

Reaction of Aldehydes and Ketones with Dichloroisopropoxyborane. Comparison of the Reducing Characteristics of Isopropoxyborane Derivatives

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Recently, we reported that boron triisopropoxide reduces simple aldehydes and ketones at 25 °C or in refluxing THF under a slow stream of nitrogen.¹ This is the first example that boron alkoxides react with carbonyl compounds in a Meerwein-Ponndorf-Verley (MPV) type fashion.²

In general, the reaction of boron triisopropoxide is much milder than that of aluminum triisopropoxide. Boron triisopropoxide only can reduce aliphatic aldehydes and ketones among the carbonyl compounds, whereas the aluminum reagent reduces most carbonyl compounds irrespective of its structure.^{2d} Therefore, the reagent might serve as a comparative partner of aluminum triisopropoxide. However, side reactions are significant under the reaction conditions and hence yields become lower as the reaction goes on.³ Furthermore, in these reactions the acetone formed should be removed from the equilibrium mixture by a slow stream of nitrogen; otherwise, the yields are often quite low. In these respects, we need to develop other boron alkoxide derivatives, which can overcome such difficulties. In the course of such efforts, we found that dichloroisopropoxyborane appears to be one of possible candidates. We wish now to report the reducing characteristics of dichloroisopropoxyborane in the reaction of selected organic compounds containing representative functional groups.

In Table 1, the reactivity of dichloroisopropoxyborane toward various aldehydes is summarized and compared to those of boron triisopropoxide. As compared in the Table, the reactivity of dichloroisopropoxyborane is found to be quite different from that of boron triisopropoxide. Thus, dichloroisopropoxyborane reduced both aliphatic and aromatic aldehydes readily to the corresponding alcohols within 1 or 3 h at 25 °C, whereas boron triisopropoxide showed a much lower reactivity toward aliphatic aldehydes and actually no reactivity toward aromatic ones. In addition to that, the side reactions, which are significant in the reaction of aldehydes with boron triisopropoxide under a stream of nitrogen, were not accompanied in this reaction even in the presence of acetone formed.

Dichloroisopropoxyborane shows also quite similar trend in the reduction of ketones, as shown in Table 2. The reactivity of the reagent toward ketones is much stronger than that of boron triisopropoxide. Simple ketones were readily reduced, but some hindered alkyl and aryl ketones very slowly and hence could not be employed for this purpose

under these reaction conditions.

However, the reagent is absolutely inert toward other organic functional groups, such as acid chlorides, carboxylic acids, amides, esters, nitriles, *etc.* Therefore, we will explore in more detail the possibility achieving a selective reduction of particular organic functional groups.

It is generally accepted that the MPV type reactions using boron triisopropoxide proceeds *via* a complex in which both the carbonyl compound and the reducing alcohol are bound to the boron ion. Thus, the carbonyl is activated upon coordination to B(III), followed by a hydride transfer from the alcoholate to the carbonyl group *via* a six-membered transition state.^{4a} From this mechanistic point of view, the coordinating capacity of boron atom to the carbonyl oxygen

Table 1. Reaction of Aldehydes with Dichloroisopropoxyborane in Methylene Chloride at 25 °C

Compound	Time (h)	Yield of alcohol (%) ^a	
		PrOBCl ₂ ^b	(PrO) ₂ B ^c
caproaldehyde	0.5	100	
	3	100	47
	24		50
	72		45
isobutyraldehyde	1	100	85
	3	100	94
	6		79
benzaldehyde	0.5	100	
	3	100	
	72		trace
<i>p</i> -nitrobenzaldehyde	0.5	100	
	3	100	
	72		trace
<i>p</i> -tolualdehyde	0.5	100	
	72		trace
<i>p</i> -chlorobenzaldehyde	0.5	96	
	3	99.9	
	72		trace
2,6-dichlorobenzaldehyde	0.5	100	
	3	100	
<i>p</i> -methoxybenzaldehyde	0.5	68	
	3	99.9	

^aAnalyzed by GC with a suitable internal standard. ^bTen % excess reagent utilized. ^cData taken from ref. 1. The reaction was carried out in THF under stream of nitrogen.

Table 2. Reaction of Ketones with Dichloroisopropoxyborane in Methylene Chloride at 25 °C

Compound	Time (h)	Yield of alcohol (%) ^a	
		ⁱ PrOBCl ₂ ^b	(ⁱ PrO) ₂ B ^c
2-butanone	0.5	100	
	3	100	
	24		75
2-heptanone	3	80	13
	6	85	18
	24	88	56
	72	99	97
cyclohexanone	0.5	100	
	6	100	90
2-methylcyclohexanone	0.5	100	
	6	100 ^d	86
3-methylcyclohexanone	0.5	99	
	6	99 ^e	82
4-methylcyclohexanone	0.5	100	
	6	100 ^f	81
norcamphor	24	52	
	72	60 ^g	0
camphor	24	50	
	72	58 ^h	0
acetophenone	24	57	
	72	75	
	120	78	trace
benzophenone	72	46	
	120	52	trace

^aAnalyzed by GC with a suitable internal standard. ^bTen % excess reagent utilized. ^cData taken from ref. 1. The reaction was run in THF under stream of nitrogen. ^dForty six % of *trans*-isomer. ^eSeventy five % of *cis*-isomer. ^fSeventy nine % of *trans*-isomer. ^gNinety six % of *exo*-isomer. ^hFifty % of *endo*-isomer.

must be one of the factors which dominate the rate of reaction. Therefore, the introduction of chlorine atom, a strong electron-withdrawing group, to boron isopropoxide increases the Lewis acidity of boron that virtually enhances the reaction rate.

In conclusion, dichloroisopropoxyborane, a chlorine-incorporated boron alkoxide, provides an effective method for the selective reduction of aldehydes and simple ketones in the presence of other functional groups. Further, the reaction of carbonyl compounds with the reagent is much faster than that of boron triisopropoxide to provide a clear reaction to the corresponding alcohol stages without any effort to remove acetone formed during the reaction.⁴

Experimental Section

All glassware used in this study was predried at 140 °C for at least 9 hours, assembled hot, and cooled under a stream of dry nitrogen prior to use. All reactions were performed under a dry nitrogen atmosphere. All chemicals used were commercial products of the highest purity available, which were further purified by standard methods before use. CH₂Cl₂ was dried and distilled. Gas chromatographic analyses were carried out with a Varian 3300 chromatograph using a 10% CW 20 M capillary column (30 m).

Preparation of Dichloroisopropoxyborane. To an oven-dried, 100 mL flask with a side-arm and a reflux condenser leading to the gas buret was placed 5 mL of a 1 M solution of HBCl₂ in CH₂Cl₂ (5 mmol) and the flask was immersed into a water bath at 25 °C. To this 0.33 g of isopropyl alcohol (5.5 mmol) was added dropwise. After the hydrogen evolution ceased, the mixture was stirred for an additional 30 min. The ¹¹B NMR spectrum of dichloroisopropoxyborane in CH₂Cl₂ showed a singlet at δ 18 ppm relative to BF₃·OEt₂.

Reduction of Carbonyl Compounds. General Procedure. The following general reaction procedure was illustrative. Into the solution of dichloroisopropoxyborane in CH₂Cl₂ (5 mmol) just prepared as above 0.48 g of benzaldehyde (4.5 mmol) and tridecane (4.5 mmol) as an internal standard were injected. At the appropriate time intervals, an aliquot of the reaction mixture was withdrawn and quenched by addition of 2 N HCl. The aqueous layer was saturated with K₂CO₃ and the organic layer was dried over anhydrous MgSO₄. GC analysis of the organic layer indicated the presence of benzyl alcohol in a yield of 100% at the period of 0.5 h or 24 h.

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References and Notes

1. Cha, J. S.; Park, J. H. *Bull. Korean Chem. Soc.* **2002**, *23*, 1051; 1377.
2. (a) Meerwein, H.; Schmidt, R. *Ann.* **1925**, *444*, 221. (b) Ponnendorf, W. *Angew. Chem.* **1926**, *39*, 138. (c) Verly, M. *Bull. Soc. Chim. Fr.* **1925**, *37*, 537. (d) Wilds, A. S. *Org. React.* **1944**, *2*, 178.
3. Aldol condensations often are possible not only between two molecules of the aldehyde but also between the aldehyde and acetone formed.¹
4. For review, see: (a) Cha, J. S. *Org. Proc. Res. Devel.* **2006**, *10*, 32. (b) Cha, J. S. *Bull. Korean Chem. Soc.* **2007**, *28*, 2162.