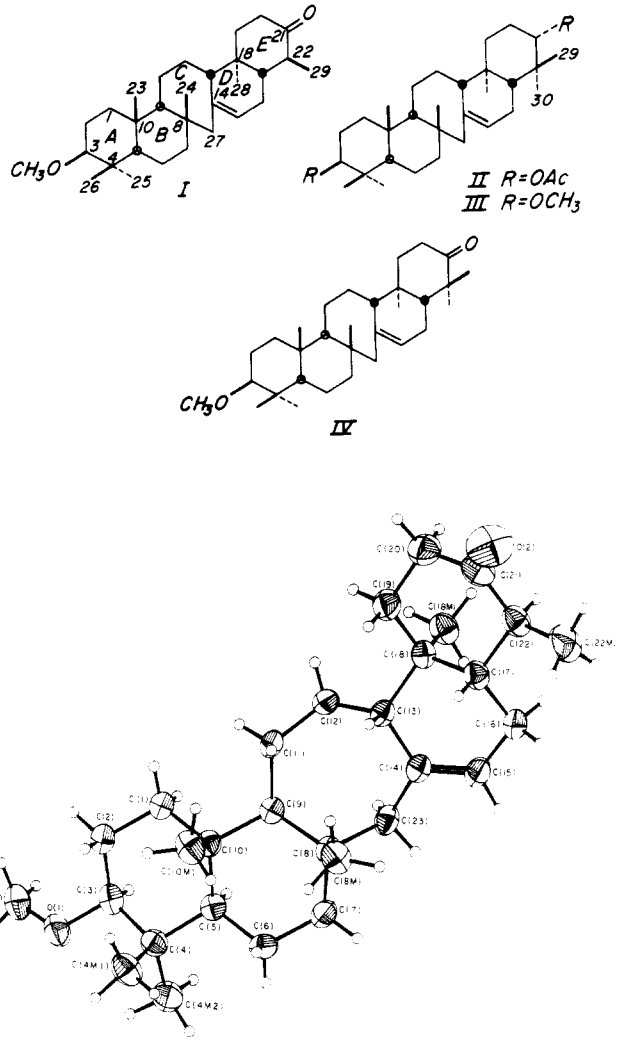


Figure 1. ORTEP diagram of 30-nor-3β-methoxyserrat-14-en-21-one (I) with nonhydrogen atoms shown as thermal vibration ellipsoids at 50% probability and hydrogen atoms shown as spheres of arbitrary size.

nonhydrogen atoms, all 48 hydrogen atoms were located from a difference Fourier synthesis. Final refinement of the structure yielded an R index [$= \sum(|F_{obsd}| - |F_{calcd}|)/\sum|F_{obsd}|$] of 0.037 for 2373 reflections with intensities greater than $1.5\sigma(I)$. An ORTEP[5] drawing of the crystallographic structure is shown in Figure 1. The full details of the X-ray analysis will be published elsewhere.

The 270-MHz ^{1}H NMR spectrum of I clearly shows that the molecule has one secondary methyl (3 H, d, J = 7 Hz) and five tertiary methyls (each 3 H, s) instead of the seven tertiary methyls previously reported from a 60-MHz spectrum.[4] The secondary methyl has the chemical shift (δ 0.97) expected for an equatorial methyl adjacent to a ketone.[6] The chemical shifts for the tertiary methyls of serratenediol diacetate (II) and similar compounds have been assigned.[7] By analogy, the chemical shifts for the tertiary methyls of serratenediol dimethyl ether[8] (III) and hence for the tertiary methyls of 3β-methoxyserrat-14-en-21-one[8] (IV) could be assigned. Table I shows that the chemical shifts for the tertiary methyls of I are similar to those of IV except for the differences expected at C-29 and C-30 due to structural differences. Especially interesting is the slight deshielding of the C-28 hydrogens, which is consistent with a C-21 ketone.

Table I. ^{1}H NMR Chemical Shifts (δ) of Serratene Methyls

methyl	III[a]	IV[a]	I[b]
C-23[c]	0.78	0.81	0.80
C-24[c]	0.83	0.82	0.83
C-25	0.83	0.92	0.90
C-26	0.96	0.95	0.96
C-28	0.68	0.75	0.75
C-29	0.83	1.05	0.97 (d)
C-30	0.96	1.09	

[a] 60 MHz, $CDCl_3$. [b] 270 MHz, $CDCl_3$. [c] Assignments may be interchanged.

Several other western white pine bark triterpenes (compounds A–G)[4] also appear to be serratenes, some of which are apparently closely related to 30-nor-3β-methoxyserrat-14-en-21-one. The structures of these compounds are presently under investigation.

Acknowledgment. We thank Professor Gibbons, Department of Biochemistry, University of Wisconsin—Madison, for the 270-MHz ^{1}H NMR spectrum, and the High Resolution Mass Spectrometry Laboratory, Florida State University, for the mass spectrum. This work was supported in part by the College of Agriculture and Life Sciences, University of Wisconsin—Madison, and the National Institutes of Health (GM-17378). The Forest Products Laboratory is maintained in cooperation with the University of Wisconsin—Madison.

Anthony H. Conner*
USDA, Forest Service
Forest Products Laboratory
Madison, Wisconsin 53705

Tuli P. Haromy, Muttaiya Sundaralingam*
Department of Biochemistry
University of Wisconsin—Madison
Madison, Wisconsin 53706
Received January 29, 1981

(5) Johnson, C. K. ORTEP II. Report ORNL-5138; Oak Ridge National Laboratory: Oak Ridge, TN, 1976.
(6) Iida, T.; Tamura, T.; Miura, N.; Matsumoto, T. *Steroids* **1977**, *29*, 453.
(7) Inubushi, Y.; Hibino, T.; Shingu, T. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1682.
(8) Rowe, J. W.; Bower, C. L. *Tetrahedron Lett.* **1965**, 2745.

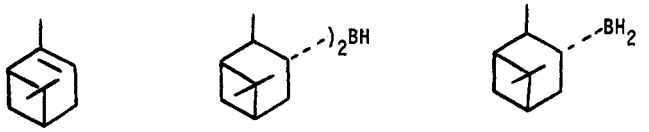
Dilongifolylborane: A New Effective Chiral Hydroborating Agent with Intermediate Steric Requirements

Summary: Dilongifolylborane, Lgf_2BH, a new effective chiral hydroborating agent, is readily synthesized from (+)-longifolene. Thus, treatment of (+)-longifolene with borane–methyl sulfide (BH_3·SMe_2) in ethyl ether rapidly precipitates snow-white crystalline Lgf_2BH: mp 160–161 °C; dimer; IR 1565 cm^{-1}. The new chiral dialkylborane achieves the successful asymmetric hydroboration of cis, trisubstituted acyclic, and trisubstituted cyclic prochiral olefins to provide alcohols, after oxidation of the intermediate organoboranes, with optical purities in the range of 60–78% ee. In the cases studied, the new asymmetric center at the alcohol position is predominantly the R enantiomer.

Sir: The functionality available through hydroboration and subsequent modification of the resulting organoborane is extensive. Monoalkyl- or dialkylboranes exhibit a remarkable stereospecificity and regioselectivity for the hydroboration of olefins. This property, coupled with the

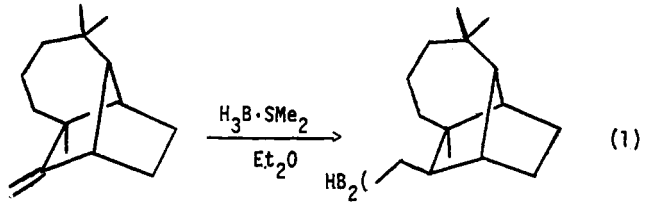
0022-3263/81/1946-2988$01.25/0

capability for asymmetric creation of chiral centers with chiral hydroborating agents, makes this reaction a most valuable one for asymmetric organic synthesis. Optically active α-pinene (1) has been used to prepare such chiral



1 2 3

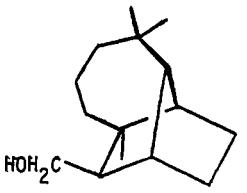
hydroborating agents. At present only two chiral hydroborating agents, viz., diisopinocampheylborane,[1,2] (Ipc_2BH, 2) and isopinocampheylborane,[3,4] ($IpcBH_2$, 3), are available for the conversion of prochiral olefins into chiral products, especially chiral alcohols. The synthesis of other chiral organoboranes using other readily available, optically active, natural products such as terpenes and steroids has remained unexplored. Here we present the synthesis and application of dilongifolylborane (Lgf_2BH, 5), a new chiral hydroborating agent, prepared (eq 1) from the potentially readily available sesquiterpene (+)-longifolene (4; Indian terpentine oil, 5–7%).



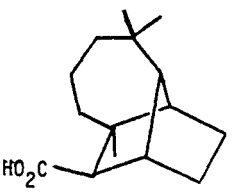
4 5 (1)

High optical purity[5] Ipc_2BH has been used for the asymmetric hydroboration of unhindered cis olefins to obtain alcohols with almost complete asymmetric induction. Unfortunately, the corresponding reactions of this reagent with more hindered trisubstituted olefins such as 2-methyl-2-butene or 1-methyl-1-cyclopentene are sluggish and mechanistically complicated, proceeding with displacement of α-pinene.[6] Moreover, the product alcohols reveal much lower optical purities,[6] in the range of 15–16% enantiomeric excess (ee). To overcome this difficulty, we developed[3,4] isopinocampheylborane ($IpcBH_2$), a less hindered, more reactive reagent. This reagent reacts readily with 2-methyl-2-butene and 1-methyl-1-cyclopentene to give, after oxidation, 3-methyl-2-butanol and *trans*-2-methylcyclopentanol in 52% and 66% ee, respectively.[3] It is an especially favorable chiral hydroborating agent for phenyl-substituted trisubstituted olefins, producing product alcohols in the range of 81–100% ee.[7] However, this reagent gives very low optical yields with relatively unhindered cis olefins, in the range of 20–25% ee.[8]

Consequently, it appeared that a chiral hydroborating agent of intermediate steric requirements might achieve favorable optical induction with both hindered and unhindered olefins. Longifolene (4) appeared to be an attractive substrate for such a reagent: (1) it contains an *exo*-methylene double bond, so that the boron atom would be attached to a primary carbon atom in the hydroborated product as compared to the secondary atom in Ipc_2BH; (2) the large steric requirements should facilitate stopping the hydroboration at the dialkylborane stage; (3) the terpene is readily available.



6



7

Longifolene (4) contains a substituted bicyclo[2.2.1]-heptane moiety, with a large bridge effectively shielding the double bond from the exo face of the molecule. Consequently, hydroboration of (+)-longifolene[9] with diborane occurs exclusively from the less hindered endo side. Longifolol[10] (6) from oxidation of the organoborane has been converted[9] to the known longifolic acid[11] (7).

Hydroboration of (+)-longifolene with borane–methyl sulfide (BH_3·SMe_2) in a 2:1 ratio in refluxing ethyl ether proceeds rapidly to the dialkylborane stage[12] (eq 1). The reaction is complete within 30 min, with snow-white crystals of dilongifolylborane (Lgf_2BH) precipitating from the reaction mixture. The supernatant liquid is removed (double-ended needle),[13] the solid is washed with Et_2O, and traces of residual solvent are removed under vacuum. Alternatively, longifolene is treated with BH_3·SMe_2 (in Et_2O, 2:1 ratio) at 0 °C. After the mixture has been allowed to stand at 25 °C for 24 h, the Lgf_2BH slowly crystallizes out as a large, heavy, shiny flakes. It is especially easy to isolate this product free of solvent.

Dilongifolylborane exhibits a reasonably high melting point, 160–161 °C (sealed, evacuated capillary). The ^{11}B NMR spectrum of the methanolyzed product indicates it to be a dialkylborane (δ 54 relative to Et_2O·BF_3). The IR spectrum (1565 cm^{-1}, Nujol mull) indicates the product to be strongly dimeric. Dilongifolylborane is only sparingly soluble in the common organic solvents, viz., pentane, THF, CCl_4, CH_2Cl_2, or $CHCl_3$. However, the suspended material is capable of achieving hydroboration. Moreover, the disappearance of the solid serves as a convenient indicator to reveal completion of the reaction.

Thus, a suspension of Lgf_2BH in THF readily reacts with *cis*-2-butene (20 °C, 1 h), and the resulting trialkylborane (^{11}B NMR δ 87 relative to Et_2O·BF_3) on oxidation furnishes (−)-(*R*)-2-butanol in very good optical yield: $[\alpha]_D$ −10.54° (neat); 78% ee (compare: Ipc_2BH,[5] 98.4% ee; $IpcBH_2$,[8] 25% ee).

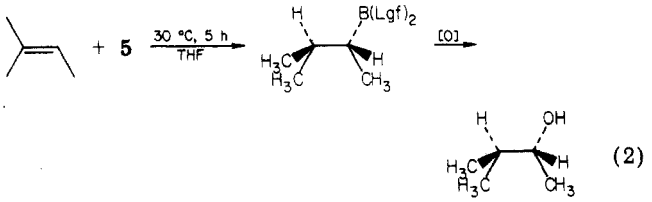
Unlike Ipc_2BH, it reacts smoothly with relatively more hindered tertiary olefins. Thus, hydroboration of 2-methyl-2-butene (trisubstituted acyclic) is complete within 5 h at 30 °C, and the organoborane after oxidation gives (−)-(*R*)-3-methyl-2-butanol (eq 2) in 70% ee (Ipc_2BH,[6] 15% ee; $IpcBH_2$,[3] 52% ee).

(1) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 486.
(2) Brown, H. C.; Ayyangar, N. R.; Zweifel, G. *J. Am. Chem. Soc.* **1964**, *86*, 397.
(3) Brown, H. C.; Yoon, N. M. *J. Am. Chem. Soc.* **1977**, *99*, 5514.
(4) Brown, H. C.; Schwier, J. R.; Singaram, B. *J. Org. Chem.* **1978**, *43*, 4395.
(5) Brown, H. C.; Yoon, N. M. *Isr. J. Chem.* **1977**, *15*, 12.
(6) Brown, H. C.; Ayyangar, N. R.; Zweifel, G. *J. Am. Chem. Soc.* **1964**, *86*, 1071.
(7) Mandal, A. K.; Jadhav, P. K.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 3543.
(8) Mandal, A. K.; Yoon, N. M. *J. Organomet. Chem.* **1978**, *156*, 183.
(9) Lhomme, J.; Ourisson, G. *Tetrahedron* **1968**, *24*, 3167.
(10) The endo epimer of longifolol, isolongifolol, is prepared by reduction of isolongifolic acid.[11]
(11) Nayak, U. R.; Dev, S. *Tetrahedron* **1963**, *19*, 2293.
(12) In one of the experiments, longifolene was treated with BH_3·SMe_2 in a 3:1 ratio, but no trialkylborane formation (^{11}B NMR) was observed.
(13) For handling of air- and moisture-sensitive compounds, see: Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M., Eds. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975; p 191.

Table I. Asymmetric Hydroboration of Representative Prochiral Olefins with Dilongifolylborane (Lgf_2BH)[a]

olefin	product alcohols				
	alcohol	yield, % (isolated)	$[\alpha]_D$, deg	% ee	config
cis-2-butene	2-butanol	71	−10.5 (neat)	78[b]	*R*
cis-3-hexene	3-hexanol	81	−5.1 (neat)	71.2[c]	*R*
2-methyl-2-butene	3-methyl-2-butanol	79	−3.5 (neat)	70[d]	*R*
2-methyl-2-pentene	2-methyl-3-pentanol	76	11.1 (neat)	75[e]	*R*
1-methyl-1-cyclopentene	*trans*-2-methylcyclopentanol	83	−27.6 (*c* 1, CH_3OH)	63[f]	1*R*,2*R*
1-ethyl-1-cyclopentene	*trans*-2-ethylcyclopentanol	81	−29.7 (*c* 5.8, C_2H_5OH)	59.6[g]	1*R*,2*R*[h]

[a] The reactions were carried out on a 50 mmol scale. The percent enantiomeric excess is based on maximum reported rotations (see footnotes *b*–*f*). [b] Leroux, P. J.; Lucas, H. J. *J. Am. Chem. Soc.* **1951**, *73*, 41; $[\alpha]^{25}_D$ −13.5° for 2-butanol. [c] Kenyon, J.; Poplett, R. *J. Chem. Soc.* **1945**, 273; $[\alpha]^{18}_D$ −7.13° for 3-hexanol. [d] Sanderson, W. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1966**, *88*, 4185; α^{27}_D +8.12° (*l* = 2, neat) for 3-methyl-2-butanol. [e] Pickard, R. H.; Kenyon, J. *J. Chem. Soc.* **1912**, *101*, 620; $\alpha^{21.4}_D$ +12.4° (*l* = 1, neat) for 2-methyl-3-pentanol. [f] Partridge, J. J.; Chadha, N. K.; Uskoković, M. R. *J. Am. Chem. Soc.* **1973**, *95*, 532; $[\alpha]^{25}_D$ +43.9° (*c* 1.00, CH_3OH) for *trans*-2-methylcyclopentanol. [g] Determined by 90-MHz NMR by use of the chiral shift reagent tris[[(heptafluoroprop-3-yl)hydroxymethylene]-*d*-camphorato]europium(III) [Eu(hfc)$_3$]. [h] The absolute configuration of *trans*-2-ethylcyclopentanol has not been established. We predict that the (−) isomer is probably 1*R*,2*R*.



(2)

(*R*)-(−), 70% ee

Similarly, 1-methyl-1-cyclopentene (trisubstituted acyclic) with Lgf_2BH gives (−)-(1*R*,2*R*)-*trans*-2-methylcyclopentanol in 63% ee (Ipc_2BH,[6] 16% ee; $IpcBH_2$; 66% ee). Asymmetric hydroboration results for the representative olefins are summarized in Table I.

The following procedure for the preparation of Lgf_2BH and asymmetric hydroboration of 2-methyl-2-butene is representative. With the usual experimental setup,[13] all operations were carried out under nitrogen in a 250-mL flask. The flask was charged with 10.5 mL of borane–methyl sulfide (100 mmol) and 92.7 mL of ethyl ether. It was cooled to 0 °C, and 47.2 mL of (+)-longifolene,[14] $[\alpha]^{25}_D$ +44.2° (*c* 4.6, $CHCl_3$); 42.8 g, 210 mmol) was added dropwise with magnetic stirring. After the mixture was allowed to stand at 25 °C for 24 h, the Lgf_2BH crystallized as heavy snow-white shiny flakes. The supernatant liquid was removed, and the solids were washed with more ethyl ether (3 × 20 mL) and then dried under vacuum (1 h/1 mm) to provide 27.8 g of Lgf_2BH (66%). To the stirred suspension of 21.1 g of dilongifolylborane (50 mmol) in 74 mL of THF in a 250-mL flask fitted with a septum inlet, magnetic stirring bar, and dry ice–acetone condenser connected to a mercury bubbler was added 5.8 mL of 2-methyl-2-butene (55 mmol). The reaction mixture was stirred at 30 °C for 5 h. The solid Lgf_2BH disappeared, and formation of trialkylborane was complete (^{11}B NMR). The organoborane was oxidized[13] by the following procedure. The reaction mixture was treated with 3 M sodium hydroxide (18.3 mL, 55 mmol), followed by dropwise addition of 30% hydrogen peroxide (20 mL, 160 mmol), maintaining the bath temperature below 40 °C. After the mixture was stirred for an additional hour at 55 °C, it was cooled to room temperature and extracted with ethyl ether (3 × 50 mL), and the organic layer was washed with water (30 mL) and brine (30 mL) and dried over anhydrous $MgSO_4$. The dried reaction mixture was distilled through a Widmer column. The distillate, free from longifolol, was then refractionated to give 3.45 g (79%) of 3-methyl-2-butanol (>97% GC purity), bp 111–112 ° (745 mm). It was further purified by preparative gas chromatography using a 10% Carbowax 20M column: n^{20}_D 1.4087 (lit. n^{20}_D 1.4089); $[\alpha]_D$ −3.49° (neat); 70% ee.

From these results (Table I), it appears that the steric requirements of the reagents decrease in the order Ipc_2BH < Lgf_2BH < $IpcBH_2$ and that optimum results in the asymmetric hydroboration are achieved when the steric requirements of the hydroborating agent and the olefin are carefully matched. Among the alcohols obtained by hydroboration with Lgf_2BH so far, the new asymmetric center at the alcohol position is consistently enriched in the *R* enantiomer (the reagent was prepared from (+)-longifolene). The new, optically active dialkylborane is evidently an excellent chiral hydroborating agent for cis, trisubstituted acyclic, and trisubstituted cyclic olefins. It appears to be the best available chiral hydroborating agent for trisubstituted acyclic olefins. The stereochemical results have been consistent and are highly promising for application to configurational assignments and stereochemical correlations.

(14) We are indebted to Dr. U. R. Nayak and Dr. H. R. Sonawane of the National Chemical Laboratory, Poona, India, and to Dr. S. N. Mehra of the Camphor and Allied Products, Bareilly, India, for generous gifts of (+)-longifolene.

(15) Postdoctoral Research Associate on Grant 2R01 GM 10937-14 from the National Institutes of Health.

Prabhakar K. Jadhav,[15] Herbert C. Brown*
Richard B. Wetherill Laboratory
Purdue University
West Lafayette, Indiana 47907
Received February 12, 1981