Chemoselective Reduction of Esters to Aldehydes by Potassium Diisobutyl-*t*-butoxyaluminum Hydride (PDBBA)

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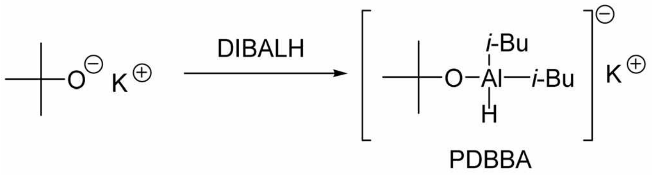
Received July 25, 2007

Key Words : Diisobutylaluminum hydride (DIBALH), Aldehyde, Ester, Partial reduction, Chemoselective reduction

The reduction of ester to aldehyde is one of the most useful synthetic transformations in organic synthesis, and a large number of reducing agents for this purpose have been reported.[1] Among them, diisobutylaluminum hydride (DIBALH),[1a] which is commercially available, is used as one of the most popular reducing agents, although this reagent provides moderate yields (48-88%) and requires a very low temperature (−78 °C). Very recently, we reported that lithium diisobutyl-*t*-butoxyaluminum hydride (LDBBA)[2] and sodium diisobutyl-*t*-butoxyaluminum hydride (SDBBA),[3] the alkoxy derivatives of DIBALH, were new partial reducing agents which could reduce various esters to aldehydes. Among them, LDBBA was especially effective for partial reduction of isopropyl esters to aldehydes in most cases with >90% yield at 0 °C, and SDBBA was also effective for partial reduction of methyl and ethyl esters in very good yield (73-93%) at 0 °C.

As a part of our research program directed toward the discovery of new reducing agents through simple modification of commercial DIBALH, we recently found that potassium diisobutyl-*t*-butoxyaluminum hydride (PDBBA) was easily prepared by reacting an equimolar amount of potassium *t*-butoxide with DIBALH in THF at 0 °C or room temperature (Scheme 1). We applied this reagent for the partial reduction of esters and nitriles to aldehydes.

We first examined the partial reduction of representative esters and nitriles such as ethyl benzoate (entry 1 in Table 2), ethyl caproate (entry 15 in Table 2), benzonitrile (entry 19 in Table 2) and capronitrile (entry 20 in Table 2) with PDBBA in THF at 0 °C. The reduction of these esters provides corresponding aldehydes in very good yield (88-89%) in 24-48 h. In contrast, nitriles were not reduced at all. It was found that PDBBA essentially did not attack nitriles at 0 °C. Therefore, partial reduction of esters to the correspondig aldehydes chemoselectively in the presence of nitriles was attempted. Indeed, as shown in Table 1, we achieved quantitative conversion of ethyl benzoate into benzaldehyde in mixtures with benzonitrile, with essentially no reduction of the benzonitrile.



Scheme 1. Preparation of PDBBA.

Accordingly, we applied PDBBA for the synthesis of aldehydes from various esters. The results for representative esters are summarized in Table 2.

As shown in Table 2, ethyl benzoate was efficiently reduced to benzaldehyde in 89% yield (entry 1 in Table 2). Under identical conditions, reduction with DIBALH alone provided only benzyl alcohol (entry 2 in Table 2). Isopropyl benzoate need larger amount of hydride (1.5 eq) than sterically unhindered esters such as ethyl benzoate, presumably due to the bulky isopropyl group (entry 3 in Table 2). Also, esters of electron-withdrawing substituents such as ethyl 4-fluorobenzoate, methyl 3-chlorobenzoate, ethyl 4-chlorobenzoate, ethyl 2-bromobenzoate, ethyl 4-bromobenzoate and ethyl 4-nitrobenzoate, and electron-donating substituents such as ethyl 2-toluate, ethyl 4-toluate and ethyl 4-methoxybenzoate were readily reduced to the corresponding aldehydes in 71-91% yield (entries 4-12 in Table 2). Among these, the reduction of ethyl 4-methoxybenzoate required a longer reaction time (48 h) than common esters. This may be attributed to the strong electron donating effect of the methoxy group. Similarly, 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 88% and 84% yield, respectively (entries 13 and 14 in Table 2). Furthermore, aliphatic esters such as ethyl caproate, isopropyl caproate, ethyl undecanoate and ethyl cyclohexanecarboxylate were efficiently reduced to the corresponding aldehydes in 78-90% yield (entries 15-18 in Table 2).

In summary, we easily prepared PDBBA by reacting commercially available DIBALH with potassium *t*-butoxide.

Table 1. Selective reduction of ethyl benzoate in the presence of benzonitrile with PDBBA at 0 °C[a,b]

compound	product	yield (%)[c]
ethyl benzoate and benzonitrile	benzaldehyde	87
	benzonitrile	99
	benzyl alcohol	12

[a] The reduction of a 1:1 mixture of ethyl benzoate and benzonitrile using 1.3 equiv of PDBBA was carried out. [b] Reacted for 24 h. [c] Yields were determined by GC.

Table 2. Yields of aldehydes from the reduction of representative esters with PDBBA at 0 °C

entry	compound	reaction condition		yield of aldehyde (%)[a]
		H$^-$/ester	time (h)	
1	ethyl benzoate	1.3	24	89
2		(1.3)	(24)	(0)[b]
3	isopropyl benzoate	1.5	24	88
4	ethyl 4-fluorobenzoate	1.3	24	85
5	methyl 3-chlorobenzoate	1.3	24	82
6	ethyl 4-chlorobenzoate	1.3	24	81
7	ethyl 2-bromobenzoate	1.3	24	87
8	ethyl 4-bromobenzoate	1.3	24	85
9	ethyl 4-nitrobenzoate	1.3	24	91
10	ethyl 2-toluate	1.3	24	90
11	ethyl 4-toluate	1.3	24	87
12	ethyl 4-methoxybenzoate	1.3	48	71
13	ethyl 2-naphthalate	1.3	24	88
14	ethyl 2-furoate	1.3	24	84
15	ethyl caproate	1.5	48	86
16	isopropyl caproate	1.5	48	84
17	ethyl undecanoate	1.5	48	90
18	ethyl cyclohexanecarboxylate	1.5	48	78
19	benzonitrile	1.5	48	no reaction
20	capronitrile	1.5	48	no reaction

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

Furthermore, we established a convenient method for the conversion of esters to corresponding aldehydes in good yield by using this new reducing agent (PDBBA). This reagent has great advantages in 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 efficient reduction of both aliphatic and aromatic esters in very good yield. Especially, we found that this reagent did not reduce nitriles, thus allowing chemoselective conversion of esters in the presence of nitriles. Therefore, PDBBA is believed to be an alternative reagent for the synthesis of aldehydes from esters and chemoselective reduction, accordingly replacing DIBALH and other reducing agents.

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 reactions 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 further purified by standard methods before use. THF was dried over sodium-benzophenone and distilled. Diisobutylaluminum hydride (DIBALH) and potassium *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.

Preparation of PDBBA. To a solution of potassium *t*-butoxide (5.89 g, 52.5 mmol) in THF (50 mL), DIBALH (50 mL, 1.0 M in hexane, 50 mmol) was added dropwise at 0 °C and the mixture was stirred for 2 h at room temperature to give a colorless homogeneous solution. The concentration of PDBBA 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.

Reduction of esters to aldehydes with PDBBA. The following procedure for reduction of ethyl benzoate with PDBBA is representative. To a solution of ethyl benzoate (0.07 mL, 0.5 mmol) in THF (5 mL) containing naphthalene as an internal standard, PDBBA (1.3 mL, 0.5 M in THF-hexane) was added at 0 °C. After 24 h, the reaction mixture was hydrolyzed with 1 N *aq* HCl (5 mL) and the product was extracted with diethyl ether (10 mL). The ether layer was dried over anhydrous magnesium sulfate. GC analysis showed an 89% yield of benzaldehyde.

Acknowledgment. This work was supported by the Research Institute for Basic Science, Kangwon National University, Korea.

References

1. (a) Zakharkin, L. I.; Khorlina, I. M. *Tetrahedron Lett.* **1962**, 619. (b) Weissman, P. M.; Brown, H. C. *J. Org. Chem.* **1966**, *31*, 283. (c) Muraki, M.; Mukaiyama, T. *Chem. Lett.* **1975**, 215. (d) Yoon, N. M.; Ahn, J. H.; An, D. K.; Shon, Y. S. *J. Org. Chem.* **1993**, *58*, 1941. (e) Yoon, N. M.; Shon, Y. S.; Ahn, J. H.; An, J. W. *Bull. Korean Chem. Soc.* **1993**, *14*, 522. (f) Ahn, J. H.; Song, J. I.; Ahn, J. E.; An, D. K. *Bull. Korean Chem. Soc.* **2005**, *26*, 377. (g) Ha, J. H.; Ahn, J. H.; An, D. K. *Bull. Korean Chem. Soc.* **2006**, *27*, 121. (h) Woo, S. M.; Kim, M. E.; An, D. K. *Bull. Korean Chem. Soc.* **2006**, *27*, 1913.
2. Kim, M. S.; Choi, Y. M.; An, D. K. *Tetrahedron Lett.* **2007**, *48*, 5061.
3. Song, J. I.; An, D. K. *Chem. Lett.* **2007**, *36*, 886.