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AN IMPROVED SYNTHESIS OF *cis*-ALKENYLBORANES *

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Summary

The hydroboration of 1-halo-1-alkynes with dialkylboranes followed by treatment with t-butyllithium proceeds readily at —78° C to afford stereochemically pure *cis*-alkenylboranes in excellent yields.

Introduction

Stereoselective syntheses involving *trans*-alkenylborane intermediates are well documented. However, until recently the lack of convenient procedures for the preparation of *cis*-alkenylboranes has precluded their use in synthesis.

Negishi has developed a synthesis of *cis*-alkenylboranes involving hydroboration of 1-halo-1-alkynes with dialkylboranes, followed by treatment with either lithium triethylborohydride or potassium tri-s-butylborohydride [1]. A disadvantage of this method is the presence of triethyl- or tri-s-butyl-borane in the reaction mixture, making it necessary to remove these by-products for subsequent conversions of the alkenyldialkylborane product.

Consequently, we undertook an investigation of the preparation of *cis*-alkenylboranes from reagents whose by-products would not involve such difficulties, either because they could be readily removed or because they would not interfere with representative reactions of organoboranes. We found that t-butyllithium is the reagent of choice in this application, since isobutylene is the innocuous by-product, readily removed by volatilization or inert to subsequent reactions of the vinylborane.

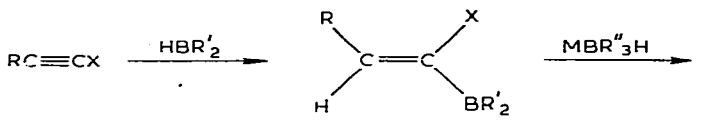
Results and discussion

Reaction of 1-halo-1-alkenyl-dicyclohexyl- and -disiamyl-boranes with t-butyllithium

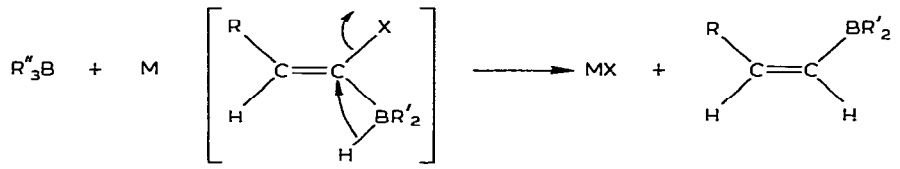
Negishi's synthesis may proceed through a metal trialkylborohydride inter-

* Dedicated to Professor Herbert C. Brown, an inspiring teacher.

mediate, I (eq. 1). This intermediate would rapidly give rise to a *cis*-alkenylborane by hydride transfer with displacement of halide.



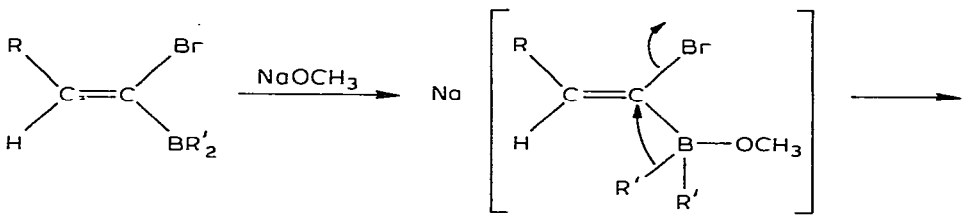
(1)



(I)

X = halogen ; M = Li, K ; R, R', R'' = alkyl

Such anionotropic rearrangements are well known in organoborane chemistry. For example, reaction of 1-halo-1-alkenylboranes with sodium methoxide followed by treatment with acetic acid produces *trans*-olefins (eq. 2) [2].



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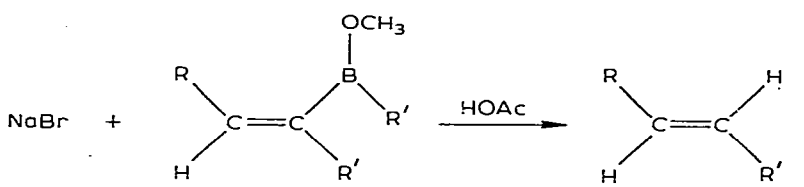


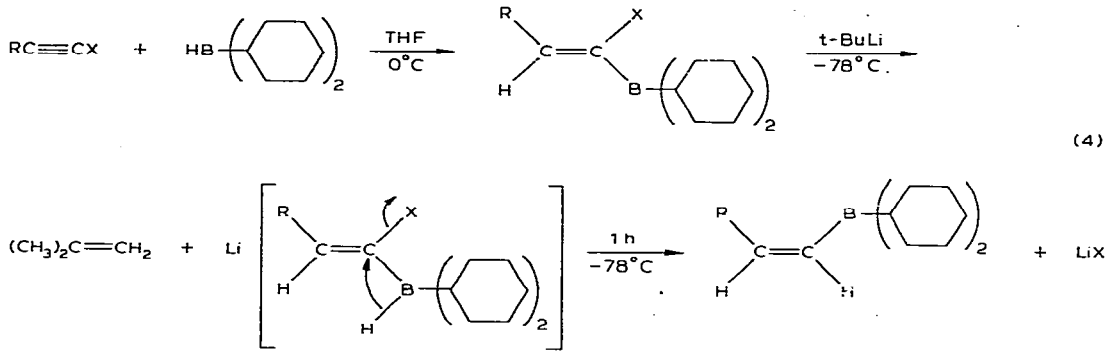
A convenient method to prepare trialkylborohydrides was first reported by Corey and his coworkers [3] and later extensively utilized by others [4]. This method involves treatment of trialkylboranes with t-butyllithium to afford the corresponding lithium trialkylborohydrides and isobutylene (eq. 3). Kramer

$$R_3B + \text{t-BuLi} \xrightarrow[-78^\circ C]{THF} Li[R_3BH] + (CH_3)_2C{=}CH_2 \qquad (3)$$

found that even highly hindered boranes are rapidly and quantitatively transformed into trialkylborohydrides at −78° C.

Therefore, we decided to explore the reaction of t-butyllithium with representative 1-halo-1-alkenylboranes. Indeed, we discovered that both the transfer of hydride to boron and subsequent rearrangement proceed with ease

at —78° C (as evidenced by precipitation of lithium halide) to provide *cis*-alkenylboranes in excellent overall yield, stereochemically pure within the limits of detection (<2%) (eq. 4).



(4)

Both 1-bromo- and 1-iodo-1-hexyne were examined as starting materials and were found to be satisfactory if they were freshly distilled. However, since both the hydroboration and the reaction with t-butyllithium were noticeably slower for the 1-bromohexyne, the 1-iodoalkynes were adopted as starting materials for the remainder of the reactions.

The *cis*-alkenylboranes prepared by this method are readily isolated in pure form. After the reaction is complete, the volatiles are removed in vacuo. To the solid which remains is added a portion of pentane. The resulting suspension is stirred for a few minutes, allowed to settle, and the supernatant liquid is carefully decanted via a double-ended needle to a centrifuge tube at —78° C. This extraction procedure is repeated twice. The combined extracts are centrifuged cold, and the clear, colorless liquid is carefully decanted to another flask via a double-ended needle. Removal of the pentane in vacuo leaves the pure *cis*-alkenylboranes (Table 1).

To test for the stereochemical purity of the products we utilized the *cis*-alkenyldicyclohexylboranes in a reaction which has been well studied for the *trans*-alkenylboranes. Thus *cis*-1-decenyldicyclohexylborane was deuterated to yield *Z*-1-*d*-1-decene in excellent yield (eq. 5). No trace of the *E* isomer was detected by ^{1}H or ^{13}C NMR.

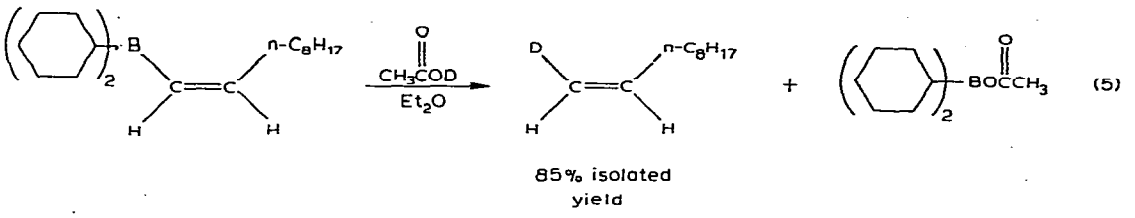
Protonolysis of alkenylboranes is known to occur with strict retention of configuration at the reaction center [5]. Therefore the *cis*-alkenylborane must be formed in a highly stereospecific manner.

In many cases the alkenylborane need not be isolated, and an in situ prepara-

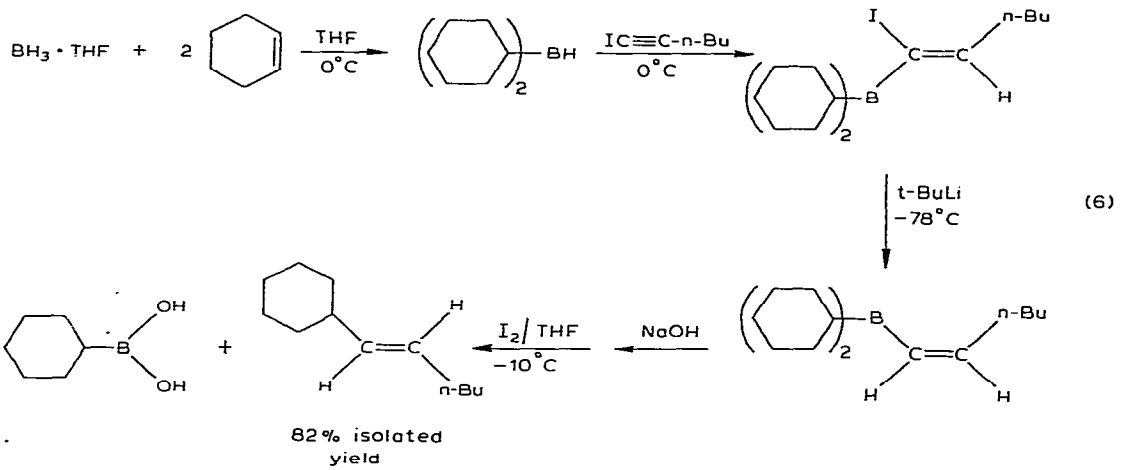
TABLE 1

PREPARATION OF *cis*-ALKENYLDICYCLOHEXYLBORANES

Halide	Product	Isolated yield (%)
1-Bromo-1-hexyne	*cis*-1-Hexenyldicyclohexylborane	92
1-Iodo-1-hexyne	*cis*-1-Hexenyldicyclohexylborane	87
1-Iodo-1-decyne	*cis*-1-Decenyldicyclohexylborane	78
1-Iodo-5-chloro-1-pentyne	*cis*-1-(5-Chloropentenyl)dicyclohexylborane	88



tion of *trans*-1-cyclohexyl-1-hexene was accomplished to demonstrate this (eq. 6).



The reaction was extended to include syntheses of *cis*-1-alkenyldisiamylboranes, although the yields were somewhat lower than those found for the dicyclohexylboranes (Table 2).

Reaction of 1-halo-1-alkenyl-9-borabicyclo[3.3.1]nonane with t-butyllithium

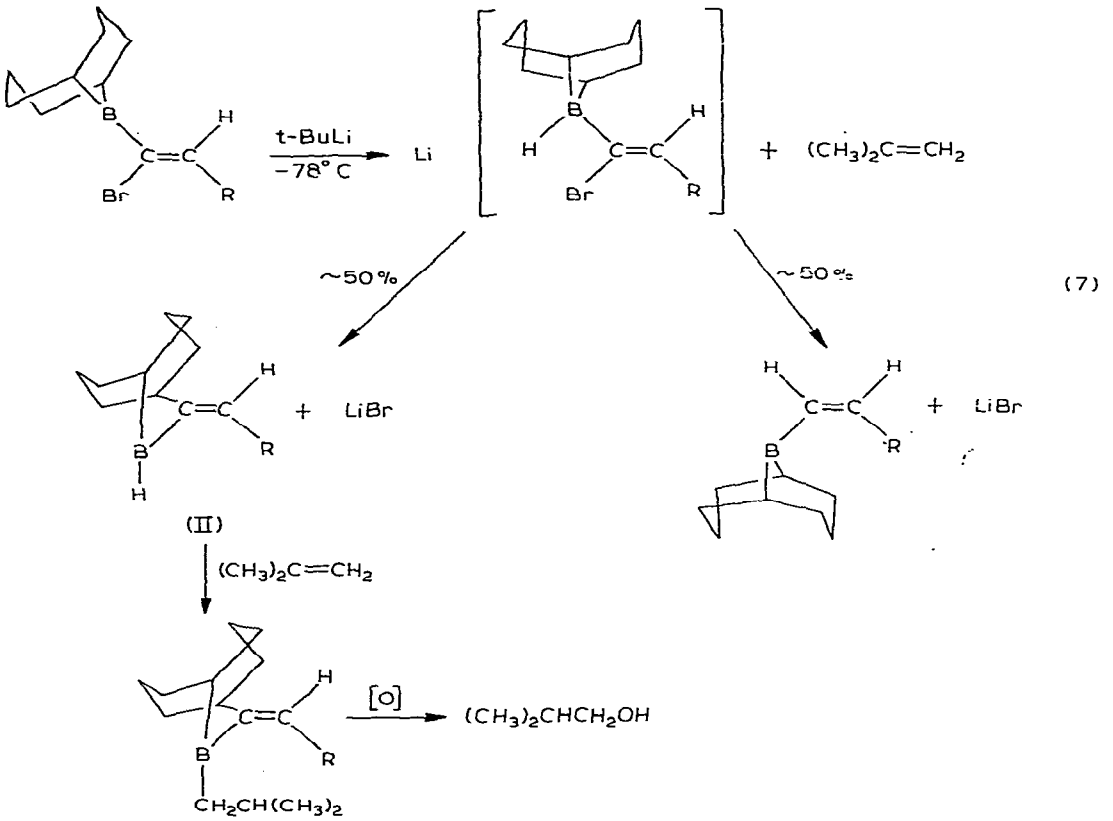
Attempts to prepare *cis*-alkenyl-9-BBN derivatives were unsuccessful due to competing cyclooctyl ring transfer (eq. 7). Thus t-butyllithium was treated with 1-bromo-1-hexenyl-9-BBN in the usual manner. The reaction mixture was quenched and tested for active hydride in an analytical gas buret [6]. The results indicated the presence of 12% active hydride, probably as compound II. Oxidation and gas chromatographic analysis of the reaction mixture revealed that 39% isobutyl alcohol was formed from the hydroboration of isobutylene evolved in the reaction. Therefore approximately 51% cyclooctyl migration is occurring in these reactions.

TABLE 2

PREPARATION OF *cis*-ALKENYLDISIAMYLBORANES

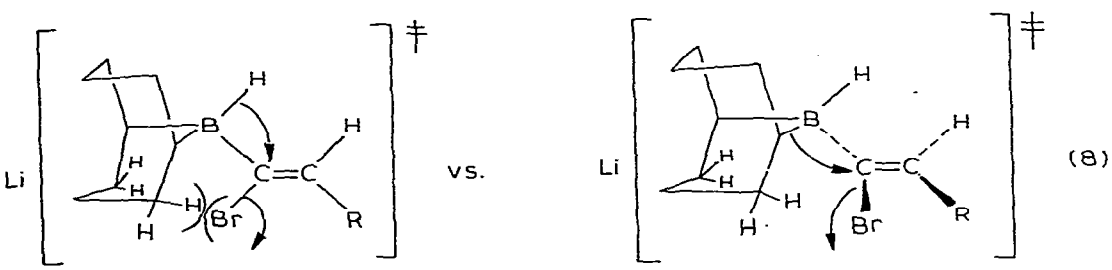
Halide	Borane	Yield (%) isolated [a]
1-Iodo-1-hexyne	*cis*-1-Hexenyldisiamylborane	70
1-Iodo-5-chloro-1-pentyne	*cis*-1-(5-Chloropentenyl)disiamylborane	68

[a] 80—90% pure by NMR.



(7)

Examination of molecular models clearly indicates that the required antiperiplanar transition state for migration of hydride has severe steric hindrance for departure of the bromide ion, while for migration of the cyclooctyl group the steric interactions are minimal (eq. 8).



(8)

Thus for the first time *cis*-alkenylboranes can be stereospecifically produced in a manner completely free of other organoboranes in the reaction mixture. This procedure will therefore greatly facilitate their use in organic synthesis.

Experimental

General comments

All reactions were carried out in pre-dried glassware (140°C, 4 h) which was

assembled hot and cooled under a stream of dry nitrogen. Reagent transfers were conducted utilizing the techniques described in Chapter 9 of ref. 6. Spectra were recorded on the following instruments: ^{1}H NMR, Varian T-60; ^{13}C NMR, Varian CFT-20; ^{11}B NMR, Varian XL-100 operating in the FT mode at 32.1 MHz; IR, Perkin—Elmer 700. Solvents (THF, ethyl ether and pentane) were distilled from lithium aluminum hydride under nitrogen before use. Alkynes used were commercially available and were distilled before use. Organolithium reagents were purchased from Alfa/Ventron and were standardized by the Watson—Eastham titration [7]. All boron hydrides and organoboron hydrides were available in this laboratory from previous work or were prepared according to published procedures [6]. The 1-halo-1-alkynes were prepared by halogenation of the corresponding 1-lithioacetylides and were distilled immediately prior to use.

Synthesis of cis-1-alkenyldialkylboranes

(i) cis-1-Hexenyldicyclohexylborane from 1-bromo-1-hexyne. To a 0°C slurry of freshly prepared dicyclohexylborane [6] in 25 ml THF was added dropwise 3.86 ml (30 mmol) of freshly distilled 1-bromo-1-hexyne. The reaction was stirred for 3 h at 0°C then for 30 min at room temperature, during which time the white precipitate of dicyclohexylborane had completely disappeared. The clear solution containing 1-bromo-1-hexenyldicyclohexylborane was then cooled to —78°C and 16.8 ml of t-butyllithium in pentane (30.0 mmol, 1.78 *M*) was added dropwise over a period of 45 min with vigorous stirring. After the addition of t-butyllithium, during which lithium bromide had precipitated, the reaction was allowed to stir for 30 min at —78°C followed by warming to room temperature and stirring for an additional 30 min. The volatiles were removed using a water aspirator followed by high vacuum for 2 h. The product was taken up in 15 ml of pentane and decanted away from the lithium bromide residue into a centrifuge tube that had been cooled to —78°C. The remaining lithium bromide was washed with 2 × 10 ml of pentane, and the washings were combined in the centrifuge tube. After centrifuging to remove any suspended lithium bromide, the clear supernatant was decanted off and the pentane removed in vacuo. The resulting clear, slightly yellow liquid gave 7.19 g (92.0%) of *cis*-1-hexenyldicyclohexylborane. ^{1}H NMR (CCl_4): δ 5.80 (multiplet, ~1.8 H); 0.9—2.0 ppm (multiplet, ~31.2 H). Complete absence of *trans*-isomer.

(ii) cis-1-Hexenyldicyclohexylborane from 1-iodo-1-hexyne. cis-1-Hexenyldicyclohexylborane was prepared in an analogous fashion to that described above except 1-iodo-1-hexyne was utilized. There was obtained 6.78 g (87.0%) of a clear, slightly yellow liquid whose ^{1}H NMR was nearly identical to that of an authentic sample. The integration of peaks was, however, much closer to the predicted value than in procedure (i).

(iii) cis-1-Hexenylbis(3-methyl-2-butyl)borane (cis-1-hexenyldisiamylborane). The intermediate *cis*-1-iodo-1-hexenyldisiamylborane was prepared by addition of 3.95 ml (30 mmol) of neat 1-iodo-1-hexyne to a —10°C solution of 30.0 mmol of disiamylborane, 1.0 *M* in THF. The hydroboration was completed by stirring for 30 min at 0°C followed by 30 min at room temperature. The solution was then cooled to —78°C and 30.0 mmol of t-butyllithium was added

dropwise as described above. After work-up, 4.99 g (70.4%) of a clear, yellow liquid was obtained. ^{1}H NMR revealed the characteristic *cis*-vinyl absorptions with the complete absence of any *trans* isomer. The integration showed the product to be about 80—90% pure. ^{1}H NMR (CCl_4); δ 5.80 (multiplet, 1.6 H); 1.0—2.0 (multiplet); 0.93 (singlet); 0.83 ppm (singlet).

(iv) cis-1-Decenyldicyclohexylborane. This was prepared in an analogous manner as previously described from 1-iodo-1-decyne on a 50.0 mmol scale. Yield: 12.04 g (77.6%); ^{1}H NMR (CCl_4); δ 5.80 (multiplet, 2 H); 1.32; 0.90 ppm

(v) cis-1-(5-Chloropentenyl)dicyclohexylborane. This was prepared in an analogous manner as previously described from 1-iodo-5-chloro-1-pentyne on a 30.0 mmol scale. Yield: 7.42 g (88.3%). ^{1}H NMR (CCl_4): δ 5.83 (multiplet, 2 H); 3.47 (triplet, *J* 6 Hz, 2 H); 1.0—2.2 ppm (multiplet, 26 H).

(vi) cis-1-(5-Chloropentenyl)disiamylborane. This was prepared in an analogous manner as previously described from 1-iodo-5-chloro-1-pentyne on a 30 mmol scale. Yield: 5.20 g (67.5%). ^{1}H NMR (CCl_4): δ 5.90 (multiplet); 3.5 (multiplet); 1.2—2.5 (multiplet); 0.93 (singlet); 0.43 ppm (singlet). Purity ~80% by NMR.

Attempted preparation of cis-1-hexenyl-9-borabicyclo[3.3.1]nonane (cis-1-hexenyl-9-BBN)

(i) The intermediate *cis*-1-bromo-1-hexenyl-9-BBN was prepared by the addition of 19.3 ml (10.0 mmol, 0.52 *M*) of 9-BBN in THF to a 0°C solution containing 1.92 ml (15.0 mmol) of 1-bromo-1-hexyne in THF. (Note: A 50% excess of the alkyne is used to suppress dihydroboration). After complete addition of the 9-BBN, the cold bath was removed and the reaction warmed to room temperature and stirred for 15 h. The solvent and unreacted 1-bromo-1-hexyne were removed under high vacuum (4 h) and a small aliquot of the residual liquid removed. ^{1}H NMR revealed the expected absorptions and integrations for *cis*-1-bromo-1-hexenyl-9-BBN. ^{1}H NMR (CCl_4): δ 7.02 (triplet, *J* 7 Hz, 1 H); 2.4 (multiplet); 1.86; 0.95 ppm (triplet). ^{11}B NMR (CCl_4): δ +77.7 (relative to $BF_3 \cdot Et_2O$). The remainder of the borane was dissolved in THF and cooled to —78°C and a stoichiometric amount of t-butyllithium was added dropwise with lithium bromide precipitating as expected. After the usual work-up as described above, an aliquot was removed and a ^{1}H NMR taken. A mixture of products was noted, with an apparent triplet at δ 5.80 ppm. There also appeared to be at least two cyclooctyl envelopes, as well as two sharp peaks at δ 0.9 and 1.1 ppm. ^{11}B NMR showed a single broad peak at δ +82.9 ppm (relative to $BF_3 \cdot Et_2O$).

(ii) Course of the reaction of t-butyllithium with cis-1-bromo-1-hexenyl-9-BBN. The usual procedure for preparing *cis*-alkenylboranes was used in treating 3.30 mmol (1.83 ml, 1.78 *M*) of t-butyllithium with 3.3 mmol of *cis*-1-bromo-1-hexenyl-9-BBN at —78°C. After stirring for 30 min at —78°C, the reaction was warmed to room temperature and stirred for 1 h. The reaction vessel was then attached to a gas buret with a Dry Ice/acetone trap and 5.0 ml of a pH 7 phosphate buffer was added. The evolved hydrogen was collected and the volume measured with corrections for water vapor pressure, atmospheric pressure, temperature, and aliquot volume displacement included. About 0.4 mmol or 12%

hydrogen was found, indicating active hydride. Addition of ethanol (3.0 ml) as a cosolvent followed by 2.0 ml of 30% hydrogen peroxide was used to oxidize any organoborane. VPC analysis using n-octane (1.07 mmol, 0.122 g) as an internal standard showed 1.28 mmol (39%) of isobutyl alcohol, a trace of n-hexanal, and several other unidentified peaks.

Reactions of cis-1-alkenyldialkylboranes

(i) Deuterolysis of cis-1-decenyldicyclohexylborane. Neat *cis*-1-decenyldicyclohexylborane (35.0 mmol) was dissolved in 15.0 ml of dry ethyl ether, cooled to 0°C followed by addition of 5.2 ml (90.0 mmol) of deuterioacetic acid (Aldrich, ~99%-*d*). The ice-bath was then removed and the reaction stirred for 3 h at room temperature. The ether was removed under aspirator vacuum followed by using high vacuum (~0.001 mmHg) with a Dry Ice/acetone trap to collect all of the volatiles including the product. The volatiles were taken up in pentane with the trap rinsed with several pentane washings. The combined organic layer was then shaken vigorously with 3 × 20 ml of 1 *N* NaOH to remove any unreacted acetic acid. After drying over anhydrous potassium carbonate, the pentane was removed by aspirator vacuum and the residue distilled, b.p., 67—69°C/17 mmHg, to afford 4.18 g (84.6%) of a clear, colorless liquid. The product was ~99% pure by VPC analysis. n_d^{20} — 1.4227. ^{1}H NMR (CCl_4); δ 5.7 (multiplet, 1 H); 4.85 (doublet, *J* 10 Hz, 1 H); 2.02 (multiplet, 2 H); 1.3 (broad singlet, 14 H); 0.85 ppm (multiplet, 3 H). ^{13}C NMR ($CDCl_3$): δ 139.10; 113.89 (triplet, $J(^{13}C—D)$ 23.5 Hz); 33.96; 32.10; 29.68; 29.49; 29.37; 29.17; 22.84; 14.13 ppm; additional small peak at δ 114.16 ppm due to undeuterated olefinic carbon). IR: 2890; 1620; 1465; 800 cm^{-1}.

(ii) In situ preparation of trans-1-cyclohexyl-1-hexene. *cis*-1-Hexenyldicyclohexylborane was prepared on a 50.0 mmol scale from 1-iodo-1-hexyne as described above. However, the borane was not isolated, but rather used directly after warming to room temperature and stirring for 30 min. After cooling to —10°C in an ice/salt bath, 30 ml (180 mmol) of 6 *M* NaOH was added to the reaction mixture. To this was added dropwise 12.7 g (50 mmol) of iodine in 50 ml of THF over a period of 20 min. After the addition was complete the cold bath was removed, and the reaction warmed to room temperature for 1 h. Pentane, 50 ml, was added and the organic layer was decanted off. The aqueous residue was washed with 3 × 30 ml pentane and the combined organic layer was dried over anhydrous magnesium sulfate. After removal of the volatiles under aspirator vacuum, the crude product was distilled, b.p. 50—52°C/1.4 mmHg. Yield: 6.79 g (81.7%). n_D^{20} — 1.4603. ^{1}H NMR (CCl_4): δ 5.38 (multiplet, 2 H); 0.8—2.2 (multiplet, 20 H). ^{13}C NMR ($CDCl_3$): δ 136.58; 127.81; 33.52; 32.54; 32.11; 26.35; 22.34; 14.03 ppm. IR (neat): 2880; 1450; 970 cm^{-1}. VPC analysis: >98% pure.

Acknowledgement

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