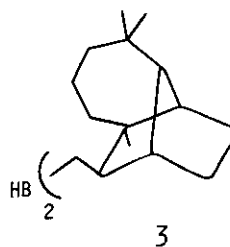
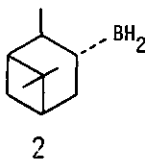
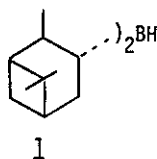


LIMONYLBORANE: THE FIRST BORABICYCLANE AS A CHIRAL HYDROBORATING AGENT[†]Prabhakar K. Jadhav^{*} and Surendra U. Kulkarni

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Abstract - The first bicyclic chiral hydroborating agent, limonylborane (LimBH) has been prepared via the cyclic hydroboration of (+)-limonene with monochloroborane, followed by hydridation with LiAlH_4 . Hydroboration of representative alkenes with LimBH proceeds with a high degree of asymmetric induction, preferentially from one enantiotopic face of the alkene, to provide products of the same absolute configuration.

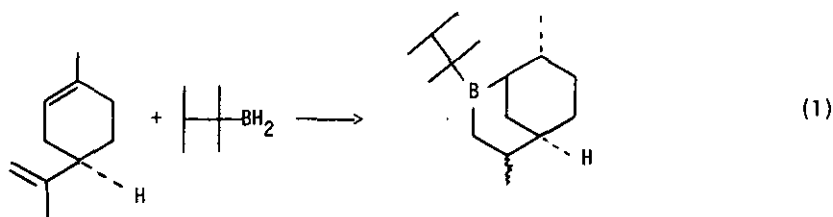
The discovery of the first chiral hydroborating agent, diisopinocampheylborane¹ (Ipc_2BH , 1), by Brown and Zweifel twenty years ago marked the beginning of a non-enzymatic, practical asymmetric synthesis. Ipc_2BH is exceptionally effective for *cis* disubstituted alkenes, achieving asymmetric hydroboration as high as 98.4% with *cis*-2-butene.² Later, the developments of new reagents and procedures enabled the preparation of the first chiral monoalkylborane, monoisopinocampheylborane³ (IpcBH_2 , 2). It achieves remarkable asymmetric induction in the hydroboration of *trans*⁴ and trisubstituted olefins.^{3,5} More recently, dilongifolylborane⁶ (Lgf_2BH , 3), prepared from (+)-longifolene, has been successfully utilized for asymmetric hydroboration of *cis* and trisubstituted olefins.



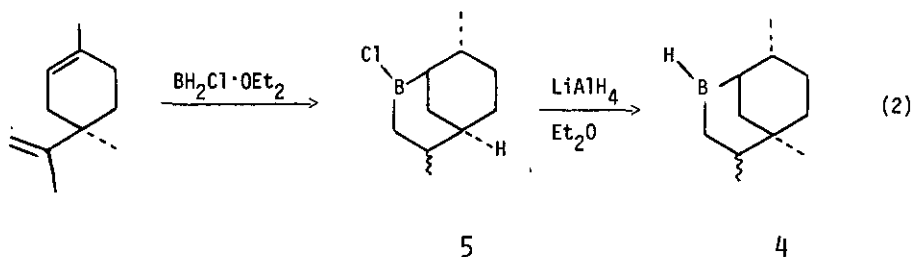
We now wish to report the preparation and hydroboration characteristics of the first bicyclic chiral hydroborating agent, 2-bora-4,8-dimethylbicyclo[3.3.1]nonane (limonylborane, LimBH, 4), from one of the most abundant monoterpenes, (+)-limonene. Cyclic hydroboration of dienes is a versatile tool for the synthesis of boraheterocycles.^{7,8} The reaction of (+)-limonene with borane does not

[†] Dedicated to Professor Herbert C. Brown on the occasion of his 70th birthday.

proceed cleanly in cyclic fashion. However, the monosubstituted hydroborating agent, *thexylborane* (ThxBH_2), leads exclusively to the cyclic hydroboration product⁹ (Eq 1).



For the synthesis of LimBH (4), monochloroborane etherate¹⁰ ($\text{BH}_2\text{Cl}\cdot\text{OEt}_2$) appeared to be an attractive cyclic hydroborating agent. Accordingly, (+)-limonene was treated with $\text{BH}_2\text{Cl}\cdot\text{OEt}_2$. Cyclic hydroboration proceeded smoothly, providing β -chloro-2-bora-4,8-dimethylbicyclo[3.3.1]nonane (LimBCl , 5) in very high yield. Subsequent hydridation¹¹ with LiAlH_4 cleanly afforded the required dialkylborane, LimBH (4) (Eq 2). It exists as the dimer (^{11}B nmr: δ 27, relative to $\text{F}_3\text{B}\cdot\text{OEt}_2$).



The ir absorption at 1560 cm^{-1} is characteristic of exceptionally stable dimers, such as those formed by 9-borabicyclo[3.3.1]nonane.¹²

The new chiral hydroborating agent was applied for the asymmetric hydroboration of representative examples from each of the four major classes of olefins. The reagent was generated *in situ* by the hydridation of LimBCl in the presence of the olefin to be hydroborated. In order to minimize cleavage of ethyl ether, two equivalents of dimethyl sulfide were used during the reaction. The hydridation of LimBCl at -25°C was almost instantaneous. However, hydroboration of 2-methyl-2-butene was complete only after 48 h at -25°C . The resulting trialkylborane (^{11}B nmr: δ 87 relative to $\text{BF}_3\cdot\text{OEt}_2$) was oxidized to provide 3-methyl-2-butanol in 66.5% enantiomeric purity. Hydroboration, followed by oxidation of 1-methylcyclopentene in two different solvents *viz* Et_2O and THF, furnish *trans*-2-methylcyclopentanol in 46% and 45% ee respectively, indicating that there is no solvent bias on the optical purity of the resulting alcohol.

The results of asymmetric hydroboration of representative prochiral olefins are summarized in Table I. The enantiomeric purities of the product alcohols appear to increase with the increase in

Table I. Asymmetric Hydroboration of Representative Prochiral Olefins with Limonylborane (LimBH)

Olefin	Alcohol	Product Alcohols			
		Yield, % (Isolated) ^a	[α] ²³ _D in deg.	% ee	Config.
2-Methyl-1-butene ^b	2-Methyl-1-butanol	75	+ 0.32(neat)	5.2 ^e	R
<i>cis</i> -2-Butene ^b	2-Butanol	78	- 7.4(neat)	55 ^f	R
<i>trans</i> -2-Butene ^b	2-Butanol	75	- 7.9(neat)	58.6 ^f	R
2-Methyl-2-butene ^b	3-Methyl-2-butanol	70	- 3.3(neat)	66.5 ^g	R
1-Methylcyclopentene ^c	<i>trans</i> -2-Methylcyclopentanol	77	-20.4(c 1, CH ₃ OH)	46 ^h	1R,2R
1-Methylcyclopentene ^d	<i>trans</i> -2-Methylcyclopentanol	85	-19.7(c 1, CH ₃ OH)	45 ^h	1R,2R

^a Isolated yields of 95% pure (gc) alcohols.

^b The reactions were carried out at -25°C on 50-mmol scale in Et₂O.

^c The reaction was carried out at 0°C on 25-mmol scale in Et₂O.

^d The reaction was carried out at 0°C on 25-mmol scale in THF. Percent enantiomeric excess based on maximum reported rotations (e + h).

^e F. C. Whitmore and J. H. Olewine, *J. Am. Chem. Soc.*, 1938, 60, 2569 report [α]²⁷_D -5.9° for 2-methyl-1-butanol.

^f P. J. Leroux and H. J. Lucas, *J. Am. Chem. Soc.*, 1951, 73, 41 report [α]²⁵_D -13.5° for 2-butanol.

^g W. A. Sanderson and H. S. Mosher, *J. Am. Chem. Soc.*, 1966, 88, 4185 report α ²⁷_D +8.12° (λ = 2, neat) for 3-methyl-2-butanol.

^h J. J. Partridge, N. K. Chadha and M. R. Uskoković, *J. Am. Chem. Soc.*, 1973, 95, 532 report [α]²⁵_D +43.9° (c 1, CH₃OH) for *trans*-2-methylcyclopentanol.

the steric requirements of olefins with the exception of 1-methylcyclopentene. Unfortunately, it is not clear at this time why the result realized with 1-methylcyclopentene is less favorable than that with 2-methyl-2-butene, although the steric requirement of the former should be greater than that of the latter. It is interesting to note that the asymmetric induction in the hydroboration of both *cis*-2-butene and *trans*-2-butene is good and comparable, 55% and 58.6% respectively, in contrast to the chiral hydroborating agents known¹³ thus far, which give excellent results only with *cis*-2-

butene (Ipc₂BH and Lgf₂BH) or only with trans-2-butene (IpcBH₂). Both of the enantiomers of limonene are readily available. Consequently, chiral centers of opposite configuration can be generated using LimBH derived from the appropriate-antipode of limonene.

The experimental procedure follows. All operations were carried out under nitrogen.¹⁴ To a solution of BH₂Cl·OEt₂ in Et₂O (440 mmol, 1.1 M solution) taken in a 1-l flask was slowly added limonene [α]²³D +120° (c 1, CH₃OH) (440 mmol, 70.5 ml) at 0°C with stirring. In 3 h at 0°C, hydroboration was complete. The solvent was removed and the residue was distilled under reduced pressure to provide LimBCl (5), a colorless liquid, 52 g (71% yield) bp 68-70°C/0.6 mm, ¹¹B nmr δ 79. To LimBCl (50 mmol, 9.23 g) at 0°C was added slowly with stirring dimethyl sulfide (100 mmol, 6.21 g) followed by 2-methyl-2-butene (50 mmol, 3.5 g) in 250 ml flask. It was then cooled to -25°C and treated with ethyl ether solution of LiAlH₄ (12.5 mmol, 52.3 ml, 0.239 M). The hydroboration was complete after 48 h at -25°C. The organoborane was oxidized by the successive addition of methanol (2 ml), 3 M sodium hydroxide (36.6 ml) and 30% H₂O₂ (48 ml). The reaction mixture was refluxed for 1 h, cooled and extracted with ethyl ether (3 x 25 ml). The residue after removal of solvent was fractionally distilled to provide 3.1 g (70% yield) of 3-methyl-2-butanol (> 96% gc purity) bp 110-112°/745 mm. It was further purified by preparative gas chromatography using a 10% Carbowax 20M column: [α]²³D -3.3 (neat), 66.5% ee.

In conclusion, the first bicyclic chiral hydroborating agent achieves a high degree of asymmetric induction in the hydroboration of cis, trans and trisubstituted alkenes. Unfortunately, like other chiral hydroborating agents,¹³ this reagent remained unsuccessful in achieving good asymmetric induction in the case of 2-methyl-1-butene. The reagent preferentially attacks from one enantiotopic face of the alkene to provide alcohols of the same absolute configuration in all cases studied. With the present knowledge of hydridation, it may be now possible to prepare chiral hydroborating agents which otherwise are not accessible by direct methods.

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