Pergamon

Tetrahedron Letters 39 (1998) 8873–8876

TETRAHEDRON
LETTERS

Organic Reaction in Water. Part 1. A Convenient Method for Reduction of Imines Using Zinc Powder

Takehito Tsukinoki*, Yoshiharu Mitoma, Satoko Nagashima, Takatoshi Kawaji†, Iwao Hashimoto† and Masashi Tashiro

Tohwa Institute for Science, Tohwa University,
1-1-1, Chikushigaoka, Minami-ku, Fukuoka 815, Japan

†Department of Industrial Chemistry, Wakayama National College of Technology,
Nojima 77, Nata-machi, Goboh, Wakayama 644, Japan

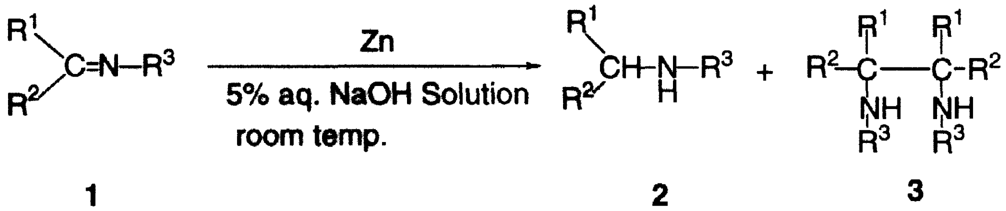
Received 25 August 1998; revised 5 September 1998; accepted 11 September 1998

Abstract: Reduction of imines was performed with zinc powder in 5% aq NaOH solution *without any organic solvents* under mild conditions, and the corresponding amines were obtained in good yields.

The reduction of imines leading to amines is effected by various methods.[1] For example, metal hydrides such as $LiAlH_4$,[2] $NaBH_4$,[2] Bu_2SnClH,[3] $(\eta\text{-}C_5H_5)_2MoH_2$,[4] and $RuHCl(PPh_3)_3$,[5] hydrogenation catalysts[6] like Pd-C and Pt, and lanthanoids such as Yb[7] are usually employed as metallic reagents in an organic solvent for preventing possible hydrolysis of imines. However, methods using metal hydrides and lanthanoids which have a moisture-sensitive character should be carried out in a dried organic solvent and/or an inert gas, and in the case of hydrogenation, the reaction should be undertaken with an expensive catalyst in an anhydrous organic solvent under high pressure. Therefore, these methods entail tedious procedures. Furthermore, recently, in connection with environmental concerns, there is growing interest in synthetic organic reactions in water *without any organic solvents* which are environmentally-friendly.[8] Water has many advantages as a solvent for organic reactions from the aspects of cost, safety, simple operation and environmental concerns as compared with use of an organic solvent, and many organic reactions such as the Diels-Alder reaction, pinacol coupling, the aldol reaction and so on have been reported.[8] We have been continuously investigating reductive dehalogenation of halogenated compounds and reductive coupling reaction of carbonyl compounds with metals in aqueous media.[9] We report here our significant finding that in 5% aq NaOH solution *without any organic solvents*, zinc powder is effective for the reduction of imines to give the corresponding amines under mild conditions with a simple procedure.

When imines **1a-q** were treated with zinc powder in 5% aq NaOH solution at room temperature, reduction proceeded and the corresponding amines **2a-q** were obtained in 53 - 88% yields (Table 1). Further, we have found that no traces of amines and carbonyl compounds formed by hydrolysis of imines were obtained in our method though imines tend to be hydrolyzed in acidic or basic solution.[10] In comparison with other con-

PII: S0040-4039(98)01904-2



Scheme 1

ventional methods, some advantages of our method are the fact that, since the reaction can be done in water at room temperature under atmospheric pressure, it is safe, and that hydrogen gas is not necessary because the proton source is water; furthermore, Zn powder is cheap compared with metal hydrides, hydrogenation catalyst and lanthanoids, and is not sensitive to oxygen and water, so its handling is very easy. In the case of aldimines **1b**-**e** having a substituent group on an aromatic ring, reaction time is shortened, but the reason for the effect of the substituent group is not clear now. As the substituent R^3 was more bulky (**1f**-**g** and **1h**-**j**), it took longer time to complete the reaction because the steric hindrance of substituent R^3 possibly prevents adsorption of the carbon-nitrogen double bond on the surface of zinc powder. The reduction of aldimines **1k**-**l** having a heterocycle was also performed. Our method is not limited to aldimines and works as well with aliphatic imine and ketimines. However, in the case of *N*-diphenylmethyleneaniline (**1p**), conversion of **1p** into amine **2p** was only 50%, even though by the treatment of **1p** under same conditions for 120 h. In addition, even though the reaction was carried out at 60 °C under ultrasonication, the formation of **2p** was not increased, but the reaction time was shortened (120→8h). Interestingly, by adding NH_4Cl to the reaction system, the reduction of **1p** smoothly proceeded to afford **2p** in 74% isolated yield. On the other hand, in the case of oxime **1q**, similarly, amine **2q** (R^3=H) which would result from overreduction was obtained in 63% yield with no trace of hydroxylamine. A small amount of diamines **3a**-**e** was formed as a by-product. In the case of imines **1f**-**g** and **1i**-**j**, the formation of diamine tended to be increased. The formation of diamines in an aqueous solution is particularly interesting, since usually dimerization of aldimines proceeds under anhydrous conditions.[11]

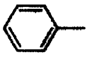
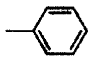
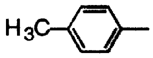
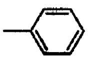
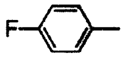
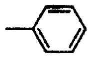
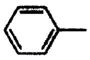
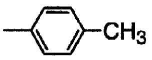
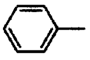
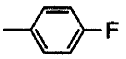
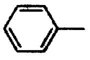
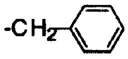
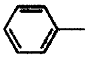
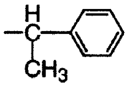
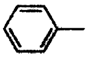
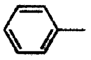
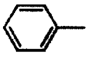
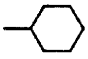
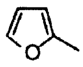
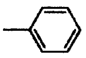
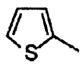
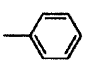
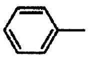
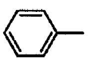
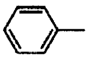
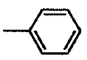
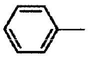
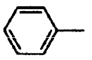
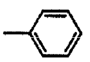
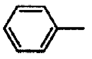
In a very diluted aqueous alkaline solution, 1% aq NaOH, reduction of **1a** occurred as well as in 5% aq NaOH, giving **2a** in 83% yield, although reaction time is prolonged (7→19h). When the reduction of **1a** in 1% aq NaOH was carried out under ultrasonic irradiation, the reaction was accelerated (19→1.5 h), but the molar ratios of product **2a** and **3a** were little affected.

In a typical procedure, to a stirred mixture of *N*-benzylideneaniline **1a** (906 mg, 5.00 mmol) and 5% aq NaOH solution (20 ml) at room temperature was gradually added commercially available zinc powder (5.00 g[12]) for 10 min. After the reaction mixture was stirred for 7 hr at room temperature, the insoluble materials were filtered off and the filtrate was extracted with ethyl acetate. The extract was washed with water, dried over ($MgSO_4$) and evaporated *in vacuo* to give a residue, which was distilled on a Kugelrohr apparatus (oven temperature:150 - 151 °C) under reduced pressure (1.3 torr), to afford *N*-benzylaniline **2a** (750 mg, 82%) and *N*, *N'*,1,2-tetraphenylethylenediamine **3a** (64 mg, 7%).

In conclusion, the reduction of imines took place with the use of low-priced zinc powder in an aqueous alkaline solution *without any organic solvents* and no production of hydrolyzed products of imines to afford the corresponding amines.

Further study on extension of this reaction and dimerization of imines is under way.

Table 1. Reduction and Coupling of Imines Using Zn Powder in Aqueous Solution without Organic Solvents[a]

Imines	R^1	R^2	R^3	Time/h[b]	Isolated Yield/%	
					2	3
1a		H-		7.2	82	7
1b		H-		0.7	85	9
1c		H-		0.7	88	5
1d		H-		2.2	83	3
1e		H-		1.2	88	4
1f		H-		1.7	67	23
1g		H-		7.2	76	15
1h		H-	$-CH_3$	0.2	53	-
1i		H-	*iso*-propyl	5.2	53	20
1j		H-		5.2	71	15
1k		H-		0.2	63	3
1l		H-		3.2	73	4
1m	$CH_3(CH_2)_4$-	H-	$-(CH_2)_5CH_3$	31.2	64	-
1n			-H	30.2	86	-
1o		CH_3-		15.2	83	6
1p[c]				5.2	74	-
1q		H-	-OH	22.2	63 (R^3=H)	-

[a]Substrate : 5.00 mmol, Zn : 5g (76.5 mmol). [b]The time (10 min) of adding Zn powder to the reaction vessel is included in the mentioned reaction time. [c] NH_4Cl (1.96 g, 36.7 mmol) was used.

References and Notes

1. a) Harada, K.; Patai, S. *The Chemistry of the Carbon Nitrogen Double Bond*; John Wiley and Sons, Inc.: New York, 1970; pp. 276-298. b) House, H. O. *Modern Synthetic Reactions*; Benjamin: Menlo Park, 1972; pp. 209-211. c) Huffman, J. W. *Comprehensive Organic Synthesis*; Pergamon Press: Oxford, 1991; vol. 8, pp. 123-124. d) March, J. *Advanced Organic Chemistry*; John Wiley and Sons, Inc.: New York, 1992; p. 918.
2. Hutchins, R. O.; Hutchins, M. K. *Comprehensive Organic Synthesis*; Pergamon Press: Oxford, 1991; vol. 8, pp. 25-78.
3. Shibata, I.; Moriuchi-Kawakami, T.; Tanizawa, D.; Suwa, T.; Sugiyama, E.; Matsuda, H.; Baba, A. *J. Org. Chem.* **1998**, 63, 383-385.
4. Minato, M.; Fujiwara, Y.; Ito, T. *Chem. Lett.* **1995**, 647-648.
5. Mizushima, E.; Yamaguchi, M.; Yamagishi, T. *Chem. Lett.* **1997**, 237-238.
6. Freifelder, M. *Catalytic Hydrogenation in Organic Synthesis Procedures and Commentary*; John Wiley and Sons, Inc.: New York, 1978; pp. 65-77.
7. Takaki, K.; Tsubaki, Y.; Tanaka, S.; Beppu, F.; Fujiwara, Y. *Chem. Lett.* **1990**, 203-204.
8. a) Li, C.-H.; Chan, T.-H. *Organic Reactions in Aqueous Media*; John Wiley and Sons, Inc.: New York, 1997; pp. 13-189. b) Lubineau, A.; Augé, J.; Queneau, Y.; *Synthesis* **1994**, 741-760. c) Li, C.-J., *Chem. Rev.* **1993**, 93, 2023-2035.
9. For example, see: a) Tashiro, M.; Nakayama, K. *J. Chem. Soc., Perkin Trans. 1.* **1983**, 2315-2318. b) Tashiro, M.; Mataka, S.; Nakamura, H.; Nakayama, K. *J. Chem. Soc., Perkin Trans. 1.* **1988**, 179-181. c) Tsuzuki, H.; Iyama, H.; Mashimo, T.; Mukumoto, M.; Tsukinoki, T.; Mataka, S.; Tashiro, M. *Chem. Express* **1993**, 8, 495-498. d) Tsukinoki, T.; Kakinami, T.; Iida, Y.; Ueno, M.;Ueno, Y.; Mashimo, T.; Tsuzuki, H.; Tashiro, M. *J. Chem. Soc., Chem. Commun.* **1995**, 209-210. e) Tsukinoki, T.; Kawaji, T; Hashimot, I.; Mataka, S.; Tashiro, M. *Chem. Lett.* **1997**, 235-236. f) Tsukinoki, T.; Kawaji, T.; Hashimoto, I.; Etoh, T.; Sahade, D. A.; Tashiro, M. Eng. Sci. Rep. Kyushu Univ. **1997**, 19, 15-18. g) Sahade, D. A.; Mataka, S.; Sawada, T.; Tsukinoki, T.; Tashiro, M. *Tetrahedron Lett.* **1997**, 38, 3745-3746.
10. a) Bruylants, A.; Medicis, E. F.; Patai, S. *The Chemistry of the Carbon Nitrogen Double Bond*; John Wiley and Sons, Inc.: New York, 1970; pp. 465-501. b) March, J. *Advanced Organic Chemistry*; John Wiley andSons,Inc.: New York, 1992; pp. 884-885.
11. Robertson, G. M. *Comprehensive Organic Synthesis*; Pergamon Press: Oxford, 1991; vol. 3, pp. 579-582.
12. When we investigated the minimum amount of Zn powder which is necessary for the reduction of **1a**, we found that the reduction took place with 654 mg of Zn powder which is twice molar of substrate under the same reaction conditions. But with equimolar Zn powder for **1a**, the starting material remained. However, other substrates besides **1a** needed 5 g of Zn powder for reduction.