Chiral Synthesis via Organoboranes. 48. Efficient Synthesis of *Trans*-Fused Bicyclic and Cyclic Ketones and Secondary Alcohols in High Optical Purities via Asymmetric Cyclic Hydroboration with Isopinocampheylchloroborane Etherate

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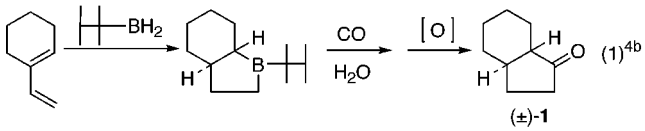
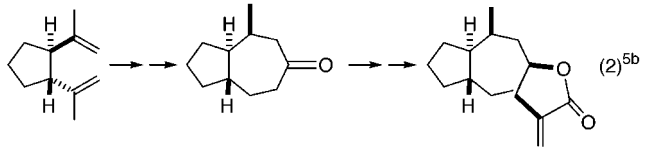
Highly stereo- and enantioselective annelation has been achieved for the synthesis of *trans*-fused bicyclic and cyclic ketones via the asymmetric cyclic hydroboration of suitable cyclic dienes, such as 1-allyl-1-cycloalkenes or 1-vinyl-1-cycloalkenes and appropriate acyclic 1,4-dienes, respectively, with enantiomerically pure isopinocampheylchloroborane etherate (IpcBHCl·Et_2O). The IpcBHCl·Et_2O (an 86−90% equilibrium mixture) was readily synthesized by the reaction of an equivalent amount of hydrochloric acid in ethyl ether (Et_2O) with optically pure isopinocampheylborane ($IpcBH_2$). The hydroboration of the terminal double bond of a representative diene with IpcBHCl·Et_2O readily provided the corresponding isopinocampheylalkylchloroborane (IpcRBCl). Subsequent hydridation of the IpcRBCl with lithium aluminum hydride (LAH, 0.25 equiv) at −20 or −25 °C generated the intermediate isopinocampheylalkylborane (IpcRBH) almost instantly, which then underwent a rapid stereospecific and enantioselective intramolecular cyclic hydroboration to provide the intermediate cyclic trialkylborane. This trialkylborane, on treatment with an aldehyde, liberated the optically pure auxiliary as α-pinene (readily recovered for recycle) to provide the corresponding cyclic borinate ester. This ester reacted smoothly with α,α-dichloromethyl methyl ether (DCME) in the presence of a hindered base (the DCME reaction) to yield, after oxidation with buffered hydrogen peroxide, the *trans*-fused bicyclic or cyclic ketone in high enantiomeric excess (ee). In another improved approach, in situ generated IpcBHCl·Et_2O, from the reduction of isopinocampheyldichloroborane ($IpcBCl_2$) with trimethylsilane (Me_3SiH), in the presence of representative dienes in Et_2O provided considerably improved optical yields of the bicyclic and cyclic ketones. The trialkylboranes obtained from suitable acyclic dienes can be easily protonolyzed to provide the secondary alcohols in high ee.

Hydroboration of alkenes is one of the fundamentally novel reactions in organic synthesis to provide organoboranes readily transformed into an array of synthetically useful compounds of interest.[2] Since the development of optically pure α-pinene-derived borane reagents, a variety of procedures have become available for the enantioselective version of this reaction.[3] On the other hand boron annulation via cyclic hydroboration of suitable dienes, developed in our group,[4] has emerged as an important synthetic tool in the synthesis of natural products.[5,6] The thexylborane ($ThxBH_2$) reagent has been used to hydroborate representative dienes to achieve a general stereospecific synthesis of *trans*-fused bicyclic ketones via the cyclic hydroboration−carbonylation protocol.[4] A noteworthy feature of this methodology is the stereospecific synthesis of thermodynamically disfavored (±)-*trans*-perhydro-1-indanone (**1**) (eq 1).[4b] This reaction has shown considerable promise for the synthesis of cyclic systems from appropriate dienes as shown in eq 2.[5b]



(1)[4b]

(±)-**1**



(2)[5b]

Asymmetric hydroboration has been studied quite extensively. However, no effort has been made to study the enantioselective version of cyclic hydroboration as a powerful and convenient synthetic tool for the stereo- and enantioselective preparation of synthetically useful *trans*-fused polycyclic systems. Since many natural products possess such cyclic systems in their structures,[5] a simple and efficient method to achieve their synthesis in highly stereocontrolled fashion is highly desirable. Thus, the

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(2) (a) Brown, H. C.; Singaram, B. *Acc. Chem. Res.* **1988**, *21*, 287. (b) Matteson, D. S. *Synthesis* **1986**, 973.

(3) (a) Brown, H. C.; Ramachandran, P. V. *Advances in Asymmetric Synthesis;* Hassner, A., Ed.; JAI Press: Greenwich, CT, 1995; Vol. 1, pp 147−210. (b) Brown, H. C.; Ramachandran, P. V. *J. Organomet. Chem.* **1995**, *500*, 1.

(4) (a) Brown, H. C.; Negishi, E. *J. Am. Chem. Soc.* **1967**, *89*, 5477. (b) Brown, H. C.; Negishi, E. *Chem. Commun.* **1968**, 594.

(5) (a) Bryson, T. A.; Reichel, C. J. *Tetrahedron Lett.* **1980**, 2381. (b) Welch, M. C.; Bryson, T. A. *Tetrahedron Lett.* **1988**, 521. (c) Pattenden, G.; Smithies, A. J.; Walter, D. S. *Tetrahedron Lett.* **1994**, *35*, 2413.

(6) (a) Reichert, C. F.; Pye, W. E.; Bryson, T. A. *Tetrahedron* **1981**, *37*, 2441. (b) Levine, E. J.; Bryson, T. A. *Heterocycles* **1982**, *18*, 271.

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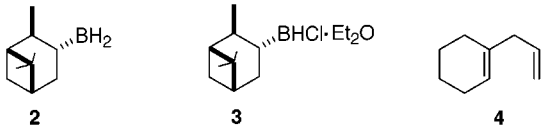
importance of this area of research led us to examine the synthesis of chiral *trans*-1-decalone by asymmetric cyclic hydroboration of 1-allyl-1-cyclohexene (**4**) with $IpcBH_2$ (**2**)[7,8] as well as the improved $IpcBHCl{\cdot}Et_2O$ (**3**) reagent in high enantiomeric purity.[9]



2 **3** **4**

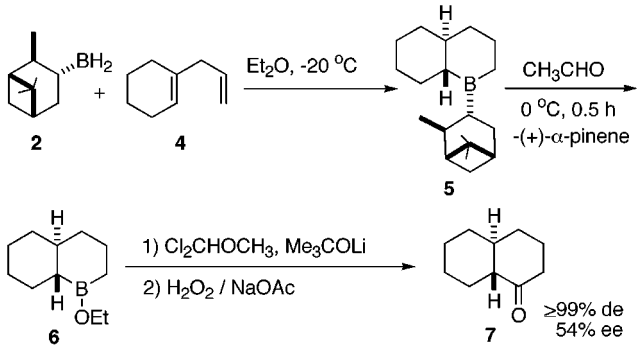
In this paper, we wish to report a detailed account of our research on the asymmetric cyclic hydroboration of appropriate dienes, *viz.*, 1-allyl-1-cycloalkenes and 1-vinyl-1-cycloalkenes, with $IpcBH_2$ (**2**) and with $IpcBHCl{\cdot}Et_2O$ (generated by two different but simple operations). We also wish to report the application of this reaction for the synthesis of cyclic ketones and secondary alcohols in significantly high optical purities.

Results and Discussion

Optically active carbonyl compounds, bearing a stereogenic center α to the carbonyl group, are important synthons for a number of natural and unnatural products. Earlier reports describe tedious routes for the synthesis of optically active *trans*-1-decalone (**7**) involving resolution procedures[10,11] and for substituted ketones as well. For example, Djerassi et al.[10] synthesized optically active *trans*-1-decalone (**7**) by the optical resolution of (±)-*cis*,*cis*-1-decalol, followed by oxidation to the corresponding *cis*,*cis*-1-decalone, equilibrated to *trans*-1-decalone of 70% optical purity. Enders et al.[12] reported the synthesis of optically active α-substituted ketones by the conversion of the ketones into the chiral hydrazones, which underwent metalation with lithium diisopropylamide to the metal derivatives. These, upon alkylation followed by ozonolysis or hydrolysis, provided chiral α-substituted ketones. Thus to explore the full scope and the generality of the asymmetric cyclic hydroboration process, we decided to synthesize in high ee representative *trans*-fused bicyclic and cyclic ketones as well as related secondary alcohols.

Synthesis of *Trans*-Fused Bicyclic Ketones. Thexylborane ($ThxBH_2$) has been utilized to synthesize *trans*-fused bicyclic ketones in a stereospecific manner from the corresponding cyclic dienes (eq 1).[4] We decided to examine the possibility of achieving asymmetric cyclic hydroboration of dienes by replacing the thexyl group of $ThxBH_2$ by the optically pure isopinocampheyl (Ipc) group from α-pinene, $IpcBH_2$ (**2**).[7] Thus, the synthesis of optically active *trans*-1-decalone (**7**) was selected as a trial case to test the practicality of achieving asymmetric cyclic hydroboration of a representative diene, 1-allyl-1-cyclohexene (**4**) (Scheme 1).

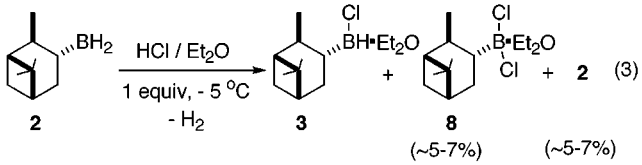
Scheme 1



2 **4** **5** **6** **7**

Optically pure isopinocampheylborane (**2**) was conveniently prepared *via* hydroboration of α-pinene.[7] Cyclic hydroboration of the diene **4** with $IpcBH_2$ (**2**) in Et_2O at −20 °C formed the corresponding cyclic trialkylborane **5**. The trialkylborane on treatment with acetaldehyde[13] underwent a clean, facile elimination of the chiral auxiliary, α-pinene, to form the corresponding cyclic borinate ester **6**. The ester **6** reacted smoothly with α,α-dichloromethyl methyl ether (DCME) in the presence of lithium *tert*-butoxide (the DCME reaction)[14] to yield, after oxidation with buffered hydrogen peroxide, optically active (+)-*trans*-1-decalone in ≥99% de and 54% ee (Scheme 1).

The asymmetric induction realized with $IpcBH_2$ (**2**) was only moderate. This unsatisfactory result led us to examine modification of the $IpcBH_2$ reagent in the hope of achieving improved optical yields. Literature reports[15] suggest that the steric and electronic environment around the boron atom in pinene-based reagents must be critical for achieving a high degree of stereoselection in asymmetric hydroboration. Accordingly, we decided to explore the effect of introducing a chlorine atom into the $IpcBH_2$ reagent. An advantage of IpcBHCl is that it would permit sequential hydroboration. Thus, the reaction of $IpcBH_2$ with a stoichiometric amount of ethereal hydrogen chloride provided isopinocampheylchloroborane etherate ($IpcBHCl{\cdot}Et_2O$) (**2**) in Et_2O at −5 °C. Systematic investigation of this new reagent showed that $IpcBHCl{\cdot}Et_2O$ exists in equilibrium with small amounts of $IpcBH_2$ and $IpcBCl_2{\cdot}Et_2O$ (**8**) (∼5−7% each)[16] (eq 3).



2 **3** **8**

Thus, the hydroboration of 1-allyl-1-cyclohexene (**4**) with $IpcBHCl{\cdot}Et_2O$ provided the corresponding IpcRBCl **9** predominantly, along with only trace amounts of the trialkylborane **5**. This dialkylchloroborane (**9**) on treatment with 0.25 equiv of $LiAlH_4$ at −20 °C underwent smooth hydridation[17] with the precipitation of LiCl,

(7) (a) Brown, H. C.; Schwier, J. R.; Singaram, B. *J. Org. Chem.* **1928**, *43*, 4395. (b) Brown, H. C.; Jadhav, P. K.; Mandal, A. K. *J. Org. Chem.* **1982**, *47*, 5074.

(8) This molecule actually exists in solution as a dimer. However, it is convenient to represent in the monomeric form.

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(13) (a) Brown, H. C.; Jadhav, P. K.; Desai, M. C. *J. Am. Chem. Soc.* **1982**, *104*, 4303. (b) Brown, H. C.; Jadhav, P. K.; Desai, M. C. *J. Org. Chem.* **1982**, *47*, 4583.

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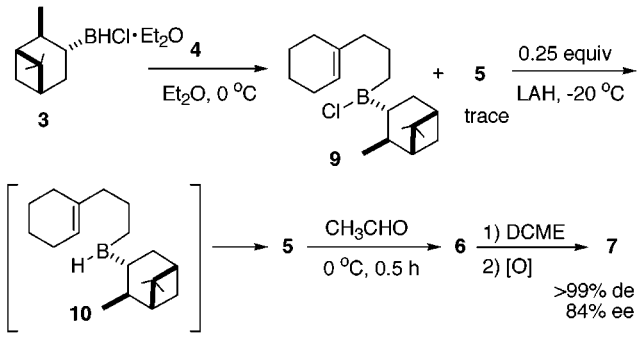
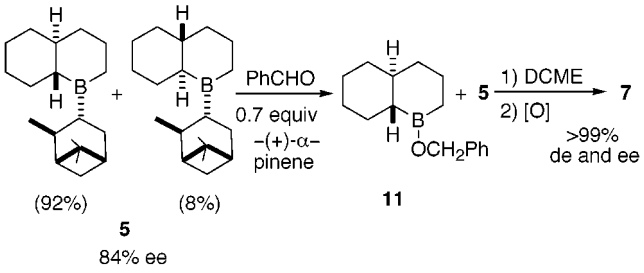
(15) (a) Houk, K. N.; Rondan, N. G.; Wu, Y.-D.; Metz, J. T.; Paddon-Row, M. N. *Tetrahedron* **1984**, *40*, 2257. (b) Egger, M.; Keese, R. *Helv. Chim. Acta* **1987**, *70*, 1843.

(16) Dhokte, U. P.; Kulkarni. S. V.; Brown, H. C. *J. Org. Chem.* **1996**, *61*, 5140.

Scheme 2



Scheme 3

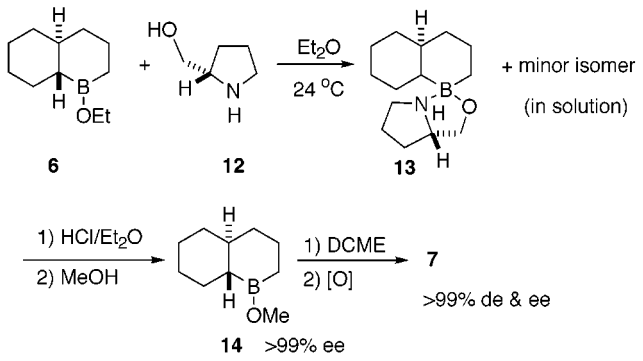


forming the corresponding dialkylborane **10** in situ, which then underwent a facile intramolecular asymmetric cyclic hydroboration to furnish the desired cyclic trialkylborane **5**. Elimination of (+)-α-pinene from **5** by treatment with acetaldehyde, followed by the DCME reaction as described earlier, afforded the (+)-*trans*-1-decalone (**7**) in ≥99% de and 84% ee (Scheme 2).

Thus, the use of preformed IpcBHCl·Et_2O improved the optical yield of (+)-*trans*-1-decalone (**7**) to 84% ee. We had previously established that the controlled treatment of diastereomeric isopinocampheylalkylborinate esters with an aldehyde results in a preferred reaction with the major isomer, upgrading the optical purity of the product borinate ester via kinetic resolution.[18] In a similar approach, indeed, the treatment of the diastereomeric trialkylborane **5** (92:8) with 0.7 equiv of PhCHO, followed by applying the DCME reaction[19] to the resulting borinate ester **11**, provided (+)-*trans*-1-decalone (**7**) in ≥99% ee (Scheme 3).

In the second approach, optically pure *trans*-1-decalone (**7**) was prepared by upgradation of the intermediate borinate ester **6**. It is known that borinate esters react with amino alcohols to form crystalline adducts.[20] Thus, the treatment of borinate ester **6** with a optically active (*S*)-(+)-2-pyrrolidinemethanol (**12**) in Et_2O at 24 °C provided the diastereomeric adducts. The major diastereomer **13** crystallized out, leaving the minor isomer in the solution. Crystalline **13** was isolated and washed with Et_2O. Treatment with HCl provided the corresponding borinic acid and the amino alcohol hydrochloride. The borinic acid, thus obtained, on esterification

Scheme 4



followed by the DCME reaction-oxidation as described earlier furnished the desired *trans*-1-decalone (**7**) in ≥99% ee (Scheme 4).[21]

For convenience, the kinetic resolution methodology was further extended for the chiral synthesis of other *trans*-fused bicyclic systems to provide the optically active bicyclic ketones **15**−**19** from appropriate dienes. The results are summarized in Table 1. By application of the upgradation methodology and controlled treatment with an aldehyde, the ee's of ketones **15**−**17** were conveniently increased to 79%, 92%, and 90%, from their initial values of 69%, 76%, and 76%, respectively (Chart 1).

Lower ee values, i.e., 31% and 56%, were realized for the formation of *trans*-fused bicyclic ketones, **19** and **18**, containing a five-membered ring, with IpcBHCl. However, the upgradation methodology provided moderate to excellent optical induction for bicyclic ketones containing the six-membered ring.

In Situ Generation of IpcBHCl·Et_2O from Reduction of $IpcBCl_2$ with Me_3SiH in Et_2O as an Improved Approach For Asymmetric Cyclic Hydroboration. Although synthesis of *trans*-1-decalone in ≥99% ee was achieved by our upgradation protocol, we decided to investigate the formation of pure IpcBHCl. Since the preformed IpcBHCl·Et_2O (≥99% ee, an 85−90% equilibrium mixture, eq 3) reagent provided ketone **7** in moderate 84% ee, it was thought that the decreased ee might be due to the ∼5−7% $IpcBH_2$ present in the equilibrium mixture.[16] Therefore, we undertook to modify the synthesis of IpcBHCl·Et_2O. It was anticipated that the asymmetric cyclic hydroboration of 1-allyl-1-cyclohexene with pure IpcBHCl·Et_2O might provide high ee for *trans*-1-decalone. Thus, stable and optically pure isopinocampheyldichloroborane[22] ($IpcBCl_2$, ≥99% ee) was prepared from the reaction of boron trichloride (BCl_3), trimethylsilane, and (+)-α-pinene (≥99% ee).[23] In situ reduction of $IpcBCl_2$ with trimethylsilane provided the intermediate IpcBHCl which immediately hydroborated diene **4**, already present in the reaction, in Et_2O at −5 °C, to provide the dialkylchloroborane **9** exclusively, without contamination with trialkylborane **5** (Scheme 5).

The pure dialkylchloroborane intermediate **9** (≥99%) was subjected to hydridation with 0.25 equiv of LAH at −25 °C in Et_2O for 4 h to provide the trialkylborane **5**. This trialkylborane **5**, following the same reaction se-

(17) (a) Kulkarni, S. U.; Lee, H. D.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 4542. (b) Brown, H. C.; Kulkarni, S. U. *J. Organomet. Chem.* **1980**, *218*, 299.

(18) Joshi, N. N.; Pyun, C.; Mahindroo, V. K.; Singaram, B.; Brown, H. C. *J. Org. Chem.* **1992**, *57*, 504.

(19) The DCME reaction−oxidation process transforms borinate esters **11** into ketones and trialkylboranes into tertiary alcohols. See also ref 14.

(20) (a) Brown, H. C.; Bhat, K. S.; Jadhav, P. K.; *J. Chem. Soc., Perkin Trans. 1* **1991**, 2633. (b) Brown, H. C.; Vara Prasad, J. V. N. *J. Org. Chem.* **1986**, *51*, 4526.

(21) For practical reasons we recommend the earlier in situ one-pot method of upgrading the borinate ester by the controlled treatment with an aldehyde.

(22) Brown, H. C.; Ramachandran, P. V.; Chandrasekharan, J. *Heteroatom Chem.* **1995**, *6*, 117.

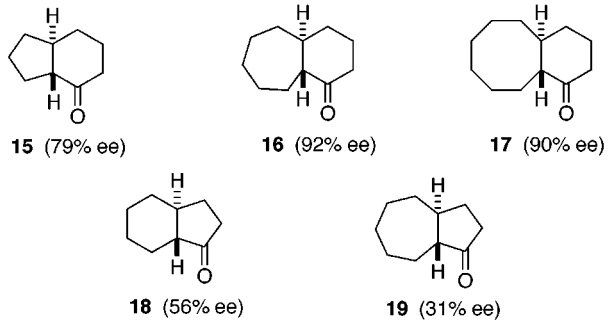
(23) Soundararajan, R.; Matteson, D. S. *Organometallics* **1995**, *14*, 4157.

Table 1. Data for the Optically Active *Trans*-Fused Bicyclic Ketones Obtained via Asymmetric Cyclic Hydroboration of Suitable Dienes

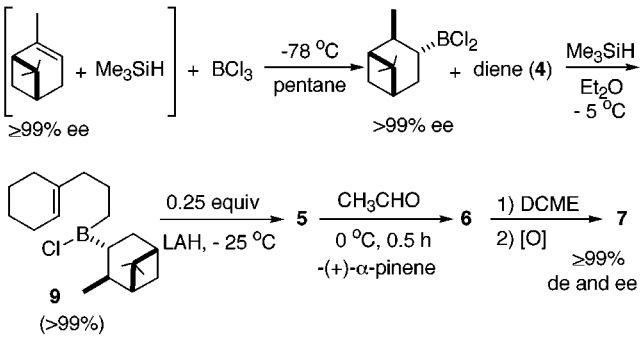
diene[a]	bicyclic ketones[b]	yield (%)[c]	% ee[d]	$[\alpha]_D$ (*c*, solvent)
1-allyl-1-cyclohexene	**7**[e]	76	84	+8.2° (0.55, EtOH)
		65[f]	≥99[f]	+10° (0.57, EtOH)
		51[g]	≥99[g]	+10°(0.53, EtOH)
		74[h]	≥99[h]	+10.2°(0.53, EtOH)
1-allyl-1-cyclopentene	**15**[i]	67	69	−7.6°(1.09, $CDCl_3$)
		55[f]	79[f]	−8.6°(1.01, $CDCl_3$)
		68[h]	81[h]	−8.7°(1.02, $CDCl_3$)
1-allyl-1-cycloheptene	**16**[i]	69	76	+15.2°(1.30, $CDCl_3$)
		53[f]	92[f]	+18.5°(1.46, $CDCl_3$)
1-allyl-1-cyclooctene	**17**[i]	62	76	+5.9°(1.13, EtOH)
		49[f]	90[f]	+7.4°(0.84, EtOH)
		59[h]	72[h]	+5.8°(1.00, EtOH)
1-vinyl-1-cyclohexene	**18**[i]	66	56[j]	+112°(1.64, $CDCl_3$)
1-vinyl-1-cycloheptene	**19**[i]	66	31[j]	+78.2°(1.64, $CDCl_3$)

[a] Dienes prepared by literature procedure and purified by fractional distillation.[29] [b] Stereoisomeric purities established by capillary GC (SPB-5 column). [c] Isolated. [d] Determined by analyzing dia-stereomeric ketals on capillary GC (SPB-5, column). [e] Analytical sample was purified on preparative GC. [f] Upgradation *via* kinetic resolution. [g] Upgradation *via* chelate formation. [h] Obtained by in situ generated IpcBHCl·Et_2O method. [i] Analytical sample was purified by HPLC. [j] Determined by analyzing menthyl carbonate of secondary alcohol on capillary GC (SPB-5 column).

Chart 1

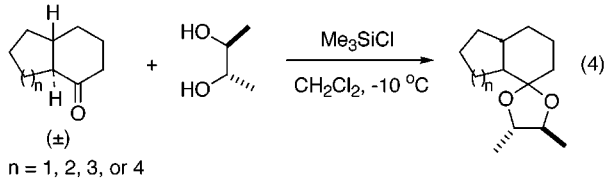


Scheme 5

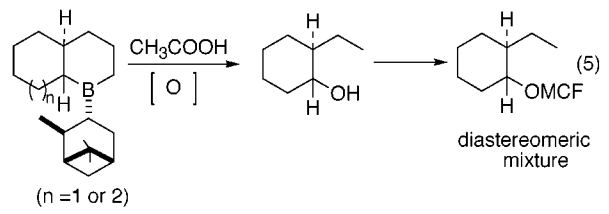


quence as shown in Scheme 2 provided (+)-*trans*-1-decalone (**7**) in ≥99% de and ee. Thus, we achieved the synthesis of (+)-*trans*-1-decalone in essentially ≥99% ee from the in situ generated IpcBHCl produced in the reaction of IpcBCl$_2$·Et$_2$O with trimethylsilane in Et$_2$O in the presence of 1-allyl-1-cyclohexene! Under similar conditions, this procedure provided ketone **15** in 81% ee, a higher value than that realized with preformed IpcBHCl·Et$_2$O. On the other hand, ketone **17** was obtained in 76% ee, a value comparable with that obtained with preformed IpcBHCl·Et$_2$O.

Determination of Enantiomeric Excess of Bicyclic Ketones. To our knowledge, of all the examples of the bicyclic ketones synthesized, only *trans*-1-decalone is known in optically pure form. Therefore, to determine the enantiomeric purities of the bicyclic ketones **7** and **15**−**17**, these ketones were conveniently converted into their corresponding diastereomeric ketals[24] by reaction with optically active (2*S*,3*S*)-(+)-2,3-butanediol and chlorotrimethylsilane at −10 °C. The diastereomeric ketals separated well on capillary GC, in comparison with 1:1 racemic ketals obtained from the racemic ketones indicating no kinetic resolution had taken place (eq 4).



However, diastereomeric ketals from the ketones **18** and **19** did not resolve on a capillary GC. Therefore, an alternative method had to be worked out to determine their ee values. Organoboranes react readily with carboxylic acids to liberate the corresponding alkanes. The first alkyl group of a trialkylborane is protonolyzed easily, followed by increased difficulty in the removal of the second and third alkyl groups. The protonolysis reaction proceeds with retention of stereochemistry of the carbon center.[25] Thus, taking advantage of this novel chemistry, the trialkylboranes intermediates, involved in the synthesis of these ketones, were subjected to selective protonolysis of the primary C−B bond with acetic acid, followed by oxidation to form the corresponding secondary alcohols. The alcohols were then converted to the menthyl carbonate[26] derivatives, which resolved well on a capillary GC. The ee of the alcohols thus obtained reflected the optical yield of the ketones obtained from these trialkylboranes (eq 5).

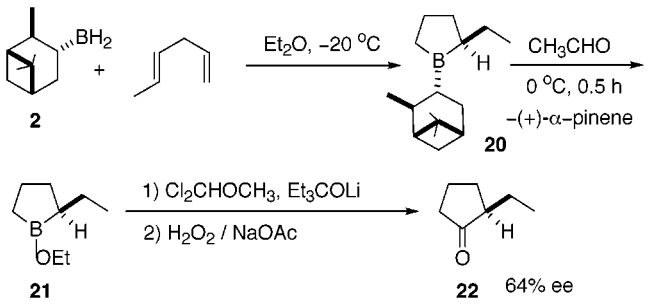


(24) Brown, H. C.; Srebnik, M.; Bakshi, R. K.; Cole, T. E. *J. Am. Chem. Soc.* **1987**, *109*, 5420.

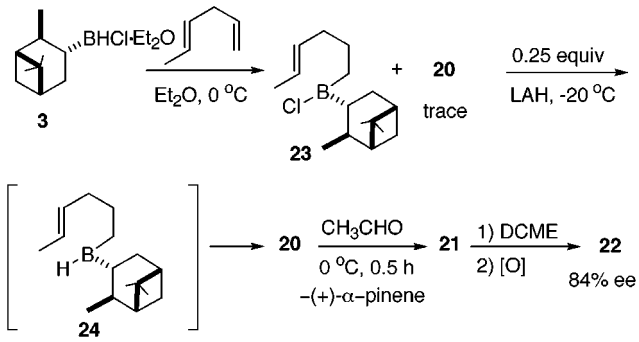
(25) (a) Brown, H. C.; Murray K. J. *J. Am. Chem. Soc.* **1959**, *81*, 4108. (b) Brown, H. C.; Murray K. J. *J. Org. Chem.* **1961**, *26*, 631. (c) Brown, H. C.; Murray, K. J. *Tetrahedron* **1986**, *42*, 5497.

(26) Westley, J. W.; Halpern, B. *J. Org. Chem.* **1968**, *33*, 3978.

Scheme 6



Scheme 7



Stereoisomeric purities of the ketones **7** and **15**−**19** were established by epimerization of the products in the presence of sodium methoxide followed by GC analyses of the equilibrated mixtures and the isolated ketones.[4b] In all cases the data revealed the absence of the *cis*-isomers.

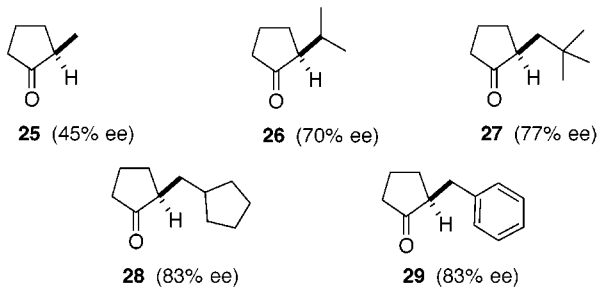
Assignment of Absolute Configuration. Kirk et al.[11] have established the absolute configuration of *trans*-1-decalone (**7**). Thus, in accord with the sign of the rotation of this ketone **7**, obtained by the asymmetric cyclic hydroboration, its absolute configuration should be (9*R*,10*S*). In analogy with *trans*-1-decalone (**7**), the absolute configuration of ketones **15**−**19** can be correlated.

Synthesis of 2-Organylcyclopentanones in High Optical Purities *via* Asymmetric Cyclic Hydroboration of Suitable 1,4-Dienes. After achieving moderate to excellent success in the asymmetric cyclic hydroboration of cyclic dienes, we decided to test the utility of the process for the synthesis of α-substituted cyclopentanones via asymmetric cyclic hydroboration of a representative examples of acyclic dienes, such as appropriate 1,4-dienes. For this study, asymmetric cyclic hydroboration of *trans*-1,4-hexadiene with $IpcBH_2$ (**2**) was selected as a typical example. The reaction was carried out at −25 °C in Et_2O to provide the corresponding trialkylborane **20**, which upon the series of reactions as described earlier for trialkylborane **5** in Schemes 1 and 2, provided optically active 2-ethylcyclopentanone (**22**) in 64% ee (Scheme 6).

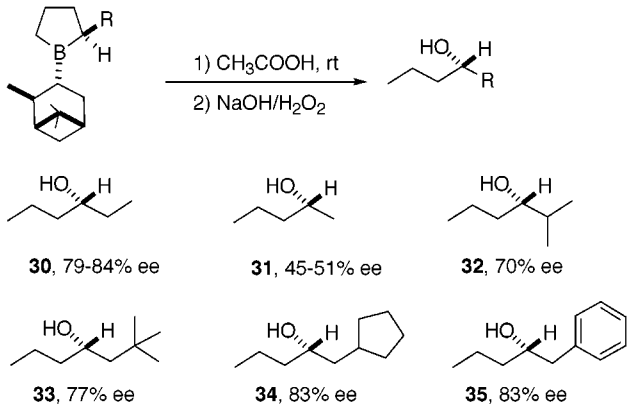
After having achieved only moderate asymmetric induction (64%) with $IpcBH_2$, it was decided to test the effectiveness of preformed IpcBHCl·Et_2O reagent in this reaction. Thus, the preformed IpcBHCl·Et_2O was used for stepwise hydroboration of *trans*-1,4-hexadiene as shown in Scheme 7.

This reaction provided the desired 2-ethylcyclopentanone (**22**) in 84% ee, a much improved value than realized with the $IpcBH_2$ reagent. However, the asymmetric cyclic hydroboration of 1,4-pentadiene and 1,4-hexadiene with in situ generated IpcBHCl, as described in Scheme 5, provided 2-methyl- (**25**) and 2-ethylcyclopentanones (**22**) in 51% and 79% ee, respectively. To establish the generality of this methodology, asymmetric cyclic hydroborations of representative 1,4-dienes were performed with preformed IpcBHCl·Et_2O to achieve the synthesis of 2-organylcyclopentanones (**26**−**29**) in moderate ee (Chart 2).

Chart 2



Scheme 8



We anticipate that it would be possible to upgrade the ee of these products by following the kinetic resolution shown in Scheme 3 and by the chelation method shown in Scheme 4.

Determination of Optical Purities of 2-Organylcyclopentanones and Synthesis of Chiral Secondary Alcohols. Organoboranes react readily with carboxylic acids to liberate the corresponding alkanes (protonolysis reaction) with retention of stereochemistry of the carbon center.[25] Thus, trialkylboranes, a product of asymmetric cyclic hydroboration of acyclic 1,4-dienes, were treated with glacial acetic acid at ambient temperature and the intermediate species were further subjected to alkaline peroxide oxidation to provide the desired secondary alcohols in high optical purities. Thus, this procedure also provided a convenient method for achieving the synthesis of secondary alcohols in moderate to good enantiomeric purities (Scheme 8).

The optical purity of the alcohols thus obtained was determined by derivatizing with (−)-menthyl chloroformate[26] or (+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid chloride (MTPA-Cl),[27] and the corresponding menthyl carbonate and MTPA ester were analyzed on a capillary GC with respect to their corresponding 1:1 diastereomeric mixtures.

(27) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

Table 2. Data for the Optically Active 2-Organylcyclopentanone Obtained *via* Asymmetric Cyclic Hydroboration of Suitable Dienes with $IpcBH_2$ (2) Reagent

diene[a]	cyclopentanone[b] or alcohol[b]	yield (%)[c]	% ee[d]	$[\alpha]_D$ (*c*, EtOH)
trans-1,4-hexadiene	**22**	59	64	−107.5° (1.08)
	30	62	45	−2.66° (2.10)
5-methyl-1,4-hexadiene	**26**	50	54	−98.5° (0.81)
	32	52	54	−12.45° (0.57)
2,2-dimethyl-3,6-heptadiene	**27**	78	60	+1.24° (1.05)
	33	75	60	+9.00° (0.50)
trans-1-cyclopentyl-1,4-pentadiene	**28**	75	64	−0.96° (1.46)
	34	72	64	−8.96° (0.60)
trans-1-phenyl-1,4-pentadiene	**29**	80	82	+1.09° (0.55)
	35	82	82	+3.09° (0.62)

[a] Dienes were prepared by literature procedure[29] and purified by fractional distillation. [b] Purified by preparative GC. [c] Isolated. [d] Determined by resolving diastereomeric MTPA ester or menthyl carbonate derivates on an SPB-5 column.

Conclusions

The asymmetric cyclic hydroboration provides a highly efficient, simple, and promising synthetic route to a variety of *trans*-fused polycyclic and cyclic systems. Thus, the asymmetric cyclic hydroboration of suitable dienes with the α-pinene-derived chloroborane reagent (IpcBHCl), obtained by simple operations, followed by the DCME reaction provide *trans*-fused bicyclic ketones and α-substituted-cyclopentanones in high stereo- and enantiomeric purities. Representative bicyclic ketones have been synthesized by utilizing this methodology, and their ee can be increased by the upgradation procedures. It appears that relatively lower asymmetric induction is achieved in the five-membered ring closure in comparison with the six-membered ring closure. This methodology provides convenient access to the 2-organylcyclopentanones in moderate to excellent optical yields. The intermediate trialkylboranes, obtained in this reaction, can be conveniently transformed by controlled protonolysis−oxidation into optically active secondary alcohols, also useful synthons in natural product synthesis.

Experimental Section

All glassware was dried at 140 °C overnight, assembled hot, and cooled to ambient temperature in a stream of nitrogen.[28] All reactions involving air- or moisture-sensitive compounds were performed under a static pressure of dry nitrogen.[28] Reported melting points are uncorrected. ^{11}B NMR spectra were recorded at 96 MHz and were referenced relative to $BF_3 \cdot Et_2O$. ^1H and ^{13}C NMR spectra for all new compounds were recorded at 200 MHz (also on 300 MHz) and 50 MHz, respectively, relative to internal tetramethylsilane (TMS). Chemical shifts in the ^1H and ^{13}C NMR spectra are reported as parts per million (ppm) downfield from TMS. Optical rotations were measured on a digital polarimeter in a 1-dm cell. Preparative HPLC was used to prepare analytical samples using a C-18 column. The mobile phase used was acetonitrile with detection at 210 nm. Capillary GC analyses were performed using the SPB-5 column (30 m).

Materials. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl and used as required. Anhydrous Et_2O, (−)-menthyl chloroformate, 1,4-penta- and hexadienes and (2*S*,3*S*)-(+)-2,3-butanediol were used as such without any further purification. Certain cyclic and acyclic dienes used in this study were prepared according to literature procedures and purified by fractional distillation.[29]

Preparation of *Trans*-Fused Bicyclic Ketones from Dienes *via* Asymmetric Cyclic Hydroboration with Preformed $IpcBHCl \cdot Et_2O$.[16] The following procedure for the preparation of (9*R*,10*S*)-(+)-*trans*-1-decalone (**7**) is representative. A solution of $IpcBH_2$ (**2**) (28.5 mL, 20 mmol) in Et_2O was cooled to −10 °C and HCl in Et_2O (7.14, 20 mmol) was added to it dropwise with stirring. After the addition was complete, the ^{11}B NMR spectrum indicated the formation of a major amount of $IpcBHCl \cdot Et_2O$ (**3**).[16] In another flask the 1-allyl-1-cyclohexene (**4**) (2.68 g, 22 mmol) was dissolved in Et_2O (10 mL) and cooled to 0 °C. To it, preformed **3** solution was added dropwise and the mixture was allowed to stir at 0 °C for 1 h, when the ^{11}B NMR spectrum indicated major formation of R_2BCl (**9**) (δ 74). The reaction mixture was cooled to −20 °C (ice−water bath), and the LAH (1.0 M, 5 mL, 5 mmol) in Et_2O was added dropwise with stirring. The stirred mixture was allowed to warm to 24 °C (12 h). The ^{11}B NMR indicated the formation of clean trialkylborane **5** (δ 81). The mixture was cooled to 0 °C and acetaldehyde (2.5 mL) added and stirred for 1 h, when the ^{11}B NMR spectrum indicated the formation of borinate ester (**6**) (δ 52). The volatiles were removed by applying reduced pressure (10 mmHg, 30 min), **6** was dissolved in Et_2O (20 mL), and the solution was cooled to 0 °C. To it α,α-dichloromethyl methyl ether (30 mmol, 2.70 mL) was added, followed by the dropwise addition of lithium *tert*-butoxide in *n*-hexanes (40 mmol, generated from *tert*-butyl alcohol and *n*-butyllithium) with stirring. The mixture was stirred at 0 °C for 1 h and then at 24 °C for 4 h. Water (10 mL) was added, and then the mixture was washed with water to pH = 7. Solvent was removed. THF (20 mL) was added followed by the addition of 3.0 M NaOAc (8.0 mL) and H_2O_2 (30%, 8.0 mL), and the mixture was stirred at 24 °C for 1 h and then at 40−50 °C for 1 h. The mixture was diluted with Et_2O (40 mL) and then washed with water (4 × 10 mL), brine (10 mL), and dried ($MgSO_4$). The solvent was removed and the residue distilled (64−66 °C, 0.5 mmHg) (lit.[10] 40 °C., 0.1 mmHg) to afford the desired ketone **7** (2.42 g, 76% yield): Mp 38 °C; $[\alpha]^{23}_D = +8.20°$ (*c* 0.55, EtOH); (lit.[11] −10 ± 1°; *c* 0.5, EtOH).

The same procedure was applied for the synthesis of *trans*-fused bicyclic ketones (**15**−**19**) from their corresponding dienes. The results of these reactions are presented in Table 1.

Similarly, by the same procedure 2-organylcyclopentanones (**22**, **25**−**29**) were prepared in 53−80% yields. All these reactions were performed on 10−15 mmol scales. All these results are summarized in Tables 2 and 3.

Asymmetric cyclic hydroboration of diene **4** and *trans*-1,4-hexadiene was performed with $IpcBH_2$ (**2**) on 10−15 mmol scale. The reaction was performed at −20 °C for 18 h to provide the trialkylborane **5** (Scheme 1) and **20** (Scheme 6). The usual workup procedure as described earlier provided (+)-*trans*-1-decalone (**7**) and 2-ethylcyclopentanone (**22**) in 50−69% and 59% yields, respectively. The optical purity (54% ee for **7** and 64% for **22**) of these ketones was determined as discussed in the later section.

General Procedure for Upgradation *via* Kinetic Resolution. The following procedure for the upgradation of (9*R*,-10*S*)-(+)-*trans*-decalone (**7**) from 84% ee to >99% ee is repre-

(28) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Syntheses Via Boranes;* Wiley-Interscience: New York, 1975. A reprinted edition, Vol. 1, Aldrich Chemical Co., Inc., Milwaukee, WI, 1997, is currently available.

(29) (a) Gream, G. E.; Serelis, A. K.; Stoneman, T. I. *Aust. J. Chem.* **1974**, *27*, 1711. (b) Brown, H. C.; Campbell, J. B., Jr. *J. Org. Chem.* **1980**, *45*, 549.

Table 3. Data for the Optically Active 2-Organylcyclopentanones Obtained *via* Asymmetric Cyclic Hydroboration of Suitable Dienes with IpcBHCl·Et_2O (3) Reagent

diene[a]	cyclopentanone[b] or alcohol[b]	yield (%)[c]	% ee[d]	$[\alpha]_D$ (*c*, EtOH)
trans−1,4-hexadiene	**22**	55	84	−137.5° (0.24)
	30	54	84	−3.40° (3.03)
5-methyl-1,4-hexadiene	**26**	53	70	−126.3° (1.05)
	32	52	54	−12.45° (0.34)
2,2-dimethyl-3,6-heptadiene	**27**	74	77	+1.5° (0.65)
	33	70	77	+11.4° (1.23)
trans−1-cyclopentyl-1,4-pentadiene	**28**	75	83	−1.20° (1.24)
	34	70	83	−11.60° (0.43)
trans−1-phenyl-1,4-pentadiene	**29**	78	83	+1.40° (0.63)
	35	80	83	+4.20° (0.57)

[a] Dienes were prepared by literature procedure[29] and purified by fractional distillation. [b] Purified by preparative GC. [c] Isolated. [d] Determined by resolving diastereomeric MTPA ester or menthyl carbonate derivates on an SPB-5 column.

sentative. A solution of diastereomeric trialkylborane (**5**) (5 mmol) in Et_2O (10 mL) was cooled to 0 °C, benzaldehyde (3.5 mmol, 0.35 mL) was added to it dropwise, and the mixture was stirred for 6 h. ^{11}B NMR indicated the formation of borinic ester (**11**) and the unreacted trialkylborane (**5**). The mixture was subjected to the DCME reaction, followed by oxidative workup as described earlier, provided the desired (+)-*trans*-1-decalone (**7**) (0.5 g, 65% yield) (Scheme 3); Mp 43 °C (lit.[11] 43 °C); $[\alpha]^{23}_D$ = +10° (*c* 0.57, EtOH) corresponding to the product of ≥99% ee.

Upgradation *via* Chelate Formation. The following procedure for the upgradation of (9*R*,10*S*)-(+)-*trans*-1-decalone (**7**) from 84% ee to ≥99% ee is representative. The borinate ester (**6**) was distilled (60−62 °C, 0.5 mmHg). To a solution of distilled **6** (5 mmol) in Et_2O (20 mL) was added (*S*)-(+)-2-pyrrolidinemethanol (**12**) (5 mmol, 0.49 mL) dropwise with stirring at 24 °C. A white precipitate appeared instantly. The mixture was allowed to stir at 24 °C for 12 h. It was then centrifuged and the supernatant layer removed. The solid was washed with ether (3 × 5 mL) using centrifugation technique. The crystalline adduct (**13**) was isolated: Mp 206−207 °C; ^{11}B NMR ($CDCl_3$) δ 5.7; ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ 5.32−5.52 (m, 1H), 3.9−4.02 (t, 1H), 3.5−3.8 (m, 1H), 3.35−3.48 (t, 1H), 2.97−3.10 (m, 2H), 2.1−0.5 (m, 20H); MS *m*/*z* 236 (M + H), 100). Anal. Calcd for $C_{14}H_{26}BNO$: C, 71.48; H, 11.06; B, 4.68; N, 5.95. Found: C, 71.59; H, 11.30; B, 4.34; N, 5.72. The amine complex (**13**) was then dissolved in Et_2O (5 mL), and HCl in Et_2O (5 mmol, 2.1 mL) was added to it to precipitate 2-pyrrolidinemethanol hydrochloride as a yellow gummy solid. The supernatant layer was transferred into another flask using a double-ended needle, and the solvent was removed under vacuum to provide the borinic acid. This acid was dissolved in *n*-pentane, MeOH (5 mL) was added, and the mixture was stirred over molecular sieves (4 Å, beads, 4−8 mesh) for 3 h. The solvent was removed under vacuum to obtain the borinate ester (**14**), which was subjected to the DCME-oxidation reaction as described earlier to provide the desired *trans*-1-decalone (**7**) (0.39 g, 51% yield): Mp 42−43; $[\alpha]^{23}_D$ = +10° (*c* 0.53, EtOH) corresponding to a product of ≥99% ee.

Hydroboration of 1-Allylcyclohexene with in Situ Generated IpcBHCl·Et_2O. The typical procedure for in situ generated IpcBHCl·Et_2O, obtained from the reduction of $IpcBCl_2$ with Me_3SiH in Et_2O, and its hydroboration with 1-allyl-1-cyclohexene follows. Neat $IpcBCl_2$ (2.19 g, 10 mmol) was placed in a flask and cooled to −5 °C, and cold (0 °C) Et_2O (9.0 mL) was added. To this resulting $IpcBCl_2$·Et_2O in solution, diene **4** (1.34 g, 11 mmol) was added, followed by liquid trimethylsilane (0.74 g, 10 mmol, collected as a liquid at −78 °C[28]). The reaction mixture was stirred for 10 min and brought to ambient temperature. ^{11}B NMR showed the formation of dialkylchloroborane (**9**) (δ 76−77) exclusively. Volatiles of the reaction mixture were removed by applying aspirator vacuum, dry Et_2O (9 mL) was introduced in the flask, and the solution was cooled to −25 °C. LAH in Et_2O (1.0 M, 2.5 mL) was added slowly from the side of the flask. The reaction mixture was stirred for 4 h and warmed to ambient temperature; the ^{11}B NMR showed the clean formation of trialkylborane **5** (δ 84). Acetaldehyde (20 mmol) was added at 0 °C, and the mixture was stirred for 30 min; ^{11}B NMR indicated the formation of borinate ester **6** (δ 52). Volatiles were removed by applying aspirator vacuum. The borinate ester **6** was dissolved in Et_2O (10 mL), and the clear Et_2O solution containing the borinate ester was transferred into another flask and cooled to 0 °C. The DCME reaction and oxidative workup as described earlier provided the required (+)-*trans*-1-decalone (**7**) (1.13 g, 74% yield) and a small amount of crude material further purified by preparative GC: Mp 41−2 °C; $[\alpha]^{23}_D$ +10.2 (*c* 0.53, EtOH).

This procedure provided a significantly improved optical yield of 81% for the bicyclic ketone **15** while ketone **17** was obtained in 72% ee. This value is comparable with that (76% ee) realized with preformed IpcBHCl·Et_2O.

(8*R*,9*S*)-(−)-*trans*-Perhydro-4-indanone (15): Yield 67% for 69% ee compound and 55% for 79% ee (after upgradation procedure) compound; bp 61−63 °C (1.0 mmHg) (lit.[4b] 45 °C, 0.5 mmHg); $[\alpha]^{23}_D$ = −7.6° (*c* 1.09, $CHCl_3$) for 69% ee and $[\alpha]^{23}_D$ = −8.6° (*c* 1.01, $CHCl_3$) for 79% ee; IR (neat) 1708 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.16−2.42 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 212.51, 58.29, 49.89, 41.66, 32.30, 30.95, 28.08, 22.65, 21.99; MS *m*/*z* 139 (M^+ + H); HRMS calcd for $C_9H_{14}O$ 138.1045, found 138.1046.

(10*R*,11*S*)-(+)-*trans*-Perhydro-1-benzocycloheptanone (16): Yield 69% of 76% ee compound and 53% of 92% ee (after upgradation) compound; bp 80−82 °C (1.0 mmHg) (lit.[4b] 70−72, 0.6 mmHg); $[\alpha]^{23}_D$ = +15.2° (*c* 1.3, $CHCl_3$) for 76% ee and $[\alpha]^{23}_D$ = +18.5° (*c* 1.46, $CHCl_3$) for 79% ee; IR (neat) 1708 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.30−2.42 (m, 18H); ^{13}C NMR ($CDCl_3$) δ 214.07, 58.21, 47.34, 41.58, 35.82, 34.85, 28.36, 26.54, 25.79, 25.52, 25.47; MS *m*/*z* 167 (M^+ + H, 100); HRMS calcd for $C_{11}H_{18}O$ 166.1358, found 166.1356.

(11*R*,10*S*)-(+)-*trans*-Perhydro-1-benzocyclooctanone (17): Yield 62% of 76% ee compound and 49% of 90% ee (after upgradation); bp 100−102 °C (0.6 mmHg); $[\alpha]^{23}_D$ = +5.9° (*c* 1.13, EtOH) for 76% ee and $[\alpha]^{23}_D$ = +7.4° (*c* 0.84, EtOH) for 90% ee compound; IR (neat) 1708 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.84−2.66 (m, 20H); ^{13}C NMR ($CDCl_3$) δ 213.63, 55.53, 44.53, 42.08, 33.93, 32.67, 27.52, 27.11, 26.77, 26.63, 25.13, 24.16; MS *m*/*z* 180 (M^+, 12.1). Anal. Calcd for $C_{12}H_{20}O$: C, 80.0; H, 11.11. Found: C, 80.01; H, 11.35.

(8*R*,9*S*)-(+)-*trans*-Perhydro-1-indanone (18): Yield 66%; bp 44−45 °C (0.4 mmHg) (lit.[4b] 43 °C, 0.5 mmHg); $[\alpha]^{23}_D$ = +112° (*c* 1.64, $CHCl_3$); IR (neat) 1738 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.97−2.43 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 219.34, 56.95, 43.60, 37.30, 32.89, 27.91, 26.10, 25.85, 25.23; MS *m*/*z* 139 (M^+ + H), 100; HRMS calcd for $C_9H_{14}O$ 138.1045, found 138.1044.

(9*R*,10*S*)-(+)-*trans*-Perhydro-1-azulenone (19): Yield 66%; bp 66−68 °C (0.2 mmHg) (lit. 68 °C, 0.2 mmHg); $[\alpha]^{23}_D$ = +78.2° (*c* 0.77, $CHCl_3$); IR (neat) 1738 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80−2.60 (m, 16H); ^{13}C NMR ($CDCl_3$) δ 222.46, 55.69, 43.94, 38.38, 35.70, 29.08, 28.46, 27.86, 27.86, 27.27, 27.00; MS *m*/*z* 153 (M^+ + H); HRMS calcd for $C_{10}H_{16}O$ 152.1201, found 152.1199.

General Procedure for Determining the Ee of Bicyclic Ketones (7, 15−17) *via* Ketal Formation. The ketone (0.1 mmol) was dissolved in methylene chloride (0.5 mL) and cooled to −10 °C. (2*S*,3*S*)-(+)-2,3-butanediol (0.3 mmol) and chlo-

rotrimethylsilane (0.6 mmol) were added sequentially. The reaction mixture was stirred at −10 °C for 0.5 h, poured into saturated $NaHCO_3$ solution, and extracted with Et_2O. The ethereal solution was dried over $MgSO_4$, filtered, and analyzed directly on capillary GC on an SPB-5 column (30 m).

(−)-2-Ethylcyclopentanone (22): Yield 59%; bp 90−92 °C (100 mmHg) (lit.[30] 92, 100 mmHg); $[\alpha]^{23}_D = -137.5°$ (*c* 0.24, EtOH); IR (neat) 1731 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.92−2.4 (m, 5H), 1.68−1.90 (m, 2H), 1.46−1.64 (m, 1H), 1.20−1.40 (m, 1H), 0.95 (t, J = 3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 50.6, 38.3, 29.0, 22.7, 20.7, 11.9. Anal. Calcd for $C_7H_{12}O$: C, 75.0; H, 10.75. Found: C, 74.69; H, 11.06. The optical yield of 80% was determined by analyzing this ketone on Chiraldex GTA (23 m) column at 61 °C (isothermal).

(−)-2-Methylcyclopentanone (25): Yield 42%; bp 137−138 °C (760 mmHg); $[\alpha]^{23}_D = -57.9°$ (*c* 1.19, $CHCl_3$) [lit.[31] $[\alpha]^{23}_D = -110.5°$ (*c* 1.19, $CHCl_3$)]; IR (neat) 1731 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.94−2.38 (m, 5H), 1.70−1.90 (m, 1H), 1.40−1.58 (m, 1H), 1.08 (dd, J = 6 Hz, 3H). This ketone was also obtained by asymmetric cyclic hydroboration of 1,4-pentadiene with in situ generated IpcBHCl as described earlier. Thus, optical yield of 51% was obtained for the ketone **25** and was determined by analyzing this ketone directly on a chiral column, Chiraldex GTA (23 m) column at 49 °C (isothermal), in comparison with its 1:1 racemic mixture.

(−)-2-Isopropylcyclopentanone (26): Yield 50%; bp 174 °C (760 mmHg) [lit.[32] 174 °C (760 mmHg)]; $[\alpha]^{23}_D = -126.3°$ (*c* 1.05, EtOH); IR (neat) 1731 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.90−2.38 (m, 6H), 1.58−1.80 (m, 2H), 1.00 (d, J = 6 Hz, 3H), 0.80 (d, J = 6 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 222, 55.4, 39.5, 27.6, 24.8, 21.3, 20.8, 18.5.

(+)-2-Neopentylcyclopentanone (27): Yield 78%; bp 130 °C (20 mmHg); $[\alpha]^{23}_D = +1.50°$ (*c* 0.65, EtOH); IR (neat) 1738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.65−2.45 (m, 8H), 1.40−1.60 (m, 1H), 0.90 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 222.8, 76.9, 47.1, 44.4, 37.7, 33.0, 30.7, 30.0, 29.9, 21.0.

(−)-2-(Cyclopentylmethyl)cyclopentanone (28): Yield 75%; bp 78−80 °C (0.5 mmHg) [lit.[33] 78 °C (0.5 mmHg)]; $[\alpha]^{23}_D = -1.20°$ (*c* 1.24, EtOH); IR (neat) 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00−2.40 (m, 18H); ^{13}C NMR ($CDCl_3$) δ 48.7, 38.4, 38.0, 36.0, 33.3, 32.0, 30.1, 25.2, 25.0, 20.8. Anal. Calcd for $C_{11}H_{18}O$: C, 79.52; H, 10.84. Found: C, 79.17; H, 11.11.

(+)-2-Benzylcyclopentanone (29): Yield 80%; bp 109−111 °C; $[\alpha]^{23}_D = +1.40°$ (*c* 0.63, EtOH); IR (neat) 1731 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.10−7.50 (m, 5H), 3.15 (dd, J = 4 Hz, and J = 2 Hz, 1H), 2.55 (q, J = 3 Hz, 1H), 2.25−2.46 (m, 2H), 1.88−2.20 (m, 3H), 1.45−1.85 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 140.3, 129.2, 129.0, 128.7, 128.6, 126.5, 76.7, 51.3, 38.5, 35.9, 29.4, 20.8. Anal. Calcd for $C_{12}H_{14}O$: C, 82.75; H, 8.06. Found: C, 82.39; H, 8.11.

General Procedure for the Synthesis of Chiral Alcohols. The following procedure for the synthesis of optically active (−)-2-pentanol (**31**) is representative. The reaction was performed on a 10 mmol scale. To the trialkylborane, formed from the reaction of preformed IpcBHCl·Et_2O with 1,4-pentadiene as described earlier, glacial acetic acid (10 mL) was added, and it was stirred at 24 °C for 10 min. The excess of acetic acid was neutralized with aqueous 3 M NaOH, and NaOH (3.0 M, 4 mL) was added followed by the addition of 30% H_2O_2 (4 mL) and the usual work up providing 1- and the desired 2-pentanol in 30:70 ratio in 48% yield. These alcohols were separated by preparative GC and characterized by ^1H NMR, IR, and GC analyses in comparison with their authentic samples: Bp 119−120 °C (lit.[34] 116−120 °C); $[\alpha]^{23}_D = -6.50°$ (*c* 0.87, EtOH); (lit.[34] −16.1°); IR (neat) 3500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3H), 1.20 (d, 3 H), 1.30−1.50 (m, 4 H), 3.70−3.90 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.2, 19.1, 23.4, 41.7, 67.8; MS *m*/*z* 88 (M^+).

(−)-3-Hexanol (30): Yield 56%; bp 134−135 °C (lit.[35] 133−134 °C); $[\alpha]^{23}_D = -3.40°$ (*c* 3.03, EtOH) (lit.[35] −7.13°); IR (neat) 3345 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.50 (s, 1H), 1.25−1.75 (m, 7H), 0.85−1.50 (m, 6H). The optical yield of 64% was determined by converting this alcohol into its MTPA ester[27] and analyzing it on an SPB-5 column (30 m).

(−)-2-Methyl-3-hexanol (32): Yield 42%; bp 145−146 °C (lit.[36] 145−146 °C); $[\alpha]^{23}_D = -16.8°$ (*c* 0.34, EtOH) (lit.[36] +21.25°); IR (neat) 3345 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.40 (s, 1H), 1.20−1.75 (m, 6H), 0.85−1.00 (m, 9H). The optical yield of 54% was determined by converting this alcohol into its menthyl carbonate[26] and analyzing it on an SPB-5 column (30 m).

(+)-2,2-Dimethyl-4-heptanol (33): Yield 75%; bp 47−49 °C (5 mmHg) [lit.[37] 46.5 °C (5 mmHg)]; $[\alpha]^{23}_D = +11.38°$ (*c* 1.23, EtOH); IR (neat) 3352 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10−1.50 (m, 7H), 0.90−1.00 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 69.6, 51.5, 42.0, 30.4, 30.3, 29.8, 23.8, 18.9, 14.1. Anal. Calcd for $C_9H_{20}O$: C, 75.0; H, 13.89. Found: C, 74.62; H, 14.22. The optical yield of 77% was determined by converting this alcohol into its MTPA ester[27] and analyzing it on an SPB-5 column (30 m).

(−)-1-Cyclopentyl-2-pentanol (34): Yield 72%; bp 120 °C (17 mmHg); $[\alpha]^{23}_D = -11.6°$ (*c* 0.43, EtOH); IR (neat) 3345 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00−2.00 (m, 16H), 0.90 (t, 3H); ^{13}C NMR ($CDCl_3$) δ 71.4, 44.2, 40.4, 37.0, 33.5, 32.8, 25.3, 25.2, 19.0, 14.3; HRMS calcd 155.1436, found 155.1435. The optical yield of 83% was determined by converting this alcohol into its menthyl carbonate[26] and analyzing it on an SPB-5 column (30 m).

(+)-Phenyl-2-pentanol (35): Yield 82%; bp 125−127 °C (15 mmHg) [lit.[38] 127 °C (15 mmHg)]; $[\alpha]^{23}_D = +4.21°$ (*c* 0.57, EtOH); IR (neat) 3385 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.15−7.40 (m, 5H), 3.80 (s, 1H), 2.80 (d, J = 6 Hz, 1H), 2.65 (q, J = 6 Hz, 1H), 1.30−1.70 (m, 5H), 0.90 (t, 3H); ^{13}C NMR ($CDCl_3$) δ 138.9, 129.7, 128.8, 128.7, 126.7, 126.2, 72.7, 44.4, 39.3, 19.3, 14.4. Anal. Calcd for $C_{11}H_{16}O$: C, 80.49; H, 9.76. Found: C, 80.26; H, 9.51. The optical yield of 82% was determined by converting this alcohol into its menthyl carbonate[26] and analyzing it on an SPB-5 column (30 m).

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Supporting Information Available: ^1H NMR spectra for compounds **7**, **13**, **15**−**19**, **22**, and **26**−**35** and ^{13}C NMR spectra for compounds **7**, **13**, **15**−**19**, **26**−**29**, and **33**−**35** (39 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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