Colloid and Nanodimensional Catalysts in Organic Synthesis: VIII.¹ Hydrogenation of C=N Bond with Hydrogen in the Presence of Colloid Nickel

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Abstract—Hydrogenation of azomethines with hydrogen at atmospheric pressure using nickel nanoparticles as catalyst was carried out. Reaction may be used for the preparation of secondary amines under mild conditions on an available catalyst. Continuation of studies will lead to development of a convenient method for the reductive amination of carbonyl compounds.

Keywords: azomethines, hydrogenation, nanoparticles, nickel

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Hydroamination is widely used for the preparation of amines and amino derivatives. In industry the reductive amination is carried out under hydrogen excess often using expensive catalysts, high pressures and temperatures. In the laboratory conditions a considerable excess of amino derivative and hydrogenating agent is used, frequently it is formic acid [2]. Metal nanoparticles can catalyze hydrogenation of some olefins [3, 4].

As is known, the first stage of reductive amination is the condensation of carbonyl compound and amine which commonly can proceed separately on an available catalysts without using special conditions. Hydrogenation of obtained azomethines or enamines proceeds easily in the presence of formic acid or complex metal hydrides. The application of gaseous hydrogen and available heterogenic catalysts demands rigid conditions for performing the reaction.

A series of methods are known for preparing secondary amines by catalytic hydrogenation of imines. For example, aldimines and ketimines are hydrogenated with hydrogen on the Raney nickel at 7 bar and 100°C or on copper chromite at 68 bar and 150°C, at 1 bar in the presence of iridium complexes [6], at 2 bar in the presence of metallic platinum [7], at 1–100 bar in the presence of various complexes of rhodium, iridium, ruthenium, and titanium [8], at 3 bar in the presence of iridium complexes and potassium isopropylate [9]. Data on hydrogenation of C=N bonds with hydrogen under mild conditions on available catalysts are absent. It is known only about the reduction of amines on nanoparticles or metal complexes using isopropanol or hydrogen *in statu nascendi* as the reducing agent [10–13].

The aim of this study was the investigation of possibility of hydrogenation under mild conditions of azomethimes and ketimines as half-products of reductive amination reaction of carbonyl compounds and primary amines.

As the starting substances the products of condensation of aniline or *p*-anizidine with benzaldehyde, methyl isobutyl ketone, cyclopentanone, and cyclohexanone, and also of cyclohexyl amine with benzaldehyde were used. The attempt to carry out hydrogenation of benzalaniline with hydrogen using nickel colloid solution in THF was unsuccessful, therefore we used the catalytic system obtained by reduction of anhydrous nickel(II) chloride with sodium borohydride in isopropanol. According to the reported data under these conditions the suspension of nickel nanoparticles [14, 15] or the nanoparticles containing also some amount of boron [16] depending on an excess of

¹ For communication VII, see [1].

sodium borohydride was formed. We have used the smallest amount of reducing agent with the purpose to minimize the metal boride content on the surface of nanoparticles. For each reaction we have used 5-10 mol % of this catalyst.

It was found that the hydrogenation of C=N bond under these conditions proceeds successfully in the course of 5-6 h while bubbling gaseous hydrogen through the mixture of azomethine and the colloid solution of nickel nanoparticles in isopropanol.



 $R^{1} = Ph, R^{2} = H, R^{3} = Ph (Ia, IIa); R^{1} = Ph, R^{2} = Me, R^{3} = i-Bu (Ib, IIb); R^{1} = Ph, R^{2}R^{3} = -(CH_{2})_{4}-(Ic, IIc); R^{1} = Ph, R^{2}R^{3} = -(CH_{2})_{5}-(Id, IId), R^{1} = 4-MeOPh, R^{2}R^{3} = -(CH_{2})_{4}-(Ie, IIe); R^{1} = Cy, R^{2} = H, R^{3} = Ph (If, IIf); R^{1} = Bu, R^{2} = H, R^{3} = Ph (Ig, IIg).$

It was shown that the structure of azomethine slightly affects its conversion under the abovementioned conditions. As is known, metal nanoparticles catalyze the reaction of transfer hydrogenation [11] while using secondary alcohols as reagents. Due to that it was necessary to check whether isopropanol used as the solvent in this reaction can be also the reducing agent. With this purpose the hydrogenation of aldimines **Ia**, **Ig** was carried out in *tert*-butanol which cannot generate hydrogen under these conditions. It was shown that substitution of solvent does not significantly influence the yield of benzylaniline. Therefore the hydrogen.

The structure of secondary amines **Ha–Hg** obtained in 68–75% yield was confirmed by ¹H NMR spectroscopy. The properties of known substances were in agreement with the reported data.

Hence, the developed procedure permits to carry out hydrogenation of azomethines at atmospheric pressure without using expensive and difficultly available catalysts. It was found recently that nano-dispersed metals and their oxides catalyze some condensation reactions [17, 18]. Hence, the probability was shown of performing the one-stage process of reductive amination of carbonyl compounds with amines using nickel nanoparticles at the atmospheric pressure of hydrogen.

EXPERIMENTAL

¹H NMR spectra of compounds synthesized were recorded on a Varian Mercury-300 spectrometer (300 MHz) in carbon tetrachloride, internal reference HMDS.

N-Benzylaniline (IIa). *a*. To a suspension of 0.5 g (0.014 mol) of sodium borohydride in 20 mL of isopropanol 0.9 g (0.007 mol) of anhydrous NiCl₂ was added, and the mixture obtained was heated to 50-60°C to form black colloid solution. After that bubbling of hydrogen was started at a rate of 20-25 mL/min, and 18.1 g (0.1 mol) of benzalaniline Ia was added. The mixture was kept at 60°C under stirring and constant bubbling of hydrogen for 8 h. After that the reaction mixture was cooled, and 1 mL of water was added to accelerate the coagulation of catalyst. The precipitate formed was filtered off, and isopropanol was removed from filtrate. The residue was distilled in a vacuum to give 13.2 g (0.072 mol, 72%) of benzylaniline **Ha** as a colorless liquid crystallizing on storage, mp 30-32°C, bp 155–157°C (25 mmHg) (mp 32°C, bp 306–307°C [19]). ¹H NMR spectrum, δ , ppm: 3.71 s (1H, NH), 4.06 s (2H, CH₂N), 6.32–7.14 m (10H, 2 C₆H₅).

b. Analogously from the suspension of 0.4 g (0.011 mol) of sodium borohydride in 15 mL of *tert*butanol, 0.65 g (0.005 mol) of NiCl₂ and 14.5 g (0.08 mol) of imine **Ia** 10.2 g (0.056 mol, 70%) of benzylaniline **IIa** was obtained, mp 29–32°C, bp 154–156°C (25 mmHg).

2-Methyl-4-(phenylamino)pentane (IIb). Analogously to **Ha** from a mixture of 0.6 g (0.0016 mol) of sodium borohydride, 25 mL of isopropanol, 1.0 g (0.008 mol) of anhydrous NiCl₂, and 17.5 g (0.1 mol) of imine **Ib** under bubbling of hydrogen for 12 h at 70°C 12.05 g (0.068 mol, 68%) of amine **IIb** was obtained, bp 169–172°C (20 mmHg). ¹H NMR spectrum, δ , ppm: 0.83–0.95 m (6H, 2CH₃), 1.05 t (3H, CH₃, *J* 6 Hz), 1.90–2.20 m (3H, CH₂, CH), 3.24 br.s (1H, NH), 3.45 m (1H, CH–N), 6.40–6.96 m (5H, C₆H₅). Found, %: C 81.37, H 10.75, N 7.88. C₁₂H₁₉N. Calculated, %: C 81.30, H 10.80, N 7.90.

N-Cyclopentylaniline (IIc). Analogously to IIa from a mixture of 0.3 g (0.008 mol) of sodium borohydride, 20 mL of isopropanol, 0.5 g (0.004 mol) of anhydrous NiCl₂, and 6.4 g (0.04 mol) of ketimine Ic under bubbling of hydrogen for 10 h at 60°C 4.2 g (0.026 mol, 66%) of amine IIc was obtained, bp 160– 162°C (20 mmHg) (bp 265–266°C [20]). ¹H NMR spectrum, δ , ppm: 1.36–2.45 m (8H, 4CH₂), 3.58 m (1H, CH–N), 3.72 s (1H, NH), 6.38–6.95 m (5H, C₆H₅).

N-Cyclohexylaniline (IId). Analogously to IIa from a mixture of 0.3 g (0.008 mol) of sodium borohydride, 15 mL of isopropanol, 0.5 g (0.004 mol) of anhydrous NiCl₂, and 10.4 g (0.06 mol) of ketimine Id under bubbling of hydrogen for 8 h at 70°C 7.3 g (0.041 mol, 69%) of amine IId was obtained, bp 165– 167°C (20 mmHg) (bp 167–168°C [20]). ¹H NMR spectrum, δ , ppm: 1.12–2.30 m (10H, 5CH₂), 3.52 m (1H, CH–N), 3.70 s (1H, NH), 6.40–6.97 m (5H, C₆H₅).

4-(Methoxy)phenylaminocyclopentane (IIe). Analogously to **Ha** from a mixture of 0.5 g (0.014 mol) of sodium borohydride, 20 mL of isopropanol, 0.9 g (0.007 mol) of anhydrous NiCl₂, and 9.5 g (0.05 mol) of imine **Ie** under bubbling of hydrogen for 10 h at 70°C 6.7 g (0.036 mol, 71%) of amine **He** was obtained, bp 179–182°C (20 mmHg). ¹H NMR spectrum, δ , ppm: 1.19–2.68 m (8H, 4CH₂), 3.34 br.s (1H, NH), 3.40 m (1H, CHN), 3.60 s (3H, OCH₃), 6.32–6.66 m (4H, Ph). Found, %: C 74.58, H 8.49, N 7.87. C₁₁H₁₅NO. Calculated, %: C 74.54, H 8.53, N 7.90.

N-Benzylaminocyclohexane (IIf). Analogously to IIa from a mixture of 0.5 g (0.014 mol) of sodium borohydride, 20 mL of isopropanol, 0.9 g (0.007 mol) of anhydrous NiCl₂ and 14 g (0.075 mol) of imine If under bubbling of hydrogen for 8 h at 70°C 10.2 g (0.056 mol, 74%) of amine IIf was obtained, bp 168– 171°C (25 mmHg). ¹H NMR spectrum, δ , ppm: 1.03– 2.35 m (10H, 5CH₂), 2.38 m (1H, CH–N), 3.05 s (2H, CH₂–N),7.05–7.22 m (5H, C₆H₅). Found, %: C 82.54, H 10.15, N 7.31. C₁₃H₁₉N. Calculated, %: C 82.48, H 10.12, N 7.40.

N-Benzylaminobutane (IIg). Analogously to IIa from a mixture of 0.5 g (0.014 mol) of sodium borohydride, 20 mL of *tert*.-butanol, 0.9 g (0.007 mol) of anhydrous NiCl₂, and 11.3 g (0.07 mol) of imine Ig under bubbling of hydrogen for 9 h at 65°C 9.8 g (0.06 mol, 86%) of amine IIg was obtained, n_D^{20} 1.5014 (n_D^{20} 1.5022 [21]).

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