the plots of log (k_1/k_2) for the two different leaving groups in Figure 3, which have slopes of 0.08 and 0.04 for the phosphorylated pyridines and phosphate esters, respectively. This behavior can be described by the cross-interaction coefficient $p_{xy} = \partial\beta_{nuc}/\partial pK_{lg} = \partial\beta_{lg}/\partial pK_{nuc}$. The values of p_{xy} are 0.023 and 0.013, from the slopes of Figure 3, and the changes in pK_a of the leaving groups of 3.5 and 3.0 for the phosphorylated pyridines and phosphate esters, respectively. These are comparable to previously reported values of $p_{xy} = 0.014$–0.020 for reactions of amines with phosphorylated pyridines but are smaller than a value of $p_{xy} = 0.043$ for reactions of pyridines with phosphate esters, based on data from two different studies (one of which involved only three pyridines).[4,5,8] The small value of p_{xy} for the phosphate esters removes the basis for the suggestion that the structure of the transition state changes more easily for reactions of phosphate esters than for phosphorylated pyridines.[8]

Insufficient data are available to determine whether there is curvature in the Brønsted plots for reactions of quinuclidines with phosphate compounds (Figures 1 and 2). However, the Brønsted plots for reactions of pyridines and primary amines with phosphorylated pyridines and with 2,4-dintrophenyl phosphate are linear within experimental error; there is no curvature over 8 pK units for the reactions of pyridines with 2,4-dinitrophenyl phosphate.[5] The upper limit for curvature in the reactions of pyridines and primary amines with phosphorylated pyridines corresponds to a direct interaction coefficient of $p_x = \partial\beta_{nuc}/-\partial pK_{nuc} \leq 0.006$.[8] This would give a decrease in β_{nuc} of only 0.03 for a 5 unit change in pK_a of the nucleophile between pyridines and quinuclidines, which would decrease β_{nuc} from 0.22 to 0.19 and from 0.17 to 0.14 for the reactions with phosphorylated 4-morpholinopyridine and 3-methoxypyridine, respectively. Thus, there is no significant Hammond effect with changing basicity of the nucleophile and the maximum change in β_{nuc} with increasing basicity would not give a negative value of β_{nuc} for the quinuclidines. Furthermore, the Brønsted line for the reactions of primary amines with phosphorylated 4-morpholinopyridine[8] overlaps the pK range for the quinuclidines that react with this compound. The different classes of amines fall on different straight lines, some of which have different slopes, for reactions with phosphate compounds.[4,5,8]

It may appear surprising that there is a significant change in β_{nuc} with changing pK_a of the *leaving group*, which corresponds to a positive cross coefficient p_{xy}, but no significant curvature in the Brønsted correlations, which means that there is no measurable change in β_{nuc} with changing pK_a of the *nucleophile* and the direct coefficient p_x is ~ 0. However, this behavior is predicted by the expected movements of the transition state parallel and perpendicular to the reaction coordinate, with changing pK_a of the nucleophile and leaving group, on a reaction surface that is defined by the observed structure–reactivity coefficients.[8]

Registry No. 3-Quinuclidinone, 3731-38-2; triethylenediamine, 280-57-9; 3-chloroquinuclidine, 42332-45-6; 3-hydroxyquinuclidine, 1619-34-7; quinuclidine, 100-76-5; triethylenediamine monocation, 33937-19-8; *p*-nitrophenyl phosphate, 36199-67-4; 2,4-dinitrophenyl phosphate, 18962-96-4; calcium 2,4-dinitrophenyl phosphate, 99618-15-2; phosphorylated 4-morpholinopyridine, 26322-06-5; phosphorylated pyridine, 26322-03-2.

Chiral Allenylboronic Esters as a Practical Reagent for Enantioselective Carbon–Carbon Bond Formation. Facile Synthesis of (−)-Ipsenol

Nobuo Ikeda, Isao Arai, and Hisashi Yamamoto*

Contribution from the Department of Applied Chemistry, Nagoya University, Chikusa, Nagoya 464, Japan. *Received August 8, 1985*

Abstract: A stereospecific synthetic route to (−)-ipsenol is described. The synthesis illustrates a new asymmetric synthetic reaction using chiral allenyl boronic esters. The scope of the synthesis as a general route to either (*R*)- or (*S*)-3-alkynol is further illustrated by several cases.

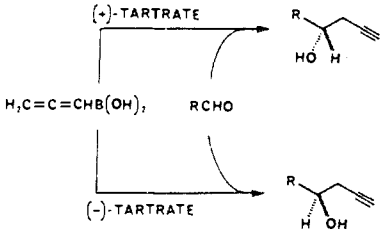
Recently we had envisioned the synthesis of a number of natural products which contain arrays of stereocenters in an open-chain arrangement. The methods of creating these stereocenters in the particular relative configuration have been termed "acyclic stereoselection".[1] Of the many potentially useful methods to this problem, addition of chiral nucleophiles to carbonyl compounds should offer the advantages of widespread applicability to a unique degree.[2] Among them, the asymmetric addition of allylic nucleophiles to the carbonyl compounds is one of the most powerful and useful synthetic methods in modern synthetic chemistry.[3] On the other hand, the propargylic reagent has never been developed to a useful level due to the lack of a satisfactory chiral system. The even greater versatility of propargylic systems[4] compared to allylic systems encouraged us to study the former type compounds in detail. Whereas it is usually difficult to differentiate the two reactive centers of allylic system, it is relatively easy to achieve reaction specifically at either one of the two reactive centers in a propargylic system.[5]

Prior to our work, efforts to find an efficient asymmetric synthesis using allenyl anion had produced very limited success. Thus, the reaction with carbonyl compounds has been extensively studied with magnesium,[6] aluminum,[7] zinc,[8] titanium,[5] and boron[9] reagents with much discussion on diastereoselectivity. Although a cyclic mechanism has generally been proposed for such a re-

(1) General review: Morrison, J. D., Ed. "Asymmetric Synthesis"; Academic Press: New York, 1983; Vol. 1–4.
(2) Solladie, G., ref 1, Chapter 6, Vol. 2, and references cited therein.
(3) Condensation of aldehydes with enantiomerically enriched allylboranes was shown to provide homoallylic alcohols: Midland, M. M.; Preston, S. B. *J. Am. Chem. Soc.* **1982**, *104*, 2330. Herold, T.; Schrott, U.; Hoffmann, R. W. *Chem. Ber.* **1981**, *114*, 359. Pearson, N. R.; Hahn, G.; Zweifel, G. *J. Org. Chem.* **1982**, *47*, 3364.
(4) Moreau, J.-L. In "The Chemistry of Ketenes, Allenes, and Related Compounds"; Patai, S., Ed.; Wiley: New York, 1980; pp 363–414.
(5) Ishiguro, M.; Ikeda, N.; Yamamoto, H. *J. Org. Chem.* **1982**, *47*, 2225.
(6) Karila, M.; Capmau, M. L.; Chodkiewicz, W. *C. R. Seances Acad. Sci., Ser. C* **1969**, *264*, 342. Saniere-Karila, M.; Capmau, M. L.; Chodkiewicz, W. *Bull. Soc. Chim. Fr.* **1973**, 3371.
(7) Guillerm-Dron, D.; Capmau, M. L.; Chodkiewicz, W. *Tetrahedron Lett.* **1972**, 37.
(8) Moreau, J.-L. *Bull. Soc. Chim. Fr.* **1975**, 1248.
(9) Favre, E.; Gaudemar, M. *J. Organomet. Chem.* **1975**, *92*, 17.

0002-7863/86/1508-0483$01.50/0

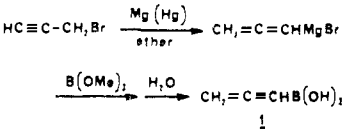
Scheme I



action, there is still a lack of information about the nature of the transition states.

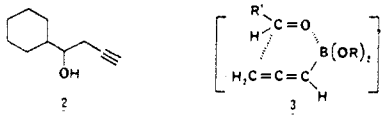
Results and Discussion[10]

Treatment of propargyl Grignard reagent with trimethylborate followed by acidic workup gave, after recrystallization with hexane–ether, a single crystalline boric acid **1** in 40–60% yield.[11] As far as can be discerned, a single compound results from this preparation. Assignment of structure follows by a clean ^{1}H NMR spectrum, and none of the acetylenic isomer is present.



1

With the structure of the boron reagent fixed, attention turns to the condensation with carbonyl compounds. The allenylboronic acid is an ambident nucleophile and the reaction can be envisioned to occur either at the α or γ position of **1**. Treatment of cyclohexanecarbaldehyde with **1** in toluene containing 4 equiv of pentanol and molecular sieves exclusively produced the homopropargylic alcohol **2** in 40% yield. This fact indicates that the reaction proceeds through the cyclic transition state **3**.



2 **3**

The potential for application of the carbonyl addition reaction of allenyl boron reagent to an asymmetric fashion appeared particularly exciting. Our earlier investigations revealed the asymmetric induction using dialkyl tartrate as an effective chiral ligand to boron to be highly efficient yet mild and regioselective (Scheme I).[10]

Encouraged by the success in the asymmetric induction of **1**, we investigated further application of the method using other tartrate esters. Thus, reactions of allenylboronic acid and a series of tartrate esters were examined with cyclohexanecarbaldehyde as the substrate. The expectation that the alkylation process of Scheme I using the more bulkyl tartrate esters would be more stereoselective than the reaction of methyl, ethyl, or isopropyl ester of tartaric acid with allenylboronic acid rests on the following assumptions: (a) that the addition of allenyl anion to the prochiral center of aldehyde is subject to steric screening, (b) that the conformation of the tetravalent boron center is as shown in Figure 1, (c) that in the most favorable geometry of the allenyl boron reagent, the alkoxy group exerts a screening influence on the prochiral α-carbon atom of carbonyl compound. Some of our results are summarized in Table I. As can be seen, a more effective ester was found to be that derived from commercially available 2,4-dimethyl-3-pentanol or cyclododecanol. The former ester gave the homopropargylic alcohol with >99% ee (entry 8 of Table I).

Condensation with aromatic aldehydes appears to be considerably less efficient than the reaction with saturated aldehydes. In addition, only low yields (<50%) of the homopropargylic alcohol

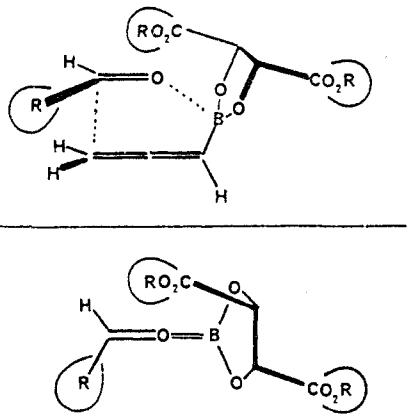
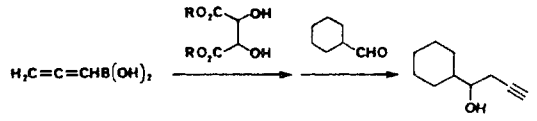


Figure 1.

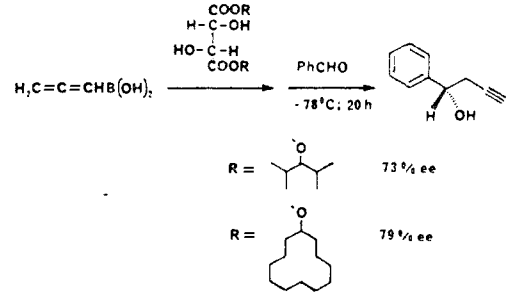
Table I. Effect of Tartrate Esters on Asymmetric Condensation[a]



entry no.	R	tartrate	yield,[b] %	% ee[c]
1	Et	L-(+)	81	91
2	*i*-Pr	L-(+)	88	92
3	cyclopentyl	L-(+)	42[d]	91
4	1-menthyl	L-(+)	37[d]	93
5	1-menthyl	D-(-)	69[d]	92
6	cyclododecyl	L-(+)	85	98
7	2,4-dimethyl-3-pentyl	L-(+)	88	98
8	2,4-dimethyl-3-pentyl	L-(+)	89[e]	>99

[a] Unless otherwise specified, all reactions were performed as described in the General Procedure subsection of the Experimental Section. [b] Isolated yields. Yields are based on allenylboronic acid. [c] Determined by GC analyses of the ester from (*S*)-(-)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride. [d] Yield is not optimal since the reaction was performed only once. [e] The reaction was performed with 3 equiv of the aldehyde.

were obtained by the reaction with a variety of unsaturated aldehydes with this bulky reagent, indicating that the use of saturated aldehyde is crucial to the success of the present reaction. It is well-known, however, that benzylic as well as allylic alcohols may be prepared with satisfactory enantioselectivities by the existing techniques,[12] which thus seemed to be complementary to our new method.



Additional results are recorded in Table II.

With a demonstrated ability for (*R*)- or (*S*)-homopropargyl alcohol formation stereospecifically, emphasis shifted toward a more general determination of the scope and limitations of this method. The synthesis of (*S*)-(-)-*ipsenol*,[13] a monoterpene aggregation pheromone isolated from the frass produced by male California five-spined ips, is an attractive target[14] since the bio-

(10) For preliminary accounts of this work, see: Haruta, R.; Ishiguro, M.; Ikeda, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1982**, *104*, 7667.

(11) Favre, E.; Gaudemar, M. *C. R. Seances Acad. Sci., Ser. C* **1966**, *262*, 1332.

(12) For example: Noyori, R.; Tomino, I.; Tanimoto, Y. *J. Am. Chem. Soc.* **1979**, *101*, 3129. Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237.

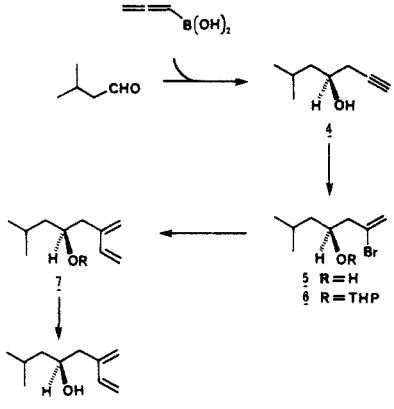
(13) Silverstein, R. M.; Rodin, J. O.; Wood, D. L. *Science* **1966**, *154*, 509. Amoore, J. E. "Molecular Basis of Odor"; Charles, C., Ed.; Thomsa: Springfield, IL, 1970.

Table II. Asymmetric Condensation of Allenyl Reagents[a]

entry no.	aldehyde (equiv)	tartrate[b]	yield,[c] %	$[\alpha]_D$ (c, $CHCl_3$)	% ee[d]
1	hexanal (1.5)	L-(+)	81	+0.39 (1.22)	94[e]
2	hexanal (5.0)	L-(+)	72	-0.49 (1.08)	97[e]
3	cyclohexane-carbaldehyde (1.5)	L-(+)	88	-9.65 (1.02)	98
4	cyclohexane-carbaldehyde (3.0)	L-(+)	89		>99
5	cyclohexane-carbaldehyde (1.5)	D-(-)	82	+9.67 (1.00)	99
6	isovaleraldehyde (1.5)	D-(-)	78		99
7	isovaleraldehyde (3.0)	D-(-)	74	-11.24 (1.35)	>99
8	(*S*)-citronellal (1.5)	L-(+)	74	+9.40 (1.18)	92[e]
9	(*S*)-citronellal (5.0)	L-(+)	90	+6.81 (1.19)	99[e]
10	(*R*)-citronellal (1.5)	L-(+)	67	+4.68 (1.07)	98[e]

[a] Unless otherwise specified, all reactions were performed as described in the General Procedure section of the Experimental Section. [b] Bis(2,4-dimethyl-3-penthyl) tartrate was used. [c] Isolated yields. Yields are based on allenylboronic acid. [d] Unless otherwise specified the % ee was determined by GC analyses of the ester from (*S*)-(-)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride. [e] Determined by HPLC analyses of the ester from (*S*)-(-)- and (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride.

Scheme II



logical activity of the racemate was inferior to the (*S*)-(-)-isomer when released in comparable quantity: the antipode proved nearly inactive.[15] The highly stereoselective synthesis of homopropargylic alcohols described above suggested the synthetic approach outlined in Scheme II. Isovaleraldehyde was converted by reaction with allenylboronic acid and bis(2,4-dimethyl-3-pentyl) tartrate into the corresponding homopropargylic alcohol **4** in 78% yield with >99% ee. The propargylic alcohol **4** was then converted to the 2-brominated alcohol **5** in 92% isolated yield by a new process of Suzuki and Hara[16] which has the advantage of being easily reproducible and avoiding formation of 1-brominated alcohol. Exposure of the alcohol with dihydropyran in methylene chloride containing a catalytic amount of *p*-toluenesulfonic acid at 0 °C for 1.5 h resulted in the olefinic tetrahydropyranyl ether **6** in quantitative yield. A solution of the ether **6** in benzene was treated with vinyl Grignard reagent and a catalytic amount of palladium tetrakis(triphenylphosphine) at ambient temperature for 2 h.[17] Isolation of the product chromatographically afforded the desired diene **7** in 96% yield. None of the isomeric by-products with respect to the olefinic linkage could be detected chromatographically or by NMR analysis. The diene **7**, upon treatment with *p*-toluenesulfonic acid in methanol, was smoothly converted to (-)-ipsenol. The infrared and NMR spectra and optical rotation of the synthetic product were identical with those obtained from natural ipsenol.[13] The optical purity of the synthetic product was shown to be >99% ee by GC analysis of the corresponding MTPA ester.

It is clear from the present results that a major improvement has been made in the methodology of asymmetric synthesis, with regard to complete stereochemical control for the carbonyl addition reaction. A number of significant applications of the new process can be foreseen, for example in the synthesis of chiral aldols which is not readily available from previous procedures.

Experimental Section

Allenyboronic Acid. The apparatus consisted of a three-necked 500-mL round-bottomed flask fitted with a 200-mL dropping funnel with a pressure-equalizing side arm, a 50-mL dropping funnel of the same type, a thermometer, an efficient magnetic stirring bar, and an inlet for dry argon. The apparatus was thoroughly swept with dry argon, and the reaction flask is charged with 225 mL of freshly distilled dry ether. Freshly distilled methyl borate (17.03 mL, 150 mmol) and dry ether (30 mL) were placed in the 50-mL dropping funnel shortly before the reaction was started. The flask was cooled to below -70 °C by a bath of dry ice and methanol and was kept below -70 °C all during the reaction. One hundred and sixty milliliters of an ethereal solution of propargylmagnesium bromide (ca. 150 mmol), freshly prepared according to "Organic Synthesis",[18] was pressure-transferred with dry argon to the 500-mL dropping funnel. The reactants were added to the vigorously stirred reaction mixture alternately in small portions, first 1/12 of methyl borate and then 1/12 of Grignard reagent, the rate of addition being as rapid as is possible without the temperature of the mixture rising above -70 °C. The addition was completed in 30 min. Stirring was continued for an additional 30 min below -70 °C after the addition of the reagent was completed. The stirred mixture, maintained at or below 0 °C with an ice bath, was hydrolyzed by the sequential addition of 10.5 mL of water during 1 min. It is then neutralized by addition of a solution of 75 mL of diluted sulfuric acid, prepared from 5.56 mL of concentrated sulfuric acid and 100 mL of water, during 10 min. The reaction mixture was turned from a white suspension to a clear bilayer solution. The mixture was transferred to a separatory funnel, the ether layer was separated, and the aqueous layer was extracted with ether two times (20 mL each). The combined ether layer and extracts were dried over magnesium sulfate and concentrated under reduced pressure with a rotary evaporator. After approximately one-tenth of the ether has been removed, the evaporator was charged with argon. A small amount of dry ether was added if some crystals of boric acid appeared. The solution was then treated with hexane (70 mL) under argon and shaken for a few minutes. Solvent was removed by syringe, and the white crystals were dissolved in ether (60 mL). The solution was transferred to the dry flask under argon and concentrated until some crystals of allenylboronic acid precipitated. A minimum amount of ether was added to dissolve the solid and the solution was treated with hexane (70 mL) and the mother liquid was removed by syringe. The same operation was repeated again and finally 10 mL of hexane was added. The resulting suspension of allenylboronic acid could be stored at -20 °C for several weeks without any deterionation. The yield of allenylboric acid was ca. 40–60% depending on the recrystalization efficiencies. Mp 150 °C dec; ^1H NMR ($CDCl_3$–Me_2SO-d_6) δ 4.48 (d, J = 5.8 Hz, 1 H), 4.51 (d, J = 7.2 Hz, 1 H), 4.83 (dd, J = 5.8 and 7.2 Hz, 1 H), 6.52 (br s, 2 H).

D-(-)- and L-(+)-Bis(2,4-dimethyl-3-pentyl) Tartrate. A mixture of D-(-)-tartaric acid (49.9 g, 333 mmol), 2,4-dimethyl-3-pentanol (186.5 mL, 1.33 mol) and concentrated hydrochloric acid (20 mL) was placed in the 500-mL round-bottomed flask and heated at 80 °C for 22 h. The reaction mixture was poured into ice-cold dilute NaOH solution and the product was extracted with ether repeatedly. The combined extracts were dried (Na_2SO_4), concentrated, and distilled to give a colorless oil (34.9 g, 30% yield): bp 168–176 °C (0.3 torr); R_f 0.45 (hexane–ether, 1:1), $[\alpha]_D$ -23.66° (5.05, MeOH); ^1H NMR (CCl_4) δ 0.93 (d, J = 6 Hz, 24 H), 1.90 (octet, J = 6 Hz, 4 H), 3.30 (d, J = 8 Hz, 2 H), 4.42 (d, J = 8 Hz, 2 H), 4.70 (dd, J = 6 Hz, 2 H); IR (CCl_4) 3535, 2970, 1740, 1255, 1130, 1093 cm^{-1}. Anal. Calcd for $C_{18}H_{34}O_6$: C, 62.40; H, 9.89. Found: C, 62.47; H, 9.82.

L-(+)-Bis(cyclododecyl) Tartrate. A mixture of L-(+)-tartaric acid (70 g, 466 mmol), cyclododecanol (258 g, 1.40 mol) and concentrated hydrochloric acid (50 mL) was heated at 110 °C for 8 h. The reaction

(14) Mori, K.; Takigawa, T.; Matsuo, T. *Tetrahedron* **1979**, *35*, 933 and references therein.
(15) Viete, J. P.; Hedden, R.; Mori, K. *Naturwissenshaften* **1977**, *63*, 43.
(16) Hara, S.; Dojo, H.; Takinami, S.; Suzuki, A. *Tetrahedron Lett.* **1983**, *24*, 731.
(17) Dang, H. P.; Linstrumelle, G. *Tetrahedron Lett.* **1978**, 191.
(18) Hopf, H.; Boehm, I.; Kleinschroth, *J. Org. Synth.* **1980**, *60*, 41.

mixture was poured into ice-cold NaOH solution and the product was extracted with ether repeatedly. The combined extracts were washed with water, concentrated in vacuo, and recrystallized from ethanol to give white crystals (149 g, 66%): R_f 0.56 (hexane–ether, 1:1); mp 123 °C; $[\alpha]_D$ +8.22° (*c* 1.17, EtOH); ^{1}H NMR (CCl_4) δ 1.40 (br s, 44 H), 2.93 (d, *J* = 8 Hz, 2 H), 4.30 (d, *J* = 8 Hz, 2 H), 5.10 (br s, 2 H); IR (CCl_4) 3545, 2940, 1740, 1260, 1130, 1100 cm^{-1}. Anal. Calcd for $C_{28}H_{50}O_6$: C, 69.67; H, 10.44. Found: C, 69.72; H, 10.39.

General Procedure of the Reaction of Allenylboronic Esters with Aldehydes. The following procedure was generally used to produce solutions of allenylboronic esters. A white suspension of allenylboronic acid in hexane (3–5 mmol) was placed in a 50-mL round-bottomed flask fitted with a three-way stopcock under argon. With gentle swirling, the system was evaporated in vacuo followed by flushing with argon. After the complete removal of solvent, the exact amount of boronic acid was weighed. Dry toluene (10 mL/3 mmol of allenylboric acid), dialkyl tartarate (2 equiv), and freshly dried molecular sieves 5A (1.5 g/3 mmol of allenylboronic acid) were added. The mixture was allowed to stand for 24 h, during which period the evolution of gas from the system was almost completed. Gentle swirling of the system was repeated time to time if needed. The resulting clear colorless solution was transferred to a dry 50-mL round-bottomed flask under argon and the residue was washed with toluene (10 mL/3 mmol of allenylboronic acid).

Condensation of Allenyl Esters with Aldehydes. To a solution of the boron reagent as prepared above was added 1.5 equiv of aldehyde at −78 °C. This reaction mixture was allowed to stand at −78 °C for 20 h. The reaction was then quenched with excess cold diluted hydrochloric acid, and the product was extracted with ether repeatedly. The aqueous layer was further extracted with ether two times. The extracts were combined, washed with water until neutral, dried over anhydrous sodium sulfate, and filtered. The solvents were removed under reduced pressure and the crude product was subjected to column chromatography on silica gel to furnish the pure alcohol.

(*S*)-4-Cyclohexyl-1-butyn-4-ol: R_f 0.28 (CH_2Cl_2); ^{1}H NMR (CCl_4) δ 1.99 (t, *J* = 2.6 Hz, 1 H, ≡CH), 2.34 (dd, *J* = 2.6 and 6 Hz, 2 H, $CH_2C\equiv$), 2.85 (s, 1 H, OH), 3.44 (br m, 1 H, CHOH); IR (CCl_4) 3600, 3320, 2930, 2850, 1450, 1430, 1390, 1350, 1310, 1260, 1110, 1095, 1050, 1000, 955, 900 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.60. Found: C, 78.84; H, 10.65.

(*S*)-4-Phenyl-1-butyn-4-ol: R_f 0.30 (dichloromethane); ^{1}H NMR (CCl_4) δ 1.87 (t, *J* = 2.6 Hz, 1 *H*, ≡CH), 2.48 (dd, *J* = 2.6 and 6.6 Hz, 2 H, $CH_2C\equiv$), 3.01 (s, 1 H, OH), 4.66 (t, *J* = 7 Hz, 1 H, CHOH), 7.23 (br s, 5 H, Ph); IR (CCl_4) 3620, 3330, 1200, 1060 cm^{-1}; exact mass calcd (M) 146.0732,found 146.0720.

(*R*)-1-Nonyn-4-ol: R_f 0.37 (CH_2Cl_2); ^{1}H NMR (CCl_4) δ 1.93 (t, *J* = 2.6 Hz, 1 H, ≡CH); 2.29 (dd, *J* = 2.6 and 6 Hz, 2 H, $CH_2C\equiv$), 2.98 (br, 1 H, OH), 3.67 (m, 1 H, CHOH); IR (CCl_4) 3600, 3320, 2940, 2870, 1465, 1382, 1258, 1125, 1075, 1045, 945 cm^{-1}; exact mass calcd (M) 140.1201, found 140.1180.

(4*R*,6*R*)-6,10-Dimethyl-9-undecen-1-yn-4-ol: R_f 0.39 (CH_2Cl_2); ^{1}H NMR (CCl_4) δ 0.93 (d, *J* = 6 Hz, 3 H, C(6)Me), 1.58 and 1.65 (2s, 3 H each, $CH_3C\equiv$), 1.90 (t, *J* = 2.6 Hz, 1 H, ≡CH), 2.26 (dd, *J* = 2.6 and 6 Hz, 2 H, $CH_2C\equiv$), 3.74 (p, *J* = 6 Hz, 1 H, CHOH), 5.01 (m, 1 H, =CH); IR (CCl_4) 3600, 3320, 2920, 1450, 1375, 1250, 1095, 1065, 1035 cm^{-1}. Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.34; H, 11.42.

(4*R*,6*S*)-6,10-Dimethyl-9-undecen-1-yn-4-ol: R_f 0.39 (CH_2Cl_2); ^{1}H NMR (CCl_4) δ 0.90 (d, *J* = 6 Hz, 3 H, C(6)Me), 1.58 and 1.65 (2 s, 3 H each, CH_3C=), 1.90 (t, *J* = 2.6 Hz, 1 H, ≡CH), 2.28 (dd, *J* = 2.6 and 6 Hz, 2 H, $CH_2C\equiv$), 3.77 (p, *J* = 6 Hz, 1 H, CHOH), 5.02 (m, 1 H, =CH); IR (CCl_4) 3600, 3320, 2910, 1450, 1380, 1070, 1030 cm^{-1}. Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.38; H, 11.38.

(*S*)-6-Methyl-1-heptyn-4-ol (4). The boron reagent was prepared as above from 2.1 g (25 mmol) of allenylboronic acid and 17.3 g (50 mmol) of D-(−)-bis(2,4-dimethyl-3-pentyl) tartrate in 160 mL of toluene. The reagent was treated with isovaleraldehyde (8.04 mL, 75 mmol) for 20 h at −78 °C and worked up as above to give (*S*)-6-methyl-1-heptyn-4-ol as a colorless liquid (2.46 g, 78% yield): R_f 0.19 (CH_2Cl_2); IR (CCl_4) 3602, 3350, 2970, 2940, 2876, 1475, 1395, 1375, 1075 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.92 (d, ; *J* = 6.6 Hz, 6 H), 1.17–1.78 (m, 3 H), 1.93 (t, *J* = 2.4 Hz, 1 H), 2.28 (dd, *J* = 2.4 and 5.8 Hz, 2 H), 2.53 (br, 1 H), 3.74 (br, 1 H); mass *m/z* 125.1028 (calcd for $C_8H_{13}O$ 125.0967). The optical purity of the product was determined by conversion to the diastereoisomeric mixture of (+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA) esters. GC analysis with a PEG-HT capillary column (25 m) showed two clearly separated peaks due to the diastereoisomers with a ratio of 99.8:0.2. The identity of the minor peak was established from the (−)-MTPA ester of the product and racemic mixture which was prepared independently.

(*S*)-2-Bromo-6-methyl-1-hepten-4-ol (5). To a solution of (*S*)-6-methyl-1-heptyn-4-ol (1.37 g, 10.8 mmol) in dichloromethane (50 mL) was added B-Br-9-BBN (20 mL of a stock solution in CH_2Cl_2, 23.5 mmol)[19] at 0 °C. The mixture was stirred at 0 °C for 3 h, and acetic acid (9 mL) was added. After being stirred for 1 h at 0 °C, reaction mixture was treated with excess NaOH solution and 30% H_2O_2 and stirred at room temperature for 30 min. The product was extracted with ether three times and organic extracts were washed with water, dried, and concentrated in vacuo. The crude product was then subjected to column chromatography on silica gel (hexane–ether) to yield the bromide as a colorless liquid (2.07 g, 92% yield): R_f 0.25 (hexane–ether, 2:1); IR (CCl_4) 3620, 3490, 2970, 2940, 2890, 1700, 1630, 1470, 1385, 1370, 1215, 1145, 1070, 1035, 895, 850 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.93 (d, *J* = 6 Hz, 6 H), 1.10–2.07 (m, 4 H), 2.45 (d, *J* = 6 Hz, 2 H), 3.92 (q, *J* = 6 Hz, 1 H), 5.48 and 5.64 (2 s, 2 H); mass *m/z* 151, 149, 122, 120, 87, 69 (100), 43.

(4*S*)-2-Bromo-6-methyl-4-(2-tetrahydropyranyloxy)-1-heptene (6). 2,6-Dihydropyran (0.97 mL, 10.6 mmol) and *p*-toluenesulfonic acid (10 mg) were added successively to a solution of (*S*)-2-bromo-6-methyl-1-hepten-4-ol (1.49 g, 7.20 mmol) in dry dichloromethane (20 mL) at 0 °C. After being stirred for 1.5 h, the reaction mixture was poured into saturated aqueous bicarbonate and the product was extracted with ether three times. The combined extracts were washed with water, dried, and concentrated in vacuo. Purification by column chromatography on silica gel (hexane–ether, 2:1 as eluent) to give the ether as a colorless oil in quantitative yield (2.12 g): R_f 0.57 (hexane–ether, 2:1); IR (CCl_4) 2960, 2875, 2860, 1635, 1465, 1455, 1441, 1385, 1370, 1320, 1260, 1205, 1186, 1170, 1135, 1120, 1080, 1040, 1030, 1100, 985, 890, 870 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.92 (d, 6 Hz, 6 H), 1.10–2.12 (m, 9 H), 2.12–2.90 (m, 2 H), 3.10–4.20 (m, 3 H), 4.58 (br, 1 H), 5.35, 5.57 (2 br s, 1 H each).

2-(4-Methyl-1-(2-tetrahydropyranyloxy)pentyl)-1,3-butadiene (7). A solution of vinyl Grignard reagent was prepared as follows: A stirred suspension of magnesium turnings (0.68 g, 28 mmol) in dry tetrahydrofuran (5 mL) was treated dropwise with a solution of vinyl bromide (1.76 g, 25 mmol) in tetrahydrofuran (20 mL). During the addition, the mixture was gently refluxed with a dry ice–methanol condenser. After the addition was completed, the mixture was stirred for an additional 30 min and 13.1 mL (ca. 13 mmol) of the solution was transferred to a mixture of the bromide **6** (1.91 g, 6.56 mmol), tetrakis(triphenylphosphine) palladium (0.38 g, 0.33 mmol) and benzene (35 mL) at room temperature. The mixture was stirred for 2 h, and the product was passed through a short column of silica gel and then careful purification by column chromatography on silica gel (hexane–ether, 10:1) afforded the diene as an oil (1.50 g, 96%): R_f 0.38 (hexane–ether, 10:1); IR (CCl_4) 3080, 2960, 2870, 1600, 1470, 1455, 1445, 1390, 1370, 1355, 1320, 1260, 1210, 1180, 1170, 1140, 1120, 1080, 1040, 1030, 1000, 905, 880 cm^{-1}; ^{1}H NMR (CCl_4) 0.77–1.10 (m, 6 H), 1.10–2.95 (m, 12 H), 3.13–4.13 (br m, 3 H), 4.57 (br s, 1 H), 4.77–5.52 (m, 3 H), 6.2 (dd, *J* = 11 and 18 Hz, 1 H).

(*S*)-(−)-Ipsenol. The diene **7** (1.42 g, 9.2 mmol) in methanol (40 mL) was treated with a catalytic amount of *p*-toluenesulfonic acid and the mixture was stirred at room temperature for 1 h. The solution was poured into ice-cold water and the product was extracted with ether repeatedly. The combined extracts were washed with bicarbonate, dried, and concentrated in vacuo. Chromatography on silica gel (hexane–ether, 10:1) gave (−)-ipsenol as a colorless liquid (1.41 g, 99% yield): R_f 0.29 (hexane–ether, 2:1); IR (CCl_4) 3600, 3480, 3100, 3020, 2960, 2940, 2880, 1820, 1600, 1470, 1390, 1370, 1280, 1230, 1180, 1140, 1070, 1030, 990, 905, 890, 850 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.89 (d, *J* = 6 Hz, 3 H), 0.92 (d, *J* = 6 Hz, 3 H), 1.27 (q, *J* = 4 Hz, 2 H), 1.47–2.13 (m, 2 H), 2.13–2.44 (m, 2 H), 3.70 (m, 1 H), 4.87–5.40 (m, 4 H), 6.33 (dd, *J* = 18 and 11 Hz, 1 H); $[\alpha]_D$ −17.5 (*c* 1.58, EtOH) (lit.[13] $[\alpha]_D$ −17.5 ± 0.7 (*c* 1, EtOH); mass (70 eV) *m/z* 154.1305 (calcd for $C_{10}H_{18}O$ 154.1359). The optical purity of the product was further determined by the conversion to its (−)- and (+)-MTPA ester followed by analyses with the PEG-HT capillary GC: >99% pure (t_r 2.83 and 2.85 h).

Acknowledgment. This work was supported by the Ministry of Education, Japanese Government (Grant-in-Aid 58470072). We are grateful to M. Ishiguro and R. Haruta for their assistance in the early stages of this work. Generous supply of sample from Takasaga Co. Ltd. also should be mentioned.

(19) Prepared according to the following: Brown, H. C.; Kulkarni, S. U. *J. Organomet. Chem.* **1979**, *168*, 281.