meric diols, α^{20}_D +14.5°, product **6**, an ethyl ketone like **4**, afforded in 15% yield (3*S*,4*R*)-**14**, oil, α^{20}_D −11.5°. Its absolute configuration is supported by the conversion via isopropylidene derivative and ozonolysis, into the optically pure aldehyde **20**, α^{20}_D +11.9° (lit.[13] −9.8° for the enantiomer). The hydroxy ketone recovered from the production of **14** showed α^{20}_D −22°. The latter material was submitted to the yeast reduction in two subsequent runs to give **14** in ca. 10% and 8% yield, respectively. The unreacted hydroxy ketone recovered at the end of this series of experiments showed α^{20}_D −56° and ^{1}H NMR studies on the material using tris[3-[(trifluoromethyl)-hydroxymethylene)]-(+)-camphorato]europium(III) indicated it to contain ca. 80% of a single enantiomer which we assign the 4*S* configuration depicted in **7**. The significance of the present results is further supported by the fact that the hydroxy ketone **21**, on yeast reduction, afforded ca. 70% yield of the 2*S*,3*R* diol **9** and the threo isomer **22**, α^{20}_D +74°, enantiomer of **11**, in ca. 6:4 ratio and which were separated by SiO_2 chromatography.

In summary, the above results point to the following conclusions. (a) For **1** and **2**, and probably for **5**, hydride addition to the carbonyl occurs on the *re* face regardless of the configuration of the adjacent chiral center. For **3**, **4**, and **6**, however, only the *R* enantiomer is reduced to a significant extent. (b) Hydride addition onto the *si* face of the carbonyl takes place in **21** irrespective of the configuration of the adjacent center. (c) Synthetic hydroxy ketones **1** and **2** are better substrates for the yeast enzymes than **3** and **4**. The first two are intermediates in the conversion of the aldehydes into diols (eq 1), whereas the second two are not formed directly from the corresponding aldehydes by yeast.

From a preparative point of view, the present work provides access to highly functionalized chiral carbonyl compounds like **7**, **15**, **16**, and **20**. Recently,[14] the enantiomer of the aldehyde **20** has been used as starting material in the synthesis of (+)-methynolide. A microbially aided synthesis of the enantiomer of **20** has been reported.[15] Furthermore, via yeast reduction of isomeric materials like **2** and **21**, the two enantiomeric forms **11** and **22** of products of potential synthetic interest for the synthesis of *N*-acyl derivatives of L- and D-vancosamine[16] become available.

Acknowledgment. We thank Farmitalia-C.Erba, Milano, for a grant (to C.Z.). This work has been financially supported by Piano Finalizzato CNR Chimica Fine e Secondaria.

(13) Colvin, E. W.; Robertson, A. D.; Wakhakar, S. *J. Chem. Soc., Chem. Commun.* **1983**, 312.
(14) Nakano, A.; Takimoto, S.; Inanaga, J.; Katsuki, T.; Ouchida, S.; Inoue, K.; Okukado, N.; Yamaguchi, M. *Chem. Lett.* **1979**, 1019.
(15) Hoffmann, R. W.; Ladner, W. *Chem. Ber.* **1983**, *116*, 1631.
(16) Fronza, G.; Fuganti, C.; Grasselli, P.; Pedrocchi-Fantoni, G. *J. Carbohydr. Chem.*, in press.

Claudio Fuganti,* Piero Grasselli, Stefano Servi Franca Spreafico, Carlo Zirotti

Istituto di Chimica del Politecnico Centro del CNR per la Chimica delle Sostanze Organische Naturali, 20133 Milano, Italy

Paolo Casati

DE.BI. (Gruppo ENI) 20060 Cassina de'Pecchi, Italy

Received January 19, 1984

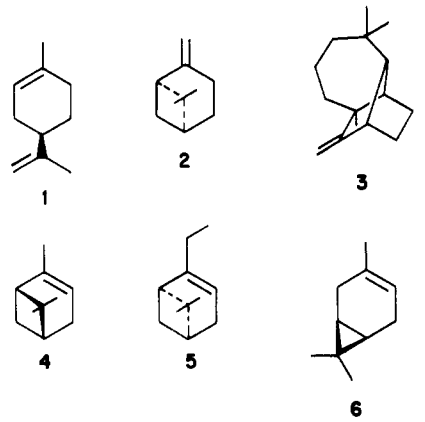
B-Allyldiisocaranylborane: A New, Remarkable Enantioselective Allylborating Agent for Prochiral Aldehydes. Synthesis of Homoallylic Alcohols Approaching 100% Enantiomeric Purities

Summary: *B*-Allyldiisocaranylborane undergoes enantioselective allylboration with a variety of aldehydes to furnish the corresponding homoallylic alcohols in 86–99% enantiomeric purities.

Sir: Several chiral *B*-allyldialkylboranes were prepared from readily available terpene hydrocarbons and treated with acetaldehyde to provide optically active 4-penten-2-ol. Among the various chiral allylboranes studied, *B*-allyldiisocaranylborane proved the most effective chiral allylborating agent. It undergoes condensation with a variety of aldehydes of different steric requirements to furnish secondary homoallylic alcohols with enantiomeric purities approaching 100%.

Homoallylic alcohols are synthetically valuable intermediates that have been used for stereoselective iodocyclization[1] and epoxidation.[2] Recently we reported that homoallylic alcohols with enantiomeric purities in the range of 83–96% are readily prepared by condensation of aldehydes with *B*-allyldiisopinocampheylborane.[3] In order to see if we could improve upon these highly promising results, we undertook exploration of other chiral *B*-allyldialkylboranes and studied the effect of the chiral ligand in this asymmetric allylboration[4] reaction.

B-Allyldialkylboranes were prepared from (+)-limonene (**1**), (−)-β-pinene (**2**), (+)-longifolene (**3**), (+)-α-pinene (**4**), (−)-10-methyl-α-pinene (**5**), and (+)-3-carene (**6**).



The preparation of the *B*-allyldialkylboranes in all these cases, except for (+)-limonene and (−)-β-pinene, is straightforward. Thus the terpene hydrocarbon is hydroborated with borane–methyl sulfide complex (BH_3·SMe_2) to the R_2BH stage, and the resulting dialkylborane is methanolyzed to provide the *B*-methoxydialkylborane. This intermediate, on subsequent treatment with allylmagnesium bromide, provides the desired *B*-allyldialkylborane. In the case of (−)-β-pinene, however, hydroboration with BH_3·SMe_2 cannot be stopped at the di-

(1) (a) Bartlett, P. A.; Jernstedt, K. K. *J. Am. Chem. Soc.* **1977**, *99*, 4829. (b) Bartlett, P. A.; Jernstedt, K. K. *Tetrahedron Lett.* **1980**, *21*, 1607. (c) Cardillo, G.; Orena, M.; Porzi, G.; Sandri, S. *J. Chem. Soc., Chem. Commun.* **1981**, 465. (d) Haslanger, M. F.; Ahmed, S. *J. Org. Chem.* **1981**, *46*, 4808.
(2) Mihelich, E. D.; Daniels, K.; Eickhoff, D. *J. Am. Chem. Soc.* **1981**, *103*, 7690.
(3) Brown, H. C.; Jadhav, P. K. *J. Am. Chem. Soc.* **1983**, *105*, 2092.
(4) For enantioselective allylboration, also see: (a) Herold, T.; Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 768. (b) Herold, T.; Schrott, U.; Hoffmann, R. W. *Chem. Ber.* **1981**, *114*, 359. (c) Hoffmann, R. W.; Herold, T. *Ibid.* 375. (d) Midland, M. M.; Preston, S. B. *J. Am. Chem. Soc.* **1982**, *104*, 2330.

0022-3263/84/1949-4089$01.50/0

Table I. Allylboration of Acetaldehyde with Chiral *B*-Allyldialkylboranes[a]

R_2B-allyl	4-penten-2-ol: % yield (isolated)	$[\alpha]^{23}_D$, deg (*c* 9.18, Et_2O)	% ee[b]	confign
B-allyllimonylborane	72	−0.70	7[c]	*R*
B-allyldi-10-pinanylborane	65	+1.07	11[c]	*S*
B-allyldilongifolylborane	67	+3.34	34[c]	*S*
B-allyldiisopinocampheylborane	74	−9.08	93[d]	*R*
B-allylbis(10-methylisopinocampheyl)borane[e]	72	+9.06	93 (99)[f]	*S*
B-allyldiisocaranylborane	72	−9.75	>99	*R*

[a] (+)-Limonene, $[\alpha]^{23}_D$ +120° (*c* 1, CH_3OH); (−)-β-pinene, $[\alpha]^{23}_D$ −21.1° (neat); (+)-longifolene, $[\alpha]^{23}_D$ +44.2° (*c* 4.6, $CHCl_3$); (−)-10-methyl-α-pinene, $[\alpha]^{23}_D$ −42.2° (neat); (+)-3-carene, $[\alpha]^{23}_D$ +18° (neat) were used to prepare the reagents. [b] The % ee has been determined[3] by ^{19}F NMR of the MTPA esters[8] of the alcohols by using a Varian XL-200 spectrometer. [c] No correction has been made for the enantiomeric purity of the starting terpenes. [d] The result is taken from ref 3. [e] The alkene **5** was readily prepared by reductive detosylation of nopol tosylate with lithium aluminum hydride. [f] Corrected value for enantiomerically pure **5**.

Table II. Allylboration of Aldehydes with *B*-Allyldiisocaranylborane

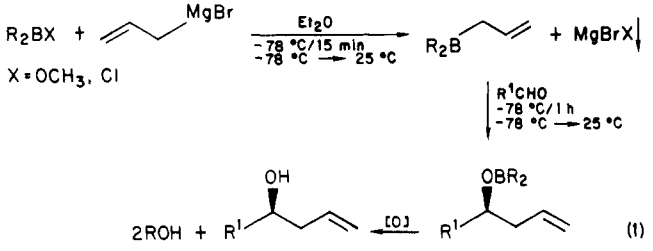
aldehyde	homoallylic alcohols: alcohol	% yield (isolated)	$[\alpha]^{23}_D$, deg	% ee[a,b]	confign
acetaldehyde	4-penten-2-ol[c]	72	−9.75 (*c* 9.16, Et_2O)	>99 (93)	*R*
propionaldehyde	5-hexen-3-ol[c]	76	+5.59 (*c* 10.75, benzene)	91 (86)	*R*
n-butyraldehyde	1-hepten-4-ol	73	+12.74 (*c* 10.21, benzene)	89 (87)	*R*
2-methylpropionaldehyde	2-methyl-5-hexene-3-ol	73	−3.62 (*c* 11.8, benzene)	97 (90)	*S*
2,2-dimethylpropionaldehyde	2,2-dimethyl-5-hexen-3-ol	80	−10.4 (*c* 10.89, benzene)	88 (83)	*S*
acrolein	1,5-hexadien-3-ol	79	+17.84 (*c* 8.57, Et_2O)	86	*S*

[a] The % ee has been determined[3] by ^{19}F NMR of the MTPA esters. [b] Figures in parentheses are % ee of the homoallylic alcohols obtained by using *B*-allyldiisopinocampheylborane.[3] [c] See ref 10.

alkylborane stage. Consequently, it was hydroborated with monochloroborane etherate[5] ($H_2BCl{\cdot}OEt_2$) to provide *B*-chlorodi-10-pinanylborane. This intermediate readily reacts with allylmagnesium bromide to furnish the desired *B*-allyldi-10-pinanylborane. *B*-Chlorolimonylborane was prepared by using the cyclic hydroboration procedure reported earlier[6] and treated with allylmagnesium bromide to provide *B*-allyllimonylborane.

In general, the formation of the allylboranes was indicated by the precipitation of the magnesium salts and confirmed by ^{11}B NMR (δ 78–85).

In all cases, the *B*-allyldialkylboranes were prepared and condensed in situ with acetaldehyde at −78 °C, and the resulting borinates were oxidized[7] with alkaline hydrogen peroxide to provide 4-penten-2-ol (eq 1; $R^1 = CH_3$).



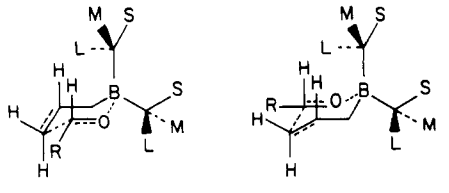
(1)

The results achieved by the asymmetric allylboration of acetaldehyde with various *B*-allyldialkylboranes are summarized in Table I. The results indicate that asymmetric inductions observed with allylboranes derived from **1**, **2**, and **3** are less satisfactory. In the case of allylboranes derived from **4**, **5**, and **6**, the boron atom is directly attached to the chiral center. Apparently this results in exceptionally high enantiomeric purity of the product alcohol.

B-Allyldiisocaranylborane proved to be the most satisfactory reagent among the allylboranes examined thus far, achieving >99% asymmetric synthesis. Consequently, its scope was explored in greater detail. The results are summarized in Table II. In general, higher values of enantiomeric excess are realized compared to *B*-allyldiisopinocampheylborane.[3] Allylboration of acrolein (α,β-unsaturated aldehyde) also occurs with high asymmetric induction (86% ee) in comparison to the literature achievement of only 50% ee.[4c]

The experimental procedure is essentially identical with that reported earlier for *B*-allyldiisopinocampheylborane.[3]

Asymmetric allylboration apparently proceeds via the initial complexation of the carbonyl oxygen with boron, followed by transfer of the allyl group from boron to the carbonyl carbon, involving a six-membered transition state. All the allylboranes, except *B*-allyllimonylborane, are symmetrical and thus presumably involve the same initial aldehyde–borane complex, irrespective of the side of the aldehyde approached by the allylborane. Consequently, the transfer of the allyl group via one of the two possible six-membered transition states (**7** and **8**) decides the absolute configuration of the product alcohol. However, the stereochemical outcome in the case of *B*-allyllimonylborane apparently depends upon both of the above-mentioned steps.



We have now achieved surprising success in these asymmetric syntheses with *B*-allyldiisocaranylborane. We are now in position to establish the full scope of this new synthesis. Hopefully, it will accommodate wide variations in the structure of the allylic moiety.[8]

(5) Brown, H. C.; Ravindran, N. *J. Am. Chem. Soc.* **1972**, *94*, 2112.
(6) Jadhav, P. K.; Kulkarni, S. U. *Heterocycles* **1982**, *18*, 169.
(7) Oxidation of all the borinates formed after allylboration was readily achieved by alkaline hydrogen peroxide in ethyl ether. However, oxidation of the alkoxydicaranylboranes was sluggish in ethyl ether and required the more polar solvent, THF, for complete oxidation.

Acknowledgment. The financial support from the National Institutes of Health is gratefully acknowledged (Grant No. GM 10937-21). We thank Glidden Organics, SCM Corporation, P.O. Box 389, Jacksonville, FL 32201, for a gift sample of (+)-3-carene of high optical purity.

Registry No. 1, 5989-27-5; 2, 18172-67-3; 3, 475-20-7; 4, 7785-70-8; 5, 38359-49-8; 6, 498-15-7; acetaldehyde, 75-07-0; *B*-allyldiisocaranylborane, 92055-65-7; *B*-allylimonylborane, 92055-66-8; *B*-allyldi-10-pinanylborane, 92055-67-9; *B*-allyldilongifolylborane, 92055-68-0; *B*-allyldiisopinocamphenylborane, 85116-38-7; *B*-allylbis(10-methylisopinocamphenyl)borane, 92055-69-1; (*R*)-4-penten-2-ol, 64584-92-5; (*S*)-4-penten-2-ol, 55563-79-6.

(8) For recent success with (3,3-dimethylallyl)diisopinocampheylborane, see: Brown, H. C.; Jadhav, P. K. *Tetrahedron Lett.* **1984**, *25*, 1215.
(9) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, 95, 512.
(10) Additional proofs for % ee and absolute configurations were obtained by catalytic (5% Pt on C) hydrogenation of (−)-4-penten-2-ol and (+)-5-hexen-3-ol to (*R*)-(−)-2-pentanol in 100% ee and (*R*)-(−)-3-hexanol in 93% ee, respectively.
(11) Research associate on Grant 2 R01 GM 10937-21 from the National Institutes of Health.

Herbert C. Brown,* Prabhakar K. Jadhav[11]
Richard B. Wetherill Laboratory
Purdue University
West Lafayette, Indiana 47907
Received May 1, 1984

Stereospecific Synthesis of Metalated Alkoxymethyl Vinyl Ethers

Summary: The thermolysis of substituted bicyclo[2.2.1]hept-5-enes provides expedient access to stannylated vinyl ethers of defined stereochemistry. Alkoxymethyl substitution on the vinyl oxygen is found to significantly improve the hydrolytic stability of several substituted vinyl ethers.

Sir: As part of a program addressing the synthesis of natural products bearing 1,2- and/or 1,3-oxygenation patterns, we sought to establish the utility of the strategy represented in Figure 1 (boxed). Recognizing the problems inherent in stereoselectively generating species I and II without competing β-elimination,[1] we considered equivalent methods of effecting the desired transformations. Following this reasoning, a sequence involving the condensation of the starting aldehyde with a vinyl ether anion (e.g., **1**)[2] to give an adduct (e.g., **2**) which might be transformed into the desired product(s) was explored. An appealing feature of this approach is the possibility of preparing polyols of complimentary stereochemistries from a single intermediate through control over the hydration of the vinyl ether adduct (**2**). Successful implementation of this scheme requires the general availability of metalated vinyl ethers of defined stereochemistry which afford condensation products sufficiently stable to allow subsequent elaboration. This requirement is addressed in the efficient, stereospecific synthesis of metalated vinyl ethers described below.

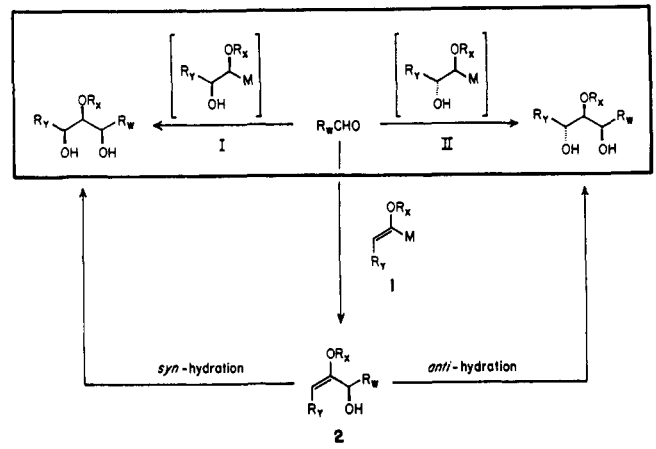


Figure 1.

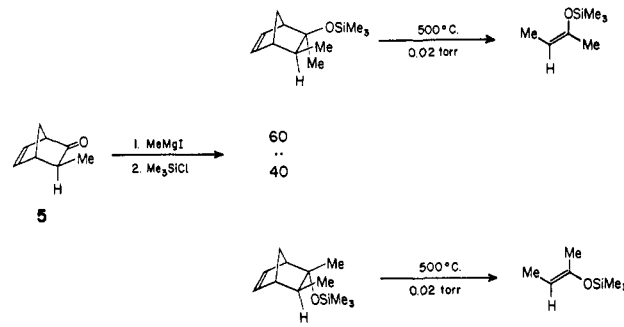


Figure 2.

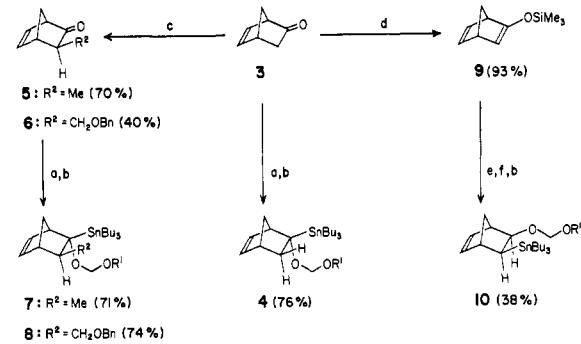


Figure 3. (a) *n*-Bu_3SnLi, THF, −78 °C.[7] (b) R^1OCH_2Cl, Hünig's base, CH_2Cl_2. (c) LDA, THF, −78 °C; MeI or $BnOCH_2I$. (d) LDA, THF, −78 °C; Me_3SiCl. (e) *n*-Bu_3SnH, AIBN, PhMe, Δ. (f) *n*-Bu_4NF, THF.

Our synthetic approach to vinyl ethers was suggested by several observations. First, Rouessac and co-workers reported that the retro-Diels–Alder reaction of silylated bicyclo[2.2.1]hept-5-en-2-ols proceeded to stereospecifically generate silyl enol ethers (Figure 2).[3] Second, related studies in our laboratories indicated that alkoxymethyl substitution on oxygen conferred enhanced stability upon vinyl ethers.[4] Third, tin–lithium exchange has been demonstrated to be an efficient means of preparing lithiated vinyl ethers.[2b,5] It was our hope that analogous tri-*n*-butylstannylated derivatives of alkoxymethyl-protected bicyclic heptenols could be prepared in a highly

(1) Examples which suppress β-elimination: (a) Nájera, C.; Yus, M.; Seebach, D. *Helv. Chim. Acta* **1984**, *67*, 289. (b) Barluenga, J.; Florez, J.; Yus, M. *J. Chem. Soc., Chem. Commun.* **1982**, 1153. (c) Barluenga, J.; Fañanás, F. J.; Villamaña, J.; Yus, M. *J. Org. Chem.* **1982**, *47*, 1560.
(2) Examples of vinyl ether anions: (a) Baldwin, J. E.; Höfle, G. A.; Lever, O. W., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 7125. (b) Wollenberg, R. H.; Albizati, K. R.; Peries, R. *J. Am. Chem. Soc.* **1977**, *99*, 7365. (c) Gould, S. J.; Remillard, B. D. *Tetrahedron Lett.* **1978**, 4353. (d) Boeckman, R. K., Jr.; Bruza, K. J. *J. Org. Chem.* **1979**, *44*, 4781. (e) Boeckman, R. K., Jr.; Bruza, K. J. *Tetrahedron* **1981**, *37*, 3997. (f) Miyata, O.; Schmidt, R. R. *Tetrahedron Lett.* **1982**, *23*, 1793. (g) Smithers, R. H. *J. Org. Chem.* **1983**, *48*, 2095. (h) Russell, C. E.; Hegedus, L. L. *J. Am. Chem. Soc.* **1983**, *105*, 943.
(3) Gringore, O.; Haslouin, J.; Rouessac, F. *Bull. Soc. Chim. Fr.* **1976**, 1523.
(4) McGarvey, G. J.; Kimura, M., unpublished results.
(5) Sonderguist, J. A.; Hsu, G. J.-H. *Organometallics* **1982**, *1*, 830.

0022-3263/84/1949-4091$01.50/0