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A FACILE REDUCTION OF AZIDES TO THE CORRESPONDING AMINES WITH Sm/NiCl₂· 6H₂O SYSTEM

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A FACILE REDUCTION OF AZIDES TO THE CORRESPONDING AMINES WITH Sm/NiCl₂·6H₂O SYSTEM

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ABSTRACT

Azides can be easily reduced to the corresponding amines with $Sm/NiCl_2 \cdot 6H_2O$ in excellent yields under mild and neutral conditions.

The reduction of azides to corresponding amines is an important reaction in organic synthesis.^{1–2} A wide variety of reagents have been used for this conversion, for example, zinc borohydride,³ lithium aluminium hydride,⁴ triethyl phosphate,⁵ sodium borohydride,⁶ lithium aminoborohydride,⁷ benzyltriethylammonium tetrathiomolybdate,⁸ etc. We also reported the reduction of azides to amines with Sm/cat. I₂,⁹ SmI₂ and Cp₂TiCl₂-Sm system.¹⁰

But some of these reagents have one or more limitations with regard to general applicability, selectivity, ready availability, operational convenience, and toxicity. For instance, LiAlH₄ is not tolerable to many functionalities

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such as CO_2R , NO_2 etc. and on the other hand, catalytic hydrogenation and diborane reduction have limitations for being applied to unsaturated compounds containing a double or a triple bond. As a result, there is always considerable interest in finding more selective methods.

Here we wish to report a novel reduction of azides to the corresponding amines with samarium-nickel chloride hexahydrate in high yield in tetrahydrofuran under mild and neutral condition.

$$R - N_3 \xrightarrow{Sm/NiCl_2 \cdot \delta H_2O} R - NH_2$$

Scheme 1.

Table 1 summarizes our results on the reduction of a number of alkyl, aryl, aroyl and arylsulfonyl azides. In all the reactions, the cleavage takes place between the N–N bond, rather than the C–N or S–N bond. At the same time, aryl, aroyl and arylsulfonyl azides containing halides, carbonyl, or sulfonyl groups are reduced to the corresponding amines or amides. The amides are not reduced further to the amines. Chloro, bromo, iodo, carbonyl and sulfonyl groups cannot be reduced under the reaction conditions and do not influence the rate of reduction. Furthermore, α , β -unsaturated acyl azides are selectively reduced with the double bond

Entry	Azides	Reduction Time (h)	Yield* (%)
1	p-ClC ₆ H ₄ N ₃	2.5	85
2	p-BrC ₆ H ₄ N ₃	2.5	83
3	$p-IC_6H_4N_3$	2.5	87
4	$p-CH_3C_6H_4N_3$	2.5	88
5	$C_6H_5N_3$	2.5	90
6	$C_7H_{15}N_3$	3	70
7	$o-NO_2C_6H_4N_3$	3	82
8	$2,4-Cl_2C_6H_3N_3$	3	83
9	C ₆ H ₅ CON ₃	2.5	85
10	m-CH ₃ C ₆ H ₄ CON ₃	2.5	83
11	$C_6H_5SO_2N_3$	2.5	85
12	p-CH ₃ C ₆ H ₄ SO ₂ N ₃	2.5	87
13	N ₃ CH ₂ COOCH ₃	3	76
14	C ₆ H ₅ CH=CHCON ₃	3	75

Table 1. Reduction of Azides to Amines with Sm/NiCl₂.6H₂O

*Isolated yield.



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remained (Entry 14), and the corresponding nitro aniline was selectively obtained without any further reduction of nitro group (Entry 7), but nitroarenes can be reduced to the corresponding amines with SmI_2 ,¹¹ Sm/cat. I₂,¹² and Cp₂TiCl₂/Sm.¹³

In conclusion, it has been found that the $Sm/NiCl_2 \cdot 6H_2O$ system can be used for the reduction of azides to amines. The advantages of this reaction are excellent yields, unique selectivity, simple operation, mild and neutral reaction condition.

EXPERIMENTAL

¹H NMR spectra were recorded on a Brucker AC 80 instrument. All NMR samples were measured in CDCl₃ using TMS as internal standard, IR spectra were determined on a Perkin-Elmer 683 spectrometer.

Metallic samarium and other chemicals were purchased from commercial sources and used without purification. All azides were prepared according to known method.¹⁴

General Procedure: Under a nitrogen atmosphere, metallic samarium powder (4.0 mmol) and nickel chloride hexahydrate (4.0 mmol) were placed in a three-necked reaction flask and THF (10 ml) was added in one portion. Azides was then added to the mixture and stirred at 40°C for a given time (Table 1). A satd. aq. $Na_2S_2O_3$ was added to quench the reaction and the mixture was extracted with ether (20 ml × 3). The organic layer was washed with brine (20 ml × 3) and dried over anhydrous Na_2SO_4 . The solvent was removed in vacuo. The residue was then purified by preparative TLC on silica gel (dichloromethane-cyclohexane as eluent) to give pure product.

p-ClC₆H₄NH₂¹⁵: mp 70°C (Lit. 71–73°C); $\delta_{\rm H}$ 3.40 (s, 2H), 6.30–7.00 (m, 4H); $v_{\rm max}/{\rm cm}^{-1}$ 3470, 3400, 1600, 1500, 1290, 830, 640.

p-BrC₆H₄NH₂¹⁵: mp 61°C (Lit. 62–64°C); $\delta_{\rm H}$ 3.40 (s, 2H), 6.25–7.15 (m, 4H); $\nu_{\rm max}/{\rm cm}^{-1}$ 3480, 3370, 1610, 1500, 1280, 810, 620.

p-IC₆H₄NH₂¹⁵: mp 62°C (Lit. 62–63°C); $\delta_{\rm H}$ 3.60 (s, 2H), 6.30–7.30 (m, 4H); $v_{\rm max}/{\rm cm}^{-1}$ 3390, 3350, 3200, 3050, 1620, 1600, 1480, 1280, 1180, 940, 810, 590.

 $\textit{p-CH}_3C_5H_4NH_2^{15}:$ mp 43°C (Lit. 44°C); δ_H 2.10 (s, 3H), 3.15 (s, 2H), 6.25–6.80 (m, 4H); ν_{max}/cm^{-1} 3460, 3400, 3010, 2960, 1610, 1490, 1310, 1260, 860, 770.

 $C_6H_4NH_2^{10}:$ Oil; δ_H 3.25 (s, 2H), 6.30–7.10 (m, 5H); ν_{max}/cm^{-1} 3410, 3350, 3020, 1640, 1600, 1500, 1280, 1200, 750, 690.

 $C_7 H_{15} N H_2^{10} :$ Oil; δ_H 0.90 (t, 3H), 1.25 (m, 10H), 2.27 (s, 2H), 2.65 (t, 2H); ν_{max}/cm^{-1} 3400, 3380, 2960, 2880, 2760, 1600, 1450, 1050, 800, 720.



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 $o\text{-NO}_2\text{C}_6\text{H}_4\text{NH}_2^{15a}$: mp 71°C (Lit. 71–72°C); δ_{H} 6.25 (s, 2H), 6.67–8.08 (m, 4H); $v_{\text{max}}/\text{cm}^{-1}$ 3470, 3320, 1630, 1570, 1500, 1430, 1350, 1250, 1100, 750.

2,4-Cl₂C₆H₃NH¹⁵₂: mp 62°C (Lit. 63°C); $\delta_{\rm H}$ 3.87 (s, 2H), 6.42–7.10 (m, 3H); $\nu_{\rm max}/{\rm cm}^{-1}$ 3430, 3300, 3200, 1620, 1580, 1470, 1400, 850, 810, 700, 640.

 $C_6H_5CONH_2^{15}$: mp 128°C (Lit. 130°C); δ_H 5.69 (s, 2H), 7.20–7.90 (m, 5H); v_{max}/cm^{-1} 3380, 3210, 1670, 1610, 1580, 1400, 650.

m-CH₃C₆H₄CONH₂¹⁵: mp 93–94°C (Lit. 94–95°C); $\delta_{\rm H}$ 2.30 (s, 3H), 6.50 (s, 2H), 7.28–7.64 (m, 4H); $v_{\rm max}/{\rm cm}^{-1}$ 3400, 3210, 1650, 1620, 1590, 1400, 750, 690, 630.

 $C_6H_5SO_2NH_2^{15}$: mp 151°C (Lit. 152–154°C); δ_H 3.30 (s, 2H), 7.30–7.95 (m, 5H); v_{max}/cm^{-1} 3310, 3240, 1550, 1450, 1320, 1300, 1160, 1100, 990, 890, 760, 680.

 $p\text{-}\mathrm{CH_3C_6H_4SO_2NH_2^{15}:}$ mp 156°C (Lit. 157°C); δ_H 2.33 (s, 3H), 3.20 (s, 2H), 7.20–7.80 (m, 4H); $v_{max}/\mathrm{cm^{-1}}$ 3320, 3240, 3020, 2920, 1600, 1480, 1400, 1310, 1170, 1090, 910, 800, 680.

 $\begin{array}{l} NH_2CH_2COOCH_3^9: \ Oil; \ \delta_H \ 2.25 \ (s, \ 2H), \ 3.35 \ (s, \ 2H) \ 3.86 \ (s, \ 3H); \\ \nu_{max}/cm^{-1} \ 3450, \ 3380, \ 2970, \ 2870, \ 1750, \ 1370, \ 1350, \ 1300, \ 1200, \ 1090, \ 1020. \end{array}$

 $C_6H_5CH = CHCONH_2^{16b}$: mp 147°C (Lit. 148–150°C); δ_H 6.39 (d, 1H), 7.10–7.50 (m, 5H), 8.00 (d, 1H); v_{max}/cm^{-1} 3360, 3180, 1670, 1600, 1490, 1400, 1250, 1120, 970, 870, 700.

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REFERENCES

- Sheradsky, T. *The Chemistry of the Azido Group*, Patai, S., Ed., Chapter 6, Interscience Publishers: New York, 1971.
- 2. Scriven, E.F.V., Ed. Azides and Nitrenes, Reactivity and Utility, Academic Press, Inc.: New York, 1984.
- 3. Ranu, B.C.; Sarkar, A.; Chakraborty, R. J. Org. Chem. 1994, 59, 4114.
- 4. Boyer, J.H. J. Am. Chem. Soc. 1951, 73, 5865.
- Mungall, W.S.; Green, G.L.; Heavner, G.A.; Letsinger, R.L. J. Org. Chem. 1975, 40, 1659.

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-------	--	----------

AZIDE REDUCTION TO CORRESPONDING AMINES

- (a) Smith, P.A.S.; Hall, J.H.; Kan, R.O. J. Am. Chem. Soc. 1962, 84, 485. (b) Gastiser, T.; Selve, C.; Delpucch, J.J. Tetrahedron Lett. 1983, 24, 1609.
- 7. Alverez, S.G.; Fisher, G.B.; Singavam, B. Tetrahedron Lett. **1995**, *36*, 2567.
- Ramesha, A.R.; Bhat, S.; Chandresekan, S. J. Org. Chem. 1995, 60, 7682.
- 9. Huang, Y.; Zhang, Y.; Wang, Y. Tetrahedron Lett. 1997, 38, 1065.
- 10. Huang, Y.; Zhang, Y. Synth. Commun. 1996, 26, 2911.
- Souppe, J.; Danon, L.; Namy, J.L.; Kagan, H.B. J. Organomet. Chem. 1983, 250, 227.
- 12. Banik, B.K.; Becker, F.F. Tetrahedron Lett. 1998, 39, 7243.
- 13. Huang, Y.; Liao, P.; Zhang, Y. Synth. Commun. 1997, 27, 1059.
- 14. Sandler, S.R.; Karo, W. *Organic Functional Group Preparations*, Vol. 1, P266, Academic Press: London, 1971.
- 15. (a) Aldrich, **1996–1997**; (b) Harris, G., et al. *Dictionary of Organic Compounds*, Fourth Completely Revised, Vol. 1–5, Eyre and Spottiswoode (Publishers) Ltd.: London.
- 16. (a) Beil. 12, 687, (b) Beils, 9, 587.

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