

## Selective Reduction of Carbonyl Compounds with *B*-Phenoxydiisopinocampheylborane: Comparison of Its Reactivity to the Cyclohexoxy Derivative

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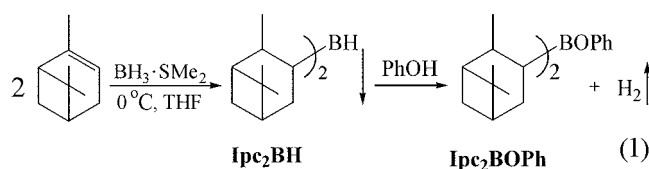
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In the previous communication,<sup>1</sup> we reported that *B*-cyclohexoxydiisopinocampheylborane, a new alicyclic derivative of diisopinocampheylborane, is one of the mildest reducing agents, which can reduce only an aldehyde function among the reducible general organic functionalities. The reagent readily reduces a variety of aldehydes at room temperature, but very slowly at 0 °C. It is evident that the reduction proceeds *via* a cyclic boatlike transition state being considered as a Meerwein-Ponndorf-Verley (MPV) type reaction.<sup>2</sup>

In the mechanistic point of view, the key step of such reactions must be the coordination of boron atom of reagent to the carbonyl oxygen of substrate. We believe that the reactivity of diisopinocampheylborane derivatives correlates to their Lewis acidity and steric requirement: stronger the coordination, faster the reduction rate. Accordingly, we decided to examine the reducing characteristics of *B*-phenoxydiisopinocampheylborane (*Ipc*<sub>2</sub>BOPh), an aromatic derivative, and compare its reactivity to that of the cyclohexoxy derivative (*Ipc*<sub>2</sub>BOC<sub>hex</sub>), in hopes of better understanding the nature of reagent and exploring its role in organic synthesis.

### Results and Discussion

*Ipc*<sub>2</sub>BOPh was prepared from  $\alpha$ -pinene by hydroboration followed by treatment with phenol in THF (Eq. 1).



The reactivity of *Ipc*<sub>2</sub>BOPh toward some representative organic functional groups are examined, and the results are summarized and compared with those obtained by *Ipc*<sub>2</sub>BOC<sub>hex</sub> in Table 1. *Ipc*<sub>2</sub>BOPh readily reduced a wide variety of aldehydes to the corresponding alcohols at 0 °C or room temperature, whereas the other functions including

ketones, acid chlorides, esters and nitriles were absolutely inert to this reagent. This chemoselectivity is actually same as that obtained by *Ipc*<sub>2</sub>BOC<sub>hex</sub>. However, the reactivity of *Ipc*<sub>2</sub>BOPh toward an aldehyde function appeared much

**Table 1.** Reaction of Aldehydes and Other Functional Compounds with *B*-Phenoxydiisopinocampheylborane (*Ipc*<sub>2</sub>BOPh) in Tetrahydrofuran at 25 °C<sup>a</sup>

Compound	Temp (°C)	Time (h)	Yield of alcohol (%) <sup>b</sup>		
			<i>Ipc</i> <sub>2</sub> BOPh	<i>Ipc</i> <sub>2</sub> BOC <sub>hex</sub>	
hexanal	0	1	94	14	
		6	99	24	
		12	99.9	26	
		25	1	99	68
		3	100		
		6	100	89	
	0	12		98	
		24		99	
		25	1	99	81
			3	99	
6				98	
12				99	
<i>o</i> -tolualdehyde	0	1	96	15	
		3	98	16	
		6	99	19	
		12	99		
		24		29	
	25	1	97	96	
		3	100	97	
		6	100	99	
		12		99	
					99
<i>p</i> -tolualdehyde	0	1	98	25	
		3	99	26	
		6	99	36	
		25	1	98	97
		3	100	98	
	25	6	100	99	
		12		99	

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Table 1. Continued

Compound	Temp (°C)	Time (h)	Yield of alcohol (%) <sup>b</sup>			
			Ip <sub>c</sub> <sub>2</sub> BOPh	Ip <sub>c</sub> <sub>2</sub> BOC <sub>hex</sub>		
<i>p</i> -chlorobenzaldehyde	0	1	92	18		
		3	98	19		
		6	99	25		
		12	99	28		
	25	24	31			
		1	93	72		
		3	99	87		
		6	99	98		
		12		100		
		24		100		
		<i>m</i> -hydrobenzaldehyde	0	0.5	98	21
				1	99	29
3	100			31		
25	6		100	38		
	0.5		99	97		
	1		100	99		
2-naphthaldehyde	0	3	100	99		
		6		18		
		12		19		
	25	24		23		
		1	99	74		
		3	99.9	88		
		6	99.9	98		
		12		99		
		24		99		
		2-heptanone	0	72	0	0
25	72		0	0		
acetophenone	0	72	0	0		
	25	72	0	0		
isophorone	0	24	0	0		
	25	24	0	0		
benzophenone	0	24	0	0		
	25	24	0	0		
hexanoyl chloride	0	24	0	0		
	25	24	0	0		
ethyl caproate	0	24	0	0		
	24	24	0	0		
benzonitrile	0	24	0	0		
	25	24	0	0		

<sup>a</sup>Ten% excess reagent utilized. <sup>b</sup>GC yield with suitable internal standard. <sup>c</sup>Data taken from ref.1. <sup>d</sup>Reacted both at 25 °C and under reflux.

stronger than that of Ip<sub>c</sub><sub>2</sub>BOC<sub>hex</sub>. Thus, the reaction of aldehydes with Ip<sub>c</sub><sub>2</sub>BOC<sub>hex</sub> at 0 °C is very slow, while Ip<sub>c</sub><sub>2</sub>BOPh can reduce aldehydes readily even at 0 °C. Such a reactivity seems to arise from the Lewis acidity difference between two derivatives: the electron-withdrawing effect of phenoxy group makes the phenoxy derivative more acidic than the cyclohexoxy derivative.

Such a phenomenon was also detected in the reaction of  $\alpha,\beta$ -unsaturated aldehydes and ketones, the results being summarized in Table 2. Ip<sub>c</sub><sub>2</sub>BOPh reduced  $\alpha,\beta$ -unsaturated

Table 2. Reaction of  $\alpha,\beta$ -Unsaturated Aldehydes and Ketone with Ip<sub>c</sub><sub>2</sub>BOPh in Tetrahydrofuran<sup>a</sup>

Compound	Temp (°C)	Time (h)	Product ratio <sup>b,c</sup> 1,2 : 1,4	Yield of allylic alcohol(%)			
				Ip <sub>c</sub> <sub>2</sub> BOPh	Ip <sub>c</sub> <sub>2</sub> BOC <sub>hex</sub> <sup>d</sup>		
crotonaldehyde	0	1	100:0	19	9		
		3	100:0	33	12		
		6	100:0	53	33		
		12	100:0	60			
		24	100:0	70	49		
		72	100:0	88	52		
	25	1	100:0	88	81		
		3	100:0	92	90		
		6	100:0	100	98		
		12	100:0	100	99		
		24	100:0		99		
2-hexenal	0	3	100:0				
		6	100:0				
		12	100:0				
	25	3	100:0				
		6	100:0				
		12	100:0				
cinnamaldehyde	0	1	100:0	93	3		
		3	100:0	95	6		
		6	100:0	99	33		
		24	100:0	99	43		
		25	1	100:0	99	86	
			3	100:0	99.9	97	
	6		100:0	99.9	99		
	12		100:0		99		
	isophorone		0	24		0	0
			25	24		0	0
	chalcone	0	24		0	0	
		25	24		0	0	
benzalacetone	0	24		0	0		
	25	24		0	0		

<sup>a</sup>Ten % excess reagent utilized. <sup>b</sup>Determined by GC using calibrated internal standard. <sup>c</sup>Normalized product ratio. <sup>d</sup>Data taken from ref. 1.

Table 3. Competitive Reduction of Aldehydes in the presence of Other Functional Compounds with Ip<sub>c</sub><sub>2</sub>BOPh in Tetrahydrofuran at 25 °C<sup>a</sup>

Starting mixture	Time (h)	Ratio of reduction products <sup>b</sup>
hexanal / 2-heptanone	12	100:0
hexanal / acetophenone	12	100:0
hexanal / benzophenone	12	100:0
hexanal / hexanoyl chloride	12	100:0
hexanal / benzonitrile	12	100:0
hexanal / ethyl benzoate	12	100:0
benzaldehyde / hexanal	1	96:0
	3	97:3(98:2) <sup>c</sup>
benzaldehyde / 2-heptanone	1	100:0
benzaldehyde / acetophenone	3	99:0
<i>o</i> -tolualdehyde / 2-heptanone	3	100:0

<sup>a</sup>Ten % excess reagent (1.1 equiv) was utilized for the competitive reaction of equimolar mixture of two compounds. <sup>b</sup>Determined by GC with appropriate internal standard; the total yield of product alcohol were 99.5%. <sup>c</sup>At 0 °C.

aldehydes cleanly to the corresponding allylic alcohols, but did not attack  $\alpha,\beta$ -unsaturated ketones at all, being exactly same results obtained by  $\text{Ipc}_2\text{BOC}_{\text{hex}}$ . However, the reactivity of  $\text{Ipc}_2\text{BOPh}$  is still stronger than that of  $\text{Ipc}_2\text{BC}_{\text{hex}}$  in these reductions.

The reagent also showed an excellent chemoselectivity between aldehydes and the other reducible organic compounds including ketones, acid chlorides, esters and nitriles, and the results are summarized in Table 3. As seen in the Table, the complete discrimination between aldehydes and ketones are remarkable. Especially, the chemoselectivity between benzaldehyde and hexanal is noteworthy (93 : 7 at 25° and 98 : 2 at 0°); the results is quite comparable to that achieved by  $\text{Ipc}_2\text{BOC}_{\text{hex}}$  (98 : 2 at 25°).

### 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 reaction were performed under a dry  $\text{N}_2$  atmosphere. All chemicals used were commercial products of the highest purity available, which were further purified by standard methods before use. THF was distilled from sodium-benzophenone ketyl prior to use. Gas chromatographic analyses were carried out with a Varian 3300 chromatograph using a 10% Carbowax 20M capillary column (30 m).

**Preparation of *B*-Phenoxydiisopinocampheylborane ( $\text{Ipc}_2\text{BOPh}$ ).** To an oven-dried, 200 mL flask with a sidearm and a reflux condenser leading to a mercury bubbler were added 5 mL of BMS (10 M, 50 mmol) and 4 mL of THF. It was cooled to 0 °C, and 17 mL (105 mmol) of  $\alpha$ -pinene was added dropwise with stirring. After the complete addition of  $\alpha$ -pinene, the stirring was stopped and the flask was stored at 0 °C for 6 h. The supernatant solution was decanted by using a double-ended needle. The crystalline lumps of  $\text{Ipc}_2\text{BH}$  was suspended in THF (20 mL), and to this was added a 5.0 M solution of phenol in THF (55 mmol) dropwise with stirring. The solid was disappeared as hydrogen evolved. The solution was diluted with THF to be 1.0 M. The  $^{11}\text{B}$  NMR spectrum of the solution showed a broad singlet at  $\delta$  54 ppm.

**General Reduction of Aldehydes with  $\text{Ipc}_2\text{BOPh}$ .** An

oven-dried, 50 mL flask, fitted with a sidearm and a bent adapter connected to a mercury bubbler, was charged with 2.5 mL of a 2.0 M aldehyde solution (5 mmol) in THF and dodecane as an internal standard. The solution was maintained in a circulating bath at either 0 or 25 °C. To this was added 5.5 mL of a stock solution of  $\text{Ipc}_2\text{BOPh}$  (5.5 mmol) in THF with stirring. At the appropriate time intervals, an aliquot (*ca.* 1 mL) was withdrawn, and the mixture was quenched by addition of acetaldehyde (0.39 mL, 7 mmol) and the mixture was stirred for 6 h. After the addition of NaOH (6 N, 5 mL), the aqueous layer was saturated with  $\text{K}_2\text{CO}_3$  and the organic layer was dried over anhydrous  $\text{MgSO}_4$ . The organic layer was then subjected to gas chromatographic analysis.

**Competitive Reduction.** The following procedure for the competitive reaction between hexanal and 2-heptanone with  $\text{Ipc}_2\text{BOPh}$  is representative. A 50 mL flask was charged with equimolar mixture of hexanal (4 mmol) and 2-heptanone (4 mmol) in 4 mL of THF. The solution was maintained at 25 °C in a water bath and 4.4 mL of a 1.0 M solution of  $\text{Ipc}_2\text{BOPh}$  (4.4 mmol) in THF was added rapidly with stirring. The reaction mixture was stirred for 12 hrs and the mixture was quenched with 3 N NaOH (2 mL) and dodecane was added (2 mmol) as an internal standard. The organo-borane derivative was oxidized by the addition of buffer solution (pH 7.0, 2 mL) and 30%  $\text{H}_2\text{O}_2$  (0.8 mL). The aqueous layer was then saturated with  $\text{K}_2\text{CO}_3$  and dried over anhydrous  $\text{MgSO}_4$ . GC analysis showed only the reduced product hexanol and unreacted 2-heptanone in a total yield of 99.5%.

### References and Notes

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