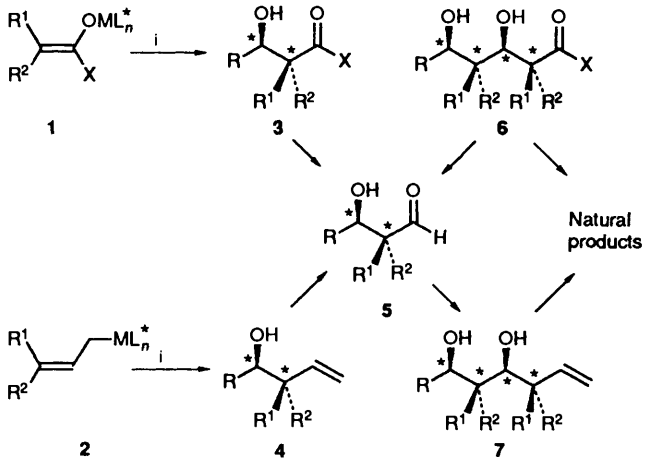
Chiral Synthesis *via* Organoboranes. Part 32. Synthesis of *B*-(Cycloalk-2-enyl)-diisopinocampheylboranes of High Enantiomeric Purity *via* the Asymmetric Hydroboration of Cycloalka-1,3-dienes. Successful Asymmetric Allylborations of Aldehydes with *B*-(Cycloalk-2-enyl)diisopinocampheylboranes†

Herbert C. Brown,* Krishna S. Bhat and Prabhakar K. Jadhav
H. C. Brown and R. B. Wetherill Laboratories of Chemistry, 1393 Brown Building, Purdue University, West Lafayette, Indiana 49707, USA

The hydroboration of cycloalka-1,3-dienes (C_nH_{2n-4}, n = 6, 7 and 8) with diisopinocampheylborane (^{d}Ipc$_2$BH or ^{l}Ipc$_2$BH) at −25 °C provides highly enantiomerically pure *B*-(cycloalk-2-enyl)diisopinocampheylboranes, $^{l\text{ or }d}$Ipc$_2$BC$_n$H$_{2n-3}$ (≥93% ee). Surprisingly, these allylic borane derivatives retain their stereochemical integrity at −25 °C although such compounds are capable of undergoing racemization through rapid allylic rearrangements. Furthermore, the *B*-(cycloalk-2-enyl)diisopinocampheylboranes achieve allylborations of aldehydes at −78 °C and afford 1-(cycloalk-2-enyl)alkan-1-ols in 90–95% ee and 100% *syn*-diastereoselectivity.

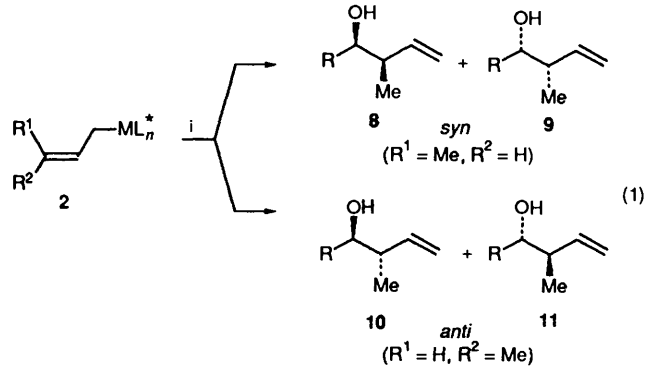
The enantio- and diastereo-selective synthesis of cyclic and acyclic compounds is a challenging area of research owing to rapidly growing demands in natural product synthesis. In recent years many different approaches have been explored towards this objective.[1,2] Among such methods, the stereoselective reactions of metal enolates and allyl/crotylorganometallic reagents **2** with aldehydes have proved extremely valuable.[2–8]



Reagent: i, RCHO

Reactions of (*Z*)- or (*E*)-crotyl metals with aldehydes generate two new chiral centres and four stereoisomers. There are two significant stereochemical aspects associated with the crotylboration reaction: the first deals with diastereoselection (**8** + **9** *vs.* **10** + **11**), and the second deals with enantioselection [**8** *vs.* **9** and **10** *vs.* **11**, eqn. (1)].[7e]

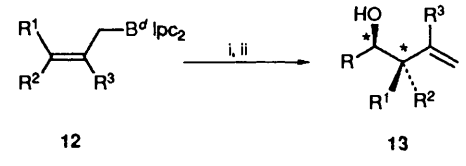
To support the many applications in natural product chemistry, our objective has been to develop new asymmetric allyl- and crotyl-organoborane reagents, which are suitable for highly enantio- and diastereo-selective synthesis. Previously, we reported allylborations utilizing various chiral reagents **12** (Ipc$_2$BR: Ipc = isopinocampheyl; **R** = allyl, 2-methylallyl, 3,3-dimethylallyl, isoprenyl and 3-methoxyallyl) which yield, upon



(1)

Reagent: i, RCHO

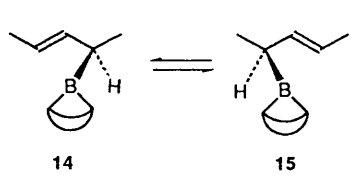
allylboration, the corresponding homoallylic alcohols **13** with optical purities in the range of 88–96% ee [eqn. (2)].[4g,4h,7]



(2)

Reagent: i, RCHO; ii, H_2O_2, OH^-

There is considerable interest in extending such highly promising asymmetric synthesis to other chiral, substituted allylorganoborane derivatives. However, there is one potential problem. The *B*-crotylborane derivatives are susceptible to rapid allylic rearrangements even at relatively low temperatures [eqn. (3)].[3b,9]



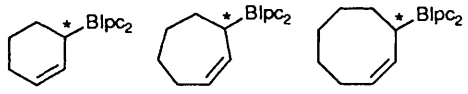
(3)

The rate of allylic isomerization of these intermediates depends on the nature of the other groups on the boron: allyldialkylborane[7] > allylalkylborinate[8b] > allylboronate.[8a]

For a long time, we were interested in extending the allylboration methodology to representative chiral *B*-(cycloalk-2-

† Submitted to mark the 150th anniversary of the Chemical Society Royal Society of Chemistry.

enyl)diisopinocampheylboranes, ^{l} or $^{d}Ipc_2BC_nH_{2n-3}$ such as **16–18**. We decided to prepare these reagents by direct hydroboration of the corresponding dienes (n = 6, 7 and 8) with diisopinocampheylborane (^{l} or $^{d}Ipc_2BH$) without any racemization. We knew that the hydroboration of cyclopenta-1,3-diene with diisopinocampheylborane provides preferentially the homoallylic derivative which is useful for the asymmetric synthesis of cyclopent-2-enol, but unsuitable for allylboration.[6c,6d] Consequently, in the present study, we report the first successful asymmetric synthesis of *B*-(cycloalk-2-enyl)diisopinocampheylboranes **16–18** in high enantiomeric purity, and their enantio- and diastereo-selective reactions with representative aldehydes. A preliminary account of a portion of this study has appeared elsewhere.[10]

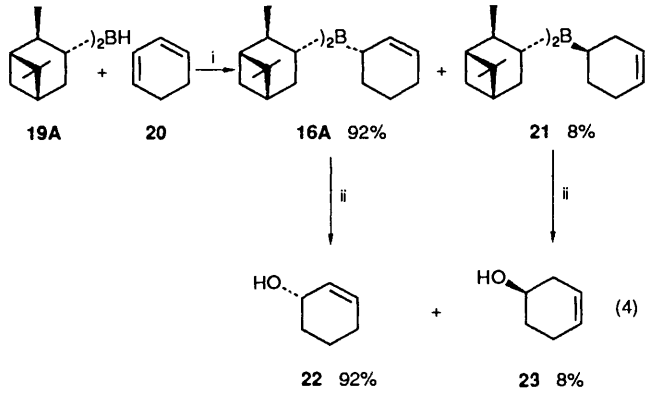


16 **17** **18**

Results and Discussion

Previously, we reported the hydroboration of cyclic dienes with several representative hydroborating agents: borane–dimethyl sulphide, 9-borabicyclononane, disiamylborane (Sia_2BH), dibromoborane–dimethyl sulphide, and dibromoborane.[11b] In that study we established that the hydroboration of cyclopenta-1,3-diene with Sia_2BH affords predominantly the homoallylic borane derivative,[6c,6d] while the hydroboration of higher cycloalka-1,3-dienes (C_nH_{2n-4}, n = 6, 7 and 8) with Sia_2BH provides preferentially the allylic borane derivatives. However, following this study, we did not explore the asymmetric hydroborations of these higher cyclic dienes. The present study reports the successful asymmetric hydroborations of cycloalka-1,3-dienes (C_nH_{2n-4}, n = 6, 7 and 8) with diisopinocampheylborane (^{l} or $^{d}Ipc_2BH$),[6c] and the utilization of the corresponding chiral organoborane derivatives for the allylboration of representative aldehydes at −78 °C.

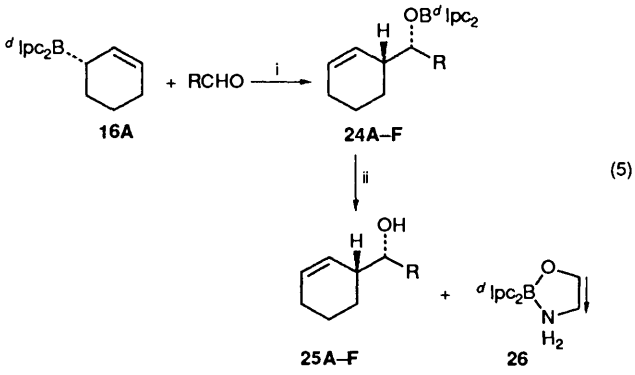
B-(*Cyclohex-2-enyl*)*diisopinocampheylboranes* **16a** *and* **16B** *and Their Reactions with Aldehydes. Preparation of* 1-(*Cyclohex-2-enyl*)*alkan-1-ols.*—Cyclohexa-1,3-diene was treated with diisopinocampheylborane, derived from (+)-α-pinene (*i.e.*, the borane **19A**, $^{d}Ipc_2BH$) at −25 °C in tetrahydrofuran (THF). The hydroboration was observed to be complete in 12 h. The reaction products were oxidized with trimethylamine *N*-oxide,[12] and after the usual work-up were analysed by GC. There was obtained a 92:8 mixture of (*S*)-(−)-cyclohex-2-enol **22** and cyclohex-3-enol **23**. The (*S*)-(−)cyclohex-2-enol **22**, obtained in pure form by preparative GC, was found to be of 93% ee.[13] Evidently, hydroboration takes place predominantly in the allylic position[11] without any racemization [eqn. (4)].



(4)

Reagents and conditions: i, THF, −25 °C, 12 h; ii, [O]

The reagent *B*-(cyclohex-2-enyl)diisopinocampheylborane **16A** reacts readily with acetaldehyde at −78 °C while the minor homoallylic derivative **21** does not, making the separation of the isomeric products extremely simple. The reagent **16A** yielded a borinic ester **24A**, which reacted with ethanolamine to provide (1*R*,1′*R*)-(+)-(cyclohex-2-enyl)ethanol **25A** as a single diastereoisomer and in 94% ee [eqn. (5)].



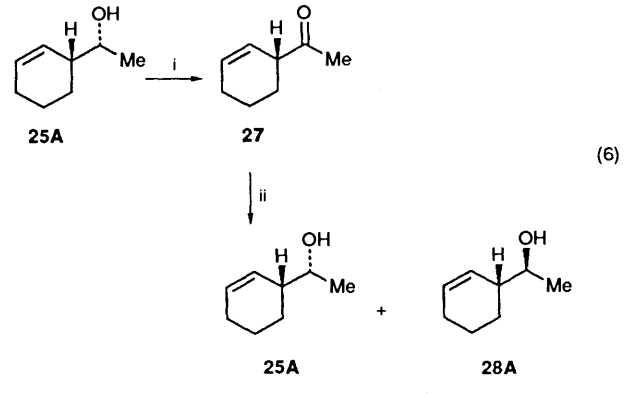
(5)

R = Me (**A**); Et (**B**); Pr^{i} (**C**); Bu^{t} (**D**); CH=CH$_2$ (**E**); Ph (**F**)

Reagents and conditions: i, −78 °C, 3 h; ii, ethanolamine

The customary procedure for isolation of the products from an allylboration reaction involves oxidation of the reaction mixture with alkaline hydrogen peroxide, followed by separation of the homoallylic alcohol from isopinocampheol by fractional distillation. In fact, this has been our preferred work-up procedure for all our previous allylborations.[7] However, in some cases, such as compound **25A**, oxidative work-up poses a problem: isopinocampheol codistills with the product (they have very similar b.p.s), making isolation of the pure product very difficult. We solved this problem by adopting the ethanolamine work-up procedure. In order to be consistent, we employed the ethanolamine work-up for all allylborations with substrate **16A**. These results are summarized in Table 1.

Determination of Diastereoisomeric Purity.—Although the *cis*-geometry of the cyclohexenyl moiety in substrate **16A** is expected to translate into a single diastereoisomer **25** in allylboration of aldehydes [equation (5)],[7d] we decided to confirm this in at least one case. Therefore, the product alcohol **25A** was reoxidized with pyridinium dichromate (PDC) to give the corresponding ketone **27**, and this was then reduced with $LiAlH_4$ to obtain an authentic mixture of diastereoisomers **25A** and **28A** [eqn. (6)].



(6)

Reagents: i, PDC; ii, $LiAlH_4$

These diastereoisomers are well resolved on a Supelcowax column on capillary GC at 85 °C, with retention times of 10.07

Table 1 Allylboration of aldehydes with *B*-(cyclohex-2-enyl)diisopinocampheylborane **16A**

Aldehyde	Alcohol	Yield (%)	% Ee[a]	Absolute config.[b]
MeCHO	1-(Cyclohex-2-enyl)ethanol **25A**	62	94	1*R*,1′*R*
EtCHO	1-(Cyclohex-2-enyl)propan-1-ol **25B**	65	93	1*R*,1′*R*
Pr^{i}CHO	1-(Cyclohex-2-enyl)-2-methylpropan-1-ol **25C**	69	90	1*R*,1′*R*
Bu^{t}CHO	1-(Cyclohex-2-enyl)-2,2-dimethylpropan-1-ol **25D**	67	90	1*S*,1′*R*
CH_2=CHCHO	1-(Cyclohex-2-enyl)prop-2-en-1-ol **25E**	58	92	1*R*,1′*R*
PhCHO	(Cyclohex-2-enyl)(phenyl)methanol **25F**	71	94	1*S*,1′*R*

[a] The percent ees were determined by ^{19}F NMR analysis of the 'α-methoxy-α-trifluoromethyl-α-phenylacetic acid' (MTPA) esters of the alcohols by using a Varian XL-200 spectrometer. [b] In all cases, addition of the cyclohexenyl group to the aldehyde takes place in the same stereochemical sense, but the Cahn–Ingold–Prelog notations for the products differ because of the priority assignments.

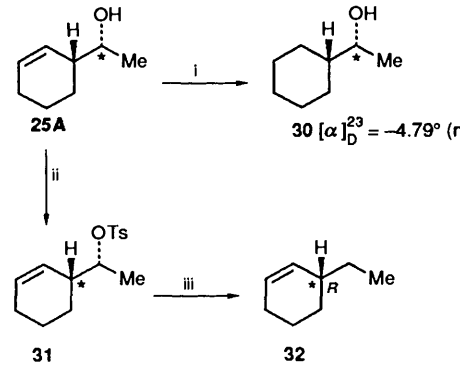
min (**25A**) and 11.13 min (**28A**). Under identical GC conditions, the actual reaction product **25A** [eqn. (5)] showed a single peak (10.14 min). Further, a comparison of the ^{13}C NMR spectra of compound **25A**, before and after the oxidation–reduction sequence [eqn. (6)], clearly indicated that product **25A** [eqn. (5)] is a single diastereoisomer. Similarly, the ^{13}C NMR spectra of the homoallylic alcohols **25B–25F** did not indicate the presence of any other diastereoisomers. These studies clearly demonstrated that the reaction of substrate **16A** with aldehydes is highly diastereoselective.

Stability of Allylic Reagent **16**.—Based on earlier reports,[3b] we expected compound **16A/16B** to be susceptible to racemization due to allylc isomerization [eqn. (7)]. However,

16A **29** (7)

we observed that at −25 °C no racemization took place; racemization of the reagent took place only when the hydroboration mixture was warmed to 25 °C: allylboration of aldehydes at −78 °C with **16A**, that is once warmed to room temperature from −25 °C, provided the product alcohols in much lower optical purities (12% ee). If the reagent **16A** was synthesized at −25 °C and then treated with aldehydes at −78 °C, no difficulty was experienced.

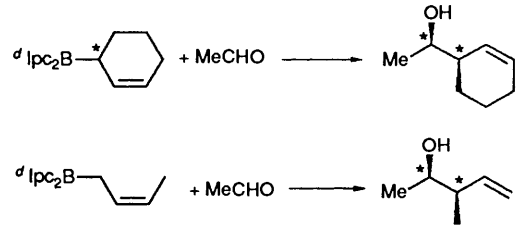
Assignment of Absolute Configurations.—Catalytic hydrogenation (5% Pt on C) of (+)-1-(cyclohex-2-enyl)ethanol **25A** to (−)-1-cyclohexylethanol **30**, $[\alpha]_D^{23}$ −4.79° (neat), showed that the absolute configuration[14,15] of the asymmetric carbon atom bearing the hydroxy group is *R*. Tosylation of the alcohol **25A**, followed by reductive detosylation of ester **31** to (*R*)-(+)-3-ethylcyclohexene **32**, $[\alpha]_D^{23}$ +20.73° (neat),[16] confirmed that the absolute configuration of the other chiral centre is also *R* [eqn. (8)].



(8)

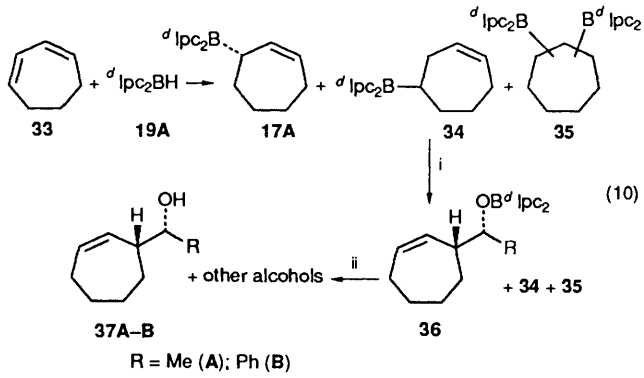
Reagents: i, H_2; ii, TsCl, Pyr; iii, H^-

The consistency observed in the stereoselectivity of allylborations utilizing *B*-(cyclohex-2-enyl)diisopinocampheylborane **16A** with various aldehydes (Table 1) confirms that there is no difference in the stereochemical course between the present reaction and the crotylboration with (*Z*)-crotyldiisopinocampheylborane which we reported earlier [eqn. (9)].[7d]



(9)

B-(*Cyclohep-2-enyl*)*diisopinocampheylboranes* **17A** *and* **17B** *and Their Reactions with Aldehydes. Preparation of* 1-(*Cycloheptt-2-enyl*)*alkan*-1-*ols*.—Cycloheptt-1,3-diene was hydroborated with ^{d}Ipc$_2$BH at −25 °C in THF. The hydroboration of this diene with Sia$_2$BH has been described elsewhere.[11b] The hydroboration was complete in 10 h, as observed by the disappearance of the solid ^{d}Ipc$_2$BH. Then the reaction mixture was cooled to −78 °C and treated with acetaldehyde. Only the allylic derivative **17A** reacted with the aldehyde, to provide compound **36**, while the other derivatives **34** and **35** remain unchanged in the reaction mixture. This mixture was directly oxidized with alkaline hydrogen peroxide* to furnish the required (1*R*,1′*R*)-1-(cycloheptt-2-enyl)ethanol **37A** as a single diastereoisomer in 36% yield. Compound **37A** was easily separated from the other, undesired compounds by preparative GC. Its optical purity was determined by capillary GC analysis to be 93% ee [eqn. (10)].



(10)

Reagents and conditions: i, RCHO, −78 °C; ii, [O]

* In these cases, we preferred the oxidative work-up to the ethanolamine work-up because the former method afforded better yields of isolated products.

Table 2 Allylboration of aldehydes with *B*-(cyclohept-2-enyl)diisopinocampheylborane **17A**

Aldehyde	Alcohol	Yield (%)	% Ee[a]	Absolute config.[b]
MeCHO	1-(Cyclohept-2-enyl)ethanol **37A**	36	93	1*R*,1′*R*
PhCHO	(2-Cyclohept-2-enyl)(phenyl)methanol **37B**	38	95	1*S*,1′*R*

[a] As for Table 1. [b] As for Table 1 (except cycloheptenyl instead of cyclohexanyl).

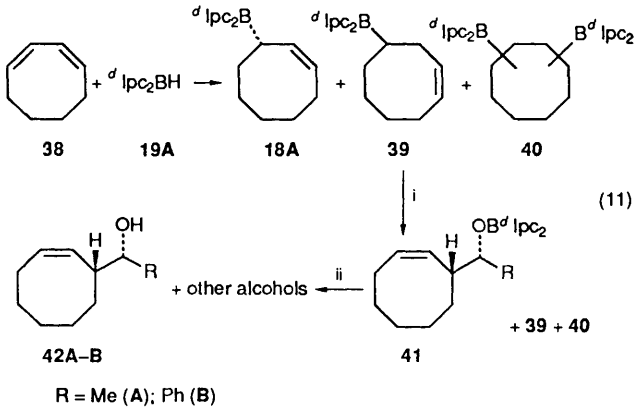
Table 3 Allylboration of aldehydes with *B*-(cyclooct-2-enyl)diisopinocampheylborane **18A**

Aldehyde	Alcohol	Yield (%)	% Ee[a]	Absolute config.[b]
MeCHO	1-(Cyclooct-2-enyl)ethanol **42A**	24	95	1*R*,1′*R*
PhCHO	(Cyclooct-2-enyl)(phenyl)methanol	28	93	1*S*,1′*R*

[a] As for Table 1. [b] As for Table 1 (except cyclooctenyl instead of cyclohexenyl).

Similarly, the hydroboration of cyclohepta-1,3-diene with $^{l}Ipc_2BH$ **19B** provided the enantiomeric reagent, which on reaction with acetaldehyde affords (1*S*,1′*S*)-1-(cyclohept-2-enyl)ethanol in comparable optical purities. Further, this synthesis was extended to benzaldehyde to provide the corresponding diastereoisomeric alcohol **37B** in 100% diastereoselectivity and 95% ee. The results are summarized in Table 2.

B-(*Cyclooct-2-enyl*)*diisopinocampheylborane* **18A** *and* **18B** *and Their Reaction with Aldehydes. Preparation of* 1-(*Cyclooct-2-enyl*)*alkan-1-ols.*—Cycloocta-1,3-diene was treated with $^{d}Ipc_2BH$ **19A** at −25 °C in THF. The hydroboration of this diene with Sia_2BH has been described elsewhere.[11b] After completion of the hydroboration, the reaction mixture was cooled to −78 °C and treated with acetaldehyde. Only the allylic derivative **18A** reacted with acetaldehyde, to provide the boronic ester **41** along with unchanged intermediate **39** and **40**. This mixture was directly oxidized with alkaline hydrogen peroxide* to obtain the required (1*R*,1′*R*)-1-(cyclooct-2-enyl)ethanol **42A** as a single diastereoisomer in 95% ee [eqn. (11)].



Reagents and conditions: i, RCHO, −78 °C; ii, [O]

Similarly, hydroboration of cycloocta-1,3-diene with $^{l}Ipc_2BH$, followed by reaction of the resulting allylborane reagent with acetaldehyde, afforded (1*S*,1′*S*)-1-(cyclooct-2-enyl)ethanol in comparable optical purities. This synthesis was extended to benzaldehyde to obtain the corresponding diastereoisomeric alcohol **42B** in 100% diastereoselectivity and in 93% ee. The results are summarized in Table 3.

The present study establishes the feasibility of the synthesis of highly enantiomerically pure *B*-(cycloalk-2-enyl)diisopinocampheylboranes **16**–**18** by hydroboration of the corresponding dienes with $^{l\ or\ d}Ipc_2BH$, without racemization. Furthermore, it demonstrates the synthetic utility of these reagents for highly enantio- and distereo-selective allylborations of representative aldehydes. We are very hopeful that this finds many applications in natural product synthesis.

Experimental

General.—The reaction flasks and other glass equipment were dried in an oven (140 °C, 12–18 h) and assembled in a stream of dry nitrogen gas. All reactions were carried out under nitrogen. Special experimental techniques used in handling air-sensitive materials are described in detail elsewhere.[17] THF was distilled over sodium benzophenone ketyl and stored under nitrogen in an ampoule. Aldehydes (Aldrich) were used without further purification. Cyclohexa-1,3-diene, cyclopenta-1,3-diene and cycloocta-1,3-diene were purchased from Aldrich and were used after being dried over molecular sieves. ^{11}B NMR spectra were recorded by using a Varian FT-80A instrument. The chemical shifts are in δ-values relative to BF_3·OEt_2. ^{1}H NMR spectra were recorded on either a Varian T-60 (60 MHz) or a Perkin-Elmer R-32 (90 MHz) instrument. *J*-Values are given in Hz. ^{13}C NMR spectra were recorded on a Varian FT-80A or XL-200 instrument. GC analysis was carried out with a Hewlett-Packard 5740 Chromatograph. Optical rotations were measured on an Autopol® III automatic polarimeter.

B-(*Cyclohex-2-yl*)*diisopinocampheylborane* **16A** *and Its Reaction with Aldehydes.* 1-(*Cyclohex-2-enyl*)*alkan-1-ols. Typical Procedure.*—Diisopinocampheylborane ($^{d}Ipc_2BH$) was prepared from (+)-α-pinene following the reported procedure.[18] To a stirred suspension of $^{d}Ipc_2BH$ (7.15 g, 25 mmol) in THF at −25 °C was added cyclohexa-1,3-diene (2.0 g, 25 mmol) dropwise. The hydroboration was complete in 12 h as indicated by the disappearance of the solid Ipc_2BH and confirmed by ^{11}B NMR (δ + 80) examination of the solution. The reaction mixture was then cooled to −78 °C and treated with acetaldehyde (1.4 cm^3, 25 mmol) dropwise. The contents were stirred at −78 °C for 3 h, the solid CO_2–acetone-bath was removed, and the mixture was allowed to warm to room temperature. ^{11}B NMR spectroscopy indicated formation of the borinate (δ + 56). The volatile materials were removed under reduced pressure (25 °C/18 mmHg/1 h, 0.05 mmHg/6 h) and the residue was dissolved in dry pentane (15 cm^3). The

* In these cases, we preferred the oxidative work-up to the ethanolamine work-up because the former method afforded better yields of isolated products.

borinate was cooled to 0 °C and treated with ethanolamine (1.5 cm^3, 25 mmol). The contents were stirred at 0 °C for 0.5 h and allowed to warm to room temperature. At this stage the reaction mixture was seeded with monoethanolamine–$BIpc_2$ adduct. ^{11}B NMR spectroscopy (δ + 13) of the reaction mixture indicated formation of the ethanolamine adduct **26**, which separated as a crystalline solid after the contents had been stirred at 25 °C for 1 h. With relatively hindered aldehydes, such as isobutyraldehyde and pivalaldehyde, the reactions were observed to be quite slow, and needed reaction times up to 24 h. The mixture was cooled to 0 °C, then filtered, and the solid was washed with cold pentane (2 × 100 cm^3). The residue, following removal of the solvent from the combined filtrate, was distilled to provide (1*R*,1′*R*)-1-(cyclohex-2-enyl)ethanol **25A** (2.07 g, 66%), b.p. 82 °C (18 mmHg); α_D^{23} −29.17° (*l* 0.5, neat), 94% ee; δ($CDCl_3$) 1.22 (3 H, d, *J* 7), 1.31–2.43 (8 H, m), 3.60–3.91 (1 H, m) and 5.46–6.01 (2 H, m); δ_C($CDCl_3$; Me_4Si) 19.95, 21.36, 23.73, 25.32, 42.90, 70.61, 128.34 and 129.87.

(1R,1′R)-1-(*Cyclohex-2-enyl*)*propan-1-ol* **25B**. Yield 65%; b.p. 72 °C (8 mmHg); α_D^{23} +32.69° (*l* 0.5, neat); 93% ee; $_H$($CDCl_3$) 1.03 (3 H, t, *J* 7), 1.36–2.53 (10 H, m), 3.36–3.60 (1 H, m) and 5.40–6.06 (2 H, m); δ_C($CDCl_3$; Me_4Si) 10.38, 21.44, 22.89, 25.33, 26.70, 40.96, 76.05, 128.91 and 130.16.

(1R,1′R)-1-(*Cyclohex-2-enyl*)-2-*methylpropan-1-ol* **25c**. Yield 69%; b.p. 68 °C (1.5 mmHg); α_D^{23} +22.65° (*l* 0.5, neat); 90% ee; δ_H($CDCl_3$) 1.00 (6 H, t, *J* 8), 1.11–2.59 (9 H, m), 3.14–3.42 (1 H, m) and 5.41–6.03 (2 H, m); δ_C($CDCl_3$; Me_4Si) 17.94, 19.42, 21.25, 22.34, 25.21, 30.04, 38.58, 79.47, 129.10 and 130.55.

(1S,1′R)-1-(*Cyclohex-2-enyl*)-2,2-*dimethylpropan-1-ol* **25D**. Yield 67%; b.p. 75 °C (1 mmHg); α_D^{23} +6.83° (*l* 0.5, neat); 90% ee; δ_H($CDCl_3$) 0.92 (9 H, s), 1.46–2.55 (8 H, m), 3.22 (1 H, br s) and 5.31–5.92 (2 H, m); δ_C($CDCl_3$; Me_4Si) 22.03, 23.02, 24.78, 27.22, 35.39, 38.69, 82.09, 130.25 and 131.76.

(1R,1′R)-1-(*Cyclohex-2-enyl*)*prop-2-en-1-ol* **25E**. Yield 58%; b.p. 76 °C (5 mmHg); α_D^{23} +41.76° (*l* 0.5, neat); 92% ee; δ_H($CDCl_3$) 1.21–2.50 (8 H, m), 3.80–4.12 (1 H, t, *J* 6) and 5.01–6.22 (5 H, m); δ_C($CDCl_3$; Me_4Si) 21.37, 24.12, 25.27, 41.51, 76.28, 115.91, 127.86, 129.82 and 139.35.

(1S,1″R)-(*Cyclohex-2-enyl*)(*phenyl*)*methanol* **25F**. Yield 71%; b.p. 82 °C (0.05 mmHg); $[\alpha]_D^{23}$ +17.72° (*c* 5, benzene); 94% ee; δ_H($CDCl_3$) 1.30–2.61 (8 H, m), 4.56 (1 H, d, *J* 7), 5.21–5.92 (2 H, m) and 7.36 (5 H, s); δ_C($CDCl_3$; Me_4Si) 21.16, 24.32, 25.27, 42.96, 77.44, 126.69, 127.25, 128.11, 129.75 and 143.17.

Hydrogenation of Compound **25A**.—A mixture of compound **25A** (0.5 g, 4 mmol) and 5% Pt–carbon (75 mg) in methanol (20 cm^3) was stirred and saturated with hydrogen by using a Brown automatic gasimeter,[19] until no more hydrogen was absorbed. The mixture was filtered and concentrated. The residue was purified to provide the known (*R*)-(−)-1-cyclohexylethanol **30**, (91%); $[\alpha]_D^{23}$ −4.79° (neat).[15]

Tosylation and Reductive Detosylation of Compound **25A**.—To a stirred solution of compound **25A** (1.3 g, 10 mmol) in THF (10 cm^3) at −78 °C was added butyllithium (2.1 mol dm^{-3}; 10 mmol) in hexane. After 1 h, a solution of tosyl chloride (1.9 g, 10 mmol) in THF (20 cm^3) was added dropwise and the reaction mixture was stirred for an additional hour; it was then gradually warmed to room temperature (2 h). To this mixture was slowly added lithium aluminium hydride in diethyl ether (1 mol dm^{-3}; 10 mmol) and the mixture was maintained at 40–45 °C while being stirred for 3 h. Finally, the mixture was poured into ice–water. The solid was filtered off and the filtrate was extracted with diethyl ether (2 × 10 cm^3). The combined extracts were washed successively with dil. HCl and brine, and dried over anhydrous $MgSO_4$. The concentration residue was purified to provide the known (*R*)-(+)-3-ethylcyclohexene **32**, $[\alpha]_D^{23}$ +20.73° (neat).[16]

Hydroboration of Cyclohexa-1,3-diene and Oxidation of Resulting Organoboranes. Cyclohex-2-enol.—To a stirred suspension of $^dIpc_2BH$ (7.15 g, 25 mmol) in THF at −25 °C was added cyclohexa-1,3-diene (2.4 cm^3, 25 mmol) dropwise. After the mixture had been kept at 12 h at −25 °C, trimethylamine *N*-oxide (7.5 g, 100 mmol) in diethyl ether (25 cm^3) was slowly added. The mixture was stirred at 0 °C for 3 h and at 25 °C for 3 h. Hydrolysis with aq. NaOH (3 mol dm^{-3}), followed by the usual work-up, provided a mixture of cyclohex-2-enol **22** and cyclohex-3-enol **23** (92:8) in 92% total yield. The 99% GC-pure sample of compound **22** was obtained by preparative GC (5% Carbowax on firebrick), $[\alpha]_D^{23}$ −104.5° (*c* 1.0, $CHCl_3$),[13] 93% ee; δ_H($CDCl_3$) 1.30–2.81 (7 H, m), 3.72–4.26 (1 H, m) and 5.53–5.91 (2 H, m); δ_C($CDCl_3$; Me_4Si) 19.05, 25.08, 32.00, 65.44, 130.98 and 130.26.

Reaction of B-(*Cyclohept-2-enyl*)*diisopinocampheylborane* **17A** *and Its Reaction with Aldehydes.* 1-(*Cyclohept-2-enyl*)*alkan-1-ol* **37A**. *Typical Procedure.*—To a stirred suspension of $^dIpc_2BH$ (25 mmol) in THF at −25 °C was added cyclohept-1,3-diene (3.2 cm^3, 25 mmol) dropwise. After being stirred at −25 °C for 30 h, the reaction mixture was cooled to −78 °C and treated with acetaldehyde (1.4 cm^3, 25 mmol). The contents were stirred at −78 °C for 3 h and then oxidized with alkaline hydrogen peroxide.* After usual work-up, the products were fractionally distilled to furnish compound **37A** (36%; 93% ee); δ_H($CDCl_3$) 1.12–2.90 (10 H, m), 4.60 (1 H, d, *J* 7), 5.42–6.08 (2 H, m) and 7.3 (5 H, s); δ_C($CDCl_3$; Me_4Si) 26.79, 28.22, 28.57, 29.92, 46.88, 77.27, 126.77, 127.30, 128.14, 132.09, 133.66 and 143.31.

(1S,1′R)-*Cyclohept-2-enyl*)(*phenyl*)*methanol* **37B**. Yield 38%; b.p. 88 °C (0.5 mmHg); $[\alpha]_D^{23}$ −40.16° (*c* 3.0, Et_2O); 95% ee; δ_H($CDCl_3$) 1.12–2.90 (10 H, m), 4.60 (1 H, d, *J* 7), 5.42–6.08 (2 H, m) and 7.3 (5 H, s); δ_C($CDCl_3$; Me_4Si) 26.79, 28.22, 28.57, 29.92, 46.88, 77.27, 126.77, 127.30, 128.14, 132.09, 133.66 and 143.31.

Reaction of B-(*Cyclooct-2-enyl*)*diisopinocampheylborane* **18A** *with Aldehydes.* 1-(*Cyclooct-2-enyl*)*alkan-1-ol* **42A**. *Typical Procedure.*—To a stirred suspension of $^dIpc_2BH$ (14.3 g, 50 mmol) in THF at −25 °C was added cycloocta-1,3-diene (6.5 cm^3, 50 mmol) dropwise. After being stirred at −25 °C for 30 h, the reaction mixture was cooled to −78 °C and treated with acetaldehyde (2.8 cm^3, 50 mmol). The contents were stirred at −78 °C for 3 h and oxidized with alkaline hydrogen peroxide.* After usual work-up, the products were fractionally distilled to furnish compound **42A** (24%); $[\alpha]_D^{24}$ −84.29° (*c* 3.1, Et_2O); 95% ee; δ_H($CDCl_3$) 1.12 (3 H, d, *J* 4), 1.36–2.62 (12 H, m), 3.65 (1 H, m) and 5.36–5.92 (2 H, m); δ_C($CDCl_3$; Me_4Si) 21.30, 25.61, 26.73, 26.91, 29.42, 31.80, 43.94, 71.53, 130.50 and 130.60.

(1S,1′R)-(*Cyclooct-2-enyl*)(*phenyl*)*methanol* **42B**. Yield 28%; b.p. 90 °C (0.5 mmHg); $[\alpha]_D^{23}$ −112.88° (*c* 2.6, Et_2O); 93% ee; δ_H($CDCl_3$) 1.02–3.06 (12 H, m), 4.53 (1 H, d, *J* 7), 5.12–5.86 (2 H, m) and 7.30 (5 H, s); δ_C($CDCl_3$; Me_4Si) 25.52, 26.67, 26.81, 29.36, 31.55, 43.34, 77.94, 126.79, 127.38, 128.17, 129.94, 130.56 and 143.62.

* In these cases, we preferred the oxidative work-up to the ethanolamine work-up because the former method afforded better yields of isolated products.

Acknowledgements

We gratefully acknowledge the financial support from the National Institutes of Health (grant GM 10937).

References

1 P. A. Bartlett, *Tetrahedron*, 1980, **36**, 3; M. T. Reetz, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 556; G. J. McGarvey, M. Kimura, T. Oh and J. M. Williams, *J. Carbohydr. Chem.*, 1984, **3**, 125; R. W. Hoffmann and K. Ditrich, *Tetrahedron Lett.*, 1984, **25**, 1781 and references therein.

2 T. Mukaiyama, *Org. React.*, 1982, **28**, 203; D. A. Evans, J. V. Nelson and T. R. Taber, *Top. Stereochem.*, 1982, **13**, 1; C. H. Heathcock in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic, New York, 1984, vol. 3, p. 111; S. Masamune and W. Choy, *Aldrichim. Acta*, 1982, **15**, 47; S. Kobayashi, H. Uchiro, Y. Fujishita, I. Shiina and T. Mukaiyama, *J. Am. Chem. Soc.*, 1991, **113**, 4247 and references therein.

3 (*a*) Y. Yamamoto, *Acc. Chem. Res.*, 1987, **20**, 243; (*b*) G. W. Kramer and H. C. Brown, *J. Org. Chem.*, 1977, **42**, 2292.

4 (*a*) R. W. Hoffmann and T. Herold, *Chem. Ber.*, 1981, **114**, 375; (*b*) M. T. Reetz and T. Zierke, *Chem. Ind.*, 1988, 663; (*c*) W. R. Roush, A. E. Watts and L. K. Hoong, *J. Am. Chem. Soc.*, 1985, **107**, 818; (*d*) W. R. Roush and L. Banfi, *J. Am. Chem. Soc.*, 1988, **110**, 3979; (*e*) R. P. Short and S. Masamune, *J. Am. Chem. Soc.*, 1989, **11**, 1892; (*f*) E. J. Corey, S.-M. Yu and S. S. Kim, *J. Am. Chem. Soc.*, 1989, **111**, 5495; (*g*) H. C. Brown, R. S. Randad, K. S. Bhat, M. Zaidlewicz and U. S. Racherla, *J. Am. Chem. Soc.*, 1990, **112**, 2389; (*h*) U. S. Racherla and H. C. Brown, *J. Org. Chem.*, 1991, **56**, 401.

5 W. R. Roush, A. D. Palkowitz and M. A. Palmer, *J. Org. Chem.*, 1987, **52**, 316; W. R. Roush and A. D. Palkowitz, *J. Am. Chem. Soc.*, 1987, **109**, 953; W. R. Roush, M. A. Adam, A. E. Watts and D. J. Harris, *J. Am. Chem. Soc.*, 1986, **108**, 3422 and references therein.

6 (*a*) R. W. Hoffmann and U. Weidmann, *Chem. Ber.*, 1985, **118**, 3966 and references therein; (*b*) R. W. Hoffmann, K. Ditrich and S. Froech, *Tetrahedron*, 1985, **41**, 5517 and references therein; (*c*) H. M. Hess and H. C. Brown, *J. Org. Chem.*, 1967, **32**, 4138; J. J. Patridge, N. K. Chadha and M. R. Uskokovic, *J. Am. Chem. Soc.*, 1973, **95**, 7171.

7 (*a*) H. C. Brown and P. K. Jadhav, *J. Am. Chem. Soc.*, 1983, **105**, 2092; (*b*) H. C. Brown, P. K. Jadhav and P. T. Perumal, *Tetrahedron Lett.*, 1984, **25**, 5111; (*c*) H. C. Brown and P. K. Jadhav, *Tetrahedron Lett.*, 1984, **25**, 1215; (*d*) P. K. Jadhav, K. S. Bhat, P. T. Perumal and H. C. Brown, *J. Org. Chem.*, 1986, **51**, 432; (*e*) H. C. Brown and K. S. Bhat, *J. Am. Chem. Soc.*, 1986, **108**, 293; (*f*) H. C. Brown, P. K. Jadhav and K. S. Bhat, *J. Am. Chem. Soc.*, 1988, **110**, 1535; (*g*) H. C. Brown and R. S. Randad, *Tetrahedron Lett.*, 1990, **31**, 455.

8 (*a*) R. W. Hoffmann and B. Landmann, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 437; (*b*) M. M. Midland and S. B. Preston, *J. Am. Chem. Soc.*, 1982, **104**, 2330; (*c*) M. Riediker and R. O. Duthaler, *Angew. Chem., Int. Ed. Engl.*, 1989, **28**, 494 and references therein.

9 B. M. Mikhailov, *Organomet. Chem. Rev., Sect. A*, 1972, **8**, 1.

10 H. C. Brown, P. K. Jadhav and K. S. Bhat, *J. Am. Chem. Soc.*, 1985, **107**, 2564.

11 For hydroboration of dienes with disiamylborane, see: (*a*) G. Zweifel, K. Nagase and H. C. Brown, *J. Am. Chem. Soc.*, 1962, **84**, 190; (*b*) H. C. Brown and K. S. Bhat, *J. Org. Chem.*, 1986, **51**, 445.

12 G. Zweifel, N. L. Polston and C. C. Whitney, *J. Am. Chem. Soc.*, 1968, **90**, 6243.

13 R. K. Hill and J. W. Morgan, *J. Org. Chem.*, 1968, **33**, 927; T. Sato, Y. Gotoh, Y. Wakabagashi and T. Fujisawa, *Tetrahedron Lett.*, 1983, **24**, 4123.

14 H. C. Brown and K. S. Bhat, *J. Am. Chem. Soc.*, 1986, **108**, 5919.

15 For absolute configuration and maximum reported rotation of 1-cyclohexylethanol, see: K. Mislow, *J. Am. Chem. Soc.*, 1951, **73**, 3954; P. A. Levene and S. A. Harris, *J. Biol. Chem.*, 1936, **113**, 55.

16 For absolute configuration and maximum reported rotation of (+)-3-ethylcyclohexene, see: J. H. Brewster, *J. Am. Chem. Soc.*, 1959, **81**, 5943; G. Buono, G. Peiffer, A. Mortreux and F. Petit, *J. Chem. Soc., Chem. Commun.*, 1980, 937; G. Cosiglio, F. Morandini and O. Piccolo, *J. Chem. Soc., Chem. Commun.*, 1983, 112.

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

18 H. C. Brown, M. C. Desai and P. K. Jadhav, *J. Org. Chem.*, 1982, **47**, 5065.

19 C. A. Brown and H. C. Brown, *J. Org. Chem.*, 1966, **31**, 398.

Paper 1/02870G
Received 14*th June* 1991
Accepted 8*th July* 1991