An efficient chemoselective production of amines from azides using AlCl₃/NaBH₄†

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A practical reagent system AlCl₃/NaBH₄ is used for the preparation of amines from azides under mild reaction condition, in excellent yields.

Modified borohydrides¹ are among the most important reducing agents in organic chemistry. A combination of NaBH₄ with several parameters¹, such as variation of metal chloride, solvent and temperature to improve its reactivity for various functional group transformations is reported. The reaction is of wide applicability and has been effected with variety of reagents. Some of them include LiAlH₄¹, zinc borohydride³, samarium iodide⁴, (BER)-nickel acetate⁵, benzyl triethylammoniumtetrathiomolybdate, ⁶Zn-NiCl₂·6H₂O·HF⁷, Zn(BH₄)₂(dabco)⁸-¹⁰, and MePh₃⁺BH₄⁻, etc. Most of the available reagents reported have some disadvantages in relation to their general applicability, selectivity and longer reaction time³. As part of our ongoing study⁹ in exploring the potential utility of modified borohydrides,

It was found that a combination of AlCl₃/NaBH₄ can efficiently reduce various azides to amine in excellent yields (Scheme 1). This is reported, in the present communication. This reagent system has an advantage of chemoselectivity, and affecting the reduction azides to amines more rapidly than the earlier method¹⁰.

The generality of the reaction is summarized in Table I. In all the reactions conducted, the AlCl₃/NaBH₄ reagent system efficiently furnished amines in good to excellent yields, (85-92%) at 35°C. Aliphatic azides required longer reaction time (2 hr), whereas aromatic azides furnished the corresponding amines in 30-45 minutes duration. The distinct advantage of this reagent system lies in its chemoselectivity towards azide function in presence of nitro (entry-4) and carboxylic acid groups (entry-5).

In conclusion, AlCl₃/NaBH₄ reagent system provides a chemoselective and efficient production of amines from azides in presence of nitro and carboxylic groups.

Experimental Section

Typical experimental procedure. Into a two necked round bottom flask equipped with magnetic bead and nitrogen balloon adapter was placed AlCl₃ (1eq), dry THF (25mL) was syringed into the flask. The contents were cooled to 0°C, NaBH₄ (3 eq) was added in portionwise to the above solution. To the reagent system at 0°C was added a solution of azide (1eq) in THF. After complete addition, ice cooling was removed and contents were brought to room temperature (35°C). The progress of the reaction was monitored by TLC, which indicated the disappearance of the azide in 30-45 minutes period. Contents were cooled to 0°C and quenched by dropwise addition of 5% aq. HCl solution. From the reaction mixture THF was evaporated in vacuo and remaining aqueous layer was extracted with ethyl acetate. The organic fractions were combined, washed successively with brine, water and dried over anhydrous Na₂SO₄. Evaporation of the solvent followed by purification of crude product by column chromatography on silica gel gave the corresponding amines (isolated yields 80-92%). All products thus obtained were characterized by IR, ¹H NMR, and mass spectral data and comparing with authentic samples.

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Note

![Scheme 1](image-url)

R⁻N₃ + AlCl₃/NaBH₄ → R⁻NH₂

THF, 0°C to 35°C

Table I

<table>
<thead>
<tr>
<th>R⁻N₃</th>
<th>Product</th>
<th>Yield (%)</th>
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<tr>
<td>Aliphatic</td>
<td>Azide</td>
<td>85-92</td>
</tr>
<tr>
<td>Aromatic</td>
<td>Azide</td>
<td>85-92</td>
</tr>
</tbody>
</table>

Scheme 1
Table 1—Production of amines from azides using AlCl₃/NaBH₄

<table>
<thead>
<tr>
<th>Entry</th>
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<td>8</td>
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<td>85%</td>
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</table>

*a All reactions were completed in 30 to 45 min period, at 35°C stirring
*b Yields (%) refer to unoptimised, isolated and chromatographically pure products
*c Reaction completed in 2 hr period.

Acknowledgement

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References
(b) Brown H C & Krishnamurthy S, Tetrahedron, 35, 1979, 567.