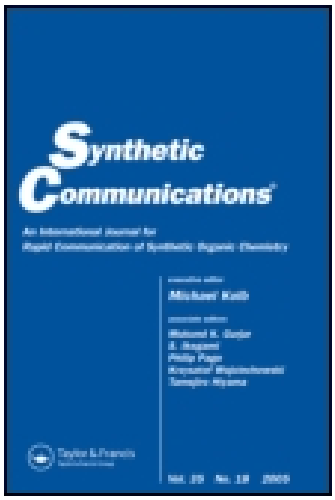

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Huayue Wu , Rener Chen [a] & Yongmin Zhang [b]

[a] Department of Chemistry , Zhejiang University at Xixi Campus, Hangzhou, 310028, P. R. China

[b] Department of Chemistry , Zhejiang University at Xixi Campus, Hangzhou, 310028, P. R. China

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A FACILE REDUCTION OF AZIDES TO THE CORRESPONDING AMINES WITH $Sm/NiCl_2 \cdot 6H_2O$ SYSTEM

Huayue Wu,* Rener Chen, and Yongmin Zhang†

Department of Chemistry, Zhejiang University at Xixi Campus, Hangzhou, 310028, P. R. China

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. I_2,[9] SmI_2 and Cp_2TiCl_2-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, $LiAlH_4$ is not tolerable to many functionalities

*Visiting scholar from Wenzhou Normal College.
†Corresponding author.

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.

$$R - N_3 \xrightarrow[THF,\ 40^\circ C]{Sm/NiCl_2 \cdot 6H_2O} R - NH_2$$

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

Table 1. Reduction of Azides to Amines with $Sm/NiCl_2 \cdot 6H_2O$

Entry	Azides	Reduction Time (h)	Yield* (%)
1	*p*-$ClC_6H_4N_3$	2.5	85
2	*p*-$BrC_6H_4N_3$	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	$C_6H_5CON_3$	2.5	85
10	*m*-$CH_3C_6H_4CON_3$	2.5	83
11	$C_6H_5SO_2N_3$	2.5	85
12	*p*-$CH_3C_6H_4SO_2N_3$	2.5	87
13	$N_3CH_2COOCH_3$	3	76
14	$C_6H_5CH{=}CHCON_3$	3	75

*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. I_2,[12] and Cp_2TiCl_2/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

^{1}H NMR spectra were recorded on a Brucker 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 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-$ClC_6H_4NH_2$[15]: mp 70°C (Lit. 71–73°C); δ_H 3.40 (s, 2H), 6.30–7.00 (m, 4H); ν_{max}/cm^{-1} 3470, 3400, 1600, 1500, 1290, 830, 640.

p-$BrC_6H_4NH_2$[15]: mp 61°C (Lit. 62–64°C); δ_H 3.40 (s, 2H), 6.25–7.15 (m, 4H); ν_{max}/cm^{-1} 3480, 3370, 1610, 1500, 1280, 810, 620.

p-$IC_6H_4NH_2$[15]: mp 62°C (Lit. 62–63°C); δ_H 3.60 (s, 2H), 6.30–7.30 (m, 4H); ν_{max}/cm^{-1} 3390, 3350, 3200, 3050, 1620, 1600, 1480, 1280, 1180, 940, 810, 590.

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.

$C_7H_{15}NH_2$[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-$NO_2C_6H_4NH_2$[15a]: mp 71°C (Lit. 71–72°C); δ_H 6.25 (s, 2H), 6.67–8.08 (m, 4H); ν_{max}/cm^{-1} 3470, 3320, 1630, 1570, 1500, 1430, 1350, 1250, 1100, 750.

2,4-$Cl_2C_6H_3NH_2$[15]: mp 62°C (Lit. 63°C); δ_H 3.87 (s, 2H), 6.42–7.10 (m, 3H); ν_{max}/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); ν_{max}/cm^{-1} 3380, 3210, 1670, 1610, 1580, 1400, 650.

m-$CH_3C_6H_4CONH_2$[15]: mp 93–94°C (Lit. 94–95°C); δ_H 2.30 (s, 3H), 6.50 (s, 2H), 7.28–7.64 (m, 4H); ν_{max}/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); ν_{max}/cm^{-1} 3310, 3240, 1550, 1450, 1320, 1300, 1160, 1100, 990, 890, 760, 680.

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

$NH_2CH_2COOCH_3$[9]: Oil; δ_H 2.25 (s, 2H), 3.35 (s, 2H) 3.86 (s, 3H); ν_{max}/cm^{-1} 3450, 3380, 2970, 2870, 1750, 1370, 1350, 1300, 1200, 1090, 1020.

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

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