SHORT PAPER

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A novel method for the chemoselective reduction of azides to amines with a Sm/CoCl$_2$ • 6H$_2$O system[†]

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Azides can be easily reduced to the corresponding amines with Sm/CoC1$_2$ • 6H$_2$O in excellent yields under mild and neutral conditions.

We and others have shown that the reduction of azides to corresponding amines is an important reaction in organic synthesis.[1–10] 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] Sm/cat. I$_2$[9], SmI$_2$ and a Cp$_2$TiC1$_2$-Sm system.[10] However, these reagents have one or more limitations with regard to general applicability, selectivity, ready availability, operational convenience, and toxicity. For instance, LiAlH$_4$ does not tolerate many functionalities such as CO$_2$R, NO$_2$ *etc*., and on the other hand, catalytic hydrogenation and diborane reduction have limitations for being applied to unsaturated compounds containing double or triple bonds. 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-cobalt chloride hexahydrate in high yield in tetrahydrofuran under mild and neutral conditions.

$$R - N_3 \xrightarrow[\text{THF, r.t.}]{\text{Sm/CoC1}_2 \bullet 6\text{H}_2\text{0}} R - NH_2$$

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 without the double bond reacting (entry 13), and the corresponding nitroaniline was selectively obtained without any further reduction of the nitro group (entry 7). Nitroarenes can be reduced to the corresponding amines with SmI$_2$[11], Sm.cat.I$_2$[12] and Cp$_2$TiCl$_2$/Sm.[13]

In conclusion, it has been found that the Sm/CoC1$_2$ · 6H$_2$O system can be used for the reduction of azides to amines. The advantages of this reaction are good yields, excellent chemoselectivity, a simple procedure and mild and neutral reaction conditions.

Table 1 Reduction of azides to amines with Sm/CoC1$_2$ • 6H$_2$O

Entry	Azides	Reaction time (min)	Yield (%)[a]
1	p-$ClC_6H_4N_3$	45	87
2	p-$BrC_6H_4N_3$	45	85
3	p-$IC_6H_4N_3$	45	88
4	p-$CH_3C_6H_4N_3$	45	90
5	$C_6H_5N_3$	45	92
6	n-$C_7H_{15}N_3$	60	71
7	o-$NO_2C_6H_4N_3$	60	90
8	$C_6H_5CON_3$	45	84
9	$C_6H_5CON_3$	60	87[b]
10	m-$CH_3C_6H_4CON_3$	45	84
11	$C_6H_5SO_2N_3$	45	83
12	$N_3CH_2COOCH_3$	60	79
13	$C_6H_5CH{=}CHCON^3$	60	81

[a] Isolated yield.

[b] The reaction was carried out on ten times scale.

Experimental

^{1}H spectra were recorded on a Bruker AC 80 instrument. All NMR samples were measured in CDC1$_3$ 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.[14]

General procedure: Under a nitrogen atmosphere, metallic samarium powder (4.0 mmol) and cobalt chloride hexahydrate (4.0 mmol) were placed in three-necked reaction flask and THF (10 ml) was added in one portion. The azides (1.3 mmol) was then added to the mixture and stirred at 40°C for a given time (Table 1). A satd. aq. Na$_2$S$_2$O$_3$ 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$_2$SO$_4$. The solvent was removed in vacuo. The residue was then purified by preparative plate chromatography on silica gel with dichloromethane-cyclohexane (3:1) as eluent to give a pure product.

p-ClC$_6$H$_4$NH$_2$;[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$_6$H$_4$NH$_2$[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$_6$H$_4$NH$_2$[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$_3$C$_6$H$_4$NH$_2$;[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$_6$H$_5$NH$_2$[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.

n-C$_7$H$_{15}$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.

o-NO$_2$C$_6$H$_4$NH$_2$[16a]; 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.

C$_6$H$_5$CONH$_2$[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.

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

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.

$NH_2CH_2COOCH_3$[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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