of the reaction mixture indicated 3.38 mmol of residual hydride, which means that 0.62 mmol of hydride per millimole of 2-heptanone had been consumed. After 3 h, the analysis showed 2.98 mmol of residual hydride, which indicated that 1.02 mmol of hydride per millimole of the compound had been consumed. These results are summarized in Table II.[9b]

General Procedure for Stereoselectivity Study. The reduction of 2-methylcyclohexanone is described here as representative. To a 100-mL round-bottom flask fitted with a sidearm and capped by a rubber septum was added 2 mL of a solution of ThxBHCl in methylene chloride (4 mmol in hydride). The flask was kept at -78 °C with the aid of a dry ice-acetone bath. To this was added 2 mL of a 1 M 2-methylcyclohexanone solution in methylene chloride (at -78 °C). The reaction mixture was kept at -78 °C for 12 h. It was then hydrolyzed by the addition of 1 mL of 3 N NaOH and 0.5 mL of 30% H_2O_2. The aqueous layer was saturated with anhydrous potassium carbonate, and the organic layer was analyzed by means of GC. The results are summarized in Table III.

Supplementary Material Available: Tables I, II, IV, V, VI, VII, VIII, IX, X, and XI, giving the rate and stoichiometry data (10 pages). Ordering information is given on any current masthead page.

Vinylic Organoboranes. 6. A General Synthesis of (*E*)-Disubstituted Alkenes or Ketones via the (*E*)-(1-Substituted-1-alkenyl)boronic Esters[1]

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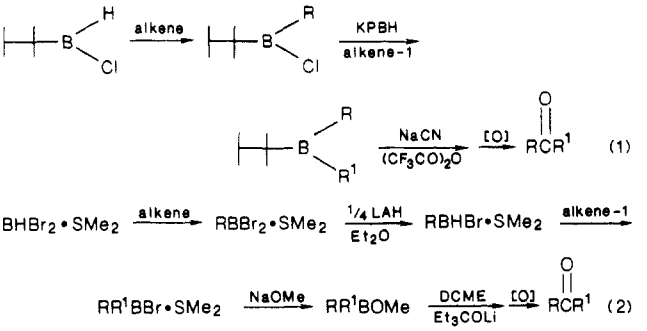
Received March 24, 1986

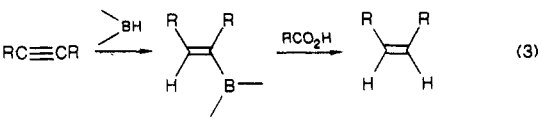
Development of a general stereospecific synthesis of (*E*)-disubstituted alkenes utilizing a variety of hydroborating agents such as monohaloborane, thexylborane, thexylchloroborane, and dibromoborane is discussed. Hydroboration of 1-halo-1-alkynes with dialkylboranes (R_2BH, **1**), thexylmonoalkylborane (ThxBHR, **6**), or alkylbromoborane (RBHBr·SMe_2, **10**) provides the corresponding *B*-(*cis*-1-halo-1-alkenyl)alkylborane derivatives (**2**, **7**, **11**), respectively. Treatment of *B*-(*cis*-1-halo-1-alkenyl)dialkylborane (**2**) with sodium methoxide results in the intramolecular displacement of bromine by one of the alkyl groups on boron to produce *B*-(*trans*-1-alkyl-1-alkenyl)alkylborinate esters **3**. Protonolysis of **3** provides *trans*-alkenes **4** in high yields and in >99% isomeric purities. Similarly, the intermediates **8** and **12** afford the *trans*-disubstituted alkenes in excellent yields and in >99% isomeric purities. Alternatively, oxidation of these vinylboron derivatives, **3**, **8**, and **12**, with alkaline hydrogen peroxide provides the corresponding ketones in excellent yields.

Recent developments in organic synthesis demand greater regio- and stereoselectivities in organic synthesis. Stereospecific synthesis of (*Z*)- and (*E*)-disubstituted alkenes has attracted considerable attention in recent years because most of the insect pheromones belong to this class of compounds with hydroxy or acetate functionality.[3] Since the presence of geometric isomers inhibits the activity of the pheromones,[4] the isomeric purity is a highly important factor in preparing the insect sex attractants.

Another valuable group of organic compounds are the carbonyl derivatives. A number of methods have been developed for the synthesis of ketones using organoboranes via carbonylation, cyanidation, or carbenoidation.[5] All of these reactions involve the conversion of two alkenes into the corresponding ketone. Recently thexylchloroborane[6] (eq 1) and dibromoborane[7] (eq 2) have been found to be the best reagents for this elegant conversion of two alkenes into the corresponding ketones.



The hydroboration reaction readily converts alkenes and alkynes into the corresponding organoboranes that can be conveniently transformed into a variety of organic functional derivatives.[8,9] Monohydroboration of internal alkynes provides the vinylboranes (eq 3). Protonolysis



of these vinylboranes proceeds with retention of configuration, thus providing a stereospecific synthesis of (*Z*)-alkenes in excellent yields.[8] Oxidation of these vinylborane intermediates affords ketones in excellent yields, thus

(1) For preliminary results, see: (a) Brown, H. C.; Basavaiah, D. *J. Org. Chem.* **1982**, *47*, 754. (b) Negishi, E.; Katz, J.-J.; Brown, H. C. *Synthesis* **1972**, 555. (c) Brown, H. C.; Lee, H. D.; Kulkarni, S. U. *Ibid.* **1982**, 195. (d) Brown, H. C.; Basavaiah, D.; Kulkarni, S. U. *J. Org. Chem.* **1982**, *47*, 3808. (e) Kulkarni, S. U.; Lee, H. D.; Brown, H. C. *Synthesis* **1982**, 193.

(2) (a) Postdoctoral research associate on Grant GM 10937 from the National Institutes of Health. (b) Postdoctoral research associate (1978-1982) Purdue University. (c) Postdoctoral research associate (1979-1982) on a grant from Albany International Chemical Division. (d) Graduate student, Purdue University (1971-1974), on grant GM 10937 from the National Institutes of Health.

(3) Mori, K. *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley-Interscience: New York, 1981; Vol. 4, pp 1-183.

(4) (a) Jacobson, M. *Science (Washington, D.C.)* **1969**, *163*, 190. (b) Roclofs, W. L.; Tette, J. P. *Nature (London)* **1970**, *226*, 1172.

(5) Kulkarni, S. U.; Basavaiah, D.; Zaidlewicz, M.; Brown, H. C. *Organometallics* **1982**, *1*, 212.

(6) Zweifel, G.; Arzoumanian, H. *J. Am. Chem. Soc.* **1967**, *89*, 5086.

(7) Brown, H. C.; Kulkarni, S. U. *J. Organomet. Chem.* **1981**, *218*, 299.

(8) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Syntheses via Boranes*; Wiley-Interscience: New York, 1975.

(9) Brown, H. C. *Pure Appl. Chem.* **1976**, *47*, 49.

0022-3263/86/1951-5270$01.50/0

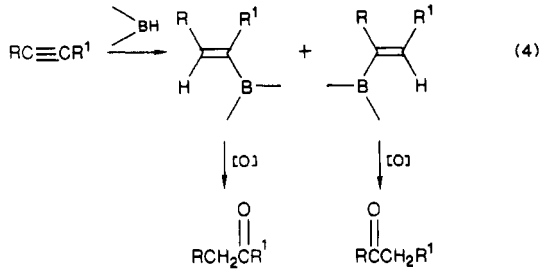
Table I. Synthesis of *trans*-Alkenes from Dialkylhaloboranes and 1-Bromo-1-alkyne[a]

alkene for R_2BX	X	1-bromo-1-alkyne	product[b,c]	yield,[d] %	bp, °C/mm	n^{20}_D
1-hexene[e]	Cl	1-bromo-1-hexyne	**4a**	79	85–87/6 [lit.[26] 213.5/760]	1.4304
2-methyl-1-pentene[e]	Cl	1-bromo-1-octyne	**4b**	77	88–90/1	1.4365
cyclopentene	Br	1-bromo-1-hexyne	**4c**	73	66–67/3	1.4526
cyclopentene	Br	1-bromo-1-octyne	**4d**	70	73–74/0.6	1.4562

[a] All reactions were carried out in 30-mmol scale. [b] Chemical purities of all compounds are >99% by GC analysis on a 6 ft × 1/4 in. column (10% SE-30). [c] Isomeric purities are >99% determined by ^{13}C NMR analysis.[22] [d] Yields of pure products isolated by distillation based on R_2BX or 1-bromo-1-alkyne. [e] Distilled R_2BX was utilized.

offering an alternate route for the synthesis of ketones.

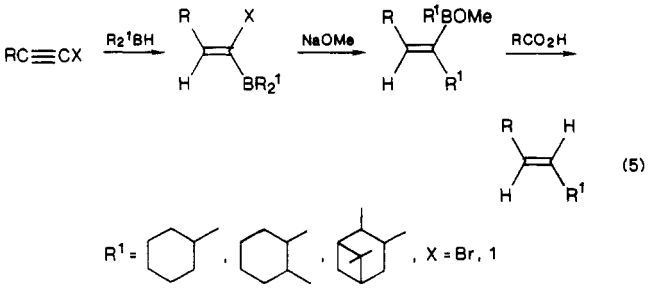
However, unsymmetrical alkynes usually give a mixture of two isomeric ketones (eq 4). A synthetic survey for the



(4)

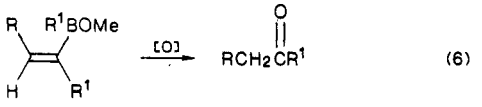
preparation of unsymmetrical ketones lies in developing a convenient method for the synthesis of pure unsymmetrical vinylborane derivatives.

The first synthesis of *B*-(*trans*-1-alkyl-1-alkenyl)alkylborinate esters was due to Zweifel and co-workers[10] (eq 5).



(5)

This method involved hydroboration of 1-halo-1-alkynes with dialkylboranes, followed by the base-induced intramolecular displacement of bromine by one of the alkyl groups on boron. The resulting *B*-(*trans*-1-alkyl-1-alkenyl)alkylborinate esters on protonolysis affords the desired *trans*-alkenes in excellent yields. Oxidation produced the desired unsymmetrical ketones (eq 6).



(6)

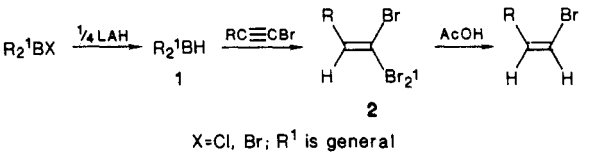
However, the applicability of this method is limited to the availability of dialkylboranes. Direct hydroboration usually fails to stop at the dialkylborane state, generally proceeding to the trialkylborane stage. Only in the case of relatively hindered alkenes does direct hydroboration stop at the dialkylborane stage. Hence, Zweifel's synthesis of *trans*-alkenes and ketones has found limited application in organic synthesis. The second disadvantage in this procedure is the loss of one of the two alkyl groups on boron. We now report solutions for both of these problems, thus providing a general and more practical synthesis of (*E*)-alkenes. Oxidation of the same boron intermediate provides a convenient route to unsymmetrical ketones.

(10) (a) Zweifel, G.; Arzoumanian, H. *J. Am. Chem. Soc.* **1967**, *89*, 5086. (b) Zweifel, G.; Fisher, R. P.; Snow, J. T.; Whitney, C. C. *Ibid.* **1971**, *93*, 6309.

Results and Discussion

The first problem was solved by a general synthesis of dialkylboranes **1**, developed recently in our laboratory, utilizing the hydridation of dialkylhaloboranes.[11]

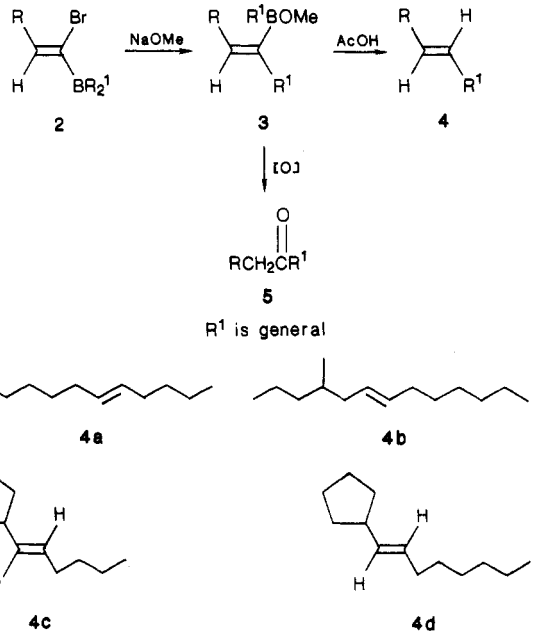
Hydroboration with Dialkylboranes. Hydroboration of 1-bromo-1-alkynes with dialkylboranes affords cleanly the monohydroborated product,[12] *B*-(*cis*-1-bromo-1-alkenyl)dialkylboranes **2**, as evidenced by the formation of *cis*-1-bromo-1-octene on protonolysis of the vinylborane **2** (eq 7). Treatment of these



(7)

X=Cl, Br; R¹ is general

intermediates (**2**) with sodium methoxide results in the intramolecular displacement of bromine by one of the alkyl groups on boron to produce *B*-(*trans*-1-alkyl-1-alkenyl)alkylborinate esters **3**, thus representing the first general synthesis of such derivatives. Protonolysis of these borinate esters (**3**) with acetic acid provides the desired *trans*-alkenes **4** in high yields and high isomeric purities (>99%) (eq 8) (Table I).



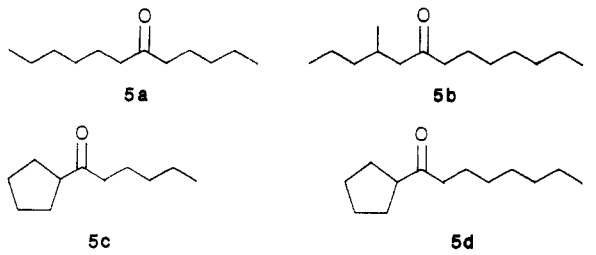
(8)

Oxidation of these unsymmetrically substituted vinylborane derivatives (**3**) with alkaline hydrogen peroxide gives ketones **5** in excellent yield. Representative ketones **5a–d** were prepared by using this method (Table II).

Thus, this modification greatly extends the applicability of Zweifel's synthesis of *trans*-alkenes and ketones. However, this procedure suffers from a loss of one of the alkyl groups on boron, thus rendering it less practical when the alkyl group is derived from a valuable alkene. This difficulty was circumvented to some extent by using thexylmonoalkylborane for the hydroboration of

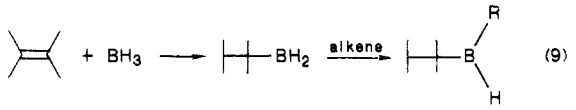
(11) Brown, H. C.; Kulkarni, S. U. *J. Organomet. Chem.* **1981**, *218*, 299.

(12) Brown, H. C.; Basavaiah, D.; Kulkarni, S. U.; Lee, H. D., unpublished results.



haloalkynes with the thexyl moiety serving as a blocking group.

Hydroboration with Thexylborane. Thexylborane[13] is a versatile reagent that can be easily prepared by the hydroboration of tetramethylethylene with BH_3. This reagent reacts with a variety of alkenes such as isobutylene 2-butene and 2-methyl-1-pentene at −25 °C to provide nearly quantitative yields of thexylmonoalkylboranes **6** (eq 9). Moreover, in certain reactions of



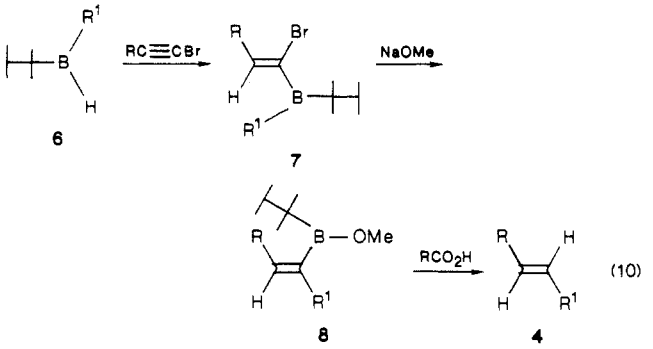
(9)

6

R = secondary or 2-substituted primary

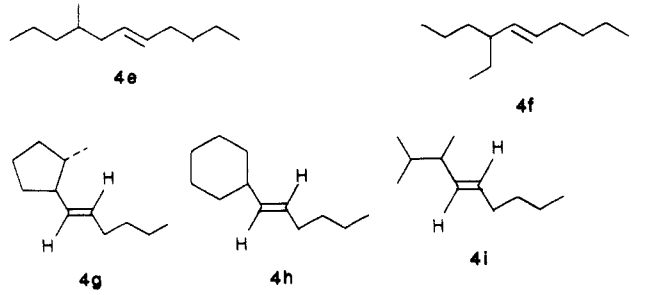
thexylboranes, which presumably involve anionotropic migrations, it has been observed that the thexyl group does not migrate from boron to carbon competitively with less hindered alkyl groups.[14]

These findings suggested the possibility that thexylmonoalkylboranes might be valuable in the synthesis of (*E*)-disubstituted alkenes (eq 10).

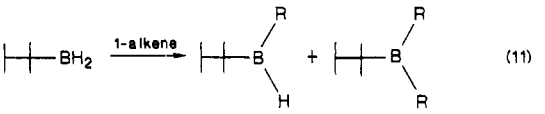


(10)

Hydroboration of 1-bromo-1-alkynes with thexylalkylborane affords cleanly *B*-(*cis*-1-bromo-1-alkenyl)thexylalkylborane (**7**). Treatment of these intermediates with sodium methoxide results in the migration of the alkyl group from boron to the adjacent vinylic carbon displacing the bromine. Thexyl-migrated product was observed only in small amounts (2–7%). Protonolysis of the vinylborane **8** proved to be slow, requiring 20–24 h in refluxing acetic acid. However, protonolysis is faster in refluxing isobutyric acid, requiring only 1–2 h. A wide variety of (*E*)-disubstituted alkenes **4e–i** were prepared in excellent yields (Table III).



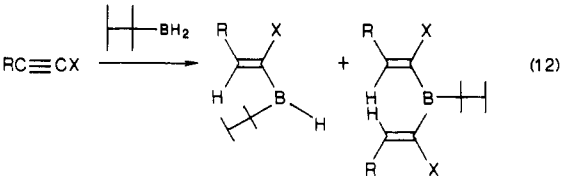
Thus, this modification solved both problems. However, the utility of this reaction sequence has been restricted to the availability of thexylmonoalkylborane. Only in the case of relatively hindered alkenes does hydroboration with thexylborane lead to pure thexylmonoalkylborane. In general, hydroboration of terminal alkenes produces a mixture of products (eq 11).



(11)

R is primary

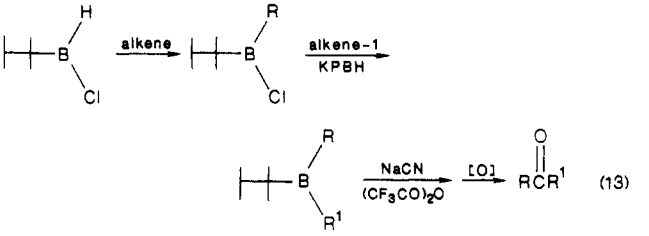
In order to overcome this difficulty, we tried to hydroborate 1-halo-1-alkyne with thexylborane in the first step, aiming at the introduction of the unhindered primary alkyl group at the second stage. Unfortunately, a competing dialkenylation of thexylborane decreases the yield of desired vinylborane (eq 12).[15] Therefore,



(12)

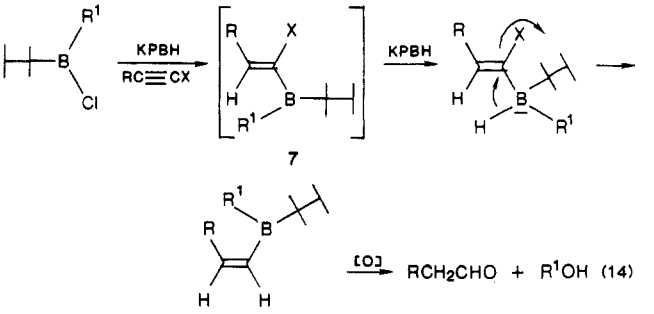
we directed our attempts to solving this problem by using thexylchloroborane, a monofunctional hydroborating agent.

Hydroboration with Thexylchloroborane. Recently, thexylchloroborane[16] (ThxBHCl·SMe_2) has been established to be an excellent hydroborating agent that hydroborates alkenes to provide thexylalkylchloroboranes. Hydridation of these intermediates with potassium triisopropoxyborohydride (KPBH) in the presence of another alkene produces the mixed dialkylthexylborane, as evidenced by the conversion to the corresponding unsymmetrical ketones by the cyanidation reaction (eq 13).



(13)

However, the hydridation of thexylalkylchloroborane in the presence of 1-halo-1-alkyne provides an undesirable side product along with ≈50% unreacted 1-halo-1-alkyne. It appears that *B*-(*cis*-1-halo-1-alkenyl)thexylalkylborane (**7**) readily captures a hydride from KPBH, followed by hydride migration to the attached vinylic carbon displacing the halogen to provide the corresponding *cis*-vinylborane (eq 14).



(14)

Indeed, we observed ≈40% of the corresponding aldehyde RCH_2CHO on oxidation.

Fortunately, this difficulty could be overcome by generating free thexylalkylborane **6** via hydridation of thexylalkylchloro-

(13) (a) Zweifel, G.; Brown, H. C. *J. Am. Chem. Soc.* **1963**, *85*, 2066. (b) Brown, H. C.; Negishi, E.; Katz, J.-J. *Ibid.* **1972**, *94*, 5893.

(14) (a) Brown, H. C.; Negishi, E. *J. Am. Chem. Soc.* **1967**, *89*, 5285. (b) Brown, H. C.; Yamamoto, Y.; Lane, C. F. *Synthesis* **1972**, 304.

(15) Brown, H. C.; Lee, H. D., unpublished results.

(16) (a) Brown, H. C.; Sikorski, J. A.; Kulkarni, S. U.; Lee, H. D. *J. Org. Chem.* **1982**, *47*, 863. (b) Zweifel, G.; Pearson, N. R. *J. Am. Chem. Soc.* **1980**, *102*, 5919.

(17) (a) Brown, C. A. *J. Am. Chem. Soc.* **1973**, *95*, 4100. (b) Potassium triisopropoxyborohydride is now available as a 1.0 M solution in THF from Aldrich Chemical Company. (c) Brown, H. C.; Nazer, B.; Sikorski, J. A. *Organometallics* **1983**, *2*, 634.

Table II. Synthesis of Ketones from Dialkylhaloboranes and 1-Bromo-1-alkyne[a]

alkene for R_2BX	X	1-bromo-1-alkyne	product,[b] %	yield,[c] %	bp, °C/mm	n^{20}_D
1-hexene[d]	Cl	1-bromo-1-hexyne	**5a**	84	67–69/0.7 [lit.[27] 125/2]	1.4300 [lit.[27] 1.4339]
2-methyl-1-pentene[d]	Cl	1-bromo-1-octyne	**5b**	83	114–116/1 [lit.[28] 136.5/10]	1.4357 [lit.[28] 1.4358]
cyclopentene	Br	1-bromo-1-hexyne	**5c**	81	77–79/0.9	1.4516
cyclopentene	Br	1-bromo-1-octyne	**5d**	80	100–102/0.8	1.4542

[a] All reactions were carried out in 30-mmol scale. [b] Chemical purities of all compounds are >99% by GC analysis on a 6-ft SE-30 column. [c] Yields of the pure products, isolated by distillation, based on R_2BX or 1-bromo-1-alkyne. [d] Distilled R_2BCl was utilized.

Table III. Synthesis of *trans*-Alkenes from Thexylmonoalkylborane (from Thexylborane) and 1-Bromo-1-alkyne[a]

alkene for thexylmonoalkylborane	1-bromo-1-alkyne	product[b,c]	yield,[d] %	n^{20}_D
2-methyl-1-pentene	1-bromo-1-hexyne	**4e**	94	1.4324
trans-3-hexene	1-bromo-1-hexyne	**4f**	93 (78)	1.4319
1-methylcyclopentene	1-bromo-1-hexyne	**4g**	94	1.4501
cyclohexene	1-bromo-1-hexyne	**4h**	85	1.4569
2-methyl-2-butene	1-bromo-1-hexyne	**4i**	86	1.4285

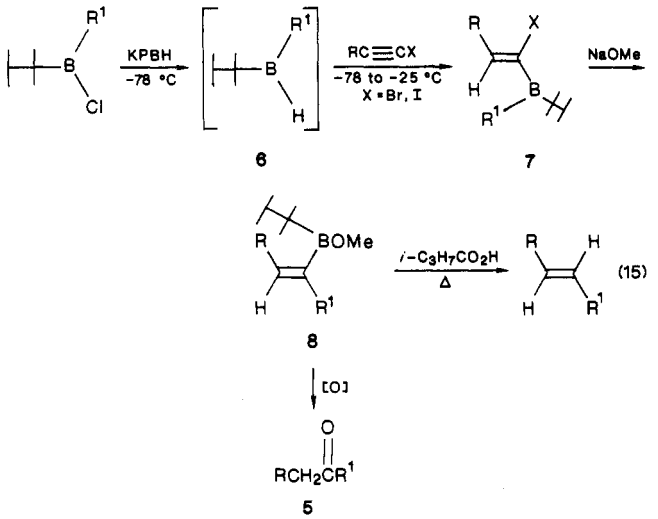
[a] All reactions were carried out in 10-mmol scale. [b] Isolated by preparative GC (10% SE-30). [c] Isomeric purities are >99% by ^{13}C NMR.[22] [d] GC yields using a suitable internal standard and values in parentheses are isolated yields.

Table IV. Synthesis of *trans*-Alkenes from Thexylmonoalklylborane (from Thexylchloroborane) and 1-Halo-1-alkyne[a]

alkene for thexylmonoalkylborane	1-halo-1-alkyne	product[b,c]	yield,[d] %	bp, °C/mm	n^{20}_D
1-hexene	1-bromo-1-octyne	**4j**	77 (90)	69–71/0.4	1.4385 [lit.[29] 1.4470]
1-octene	1-iodo-1-octyne	**4k**			
1-octene	1-bromo-1-hexyne	**4l**	76	56–61/0.1	1.4365 [lit.[30] 1.4382]
4-pentenyl acetate	1-iodo-1-butyne	**4m**	74[e]	71–72/0.5 [lit.[31] 58–60/0.05]	1.4352 [lit.[31] 1.4386]
4-pentenyl acetate	1-bromo-1-hexyne	**4n**	71[e]	82–83/0.2	1.4405
safrole	1-iodo-1-butyne	**4o**	79[f]	106–108/0.3	1.5170

[a] All reactions were carried out in 20-mmol scale. [b] Chemical purities of all compounds are >96% on a 12 ft × $^1/_8$ in. column packed with 10% SE-30. [c] Isomeric purities are >99% by ^{13}C NMR.[22] [d] Yields of pure isolated products based on 1-halo-1-alkyne and the values in the parentheses are the GC yields. [e] Protonolysis was carried out with acetic acid. [f] ^1H NMR ($CDCl_3/Me_4Si$): δ 0.95 (t, 3 H), 1.4–2.4 (m, 6 H), 2.50 (t, 2 H), 5.4 (m, 2 H), 5.78 (s, 2 H), 6.4–6.8 (m, 3 H).

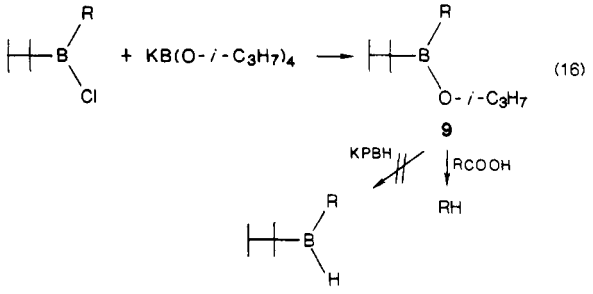
borane at −78 °C with potassium triisopropoxyborohydride (KPBH). It is necessary to carry out the hydridation of −78 °C in order to minimize disproportionation or dehydroboration of thexylalkylborane **6**, both of which are facile.[18] Subsequent treatment with 1-halo-1-alkyne at 25 °C affords the desired *B*-(*cis*-1-halo-1-alkenyl)thexylalkylborane **7**. Treatment with sodium methoxide induces the migration of R selectively, resulting in the formation of *B*-(*trans*-1-alkyl-1-alkenyl)thexylborinate (**8**). Protonolysis with 2-methylpropionic acid afforded the desired (*E*)-alkene, **4** (eq 15). Alkaline hydrogen peroxide oxidation of



(15)

8 provided the ketones **5** in excellent yields. Only <1% of thexyl-migrated product was observed when R is primary, while around 2–7% was observed when R is secondary. We also examined the hydroboration of chloro-, bromo-, and iodo-1-alkynes with thexylalkylborane and established that 1-bromo- and 1-iodo-1-alkynes work well, while 1-chloro-1-alkyne reacts more slowly and provides lower yields.[1e]

GC analysis of the crude product revealed the presence of 5–10% of impurities, generally RH, or the unreacted 1-halo-1-alkyne. These impurities arise from the side reaction (eq 16),



(16)

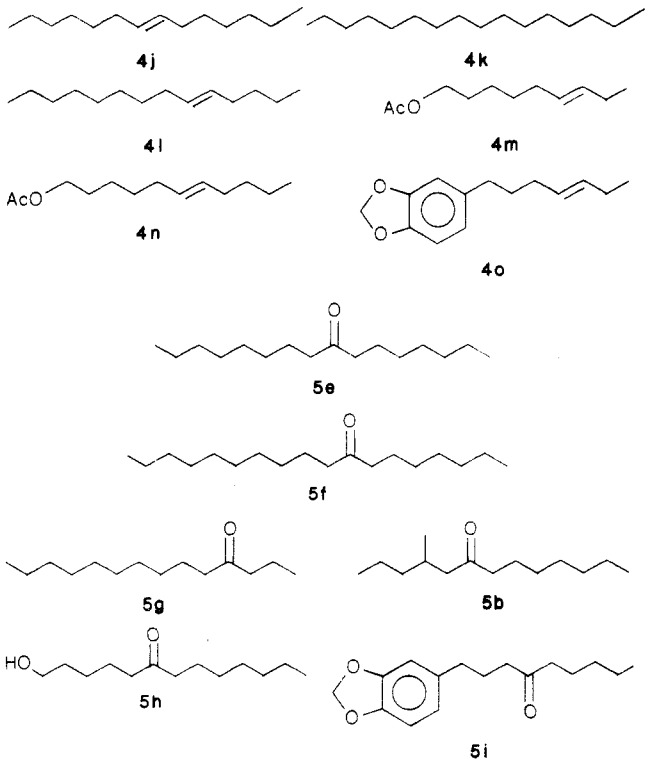
caused by the presence of 5–10% of potassium tetraisopropoxyborate in potassium triisopropoxyborohydride (KPBH). The 1-halo-1-alkyne corresponding to the amount of **9** remains unreacted. However, a careful distillation provides pure (*E*)-alkene **4** free from such impurities.

Fortunately, it is now possible to prepare potassium triisopropoxyborohydride[17a,b] free from the impurity.[17c]

A representative selection of (*E*)-alkenes **4j–o** were prepared in excellent yields (Table IV). A number of ketones **5b,e–i** were also prepared in excellent yields (Table V).

Thexylchloroborane thus circumvented both significant problems involved in the original Zweifel's synthesis of (*E*)-alkenes and ketones. But the thexyl group is lost in this modification. Although the thexyl group acts as a blocking group, it does not allow application of this approach to the further utilization of **8**, intermediates of considerable value for other applications. To solve this problem, we then examined the use of an easily replaceable blocking group on boron, a group such as halogen.

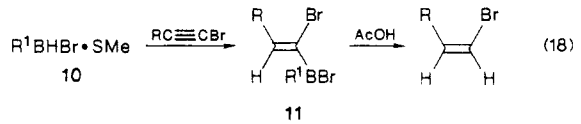
(18) (a) Brown, H. C.; Negishi, E.; Katz, J.-J. *J. Am Chem. Soc.* **1975**, *97*, 2791. (b) Brown, H. C.; Katz, J.-J.; Lane, C. F.; Negishi, E. *Ibid.* **1975**, *97*, 2799.



Hydroboration with Alkylbromoboranes. Recently we reported the preparation of a new class of partially alkylated haloborane reagents ($RBHBr{\cdot}SMe_2$, **10** via controlled hydridation of the corresponding alkyldibromoborane ($RBBr_2{\cdot}SMe_2$) for the synthesis of mixed dialkylbromoboranes and trialkylboranes (eq 17).[5]

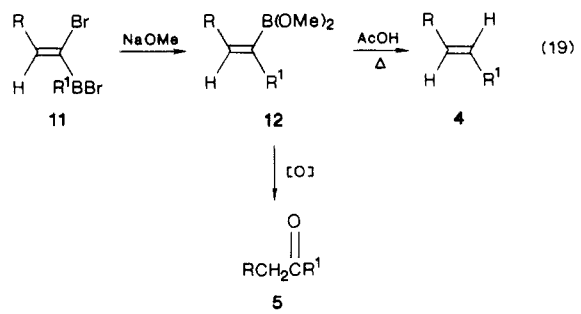
$$RBBr_2{\cdot}SMe_2 \xrightarrow[Et_2O]{^1/_4\,LiAlH_4} \underset{\mathbf{10}}{RBHBr{\cdot}SMe_2} \xrightarrow{\text{alkene-1}} RR^1BBr \rightarrow \rightarrow RR^1R^2B \quad (17)$$

Consequently, we examined the utilization of these alkylbromoboranes **9** for the synthesis of (*E*)-disubstituted alkenes and ketones. Hydroboration of 1-bromo-1-alkynes with alkylbromoboranes **10** leads cleanly to the formation of *B*-(*cis*-1-bromo-1-alkenyl)alkylbromoboranes **11**, as evidenced by the formation of *cis*-1-bromo-1-octene in excellent yields on protonolysis of the vinylborane **11** ($R^1 = n\text{-}C_6H_{13}$) (eq 18).[10]



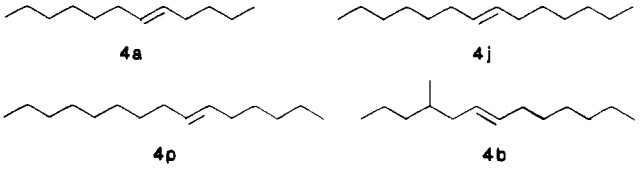
(18)

Treatment of the vinylborane **11** with sodium methoxide induces the migration of the alkyl group from boron to the vinylic carbon with displacement of bromide, providing *B*-(*trans*-1-alkyl-1-alkenyl)boronate esters **12**, which are not available by direct hydroboration, thus representing the first general and one-pot synthesis of such derivatives (eq 19).

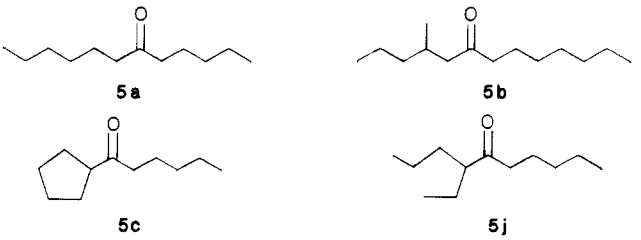


(19)

Protonolysis was achieved by heating the vinylborane **12** with acetic acid under reflux. Representative (*E*)-alkenes **4a,b,j,p** were prepared from the corresponding alkenes and 1-bromo-1-alkynes (Table VI). Alternatively, simple oxidation of these intermediates



with alkaline hydrogen peroxide produced the corresponding ketones **5a–c,j** in excellent yields (Table VII).



Thus, the alkylbromoboranes ($RBHBr{\cdot}SMe_2$, **10**) obtained via the controlled hydridation of alkyldibromoboranes offer advantages over the other three reagents, surmounting the two major problems that are associated with the original Zweifel's synthesis of (*E*)-alkenes and ketones.

The present methods describe the development of synthetic methodology for the stereospecific synthesis of (*E*)-disubstituted alkenes and unsymmetrical ketones. Thexylchloroborane and dibromoborane proved to be better reagents and dibromoborane in particular offers greater advantages for the further application of the vinylborane intermediates **11**. Applications of these vinylboranes **11** are under study now in our laboratory. We also developed a stereospecific synthesis of (*Z*)-disubstituted alkenes[19] utilizing these hydroborating agents. We are presently exploring the possibilities of applying these methods for the synthesis of various insect pheromones and other biologically active molecules.

Experimental Section

The reaction flasks and other glassware required for the experiments were predried at 150 °C for several hours, assembled hot, and cooled under a stream of dry nitrogen. Syringes were assembled and fitted with needles while hot then cooled under nitrogen. All reactions were carried out under a static pressure of nitrogen in flasks fitted with a septum-covered side arm by using standard techniques for handling air-sensitive materials.[8]

Materials. The alkenes were obtained either from the Chemical Samples Division of Albany Internationals or from Aldrich Chemical Company. The alkynes, from Farchan Acetylenes, were converted into 1-halo-1-alkynes by literature procedure.[20] Commercial potassium triisopropoxyborohydride (KPBH) was obtained from Aldrich. Alternatively, potassium triisopropoxyborohydride (KPBH) was prepared from potassium hydride and triisopropoxyborane in THF.[17b,c]

Analyses. The melting and boiling points were uncorrected. GC analyses were carried out on a Varian 1400 gas chromatograph (column 12 ft × $^1/_8$ in. packed with 10% SE-30 on Chromosorb WHF) or on a Hewlett Packard 5750 research chromatograph (column 6 ft × $^1/_4$ in. packed with 10% SE-30 on Chromosorb W AWDMCS). ^1H NMR and ^{13}C NMR were recorded on Varian T-60 and FT-80A spectrometers, respectively.

Preparation of (6*E*)-4-Methyl-6-tridecene (4b) Using Monochloroborane ($BH_2Cl{\cdot}SMe_2$). To 30 mmol of bis(2-methyl-1-pentyl)chloroborane (6.48 g) obtained via hydroboration of 2-methyl-1-pentene with $BH_2Cl{\cdot}SMe_2$[21] in THF at 0 °C was

(19) Brown, H. C.; Basavaiah, D.; Kulkarni, S. U., manuscript in preparation.

(20) 1-Bromo-1-alkynes were prepared according to the literature procedure: Schulte, E. E.; Goes, M. *Arch. Pharm. (Weinheim, Ger.)* **1959**, *290*, 118. The iodoalkynes were prepared by the action of *n*-BuLi on the corresponding 1-alkyne, followed by treatment with iodine. The chloroalkynes were prepared by the action of *p*-toluenesulfonyl chloride on the corresponding alkynyllithium.

(21) Brown, H. C.; Ravindran, N.; Kulkarni, S. U. *J. Org. Chem.* **1979**, *44*, 2417.

Table V. Synthesis of Ketones from Alkenes and 1-Halo-1-alkynes via Thexylchloroborane[a]

alkene	1-halo-1-alkyne	product[b]	yield,[c] %	mp, °C[d] or bp, °C/mm	n^{20}_D
1-octene	1-iodo-1-octyne	**5e**	(91)		
	1-bromo-1-octyne		(88)		
	1-chloro-1-octyne		(74)		
1-decene	1-iodo-1-octyne	**5f**	81	44–45 [lit.[32] 44.8–46]	
1-decene	1-iodo-1-butyne	**5g**	80	24–25 [lit.[33] 24.5–25.7]	
2-methyl-1-pentene	1-bromo-1-octyne	**5b**[e]	87	85–87/0.3 [lit.[28] 136.5/10]	1.4353 [lit.[28] 1.4358]
4-pentenyl acetate	1-bromo-1-octyne	**5h**	81[f]	49–50.5	
safrole	1-bromo-1-hexyne	**5i**[g]	86[h]	130–132/0.1	1.5090

[a] All reactions were carried out in 20-mmol scale. [b] Chemical purities are >98% by GC analysis on a 12 ft × $^1/_8$ in. (10% SE-30) column. [c] Yields of the pure distilled or crystallized products based on the haloalkyne. Values in the parentheses are GC yields. [d] Further crystallization did not increase the melting point. [e] Contained ~2% of the thexyl-migrated ketone. In other cases, the corresponding impurities were <1%. [f] Recrystallized twice from pentane. The hydroxy ketone was obtained. [g] ^{1}H NMR ($CDCl_3/Me_4Si$): δ 0.7–2.1 (m, 11 H), 2.1–2.8 (m, 6 H), 5.81 (s, 2 H), 6.5–6.8 (m, 3 H). [h] Recovered as a solid at low temperatures, dried in dessicator, distillation provides lower yields.

Table VI. Synthesis of *trans*-Alkenes from Alkyldibromoborane and 1-Bromo-1-alkyne[a]

alkene for $RBBr_2{\cdot}SMe_2$	1-bromo-1-alkyne	product[b,c]	yield,[d] %	bp, °C/mm	n^{20}_D
1-hexene	1-bromo-1-hexyne	**4a**	67	88–89/5.5 [lit.[26] 213.5/760]	1.4315
1-hexene	1-bromo-1-octyne	**4j**	73	76–77/0.6	1.4382
1-octene	1-bromo-1-heptyne	**4p**	72	100–102/0.5	1.4398
2-methyl-1-pentene	1-bromo-1-octyne	**4b**	70	74–76/0.5	1.4370

[a] All reactions were carried out on 25-mmol scale. [b] Chemical purities of all compounds are >98% by GC analysis on a 6 ft × $^1/_8$ in. SE-30 column. [c] Isomeric purities are >96% by ^{13}C NMR analysis. [d] Yields of pure products isolated by distillation based on alkene or 1-bromo-1-alkyne.

added slowly 7.5 mmol of $LiAlH_4$ in THF with stirring under nitrogen. After 1 h at 0 °C, the resulting dialkylborane was slowly transferred to the solution of 1-bromo-1-octyne (5.67 g, 30 mmol) in THF at −78 °C. The reaction mixture was allowed to warm to 0 °C, and the stirring was continued for an additional 3 h at 0 °C. Sodium methoxide (75 mmol) in methanol was added at 0 °C and stirred for 1 h at room temperature. Acetic acid, 3 mL, was added to neutralize any excess sodium methoxide. Solvents and volatile materials were removed under vacuum. Acetic acid (40 mL) was added and the mixture heated under reflux for 3 h. The reaction mixture was cooled and the usual workup[6] afforded (6*E*)-4-methyl-6-tridecene (**4b**, 4.52 g, 77%): bp 88–90 °C (1 mm); n^{20}_D 1.4365. GC analysis on a 6 ft × $^1/_4$ in. column packed with 10% SE-30 indicated 100% chemical purity. ^{1}H NMR ($CDCl_3/Me_4Si$): δ 0.68–1.65 (m, 22 H), 1.78–2.34 (m, 4 H), 5.37 (m, 2 H). ^{13}C NMR ($CDCl_3/Me_4Si$): δ 13.81, 14.08, 19.22, 20.01, 22.50, 28.69, 29.52, 31.64, 32.51, 32.83, 38.81, 40.00 (alkyl C), 128.64, 131.44 (C=C). Only two signals for two vinylic carbons (nonequivalent) reveal the absence of any significant amounts of the corresponding *Z* isomers.[22]

Preparation of (5*E*)-4-Ethyl-5-decene (4f) Using Thexylborane. To 30 mmol of thexylborane[11] (14.7 mL, 2.05 M) were added sequentially *trans*-3-hexene (2.52 g, 30 mmol, −25 °C, 1 h), 1-bromo-1-hexyne (4.83 g, 30 mmol, −25 °C, 1 h), and sodium methoxide (2.43 g, 45 mmol in 30 mL methanol, −25 °C, 5 min, then 25 °C, 1 h). After removing the solvents and other volatile materials, 2-methylpropionic acid (30 mL) was added and the reaction mixture was heated under reflux for 1 h. The cooled mixture was poured into water (100 mL), neutralized by adding a saturated solution of potassium carbonate, and extracted with pentane (3 × 60 mL). The organic layer was washed with a saturated aqueous solution of potassium carbonate and water and dried with magnesium sulfate. Distillative workup provided (5*E*)-4-ethyl-5-decene (**4f**), 3.93 g (78%): bp 49–51 °C (0.4 mm); n^{20}_D 1.4319. GC analysis indicated >99% chemical purity. ^{1}H NMR ($CDCl_3/Me_4Si$): δ 0.7–1.1 (m, 9 H), 1.1–1.65 (m, 10 H), 1.65–2.3 (m, 3 H), 4.8–5.7 (m, 2 H).

Preparation of (*E*)-7-Tetradecene (4j) via Thexylchloroborane. To 20 mmol of thexylchloroborane (9.22 mL, 2.17 M) in CH_2Cl_2 was added 1-hexene (2.5 mL, 20 mmol) at 0 °C. The reaction mixture was stirred for 2 h at room temperature, cooled to −78 °C, and diluted with 20 mL of THF. To the well-stirred solution was added a 0.86 M solution of potassium triisopropoxyborohydride (23.2 mL, 20 mmol), also cooled to −78 °C. The mixture was thoroughly stirred for 10 min, 1-bromo-1-octyne[23] (3.6 g, 19 mmol) was added, and the solution was again stirred well. After 10 min, the flask was brought to −25 °C and maintained at this temperature for 2 h with vigorous stirring. To this mixture was added 15 mL of sodium methoxide in methanol (4 M, 60 mmol) dropwise at −25 °C, and the reaction mixture was allowed to warm up to room temperature. After 1 h, the solvents were removed completely under aspirator vacuum, 2-methylpropionic acid (30 mL) was added, and the reaction mixture heated under reflux for 6 h. The cooled mixture was poured into water (100 mL), neutralized by adding a saturated solution of sodium hydrogen carbonate, and extracted with pentane. The organic layer was washed with sodium hydrogen carbonate solution, followed by washing with water, and dried over anhydrous magnesium sulfate. Distillation provided (*E*)-7-tetradecene (**4j**), 2.99 g (77%): bp 69–70 °C (0.4 mm); n^{20}_D 1.4385.

GC analysis on a 12 ft × $^1/_8$ in. column packed with 10% SE-30 indicated >98% chemical impurity. ^{1}H NMR ($CDCl_3/Me_4Si$): δ 0.7–1.6 (m, 22 H), 1.9–2.2 (m, 4 H), 5.4 (m, 2 H). ^{13}C NMR ($CDCl_3/Me_4Si$): δ 13.78, 22.51, 28.74, 29.53, 31.67, 32.46 (alkyl C), 130.11 (C=C). The single vinylic carbon (130.11) reveals the absence of any significant amounts of the corresponding *Z* isomer.[22]

Preparation of (*E*)-6-Undecen-1-yl Acetate (4n) via Thexylchloroborane. The preparation of thexylmonoalkylborane (**5n**) from thexylchloroborane and 4-pentenyl acetate, the hydroboration of 1-bromo-1-hexyne with **5n**, and subsequent conversion of **7n** by the action of sodium methoxide were carried out as described in the case of **4j**. The reaction mixture was cooled to 0 °C and water (100 mL) was added slowly with vigorous stirring. The aqueous layer was saturated with sodium chloride and extracted with diethyl ether. The combined organic extract was washed with water and dried over anhydrous sodium sulfate. The solvents and volatile materials were removed on a rotovapor and the residue was heated under reflux with glacial acetic acid (30 mL) for 20 h. The product was isolated as described for **4j**. Distillation provides (*E*)-6-undecenyl acetate (**4n**), 3.3 g (82%): bp 82–84 °C (0.3 mm); n^{20}_D 1.4405. GC analysis on a 12 ft × $^1/_8$ in. column packed with 10% SE-30 indicated >99% chemical purity. ^{1}H NMR ($CDCl_3/Me_4Si$): δ 0.7–1.7 (m, 13 H), 1.7–2.2 (m + s, 7 H), 4.03 (t, 2 H), 5.4 (m, 2 H).

Preparation of (6*E*)-4-Methyl-6-tridecene (4b) Using Dibromoborane ($BHBr_2{\cdot}SMe_2$). To 25 mmol of 2-methyl-1-pentyldibromoborane–dimethyl sulfide prepared from 2-

(22) In a mixture of isomers, the vinylic carbons of *trans*-alkenes can be distinguished from the corresponding carbons of the *cis*-alkenes. Dorman, D. E.; Jautelat, M.; Roberts, J. D. *J. Org. Chem.* **1971**, *36*, 2757.

(23) When a freshly prepared pure solution of potassium triisopropoxyborohydride is used, 20 mmol of the haloalkyne can be added. The yield of 4 is slightly better.

Table VII. Synthesis of Ketones from Alkyldibromoboranes and 1-Bromo-1-alkynes[a]

alkene for $RBBr_2 \cdot SMe_2$	1-bromo-1-alkyne	product[d]	yield,[c] %	bp, °C/mm	n^{20}_D
1-hexene	1-bromo-1-hexyne	**5a**	76	78–79/0.5 [lit.[27] 125/12]	1.4305 [lit.[27] 1.4339]
2-methyl-1-pentene	1-bromo-1-octyne	**5b**	75	100–101/0.5 [lit.[28] 136.5/10]	1.4361 [lit.[28] 1.4358]
cyclopentene	1-bromo-1-hexyne	**5c**	76	74–76/0.6	1.4506
cis-3-hexene	1-bromo-1-hexyne	**5j**	78	72–73/0.5	1.4295

[a] All reactions were carried out in 25-mmol scale. [b] Chemical purities of all compounds are >98% by GC analysis (6 ft × $^1/_4$ in. column, 10% SE-30). [c] Yields of pure products isolated by distillation based on alkene or 1-bromo-1-alkyne.

methyl-1-pentene and dibromoborane–dimethyl sulfide[24] were added at 0 °C 2.5 mL of Me_2S and 20 mL of Et_2O, followed by a slow addition of $LiAlH_4$ in Et_2O (6.25 mmol) with stirring. The reaction was allowed to proceed for 3 h at 0 °C, followed by 1 h at room temperature. The resulting alkylbromoborane was slowly transferred to a solution of 1-bromo-1-octyne (4.72 g, 25 mmol) in Et_2O (5 mL) at 0 °C. After 1 h at room temperature, the reaction mixture was added to the solution of sodium methoxide (80 mmol, 18.2 mL, 4.4 M) in methanol at 0 °C and stirred at room temperature for 1 h. Acetic acid (3 mL) was slowly added to neutralize any excess sodium methoxide. Solvents and volatile materials were removed under reduced pressure. Acetic acid (30 mL) was added and heated under reflux for 3 h. The reaction mixture was cooled and the usual workup afforded, after distillation, 3.44 g (70%) of (6*E*)-4-methyl-6-tridecene (**4b**): bp 74–76 °C (0.5 mm); n^{20}_D 1.4370. GC analysis on a 6 ft × $^1/_4$ in. column (10% SE-30) indicated 100% chemical purity. ^1H NMR ($CDCl_3/Me_4Si$): δ 0.68–1.65 (m, 22 H), 1.78–2.34 (m, 4 H), 5.37 (m, 2 H). ^{13}C NMR ($CDCl_3/Me_4Si$):[25] δ 13.85, 14.09, 19.22, 20.02, 22.52, 28.74, 29.54, 31.67, 32.53, 32.83, 38.82, 40.04 (alkyl C), 128.66, 131.46 (C=C). Only two signals for two vinylic carbons (nonequivalent) reveal the absence of any significant amounts of the corresponding *Z* isomer.[21]

Preparation of 4-Methyl-6-tridecanone (5b) via Monochloroborane ($BH_2Cl \cdot SMe_2$). To 30 mmol of distilled bis(2-methyl-1-pentyl)chloroborane[21] (6.48 g) in THF at 0 °C was added slowly 7.5 mmol of $LiAlH_4$ in THF (7.65 mL, 0.98 M) with stirring under nitrogen.[8] After 1 h at 0 °C, the resulting dialkylborane was slowly transferred to a solution of 1-bromo-1-octyne (5.67 g, 30 mmol) in THF at −78 °C. The reaction mixture was allowed to warm to 0 °C and the stirring was continued for an additional 3 h at 0 °C. Then 25 mL of aqueous sodium hydroxide (3 M) solution was slowly added to 0 °C, and the solution was stirred at room temperature for 1 h. The usual oxidation[3] afforded 4-methyl-6-tridecanone (**5b**) (5.27 g, 83%): bp 114–116 °C (1 mm); n^{20}_D 1.4357 [lit.[22] bp 136.5 °C (10 mm); n^{20}_D 1.4358]. GC analysis on a 6 ft × $^1/_4$ in. column packed with 10% SE-30 showed 100% chemical purity. ^1H NMR ($CDCl_3/Me_4Si$): δ 0.68–1.95 (m, 24 H), 2.0–2.44 (m, 4 H); ^{13}C NMR ($CDCl_3/Me_4Si$): δ 13.86, 13.98, 19.67, 19.96, 22.47, 23.69, 28.82, 29.00, 29.12, 31.62, 39.19, 43.22, 50.13 (alkyl C), 201.71 (C=O).

Preparation of *cis*-1-Bromo-1-octene via Di-*n*-hexylborane [$(n\text{-}C_6H_{13})_2BH$]. Hydroboration of 20 mmol of 1-bromo-1-octyne (3.78 g) in THF was carried out with di-*n*-hexylborane (20 mmol) obtained via the hydridation of di-*n*-hexylchloroborane[21] (20 mmol) with $LiAlH_4$ (5 mmol) in the same way as in th e preparation of **4b**. Then the solvent THF was removed under vacuum. Acetic acid, 15 mL, was added, and the solution was heated under reflux for 2.5 h. Aqueous sodium hydroxide (50 mL, 6 M) was added at 0 °C and extracted with pentane. The organic layer was dried over anhydrous K_2CO_3. The solvent was removed and the distillation afforded 3.24 g of *cis*-1-bromo-1-octene (85%): bp 80–82 °C (11 mm); n^{20}_D 1.4623. GC analysis on a 6 ft × $^1/_4$ in. column packed with 10% SE-30 indicated 100% chemical purity. ^1H NMR ($CDCl_3/Me_4Si$): δ 0.71–1.7 (m, 11 H), 1.96–2.43 (m, 2 H), 6.16 (m, 2 H).

Preparation of 6-Oxotridecan-1-ol (5h) via Thexylchloroborane ($ThxBHCl \cdot SMe_2$). To 2.82 mL (20 mmol) of 4-pentenyl acetate was added 9.22 mL solution of $ThxBHCl \cdot SMe_2$ in CH_2Cl_2 (20 mmol, 2.17 M) at 0 °C under nitrogen. The mixture was stirred for 2 h at 25 °C, cooled to −78 °C, and diluted with 20 mL of THF. This solution was added to 20 mL of KPBH solution (20 mmol, 1.0 M) at −78 °C, the mixture was stirred for 10 min, and 3.1 mL of 1-bromo-1-octyne (19 mmol) was added.[23] The mixture was thoroughly stirred, maintained at −78 °C for 10 min, and finally brought to −25 °C, where it was maintained for 2 h with vigorous stirring. Then, 15 mL of NaOMe in MeOH (60 mmol, 4.0 M) was added dropwise, and the solution was allowed to warm up to room temperature where it was maintained for 1 h with stirring.

The reaction mixture was oxidized by adding 50 mL of THF, 25 mL of NaOH (75 mmol, 3 M), and 25 mL of H_2O_2 (excess, 30% solution) at 0 °C, followed by stirring at 25 °C for 1 h and under reflux for 10 h. The organic layer was separated, the aqueous layer was extracted with pentane (3 × 50 mL), and the combined organic extract was washed with water (2 × 50 mL) and dried over anhydrous K_2CO_3. The solvents were removed on a rotovapor and the residue was crystallized from pentane at −78 °C. 6-Oxotridecan-1-ol (**5h**) was obtained in 81% yield (3.3 g), mp 49–50.5 °C. GC analysis on a 12 ft × $^1/_8$ in. column packed with 10% SE-30 indicated >99% purity. ^1H NMR ($CDCl_3/Me_4Si$): δ 0.7–1.8 (m, 19 H), 2.11 (t, J = 5 Hz, 1 H); 2.40 (t, J = 6 Hz, 4 H); 3.6 (m, 2 H). ^{13}C NMR ($CDCl_3/Me_4Si$): δ 13.97, 22.58, 23.55, 23.91, 25.45, 29.04, 29.23, 31.67, 32.42, 42.65, 42.77 (alkyl C), 62.18 (COH), 200.73 (C=O).

Preparation of 4-Methyl-6-tridecanone (5b) via Dibromoborane–Dimethyl Sulfide ($BHBr_2 \cdot SMe_2$). To 25 mmol of 2-methyl-1-pentyldibromoborane–dimethyl sulfide,[24] prepared from 2-methyl-1-pentene (3.1 mL, 25 mmol) and 25 mmol of dibromoborane–dimethyl sulfide (13.8 mL, 1.81 M), were added at 0 °C 2.5 mL of SMe_2 and 20 mL of Et_2O, followed by a slow addition of 6.25 mmol of $LiAlH_4$ in Et_2O (6.8 mL, 0.92 M) with stirring under nitrogen. The reaction was allowed to proceed for 3 h at 0 °C and 1 h at room temperature. The resulting alkylbromoborane was slowly transferred to the solution of 1-bromo-1-octyne (4.72 g, 25 mmol) in Et_2O (5 mL) at 0 °C. After 1 h at room temperature, the reaction mixture was slowly added to an aqueous solution of sodium hydroxide (26.6 mL, 3 M) at 0 °C and stirred at room temperature for 1 h. The usual oxidation[8] with hydrogen peroxide afforded 3.9 g (75%) of 4-methyl-6-tridecanone (**5b**): bp 100–101 °C (0.5 mm); n^{20}_D 1.4361 [lit.[22] bp 136.5 °C (10 mm); n^{20}_D 1.4358]. GC analysis on a 6 ft × $^1/_4$ in. column packed with 10% SE-30 indicated 100% chemical purity. ^1H NMR and ^{13}C NMR were consistent with the structure.

Preparation of *cis*-1-Bromo-1-octene via *n*-Hexylbromoborane ($n\text{-}C_6H_{13}BHBr \cdot SMe_2$). Hydroboration of 20 mmol of 1-bromo-1-octyne (3.78 g) in Et_2O was carried out with n-$C_6H_{13}BHBr \cdot SMe_2$ (20 mmol) obtained via the hydridation of $n\text{-}C_6H_{13}BBr_2 \cdot SMe_2$ (20 mmol)[24] with $LiAlH_4$ (5 mmol) in ether, as mentioned in the preparation of **5b**. Acetic acid (4 mL) was added at 0 °C and ether was removed under vacuum. Then acetic acid (15 mL) was added and heated under reflux for 3 h. The usual workup afforded 3.1 g (82%) of *cis*-1-bromo-1-octene: bp 81–82 °C (11 mm); n^{20}_D 1.4620. GC analysis on a 6 ft × $^1/_4$ in. column packed with 10% SE-30 indicated >98% chemical purity. ^1H NMR was consistent with the structure.

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