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Efficient Reduction of Azides with Samarium diiodide

Catherine Goulaouic-Dubois and Manfred Hesse*

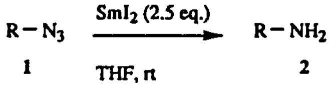
Organisch-chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich

Abstract: Reduction of alkyl, aryl and aroyl azides to the parent primary amines or amides, respectively, occurs in good yield upon treatment with an excess of SmI_2 in THF at room temperature. A radical mechanism is proposed.

The reduction of azides to amines is an important transformation in synthetic organic chemistry to introduce an amino group.[1] A wide variety of reducing agents (e.g., $LiAlH_4$,[1] H_2/Lindlar catalyst,[2] Cr^{II}/H^+,[3] Zn/HCl,[3] PPh_3/H_2O,[4] H_2S/pyridine,[5] Bu_3SnH/AIBN,[6] $NaBH_4$/phase transfer catalyst,[7] Mg or Ca/MeOH[8]) have been reported for this conversion 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.[9-12]

Although SmI_2[13] reduces various nitrogen functionality (nitro group,[14,15] imines,[14a] oximes,[14a] hydrazones[14a,16] and isoxazoles[17]), there are, to our knowledge, no literature examples for the reduction of azido group with this reagent.

In this report, we describe the efficient reduction of alkyl, aryl and aroyl azides upon treatment with SmI_2 in THF, at room temperature, to the corresponding primary amines and amides (Scheme 1).



$$\underset{1}{R-N_3} \xrightarrow[\text{THF, rt}]{SmI_2\text{ (2.5 eq.)}} \underset{2}{R-NH_2}$$

R = alkyl, aryl and aroyl

Scheme 1.

Our work concerning the reduction of several organic azides using SmI_2 is summarised in Table 1. The high yields of the reduction products demonstrate the efficiency of this new method. Azides are selectively reduced in the presence of a double bond (entry 8), an aromatic chloro group (entries 6 and 10) or an aromatic methoxy group (entries 7 and 11). Reduction of aryl and aroyl azides containing electron donating (4-OMe, entries 7 and 11) or electron withdrawing groups (4-Cl, entries 6 and 10) indicates that electronic environment in *para* position of the aryl group does not influence the rate of reduction. Even the less reactive heptyl and decyl azides were reduced within 1 h.

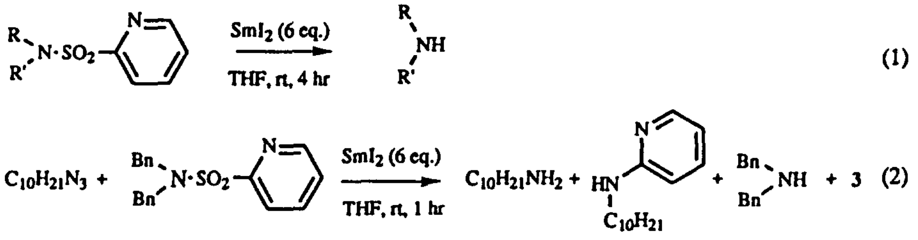
Table 1. Reduction of RN_3 (**1**) to Amines or Amides (**2**) with Samarium diiodide.

Entry	Azide	R	Reaction time (min)	Isolated yield[a] (2) (%)
1	**1a**	$C_{10}H_{21}$	60	85
2	**1b**	C_7H_{15}	60	90
3	**1c**	C_6H_{11}	30	88
4	**1d**	$C_6H_5CH_2$	20	90
5	**1e**	C_6H_5	10	90
6	**1f**	pClC$_6$H$_4$	10	88
7	**1g**	pCH$_3$OC$_6$H$_4$	10	84
8	**1h**	$C_6H_5CH{=}CHCH_2$	60	93[b]
9	**1i**	C_6H_5CO	10	79
10	**1k**	pClC$_6$H$_4$CO	10	75
11	**1l**	pCH$_3$OC$_6$H$_4$CO	10	82

a) The reactions were performed using 2.5 equiv. of SmI_2 (except entry 8). b) 5 equiv. of SmI_2 were required.

By analogy to the known radical reduction of azides using Bu_3SnH/AIBN,[6] the mechanism in case of SmI_2 probably involves an one-electron transfer to the azido group which lead to an aminyl radical by the loss of N_2. The presence of such a transient radical species has already been evocated.[18]

We recently described the SmI_2 induced deprotection of pyridine-2-sulfonamide (Scheme 2, equation 1).[19]



1a **3** **2a** **5** **4**

2a/**5** = 52:48 **3**/**4** = 59:41

2a+**5**/**1a** = 100:0

Ratios were determined from isolated yield of each compound.

Scheme 2.

In the course of our work concerning the synthesis of polyamines, we tried to investigate the selectivity between the cleavage of a pyridine-2-sulfonyl group and the reduction of an azido group. An equimolar mixture of decylazide **1a** and *N,N*-dibenzyl-pyridine-2-sulfonamide **3**[19] was treated with 6 eq. of SmI_2 at room temperature (Scheme 2, equation 2). This reaction yielded 47% of decylamine **2a** and 43% of decyl-pyridine-2-yl-amine **5**[20] (based on initial amount of **1a**). This unexpected product could arise from a coupling between an aminyl radical and the compound **3**. We cannot conclude definitely whether the crucial nitrogen-carbon bond forming step in this reaction resulted from the coupling of compound **3** with an aminyl radical or an amidosamarium species. The reaction was quenched after total consumption of the azide **1a** whereby half of the starting sulfonamide **3** was recovered unchanged. This competitive process clearly illustrates that reduction of the azide **1a** occurs faster than deprotection of the sulfonamide **3**.

In conclusion, we have demonstrated that SmI_2 is an efficient alternative method for the reduction of alkyl, aryl and aroyl azides to the corresponding primary amines and amides in the presence of other sensitive functional groups.

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20. 5: ^{1}H NMR ($CDCl_3$) δ 0.90 (*t*, *J*= 6.5 Hz, 3 H), 1.26-1.42 (*m*, 14 H), 1.62 (*p*, *J*=6.5 Hz, 2 H), 3.25 (*q*, *J*=6.5 Hz, 2 H), 4.52 (b*s*, 1 H), 6.37 (*d*, *J*=8.4 Hz, 1 H), 6.53-6.58 (*m*, 1 H), 7.39-7.42 (*m*, 1 H), 8.06-8.10 (*m*, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.97, 22.55, 26.95, 29.18, 29.27, 29.44, 31.77, 42.22, 106.22, 112.44, 137.43, 147.81, 158.83; CI-MS m/z 234 $(M+H)^+$.
21. *General procedure of the reduction of azides with SmI_2.* A typical experimental procedure for reducing azide is described below. To a 0.1 M solution of SmI_2 in THF[22] (25 mL; 2.5 mmol) was added dropwise a well-degassed solution of benzyl azide (133 mg; 1 mmol) in THF, under argon, at room temperature. After stirring for 20 min, the reaction mixture was quenched with a cold saturated solution of K_2CO_3. The aqueous layer was extracted three times with 50 mL of chloroform and the combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography purification (silica gel, chloroform:methanol:ammonia water 25% 90:10:0.5) gave benzylamine identified by comparison with authentic sample (IR, ^{1}H NMR) in 90% yield (96 mg).
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