

## Selective Conversion of Aromatic Nitriles to Aldehydes by Lithium *N,N'*-Dimethylethylenediaminoaluminum Hydride

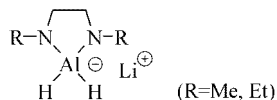
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The conversion of nitriles into aldehydes is one of the most important tools in organic synthesis. A large number of methods have been proposed to achieve such purposes.<sup>1</sup> Among them, two examples, using potassium 9-*sec*-amylboratabicyclo[3.3.1]nonane (K 9-*sec*-Am-9-BBNH)<sup>1-i</sup> and lithium tris(dihexylamino)aluminum hydride (LTDHA)<sup>1-j</sup>, for the chemoselective reduction of aromatic nitriles to the corresponding aldehydes have appeared in which aliphatic nitriles remain intact.<sup>1-i,j</sup> In the course of a systematic study of the reduction of lithium *N,N'*-dialkylethylenediaminoaluminum hydrides, the cyclic diamino-derivatives of lithium aluminum hydride, toward selected organic compounds containing representative functional groups, we found that the reagents possess interesting reducing characteristics, indicating excellent selectivity. Especially, the *N*-methyl



derivative (LDMEDAH) exhibited such an excellent chemoselectivity in the reduction of nitriles: one mole of LDMEDAH (two moles of hydride) in THF at 0 °C reduces one mole of aromatic nitriles with the immediate consumption of only one equivalent of hydride to the corresponding aldehydes, whereas the reagent did not show any reactivity toward aliphatic nitriles. This remarkable difference in the rate of reduction of aromatic and aliphatic nitriles suggests the possibility of achieving the selective reduction of aromatic nitriles to aldehydes in the presence of aliphatic nitriles under preparative conditions, similar to the cases of selective reduction by K 9-*sec*-Am-9-BBNH and LTDHA.<sup>1-j</sup> This communication reports such chemoselective transformations of aromatic nitriles to the corresponding aldehydes by utilizing LDMEDAH which is readily prepared by treatment of LiAlH<sub>4</sub> with one equivalent of *N,N'*-dimethylethylenediamine in THF at -78 °C.<sup>2</sup>

We first examined the reaction of benzonitrile with a half equivalent of the reagent (*i.e.*, one equivalent of hydride) at 0 °C. The reaction generated only about 50% yield of benzaldehyde along with the unreacted starting nitrile. We then examined the reaction of benzonitrile with one equivalent of the reagent (*i.e.*, two equivalents of hydride) and found that almost quantitative yield of benzaldehyde was generated. These results indicate that the first mole of hydride of the

reagent attacks benzonitrile to give a benzaldehyde intermediate, but the second mole of hydride is not involved in this reduction. Accordingly, we performed all the following reactions of representative nitriles with one equivalent of the reagent.<sup>3</sup>

The reagent, LDMEDAH, reduces unsubstituted aromatic nitriles, such as benzonitrile and naphthonitrile, to the corresponding aldehydes in essentially quantitative yields in 0.5 h at 0 °C, as shown in Table 1. Dinitriles, such as phthalo-, isophthalo- and terephthalonitriles, are reduced to dialdehydes in yields of 92-95%. Ring substituted derivatives are readily accommodated. Thus, chloro- and methoxybenzonitriles are converted into the corresponding aldehydes

**Table 1.** Yield of Aldehydes in the Reduction of Representative Nitriles with Lithium *N,N'*-Dimethylethylenediaminoaluminum Hydride in Tetrahydrofuran at 0 °C<sup>a</sup>

| Compound                      | Time (h) | Yield of aldehyde (%) <sup>b</sup>     |
|-------------------------------|----------|--|
| benzonitrile                  | 0.5      | 98                                     |
|                               | 1.0      | 99 (81) <sup>c</sup> , 48 <sup>d</sup> |
| 1-naphthonitrile              | 0.5      | 98                                     |
|                               | 1.0      | 98                                     |
| phthalonitrile                | 0.5      | 92                                     |
|                               | 1.0      | 92                                     |
| isophthalonitrile             | 0.5      | 95                                     |
|                               | 1.0      | 95                                     |
| terephthalonitrile            | 0.5      | 94                                     |
|                               | 1.0      | 95                                     |
| <i>p</i> -chlorobenzonitrile  | 0.5      | 98                                     |
|                               | 1.0      | 99                                     |
| 2,6-dichlorobenzonitrile      | 0.5      | 98                                     |
|                               | 1.0      | 97                                     |
| <i>p</i> -methoxybenzonitrile | 0.5      | 93                                     |
|                               | 1.0      | 94                                     |
| <i>o</i> -tolunitrile         | 0.5      | 100                                    |
|                               | 1.0      | 99 (82) <sup>f</sup>                   |
| <i>m</i> -tolunitrile         | 0.5      | 99                                     |
|                               | 1.0      | 99                                     |
| <i>p</i> -tolunitrile         | 0.5      | 100                                    |
|                               | 1.0      | 100                                    |
| 2-cyanopyridine               | 0.5      | trace                                  |
| 4-cyanopyridine               | 0.5      | trace                                  |
| hexanenitrile                 | 1.0      | trace                                  |
| decanenitrile                 | 1.0      | 0                                      |
| isovaleronitrile              | 1.0      | trace                                  |

<sup>a</sup>Reacted with 1 equiv of the reagent for mononitrile and 2 equiv for dinitrile. <sup>b</sup>Analyzed by GC with an internal standard and authentic samples. <sup>c</sup>Isolated yield on distillation. <sup>d</sup>Reacted with 0.5 equiv of the reagent.

**Table 2.** Selective Reaction of Aromatic Nitriles in the Presence of Aliphatic Nitriles with Lithium *N,N'*-Dimethylethylenediaminoaluminum Hydride in Tetrahydrofuran at 0 °C<sup>a,b</sup>

| Compound                                | Product                | mol% <sup>c</sup> |
|---|------------------------|-------------------|
| benzonitrile and hexanenitrile          | benzaldehyde           | 98                |
|   | benzonitrile           | trace             |
|   | hexanal                | trace             |
| <i>p</i> -tolunitrile and decanenitrile | hexanenitrile          | 100               |
|   | <i>p</i> -tolualdehyde | 100               |
|   | <i>p</i> -tolunitrile  | 0                 |
|   | decanal                | 0                 |
|   | decanenitrile          | 99                |

<sup>a</sup>One equiv of the reagent per mixture of 1 equiv in each of the compounds was utilized. <sup>b</sup>Reacted for 1 h. <sup>c</sup>Determined by GC analysis with an internal standard and authentic samples.

in nearly quantitative yields. Tolunitriles, regardless of the position of the methyl substituent, are also readily reduced to give the corresponding aldehydes in better than 99% yields. However, the reagent failed to produce the desired aldehydes from the reaction of cyanopyridines because of attack on the pyridine ring. On the other hand, the results appeared in the reaction of aliphatic nitriles with this reagent are somewhat unexpected: the reagent does not show any reactivity toward aliphatic nitriles examined under these reaction conditions.

As mentioned above, the reagent essentially does not attack aliphatic nitriles at 0 °C; however, aromatic nitriles are readily reduced to the aldehyde stages under the identical reaction conditions. Therefore, we attempted to convert aromatic nitriles to the corresponding aldehydes chemoselectively in the presence of aliphatic nitriles intact. Indeed, as shown in Table 2, we achieved up to 98-100% conversion of aromatic nitriles into aldehydes in mixtures with aliphatic nitriles, with essentially no reduction of the aliphatic nitriles, with a limiting amount of reagent.<sup>4</sup>

In summary, we have developed a newly-devised cyclic diamino-derivative of lithium aluminum hydride and found that the reagent reduces aromatic nitriles to aldehydes in essentially quantitative yields whereas aliphatic nitriles remain unattacked. A systematic study on the general reducing characteristics of the reagent toward organic compounds is currently underway.

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- The procedure for the preparation of lithium *N,N'*-dimethylethylenediaminoaluminum hydride (LDMEDAH) in THF is following. To an oven-dried, 200-mL flask fitted with a side arm and a stopcock leading to a mercury bubbler was added 50 mL of 2 M solution of LAH in THF and the solution was cooled to -78 °C using dry ice-acetone bath. To this solution was added 101 mL of a precooled 1 M solution of *N,N'*-dimethylethylenediamine in THF dropwise. After the hydrogen evolution, the resulting LDMEDAH solution was diluted with THF to be 0.5 M, and the <sup>27</sup>Al NMR spectrum of the solution showed a triplet ( $J_{Al-H} = 170$  Hz) centered at  $\delta$  78 ppm relative to  $[Al(H_2O)_6]^{3+}$ .
- The following procedure for the reduction of benzonitrile is representative. An oven-dried, 50-mL flask, equipped with a side arm, a condenser, and an adapter connected to a mercury bubbler, was flushed with nitrogen and charged with 8.4 mL of the reagent solution (4.2 mmol) and *n*-dodecane as an internal standard. The solution was cooled to 0 °C in an ice-water bath and 4 mL of a precooled 1 M solution of benzonitrile (4 mmol) in THF was added with stirring. At the appropriate time interval of 0.5 and 1.0 h, an aliquot was withdrawn and quenched with 3 N HCl. The organic layer was dried over anhydrous MgSO<sub>4</sub> and subjected to GC analysis to indicate the presence of benzaldehyde in yields of 98% and 99%, respectively (Table 1).
- The following procedure for the competitive reaction between benzonitrile and hexanenitrile is representative. In the usual setup, a 50-mL of the reagent (4.2 mmol) in THF and *n*-dodecane, and the solution was cooled to 0 °C. To this solution 4 mL of a precooled equimolar mixture of benzonitrile and hexanenitrile (4 mmol each) was added rapidly with stirring. The reaction mixture was stirred for 1 h at 0 °C and then quenched with water. The aqueous layer was saturated with anhydrous K<sub>2</sub>CO<sub>3</sub> and a part of organic layer was analyzed by GC for nitriles. The rest of organic layer was washed with excess 3 N HCl and dried over anhydrous MgSO<sub>4</sub>. The organic layer was then subjected to GC analysis for aldehydes. The combined GC analysis indicated a 98% yield of benzaldehyde and a 100% unreacted hexanenitrile.