

New Synthetic Method of Aldehydes from Tertiary Amides by Lithium Diisobutylpiperidinoaluminumate (LDBPA)

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Partial reduction of tertiary amides into aldehyde is one of the most important and highly desirable means in organic synthesis, and a large number of reducing agents for this have been reported.¹ Among them, a commercially available diisobutylaluminum hydride (DIBAH)^{1f} is commonly used for the preparation of aldehydes from tertiary amides in 50–70% yields.

Previously, we have reported that lithium diisobutyl-di-alkylaminohydroaluminates, the amino-derivatives of DIBAH, are new partial reducing agents, which can reduce various esters into aldehydes. Among them, lithium diisobutyl-piperidinoaluminumate (LDBPA) was most effective for partial reduction of esters to aldehydes in moderate to good yields at 0 °C² and also LDBPA was effective for partial reduction of aromatic nitriles in almost quantitative yield.³ As a part of our research program directed toward the discovery of new reducing agents through the simple modification of commercial DIBAH, we have studied the reducing characteristics of LDBPA with tertiary amides and found that LDBPA smoothly reduced tertiary amides to aldehydes at 0 °C. Herein, we wish to report a new alternative and efficient method for partial reduction of tertiary amides to aldehydes by LDBPA under mild condition (Scheme 1).

Results and Discussion

The LDBPA is readily prepared by a simple reaction of

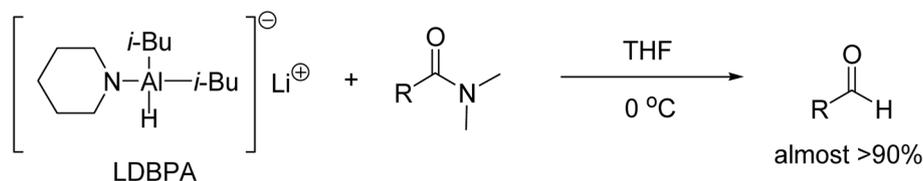
DIBAH with lithium piperilide in THF at 0 °C or room temperature (Scheme 2).

We first examined LDBPA for the conversion of aldehyde from *N,N*-dimethyl benzamide and found that LDBPA reduced *N,N*-dimethyl benzamide to give the corresponding aldehyde in quantitative yield (Entry 1 of Table 1). Using the same methodology, we applied this reducing agent for the

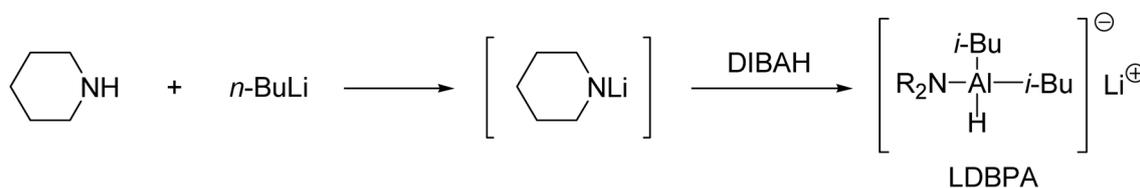
Table 1. Reduction of representative tertiary amides with LDBPA at 0 °C

entry	compound	reaction condition		yield of aldehyde (%) ^a
		H ⁻ /ester	time (h)	
1	<i>N,N</i> -dimethyl benzamide	1.5	1	99
2	<i>N,N</i> -dimethyl 4-chlorobenzamide	1.5	1	92
3	<i>N,N</i> -dimethyl 4-chlorobenzamide	1.5	1	97
4	<i>N,N</i> -dimethyl 4-methoxybenzamide	1.5	1	90
5	<i>N,N</i> -dimethyl 3-toluamide	1.5	1	96
6	<i>N,N</i> -dimethyl 3-nitrobenzamide	1.5	1	30
7	<i>N,N</i> -dimethyl 2-naphthylamide	1.5	1	98
8	<i>N,N</i> -dimethyl 2-furoamide	1.5	1	91
9	<i>N,N</i> -dimethyl caproamide	1.5	1	89
10	<i>N,N</i> -dimethyl dodecanoamide	1.5	1	99
11	<i>N,N</i> -dimethyl cyclohexanecarboxamide	1.5	1	76
12	<i>N,N</i> -dimethyl cinnamamide	1.5	1	29

^aYields were determined by GC.



Scheme 1



Scheme 2

synthesis of aldehydes from the various tertiary amides at 0 °C. The results for representative tertiary amides are summarized in Table 1.

As shown in Table 1, tertiary amides of electron withdrawing substituents such as *N,N*-dimethyl 4-chlorobenzamide and *N,N*-dimethyl 4-bromobenzamide, and electron donating substituents such as *N,N*-dimethyl 4-methoxybenzamide and *N,N*-dimethyl 3-tolubenzamide were readily reduced to the corresponding aldehydes in 90-97% (entries 2-5). However, *N,N*-dimethyl 3-nitrobenzamide gave only 30% yield of 3-nitrobenzaldehydes (entry 6). Also, reduction of other aromatic tertiary amides such as *N,N*-dimethyl 2-naphthylamide, a poly aromatic tertiary amide and *N,N*-dimethyl 2-furoamide, a heterocyclic tertiary amide gave the corresponding aldehydes in 98% and 91% yield, respectively (entries 7 and 8). Similarly, reduction of aliphatic amides such as *N,N*-dimethyl caproamide, *N,N*-dimethyl dodecanoamide and *N,N*-dimethyl cyclohexancarboxamide were smoothly reduced to the corresponding aldehydes in 76-99% yield (entries 9-11). On the other hand, *N,N*-dimethyl cinnamamide, an α,β -unsaturated tertiary amide gave only 29% yield of cinnamaldehydes (entry 12). This is very similar to other reducing agents such as lithium di- and triethoxyaluminium hydride^{1c} and sodium diethyldihydroaluminumate (SDDA)^{1e} gave only 7%, 9% and 34% of cinnamaldehyde from *N,N*-dimethyl cinnamamide, respectively.

In summary, we have easily prepared LDBPA from the reaction of commercially available DIBAH with lithium piperilide. This reagent proved to be one of effective partial reducing agents for tertiary amides to aldehydes. Therefore, LDBPA is believed to be an alternative reagent for the synthesis of aldehydes from tertiary amides instead of DIBAH in organic synthesis.

Experimental Section

General. All glassware used was dried thoroughly in an oven, assembled hot, and cooled under a stream of dry nitrogen prior to use. All reaction and manipulation of air and moisture sensitive materials were carried out using standard techniques for handling air sensitive materials. All chemicals were commercial products of the highest pure which were purified further by standard methods before use. THF was dried over sodium-benzophenone and distilled. Diisobutylaluminium hydride (DIBAH) and *n*-butyllithium

were purchased from Aldrich Chemical Company. Tertiary amides were prepared by the method of Brown and Tsukamoto.^{1c} GC analyses were performed on a Doman DS 6200 FID chromatograph, using a HP-1 (Crosslinked methyl siloxane) capillary column (30 m). All GC yields were determined with use of a suitable internal standard and authentic mixture.

Preparation of lithium diisobutylpiperidinoaluminumate (LDBPA). To a solution of piperidine (0.50 mL, 5 mmol) in THF (2.5 mL) was added *n*-butyllithium (2.0 mL, 2.5 M in hexane, 5 mmol) at 0 °C. After being stirred for 1h at room temperature, DIBAH (5 mL, 1.0 M in hexane, 5 mmol) was added dropwisw to the reaction mixture at 0 °C and the mixture was stirred for 2h at room temperature to give colorless homogeneous solution.

Reduction of tertiary amides with LDBPA to aldehydes. The following procedure for the reduction of *N,N*-dimethyl benzamide with LDBPA is representative. To a solution of *N,N*-dimethyl benzamide (0.75 g, 0.5 mmol) in THF (5 mL) containing naphthalene as an internal standard was added LDBPA (1.5 mL, 0.5 M in THF-hexane) at 0 °C. After 1h, the reaction mixture was hydrolyzed with 5 mL of 1 N HCl (aq) and the product was extracted with 10 mL of diethyl ether. The ether layer was dried over anhydrous magnesium sulfate. GC analysis showed a 99% yield of benzaldehyde.

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