extracted with ether (2 × 50 mL). The combined ether extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo, leaving 15 mg of residue which was purified by chromatography using 10 g of silicAR CC-7. Elution with ether–hexane (1:1) afforded 11.8 mg (31%) of compactin (**1**): mp 150–151 °C [lit.[1] mp 152 °C]; R_f 0.50 (ether); $[\alpha]_D$ +291.0° (*c* 0.205, acetone) [lit.[1] $[\alpha]_D^{22}$ + 283° (*c* 0.84, acetone)].

Acknowledgment. This investigation was supported by Public Health Service Research Grant CA 28865 from the National Cancer Institute. We are indebted to Prof. E. H. Goh (Department of Pharmacology, Indiana University) for a generous gift of natural compactin. We thank Dr. M. Ubakata and P. Hipskind for experimental assistance during the early stages of this investigation. The 360-MHz NMR instrument (Nicolet) used in the above studies was purchased in part through funds provided by the National Science Foundation (Grant CHE-81-05004).

Registry No. 1, 73573-88-3; **7**, 73541-95-4; **23**, 84751-39-3; (*E*)-**62**, 84800-51-1; (*Z*)-**62**, 84751-58-6; (±)-**66**, 84751-42-8; **67**, 84751-55-3; **68**, 84799-47-3; **69**, 84751-43-9; **70**, 103530-11-6; **72**, 86030-92-4; **73**, 91312-60-6; **74**, 103456-59-3; **75**, 103438-11-5; **76**, 84751-44-0; **77**, 84751-56-4; **79** (R = CH_3), 84751-45-1; **80** (isomer 1), 103438-13-7; **80** (isomer 2), 103438-14-8; **81**, 103438-15-9; **82**, 84751-57-5; (*E*)-**83**, 84751-46-2; (*Z*)-**83**, 103530-09-2; (*E*)-**84**, 103438-16-0; (*Z*)-**84**, 103530-10-5; **85**, 84751-40-6; **86**, 103438-17-1; **87**, 84751-47-3; **87** (sulfenate), 84751-59-7; **90** (R = H), 84799-48-4; **90** (R = Ac), 103438-18-2; **90** (R = COPh), 84751-48-4; **91**, 84751-49-5; **94**, 84751-51-9; **95**, 84751-50-8; **96**, 84751-52-0; **97**, 84751-53-1; **97** (lactol isomer 1), 103438-19-3; **97** (lactol isomer 2), 103530-60-5; methyl 2,4-dideoxy-3-*O*-methyl-α-D-*erythro*-hexopyranoside, *p*-toluenesulfonate, 103438-12-6; ((trimethylsilyl)propargylidene)triphenylphosphonium bromide, 42134-49-6; 2,2′-dimethyl-2,2′-azopropionitrile, 78-67-1; D-(−)-phenylglycinol, 56613-80-0; 1,8-diazabicyclo[5.4.0]undec-7-ene, 6674-22-2; 2,6-di-*tert*-butyl-4-methylphenol, 128-37-0; (*S*)-2-methylbutyric anhydride, 84131-91-9.

Supplementary Material Available: Experimental details and spectral and analytical data for **25**, **31**, **32**, **34–36**, **38**, **40**, **43**, **44**, **46–50**, **55**, and **56** and spectral data for **1**, **23**, **62**, **69**, **72**, **74–77**, **79–87**, **90**, **91**, and **94–97** (22 pages). Ordering information is given on any current masthead page.

Chiral Synthesis via Organoboranes. 7. Diastereoselective and Enantioselective Synthesis of *erythro*- and *threo*-β-Methylhomoallyl Alcohols via Enantiomeric (*Z*)- and (*E*)-Crotylboranes

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Contribution from the Richard B. Wetherill Laboratory, Purdue University, West Lafayette, Indiana 47907. *Received March 5, 1986*

Abstract: Isomerically pure (*Z*)- and (*E*)-crotylpotassiums have been prepared by metalation of (*Z*)- and (*E*)-2-butene using a modified Schlosser procedure. The enantiomerically pure (*Z*)-crotyldiisopinocampheylboranes **16A** and **16B** have been prepared by employing methoxydiisopinocampheylboranes [**20A** or **20B**, prepared from either (+)- or (−)-α-pinene] and (*Z*)-crotylpotassium (**19**), prepared as indicated above. These enantiomeric (*Z*)-crotylboranes, **16A** and **16B**, the first such derivatives to be synthesized, retain their stereochemical identity under the reaction conditions and have been successfully condensed with various aldehydes, such as acetaldehyde, propionaldehyde, acrolein, and benzaldehyde, in a regioselective and stereoselective manner to yield the corresponding *erythro*-β-methylhomoallyl alcohols in ≥99% diastereoselectivities and ≥95% enantioselectivities. Similarly, the enantiomeric (*E*)-crotyldiisopinocampheylboranes **17A** and **17B** have been prepared from **20A** or **20B** and the pure (*E*)-crotylpotassium (**23**) derived from (*E*)-2-butene. Again, these boranes, **17A** and **17B**, add to representative aldehydes such as acetaldehyde, propionaldehyde, acrolein, and benzaldehyde in a similar fashion to yield the corresponding *threo*-β-methylhomoallyl alcohols in ≥99% diastereoselectivities and 95% enantioselectivities. Further, (*Z*)- and (*E*)-crotyldiisocaranylboranes (**16C** and **17C**) have been prepared and condensed with propionaldehyde to furnish the *erythro*- and *threo*-β-methylhomoallyl alcohols **8B** and **11B**, respectively, in ≥99% diastereoselectivities and improved enantioselectivities (97%).

β-Methylalkanol units of both erythro and threo configurations[2-4] are a characteristic structural element of numerous macrolide and polyether antibiotics.[5] This has aroused interest in the development of new synthetic methods which allow the stereoselective synthesis of β-methylalkanols. Even today there are conspicuous gaps in the registry of organic synthetic methods. Special attention has been given to those reactions in which new carbon–carbon bonds are formed via aldol addition, which constituted one of the fundamental bond constructions in biosynthesis[6,7] (eq 1 and 2). Hence, there has been a renewed interest in the development of stereoregulated aldol and related condensation reactions. Among such condensations are the reactions of allylic organometallic reagents with aldehydes, affording the

(1) Postdoctoral research associate on Grant GM 10937-23 from the National Institutes of Health.

(2) The terms erythro and threo are used in the sense defined by Heathcock.[3] This terminology is used by most of the groups working on aldol-type additions. It should be made clear that this usage is contrary to the rules defined by *Chemical Abstracts* or *Beilstein*.[4]

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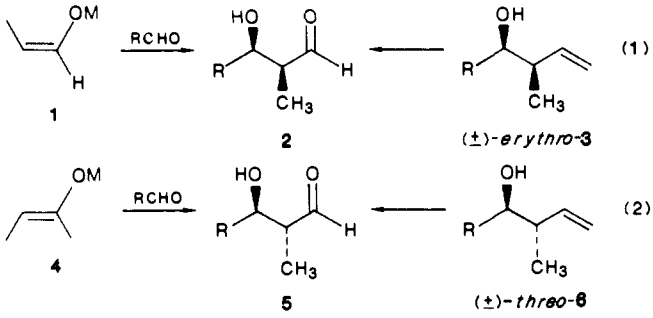
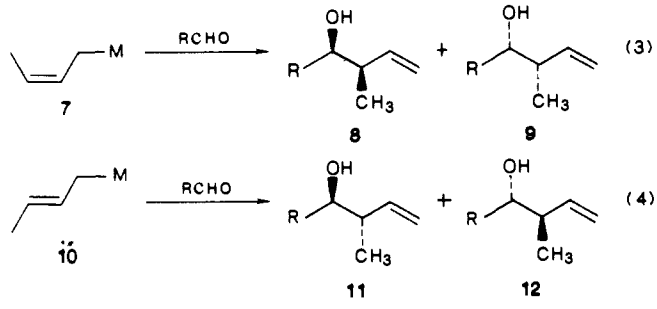


corresponding homoallyl alcohols[8-10] (eq 1 and 2). Reactions of this type have significant advantages over aldol condensations, in that newly formed alkenes may be readily transformed into aldehydes. In addition, the alkenes may be selectively epoxidized, thus readily introducing a third chiral center.

The reactions of crotylmetal reagents with carbonyl compounds are of considerable interest in the context of acyclic stereoselective synthesis of β-methylhomoallyl alcohols.[9d-i,10] This transformation, like the aldol reaction, generates two new stereochemical relationships and potentially four stereoisomeric products (eq 3 and 4). Consequently, there are two significant stereochemical aspects



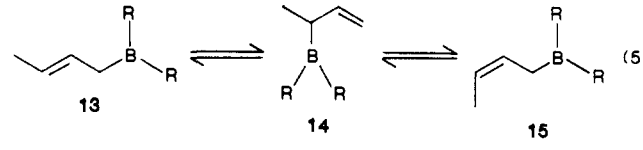
associated with the reaction. The first deals with internal stereochemical control or diastereoselection, **8** + **9** vs. **11** + **12**, and the second deals with absolute stereochemical control for a given diastereomer or enantioselection, **8** vs. **9** or **11** vs. **12**.

Our objective of research in this area required to support applications in natural products chemistry is the development of methodology and/or reagents suitable for synthesis of each diastereomeric relationship with exceptional enantioselectivity. Although considerable effort has been devoted to the elucidation of the stereochemistry of the reaction of crotylmetal compounds with achiral aldehydes, the stereoselectivity which has been achieved in such syntheses has usually been quite low.[9d,h] Hence, the development of new crotyl organometallic reagents possessing high regio- and stereoselectivities remains a desirable goal in organic synthesis.

Useful reagents of this type should fulfill the following conditions: (i) each of the stereoisomeric reagents **7** and **10** should be conveniently available, (ii) the stereoisomeric reagents **7** and **10** should not equilibrate under the reaction conditions required, (iii) each of the reagents **7** and **10** should add to aldehydes stereoselectively and should be irreversible, and (iv) chiral modification of the reagents **7** and **10** should easily be achieved. Of the numerous allylic organometallic reagents that have been considered, the allylboronic esters and allyldialkylboranes appear particularly well suited for applications in acyclic streoselective synthesis.

We discovered that the simple allylic derivatives allyldiisopinocampheylboranes,[11] methallyldiisopinocampheylboranes,[12] (3,3-dimethylallyl)diisopinocampheylboranes,[13] and 2-cyclohexenyldiisopinocampheylboranes[14] are readily synthesized and yield the various homoallylic alcohols on treatment with achiral aldehydes, with exceptionally high optical purities.[15] There was considerable interest in extending such asymmetric synthesis to the enantioselective synthesis of both *erythro*- and *threo*-β-methylhomoallyl alcohols. Indeed, a number of experimental approaches have been reported with only partial success. These include the addition of optically active 2-crotylboron[9g,i,16] or 2-crotylsilane derivatives to aldehydes[17] and the [2,3]-Wittig sigmatropic rearrangement of chiral 2-crotyl ethers.[18] However, these methods involve difficulties in the preparation of enantiomerically pure starting material or incomplete chiral selectivity during the carbon–carbon bond formation.

The *B*-crotyl derivatives generally exist as an interconvertible mixture of isomers which add to aldehyde to afford a mixture of regioisomers. The reason is the fast equilibration of pure (*E*)- and (*Z*)-crotylboron derivatives **13** and **15** via a simple borotropic rearrangement involving the 1-methylallyl compound **14** as an intermediate (eq 5). The rate of isomerization of these inter-



mediate derivatives varies greatly with the nature of the other groups on boron: allyldialkylborane > allylalkylborinate > allylboronate. Further, the rate of reaction with aldehydes varies in the same order.[14] Allyldialkylboranes react readily at −78 °C. The optical purity achieved is considerably greater the lower the reaction temperature. Thus, a major problem in our approach, as compared to use of the more stable but less reactive allylalkylborinate and allylboronate, was the lack of any knowledge about the practical synthesis of isomerically stable (*Z*)- and (*E*)-crotyldiisopinocampheylboranes. Recently, we communicated the successful conversion of (*Z*)- and (*E*)-2-butene into (*Z*)- and (*E*)-crotylpotassium. These derivatives could be converted into optically pure (*Z*)- and (*E*)-crotyldiisopinocampheylboranes (**16A,B** and **17A,B**) at low temperature. These then underwent a successful reaction with acetaldehyde to yield the enantiomeric 3-methyl-4-penten-2-ol in high optical purities.[19] With the success of these initial experiments, we undertook to explore the scope by applying the reaction of the reagents **16A,B** and **17A,B** to representative aldehydes: propionaldehyde, acrolein, and benz-

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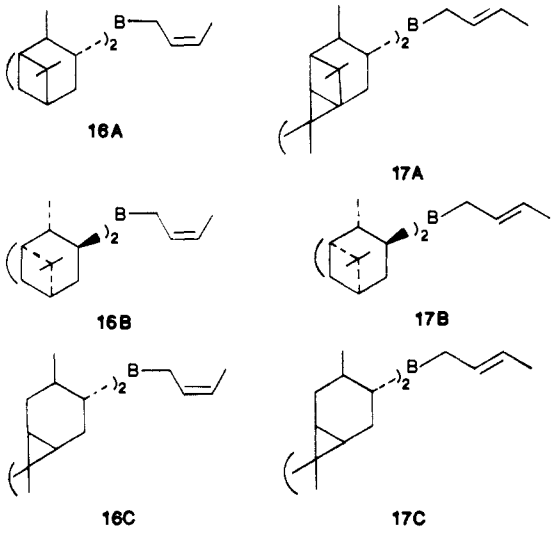
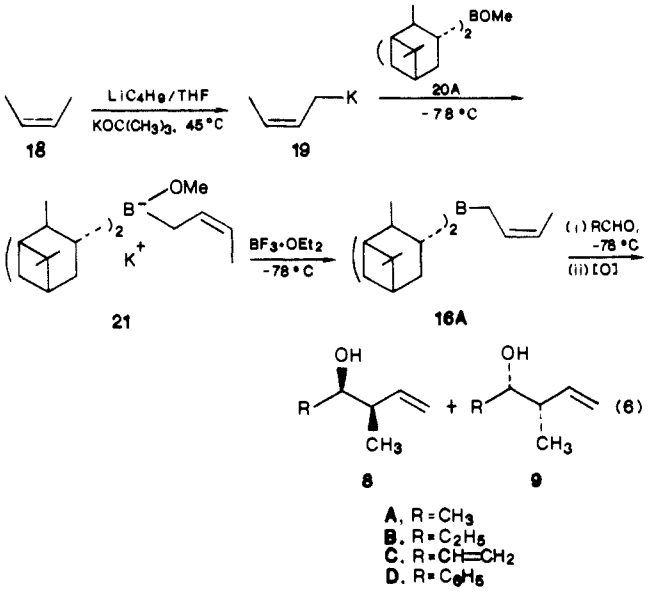


aldehyde, in addition to the acetaldehyde examined previously. We also synthesized and examined (*Z*)- and (*E*)-crotyldiisocaranylboranes (**16C** and **17C**) to see if this synthesis possessed possible advantages in controlling enantioselectivity.

For recent related studies describing the synthesis of the crotylboronates utilizing tartaric esters as the chiral auxiliary and their reactions with ketal derivatives of glyceraldehyde, see W. R. Roush et al.[10a,d]

Results and Discussion

(*Z*)-Crotyldiisopinocampheylboranes (16A and 16B) and Their Reaction with Aldehydes. Preparation of *erythro*-β-Methylhomoallyl Alcohols. Synthetic access to the (*Z*)-crotyldiisopinocampheylborane **16A** was made possible by the principal studies of Schlosser,[20] who converted (*Z*)-2-butene to (*Z*)-2-butenol via crotylboronate. In our procedure, the access to the required reagent, **16A**, was gained via the sequence in eq 6. (*Z*)-2-Butene



was metalated with a mixture of *n*-butyllithium and potassium *tert*-butoxide[21] in THF at −45 °C by using a modification of the Schlosser procedure.[22] The resulting organometallic (*Z*)-crotylpotassium (**19**) was treated with *B*-methoxydiisopinocampheylborane [**20A**, derived from (+)-α-pinene] at −78 °C. The ^{11}B NMR spectrum indicates the formation of the "ate" complex, **21**. It is known that such ate complexes react with 1.33 equiv of boron trifluoride etherate and generate trialkylborane.[23] Hence, the ate complex **21** was treated with boron trifluride etherate, and then the resulting crotyldialkylborane **16A** was immediately treated with acetaldehyde at −78 °C. The reaction mixture, upon the usual workup, furnished *erythro*-3-methyl-4-penten-2-ol (**8A**) with 99% diastereoselectivity and 95% enantioselectivity (Table I). Use of *B*-methoxydiisopinocampheylborane derived from (−)-α-pinene (**20B**) provided enantiomeric *erythro*-3-methyl-4-penten-2-ol (**9A**) in 99% diastereoselectivity and 96% enantioselectivity (Table I).

Furthermore, no difficulty was observed in extending this synthesis to other repesentative aldehydes, such as propionaldehyde, acrolein, and benzaldehyde. In all cases, comparable optical purities and erythro selectivities were realized (Table I).

(*E*)-Crotyldiisopinocampheylboranes (17A and 17B) and Their Reaction with Aldehydes. Preparation of *threo*-β-Methylhomoallyl Alcohols. The same modified Schlosser procedure[22] successfully metalated (*E*)-2-butene (**22**) at −45 °C (eq 7). The resulting organometallic, (*E*)-crotylpotassium (**23**), was treated with *B*-methoxydiisopinocampheylborane (**20A**)[15] at −78 °C. The resulting ate complex, **24**, was treated with 1.33 equiv of boron trifluoride etherate, and the resulting crotyldialkylborane, **17A**, was immediately treated with acetaldehyde at −78 °C. The reaction mixture, upon the usual workup, furnished *threo*-3-

Table I. Preparation of *erythro*-β-Methylhomoallyl Alcohols[a] **8** and **9**

precursor of (*Z*)-crotylborane reagent	aldehyde (RCHO)	*erythro*-alcohols[b] yield, %	R[c]	8:9
(+)-α-pinene	CH_3CHO	75	A	95:5
(−)-α-pinene	CH_3CHO	72	A	4:96
(+)-α-pinene	C_2H_5CHO	70	B	95:5
(−)-α-pinene	C_2H_5CHO	78	B	4:96
(+)-α-pinene	CH_2=$CHCHO$	63	C	95:5
(+)-α-pinene	C_6H_5CHO	72	D	94:6[d]
(+)-Δ^3-carene	C_2H_5CHO	75	B	97:3

[a] Diastereomeric ratios were determined by capillary GC analysis of the alcohols using a Supelcowax 10 column, 15 M × 0.25 mm. In the benzaldehyde condensation product, the diastereomeric ratios were determined by capillary GC analysis of the alcohol using a methylsilicon column, 50 M × 0.25 mm. [b] Enantiomeric ratios were determined by GC analysis of the α-methoxy-α-(trifluoromethyl)phenylacetic acid esters of the alcohols using a methylsilicon column, 50 M × 0.25 mm. [c] See eq 6 and 8. [d] Enantiomeric ratios were determined by GC analysis of the α-methoxy-α-(trifluoromethyl)phenylacetic acid ester of the alcohol using a Supelcowax 10 column, 15 M × 0.25 mm.

Table II. Preparation of *threo*-β-Methylhomoallyl Alcohols[a] **11** and **12**

precursor of (*E*)-crotylborane reagent	aldehyde (RCHO)	*threo*-alcohol[b] yield, %	R[c]	11:12
(+)-α-pinene	CH_3CHO	78	A	95:5
(−)-α-pinene	CH_3CHO	76	A	4:96
(+)-α-pinene	C_2H_5CHO	70	B	95:5
(−)-α-pinene	C_2H_5CHO	69	B	4:96
(+)-α-pinene	CH_2=$CHCHO$	65	C	95:5
(+)-α-pinene	C_6H_5CHO	79	D	94:6[d]
(+)-Δ^3-carene	C_2H_5CHO	79	B	97:3

[a] Diastereomeric ratios were determined by capillary GC analysis of the alcohols using a Supelcowax 10 column, 15 M × 0.25 mm. In the benzaldehyde condensation product, the diasteromeric ratios were determined by capillary GC analysis of the alcohol using a methylsilicon column, 50 M × 0.25 mm. [b] Enantiomeric ratios were determined by GC analysis of the α-methyl-α-(trifluoromethyl)phenylacetic acid esters of the alcohols using a methylsilicon column, 50 M × 0.25 mm. [c] See eq 7 and 9. [d] Enantiomeric ratios were determined by GC analysis of the α-methyl-α-(trifluoromethyl)phenylacetic acid ester of the alcohol using a Supelcowax 10 column, 15 M × 0.25 mm.

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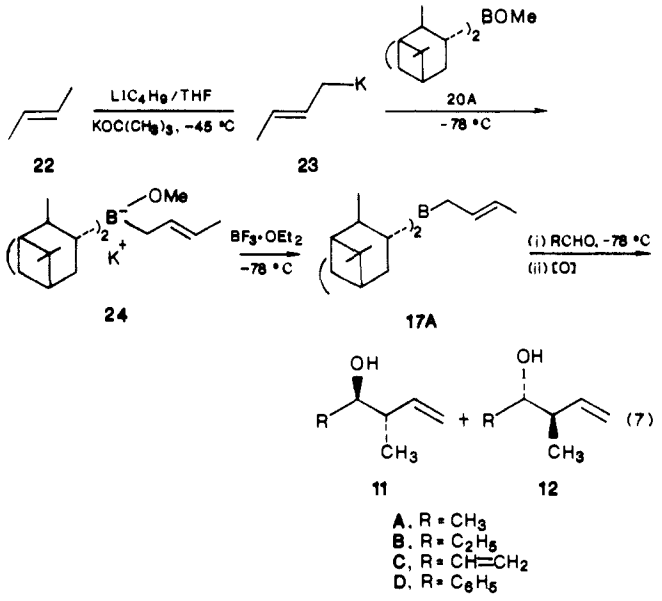


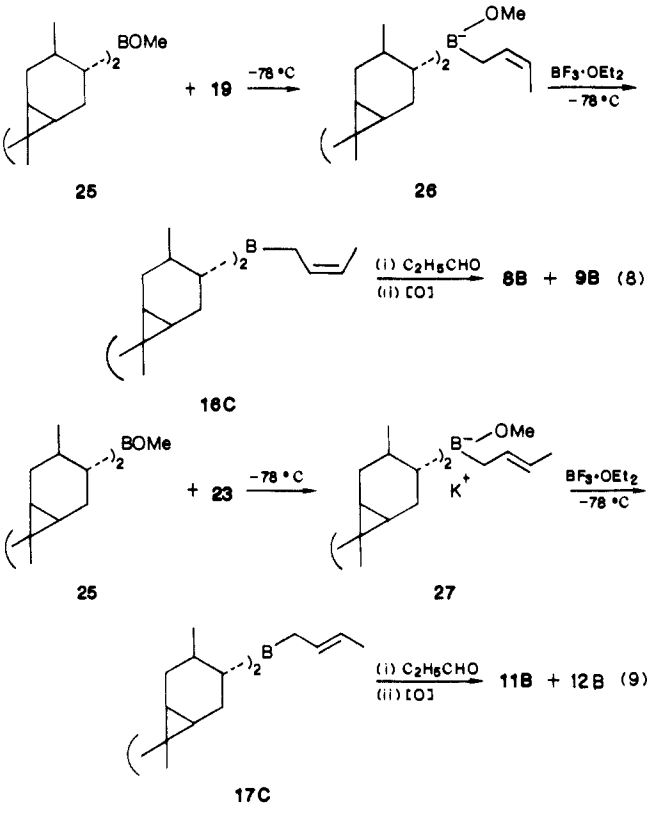
methyl-4-penten-2-ol (**11A**) with ≥99% diastereoselectivity and 95% enantioselectivity (Table II). Use of *B*-methoxydiisopinocampheylborane derived from (−)-α-pinene (**20B**), provided enantiomeric *threo*-3-methyl-4-penten-2-ol (**12A**) in ≥99% diastereoselectivity and 96% enantioselectivity (Table II).

Again, no difficulty was observed in extending the synthesis to other representative aldehydes, such as propionaldehyde, acrolein, and benzaldehyde. In all cases, comparable optical purities and threo selectivities were realized. The results are summarized in Table II.

Enantiomeric (*Z*)- and (*E*)-Crotyldiisocaranylboranes (16C and 17C) and Their Reaction with Propionaldehyde. Recently we have reported that *B*-allyldiisocaranylborane undergoes condensation with some aldehydes of different steric requirements to furnish secondary homoallylic alcohols, with improved enantiomeric purities approaching 100%.[24] In order to see if we could improve upon the enantioselectivities in the preparation of *erythro*- and *threo*-β-methylhomoallylic alcohols, we undertook the preparation of **16C** and **17C**. Indeed, we could prepare the reagents **16C** and **17C** without difficulty by following a procedure similar to that used to prepare the reagents **16A** and **17A** (eq 8 and 9). The condensation of **16C** and **17C** with propionaldehyde provided **8B** and **11B**, respectively, in ≤99% diastereoselectivities and 97% enantioselectivities (Tables I and II).

It is clear from the results that reagents **16** and **17**, the first such derivatives to be synthesized, retain their stereochemical identity under the reaction conditions and successfully add to aldehydes in a regioselective and stereoselective manner to yield the *erythro*- and *threo*-β-methylhomoallyl alcohols in very high diastereoselectivities and enantioselectivities. Further, the stereochemistry at the two asymmetric centers existing in the β-methylhomoallyl alcohols can be controlled simply by selecting the appropriate chiral ligands.

Although it was not a primary objective of this study to examine the mechanism, it seems clear that these asymmetric crotylborations of aldehydes must proceed via an initial complexation of the carbonyl oxygen with boron, followed by transfer of the crotyl group from boron to the carbonyl carbon by a mechanism involving a six-membered transition state.[9d] In the allylboration of aldehydes, we postulated that, depending on the nature of α-pinene [(+) or (−)], one of the two possible six-memebered transition states (**28** and **29**, Figure 1) predominates, determined by the geometry of the asymmetric isopinocampheyl group, and decides the absolute configuration of the product alcohols.[24] On the other hand, the crotyl system has one extra methyl group. Consequently, there will be eight possible transition states, only four of which (**30–33**) will predominate, determined by the geometry of the isopinocampheyl groups (Figure 2). These four transition states lead to the four different diastereomeric products realized in this study.



In conclusion, this one-pot synthesis of enantiomeric β-methylhomoallylic alcohols is operationally very simple, making use of readily available chemicals and providing access to all four possible stereoisomers by simply selecting either (*E*)- or (*Z*)-2-butene and the proper antipode of α-pinene for the preparation of the reagents. Further, it demonstrates the superior chiral-directing property of the 3-pinanyl and 3-caranyl groups in asymmetric synthesis. Reagents **16** and **17** are the most highly enantioselective and diastereoselective crotyldialkylborane reagents reported to date. Extension of this study to other classes of reactions, including chiral aldehydes, is in progress and will be reported in due course of time.

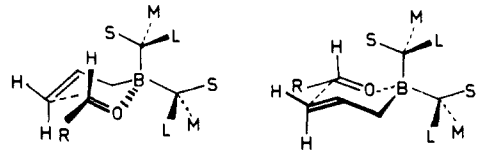
Experimental Section

General. The reaction flasks and other glass equipment were dried in an oven (140 °C, 12–18 h) and assembled in a stream of dry nitrogen gas. All reactions were carried out under an atmosphere of nitrogen. Special experimental techniques used in handling air-sensitive materials are described in detail elsewhere.[25] Tetrahydrofuran (THF) was distilled over benzophenone ketyl and stored under nitrogen atmosphere in an ampule. Aldehydes (Aldrich) were used as received. ^{11}B NMR spectra were recorded by using a Varian FT-80A instrument. The chemical shifts are in δ relative to $BF_3 \cdot OEt_2$. ^1H NMR spectra were recorded on either a Varian T-60 (60 MHz) or a Perkin-Elmer R-32 (90 MHz) instrument. ^{13}C NMR spectra were recorded on a Varian FT-80A or XL-200 instrument. GC analysis was carried out with a Hewlett-Packard 5740 chromatograph using (a) a 9-ft × 0.125-in. column packed with 10% Carbowax 20M on Chromosorb W (100–120 mesh) or (b) a 9-ft × 0.125-in. column packed with 10% SE-30 on Chromosorb W (100–120 mesh). Homoallylic alcohols were purified to 100% GC pure by preparative GC using either (a) a 6-ft × 0.5-in. column packed with 20% Carbowax W (60–80 mesh) or (b) a 6-ft × 0.5-in. column packed with 20% SP-2100 on Chromosorb W (60–80 mesh).

Optical Purity Determination. Diastereomeric ratios were determined by capillary GC analysis using the columns (a) Supelcowax 10, 15 M × 0.25 mm, or (b) methylsilicon, 50 M × 0.25 mm. Enantiomeric ratios were determined by GC analysis of α-methoxy-α-(trifluoromethyl)-

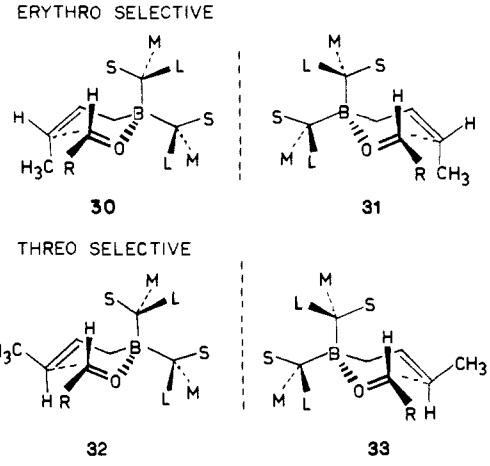
(24) Brown, H. C.; Jadhav, P. K. *J. Org. Chem.* **1984**, *49*, 4089.

(25) For handling air- and moisture-sensitive compounds, see: Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Syntheses via Boranes*; Wiley-Interscience: New York, 1975; p 191.



28 29

Figure 1. Two possible transition states for the reaction of one of the optical isomers of allyldiisopinocampheylborane with aldehydes.



30 31

32 33

Figure 2. Four transition states for the reaction of both possible optical isomers of (*Z*)- and (*E*)-crotyldiisopinocampheylboranes with aldehydes.

phenylacetic acid esters of the alcohols using the columns (a) Supelcowax 10, 15 M × 0.25 mm, or (b) methylsilicon, 50 M × 0.25 mm.

(*Z*)-Crotyldiisopinocampheylborane (16A) and Its Reaction with Aldehydes. *erythro*-β-Methylhomoallyl Alcohols. Typical Procedure. To a stirred mixture of potassium *tert*-butoxide (2.8 g, 25 mmol, dried at 80 °C/0.5 mm for 8 h), THF (7 mL), and *cis*-2-butene (4.5 mL, 50 mmol), *n*-butyllithium in THF (2.3 M, 25 mmol) was added at −78 °C. After complete addition of *n*-butyllithium, the mixture was stirred at −45 °C for 10 min. The resulting solution was recooled to −78 °C, and to it was added dropwise methoxydiisopinocampheylborane in ether [1 M, 30 mmol, derived from (+)-α-pinene, **20A**]. After the reaction mixture was stirred at −78 °C for 30 min, boron trifluoride etherate (4 mL, 33.5 mmol) was added dropwise. Then acetaldehyde (2 mL, 35 mmol) was added dropwise at −78 °C. The mixture was now stirred at −78 °C for 3 h and then treated with 18.3 mL (55 mmol) of 3 N NaOH and 7.5 mL of 30% H_2O_2, and the contents were refluxed for 1 h. The organic layer was separated, washed with water (30 mL) and brine (30 mL), and dried over anhydrous $MgSO_4$. The residue, after removal of the solvent, was carefully fractionated to furnish [2*R*,3*R*]-3-methyl-4-penten-2-ol (**8A**): yield 75%; bp 78 °C/85 mm; erythro selectivity ≥99%, 100% pure erythro material was obtained by preparative GC; enantioselectivity 96%; $[\alpha]^{23}_D$ +19.40° (neat, *l* 0.5); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.85, 19.96, 44.87, 70.78, 115.06, 140.62.

[3*R*,4*R*]-4-Methyl-5-hexen-3-ol (8B): yield 70%; bp 105 °C (bath temperature)/80 mm; $[\alpha]^{23}_D$ +18.60° (neat, *l* 0.5); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 10.42, 14.31, 26.97, 43.30, 76.28, 114.95, 141.36.

[3*R*,4*R*]-4-Methyl-1,5-hexadien-3-ol (8C): yield 63%; bp 110 °C (bath temperature)/85 mm; $[\alpha]^{23}_D$ +27.16° (neat, *l* 0.5); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 15.07, 43.70, 76.25, 115.56, 115.71, 139.03, 140.38.

[1*S*,2*R*]-2-Methyl-1-phenyl-3-buten-1-ol (8D): yield 72%; bp 125 °C (bath temperature/10 mm; ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.31, 44.65, 77.37, 115.28, 126.60, 127.27, 128.00, 140.40, 142.75.

(*E*)-Crotyldiisopinocampheylborane (17A) and Its Reaction with Aldehydes. *threo*-β-Methylhomoallyl Alcohols. Typical Procedure. To a stirred mixture of potassium *tert*-butoxide (2.8 g, 25 mmol, dried at 80 °C/0.5 mm for 8 h), THF (7 mL), and *trans*-2-butene (4.5 mL, 50 mmol), *n*-butyllithium in the THF (2.3 M, 25 mmol) was added at −78 °C. After complete addition of *n*-butyllithium, the mixture was stirred at −45 °C for 10 min. The resulting solution was recooled to −78 °C, and to it was added **20A** (1 M in ether, 30 mmol). After the reaction mixture was stirred at −78 °C for 30 min, boron trifluoride etherate (4 mL, 33.5 mmol) was added dropwise. Then acetaldehyde (35 mmol) was added dropwise at −78 °C. The mixture was then stirred at −78 °C for 4 h and worked out as above to furnish [2*R*,3*S*]-3-methyl-4-penten-2-ol (**11A**): yield 78%; bp 78 °C/85 mm; threo selectivity 96%; $[\alpha]^{23}_D$ +9.141° (neat, *l* 0.5); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 15.72, 19.94, 45.64, 70.72, 115.76, 140.73.

[3*R*,4*S*]-4-Methyl-5-hexen-3-ol (11B): yield 70%; bp 100 °C (bath temperature)/80 mm; $[\alpha]^{23}_D$ +0.620° (neat, *l* 0.5); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 10.10, 16.36, 27.07, 43.72, 76.15, 115.95, 140.52.

[3*R*,4*S*]-4-Methyl-1,5-hexadien-3-ol (11C): yield 65%; bp 110 °C (bath temperature)/85 mm; $[\alpha]^{23}_D$ +7.31° (neat, *l* 0.5); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 15.73, 44.05, 76.53, 115.99, 116.10, 139.22, 140.51.

[1*S*,2*S*]-2-Methyl-1-phenyl-3-buten-1-ol (11D): yield 79%; bp 120 °C (bath temperature)/10 mm; ^{13}C NMR ($CDCl_3$, Me_4Si) δ 16.40, 45.94, 77.82, 116.32, 126.85, 127.51, 128.15, 140.68, 142.65.

***B*-Methoxydiisocaranylborane (25).** A 250-mL flask equipped with a side arm and a magnetic stirring bar was charged with $BH_3{\cdot}SMe_2$ (10 mL, 10 M, 100 mmol) and 90 mL of THF. It was cooled to 0 °C in an ice bath, and Δ^3-carene [37.92 mL, 120 mmol, $[\alpha]^{23}_D$ +14.8° (neat)] was added dropwise with magnetic stirring. The flask was maintained at 0 °C without stirring for 20 h. A white crystalline solid separated out. The optical purity of the diisocaranylborane was upgraded as previously described.[26] The supernatant liquid was removed by a double-ended needle, and the crystals were washed with ice-cold ethyl ether (3 × 25 mL). The solid diisocaranylborane thus obtained was taken up in THF (70 mL), and methanol (8 mL, 200 mmol) was added dropwise at 0 °C. After complete addition of methanol, the reaction mixture was stirred at 0 °C for 2 h or until all of the solid disappeared. Then slowly the reaction mixture was warmed to room temperature and was stirred at 25 °C for 1 h. The solvents were removed under vacuum (14 mmHg, 1 h; 1 mmHg, 12 h). The residue, **25** (68% yield), was dissolved in sufficient anhydrous ethyl ether to make a 1 M standard solution.

(*Z*)-Crotyldiisocaranylborane (16C) and Its Reaction with Propionaldehyde. Preparation of 8B in High Enantiomeric Purities. To the (*Z*)-crotylpotassium (**19**) prepared as above (see the preparation of 16A), **25** in ether (1 M, 30 mmol) was added dropwise at −78 °C. After the reaction mixture was stirred at −78 °C for 30 min, boron trifluoride etherate (4 mL, 35.5 mmol) was added dropwise. Then propionaldehyde (2.16 mL, 30 mmol) was added dropwise. After complete addition of propionaldehyde, the mixture was stirred at −78 °C. The usual alkaline hydrogen peroxide workup (18 mL of 3 N NaOH and 8 mL of 30% H_2O_2) provided **8B** in 78% yield with diastereoselectivities of ≥99% and enantioselectivities of 97%.

(*E*)-Crotyldiisocaranylborane (17C) and Its Reaction with Propionaldehyde. Preparation of 11B in High Enantiomeric Purities. The procedure is very similar to the one used for the preparation of **17A**. (*E*)-Crotylpotassium (**23**), prepared as above, was treated with **25** in ether at −78 °C. Then ate complex **27** was reacted with boron trifluoride etherate, and the resulting crotylborane, **17C**, was immediately condensed with propionaldehyde at −78 °C. The reaction mixture on alkaline hydrogen peroxide workup provided **11B** in 79% yield with ≥99% diastereoselectivities and 97% enantioselectivities.

Acknowledgment. The financial support from the National Institutes of Health (Grant GM 10937-23) is gratefully acknowledged.

(26) Jadhav, P. K.; Vara Prasad, J. V. N.; Brown, H. C. *J. Org. Chem.* **1985**, *50*, 3203.