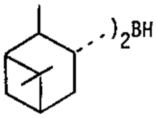
LIMONYLBORANE: THE FIRST BORABICYCLANE AS A CHIRAL HYDROBORATING AGENT†

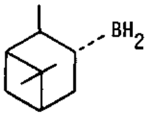
Prabhakar K. Jadhav* and Surendra U. Kulkarni
Department of Chemistry, Purdue University, West Lafayette, Indiana 47907, U.S.A.

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.

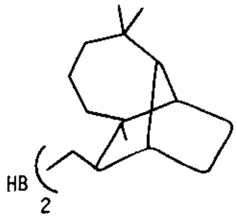
The discovery of the first chiral hydroborating agent, diisopinocampheylborane[1] (Ipc_2BH, 1), by Brown and Zweifel twenty years ago marked the beginning of a non-enzymatic, practical asymmetric synthesis. Ipc_2BH is exceptionally effective for cis disubstituted alkenes, achieving asymmetric hydroboration 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, monoisopinocampheylborane[3] ($IpcBH_2$, 2). It achieves remarkable asymmetric induction in the hydroboration of trans[4] and trisubstituted olefins.[3,5] More recently, dilongifolylborane[6] (Lgf_2BH, 3), prepared from (+)-longifolene, has been successfully utilized for asymmetric hydroboration of cis and trisubstituted olefins.



1



2



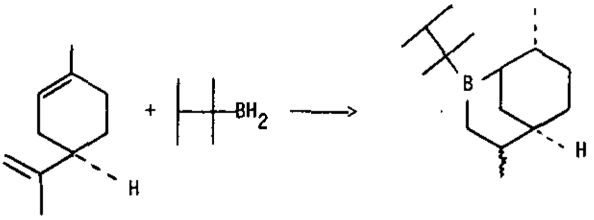
3

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

---

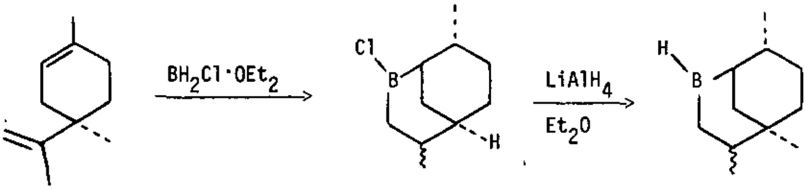
† Dedicated to Professor Herbert C. Brown on the occasion of his 70th birthday.

proceed cleanly in cyclic fashion. However, the monosubstituted hydroborating agent, thexylborane ($ThxBH_2$), leads exclusively to the cyclic hydroboration product[9] (Eq 1).



(1)

For the synthesis of LimBH (4), monochloroborane etherate[10] ($BH_2Cl\cdot OEt_2$) appeared to be an attractive cyclic hydroborating agent. Accordingly, (+)-limonene was treated with $BH_2Cl\cdot OEt_2$. Cyclic hydroboration proceeded smoothly, providing B-chloro-2-bora-4,8-dimethylbicyclo[3.3.1]nonane (LimBCl, 5) in very high yield. Subsequent hydridation[11] with $LiAlH_4$ cleanly afforded the required dialkylborane, LimBH (4) (Eq 2). It exists as the dimer (^{11}B nmr: δ 27, relative to $F_3B\cdot OEt_2$).



(2)

5 4

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 $BF_3\cdot OEt_2$) 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)

	Product Alcohols				
Olefin	Alcohol	Yield, % (Isolated)[a]	$[\alpha]^{23}$D in deg.	% ee	Config.
2-Methyl-1-butene[b]	2-Methyl-1-butanol	75	+ 0.32(neat)	5.2[e]	R
cis-2-Butene[b]	2-Butanol	78	- 7.4(neat)	55[f]	R
trans-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]	*trans*-2-Methylcyclopentanol	77	-20.4(c 1, CH_3OH)	46[h]	1R,2R
1-Methylcyclopentene[d]	*trans*-2-Methylcyclopentanol	85	-19.7(c 1, CH_3OH)	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 Et_2O.

[c] The reaction was carried out at 0°C on 25-mmol scale in Et_2O.

[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 $[\alpha]^{27}$D -5.9° for 2-methyl-1-butanol.

[f] P. J. Leroux and H. J. Lucas, *J. Am. Chem. Soc.*, 1951, **73**, 41 report $[\alpha]^{25}$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° (ℓ = 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 $[\alpha]^{25}$D +43.9° (c 1, CH_3OH) 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 known[13] thus far, which give excellent results only with *cis*-2-

butene (Ipc_2BH and Lgf_2BH) or only with trans-2-butene ($IpcBH_2$). 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 $BH_2Cl \cdot OEt_2$ in Et_2O (440 mmol, 1.1 M solution) taken in a 1-ℓ flask was slowly added limonene $[\alpha]^{23}D$ +120° (c 1, CH_3OH) (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, ^{11}B 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 $LiAlH_4$ (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% H_2O_2 (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: $[\alpha]^{23}D$ -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.

Acknowledgements - The authors are indebted to Professor Herbert C. Brown for providing laboratory facilities, advice and encouragement during this study. Financial support from the National Institutes of Health (grant GM 10937) and Purdue University is gratefully acknowledged.

References

1. H. C. Brown and G. Zweifel, J. Am. Chem. Soc., 1961, 83, 486.
2. H. C. Brown and N. M. Yoon, Israel J. Chem., 1977, 15, 12.
3. H. C. Brown and N. M. Yoon, J. Am. Chem. Soc., 1977, 99, 5514.
4. H. C. Brown and P. K. Jadhav, J. Org. Chem., 1981, 46, 0000.
5. A. K. Mandal, P. K. Jadhav and H. C. Brown, J. Org. Chem., 1980, 45, 3543.
6. P. K. Jadhav and H. C. Brown, J. Org. Chem., 1981, 46, 2988.

7. E. Negishi, S. U. Kulkarni and H. C. Brown, Heterocycles, 1976, 5, 883.

8. H. C. Brown and E. Negishi, Tetrahedron, 1977, 33, 2331.

9. H. C. Brown and C. D. Pfaffenberger, J. Am. Chem. Soc., 1967, 89, 5475.

10. H. C. Brown and N. Ravindran, J. Am. Chem. Soc., 1976, 98, 1785.

11. H. C. Brown and S. U. Kulkarni, J. Organometal. Chem., in press.

12. H. C. Brown and C. F. Lane, Heterocycles, 1977, 7, 453.

13. H. C. Brown, P. K. Jadhav and A. K. Mandal, Tetrahedron, 1981, 37, 0000.

14. For handling of air and moisture sensitive compounds, see 'Organic Syntheses via Boranes,' H. C. Brown, G. W. Kramer, A. B. Levy and M. M. Midland, eds., Wiley-Interscience, New York, 1975, p. 191.

Received, 3rd October, 1981