ISSN 1070-3632, Russian Journal of General Chemistry, 2017, Vol. 87, No. 11, pp. 2546–2551. © Pleiades Publishing, Ltd., 2017.
Original Russian Text © Yu.V. Popov, V.M. Mokhov, S.E. Latyshova, A.O. Panov, P.M. Shirkhanyan, 2017, published in Zhurnal Obshchei Khimii, 2017, Vol. 87, No. 11, pp. 1804–1809.

Colloid and Nanosized Catalysts in Organic Synthesis: XVII.[1] Reductive Amination of Carbonitriles in the Presence of Supported Nickel Nanoparticles

Yu. V. Popov*, V. M. Mokhov, S. E. Latyshova, A. O. Panov, and P. M. Shirkhanyan

Volgograd State Technical University, pr. Lenina 28, Volgograd, 400131 Russia
**e-mail: tons@vstu.ru*

Received May 15, 2017

Abstract—Reductive amination of carbonitriles catalyzed by nickel nanoparticles applied onto a solid support in a plug flow reactor in the gas phase or the gas–liquid–solid catalyst system occurs at atmospheric pressure of hydrogen affording the nonsymmetrical secondary or tertiary amines. The effect of the support type on the target product yield and conversion of the substrate has been studied.

Keywords: catalysis, nanoparticles, nickel, nitrile, amine, reductive amination

DOI: 10.1134/S1070363217110068

Hydrogenation of carbonitriles is accompanied by the formation of symmetrical secondary and tertiary amines (along with primary ones), due to the interaction of the formed primary and secondary amines with aldimines [2, 3]. Purposeful introduction of other amines into the hydrogenated mixture can afford nonsymmetrical di- and trialkylamines.

For example, hydrogenation of benzonitrile in the presence of *n*-butylamine (catalysis by Rh/C, room temperature, pressure 3 at, *n*-octane medium) has given *n*-butylbenzylamine in a quantitative yield [2]. The process can be catalyzed by Pt and Cu as well [4–6]. For example, reductive amination of nitriles catalyzed by Pt/C has been performed in a plug flow reactor at 105°C and hydrogen (reductant) overpressure 6 atm with toluene as solvent [4]. The products yield was up to 81% at the nitriles conversion up to 99%. Furthermore, the preparation of alkylarylamines via reductive amination of nitriles in the presence of copper catalyst formed *in situ* via reduction of Cu $(OTf)_2$ has been described (45°C, 20 h, water as solvent, and the dimethylamine–borane complex as the reductant; the products yield up to 60% at the nitriles conversion up to 78%) [6].

Various adoptions of reductive amination of nitriles have been described in the literature. For instance, the application of reductive amination of nitriles for selective synthesis of imines catalyzed by Ru-based metal complex catalyst has been studied; the products yield was up to 90% at the nitriles conversion up to 99% [7]. *N*-Alkylanilines have been prepared via hydrogenation of aromatic nitro compounds in the presence of nitriles catalyzed by Pd/C or Rh/C: for instance, *N*-*n*-propylaniline has been prepared within 19 h in a quantitative yield [3].

We have earlier performed liquid-phase hydrogenation of carbonitriles in the presence of primary and secondary amines leading to the reductive amination of the nitriles [8]. However, this process is accompanied by the formation of substantial amount of side products due to the low concentration of hydrogen dissolved in the liquid phase and long reaction time (10–16 h).

It should be noted that the above-described processes demand either increased pressure or long reaction duration. In view of that, this study aimed to investigate the process of formation of nonsymmetrical secondary and tertiary amines via reductive amination of nitriles by hydrogen at atmospheric pressure in a plug flow reactor in the presence of nickel nanoparticles applied on a support.

Active carbon (BAU-A grade) and an aluminosilicate cracking catalyst (Ceokar-2, 1.0–1.5 mm

---

[1] For communication XVI, see [1].

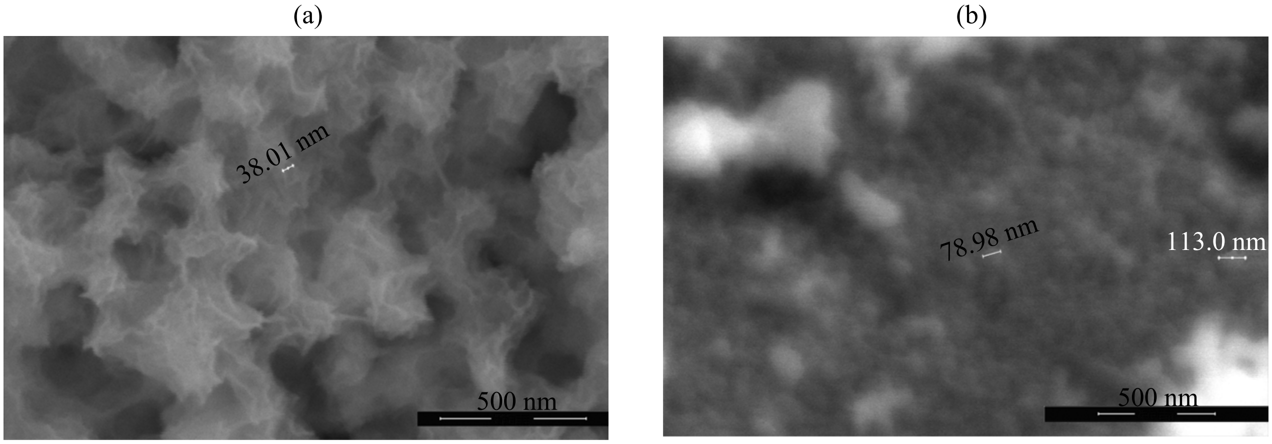


Fig. 1. SEM images of the catalysts surface: (a) Ni/C and (b) Ni/Ceokar-2.

fraction) were used as the supports. The catalysts were prepared via impregnation of the support with an aqueous solution of nickel(II) chloride, followed by separation of the impregnated carrier by filtration and reduction of nickel ions with sodium borohydride aqueous solution, as described elsewhere [1].

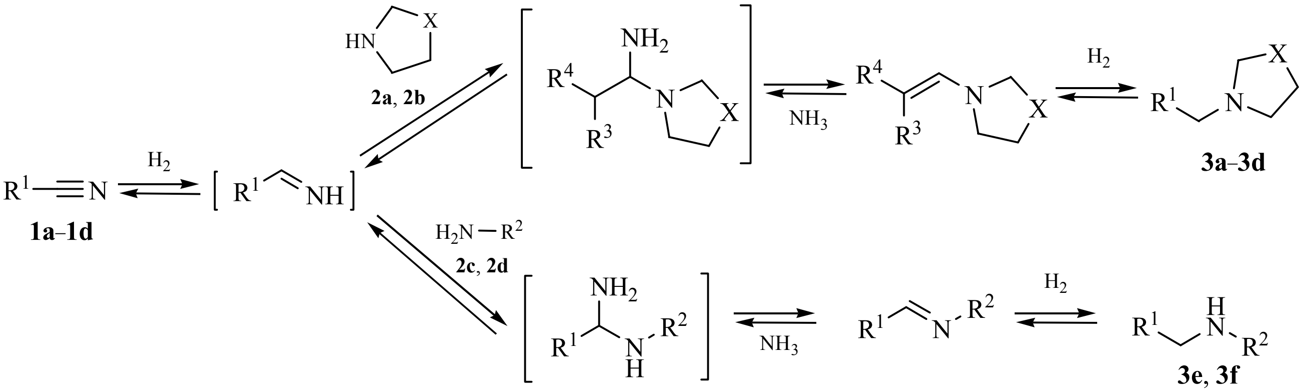
The catalysts surface was examined by means of SEM. It was revealed that nickel was chaotically distributed inside the pores of the BAU-A carbon forming nanostructured aggregates with about 40 nm particles (see Fig. 1a). The catalyst surface on the average contained 2 wt % of nickel.

In the case of the nickel catalyst applied onto Ceokar-2, the support surface contained larger 200–1000 nm agglomerates as well as smaller 80–100 nm particles (Fig. 1b); however, these particles were more uniformly distributed over the surface as compared to the Ni^0/C sample. The modified Ceokar-2 sample contained 7 wt % of nickel on the average.

To prepare various nonsymmetrical amines we performed reductive amination of nitriles **1a–1d** with cyclic secondary amines **2a**, **2b** as well as of nitriles **1a**, **1c** with primary amines **2c**, **2d** in the presence of the Ni^0/C or Ni^0/Ceokar-2 catalyst. The reaction was performed at atmospheric pressure and 120–240°C, specific feeding rate of the starting nitrile and amine being 0.9–3.6 mL h^{-1} g_{cat}^{-1} and that of hydrogen being 1.5–6 L h^{-1} g_{cat}^{-1}.

The obtained data in the yield of target products **3a–3f** and conversion of nitriles **1a–1d** are collected in the Table. Basing on these data and the reference information [2–6] we suggested the scheme of the main reaction in the presence of the Ni^0/C and Ni^0/Ceokar-2 catalysts (Scheme 1).

Scheme 1.



R^1 = Pr (**1a**, **3a**, **3e**), Bu (**1b**, **3b**), *i*-Pr (**1c**, **3c**, **3f**), Ph (**1d**, **2d**, **3f**); R^2 = Cy (**2c**, **3e**), Ph (**2d**, **3f**); X = $–CH_2O–$ (**2a**, **3a**, **3b**), $–CH_2–$ (**2b**, **3c**, **3d**); R^3 = H, R^4 = Et (with R^1 = Pr); R^3 = H, R^4 = Pr (with R^1 = Bu); R^3 = R^4 = Me (with R^1 = *i*-Pr).

Conversion of the starting nitriles and yields of the reaction products in the presence of nickel catalysts

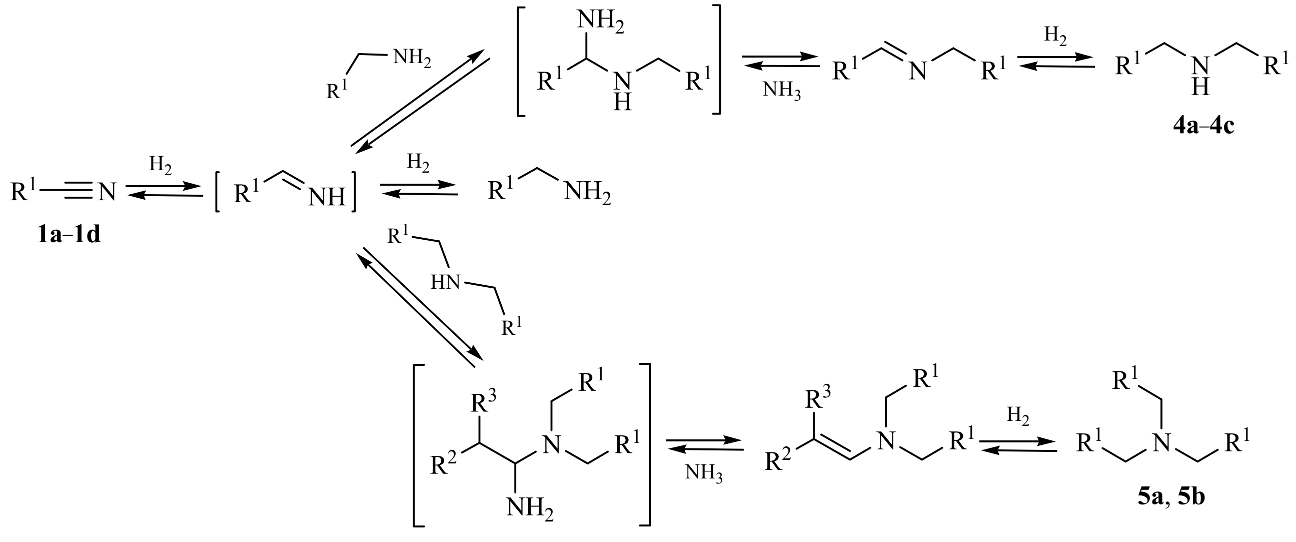
Nitrile	Amine	Reaction product	Catalyst	*t*, °C	Nitrile : amine : H_2 molar ratio	Nitrile conversion, %	Selectivity, %	Yield, %
1a	**2a**	**3a**	Ni^0/C	120	1 : 1 : 15	93	48	45
			Ni^0/C	120	1 : 2 : 20	92	82	75
			Ni^0/Ceokar-2	200	1 : 2 : 6	82	82	67
1b	**2a**	**3b**	Ni^0/C	120	1 : 2 : 20	81	95	77
			Ni^0/Ceokar-2	185	1 : 2 : 6	89	88	78
1c	**2b**	**3c**	Ni^0/Ceokar-2	200	1 : 2 : 10	75	80	60
1d	**2b**	**3d**	Ni^0/Ceokar-2	200	1 : 2 : 12	100	38	38
1a	**2c**	**3e**	Ni^0/C	150	1 : 1 : 15	92	49	45
			Ni^0/Ceokar-2	220	1 : 1 : 5	83	63	52
1c	**2d**	**3f**	Ni^0/Ceokar-2	240	1 : 2 : 10	83	75	62

The data shown in the table revealed significant effect of the structure of the starting compounds and their ratio as well as temperature on the conversion of the substrates, selectivity of the target reaction, and the yield of the reductive amination of the carbonitrile.

The yield of alkylmorpholine **3a** was of 67% in the reaction of reductive amination of nitrile **1a** with amine **2a** catalyzed by Ni^0/Ceokar-2 at 200°C, whereas the yield *N*-isobutylmorpholine and *N*-isobutylpiperidine under the same conditions was less than satisfactory. The reaction of nitrile **1c** with pyrrolidine **2b** on Ni^0/Ceokar-2 afforded *N*-isobutylpyrrolidine **3c** in 60% yield. Amine **2b** underwent the reaction with benzonitrile **1d**, but the yield of the target product was as low as 38%.

The poor selectivity of the formation of *N*-*n*-butylcyclohexylamine **3e** via the reaction of reductive amination of butyronitrile **1a** with primary amine **2c** was due to the side reaction of disproportionation of the latter with the formation of dicyclohexylamine. However, the disproportionation was not observed in the case of aniline. Aniline **2d** exhibited low activity in the reaction, likely due to the low basicity, and the satisfactory yield was attained only at heating to far above 200°C.

Scheme 2.



R^1 = Pr (**1a**, **4a**, **5a**), Bu (**1b**, **4b**, **5c**), *i*-Pr (**1c**), Ph (**1d**); R^2 = H, R^3 = Et (with R^1 = Pr); R^2 = H, R^3 = Pr (with R^1 = Bu); R^2 = R^3 = Me (with R^1 = *i*-Pr).

Chromato-mass spectrometry revealed that the side products (symmetrical di- and trialkylamines) were formed upon hydrogenation of the starting nitriles **1a–1d** (Scheme 2).

The Ni^0/C and Ni^0/Ceokar-2 catalysts were found active at different temperatures. For example, the optimal temperature range of 120–150°C was found for Ni^0/C, whereas further heating led to significant decrease in the target products yield due to the catalyst deactivation. That feature is typical for hydrogenation of nitriles and has been discussed in the literature [9, 10]. However, the comparable yield of the target products in the presence of Ni^0/Ceokar-2 was attained at 180–240°C, the nitriles conversion being increased with heating. For example, the yield of alkylmorpholine **3a** at 200°C equaled 67%. It was found that the Ni^0/Ceokar-2 catalyst remained active during 14 h in the reaction of reductive amination of valeronitrile **1b** with morpholine **2a** at 185°C, in contrast to Ni^0/C.

Furthermore, according to the data collected in the Table, the formation of the symmetrical amines **4a–4c**, **5a**, **5b** from the nitriles in the case of non-disproportionating amines **2a**, **2b**, **2d** could be suppressed in the excess of the latter. For example, in the case of the reaction of amine **2a** with nitrile **1a** afforded alkylmorpholine **3a** in the yield increasing from 45 to 75% when the amine to nitrile ratio was changed from equimolar to twofold excess of amine **2a**. In view of the possibility of the disproportionation reaction, the 1 : 1 ratio of the reactants was optimal for the primary amines, since both side reactions were suppressed under these conditions.

In the case of the Ni^0/C catalyst, 15–20-fold molar excess of hydrogen with respect to the starting nitrile was found to be optimal. The decrease in hydrogen excess resulted in rapid deactivation of the catalyst. The relatively higher stability of the Ni^0/Ceokar-2 catalyst allowed the use of less hydrogen (6–12-fold excess with respect to nitrile).

The difference in the activity and stability of the studied catalysts could be explained by the formation of larger nickel particles in the case of the Ni^0/Ceokar-2 sample, reducing the catalytic activity but enhancing the catalyst stability.

In summary, we found that reductive amination of carbonitriles catalyzed by nickel nanoparticles on active carbon or aluminosilicate carrier occurred rapidly in a plug flow reactor in a gas phase or in a gas–liquid system at atmospheric pressure, affording nonsymmetrical secondary or tertiary amines with 38–78% yield, the nitriles conversion being 75–100%.

EXPERIMENTAL

Chromato-mass spectral analysis was performed using a Saturn 2100 T/GC3900 instrument (EI, 70 eV). Quantitative GLC analysis was performed using a Kristallyuks–4000M chromatograph (t_s 100–210°C, t_{evap} 250°C, polar column HP-5, l_{col} 50 m, d_{col} 0.32 mm, nitrogen as carrier gas, flame ionization detector, t_{FID} 250°C, acetonitrile as solvent). Scanning electron microscopy studies were performed using a FEI Versa 3D DualBeam instrument (working distance 10 mm, ETD detector of secondary electrons, CBS detector of backscattered electrons, EDS elemental analysis method).

Ni^0/C catalyst was prepared by impregnation of BAU-A active carbon (fraction 1–15.5 mm) with aqueous solution of $NiCl_2 \cdot 6H_2O$ during a day (0.2 g of the nickel chloride hydrate per 0.5 g of the carbon). The precipitate was filtered off, washed with distilled water, and treated with aqueous solution of $NaBH_4$ at 20–25°C during 20–30 min.

Ni^0/Ceokar-2 catalyst was prepared similarly, from 2 g of the cracking catalyst Ceokar-2 (fraction 1–1.5 mm) and 0.5 g of nickel(II) chloride hexahydrate.

Reductive amination of nitriles 1a–1f. A reduced moist catalyst was loaded into the reactor and dried in a hydrogen stream at 120°C just before the reaction. The reaction was performed in a plug flow reactor at atmospheric pressure and temperature 100–240°C. The laboratory-scale reactor was a 12Kh18N10T steel pipe of inner diameter 9 mm placed in an electric oven with heating zone height 50 mm. The reactor temperature was monitored using a thermocouple. The hydrogen feeding was controlled using a GV-7 hydrogen generator.

A mixture of the corresponding catalyst, nitrile, and amine was loaded into the reactor and heated at 100–240°C under hydrogen flow. The reaction course was monitored by means of chromato-mass spectrometry.

Reductive amination of butyronitrile 1a. *a.* Nitrile : amine : hydrogen ratio 1 : 1 : 15, catalyst Ni^0/C, reaction temperature 120°C, feeding rate of a mixture of butyronitrile **1a** and morpholine **2a** 3.6 mL h^{-1} g_{cat}^{-1}, hydrogen feeding rate 6 L h^{-1} g_{cat}^{-1}. Nitrile **1a** conversion 93%. Yield: 45% of *N*-*n*-butylmorpholine **3a**, 31% of di-*n*-butylamine **4a**, and 15% of tri-*n*-butylamine **5a**.

***N-n*-Butylmorpholine (3a).** Mass spectrum, *m*/*e* (I_{rel}, %): 143.9 (10) [*M* + 1], 142.7 (3) [*M*], 99.9 (100), 70.0 (16).

Di-*n*-butylamine (4a). Mass spectrum, *m*/*e* (I_{rel}, %): 130.8 (2) [*M* + 2], 129.8 (15) [*M* + 1], 128.6 (2) [*M*], 99.8 (8), 85.8 (100), 70 (15), 56.9 (33), 44.1 (20), 43.0 (20), 41.1 (34).

Tri-*n*-butylamine (5a). Mass spectrum, *m*/*e* (I_{rel}, %): 184.0 (2), 141.8 (100), 99.9 (75), 58.0 (55), 44.0 (11), 41.0 (8).

b. Nitrile : amine : hydrogen ratio 1 : 2 : 20, catalyst Ni^0/C, reaction temperature 120°C, feeding rate of a mixture of butyronitrile **1a** and morpholine **2a** 3.6 mL h^{-1} $g_{cat}{}^{-1}$, hydrogen feeding rate 6 L h^{-1} $g_{cat}{}^{-1}$. Nitrile **1a** conversion 92%. Yield: 75% of *N*-*n*-butylmorpholine **3a**, 11% of di-*n*-butylamine **4a**, and 5% of tri-*n*-butylamine **5a**.

c. Nitrile : amine : hydrogen ratio 1 : 2 : 6, catalyst Ni^0/Ceokar-2, reaction temperature 200°C, feeding rate of a mixture of butyronitrile **1a** and amine **2a** 0.9 mL h^{-1} $g_{cat}{}^{-1}$, hydrogen feeding rate 0.5 L h^{-1} $g_{cat}{}^{-1}$. Nitrile **1a** conversion 82%. Yield: 67% of *N*-*n*-butylmorpholine **3a**, 12% of di-*n*-butylamine **4a**, and 2% of tri-*n*-butylamine **5a**.

d. Nitrile : amine : hydrogen ratio 1 : 1 : 15, catalyst Ni^0/C, reaction temperature 150°C, feeding rate of a mixture of butyronitrile **1a** and cyclohexylamine **2c** 3.3 mL h^{-1} $g_{cat}{}^{-1}$, hydrogen feeding rate 6 L h^{-1} $g_{cat}{}^{-1}$. Nitrile **1a** conversion 92%. Yield: 45% of *N*-*n*-butylcyclohexylamine **3e**, 47% of di-*n*-butylamine **4a**, and 10% of dicyclohexylamine.

***N-n*-Butylcyclohexylamine (3e).** Mass spectrum, *m*/*e* (I_{rel}, %): 156.8 (4) [*M* + 2], 155.9 (33) [*M* + 1], 154.8 (3) [*M*], 111.9 (100), 83.0 (2), 70.2 (6), 57 (3), 56.1 (15), 41.1 (10).

Dicyclohexylamine. Mass spectrum, *m*/*e* (I_{rel}, %): 183.0 (1) [*M* + 2], 182.0 (11) [*M* + 1], 180.8 (12) [*M*], 152.0 (6), 138.0 (100), 82.0 (4), 56.1 (27), 44.1 (3), 41.1 (6).

e. Nitrile : amine : hydrogen ratio 1 : 1 : 5, catalyst Ni^0/Ceokar-2, reaction temperature 220°C, feeding rate of a mixture of butyronitrile **1a** and cyclohexylamine **2c** 0.9 mL h^{-1} $g_{cat}{}^{-1}$, hydrogen feeding rate 0.5 L h^{-1} $g_{cat}{}^{-1}$. Nitrile **1a** conversion 83%. Yield: 52% of *N*-*n*-butylcyclohexylamine **3e**, 22%. of di-*n*-butylamine **4a**, 9% of tri-*n*-butylamine **5a**, and 4% of dicyclo-hexylamine.

Reductive amination of valeronitrile 1b. *a.* Nitrile : amine : hydrogen ratio 1 : 2 : 20, catalyst Ni^0/C, reaction temperature 120°C, feeding rate of a mixture of nitrile **1b** and morpholine **2a** 3.6 mL h^{-1} $g_{cat}{}^{-1}$, hydrogen feeding rate 6 L h^{-1} $g_{cat}{}^{-1}$. Nitrile **1b** conversion 81%. Yield: 77% of *N*-*n*-pentylmorpholine **3b** and 4% of tri-*n*-pentylamine **5b**.

***N-n*-Pentylmorpholine (3b).** Mass spectrum, *m*/*e* (I_{rel}, %): 158.1 (28) [*M* + 1], 100.1 (100), 99.2 (7), 70.1 (12).

Tri-*n*-pentylamine (5b). Mass spectrum, *m*/*e* (I_{rel}, %): 228.2 (14) [*M* + 1], 170.0 (100), 114.0 (55), 58.0 (40), 171.0 (12).

b. Nitrile : amine : hydrogen ratio 1 : 2 : 6, catalyst Ni^0/Ceokar-2, reaction temperature 185°C, feeding rate of a mixture of nitrile **1b** and amine **2a** 0.9 mL h^{-1} $g_{cat}{}^{-1}$, hydrogen feeding rate 0.5 L h^{-1} $g_{cat}{}^{-1}$. Nitrile **1b** conversion 89%. Yield: 78% of *N*-*n*-pentylmorpholine and 9% of tri-*n*-pentylamine **5b**.

Reductive amination of isobutyronitrile 1c. *a.* Nitrile : amine : hydrogen ratio 1 : 2 : 10, catalyst Ni^0/Ceokar-2, reaction temperature 200°C, feeding rate of a mixture of nitrile **1c** and pyrrolidine **2b** 0.9 mL h^{-1} $g_{cat}{}^{-1}$, hydrogen feeding rate 0.75 L h^{-1} $g_{cat}{}^{-1}$. Nitrile **1c** conversion 75%. Yield: 60% of *N*-isobutylpyrrolidine **3c**, 10% of *N*-isobutylideneisobutylamine, and 5% of diisobutylamine **4c**.

***N*-Isobutylpyrrolidine (3c).** Mass spectrum, *m*/*e* (I_{rel}, %): 128.0 (19) [*M* + 1], 126.9 (2) [*M*], 84.0 (100), 42.0 (8).

***N*-Isobutylideneisobutylamine.** Mass spectrum, *m*/*e* (I_{rel}, %): 127.8 (13) [*M* + 1], 126.7 (4) [*M*], 111.9 (8), 83.9 (100), 82.1 (8), 70.0 (10), 67.0 (11), 57.0 (46), 56.0 (38), 55.0 (15), 42.0 (23), 41.1 (43), 40.1 (4).

Diisobutylamine (4c). Mass spectrum, *m*/*e* (I_{rel}, %): 129.8 (12) [*M* + 1], 128.9 (3) [*M*], 126.8 (1), 100.8 (29), 99. 8 (75), 85.8 (22), 73.9 (100), 73.0 (19), 72.0 (38), 57.9 (10), 56.9 (26), 56.0 (23), 55 (37). 46.0 (39), 43.0 (19), 41.1 (40).

b. Nitrile : amine : hydrogen ratio 1 : 2 : 10, catalyst Ni^0/Ceokar-2, reaction temperature 240°C, feeding rate of a mixture of nitrile **1c** and aniline **2d** 0.9 mL h^{-1} $g_{cat}{}^{-1}$, hydrogen feeding rate 0.75 L h^{-1} $g_{cat}{}^{-1}$. Nitrile **1c** conversion 83%. Yield: 62% of *N*-isobutylaniline **3f**, 19% of diisobutylamine **4c**, and 2% of *N*-isobutylideneisobutylamine.

***N*-Isobutylaniline (3f).** Mass spectrum, *m*/*e* (I_{rel}, %): 150.8 (3) [*M* + 2], 149.9 (28) [*M* + 1], 149.0 (29) [*M*], 107.0 (8), 106.0 (100), 77.0 (8), 51.1 (6), 50.2 (3), 41.2 (2).

Reductive amination of benzonitrile 1d. Nitrile : amine : hydrogen ratio 1 : 2 : 12, catalyst Ni^0/Ceokar-2, reaction temperature 200°C, feeding rate of a mixture of nitrile **1d** and pyrrolidine **2b** 0.9 mL h^{-1} $g_{cat}{}^{-1}$, hydrogen feeding rate 1 L h^{-1} $g_{cat}{}^{-1}$. Nitrile **1d** conversion 100%. Yield: 38% of *N*-benzylpyrrolidine **3d**, 38% of benzylamine, and 24% of dibenzylamine **4d**.

***N*-Benzylpyrrolidine (3d).** Mass spectrum, *m*/*e* (I_{rel}, %): 162.0 (11) [*M* + 1], 160.9 (38) [*M*], 91.0 (100), 84.0 (47), 70.0 (48), 64.9 (28), 42.0 (26).

Dibenzylamine (4d). Mass spectrum, *m*/*e* (I_{rel}, %): 197.9 (18) [*M* + 1], 197.0 (8) [*M*], 196.0 (25), 105.9 (72), 91.0 (100), 65.0 (21).

REFERENCES

1. Popov, Yu.V., Mokhov, V.M., Latishiva, S.E., Panov, A.O., and Pletneva, M.Yu., *Russ. J. Gen. Chem*., 2017, vol. 87, no. 10, p. 2276. doi 10.1134/S107036321710005X
2. Rylander, P., Hasbrouck, L., and Karpenko, I., *Ann. N. Y. Acad. Sci*., 1973, vol. 214, p. 100. doi 10.1111/j.1749-6632.1973.tb49523.x
3. Sajiki, H., Ikawa, T., and Hirota, K., *Org. Lett*., 2004, vol. 6, no. 26, p. 4977. doi 10.1021/ol047871o
4. Sharma, S.K., Lynch, J., Sobolewska, A.M., Plucinski, P., Watson, R.J., and Williams, J.M.J., *Catal. Sci. Technol*., 2013, vol. 3, p. 85. doi 10.1039/c2cy20431b
5. Lu, S., Wang, J., Cao, X., Li, X., and Gu, H., *Chem. Commun*., 2014, vol. 50, p. 3512. doi 10.1039/C3CC48596J
6. Van der Waals, D., Pettman, A., and Williams, J.M.J., *RSC Adv*., 2014, vol. 4, no. 94, p. 51845. doi 10.1039/C4RA11193A
7. Srimani, D., Feller, M., Ben-David, Y., and Milstein, D., *Chem. Commun*., 2012, vol. 48, p. 11853. doi 10.1039/c2cc36639h
8. Popov, Yu.V., Mokhov, V.M., and Shcherbakova, K.V., *Russ. J. Gen. Chem*., 2016, vol. 86, no. 4, p. 798. doi 10.1134/S107036321604006X
9. McCarty, J.G. and Wise, H., *J. Catal*., 1979, vol. 57, p. 406. doi 10.1016/0021-9517(79)90007-1
10. Kock, J.H.M., Bokx, P.K., Boellaard, E., Klop, W., and Geus, J.W., *J. Catal*., 1985, vol. 96, p. 468. doi 10.1016/0021-9517(85)90314-8