Catalysis Letters Vol. 104, Nos. 1–2, October 2005 (© 2005)
DOI: 10.1007/s10562-005-7431-4

Activity and selectivity control in reductive amination of butyraldehyde over noble metal catalysts

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Received 1 June 2005; accepted 20 June 2005

Approaches to control selectivity and activity in the catalytic reductive amination of butyraldehyde with ammonia over carbon supported noble metal catalysts (Ru, Rh, Pd, and Pt) were explored. Detailed analysis of the reaction network shows that the Schiff base *N*-[butylidene]butan-1-amine is the most prominent initial product and, only after nearly all butyraldehyde had been converted to *N*-[butylidene]butan-1-amine, amines are detected in the product mixture. From this intermediate, good hydrogenolysis catalysts (Ru, Rh) produce mostly butylamine, while catalysts less active in hydrogenolysis (Pd, Pt) lead to the hydrogenation of *N*-[butylidene]butan-1-amine to mostly dibutylamine.

KEY WORDS: reductive amination; butyraldehyde; amines; noble metal catalysts; carbon supports.

1. Introduction

The reductive amination of aldehydes and ketones is one of the most important synthetic routes to amines. The reaction is conventionally claimed to proceed through an intermediately formed imine, which is reduced with hydrogen to the primary amine (scheme 1). Secondary and tertiary amines are assumed to be formed by sequential reactions with the aldehyde or ketone present in the reaction mixture. However, there is evidence that precursors to secondary and tertiary amines could be present at concentrations much higher than the amount of secondary and tertiary amines obtained [1–3]. Thus, the reaction paths, which lead to the final product, and determine the selectivity of a particular catalyst, are still ambiguous.

Homogeneous and heterogeneous catalysts are known for the reductive amination of carbonyl compounds. Homogeneous catalysts are based mostly on cobalt and rhodium complexes, [2,4–6] which, with chiral ligands, are also suitable for the stereoselective reductive amination of prochiral ketones [7–11]. With respect to solid catalysts numerous reports exist on supported and bulk transition metal catalysts [3,12–20] most of the information being, however, in the patent literature (see, e.g., nickel [21–26] cobalt [25,27,28] and noble metal based [25,29–32] catalysts). Metal sulfides of Fe, Co, Ni, Rh, W, Re, and Pt were also used in the reductive amination of ketones [33–35]. The relative inactivity of these catalysts for the hydrogenation of aromatic rings, ketones, nitriles, esters, and other unsaturated functional groups allows to achieve high selectivities in case of multifunctional compounds. However, conflicting information on the activity and selectivity of catalysts [31] shows that a largely unexplored potential for optimization of the reaction exists. Here, we show first insights into factors controlling the reductive amination of butyraldehyde (used as model substrate) over supported group VIII noble metal catalysts.

2. Experimental

2.1. Catalysts

Ru, Rh, Pd, and Pt catalysts supported on charcoal and graphite (5 wt%) were obtained from Johnson Matthey Specialty Products (Product No. 60081, 61449, 96422, 34998, 53099, 61449). If not stated otherwise in the text, the graphite support was "high surface area graphite" as specified by the manufacturer. The chemical and physicochemical properties of the materials are compiled in table 1. Graphite and charcoal were chosen as catalyst support in order to minimize support effects usually observed with refractory oxide supports. In particular, it is important to avoid acid or base catalyzed side reactions of the substrate, such as aldol condensation.

2.2. Catalytic tests

The catalyst (corresponding to $n_{\mathrm{M}} = 2.22\times10^{-5}$ mol for M = Rh, Pd, Pt and $n_{\mathrm{Ru}} = 2.22\times10^{-4}$ mol) was dried for 1 h at 130 °C in vacuum and loaded into a stainless

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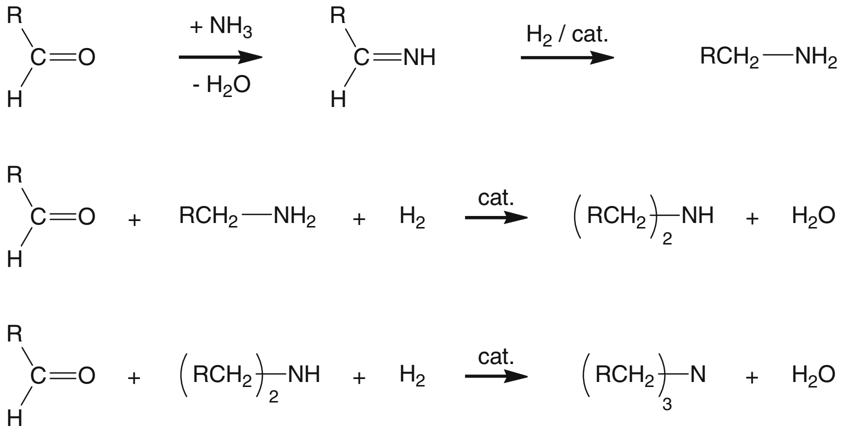


Scheme 1. Main reactions during the catalytic reductive amination of aldehydes with ammonia and hydrogen.

Table 1

Physicochemical characteristics of the catalysts investigated [36]. Data refer to dry catalyst

Catalyst	Metal loading 10^{-3} mol g^{-1}	Metal atoms exposed 10^{-3} mol g^{-1}	Metal surface area m^2 g^{-1}	Dispersion %	BET area m^2g^{-1}
Rh/charcoal	0.49	0.25	11.1	50	818
Rh/graphite	0.49	0.21	9.5	43	95
Ru/graphite	0.49	0.22	8.0	44	42
Pt/graphite	0.26	0.11	5.0	40	80
Pt/graphite (LSA)	0.26	0.07	3.5	28	57
Pd/graphite	0.47	0.24	11.4	51	88

Graphite LSA: "low surface area graphite" as specified by Johnson Matthey Specialty Products.

steel autoclave with 65 mL volume. After addition of butyraldehyde (Merck, >99% purity, 2 cm^3, 0.02 mol) and ethanol (8 cm^3) the autoclave was flushed with nitrogen. Subsequently, ammonia (5.5 g, 0.33 mol) was weighed into the autoclave. The autoclave was placed in a preheated oil bath (323 and 353 K) and, after the mixture had reached the reaction temperature, rapidly pressurized with hydrogen to 50 bar. The pressure was maintained at 50 bar and the hydrogen consumption recorded. The liquid phase was sampled and analyzed with a Hewlett Packard 5890A gas chromatograph equipped with a DB Wax 1701 column and FID detector. Reaction intermediates were identified by GC/MS analysis. If not stated otherwise, data are given for experiments performed at 353 K and 50 bar. Mass transfer limitations of hydrogen across the gas–liquid interphase were excluded by varying the speed of stirring.

3. Results and discussion

3.1. *Reductive amination with carbon supported noble metal catalysts*

Carbon supported catalysts containing 5 wt% Ru, Rh, Pd, or Pt were explored with respect to activity and selectivity for the reductive amination of butyraldehyde with ammonia and hydrogen. The hydrogen consumption (normalized to the number of exposed metal atoms) indicates that rhodium and platinum are the most active metals, while palladium and, in particular, ruthenium are less active (table 2).

The product distribution at full conversion and close to 100% overall yield is shown in figure 1. Butylamine, dibutyl-, and tributylamine were the main reaction products. Thus, on first sight the main reaction can indeed be described by the addition of ammonia to butyraldehyde and hydrogenation of the formed butan-1-imine. Higher amines are formed by consecutive addition of butyl- and dibutylamine to butyraldehyde and subsequent reduction. The selectivity to butylamine was high over rhodium and ruthenium based catalysts, while dibutylamine was obtained with a relatively high selectivity over platinum based catalysts. A mixture of butyl-, dibutyl-, and tributylamine was formed over the palladium based catalyst. For rhodium and platinum based catalysts the selectivities were nearly identical for charcoal and graphite supports. Thus, we conclude that the selectivity depends primarily on the metal and is hardly influenced by the supports used in this study. Further, the present data suggest that the reaction is not sensitive to particle size effects, i.e., the reaction is structure insensitive.

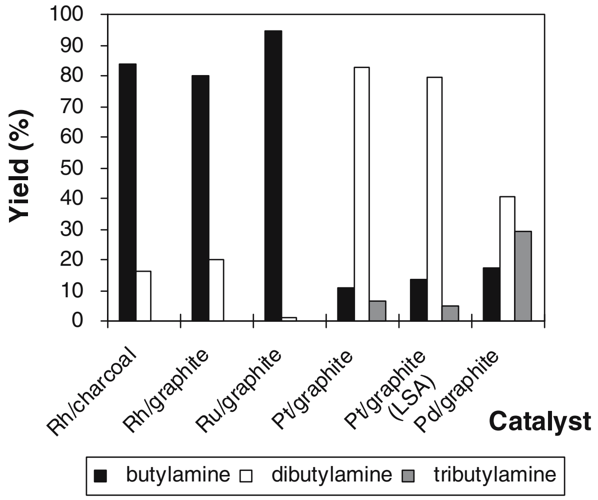


Figure 1. Yield of amine in the reductive amination of butyraldehyde over carbon supported group VIII noble metal catalysts at 100% conversion.

Table 2

Initial rate of hydrogen uptake and TOF for the formation of butyl-, dibutyl- and tributylamine

Catalyst	Rate of hydrogen uptake 10^3 mol$_{H_2}$ (mol$_{M,surface}$ h)$^{-1}$	Turnover frequency (TOF)		
		Butylamine 10^3 mol (mol$_{M,surface}$ h)$^{-1}$	Dibutylamine 10^3 mol (mol$_{M,surface}$ h)$^{-1}$	Tributylamine 10^3 mol (mol$_{M,surface}$ h)$^{-1}$
Rh/charcoal	11.0	12.0	2.16	0
Rh/graphite	14.5	3.49	0.96	0
Ru/graphite	0.28	0.22	0.003	0
Pt/graphite	11.6	0.57	4.42	0.34
Pt/graphite (LSA)	3.13	0.75	4.25	0.26
Pd/graphite	0.52	0.07	0.16	0.11

The turnover frequency (TOF) with respect to the formation of butyl-, dibutyl-, and tributylamine is also given in table 2. Similar to hydrogen uptake, the rate of product formation (sum of all three amines) depended strongly on the choice of metal, decreasing in the sequence platinum, rhodium, palladium and ruthenium (graphite supported catalysts). The rate of product formation was similar for the two platinum based catalysts, with Pt/graphite (low surface area, LSA) showing a slightly higher rate for butylamine formation. However, there were significant differences when the support was changed from graphite to charcoal. This is illustrated by the fact that the rate of butylamine (dibutylamine) formation was 3.4 (2.3) times higher for Rh/charcoal than Rh/graphite. The rate of product formation and the hydrogen uptake are not directly correlated indicating that the two observables describe different processes.

3.2. *Evolution of products with reaction time*

A more detailed kinetic study was focused on Rh/charcoal, Rh/graphite, and Pt/graphite. The amine yield in the reductive amination of butyraldehyde at 353 K and 50 bar total pressure (28 bar H_2 pressure [37]) over Rh/graphite is given as a function of reaction time in figure 2. It is important to note that the reaction has an induction period with respect to the detection of amines in the liquid phase, which is not reflected in the fast

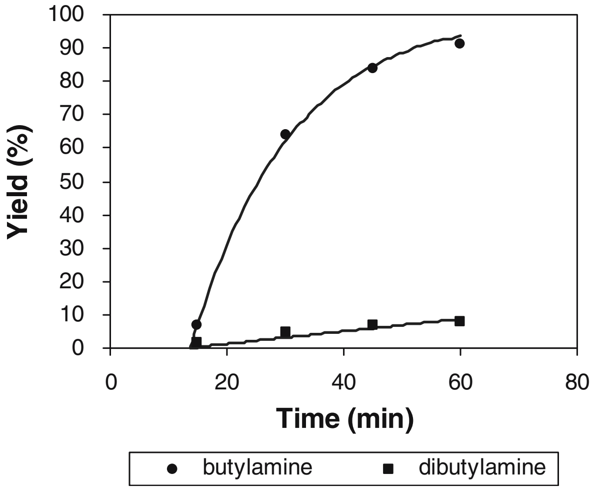


Figure 2. Yield of butyl- and dibutylamine versus reaction time on Rh/graphite catalyst ($n_{Rh} = 1.11 \times 10^{-5}$ mol).

hydrogen consumption at the beginning of the reaction. The yield of butylamine and dibutylamine increased in parallel according to approximate first order kinetics. The primary amine was not consumed at higher conversions or longer reaction times indicating that both amines are apparent primary and stable reaction products.

When the experiment was performed at 323 K and 50 bar (38 bar H_2 pressure [37], the apparent induction period was longer and the selectivity to primary amine lower, compared to those obtained at 353 K. For comparison, the time–concentration profile for the formation of butylamine on Rh/graphite at 323 and 353 K is shown in figure 3. It is noteworthy that, at 323 K, the concentration of butylamine increased linearly with time indicating approximate zero order kinetics.

When Pt/graphite was used as catalyst, dibutylamine was the main reaction product whereas only small amounts of butylamine and tributylamine were formed (Figure 4). As with the Rh/graphite catalyst, the yield of butylamine and dibutylamine increased in parallel with the reaction time suggesting primary reaction products.

3.3. Reaction pathways

Rapid H_2 consumption at short reaction times and time delayed, but parallel formation of butyl- and dibutylamine suggested the presence of a common reaction intermediate. By following the course of the reaction with GC/MS analysis, the Schiff base *N*-[butylidene]butan-1-amine ($CH_3CH_2CH_2CH=N–CH_2CH_2CH_2CH_3$) was identified as key intermediate. In contrast, the intermediate butan-1-imine expected on the basis of scheme 1 was not detected, which may be related to its high reactivity.

Hydrogen consumption and concentration of the key components in the reaction mixture are shown in figure 5 as a function of reaction time (Rh/charcoal). At the beginning of the reaction, at a reasonable level of hydrogen consumption (20–25%), primary or secondary amines were detected only in very low concentrations. The hydrogen consumed before a product is observed is equivalent to the amount needed to convert approximately 50% of the aldehyde into butylamine (probably via 1-aminobutan-1-ol and/or butan-1-imine), which immediately reacts with the remaining butyraldehyde to the Schiff base. At this stage of the reaction, most of the converted butyraldehyde was found as *N*-[butylidene]butan-1-amine. The concentration of amines increased only once this process was almost completed, the sequential steps being similar to those observed during the reductive amination of benzaldehyde over Pd/C catalysts [20].

The results depicted in figure 5 suggest that butylamine and dibutylamine are both formed from *N*-[butylidene]butan-1-amine, as increasing concentration of the amines correlates with decreasing concentration of the Schiff base. Butylamine and dibutylamine are probably formed by addition of ammonia to *N*-[butylidene]butan-1-amine followed by hydrogenolysis of the resulting geminal diamine and direct hydrogenation of *N*-[butylidene]butan-1-amine on the catalyst surface, respectively (scheme 2). Further, the imine–enamine tautomerism should be considered in the formation of dibutylamine as enamines are hydrogenated much faster than Schiff bases.

The selectivity to primary and secondary amines appears to be governed by the relative rate of the two competitive (parallel) reaction pathways of the intermediately formed Schiff base. If the catalyst binds the Schiff base (or the enamine) strongly, the hydrogenation towards the secondary amine will be the dominant pathway. Weaker chemisorption of the Schiff base (or of the enamine) on the catalyst surface will lead to a lower rate of *N*-[butylidene]butan-1-amine hydrogenation and, therefore, to less secondary amine. The results of the

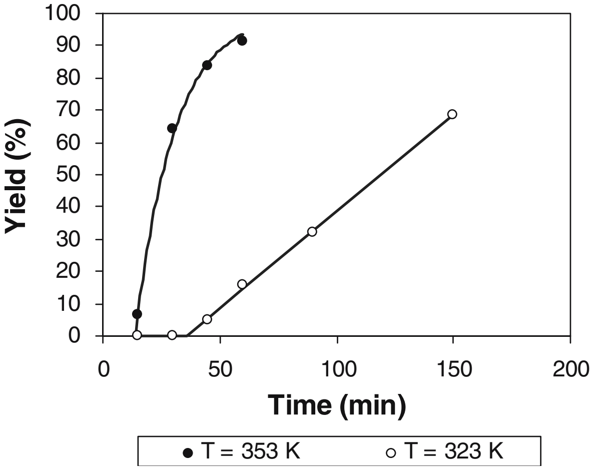


Figure 3. Formation of butylamine in the reductive amination of butyraldehyde over Rh/graphite catalyst at 323 and 353 K ($n_{Rh} = 1.11 \times 10^{-5}$ mol).

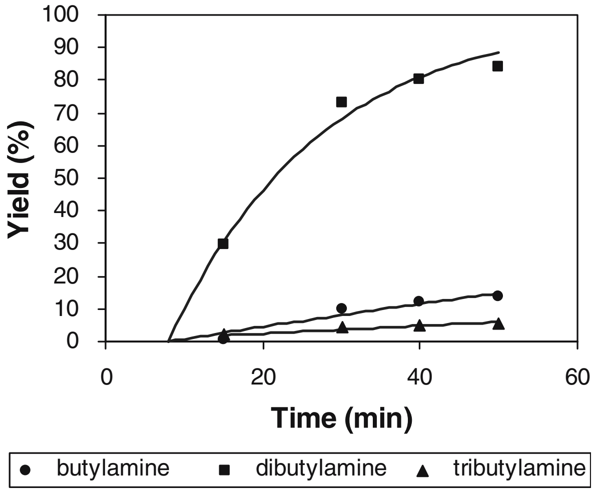


Figure 4. Yield of butyl-, dibutyl-, and tributylamine during the reductive amination of butyraldehyde over Pt/graphite catalyst ($n_{Pt} = 1.11 \times 10^{-5}$ mol).

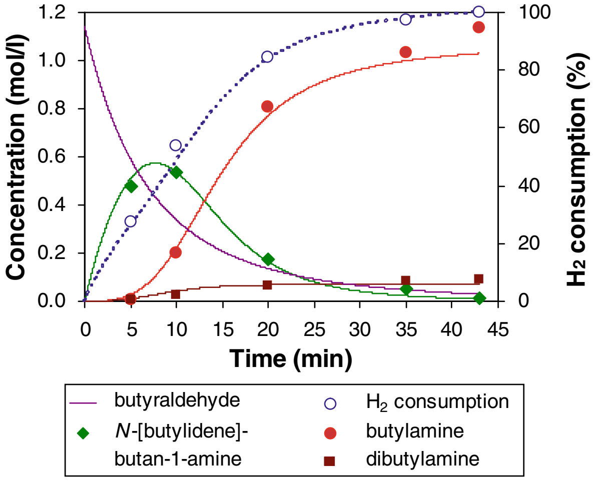
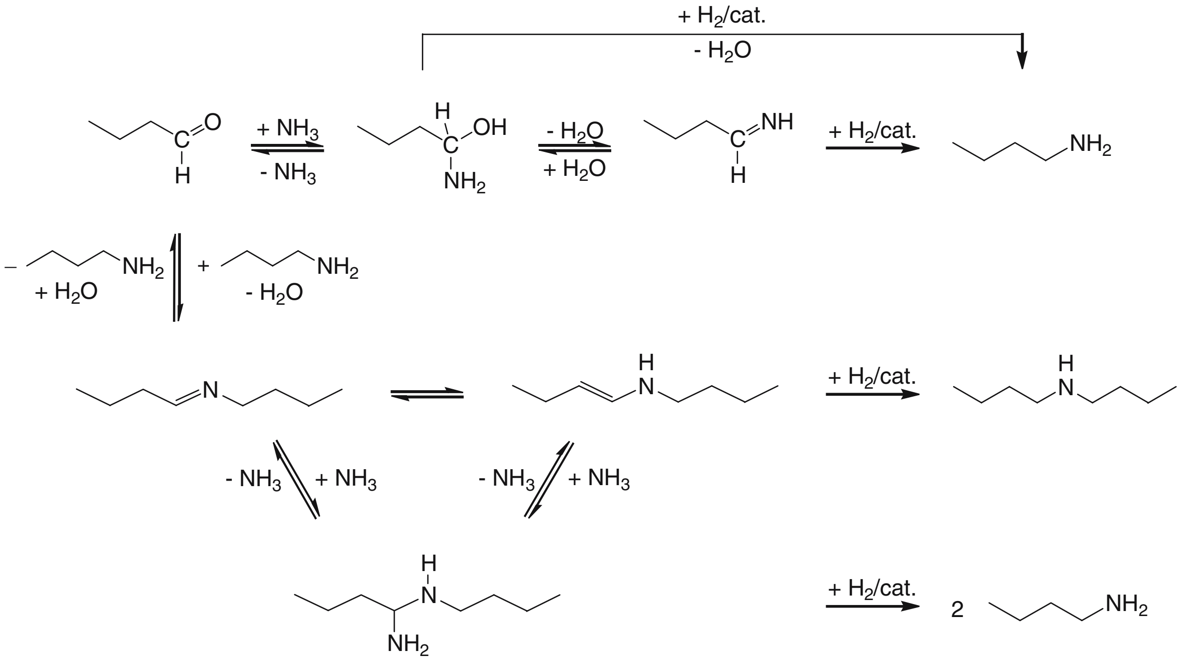


Figure 5. Amount of hydrogen consumed (in % of total) and concentration of key components during the reductive amination of butyraldehyde over Rh/charcoal ($n_{Rh} = 5.55 \times 10^{-6}$ mol).

experiments with Rh/graphite which were done at two different temperatures (323 and 353 K) supports our speculation (see figure 3). The selectivity towards butylamine is much higher at 353 K (93.5%) than at 323 K (68.4%). At higher temperatures the adsorption–desorption equilibrium of the Schiff base is shifted much more towards free *N*-[butylidene]butan-1-amine than at lower temperatures. As a result, higher temperatures will lead to lower hydrogenation rates and to less secondary amine. In consequence, the amination–hydrogenolysis of *N*-[butylidene]butan-1-amine will dominate, and the selectivity towards primary amine will be higher. At lower temperatures, a considerable amount of the Schiff base is adsorbed on the catalyst surface, and through hydrogenation a corresponding quantity of secondary amine results. Alternatively, the higher selectivity towards primary amine with increasing temperature could be explained by assuming that the hydrogenolysis has a higher energy of activation than hydrogenation [38].

We conclude that metals, which are good hydrogenolysis catalysts, such as rhodium and ruthenium, [38,39] are selective for producing butylamine, while catalysts, which are good hydrogenation catalysts, such as platinum and palladium, [38,39] catalyze the preferential formation of dibutyl- and tributylamine. At the beginning of the reaction, the primary amine is formed on a



Scheme 2. Reaction pathways for the reductive amination of butyraldehyde on carbon supported rhodium catalysts.

good hydrogenolysis catalyst mostly through hydrogenolysis of 1-aminobutan-1-ol, while on a good hydrogenation catalyst butylamine is produced mostly via hydrogenation of butan-1-imine. The initially formed, but undetectable butylamine, reacts fast with butyraldehyde and gives *N*-[butylidene]butan-1-amine. A good hydrogenation catalyst will be able to hydrogenate *N*-[butylidene]butan-1-amine to dibutylamine, while on a hydrogenolysis catalyst the rate of hydrogenation is low. In the latter case, the reaction of *N*-[butylidene]butan-1-amine with ammonia dominates leading to a geminal diamine, which is then hydrogenolyzed on the catalyst surface to butylamine.

4. Conclusions

Reductive amination of butyraldehyde on supported noble metal catalysts (Ru, Rh, Pd, and Pt) proceeds via a complex network of reactions which can be controlled by the choice of the catalyst. Charcoal provides a better support than graphite by stabilizing smaller metal particles. This causes higher activity with respect to amine formation, but does not influence the selectivity of the catalyst. The apparent induction period observed for the product formation is caused by the formation of *N*-[butylidene]butan-1-amine as key intermediate. Butyl- and dibutylamine are primary reaction products of this intermediate and, with all catalyst studied, are not interconverted. The selectivity is governed by the relative rate of the competitive (parallel) reaction pathways of the Schiff base as given in scheme 2. Metals, such as rhodium and ruthenium, tend to hydrogenolyze the geminal diamine, which results from reaction of the Schiff base with excess ammonia, to yield the primary amine. Metals that have a high hydrogenation capacity (Pt and Pd) tend to hydrogenate the intermediate Schiff base to the secondary amine.

Acknowledgment

The financial support of DSM for this work is greatly appreciated.

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