Chinese Chemical Letters Vol. 12, No. 8, pp 659 – 662, 2001

Chemoselective Reduction of Azides to Amines Using Sm/TMSCl System in the Presence of Trace Amounts of Water

Jin Chang DING*, Hua Yue WU

Department of Chemistry, Wenzhou Normal College, Wenzhou 325027

Abstract: Azides can be easily reduced to the corresponding amines with Sm/TMSCl/H_2O (trace) system in excellent yields under mild and neutral conditions.

Keywords: Azides, amines, Sm/TMSCl/H_2O (trace) system.

Samarium diiodide and organosamarium compounds have been widely employed as useful reagents in organic synthesis[1]. However, relatively few reports on the direct use of samarium metal in organic synthesis have been reported[2], because the surface of samarium metal is inactive[3]. In order to improve the activity of samarium, some additives, such as $HgCl_2$[4], NH_4Cl (aq.)[5], or TMSCl[6] were added.

The reduction of azides to the corresponding amines is an important reaction in organic synthesis[7-16]. A wide variety of reductants have been used, such as zinc borohydride[9], lithium aluminium hydride[10], triethyl phosphate[11], sodium borohydride[12], lithium aminoborohydide[13], benzyltriethylammonium tetrathiomolybdate[14], Sm/cat.I_2[15], SmI_2 and Cp_2TiCl_2-Sm system[16], *etc*. However, these reagents have one or more limitations with regard to general applicability, selectivity, ready availability, operational convenience and toxicity. As a result, there is always considerable interest in finding more selective methods.

Herein we wish to report a novel reduction of azides to the corresponding amines using Sm/TMSCl system in the presence of trace amounts of water. The reaction condition is mild and the yields are high (**Scheme**).

Scheme

$$\text{R-N}_3 \xrightarrow[\text{THF, r. t.}]{\text{Sm/TMSCl/H}_2\text{O (trace)}} \text{R-NH}_2$$

The results of reduction of azides to amines using Sm/TMSCl/H_2O (trace) system are summarized in the **Table**. We found that a number of alkyl, aryl, aroyl and arylsulfonyl azides could be easily reduced to the corresponding products. In all of the reactions, the N-N bonds were cleaved rather than the C-N or S-N bonds. At the 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. Substituents such as chloro, bromo, iodo, carbonyl and sulfonyl groups can not be reduced under the reaction conditions and do not influence the rate of reduction. Furthermore, α,β-unsaturated acyl azides are selectively reduced without affecting the double bond. Interestingly, addition of trace amounts of water not only accelerates the rate of the reduction, but also increases the yields of products.

Table Reduction of azides to amines with Sm/TMSCl/H_2O (trace) system

Entry	Azides	Reaction times (T)	Yields (%)[a]
1	$C_6H_5N_3$	2	92
2	*p*-$ClC_6H_4N_3$	2	88
3	*p*-$BrC_6H_4N_3$	2	86
4	*p*-$IC_6H_4N_3$	2	90
5	*p*-$CH_3C_6H_4N_3$	2	91
6	*n*-$C_7H_{15}N_3$	4	76
7	$C_6H_5CON_3$	2	87
8	$C_6H_5CON_3$	5	80[b]
9	*m*-$CH_3C_6H_4CON_3$	2	84
10	$C_6H_5SO_2N_3$	2	82
11	$N_3CH_2COOCH_3$	2	78
12	$C_6H_5CH{=}CHCON_3$	2	83

[a] Isolated yield. [b] No trace amounts of water was added.

In conclusion, it has been found that Sm/TMSCl/H_2O (trace) system can be used for the chemoselective reduction of azides to the corresponding amines. The notable advantages of this reaction are its simplicity, mild reaction conditions and good yields.

Experimental

The Themometer was uncorrected. ^1H NMR spectra were recorded on a Bruker AC 80 instrument. All NMR samples were measured in $CDCl_3$ 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 methodology[17].

General Procedure

Under nitrogen atmosphere, powdered samarium (180 mg, 1.2 mmol) and azides (1.0 mmol) were placed in a round bottom flask, and then THF (5 mL), TMSCl (1mL) and H_2O (50 μL) were added in one portion. The mixture was stirred at room temperature for the time indicated in the **Table**. 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 layer chromatography on silica gel with dichloromethane-cyclohexane (3:1) as eluent to give a pure product.

$C_6H_5NH_2$[16]: oil; ^1H NMR($CDCl_3$, δ ppm): 3.25 (s, 2H), 6.30-7.10 (m, 5H). IR (CCl_4): 3410, 3350 cm^{-1}.

***p*-$ClC_6H_4NH_2$**: mp 70°C (Lit.[18] 71-73°C); ^1H NMR ($CDCl_3$, δ ppm): 3.40 （s, 2H）, 6.31-7.00 (m, 4H). IR (KBr): 3470, 3400 cm^{-1}.

***p*-$BrC_6H_4NH_2$**: mp 62°C (Lit.[18] 62-64°C); ^1H NMR ($CDCl_3$, δ ppm): 3.41 (s, 2H), 6.24-7.15 (m, 4H). IR (KBr): 3480, 3370 cm^{-1}.

***p*-$IC_6H_4NH_2$**: mp 62°C (Lit.[18] 62-63°C); ^1H NMR ($CDCl_3$, δ ppm): 3.60 (s, 2H), 6.30-7.30 (m, 4H). IR (KBr): 3390,3350 cm^{-1}.

***p*-$CH_3C_6H_4NH_2$**: mp 43°C (Lit.[18] 44°C); ^1H NMR ($CDCl_3$, δ ppm): 2.10 (s, 3H), 3.15 (s, 2H), 6.25-6.80 (m, 4H). IR (KBr): 3460, 3400 cm^{-1}.

***n*-$C_7H_{15}NH_2$**: oil; ^1H NMR ($CDCl_3$, δ ppm): 0.90 (t, 3H), 1.25 (m, 10H), 2.27 (s, 2H). 2.65 (t, 2H). IR (CCl_4): 3400, 3380 cm^{-1}.

$C_6H_5CONH_2$: mp 128°C (Lit.[18] 130°C); ^1H NMR($CDCl_3$, δ ppm): 5.68 (s, 2H), 7.20-7.90 (m, 5H). IR (KBr): 3380, 3210, 1670 cm^{-1}.

***m*-$CH_3C_6H_4CONH_2$**: mp 93-94°C (Lit.[18] 94-95°C); ^1H NMR($CDCl_3$, δ ppm): 2.30 (s, 3H), 6.50 (s, 2H), 7.28-7.64 (m, 4H). IR (KBr): 3400, 3210, 1650 cm^{-1}.

$C_6H_5SO_2NH_2$: mp 151°C (Lit.[18] 152-154°C); ^1H NMR($CDCl_3$, δ ppm): 3.30 (s, 2H), 7.30-7.95 (m, 5H). IR (KBr): 3310, 3240 cm^{-1}.

$NH_2CH_2COOCH_3$[15]: oil; ^1H NMR($CDCl_3$, δ ppm): 2.26 (s, 2H), 3.35 (s, 2H), 3.86 (s, 3H). IR (CCl_4): 3450, 3380, 1750 cm^{-1}.

$C_6H_5CH=CHCONH_2$: mp 147°C (Lit.[19] 148-150°C); ^1H NMR($CDCl_3$, δ ppm): 6.38 (d, 1H), 7.10-7.50 (m, 5H), 8.00 (d, 1H). IR (KBr): 3360, 3180, 1670 cm^{-1}.

References

1. (a) H. B. Kagan, J. L. Namy, *Tetrahedron*, **1986**, *42*, 6573.
   (b) G. A. Molander, *Chem. Rev.*, **1992**, *92*, 29.
   (c) G. A. Molander, *Organic Reaction*, **1994**, *46*, 211.
   (d) G. A. Molander, C. R. Harris, *Chem. Rev.*, **1996**, *96*, 307.
2. (a) R. Yanada, N. Negoro, K. Yanada, T. Fujita, *Tetrahedron Lett.*, **1997**, *38*, 3271.
   (b) R. Yanada, N. Negoro, K. Yanada, T. Fujita, *Tetrahedron Lett.*, **1996**, *37*, 9313.
   (c) M. Lautens, P.H. Delanghe, *J. Org. Chem.*, **1995**, *60*, 2474.
3. Z. Hou, K. Takamine, Y. Fujiwara, *Chem. Lett.*, **1987**, 305.
4. (a) G. A. Molander, L. S, Harring, *J. Org. Chem.*, **1989**, *54*, 3525.
   (b) D. L. J. Clive, S. Daigneault, *J. Org. Chem.*, **1991**, *56*, 3801.
5. L. Wang, Y. Zhang, *Tetrahedon Lett.*, **1998**, *39*, 5257.
6. (a) L. Wang, Y. Zhang, *Tetrahedron*, **1998**, *54*, 11129.
   (b) M. Lautens, Y. Ren, *J. Org. Chem.*, **1996**, *61*, 2210.
7. T. Sheradsky, *The Chemistry of the Azides Group*. Patai, S., Ed., Interscience Publishers, New York, **1971**, Chap. 6.
8. E. F. V. Scriven, Ed. *Azides and Nitrenes, Reactivity and Utility*. Academic Press, Inc., New York, **1984**.
9. B. C. Ranu, A. Sarkar, R. Chakaraborty, *J. Org. Chem.*, **1994**, *59*, 4114.
10. J. H. Boyer, *J. Am. Chem. Soc.*, **1951**, *73*, 5863.
11. W. S. Mungall, G. L. Green, G. A. Heavner, R. L. Letsinger, *J. Org. Chem.*, **1975**, *40*, 1659.
12. (a) P. A. S. Smith, J. H. Hall, R. O. Kan, *J. Am. Chem. Soc.*, **1962**, *84*, 485.
    (b) T. Gastiser, C. Selve, J. J. Delpucch, Tetrahedron Lett., **1983**, *24*, 1609.
13. S. G. Alverez, G.B. Fisher, B. Singavam, *Tetrahedron Lett.*, **1995**, *36*, 2567.

14. A. R. Ramesha, S. Bhat, S. Chandresekan, *J. Org. Chem.*, **1995**, *60*, 7682.
15. Y. Huang, Y. Zhang, Y. Wang, *Tetrahedron Lett.*, **1997**, *38*, 1065.
16. Y. Huang, Y. Zhang, *Synth. Commun.*, **1996**, *26*, 2911.
17. S. R. Sandler, W. Karo, *Orgnic Functional Group Preparations, Vol. II*. Academic Press, London, **1971**, p.266.
18. (a) Aldrich **1996-1997**;
    (b) G. Harris, *et al*., *Dictionary of Organic Compounds, Fourth Completely Revised*, *Vol. 1-5*. London, Eyre and Spottiswoode Ltd.
19. *Beilsteins Handbuckh de Oganishen Chemie*, **H9**, 587.

Received 1 February, 2001