Pergamon

Tetrahedron Letters, Vol. 37, No. 26, pp. 4559-4560, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)00844-1

A New Method for the Chemoselective Reduction of Aryl and Aroylazides

Mukulesh Baruah, Anima Boruah, Dipak Prajapati, Jagir S. Sandhu*
and Anil C. Ghosh.

Regional Research Laboratory, Jorhat 785 006, Assam, India.

Abstract: Reduction of aryl and aroyl azides to the parent primary amines or amides respectively occurs in excellent yield upon treatment with a new reduction system consisting of $Fe\text{-}NiCl_2 6H_2O\text{-}THF$. Copyright © 1996 Published by Elsevier Science Ltd

Reduction of azides to amines is an important reaction in organic synthesis, especially in carbohydrate and nucleoside chemistry[1]. There are many reports on this conversion describing the use of , for example, lithium aluminium hydride[2], triethyl phosphate[3], sodium hydrogen telluride[4], catalytic hydrogenation[5], triphenyl phosphine[6], sodium borohydride/phase-transfer catalyst[7] and transfer hydrogenation[8] have been reported. But most of them have some disadvantages in relation to their general applicability, selectivity, availability, operational convenience or toxicity. As a result, there is always considerable interest in finding more selective methods. Herein we report a novel reduction system consisting of iron-nickel chloride hexahydrate in tetrahydrofuran for the chemoselective reduction of various aryl and aroyl azides. The reductions generally proceeded with high yields and showed selectivity over other labile substituents.

$$\underset{\mathbf{1}}{\mathrm{R\text{-}N_3}} \xrightarrow{\mathrm{Fe/NiCl_2 6H_2O\text{-}THF}} \underset{\mathbf{2}}{\mathrm{R\text{-}NH_2}}$$

R=Aryl, Aroyl

In a typical procedure, to a mixture of iron powder (10 mmol) and nickel chloride hexahydrate (15 mmol) was added a solution of the phenyl azide (1 mmol) in freshly distilled tetrahydrofuran. A vigorous exothermic reaction takes place immediately which is controlled by keeping the reaction in an ice bath. After about 30 minutes when TLC of the reaction mixture showed disappearance of the starting material the reaction mixture is diluted with THF (100 ml) and filtered. Evaporation of the filtrate gave the corresponding aniline which is further purified by chromatography. Similar treatment of other aryl or aroyl azides gave the corresponding amines or amides respectively in 80-90% yields(Table 1).

The excellent yields of the reduction products demonstrate the efficiency of this new method. Azides are selectively reduced in the presence of a double bond (entry 9) or an aromatic methoxy group (entry 3&10). In case of nitro substituted aromatic azides, the corresponding nitro aniline was selectively obtained without any further reduction of nitro group (entry 7).Furthermore, haloaromatic azides showed remarkable selectivity to give the amine without any further dehalogenation (entry 4&5). In addition it was worth commenting that 4-acetylphenylazide was also selectively converted to the 4-aminoacetophenone without any further reduction and the sensitive carbonyl group remains intact. However, the reduction of 4-nitrophenol did not proceed successfully with this reduction system. The use of aluminium in combination with nickel chloride hexahydrate in tetrahydrofuran is equally effective in these reactions and the corresponding primary amines or amides were obtained in almost comparable yields.

In conclusion, the present results demonstrate the novelty of iron-nickel chloride hexahydrate combination system which shows unique selectivity and constitute a useful alternative to the commonly accepted procedure[9,10] for the synthesis of various primary amines or amides in excellent yields.

Table 1: Reduction of RN_3-(1) to Amines or Amides (2) with Fe-$NiCl_26H_2O$ System.

Entry	Azide	R	Reaction time (min)	Isolated Yield (%)
1	1a	C_6H_5	30	85
2	1b	p-$CH_3COC_6H_4$	50	80
3	1c	p-$CH_3OC_6H_4$	45	90
4	1d	p-ClC_6H_4	50	85
5	1e	m-ClC_6H_4	45	82
6	1f	m-$CH_3C_6H_4$	60	80
7	1g	p-$NO_2C_6H_4$	30	85
8	1h	$C_6H_5CH=CH-CH_2$	50	78
9	1i	C_6H_5CO	25	90
10	1j	p-$CH_3OC_6H_4CO$	30	85
11	1k	p-HO-C_6H_4	60	15

References

1 Grundmann, C., in: Houben-weyl. *Methoden der Organischen Chemie,* 4th ed., Muller, E. (ed), Vol. 10/3, Georg Thieme Verlag. Stuttgart, **1965**, p. 822.

2 Boyer, J. H., *J. Am. Chem. Soc.*, **1951,** *73,* 5865.

3 Mungall, W. S., Greene, G. L., Heavner, G. A., Letsinger, R. L., *J. Org. Chem.*, **1975,** *40,* 1659.

4 Vaultier, M., Knouzi, N., Carrie, R., *Tetrahedron Lett.*, **1983,***24,* 763.

5 Koziara, A., Pacewicka, K. O., Zawadzki, S., Zwierzak, A., *Synthesis,* **1985,** 202.

6 Rolla, F., *J. Org. Chem.*, **1982,** *47,* 4327.

7 Gastiser, T., Selve, C., Delpucch, J. J., *Tetrahedron Lett.*, **1983,** *24,* 1609.

8 Suzuki, H., Takaoka, K., *Chem. Lett.*, **1984,** 1733 and references cited therein.

9 For most recent report see: Salunkhe, A. M., Brown, H. C., *Tetrahedron Lett.*, **1995,** *36,* 7987.; Afonso, C. A. M., *Tetrahedron Lett.*, **1995**, *36,* 8857.; Benati, L., Montevecchi, P. C., Nanni, D., Spagnolo, P., Volta, M., *Tetrahedron Lett.*, **1995,** *36,* 7313.

10 For other methods using Lindlar Catalyst see: Corey, E. J., Nicolaou, K. C., Balanson, R. D., Machida, Y., *Synthesis,* **1975,** 590.; Using CrII/H+ see: Kirk, D. N., Wilson, M. A., *J. Chem. Soc., Chem. Commun.*, **1970,** 590.; Using Bu_3SnH/AIBN see: Samano, M. C., Robins, M., *Tetrahedron Lett.*, **1991,** *32,* 6293.; Using Mg or Ca/MeOH see: Maiti, S. N., Spevak, P., Reddy, A. V. N., *Synth. Commun.*, **1988,** *18,* 1201.

(*Received in UK* 7 *March* 1996; *revised* 1 *May* 1996; *accepted* 3 *May* 1996)