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Colloid and Nanosized Catalysts in Organic Synthesis: IX.[1] Hydrogenation of Enamines with Hydrogen at Atmospheric Pressure

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Abstract—Hydrogenation of enamines with hydrogen at atmospheric pressure was performed using nickel nanoparticles as a catalyst. The reaction may be used to produce tertiary amines under mild conditions using an accessible catalyst.

Keywords: nickel nanoparticles, catalysis, hydrogenation, enamine, tertiary amine

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Synthesis of tertiary amines via reductive amination of ketones has been well known [2]. At the first stage a ketone reacts with a secondary amine to afford enamine. This stage often occurs under mild conditions with readily accessible catalysts. However, the hydrogenation stage requires severe conditions (high hydrogen pressure) or use of the complex metal hydrides [3, 4] as the catalysts, or formic acid [5].

Several methods of rhodium-catalyzed hydrogenation of enamines in methanol at atmospheric pressure [6] or reductive amination of carbonyl compounds with secondary amines and hydrogen at pressure of 50 atm [7] are available. Enamines of 1-methyl-5-aryl-2,3-dihydropyrrole series can be hydrogenated by hydrogen at atmospheric pressure using iridium catalyst [8]. Palladium- and platinum-catalyzed hydrogenation of enamines at atmospheric pressure has been also investigated [9, 10]. However, the drawback of the above-mentioned methods is the use of expensive palladium or platinum catalysts.

The aim of this work was to investigate the possibility of enamines hydrogenation under mild conditions using cheaper catalysts. It was previously shown that finely dispersed metal particles catalyzed alkenes hydrogenation under mild conditions [11]. Unlike alkenes, the enamines molecules contain the substituted nitrogen moiety at the C=C double bond. Since substitution of olefins dramatically reduced their ability towards hydrogenation [12], we expected that hydrogenation of enamines under mild conditions could be subject to certain complications.

Enamines formed by reacting enolisable aldehydes or ketones with secondary amines under acid catalysis were used as substrates.

The colloid nickel catalyst was prepared in situ from nickel chloride and sodium borohydride [13]. Hydrogenation of enamines was carried out by bubbling gaseous hydrogen through a solution of the enamine in isopropanol at 50–60°C during 5–6 h in the presence of nickel nanoparticles (Scheme 1).

Shorter reaction time or lower temperature (down to ~20°C) reduced degree of conversion of the starting enamine. The catalyst load as low as 10 mol % with respect to the enamine was found to be sufficient; the reaction proceeded efficiently when anhydrous solvent and dry hydrogen were applied.

Structure of the synthesized tertiary amines was confirmed by ^{1}H NMR spectroscopy; properties of the known substances coincided with the literature data [14–18].

To conclude, the use of nickel nanoparticles as a cheap and available catalyst for enamines hydrogenation allows performing the process at atmospheric

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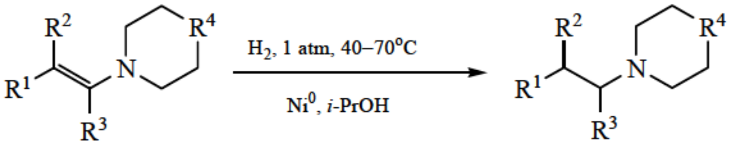
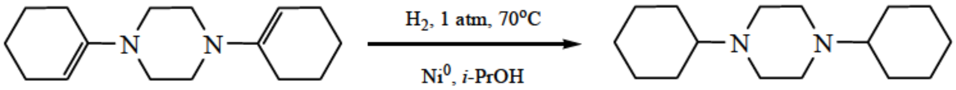
[1] For communication VIII, see [1].

Scheme 1.



Ia–If **IIa–IIf**

$R^1 = R^2 = CH_3$, $R^3 = H$, $R^4 = CH_2$ (**Ia, IIa**); $R^1 = R^2 = CH_3$, $R^3 = H$, $R^4 = O$ (**Ib, IIb**); $R^1–R^3 = (CH_2)_4$, $R^2 = H$, $R^4 = CH_2$ (**Ic, IIc**); $R^1–R^3 = (CH_2)_4$, $R^2 = H$, $R^4 = O$ (**Id, IId**); $R^1–R^3 = (CH_2)_3$, $R^2 = H$, $R^4 = O$ (**Ie, IIe**); $R^1 = H$, $R^2 = Pr$, $R^3 = CH_3$, $R^4 = O$ (**If, IIf**).



Ig **IIg**

pressure. Nanosized metals or their oxides have been known to catalyze some condensation reactions [19, 20]. Hence, the investigation of possibility of one-step hydroamination of enolisable ketones with secondary amines using colloidal catalyst (resistant to deactivation with the evolving water) is prospective. It will allow developing a scalable and cost-efficient approach towards synthesis of tertiary amines.

EXPERIMENTAL

^{1}H NMR spectra of the solutions in CCl_4 were recorded with a Varian Mercury-300 (300 MHz) spectrometer with HMDS as internal reference.

***N*-Isobutylpiperidine (IIa).** 1 g (0.008 mol) of anhydrous nickel(II) chloride was added to a suspension of 0.58 g (0.016 mol) of sodium borohydride in 20 mL of isopropanol. Then 14.1 g (0.1 mol) of enamine **Ia** was added 14.1 g to the formed black colloid solution of the catalyst. The mixture was bubbled with hydrogen (20–25 mL/min) at 50°C during 5 h. Then 2 mL of water was added, and the mixture was stirred during 1 h. The precipitate formed was filtered off, and isopropanol was distilled off. The residue was distilled at atmospheric pressure. Yield 12.7 g (0.09 mol, 90%), bp 162–164°C, n_D^{20} 1.4414 {bp 43.0–43.5°C (10 mmHg), n_D^{20} 1.4418 [14]}. ^{1}H NMR specrtum, δ, ppm: 0.49 t (6H, $2CH_3$, *J* 6.9 Hz), 1.04 s (2H, CH_2), 1.17 s (4H, $2CH_2$), 1.34–1.41 m (1H, CH), 1.60 d (2H, CH_2N, *J* 7.5 Hz), 1.91 t [4H, $(CH_2)_2N$, *J* 8.5 Hz].

***N*-Isobutylmorpholine (IIb)** was prepared similarly from 0.6 g (0.017 mol) of $NaBH_4$ in 20 mL of isopropanol, 1 g (0.008 mol) of $NiCl_2$, and 15.7 g (0.11 mol) of enamine **Ib**. Yield 14.6 g (0.102 mol, 93%), bp 66–68°C (17 mmHg), n_D^{20} 1.4414 {bp 62–64°C (17 mmHg), n_D^{20} 1.4421 [14]}. ^{1}H NMR spectrum, δ, ppm: 0.78–0.88 m (6H, $2CH_3$), 1.65–1.73 m (1H, CH), 1.97 d (2H, CH_2N, *J* 9.6 Hz), 2.26 t [4H, $(CH_2)_2N$, *J* 5 Hz], 3.52 t [4H, $(CH_2)_2O$, *J* 4.8 Hz].

***N*-Cyclohexylpiperidine (IIc)** was prepared similarly from 0.58 g (0.016 mol) of $NaBH_4$ in 20 mL of isopropanol, 1 g (0.008 mol) of $NiCl_2$, and 16.5 g (0.1 mol) of enamine **Ic**; the reaction was performed at 60°C for 6 h. Yield 15.4 g (0.092 mol, 92%), bp 233–235°C (bp 234°C [15]). ^{1}H NMR spectrum, δ, ppm: 1.06–1.71 m (16H, $8CH_2$), 2.12 m (1H, CHN), 2.36 t [4H, $(CH_2)_2N$, *J* 8.7 Hz].

***N*-Cyclohexylmorpholine (IId)** was prepared similarly from 0.58 g (0.016 mol) of $NaBH_4$ in 20 mL of isopropanol, 1 g (0.008 mol) of $NiCl_2$, and 26.7 g (0.15 mol) of enamine **Id**. Yield 21.3 g (0.126 mol, 84%), colorless liquid, bp 140–142°C (25 mmHg) {bp 111–112°C (12 mmHg) [16]}. ^{1}H NMR spectrum, δ, ppm: 1.03–1.77 m (10H, $5CH_2$), 2.00–2.07 m (1H, CHN), 2.40 t [4H, $(CH_2)_2N$, *J* 8.1 Hz], 3.48 t (4H, CH_2O, *J* 8.3 Hz).

***N*-Cyclopentylmorpholine (IIe)** was prepared similarly from 0.58 g (0.016 mol) of $NaBH_4$ in 20 mL of isopropanol, 1 g (0.008 mol) of $NiCl_2$, and 26.7 g (0.17 mol) of enamine **Ie**. Yield 21.1 g (0.136 mol, 75%), bp 131–133°C (25 mmHg) {bp 69–73°C (4.4 mmHg) [17]}. ^{1}H NMR spectrum, δ, ppm: 1.27–1.84 m (8H, $4CH_2$), 2.31 t [4H, $(CH_2)_2N$, *J* 9.5 Hz], 2.67–2.71 m (1H, CHN), 3.49 t [4H, $(CH_2)_2O$, *J* 10 Hz].

***N*-(2-Hexyl)morpholine (IIf)** was prepared similarly from 0.58 g (0.016 mol) of $NaBH_4$ in 20 mL of isopropanol, 1 g (0.0077 mol) of $NiCl_2$, and 26.5 g (0.15 mol) of enamine **If**. Yield 21.3 g (0.125 mol, 78%). ^{1}H NMR spectrum, δ, ppm: 0.80–0.94 m (6H,

$2CH_3$), 1.25–1.79 m (6H, $3CH_2$), 2.25–2.38 m [5H, $(CH_2)_2N$, CHN], 3.41 d.t [4H, $(CH_2)_2O$, J_1 9, J_2 28 Hz]. Found, %: C 78.06; H 13.64; N 8.30. $C_{11}H_{23}N$. Calculated, %: C 78.03; H 13.69; N 8.27.

***N,N*-Dicyclohexylpiperazine IIg** was prepared similarly from 0.58 g (0.016 mol) of $NaBH_4$ in 20 mL of isopropanol, 1 g (0.008 mol) of $NiCl_2$, and 25 g (0.1 mol) of enamine **Ig**; the reaction was performed at 70°C for 6 h. Yield 21.75 g (0.087 mol, 87%), colorless, bp 242–246°C (20 mmHg), mp 115–117°C {bp 170–200°C (5–10 mmHg), mp 118°C [18]}. ^1H NMR spectrum, δ, ppm: 1.10–1.72 m (20H, $10CH_2$), 2.05 m (2H, 2CHN), 2.39 t [8H, $2(CH_2)_2N$].

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REFERENCES

1. Mokhov, V.M. and Popov, Yu.V., *Russ. J. Gen. Chem.*, 2014, vol. 84, no. 10, p. 1921. DOI: 10.1134/S1070363214100090.
2. Tarasevich, V.A. and Kozlov, N.G., *Russ. Chem. Rev.*, 1999, vol. 68, no. 1, p. 55. DOI: 10.1070/RC1999v068n01ABEH000389.
3. Abdel-Magid, A.F., Carson, K.G., Harris, B.D., Maryanoff, C.A., and Shah, R.D., *J. Org. Chem.*, 1996, vol. 61, p. 3849. DOI: 10.1021/jo960057x.
4. Gavrilov, M.S., Shklyaev, V.S., and Aleksandrov, B.B., *Chem. Heterocyclic Compd.*, 1987, vol. 23, no. 8, p. 871. DOI: 10.1007/BF00473462.
5. Nilsson, A. and Carlson, R., *Acta Chim. Scand. (B)*, 1985, vol. 39, no. 3, p. 187. DOI: 10.3891/acta.chem.scand.39b-0187.
6. Tararov, V.I., Kadyrov, R., Riermeier, T.H., Holz, J., and Borner, A., *Tetrahedron Lett.*, 2000, vol. 41, no. 14, p. 2351. DOI: 10.1016/S0040-4039(00)00197-0.
7. Tararov, V.I., Kadyrov, R., Riermeier, T.H., and Borner, A., *Adv. Synth. Catal.*, 2002, vol. 344, no. 2, p. 200. DOI: 10.1002/1615-4169(200202)344.
8. Hou, G.-H., Xie, J.-H., Yan, P.-Ch., and Zhou, Q.-L., *J. Am. Chem. Soc.*, 2009, vol. 131, no. 4, p. 1366. DOI: 10.1021/ja808358r.
9. Horwell, D.C. and Timms, G.H., *Synth. Commun.*, 1979, vol. 9, no. 3, p. 223. DOI: 10.1080/00397917908066700.
10. Cohen, J.H., Abdel-Magid, A.F., Almond, H.R., and Maryanoff, C.A., *Tetrahedron Lett.*, 2002, vol. 43, no. 11, p. 1977. DOI: 10.1016/S0040-4039(02)00172-7.
11. Mokhov, V.M., Popov, Yu.V., and Nebykov, D.N., *Russ. J. Gen. Chem.*, 2014, vol. 84, no. 4, p. 622. DOI: 10.1134/S1070363214040033.
12. Corey, E.J., Actuwa, K., and Katzenellenbogen, J.A., *J. Am. Chem. Soc.*, 1969, vol. 91, p. 4318. DOI: 10.1021/ja01043a068.
13. Mokhov, V.M., Popov, Yu.V., and Nebykov, D.N., *Russ. J. Gen. Chem.*, 2014, vol. 84, no. 9, p. 1656. DOI: 10.1134/S1070363214090023.
14. Stamhuis, E.J., Maas, W., and Wynberg, H., *J. Org. Chem.*, 1965, vol. 30, no. 7, p. 2160. DOI: 10.1021/jo01018a010.
15. Reynolds, D.D. and Kenyon, W.O., *J. Am. Chem. Soc.*, 1950, vol. 72, no. 4, p. 1597. DOI: 10.1021/ja01160a046.
16. Blicke, F.F. and Zienty, F.B., *J. Am. Chem. Soc.*, 1939, vol. 61, no. 4, p. 771. DOI: 10.1021/ja01873a004.
17. Kim S., Oh, Ch.H., Ko, J.S., Ahn, K.H., and Kim, Y.J., *J. Org. Chem.*, 1985, vol. 50, no. 11, p. 1927. DOI: 10.1021/jo00211a028.
18. Bain, J.P. and Pollard, C.B., *J. Am. Chem. Soc.*, 1939, vol. 61, no. 10, p. 2704. DOI: 10.1021/ja01265a039.
19. Choudary, B.M., Kantam, M.L., Ranganath, K.V.S., Mahendar, K., and Sreedhar, B., *J. Am. Chem. Soc.*, 2004, vol. 126, p. 3396. DOI: 10.1021/ja038954n.
20. Kidwai, M., Bhardwaj, S., Mishra, N.K., Bansal, V., Kumar, A., and Mozumdar, S., *Catal. Commun.*, 2009, vol. 10, no. 11, p. 1514. DOI: 10.1016/j.catcom.2009.04.006.