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A procedure for the conversion of azides to amines, which uses NaBH₄ and catalytic amounts of tin(IV) 1,2-benzenedithiolate, is disclosed. Primary, secondary, tertiary, aromatic, and heteroaromatic azides are reduced in excellent yields under very mild conditions.

Years ago we reported on new tin(II) complexes of the general formula [Et₃NH][Sn(SR)₃],³ which reduce azides and nitro compounds but not carbonyl groups. Azides, even the most hindered ones, react completely within a few minutes at room temperature in a plethora of solvents, to afford amines in practically quantitative yields. These tin reagents can be readily obtained (i) by adding RSH and Et₃N to insoluble, polymeric Sn(SR)₂,³a,b (ii) by mixing SnCl₂, RSH, and Et₃N in a 1:3:3 ratio,³c and (iii) by treating phosphites with RN₃.⁴


phines with tin(IV) thiolates, i.e., by the reaction $R_3P + Sn\ \text{(SR)}_3 \to R_3P\cdot\text{SR} + Sn\ \text{(SR)}_2$ [4]. This finding came from a simple starting idea: that the ability to transfer electrons of anionic species such as $Sn\text{(SR)}_2^-$ (in general, of species $SnX_2^-$ or $SnX_2^2-$) had to be much greater than that of neutral molecules or salts such as $Sn\text{(SR)}_3$ and $SnX_2$. Most of these tin(II)—thiolate complexes have turned out to be the fastest reducing agents for azides reported so far.\textsuperscript{3,4,5}

We report now on an improvement based on the use of a catalytic amount of tin(IV) bis(1,2-benzenedithiolate), henceforward $Sn\text{(BDT)}_2$ or 1, and a common reducing agent, instead of a stoichiometric amount or an excess of tin(II)—thiolate complexes. It should significantly decrease the amount of tin waste, which is of great value with respect to environmental and practical concerns.

Compound 1 is a red solid,\textsuperscript{6} insoluble in most solvents but soluble in the presence of Lewis bases, i.e., by coordination with donor ligands.\textsuperscript{7} It has been easily prepared by mixing $SnCl_2\cdot5H_2O$ and 1,2-benzenedithiol in water, in a 1:2 ratio;\textsuperscript{8} this dithiol is commercially available but it was also prepared in our laboratory\textsuperscript{9} in large amounts from thiophenol, according to the procedure of Block et al.\textsuperscript{8} When a suspension of 1 in THF at room temperature is treated with an equimolar amount of NaBH\textsubscript{4} in H\textsubscript{2}O or MeOH, yellow solutions are formed that show a strong reducing power against azides: benzyl azide is converted to benzylamine in few minutes. In the absence of 1, under the same conditions, benzyl azide is not reduced by NaBH\textsubscript{4}, M\textsubscript{e}2S\textsubscript{4} solutions are formed that show a strong reducing power. See: Urpí, F.; Vilarrasa, J. Tetrahedron Lett. 1990, 31, 7407.

The active species involved in the above-mentioned reduction of benzyl azide with equimolar amounts of 1 and NaBH\textsubscript{4} should arise from the cleavage of one of the $Sn-S$ bonds of 1 by the reducing agent (transfer of hydride from borohydride ion). It may be a tin(II)—thiolate complex such as 2 or the corresponding dianion, depending on the amount of borohydride ions added and/or the medium basicity.

Going further, the strong reducing power of the active species and the compatibility of borohydride ion with some protic solvents prompted us to carry out the azide reductions in a catalytic mode. In practice, the reduction of benzyl azide with 1–20 mol % of 1 appeared to be rather efficient even in the first trial experiments. A plausible mechanism is summarized in Scheme 1, where it is shown that reaction intermediate 3 requires a proton source to give the amine and regenerate the catalyst (1), which is converted again to the active species (turnover).

The reactions were carried out on 1 mmol of azide in THF at ca. 15 °C, in the presence of 1 (5 or 10 mol %), by adding 0.67, 1.0, or 1.5 mmol of NaBH\textsubscript{4} in buffered cold water.\textsuperscript{10} The procedure was applied to a variety of azides, as shown in Table 1. Conversions of azides to the corresponding amines\textsuperscript{11} were generally quantitative. It is worth noting the following.

(i) At pH 10 (entry 1), reduction of benzyl azide took place within 30 min, even when only 0.05 mmol of 1 and 0.67 mmol of NaBH\textsubscript{4} per millimole of azide were utilized.

(ii) At pH 7 (entry 3), the reduction was slower. An excess of NaBH\textsubscript{4} (1.5 mmol/mmol of azide) was necessary to compensate for the loss of borohydride ions by reaction with

\textsuperscript{(4)} The $R_3P/\text{Sn(SR)}_3$ combination shows, as expected, both dehydrating and reducing power. See: Urpi, F.; Vilarrasa, J. Tetrahedron Lett. 1990, 31, 7407.

\textsuperscript{(5)} These methods were developed in connection with a project on the direct macroalactamization of carbonyl-activated o-azido acids, by reduction of the azido group and cyclization in situ, as we needed chemo- or stereoselective and strong enough for carrying out quickly the azido group and cyclization in situ, as we needed reagents for the direct macroalactamization of carbonyl-activated o-azido acids, by reduction of the azido group and cyclization in situ, as we needed reagents.

\textsuperscript{(6)} Brown, H. P.; Austin, J. A. Am. Chem. Soc. 1940, 62, 673. Further data for $Sn\text{(BDT)}_2$ (I): darkens at 294–296 °C; $\delta$ H NMR (DMSO-$d_6$, 200 MHz) $\delta$ 6.82 (m, 2 H, AA’), 7.37 (m, 2 H, XX’).


\textsuperscript{(9)} These reagents convert the most reactive azides to amines on heating and/or when they are used in large excesses for many hours. The only related system we have found that works efficiently, without tin and without heating, is a mixture of 1,2-benzenedithiol (1.5 equiv) and $Me_2S\cdotBH_3$ (1.5 equiv) in THF at room temperature benzyl azide is reduced in 5 h.
the protons of the medium. Nevertheless, in such a case, with 10 mol % of catalyst, disappearance of the azide was complete in ca. 60 min (see entry 3 of Table 1). In other words, even though the reduction is faster at pH 10,12 for substrates prone to hydrolysis or sensitive to basic media there is the possibility of operating at neutral pH.

(iii) A secondary azide, 1-phenylethyl azide (entry 5), and tertiary azides (entries 9 and 10) seem to react only slightly slower than primary azides. The aromatic (entry 6) and heteroaromatic azides (entries 7 and 8) checked in this work react rapidly. It is probable that more hindered azides and aromatic azides with strong electron-donating substituents react slowly, perhaps too slowly, under the conditions of Table 1, but in such cases larger amounts of 1 and NaBH₄ could be employed.

(iv) At the end, the catalyst (1) can be recovered from the aqueous solution by acidification and filtering off the red solid that precipitates; it is reusable.

In summary, the catalytic process disclosed here, clearly amenable to a larger scale, allows one to convert azides into amines in practically quantitative yields. Obviously, to transform R−NNN to R−NH₂ and N₂, two hydrogens are always needed, which may come from H₂ (catalytic hydrogenation) or from H⁺/H₂O (reduction followed by protonation). As our initial objective was the development of a new, mild procedure within the second alternative, in one pot, with all the reagents inside, the reducing agent had to be quite compatible with the proton source (protic solvent). Thus, borohydride ion was a reasonable choice, but it is not sufficiently active against azides. Use of 1 as a catalyst has solved the problem.

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(12) At pH 9 and pH 8, with 5 mol % of catalyst and 1 mmol of NaBH₄ per millimole of benzyl azide, the complete disappearance of the azide required ca. 60 min (data not included in Table 1).

Table 1. Reduction of Azides to Amines in THF−H₂O at ca. 15 °C, with NaBH₄ and 1

<table>
<thead>
<tr>
<th>Entry</th>
<th>Azide</th>
<th>1 mol%</th>
<th>NaBH₄ molar ratio</th>
<th>pH</th>
<th>Time, min</th>
<th>Amine, yield (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>PhN₃</td>
<td>5</td>
<td>0.67</td>
<td>10</td>
<td>30</td>
<td>97</td>
</tr>
<tr>
<td>2</td>
<td>PhN₃</td>
<td>5</td>
<td>1.0</td>
<td>10</td>
<td>30</td>
<td>100⁴</td>
</tr>
<tr>
<td>3</td>
<td>PhN₃</td>
<td>10</td>
<td>1.5</td>
<td>7</td>
<td>60</td>
<td>95</td>
</tr>
<tr>
<td>4</td>
<td>(CH₂)₂N₃</td>
<td>10</td>
<td>1.0</td>
<td>10</td>
<td>45</td>
<td>94</td>
</tr>
<tr>
<td>5</td>
<td>PhN₃</td>
<td>5</td>
<td>1.0</td>
<td>10</td>
<td>40</td>
<td>95</td>
</tr>
<tr>
<td>6</td>
<td>MeO₂C−N₃</td>
<td>10</td>
<td>1.0</td>
<td>10</td>
<td>15</td>
<td>100</td>
</tr>
<tr>
<td>7</td>
<td>N₂N₃</td>
<td>10</td>
<td>1.0</td>
<td>10</td>
<td>30</td>
<td>100</td>
</tr>
<tr>
<td>8</td>
<td>N₂N₃</td>
<td>5</td>
<td>0.67</td>
<td>10</td>
<td>40</td>
<td>100</td>
</tr>
<tr>
<td>9</td>
<td>OCO−N₃</td>
<td>10</td>
<td>1.0</td>
<td>10</td>
<td>60</td>
<td>96</td>
</tr>
<tr>
<td>10</td>
<td>OH−N₃</td>
<td>5</td>
<td>1.0</td>
<td>10</td>
<td>30</td>
<td>96⁴</td>
</tr>
</tbody>
</table>

⁴ This reaction was repeated in THF−MeOH with the same result, although larger amounts of NaBH₄ were required. ⁵ This product is somewhat volatile; removal of the solvent (ref 10) should be performed carefully.