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## Colloidal and Nanosized Catalysts in Organic Synthesis: XX.<sup>1</sup> Continuous Hydrogenation of Imines and Enamines Catalyzed by Nickel Nanoparticles

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Abstract—Nickel nanoparticles on the BAU-A active carbon or NaX zeolite catalyze hydrogenation of imines and enamines in a flow reactor in a gas phase or in a gas–liquid–solid catalyst system. The process occurs at atmospheric pressure of hydrogen and gives secondary or tertiary amines in a high yield.

**Keywords**: nickel nanoparticles, hydrogenation, enamines, imines, zeolite **DOI:** 10.1134/S1070363218100018

Synthesis of secondary and tertiary amines via reductive amination of carbonyl compounds has been widely described [2]. The first stage of the process is the condensation of an aldehyde or ketone with a primary amine affording an imine or with a secondary amine yielding an enamine. Such reactions are often performed separately on available catalysts. However, hydrogenation of imines and enamines with hydrogen occurs under harsh conditions, and in the laboratory conditions it proceeds easily using complex metal hydrides as a reductant [3, 4]. For example, hydrogenation of enamines with hydrogen in the presence of rhodium metal complex catalysts occurs in methanol at atmospheric pressure within 10 h [5]. Reductive amination of aldehydes and ketones with secondary amines and hydrogen using the same complexes occurs at a pressure up to 50 atm [6]. Hydrogenation of enamines on palladium and platinum catalysts at atmospheric pressure has been studied as well [7, 8]. It has been shown that colloidal nickel particles catalyze hydrogenation of enamines with hydrogen under sufficiently mild conditions [9].

Several approaches to catalytic hydrogenation of imines are known. For example, the C=N bond of aldimines and ketimines can be reduced with hydrogen on the Raney nickel at a pressure of 7 at and a

temperature of 100°C or on copper chromite at 68 at and 150°C [11], using iridium complexes at 1–3 at [12, 13], with metal platinum at 2 at [14], or at 1–100 at in the presence of various rhodium, iridium, ruthenium, and titanium complexes [15].

Titanocene catalysts have revealed activity in the hydrogenation of a range of acyclic as well as cyclic imines. High selectivity (95–99%) have been achieved for a series of cyclic imines in the presence of 1 mol % of Ti at 10–15 at. However, acyclic imine substrates have been obtained as mixtures of isomers, leading to the decrease in selectivity (53–78%) when using the same catalyst [16].

Reduction of imines in the presence of metal nanoparticles or complexes using isopropanol or nascent hydrogen as the reducing agent [17–19] as well as via bubbling hydrogen through a solution of imine under catalysis with nickel nanoparticles [20] has been described.

This study aimed to investigate the continuous hydrogenation of imines and enamines in plug-flow reactor reactor with gaseous hydrogen under mild conditions using nickel nanoparticles immobilized on a solid support as the catalyst. The reaction was performed in a stream of 12–120-fold excess of hydrogen under atmospheric pressure and a temperature of 140–180°C in the presence of the catalyst. The BAU-A active

<sup>&</sup>lt;sup>1</sup> For communication XIX, see [1].



 $R^1 = R^2 = CH_3, R^3 = H, R^4 = CH_2, (1a, 2a), R^1 = CH_3, R^2 = R^3 = H, R^4 = CH_2O (1b, 2b).$ 

carbon (Ni<sup>0</sup>/C<sub>act</sub>) or NaX zeolite (Ni<sup>0</sup>/NaX) served as the catalyst support. The catalyst was obtained via impregnation of the carrier with aqueous solution of nickel(II) chloride during 5–6 h followed by filtering off and treatment with aqueous solution of sodium borohydride at 20–25°C during 10–12 min; the size of nickel particles formed at the carrier surface was 70– 120 nm in the case of carbon [21] and 25–60 nm in the case of zeolite. The moist catalyst was charged in the reactor and dried in the hydrogen stream directly before the reaction. The laboratory-scale reactor was a metallic pipe of the inner diameter 9 mm and heating zone height 20 mm placed in an electric oven. The catalyst layer surrounded by the inert filler (quartz packing) occupied the middle part of the reactor.

Scanning electron microscopy study of the surface of the catalyst prepared via nickel ions reduction on the zeolite (Ni<sup>0</sup>/NaX) revealed the presence of 23– 60 nm nickel nanoparticles. The composition of the surface part of the catalyst was determined by means of energy-dispersive X-ray analysis: the content of nickel in the regions of the nickel nanoparticles location was 27–35%, being 19% over entire support surface.

*N*-(2-Methylprop-1-enyl)pyrrolidine **1a** and *N*-(prop-1-enyl)morpholine **1b** were used as the hydrogenation substrates. The reaction was performed at the enamines **1a**, **b** loading 3.6 mL/h and the hydrogen loading 2 L/h at 140–160°C, the catalyst content being 0.5 g (Ni<sup>0</sup>/C<sub>act</sub>) or 2 g (Ni<sup>0</sup>/NaX). The composition of the resulting mixture was determined by means of chromato–mass spectrometry.

Hydrogenation of enamine **1a** using the Ni<sup>0</sup>/C<sub>act</sub> as the catalyst resulted in the almost complete conversion of the substrate (98%) and the yield of the corresponding amine **2a** 98% (Scheme 1). Hence, the Ni<sup>0</sup>/C<sub>act</sub> catalyst revealed high activity in the preparation of cyclic tertiary amines. When using the Ni<sup>0</sup>/NaX catalyst, the yield of amine **2a** under the same condi-

Scheme 2.



R<sup>1</sup> = Ph, R<sup>2</sup> = H, R<sup>3</sup> = Et (a), R<sup>1</sup> = *t*-Bu, R<sup>2</sup> = H, R<sup>3</sup> = *i*-Pr (b), R<sup>1</sup> = Bu, R<sup>2</sup> = H, R<sup>3</sup> = Pr (c), R<sup>1</sup> = 1-C<sub>6</sub>H<sub>13</sub>, R<sup>2</sup> = H, R<sup>3</sup> = Pr (d), R<sup>1</sup> = 4-EtPh, R<sup>2</sup> = H, R<sup>3</sup> = Pr (e), R<sup>1</sup> = 2-EtPh, R<sup>2</sup> = H, R<sup>3</sup> = Pr (f).

tions was 76%. Hydrogenation of enamine **1b** with the Ni<sup>0</sup>/NaX catalyst at 160°C and 8-fold excess of hydrogen led to the formation of the product **2b** in 90% yield.

Aldimines and ketimines are further intermediates in the reductive amination of carbonyl compounds. Hydrogenation of imines was performed in a plug-flow reactor at 140–180°C with 12–20-fold excess of hydrogen at its atmospheric pressure in the presence of both above-mentioned catalysts. Imines **3a–f** served as the substrates; their hydrogenation afforded the corresponding secondary amines **4a–f** in a yield up to 98% (Scheme 2).

It was found that the Ni<sup>0</sup>/C<sub>act</sub> catalyst was efficient in the reactions of the formation of *N*-propylaniline or *p*-ethyl-*N*-butylaniline (yield 98 and 75%, respectively, at 180°C).

The effect of the substituent location in an aromatic ring was studied using p- and o-ethyl-N-butylanilines. It was found that ethyl group in the *ortho*-position significantly reduced the yield of the target product (secondary amine) in the hydrogenation reaction: the yield of p-ethyl-N-butylaniline **4e** was 75%, that of oethyl-N-butylaniline **4f** being 7%, other conditions being the same.

Synthesis of *N*-butylhexylamine was performed at  $180^{\circ}$ C using the Ni/NaX catalyst. The conversion of the starting imine was almost complete (99.8%), but the formation of the side products decreased the yield of the target product **4d** to 25%. The side products included tributylamine (30%) and dibutylhexylamine (15%).

Hydrogenation of isobutyl-*tert*-butylimine **3b** was performed at 140°C using the Ni/C<sub>act</sub> catalyst. The yield of the target secondary amine was 68% at the imine conversion 87%. Using the Ni<sup>0</sup>/NaX catalyst, the conversion of the sterically hindered **3b** could not be improved; the yield of amine **4b** was 42% at 200°C. Nevertheless, the Ni<sup>0</sup>/NaX catalyst afforded hydrogenation of sterically non-hindered imines with high yields. For example, hydrogenation of butylidenebutylimine **4c** at 200°C gave dibutylamine in 95% yield.

In summary, the elaborated method allowed hydrogenation of azomethines and enamines at atmospheric pressure of hydrogen with the target products yield up to 98% avoiding the use of expensive and difficultly available catalysts. Nanodisperse metals and their oxides are known to catalyze certain condensation reactions [22, 23], therefore it seems promising to investigate the possibility of single-stage reductive amination of carbonyl compounds with primary or secondary amines using a heterogeneous catalyst based on nickel nanoparticles, stable against deactivation with the formed water. This will aid in development of a technological and efficient approach to the synthesis of a series of secondary and tertiary amines.

## EXPERIMENTAL

Chromato-mass spectroscopy analysis was performed using a Saturn 2100 T/GC3900 instrument (EI, 70 eV). Scanning electron microscopy studies were performed using a FEI Versa 3D DualBeam instrument. Elemental analysis of the catalyst was performed by means of energy-dispersive X-ray spectroscopy.

**Catalysts preparation** was carried out via impregnation of a solid support (active carbon or 1–1.2 mm fraction of the NaX zeolite) with aqueous solution of nickel(II) chloride hexahydrate during 5–6 h (0.2 g of the nickel salt per 0.5 g of the carbon or 0.5 g of the nickel salt per 2 g of the zeolite), filtration and washing of the modified carrier, and its treatment with aqueous solution of sodium borohydride at 20–25°C during 10 min. The so prepared moist catalyst was loaded in the reactor and dried in a hydrogen stream at 120–140°C just prior to the reaction.

**Hydrogenation** (general procedure). The reaction was performed in a plug-flow reactor at atmo-spheric pressure at temperature 140–200°C. Under these conditions the reaction could proceed in the gas phase as well as in the gas–liquid–solid catalyst system, depending on the boiling point of the substrate. The laboratory-scale reactor was a 12Kh18N10T steel pipe of internal diameter 9 mm and the heating zone height 50 mm placed in an electric oven. The catalyst was loaded into the reactor, and the stream of hydrogen was simultaneously applied (the hydrogen feeding rate was controlled using a GV-7 hydrogen generator); liquid substrates **1a**, **1b**, or **3a–3f** were supplied using a Watson Marlow 120S peristaltic pump. The reactor temperature was monitored using a TKhA thermocouple.

**N-Isobutylpyrrolidine (2a).** *a.* Catalyst Ni<sup>0</sup>/C<sub>act</sub> mass 0.5 g, temperature 140°C, hydrogen feeding rate 4 L g<sub>cat</sub><sup>-1</sup> h<sup>-1</sup>, enamine **1a** feeding rate 3.6 mL g<sub>cat</sub><sup>-1</sup> h<sup>-1</sup>. The enamine conversion 98%, selectivity 100%, yield of the target product 98%. Mass spectrum, *m/e* (*I*<sub>rel</sub>, %): 129.0 (5)  $[M + 2]^+$ , 128.0 (60)  $[M + 1]^+$ , 126.1 (17)  $[M - 1]^+$ , 125.2 (3.5), 84.2 (100), 83.2 (17.5), 82.2 (7).

*b.* Catalyst Ni<sup>0</sup>/NaX mass 2 g, temperature 180°C, hydrogen feeding rate 1 L  $g_{cat}^{-1}$  h<sup>-1</sup>, enamine **1a** feeding rate 3.6 mL  $g_{cat}^{-1}$  h<sup>-1</sup>. The enamine conversion 76%, selectivity 100%, yield of the target product 76%.

*N*-Propylmorpholine (2b). Catalyst Ni<sup>0</sup>/NaX mass 2 g, temperature 160°C, hydrogen feeding rate 1 L  $g_{cat}^{-1} h^{-1}$ , enamine 1b feeding rate 0.9 m L  $g_{cat}^{-1} h^{-1}$ . The enamine conversion 90%, selectivity 100%, yield of the target product 90%. Mass spectrum, *m/e* (*I*<sub>rel</sub>, %): 128.8 (7) [*M* + 2]<sup>+</sup>, 128.0 (23) [*M* + 1]<sup>+</sup>, 127.1 (2) [*M*]<sup>+</sup>, 99.9 (100), 84.0 (3), 72.1 (6), 70.0 (18), 56.0 (8), 42.0 (6.5).

*N*-1-Propylaniline (4a). Catalyst Ni<sup>0</sup>/C<sub>act</sub> mass 0.5 g, temperature 180°C, hydrogen feeding rate 4 L  $g_{cat}^{-1}$  h<sup>-1</sup>, imine 3a feeding rate 3.6 mL  $g_{cat}^{-1}$  h<sup>-1</sup>. The imine conversion 99.8%, selectivity with respect to the amine 98%, yield of the target product 98%. Mass spectrum, *m/e* (*I*<sub>rel</sub>, %): 136.9 (7) [*M* + 2]<sup>+</sup>, 136.0 (59) [*M* + 1]<sup>+</sup>, 135.0 (50) [*M*]<sup>+</sup>, 107.0 (9), 106.0 (100), 79.0 (11), 77.0 (12), 51.0 (7).

**Isobutyl-***tert***-butylamine (4b).** *a*. Catalyst Ni<sup>0</sup>/C<sub>act</sub> mass 0.5 g, temperature 140°C, hydrogen feeding rate 4 L g<sub>cat</sub><sup>-1</sup> h<sup>-1</sup>, imine **3b** feeding rate 3.6 mL g<sub>cat</sub><sup>-1</sup> h<sup>-1</sup>. The imine conversion 87%, selectivity with respect to the amine 77%, yield of the target product 68%. Mass spectrum, *m/e* (*I*<sub>rel</sub>, %): 130.8 (5) [*M* + 2]<sup>+</sup>, 129.9 (45) [*M* + 1]<sup>+</sup>, 127.8 (1) [*M*]<sup>+</sup>, 115.0 (10.4), 114.0 (100), 85.8 (6.5), 74.0 (1), 58.0 (37).

*b*. Catalyst Ni<sup>0</sup>/NaX mass 2 g, temperature 200°C, hydrogen feeding rate 1 L  $g_{cat}^{-1}$  h<sup>-1</sup>, imine **3b** feeding rate 3.6 mL  $g_{cat}^{-1}$  h<sup>-1</sup>. The imine conversion 48%, selectivity with respect to the amine 87%, yield of the target product 42%.

**Di-***n***-butylamine (4c)**. Catalyst Ni<sup>0</sup>/NaX mass 2 g, temperature 180°C, hydrogen feeding rate 1 L  $g_{cat}^{-1} h^{-1}$ , imine **3c** feeding rate 0.9 mL  $g_{cat}^{-1} h^{-1}$ . The imine conversion 97%, selectivity with respect to the amine 98%, yield of the target product 95%. Mass spectrum, *m/e* ( $I_{rel}$ , %): 130.0 (26) [M + 1]<sup>+</sup>, 128.7 (2) [M]<sup>+</sup>, 44.1 (100), 85.9 (39), 41.1 (31), 42.0 (17), 57.0 (62), 43.0 (5).

*N*-Butylhexylamine (4d). Catalyst Ni<sup>0</sup>/NaX mass 2 g, temperature 180°C, hydrogen feeding rate 1 L g<sub>cat</sub><sup>-1</sup> h<sup>-1</sup>, imine 3d feeding rate 0.9 mL g<sub>cat</sub><sup>-1</sup> h<sup>-1</sup>. The imine conversion 99.8%, selectivity with respect to the target amine 25%, yield of the target product 25%. Mass spectrum, *m/e* ( $I_{rel}$ , %): 158.8 (12) [M + 2]<sup>+</sup>, 158.0 (100) [M + 1]<sup>+</sup>, 113.8 (3), 85.8 (3), 44.2 (57), 41.2 (3). Selectivity with respect to tri-1-butylamine 30%, yield 30%. Mass spectrum, *m/e* ( $I_{rel}$ , %):186.9 (11) [M + 2]<sup>+</sup>, 186.0 (100) [M + 1]<sup>+</sup>, 185.0 (3) [M]<sup>+</sup>, 114.2 (6), 113.2 (5), 44.2 (80), 41.2 (6). Selectivity with respect to dibutylhexylamine 15%, yield 15%. Mass spectrum, *m/e* ( $I_{rel}$ , %): 214.8 (11) [M + 2]<sup>+</sup>, 214.1 (100) [M + 1]<sup>+</sup>, 115.1 (3), 114.2 (22), 113.2 (4), 44.2 (60), 41.2 (5).

*p*-Ethyl-*N*-butylaniline (4e). Catalyst Ni<sup>0</sup>/C<sub>act</sub> mass 0.5 g, temperature 180°C, hydrogen feeding rate 4 L g<sub>cat</sub><sup>-1</sup> h<sup>-1</sup>, imine **3e** feeding rate 3.6 mL g<sub>cat</sub><sup>-1</sup> h<sup>-1</sup>. The imine conversion 95%, selectivity with respect to the target amine 77%, yield of the target product 74%. Mass spectrum, *m/e* ( $I_{rel}$ , %): 178.8 (10) [M + 2]<sup>+</sup>, 177.8 (100) [M + 1]<sup>+</sup>, 176.9 (28) [M]<sup>+</sup>, 176.0 (5) [M - 1]<sup>+</sup>, 134.1 (21), 106.0 (4). Selectivity with respect to *p*-ethyl-*N*,*N*-dibutylaniline 23%, yield 22%. Mass spectrum, *m/e* ( $I_{rel}$ , %): 234.0 (2) [M + 1]<sup>+</sup>, 233.0 (15) [M]<sup>+</sup>, 232.1 (100) [M - 1]<sup>+</sup>, 175.0 (8), 174.0 (5), 160.0 (5), 129.8 (2).

*o*-Ethyl-*N*-butylaniline (4f). Catalyst Ni<sup>0</sup>/C<sub>act</sub> mass 0.5 g, temperature 180°C, hydrogen feeding rate 4 L g<sub>cat</sub><sup>-1</sup> h<sup>-1</sup>, imine 3f feeding rate 3.6 mL g<sub>cat</sub><sup>-1</sup> h<sup>-1</sup>. The imine conversion 75%, selectivity with respect to the target amine 11%, yield of the target product 7%. Mass spectrum, *m/e* ( $I_{rel}$ , %): 178.8 (11) [M + 2]<sup>+</sup>, 177.8 (100) [M + 1]<sup>+</sup>, 177.2 (48) [M]<sup>+</sup>, 176.3 (8) [M – 1]<sup>+</sup>, 134.0 (29), 105.8 (5). Selectivity with respect to *o*-ethyl-*N*,*N*-dibutylaniline 47%, yield 47%. Mass spectrum, *m/e* ( $I_{rel}$ , %): 232.0 (2) [M – 1]<sup>+</sup>, 231.0 (16), 230.0 (100), 229.3 (68), 214.2 (30), 200.2 (9), 131.9 (9), 106.0 (6).

## CONFLICT OF INTERESTS

No conflict of interests was declared by the authors.

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