

Partial and Chemoselective Reduction of Nitriles with Metal Diisobutyl-*t*-butoxyaluminum Hydrides

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Received August 18, 2008

Key Words : Diisobutylaluminum hydride (DIBALH), Aldehyde, Nitrile, Partial reduction, Chemoselectivity

Recently, we have reported that a new class of reducing agents, metal diisobutyl-*t*-butoxyaluminum hydrides such as lithium diisobutyl-*t*-butoxyaluminum hydride (LDBBA),^{1a} sodium diisobutyl-*t*-butoxyaluminum hydride (SDBBA),^{1b} and potassium diisobutyl-*t*-butoxyaluminum hydride (PDBBA),^{1c,d} the *t*-butoxy derivatives of DIBALH, are new effective partial reducing agents which can reduce various esters to aldehydes in high yields. Among them, LDBBA was especially effective for partial reduction of isopropyl esters to aldehydes usually in higher than 90% yield at 0 °C. Also, SDBBA and PDBBA were effective for partial reduction of common methyl and ethyl esters in very good yield (71-93%) at 0 °C. Accordingly, we decided to extend our investigation to the reduction of nitriles (Scheme 1) because partial reduction of nitriles into aldehydes is one of important and highly desirable means in organic synthesis, and a large number of reducing agents for this have been reported.²

Results and Discussion

As shown in Table 1, we first tried partial reduction of benzonitrile with LDBBA, SDBBA and PDBBA in THF at room temperature, respectively. And we obtained the best result with LDBBA in 6 h at room temperature. Using the same methodology, the partial reduction of other aromatic and aliphatic nitriles to the corresponding aldehydes was carried out. The results for representative nitriles are summarized in Table 2.

As shown in Table 2, aromatic benzonitriles of electron withdrawing and donating substituents were smoothly reduced to the corresponding aldehydes in very good yields (entries 1-10 in Table 2). Among them, the reduction of 2-tolunitrile, 2-methoxybenzonitrile and 1-cyanonaphthalene required longer reaction time and/or large amount of hydride

than other nitriles (entries 5, 8 and 10 in Table 2). This may be attributed to the electron donating effect of methyl, methoxy or naphthyl group and steric hindrance effect. In con-

Table 1. Reduction of benzonitrile with metal diisobutyl-*t*-butoxyaluminum hydrides at room temperature

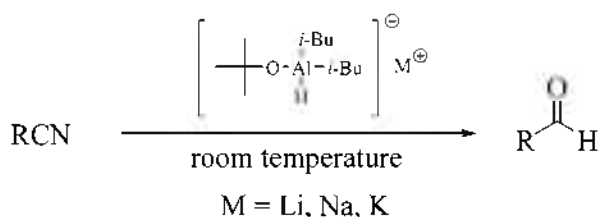
Compound	Hydride	Reaction condition		Yield of aldehyde (%) ^a
		H ⁻	time (h)	
benzonitrile	LDBBA	1.5	3	76
		2.0	1	79
		2.0	3	81
SDBBA	SDBBA	2.0	6	98
		2.0	12	63
		2.0	24	71
		3.0	6	57
		3.0	12	73
		3.0	24	80
PDBBA	PDBBA	3.5	24	70
		1.3	24	no reaction
		1.5	24	no reaction
		1.5	24	no reaction
		2.0	24	no reaction
		3.0	24	no reaction

^aYields were determined by GC.

Table 2. Yields of aldehydes in the reduction of representative nitriles with LDBBA at room temperature

Entry	Compound	Reaction condition		Yield of aldehyde (%) ^a
		H ⁻ /nitrile	time (h)	
1	benzonitrile	2.0	6	98
2	2-chlorobenzonitrile	2.0	6	96
3	3-chlorobenzonitrile	2.0	6	96
4	4-chlorobenzonitrile	2.0	6	95
5	2-tolunitrile	5.0	12	67
6	3-tolunitrile	2.0	6	97
7	4-tolunitrile	2.0	6	95
8	2-methoxybenzonitrile	5.0	24	75
9	4-methoxybenzonitrile	3.0	6	96
10	1-cyanonaphthalene	3.0	6	76
11	capronitrile	2.0	6	no reaction
12	dodecanenitrile	2.0	6	no reaction

^aYields were determined by GC.



Scheme 1

Table 3. Selective reduction of benzonitrile in the presence of capronitrile with LDBBA at room temperature^{a,b}

compound	product	yield (%) ^c
benzonitrile and capronitrile	benzaldehyde	98
	benzonitrile	0
	caproaldehyde	0
	capronitrile	99

^aThe reduction of a 1:1 mixture of benzonitrile and capronitrile using 2.0 equiv of the LDBBA was carried out. ^bReacted for 6 h. ^cYields were determined by GC.

trast, aliphatic nitriles, such as capronitrile and dodecanitrile are totally resistant to LDBBA (entries 11 and 12 in Table 2). The results indicate that LDBBA could selectively reduce aromatic nitriles in the presence of aliphatic nitriles. Indeed, when LDBBA was reacted with a 1:1 mixture of benzonitrile and capronitrile at room temperature, the reaction afforded only benzaldehyde with essentially no reduction of the capronitrile (Table 3).

This study has shown that LDBBA and SDBBA are new partial reducing agents for the direct transformation of aromatic nitriles to the corresponding aldehydes in very good yields at room temperature. LDBBA has proved superior to SDBBA in terms of chemical yield. It should be noted that LDBBA does not react with aliphatic nitriles at all. Therefore, LDBBA is believed to be unique and alternative reagent for reducing aromatic nitriles to the corresponding aldehydes without affecting aliphatic nitriles.

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. Diisobutylaluminum hydride (DIBALH), *n*-butyllithium, *t*-BuOH, sodium *t*-butoxide and potassium *t*-butoxide were purchased from Aldrich Chemical Company. GC analyses were performed on a Donam DS 6200 or Younglin Acme 6000M 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. The concentration of metal diisobutyl-*t*-butoxyaluminum hydrides 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.

Preparation of LDBBA. To a solution of *t*-butyl alcohol (5.16 mL, 55 mmol) in THF (25 mL) was added *n*-butyllithium (20 mL, 2.5 M in hexane, 55 mmol) at 0 °C. After being stirred for 1 h at room temperature, DIBALH (50 mL, 1.0 M in hexane, 50 mmol) was added dropwise to the reaction mixture at 0 °C and the mixture was stirred for 2 h at

room temperature to give a colorless homogeneous solution.

Preparation of SDBBA and PDBBA. To a solution of sodium *t*-butoxide (5.05 g, 52.5 mmol) or 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.

Stability of new hydrides. The LDBBA, SDBBA and PDBBA solutions were stable in the refrigerator for 6 months without any appreciable loss of hydride content.

Reduction of nitriles to aldehydes. The following procedure for the reduction of benzonitrile with LDBBA is representative. To a solution of benzonitrile (0.051 mL, 0.5 mmol) in THF (5 mL) containing naphthalene as an internal standard was added LDBBA (2.17 mL, 0.46 M in THF-hexane) at room temperature. After 6 h, 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 98% yield of benzaldehyde.

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