New Method for Synthesis of Aldehydes from Esters by Sodium Diisobutyl-*t*-butoxyaluminum Hydride

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A new reducing agent, sodium diisobutyl-*t*-butoxyaluminum hydride (SDBBA), easily prepared by addition of sodium *t*-butoxide to DIBALH in THF at 0 °C or room temperature, readily reacts with representative esters to give the corresponding aldehydes in very good yields under mild conditions (0 °C).

Partial reduction of ester to aldehyde is one of the most important and highly desirable methods in organic synthesis, and a large number of reducing agents for this purpose have been reported. Among them, diisobutylaluminum hydride (DIBALH),[1] which is commercially available, is used as one of the most popular reducing agents. However, the yields of aromatic aldehydes (48–70%) are considerably lower than those of aliphatic aldehydes (80–88%) and this reagent requires a very low temperature (−78 °C). It has also been reported that several substituted metal hydrides for partial reduction of esters, such as lithium tri-*t*-butoxyaluminum hydride (LTBA),[2] bis(4-methyl-1-piperazinyl)aluminum hydride,[3] and sodium diethylpiperidinohydroaluminate (SDP A),[4] can be used. Of these reagent, LTBA can be applied only for phenyl esters and bis(4-methyl-1-piperazinyl)aluminum hydride required elevated reaction temperature (65 °C). Additionally sodium diethyldihydroaluminate (SDDA), which is the precursor for synthesis of SDPA, is not commercially available. And, also these reagents cannot achieve very general reduction of both aliphatic and aromatic esters.

Recently, we have reported that lithium diisobutylpiperidinohydroaluminate (LDBPA) was readily prepared by the reaction of lithium piperilide with DIBALH and exhibits excellent reducing ability of various aromatic nitriles[5b] and tertiary amides[5c] to the corresponding aldehydes in almost quantitative yield. However, the LDBPA was less effective for the partial reduction of esters (47–83%)[5a] than other carboxylic acid derivatives such as nitriles and tertiary amides. In the course of our program for developing a new and better selectivity for the partial reduction of esters to aldehydes than LDBPA, we found that sodium diisobutyl-*t*-butoxyaluminum hydride (SDBBA)[6] easily prepared from commercially available DIBALH smoothly reduced esters to aldehydes in very good yields at 0 °C. Herein, we wish to report a new alternative and efficient method for partial reduction of esters to aldehydes by SDBBA under mild conditions.

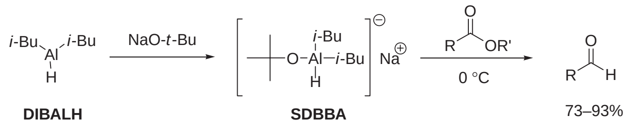
SDBBA was easily prepared by reacting an equimolar amount of sodium *t*-butoxide with DIBALH in THF at 0 °C or room temperature (Scheme 1). Next, we examined partial reduction of representative aromatic and aliphatic esters, such as ethyl benzoate (Entry 1 in Table 1) and ethyl hexanoate (Entry 13 in Table 1), with SDBBA in THF at 0 °C. The reduction of these esters provides corresponding aldehydes in very good yields in 6–12 h. Thus, we applied SDBBA for the synthesis of aldehydes from various esters. The results for representative esters are summarized in Table 1.

As shown in Table 1, ethyl benzoate was smoothly reduced to produce benzaldehyde in 84% yield (Entry 1 of Table 1).[8] Under identical conditions, reduction with DIBALH itself provided only benzyl alcohol (Entry 2 of Table 1). The case of

Table 1. Yields of aldehydes in the reduction of representative esters with SDBBA at 0 °C[7]

Entry	Ester	Product	Reaction condition		Yield/%[a]
			H^-/Ester	Time/h	
1	Ethyl benzoate	Benzaldehyde	1.2	6	34
2			(1.2)	(6)	(0)[b]
3	Isopropyl benzoate	Benzaldehyde	1.5	24	85
4	Ethyl 4-fluorobenzoate	4-Fluorobenzaldehyde	1.2	6	91
5	Methyl 3-chlorobenzoate	3-Chlorobenzaldehyde	1.2	6	91 (79)[c]
6	Ethyl 2-bromobenzoate	2-Bromobenzaldehyde	1.2	6	91
7	Ethyl 4-bromobenzoate	4-Bromobenzaldehyde	1.2	6	92
8	Ethyl 4-nitrobenzoate	4-Nitrobenzaldehyde	1.2	6	90 (77)[c]
9	Ethyl 2-toluate	2-Methylbenzaldehyde	1.2	6	83
10	Ethyl 4-methoxybenzoate	4-Methoxybenzaldehyde	1.2	24	73
11	Ethyl 2-naphthalate	2-Naphthylaldehyde	1.2	1	89
12	Ethyl 2-furoate	2-Furoylaldehyde	1.2	1	83
13	Ethyl hexanoate	hexanal	1.2	12	91
14	Isopropyl hexanoate	hexanal	1.5	12	94
15	Ethyl undecanoate	Undecanal	1.2	12	93
16	Ethyl cyclohexanecarboxylate	Cyclohexanecarboxaldehyde	1.2	12	81

[a]Yields were determined by GC. [b]Yields obtained with DIBALH alone are shown in parentheses. [c]Isolated yields.



Scheme 1.

isopropyl benzoate needed a larger amount of hydride (1.5 equiv.) and a longer reaction time (24 h) than unhindered esters such as ethyl benzoate, presumably due to the bulky isopropyl group (Entry 3 in Table 1). Also, esters of electron-withdrawing substituents such as ethyl 4-fluorobenzoate, methyl 3-chlorobenzoate, ethyl 2-bromobenzoate, ethyl 4-bromobenzoate, and ethyl 4-nitrobenzoate, and electron-donating substituents such as ethyl 2-toluate and ethyl 4-methoxybenzoate were readily reduced to the corresponding aldehydes in 73–92% yields (Entries 4–10 of Table 1). Among them, the reduction of ethyl 4-methoxybenzoate required a longer reaction time (24 h) than that of common esters. This may be attributed to the strong electron-donating effect of the methoxy group. Reduction of other aromatic esters such as ethyl 2-naphthalate, a poly-aromatic ester and ethyl 2-furoate, a heterocyclic ester gave the corresponding aldehydes in 89% and 83% yield, respectively (Entries 11 and 12 in Table 1). Furthermore, aliphatic esters such as ethyl hexanoate, isopropyl hexanoate, ethyl undecanoate and ethyl cyclohexanecarboxylate were smoothly reduced to the corresponding aldehydes under the same reaction conditions in 81–94% yields (Entries 13–16 in Table 1).

In summary, we easily prepared SDBBA by reacting commercially available DIBALH with sodium *t*-butoxide. Furthermore, we have established a convenient method for the conversion of esters to corresponding aldehydes in very good yields by the new reducing agent (SDBBA). Especially, this reagent has the great advantage that this aldehyde synthesis can be carried out at 0 °C instead of a very low temperature (−78 °C) or a very high temperature (reflux) and it can achieve very general reduction of both aliphatic and aromatic esters in very good yields. Therefore, SDBBA is believed to be a reagent of choice for the synthesis of aldehydes from esters, instead of DIBALH, LDBPA, and other reducing agents.

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References and Notes

1 L. I. Zakharkin, I. M. Khorlina, *Tetrahedron Lett.* **1962**, *3*, 619.

2 P. M. Weissman, H. C. Brown, *J. Org. Chem.* **1966**, *31*, 283.

3 M. Muraki, T. Mukaiyama, *Chem. Lett.* **1975**, 215.

4 a) N. M. Yoon, J. H. Ahn, D. K. An, Y. S. Shon, *J. Org. Chem.* **1993**, *58*, 1941. b) N. M. Yoon, Y. S. Shon, J. H. Ahn, J. W. An, *Bull. Korean Chem. Soc.* **1993**, *14*, 522.

5 a) J. H. Ahn, J. I. Song, J. E. Ahn, D. K. An, *Bull. Korean Chem. Soc.* **2005**, *26*, 377. b) J. H. Ha, J. H. Ahn, D. K. An, *Bull. Korean Chem. Soc.* **2006**, *27*, 121. c) S. M. Woo, M. E. Kim, D. K. An, *Bull. Korean Chem. Soc.* **2006**, *27*, 1913.

6 To a solution of sodium *t*-butoxide (5.05 g, 52.5 mmol) in THF (25 mL) was added dropwise DIBALH (50 mL, 1.0 M in hexane, 50 mmol) at 0 °C and the mixture was stirred for 2 h at room temperature to give a colorless homogeneous solution. The concentration of SDBBA solution in THF–hexane was measured gasometrically by hydrolysis of an aliquot of the solution with a hydrolyzing mixture of *t*-butyl alcohol–THF (1:1) at 0 °C.

7 All glassware used was dried thoroughly in an oven, assembled hot, and cooled under a stream of dry nitrogen prior to use. All reactions and manipulation of air- and moisture-sensitive materials were carried out by 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. Diisobutylaluminum hydride (DIBALH) and sodium *t*-butoxide were purchased from Aldrich Chemical Company. 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 the use of a suitable internal standard and authentic mixture.

8 The following procedure for the reduction of ethyl benzoate with SDBBA is representative. To a solution of ethyl benzoate (0.07 mL, 0.5 mmol) in THF (5 mL) containing naphthalene as an internal standard was added LDBPA (1.2 mL, 0.5 M in THF–hexane) at 0 °C. After 6 h, the reaction mixture was hydrolyzed with 5 mL of 1 M 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 an 84% yield of benzaldehyde.