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CHIRAL SYNTHESIS *VIA* ORGANOBORANES. 26. AN EFFICIENT SYNTHESIS OF ISOPRENYL DERIVATIVES OF BORANE – VALUABLE REAGENTS FOR THE ISOPRENYLBORATION OF ALDEHYDES. A CONVENIENT ROUTE TO BOTH ENANTIOMERS OF IPSENOL AND IPSDIENOL IN HIGH OPTICAL PURITY†

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Abstract: Preparation of *B*-isoprenyldialkylboranes is achieved by adopting the Brandsma modification of the Schlosser procedure, namely metallation of isoprene with potassium 2,2,5,5-tetramethylpiperidide followed by sequential treatment with *B*-methoxydialkylborane and boron trifluoride-etherate. These reagents are used for the convenient isoprenylation of aldehydes. Reaction of isovaleraldehyde and β, β-dimethylacrolein with *B*-2'isoprenyldiisopinocampheylborane provides both ipsenol and ipsdienol, respectively in 65% yields and 96% ee.

The discovery of the hydroboration reaction has led to the creation of an array of versatile organoboranes providing a valuable synthetic tools for organic chemists.[2] Unlike many other organometallic reagents, boron reagents are both well behaved and easily controlled.

Chiral Allyl- and Crotylboration

A most important reaction that we have studied in detail over the past decade is allylboration.[3a] This provides a remarkably simple procedure for the formation of carbon-carbon bonds which has been utilized for a considerable number of organic syntheses.[3] A decade ago R. W. Hoffman designed chiral allylboronates starting from camphor for allylboration of aldehydes.[4] However the enantiomeric excesses (ee) of the product homoallylic alcohols were not satisfactory (45-77% ee). We introduced chiral dialkylallylboranes for the allylboration of aldehydes with considerable success (≥90% ee).[5] The allylborane reagent, *B*-allyldiisopinocampheylborane, **1**, was synthesized by a reaction of either *B*-methoxydiisopinocampheylborane or *B*-chlorodiisopinocampheylborane with allylmagnesium bromide. Using a similar method we synthesized various dialkylallylborane reagents with different chiral auxilliaries as the alkyl group. Differences in enantiomeric excesses in the product homochiral alcohols were observed when the terpenic alkyl groups were varied.[6]

Using a different procedure, we prepared diisopinocampheylmethallylborane, **2** and studied methallylboration reaction.[7] The reagent was prepared by treating *B*-methoxydialkylborane with methallyl lithium. Once again, α-pinene proved successful as the chiral auxilliary in providing 2-methyl-1-alken-4-ols in >90% ee.

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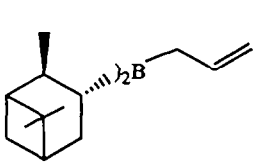
†This paper is dedicated to Professor W. D. Ollis in appreciation of his many outstanding contributions to organic chemistry and to the highly stimulating annual Sheffield Stereochemistry Symposium.



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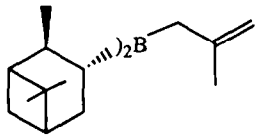

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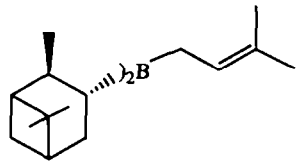
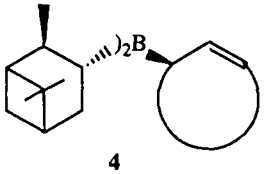


3

Again, by preparing 3,3-dimethylallyldiisopinocampheylborane, **3** and condensing with aldehydes, we obtained 3,3-dimethyl-1-alken-4-ols in >90% ee.[8] This provided a route to prepare "irregular" terpenes with non-head-to-tail union of isoprene units. The reagent **3** was prepared very easily by direct hydroboration of 3-methyl-1,2-butadiene with diisopinocampheylborane. We demonstrated the utility of this reaction for the first asymmetric synthesis of (–)- and (+)-artemesia alcohol, the acyclic monoterpene alcohol isolated from *Artemisia annua L.* and *Artemisia herba-alba*, respectively.[8,9]

We continued our success in various types of allylboration reactions with the synthesis of stereochemically stable allylic boranes such as *B*-2-cycloalken-1-yldiisopinocampheylborane, **4**.[10] We synthesized diastereomerically pure (100% erythro) 1-(2-cycloalkenyl)-1-alkanols in >94% ee using these reagents. The reagent was synthesized by hydroboration of 1, 3-cycloalkadienes with (+)- or (–)-diisopinocampheylborane.

β-methylalkanol units of both *erythro* and *threo* configurations are a characterisitc structural element of numerous macrolide and polyether antibiotics.[11] This aroused our interest in the development of isomerically pure [*E*] and [*Z*]-crotylboranes, **5** and **6**, respectively which could be utilized for crotylboration of aldehydes into pure *threo*- or *erythro*-β-methylhomoallyl alcohols, respectively. Schlosser previously had successfully converted *Z*-butene to *Z*-crotylpotassium by treatment with his reagent pair.[12] He successfully converted this intermediate into [*Z*]-crotyl boronate and cleanly oxidized into pure Z-buten-1-ol. However, application of this procedure to *E*-butene gave only mixtures of [*E*] and [*Z*] crotyl potassium. Fortunately, we discovered that by careful control of the temperature, maintaining at –45 °C during the metallation step, both [*Z*]– and [*E*]-2-butene can be successfully metallated to give pure [*Z*]- and [*E*]-crotylpotassium.[13] This metallated intermediate was then treated with methoxydialkylborane to form the 'ate' complex, followed by liberation of the trialkylborane using BF_3·EE.[14]



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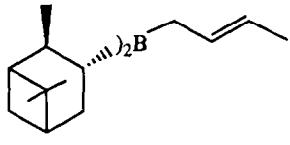

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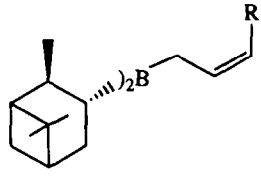


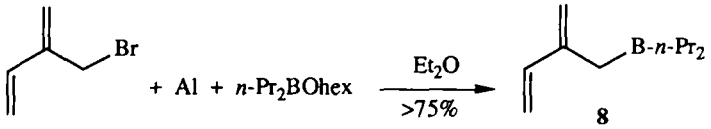
R = Me, **6**
R = OMe, **7**

We synthesized *threo*-β-methoxyhomoallyl alcohols in ≥99% diastereoselectivities and ≥95% enantioselectivities by treating (*Z*)-γ-methoxyallyldiisopinocampheylborane, **7** with aldehydes.[15] This reagent was prepared from *B*-methoxydiisopinocampheylborane and lithiated allyl methyl ether.

Achiral Isoprenylboration

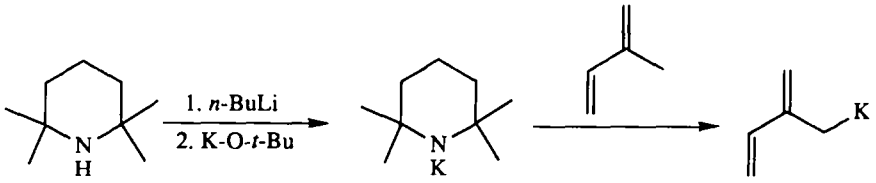
Isoprenylation is an important step encountered in the synthesis of many natural products. Accordingly, searches for a practical procedure for the synthesis of the isoprenyl anion have attracted the attention of many research groups.[16] Several different metal atoms have been used to achieve the incorporation of the isoprene unit

into various molecules. Katzenellenbogen and Lenox prepared isoprenyllithiums by reduction of the corresponding mesitoates with lithium metal in THF at 0 °C.[17] Katzenellenbogen subsequently utilized allyl bromide and magnesium or zinc as another source of the allylic anion.[18] An allylation reaction using allylstannanes in the presence of a Lewis acid, has been described by Sakurai *et. al.*[19] A highly convenient isoprenylation of carbonyl compounds using silyl derivatives has also been described by Sakurai.[20] The isoprenylation of aldehydes with di-*n*-propylisoprenylborane was reported recently by Bubnov and E'tinger.[21] However, synthesis of their reagent, **8** involves the cumbersome preparation of di-*n*-propylhexoxyborane, followed by treatment with 2-bromomethyl-1,3-butadiene and $HgCl_2$-activated aluminum turnings.



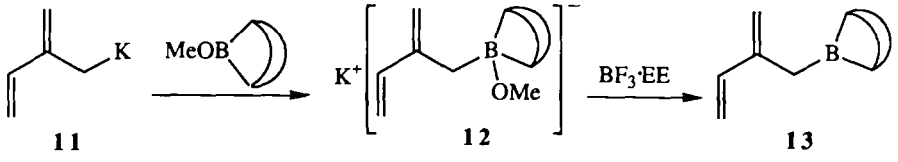
8

We felt that our modified Schlosser procedure, used for the preparation of [*E*]- and [*Z*]-crotylpotassium,[13] could be extended to the preparation of isoprenylpotassium. Unfortunately, our first efforts in this direction failed, confirming similar failures described in the literature.[22] Recently, Brandsma and his coworkers successfully modified the procedure to permit the synthesis of isoprenylpotassium.[23] Application of the Schlosser reaction to 2,2,5,5-tetramethylpiperidine, **9** provides the potassium salt, **10**. The potassium amide, **10** cleanly converts isoprene into the desired isoprenylpotassium, **11**.



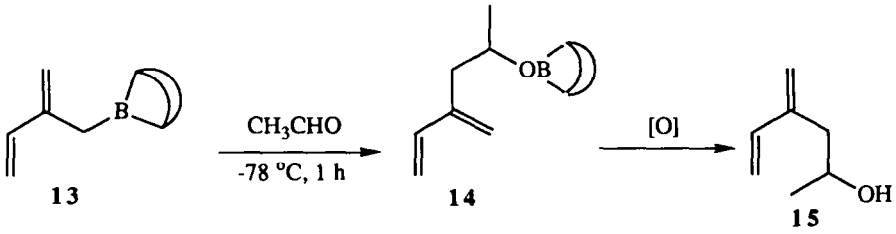
9 **10** **11**

We then tested our standard procedure for converting such potassium derivatives into the desired boron reagents. Treatment of *B*-methoxy-9-borabicyclo[3.3.1]nonane (*B*-OMe-9-BBN) with isoprenylpotassium provided the desired 'ate' complex, **12** (^{11}B NMR: δ 2.5). Addition of a controlled quantity of BF_3·EE gave the desired B-isoprenyl-9-BBN, **13** (^{11}B: δ 78).



11 **12** **13**

The homogeneity of the product was tested by treating it with one equivalent of acetaldehyde at –78 °C. Reaction is practically instantaneous, as shown by the ^{11}B NMR spectrum (δ 54). Typical of allylboranes, **13** reacts with acetaldehyde with allylic rearrangement to provide the borinate intermediate, **14**, presumably *via* a six membered transition state.[6] Oxidation of the intermediate **14** with alkaline hydrogen peroxide, followed by distillation gives the desired isoprenyl derivative, 4-methylene-5-hexene-2-ol, **15** (bp 67-68 °C/19 mmHg) in 65% yield. Its ^1H NMR and ^{13}C NMR are entirely consistant with the structure indicated.

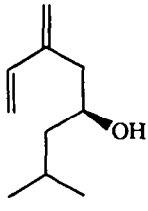


13 14 15

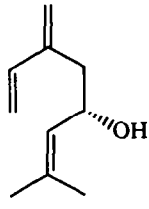
The reliability of the reaction of the reagent **13** with aldehydes was further tested with a number of representative aldehydes of varying steric and electronic environments. Thus, 2-methylpropionaldehyde undergoes condensation with **13** at –78 °C in 1 h to provide 5-methylene-6-hepten-3-ol (bp 90-93 °C/25 mmHg) in 65% yield. Similarly, reaction of **13** with benzaldehyde provides 3-methylene-1-phenyl-4-penten-1-ol (bp 70 °C/1 mmHg) in 60% yield. Table 1 summarizes the results with representative aldehydes isoprenylated with **13**.

Table 1. Isoprenylation of Aldehydes With *B*-2'-Isoprenyl-9-BBN, 13.

aldehyde	product	isolated yield, %	bp, °C/ mmHg	^{1}H NMR
acetaldehyde	4-methylene-5-hexen-2-ol	65	67-68/19	1.2 (3H, d, J = 6 Hz), 2.3 (2H, m), 3.9 (1H, m) 4.8 - 5.3 (4H, m), 6.3 (1H, dd, J = 12 Hz)
2-methyl-propionaldehyde	2-methyl-5-methylene-6-hepten-3-ol	65	90-93/25	0.96 (6H, d, J = 6 Hz), 1.6-2.5 (3H, m), 3.65 (1H, m), 4.9-5.3 (4H, m), 6.3 (1H, dd, J = 12 Hz
benzaldehyde	3-methylene-1-phenyl-4-penten-1-ol	60	70/1	2.8 (2H, m), 4.8 (1H, br t), 5.0-5.4 (4H, m), 6.4 (1H, dd, J =12 Hz), 7.3 (5H, s)
isovaleraldehyde	2-methyl-6-methylene-7-octen-4-ol (ipsenol)	65	92-94/19	0.88 (3H, d, J = 6 Hz), 0.92 (3H, d, J = 6 Hz) 1.2 (2H, m), 1.8 (2H, m), 3.72 (1H, m), 5-5.3 (4H, m 6.3 (1H, dd, J = 12 Hz)
β,β-dimethylacrolein	2-methyl-6-methylene-2,7-octadien-4-ol (ipsdienol)	60	51-54/1.5	1.66 (3H, d, J = 6 Hz), 1.72 (3H, d, J = 6Hz), 2.39 (2H, d, J = 7 Hz), 4.46 (1H, m), 4. 95-5.36 (5H, m), 6.32 (1H, dd, J = 12 Hz)



Ipsenol, **16**



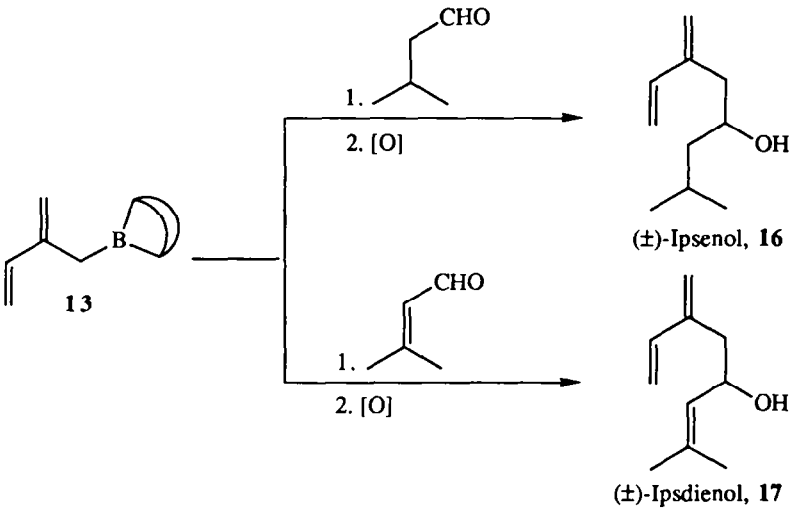
Ipsdienol, **17**

2-Methyl-6-methylene-7-octene-4-ol, ipsenol, **16**, and 2-methyl-6-methylene-2,7-octadien-4-ol, ipsdienol, **17** are two of the aggregation pheromones isolated from the bark beetle *Ips paraconfusus* Lanier whose structures have been elucidated by spectral data and confirmed by synthesis.[24] Skattebol and coworkers synthesized racemic **16** and **17** by the combination of a 6 C fragment, 3-methylene-4-pentenal with the 4 C fragment derived from isobutyl bromide and isobutenyl bromide, respectively *via* the Grignard reagent.[25] Katzenellenbogen and coworkers synthesized achiral **16** and **17** *via* a Reformatsky reaction of 2-bromomethyl-1,3-butadiene with isovaleraldehyde and 3-methyl-2-butenal, respectively.[17] Synthesis of (±)-ipsenol *via* a sulfurated Grignard reagent is described by Cazes and coworkers.[26] Sakurai utilized an isoprenylsilane to synthesize racemic **16** and **17**.[20,27] Krief and Halazy synthesized ipsenol using a selenocyclobutane.[28] Masaki and coworkers synthesized racemic **17** by the

allylic oxidation of the *gem* dimethyl olefin *via* addition of benzenesulfenyl chloride.[29] The most recent synthesis of racemic ipsenol and ipsdienol was reported by Brandsma and coworkers using dilithiated isopropenylacetylene.[30]

Recently, Bubnov had shown[21] the utility of dipropylisoprenylborane for the synthesis of racemic ipsenol, and ipsdienol. We decided to utilize reagent **13** for the synthesis of **16** and **17**. As expected, **13** reacts cleanly with isovaleraldehyde and β, β-dimethylacrolein under the standard conditions (THF/hexane, –78 °C, 1 h) to furnish the corresponding borinate intermediates. These intermediates are oxidized with alkaline hydrogen peroxide to provide a 65% isolated yields of racemic **16** and **17**, repectively (Scheme 1).

Scheme 1



Though many syntheses of racemic ipsenol and ipsdienol are available in the literature,[21, 25-30] it was Mori who first synthesized both of these pheromones in optically active form and assigned their configurations.[31,32] While the natural ipsenol with the *S* configuration is levorotatory,[31] the natural ipsdienol with the *S* configuration is dextrorotatory.[32] Field tests using optically active ipsenol and ipsdienol have been conducted and the pheromonal chirality and integrity of aggregation responses reported.[33] Again, it has been demonstrated that the five-spined engraver beetle, *Ips grandicollis*, aggregates only in response to (*S*)-ipsenol.[34] Ipsenol and ipsdienol constitute aggregation pheromones of the spruce-infesting bark beetle, *Ips typographus* [35]and ipsdienol of unknown configuration and optical purity is present in the population attractant of *Ips sexdentatus*.[36]

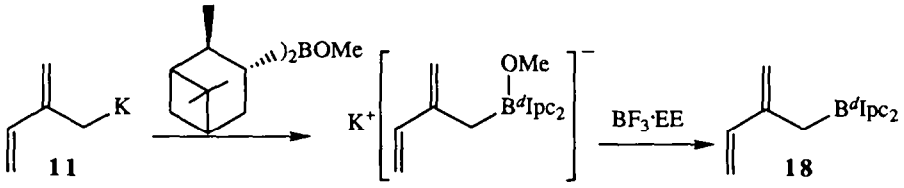
Mori's initial synthesis of ipsenol, starting from leucine, is both lengthy and cumbersome. Moreover, the chemical (~5%) and optical yields (80%) are low.[31a] Later, Mori modified his procedure to obtain optically pure **1** (≥99% ee), but the overall yield still remained low.[31b] Ipsdienol was synthesized by Mori in 38% ee using D-mannitol as the starting substrate.[32a] A synthesis of *S*-(+)-ipsdienol starting from (*R*)-malic acid gave 90% ee for the pheromone.[32b] More enantioselective syntheses have been reported since then. Ohloff and Giersch prepared ipsdienol in 91% ee (*R*) and 80% ee (*S*) from the enantiomers of verbenone *via* the corresponding β-pinene-4-ols.[37] Norin prepared racemic ipsdienol *via* sensitized photooxidation of commercially available myrcene followed by acid catalyzed rearrangement.[38] Oxidation of the *tertiary* alcohol obtained from photooxidation to myrcenone, followed by asymmetric reduction of the carbonyl moiety using Noyori's Binal-H[39] provided both enantiomers of ipsdienol in 63% ee. Modified Binal-H provided ipsdienol of even lower optical purity.[38] Hisashi Yamamoto's condensation of isovaleraldehyde with the tartrate ester of allenyl boronic acid provided the corresponding homopropargylic

alcohol which was further elaborated to the 2-brominated alcohol. Protection of the alcohol as the tetrahydropyranyl ether followed by treatment with the vinyl Grignard reagent and deprotection furnished (–)-ipsenol in >99% ee.[40] Recently, Bubnov reported a chiral synthesis of the enantiomeric pairs of ipsenol and ipsdienol utilizing isoprenylation *via* a boron reagent with tartrate ester as the chiral auxilliary.[41] However, the optical purities of the products were low (46-63% ee).

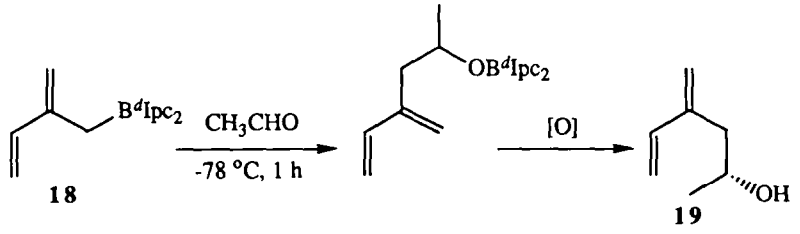
The demonstrated utility of B-2'-isoprenyl-9-borabicyclo[3.3.1]nonane for the isoprenylation of aldehydes, which provided a highly convenient synthesis of racemic ipsenol and ipsdienol in high yields, prompted us to undertake the synthesis of these pheromones in optically active form. As part of our 'Chiral Synthesis *via* Organoboranes' program,[42] we tested the isoprenylation reaction for the synthesis of chiral isoprenyl alcohols.

Chiral Isoprenylboration. Synthesis of Enantiomers of Ipsenol and Ipsdienol.

We have had considerable success employing α-pinene as a chiral ligand[43] which suggested that the isopinocampheyl (Ipc) moiety might prove useful for the isoprenylation reaction also. Using a procedure similar to the one used for the preparation of **13**, the reagents *B*-2'-isoprenyldiisopinocampheylboranes, $^{d\ or\ l}Ipc_2BIpn$,[44] **18** or **20**, respectively are synthesized by the reaction of 2'-isoprenylpotassium, **11** with *B*-methoxydiisopinocampheylborane ($^{d\ or\ l}Ipc_2BOMe$) followed by treatment with BF_3·EE.



Reagent **18**, upon condensation with several representative aldehydes, provides the corresponding chiral homoallylic alcohols. For example, a reaction of **18** with acetaldehyde at –78 °C, for 1 h, provides the borinate which following alkaline hydrogen peroxide oxidation, affords (*R*)-4-methylene-5-hexen-2-ol, **19**, in 65% isolated yield and 90% ee: $\alpha_D^{23} = -19.24^o$ (neat). The ee value was established either by capillary GC examination of diastereomeric α-methoxy-α-trifluoromethylphenylacetates (MTPA)[45] or (–)-menthylchloroformate (MCF) derivatives[46] or by comparison of the observed optical rotation with those reported in the literature. The results are summarized in Table 2.



$\alpha_D^{23} = -19.24^o$ (neat)

90% ee

This synthetic methodology was then applied to the preparation of both enantiomers of the pheromones ipsenol and ipsdienol by reacting the stereoisomers of *B*-2'-isoprenyldiisopinocampheylborane, **18** or **20**, with isovaleraldehyde and β,β-dimethylacrolein, respectively.[47] However, in this case the product alcohols were isolated by a non-oxidative workup: i.e. addition of acetaldehyde to the reaction mixture, converting the borinate intermediate

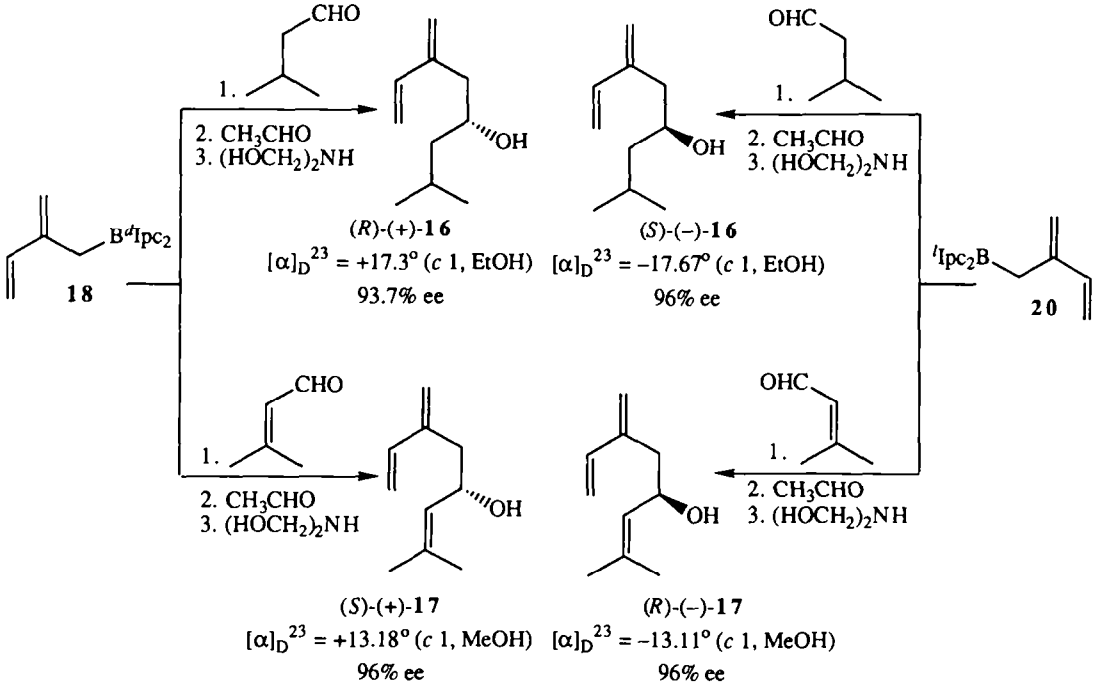
into the corresponding boronate, with simultaneous displacement of α-pinene. Addition of diethanolamine precipitated the boron components and the products were isolated from the filtrate by distillation. (*S*)-(-)-Ipsenol was isolated in 60% yield and in 96% ee while the enantiomer was isolated in 65% yield and in 94% ee. Both isomers of ipsdienol were synthesized in 60% yield and in 96% ee (Scheme 2).

Table 2. Asymmetric Isoprenylation of Representative Aldehydes With $^{d\ or\ l}Ipc_2BIpn$, 18 or 20.

aldehyde	product	yield,[a] %	$[\alpha]_D^{23}$	% ee	confign.
acetaldehyde	(–)-4-methylene-5-hexene-2-ol	65	–19.24° (neat)[b]	90[c]	*R*[d]
2-methyl-propionaldehyde	(–)-2-methyl-5-methylene-6-hepten-3-ol	65	–10.26° (neat)[b]	92[e]	*S*[d]
benzaldehyde	(–)-3-methylene-1-phenyl-4-penten-1-ol	60	–23.56° (*c* 1, MeOH)	93[e]	*S*[d]
isovaleraldehyde	(+)-2-methyl-6-methylene-7-octen-4-ol	60	+17.30° (*c* 1, EtOH)	94[c]	*R*[f]
isovaleraldehyde	(–)-2-methyl-6-methylene-7-octen-4-ol (ipsenol)[g]	65	–17.67° (*c* 1, EtOH)	96[c]	*S*[f]
β,β-dimethylacrolein	(+)-2-methyl-6-methylene-2,7-octadien-4-ol (ipsdienol)	60	+13.18° (*c* 1, MeOH)	96[h]	*S*[i]
β,β-dimethylacrolein	(–)-2-methyl-6-methylene-2,7-octadien-4-ol[g]	60	–13.11° (*c* 1, MeOH)	96[h]	*R*[i]

[a]Isolated yield. [b]Observed rotation. [c]Determined as (–)-MCF derivative on a capillary GC. [d]Based on analogy with entries 4-7. [e]Determined as (*R*)-(+)-α-methoxy-α-(trifluoromethyl)-phenylacetates (MTPA) on a capillary GC. [f]From ref. 31. [g]For the reagent **20**. [h]Determined by comparison with maximum rotation reported: ref. 32b. [i]From ref. 32.

Scheme 2.



Our facile synthesis of both enantiomers of the reagent **18** from inexpensive and readily available substances makes the synthesis of either enantiomers of **16** and **17** very attractive. The entire reaction sequence is carried out in one-pot and scaling up poses no problems. The chemical purity, yield, and optical purity of the products are very high. The chiral auxilliary can be easily recovered and may be recycled. All these make this approach to optically active Ipsenol and Ipsdienol advantageous to the other procedures previously reported.

In conclusion, we have extended our allylboration reaction for the isoprenylation of aldehydes. We have developed an efficient synthesis of *B*-isoprenyldialkylboranes, adopting the Brandsma modification of the Schlosser metallation procedure, namely metallation of isoprene with potassium 2,2,5,5-tetramethylpiperidide followed by sequential treatment with *B*-methoxydialkylborane and boron trifluoride-etherate. Utilizing this methodology we have developed a one-pot synthesis of both enantiomers of the pheromones of the bark beetle *Ips paraconfusus* Lanier, ipsenol and ipsdienol in 96% ee and 65% yields. This asymmetric isoprenylation of aldehydes further indicates the remarkable synthetic utility of chiral organoboranes.

Experimental Section

General Methods. Techniques for handling air-sensitive compounds have been previously described.[48] Spectroscopic measurements (^{1}H and ^{11}B NMR and IR) were made with standard instruments. GC analyses were done on a Varian Aerograph Series 1200 gas chromatograph having a flame ionization detector and integrated with a Hewlett-Packard 3380 S integrator. GC columns, 1/8"x12', were packed with 10% SP-2100 on Chromosorb W (80-100 mesh) or 5% Carbowax 1540 on Chromosorb W (80-100 mesh). Analyses of the MTPA esters or MCF derivatives were performed on a Hewlett-Packard 5890A gas chromatograph using a Supelcowax glass capillary column (15 m), methylsilicone capillary column (50 m) or a SPB-5 capillary column (30 m) at appropriate temperatures and integrated using a Hewlett-Packard 3390A integrator.

Materials. THF was distilled from sodium benzophenone ketyl and stored under nitrogen in an ampule. BMS, 9-BBN, α-pinene, 2,2,5,5-tetramethylpiperidine (TMP), *n*-butyllithium, *t*-BuOK, BF_3·EE, acetaldehyde, 2-methylpropionaldehyde, benzaldehyde, isovaleraldehyde, β,β-dimethylacrolein (3-methyl-2-butenal), α-methoxy-α-trifluromethylphenylacetic acid (MTPA), menthyl chloroformate (MCF) were all obtained from Aldrich Chemical Co. MTPA was converted to the acid chloride using the literature procedure.

The following procedure for the preparation of Ipsenol is representative:

***B*-Isoprenyl-9-BBN, 13:** 2,2,5,5-Tetramethylpiperidine (TMP) (3.5 g, 4.2 mL, 25 mmol) was added at 0 °C to a solution of *n*-butyllithium (10.8 mL of 2.3 *M* solution in hexane, 25 mmol) in a mixture of THF (5.5 mL) and hexane (2.5 mL) contained in a 200 mL round-bottomed flask fitted with a side-arm and connecting tube as usual.[48] After 15 minutes, the solution of LiTMP was cooled to –78 °C and a solution of *t*-BuOK (2.8 g, 25 mmol in 15 mL THF) was added slowly to provide a clear yellow solution of the potassium salt of TMP. Subsequently, isoprene (3.7 mL, 37 mmol) was added slowly to the reaction mixture over a period of five minutes while keeping the temperature of the now red solution between –78 to –60 °C. After completion of the addition, the dry ice-acetone bath was replaced by a $CHCl_3$/liquid nitrogen bath (–60 °C) and stirred for an additional 15 minutes to ensure complete metallation.[23] The potassium salt of isoprene was recooled to –78 °C and 25 mL of a 1 *M* solution of *B*-methoxy-9-BBN in THF was added slowly over a period of five minutes. The ^{11}B NMR spectrum of the mixture showed a singlet at δ 2.5 corresponding to an 'ate' complex. This 'ate' complex was treated with 1.33 equiv of BF_3·EE (4 mL, 33 mmol) at –78 °C (5 min) to provide the isoprenylborane **13** as a thick slurry (^{11}B NMR: δ 78 ppm). This reagent was used as such for isoprenylation of aldehydes.

(±)-2-methyl-6-methylene-7-octen-4-ol, Racemic Ipsenol: Isovaleraldehyde (2.15 g, 2.68 mL, 25 mmol) in ether (6 mL) was added dropwise to a rapidly stirred solution of **13**, maintained at –78 °C. Stirring was continued for 1 h, when the ^{11}B NMR spectrum of an aliquot showed a peak at δ 52 ppm corresponding to a borinate indicating completion of the reaction. The reaction mixture was warmed to room temperature, quenched with methanol and oxidized with alkaline H_2O_2. The usual workup,[48] followed by distillation (bp 92-94 °C/19 mmHg) provided **16**. Yield: 2.5 g, 65%.

Following are the physical properties of the product alcohols from isoprenylation of various aldehydes.

(±)-4-Methylene-5-hexen-2-ol: Yield: 65%. bp 67-68 °C/19 mmHg.
^{1}H NMR: ($CDCl_3$), δ: 1.2 (3H, d, J = 6Hz), 2.3 (2H, m), 3.9 (1H, m), 4.8 - 5.3 (4H, m), 6.3 (1H, dd, J = 12 Hz).
^{13}C NMR: ($CDCl_3$), δ: 22.94, 41.69, 65.96, 114.0, 118.09, 138.59, 143.25

2-methyl-5-methylene-6-hepten-3-ol: Yield: 65%. bp 90-93 °C/25 mmHg.

^{1}H NMR: ($CDCl_3$), δ: 0.96 (6H, d, J = 6 Hz), 1.6-2.5 (3H, m), 3.65 (1H, m), 4.9-5.3 (4H, m), 6.3 (1H, dd, J = 12 Hz). ^{13}C NMR: ($CDCl_3$), δ: 17.58, 18.67, 33.51, 36.8, 74.03, 114.13, 118.21, 138.54, 143.67

3-methylene-1-phenyl-4-penten-1-ol: Yield: 60%. bp 70 °C/1 mmHg.
^{1}H NMR: ($CDCl_3$), δ: 2.8 (2H, m), 4.8 (1H, br t), 5.0-5.4 (4H, m), 6.4 (1H, dd, J = 12 Hz), 7.3 (5H, s)

2-methyl-6-methylene-7-octen-4-ol: Yield: 65%. bp 92-94 °C/19 mmHg.
^{1}H NMR: ($CDCl_3$), δ: 0.88 (3H, d, J = 6 Hz), 0.92 (3H, d, J = 6 Hz), 1.2 (2H, m), 1.8 (2H, m), 3.72 (1H, m), 5.0-5.3 (4H, m), 6.3 (1H, dd, J = 12 Hz). ^{13}C NMR: ($CDCl_3$), δ: 22.26, 23.63, 24.87, 40.79, 46.69, 67.88, 114.59, 118.86, 139.05, 143.7

2-methyl-6-methylene-2,7-octadien-4-ol: Yield: 60%. bp 51-54 °C/1.5 mmHg.
^{1}H NMR: ($CDCl_3$), δ: 1.66 (3H, d, J = 6 Hz), 1.72 (3H, d, J = 6 Hz), 2.39 (2H, d, J = 7 Hz), 4. 46 (1 H, m), 4. 95-5.36 (5H, m), 6.32 (1H, dd, J = 12 Hz). ^{13}C NMR: ($CDCl_3$), δ: 18.52, 25.96, 40.4, 67.05, 114.4, 119.08, 128.18, 135.58, 139.24, 149.3

B-Isoprenyldiisopinocampheylborane, ^{d}Ipc$_2$BIpn, 18: This reagent was prepared using a procedure similar to the one used for the preparation of the achiral reagent **13**. Isoprenylpotassium, **11** (25 mmol) was treated with *B*-methoxydiisopinocampheylborane, prepared from (+)-α-pinene (25 mmol) in THF at –78 °C. ^{11}B NMR showed a singlet at δ 2ppm corresponding to an 'ate' complex. This 'ate' complex was treated with 1.33 equiv of BF_3·EE (4 mL, 33 mmol) at –78 °C (5 min) to provide **18** as a thick slurry. This was used as such for asymmetric isoprenylation of aldehydes.

***(R)*-(+)-2-Methyl-6-methylene-7-octen-4-ol, (+)-Ipsenol, (+)-16:** Isovaleraldehyde (2.15 g, 2.68 mL, 25 mmol) in ether (6 mL) was added dropwise to a rapidly stirred solution of **18**, maintained at –78 °C. Stirring was continued for 1 h, when the ^{11}B NMR spectrum of an aliquot showed a peak at δ 52 ppm corresponding to a borinate indicating completion of the reaction. The reaction mixture was warmed to 0 °C and acetaldehyde (2.1 mL, 37.5 mmol) was added when one equiv of α-pinene was eliminated. ^{11}B NMR showed a peak at δ 32 ppm corresponding to a boronate. THF was substituted with EE and 1.1 equiv of diethanolamine (2.6 mL, 27.5 mmol) was added and stirred for 2 h. The precipitated boron components were filtered and the filtrate was concentrated and distilled (92-94 °C/19 mmHg) to yield 2.3 g (60%) of **16**. $[\alpha]_D$ = +17.3° (*c* 1, MeOH) which corresponds to 93.7% ee. The spectral properties of (+)-**16** were identical to the racemic sample prepared as detailed above.

***(S)*-(+)-2-Methyl-6-methylene-2,7-octadien-4-ol, (+)-Ipsdienol, (+)-17:** β,β-dimethylacrolein (2.15 g, 2.68 mL, 25 mmol) in ether (6 mL) was added dropwise to a rapidly stirred solution of **18**, maintained at –78 °C. Stirring was continued for 1 h, when the ^{11}B NMR spectrum of an aliquot showed a peak at δ 52 ppm corresponding to a borinate indicating completion of the reaction. The reaction mixture was warmed to 0 °C and acetaldehyde (2.1 mL, 37.5 mmol) was added when one equiv of α-pinene was eliminated. ^{11}B NMR showed a peak at δ 32 ppm corresponding to a boronate. THF was substituted with EE and 1.1 equiv of diethanolamine (2.6 mL, 27.5 mmol) was added and stirred for 2 h. The precipitated boron components were filtered and the filtrate was concentrated and distilled (51-54 °C/1.5 mmHg) to yield 2.3 g (60%) of **17**. $[\alpha]_D$ = +13.18° (*c* 1, MeOH) which corresponds to 96% ee. The spectral properties of (+)-**17** were identical to racemic **17** prepared using reagent **13**.

B-Isoprenyldiisopinocampheylborane, ^{l}Ipc$_2$BIpn, 20: This reagent was prepared using a procedure similar to the one used for the preparation of the achiral reagent **18**. *B*-methoxydiisopinocampheylborane, prepared from (-)-α-pinene was used instead of the methoxy derivative prepared form (+)-α-pinene and the same reaction sequence was followed to obtain **20** as a thick slurry. This was used as such for asymmetric isoprenylation of aldehydes.

***(S)*-(–)-2-Methyl-6-methylene-7-octen-4-ol, (–)-Ipsenol, (–)-16:** This isomer of Ipsenol was prepared from **20** using the same reaction sequence used for the preparation of (+)-**16**. bp.92-94 °C/19 mmHg). Yield 2.5 g (65%), $[\alpha]_D$ = –17.67° (*c* 1, MeOH) which corresponds to 96% ee. The spectral properties of (–)-**16** were identical to the racemic sample prepared as reported above.

***(R)*-(–)-2-Methyl-6-methylene-2,7-octadien-4-ol, (–)-Ipsdienol, (–)-17:** This isomer of Ipsdienol was synthesized from **20** using the same reaction sequence as was used for the preparation of (+)-**17**. bp. (51-54 °C/1.5 mmHg). Yield 2.3 g (60%), $[\alpha]_D$ = –13.11° (*c* 1, MeOH) which corresponds to 96% ee. The spectral properties of (–)-**17** were identical to racemic **17** prepared from **13**.

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