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Reaction of primary amines with Pt/C catalyst in water under microwave irradiation: a convenient synthesis of secondary amines from primary amines

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Abstract—Upon microwave irradiation in water, Pt/C converts primary amines into secondary amines in good yield via *retro*-reductive and reductive amination.

Recently, we reported that some amines can be directly converted to ketones under microwave irradiation in the presence of catalytic amount of Pd/C and water.[1] In this reaction, the products were strongly dependent on the number of hydrogens on the α-carbon adjacent to nitrogen of starting amines. Amines having one hydrogen atom on the α-carbon were converted to corresponding ketones and amines having two hydrogen atoms on the α-carbon were derived to secondary amines. As a further extension of this method, we have developed a convenient synthesis of secondary amines from primary amines. Although many protocols for the preparation of secondary amines from primary amines have been reported, these require the use of organic solvents and long reaction times.[2]

Table 1 lists the preliminary results of the reaction of *n*-butylamines with four types of catalysts (Pd/C, Ru/C, Rh/C, and Pt/C, 5 wt % of metal content). The reactions were conducted in the presence of the catalysts in water under microwave irradiation (2.45 GHz 50 W) using a pressure resistant glass ampoule. When *n*-butylamine (**1**) was reacted with the catalysts described above in water under microwave irradiation, desired di-*n*-butylamine (**2**) was obtained along with butylidenebutylamine (**3**) and tri-*n*-butylamine (**4**) (entries 1–3 and 5). The conversions of **1** and yields of **2** were dependent on the kind of metal catalyst used. The Pt/C catalyst among them showed high conversion and selectivity toward the desired secondary amine. In the case of Pt/C catalyst used (entry 5), the temperature of ampoule surface measured by infrared thermo detector rose to 158 °C upon continuous microwave irradiation at 50 W for 60 min. In order to compare conventional oil bath heating, we examined the reaction using preheated (158 °C) oil bath for 60 min (entry 7). The reaction proceeded to give **2** in high selectivity; however, the conversion of the starting amine was low (30%) compared with the reaction using microwave heating (76%, entry 5). It is obvious that microwave heating showed the advantage compared with conventional microwave heating. The formation of **3** seemed to be due to lack of hydrogen for subsequent hydrogenation of **3** to form **2** (entries 1–7). It has been reported that a combination of aluminum powder and water can be used as a substitute for hydrogen gas.[3] Thus, we added a small amount of aluminum powder into the reaction. The addition of aluminum powder worked effectively and the reaction was accelerated and selectively gave the desired **2** in good yield (entry 8) and the reaction time was considerably shortened compared with the reactions without aluminum powder (entries 4 and 6). It was found that the catalyst combination of Pt/C and aluminum was effective

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Keywords: Microwave; Platinum supported on activated carbon; Amination; Water; Reductive amination; *retro*-Reductive amination.

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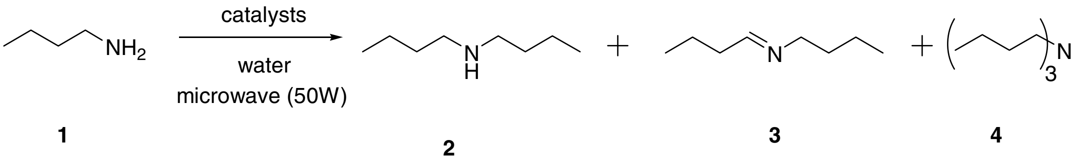
Table 1. The preliminary results of the reaction of *n*-butylamine



Entry	Catalysts[a]	Time (min)	Conversion [b] (%)	Relative yields [b] (%)		
				2	**3**	**4**
1	Pd/C	60	20	39	44	17
2	Ru/C	60	41	60	36	4
3	Rh/C	60	40	34	57	9
4	Pt/C	15	29	81	19	Trace
5	Pt/C	60	76	94	3	3
6[c]	Pt/C	15	4	48	52	Trace
7[c]	Pt/C	60	30	92	8	Trace
8[d]	Pt/C	15	80	93	0	7

Conditions: *n*-butylamine (100 mg), catalysts (50 mg), water (2 ml), continuous microwave irradiation at 50 W.

[a] Metal (5 wt %) supported on activated carbon was used.

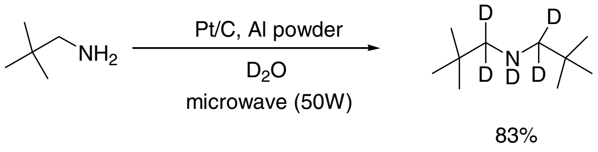
[b] Identification and quantification of the products were determined by GC and GC–MS analyses, and relative yields were based on peak area ratio.

[c] Preheated oil bath (158 °C) was used.

[d] Aluminum powder (30 mg) was used as an additive.

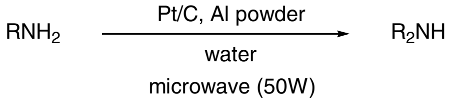
for selective transformation of **1** to **2** under microwave irradiation in water.[4]

The reaction is generally applicable to other amines as summarized in Table 2. Thus, *n*-pentylamine, *n*-hexylamine, isobutylamine, and neopentylamine (bearing primary methylenes adjacent to amines) were converted to corresponding secondary amines in good yields (entries 1–3 and 5). Tertiary amines were the main side products. When amines having secondary alkyl group (*sec*-butylamine, 3-pentylamine, cyclopentyl, and cyclohexylamine (entries 4 and 6–8)) were reacted under similar conditions, the selectivity to secondary amines was fairy low and main products were ketones. However, the reactions were quite fast. Furthermore, the reaction of benzylamine under similar condition did not give the expected dibenzylamine, only benzene and toluene were obtained (entry 9). In this reaction, benzaldehyde was observed as a transient product in the middle of the reaction. These results indicate that the formation of imine followed by hydrolysis yielding carbonyl compound is a key step in the case of latter substrates. Thus, water is not only a solvent but also a mediator for promoting the reactions. When D_2O was used instead of H_2O to the reaction of neopentylamine, deuterated dineopentylamine was obtained in 83% yield (Scheme 1).



Scheme 1.

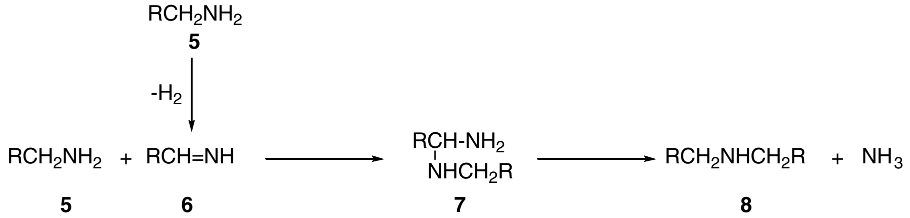
Table 2. Reaction of amines with Pt/C in water under microwave irradiation



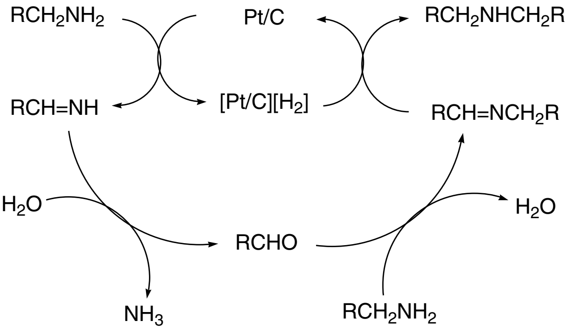
Entry	R	Time (min)	Conversion[a] (%)	Relative yield[a] (%)	
				R_2NH	Side products
1	*n*-Pentyl	30	87	84	Tripentylamine (14)
2	*n*-Hexyl	30	75	68	Trihexylamine (26)
3	Isobutyl	30	97	100	
4	*sec*-Butyl	10	100	37	2-Butanone (58)
5	*neo*-Pentyl	60	87	86	*neo*-Pentanenitrile (14)
6	3-Pentyl	10	100	21	3-Pentanone (71)
7	Cyclopentyl	10	76	51	Cyclopentanone (32)
8	Cyclohexyl	10	90	29	Cyclohexanone (67)
9	Benzyl	30	100	0	Benzene (46), toluene (53)

Conditions: amine (100 mg), Pt/C (50 mg), Al powder (30 mg), water (2 ml), continuous microwave irradiation at 50 W.

[a] Identification and quantification of the products were determined by GC and GC–MS analyses, and relative yields were based on peak area ratio.



Scheme 2.



Scheme 3.

In the literature, some have proposed aminal (**7**) as an intermediate formed by the reaction of amine (**5**) and imine (**6**) generated by the dehydrogenation of **5** in organic solvent or under neat conditions (Scheme 2).[2] On the other hand, the reactions using water as a solvent seem to proceed via different intermediates. Scheme 3 depicts a plausible reaction pathway of Pt/C catalyzed reaction of primary amine to secondary amine in water under microwave irradiation. Oxidative removal of dihydrogen, which is initially formed in situ in the reaction of starting alkylamine with Pt/C, produces an imine. The imine is hydrolyzed to afford an aldehyde derivative as an intermediate and ammonia. The aldehyde immediately reacts with starting amine to give alkylidenealkylamine. The Pt/C-dihydrogen species hydrogenates the alkylidenealkylamine to give a secondary amine and regenerate fresh Pt/C catalyst. Thus addition of aluminum helps to produce additional dihydrogen for the hydrogenation reaction. As shown in Scheme 3, the first part of the reaction (from primary amine to aldehyde) is *retro*-reductive amination (oxidative deamination) and the second part of the reaction (from aldehyde to secondary amine) is reductive amination.[5] Thus, in this unique reaction contrasting processes (*retro*-reductive and reductive amination) seem to occur concurrently in one pot.

In summary, we have demonstrated the convenient synthesis of secondary amines from primary amines with a catalytic amount of Pt/C and aluminum powder in water under microwave irradiation conditions. The presently developed method should be very useful since the reaction proceeds very rapidly and shows high secondary amine selectivity. Further investigations into the application of the methodology to other substrates are in progress in our laboratories.

References and notes

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4. The typical experimental procedure is as follows (i.e., Table 1 entry 8): A mixture of 100 mg (1.37 mmol) of *n*-butylamine, 50 mg of 5 wt % of Pt/C, 30 mg (1.1 mmol) of aluminum powder, and 2 ml of water in a pressure resistant glass ampoule equipped with rubber septum and aluminum cap is introduced into the cavity of microwave apparatus (CEM Discover, 2.45 GHz, CEM corporation, NC USA). The reaction mixture was irradiated by microwave (50 W) continuously for 15 min. The reaction vessel was cooled in an ice-water bath and the organic materials were extracted with ether. The ether fraction was analyzed by GC (FID detector) and GC–MS for identification and quantification of products.
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