black mixture is poured into saturated aqueous NH_4Cl. Ether is added and the organic layer is washed (dilute HCl, then saturated NH_4Cl) and dried. Evaporation of the solvent and purification of the crude mixture by silica gel chromatography affords the pure product identified by the usual spectral techniques and through comparison with authentic samples.

Table I gives some examples of the observed results. Usually no 1,2 adduct, i.e., the allylic alcohol, can be detected. However, this simple and easily performed reaction suffers from the formation in several cases of polar byproducts having complex structures (IR and NMR), resulting from further reactions of the intermediate enolate.

Minimization of these undesired condensations was attempted by sonication at lower temperatures in less polar solvents (hexane–THF mixtures). It was observed that the reaction of the organolithio intermediate with the Cu^I derivative was dramatically slowed down at −30 °C and a large amount of allylic alcohol was formed at this temperature. Thus, a narrow balance exists between the requirements of rapid formation of the organocopper reagent and a decreased reactivity of the enolate. Although satisfactory yields can often be obtained with this procedure, we investigated a second method (method B) in which the organocopper reagent is generated in a first step and then treated with the enone. Thus, a mixture of 1.5 mmol (195 mg) of C_5H_7Cu, 3 mmol (480 mg) of HMP 1.5 mmol of an alkyl halide, and 45 mg (3 equiv) of lithium sand in 6 mL of dry THF–diethyl ether (1:1) is sonicated[9b] at −40 °C (ethanol–liquid nitrogen) for 10–30 min under an argon atmosphere. After consumption of the lithium, 1 mmol of the enone in 1 mL of dry THF is added dropwise with a syringe and sonication is continued for an additional 10 min. The mixture is then worked up as described above, and the reaction products are isolated by silica gel chromatography. Results are given in Table I. In most cases, the crude β-alkylated ketone is obtained in high purity as shown by analytical methods (IR, TLC) and almost no contamination (<5%) by the allylic alcohol is observed. This procedure also reduces considerably the amount of polar byproducts. In contrast, an experiment run with *n*-butyl bromide at 0 °C rapidly gave a black mixture that left 2-cyclohexenone unchanged, probably due to the well-documented decomposition at this temperature of the organocopper derivatives.

Sonication has an essential role in the process. As shown above, replacement of low-intensity sonication by more energetic irradiation has a pronounced effect on the reaction. In addition, the use of magnetic stirring in lieu of ultrasonic waves results in a much slower reaction with a different product distribution (increased 1,2 addition and lower conversion).

The cavitation effects[10] of acoustic waves are known to promote the erosion of metallic surfaces and are undoubtedly responsible for the rapid consumption of lithium. In summary, diverse organocopper reagents can be rapidly and efficiently prepared from the corresponding halides and used effectively in conjugate addition reactions with enones.[14] Extensions of this work is presently under investigation.

(10) See for instance: Weissler, A. *J. Acoust. Soc. Am.* **1953**, *25*, 651. Bebtchuk, A. S.; Borisov, Yu.Ya.; Rosenberg, L. D. *Akoust Zh.* **1958**, *4*, 361.
(11) Suzuki, M.; Suzuki, T.; Kawagishi, T.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1247.
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(13) House, H. O.; Fischer, W. F. *J. Org. Chem.* **1969**, *34*, 3615.
(14) In the present state of this work, a limitation has been found with methyl bromide and iodide which give poor and/or irreproducible yields.

Acknowledgment. We thank Dr. A. E. Greene for many useful comments. Financial support from the CNRS (LA 332) is gratefully acknowledged.

Registry No. 2-Cyclohexenone, 930-68-7; 2-cyclopentenone, 930-30-3; 3-methylenebicyclo[2.2.1]heptan-2-one, 5597-27-3; 3,5,5-trimethyl-2-cyclohexen-1-one, 78-59-1; butyl bromide, 109-65-9; bromoethene, 593-60-2; *tert*-butyl bromide, 507-19-7; heptyl bromide, 629-04-9; bromobenzene, 108-86-1; 3-butylcyclohexanone, 39178-69-3; 3-ethenylcyclohexanone, 1740-63-2; 3-*tert*-butylcyclopentanone, 5581-94-2; 3-heptylcyclopentanone, 82741-92-2; 3-benzylbicyclo-[2.2.1]heptan-2-one, 82741-93-3; 3-(2-propenyl)cyclohexanone, 20498-05-9; 3-(2-propenyl)-3,5,5-trimethylcyclohexanone, 62394-27-8; lithium, 7439-93-2; copper iodide, 7681-65-4; 3-bromo-1-propene, 106-95-6; C_5H_7Cu-2HMPT, 67840-54-4.

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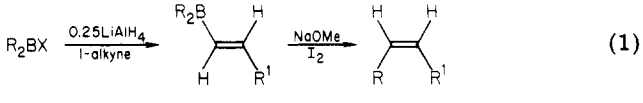
A General and Stereospecific Synthesis of Cis Alkenes via Stepwise Hydroboration: A Simple Synthesis of Muscalure, the Sex Pheromone of the Housefly (*Musca domestica*)

Summary: Base-induced iodination of the vinylborane intermediates, conveniently obtained via the hydroboration of 1-alkynes with alkylbromoboranes ($RBHBr{\cdot}SMe_2$), provides cis-disubstituted alkenes in good yields. Muscalure, the insect pheromone of the housefly (*Musca domestica*), has been prepared in 59% yield.

Sir: Recent developments[1] in the synthesis and application of insect pheromones have stimulated a search for simple methods to achieve the stereospecific synthesis of *Z* and *E* alkenes, structural features possessed by many insect pheromones. The application of organoboranes to carbon–carbon bond formation has been well-documented and a wide variety of synthetic methods for carbon skeletal assemblage via organoboranes are becoming available.[2] We recently reported[3] a general synthesis of cis-disubstituted alkenes via the iodine-induced transfer of dialkylvinylboranes, produced by the hydridation of dialkylhaloboranes in the presence of 1-alkynes, thus generalizing the elegant Zweifel[4] cis-alkene synthesis (eq 1).



(1)

This procedure suffers from two significant disadvantages. (1) Monohydroboration of 1-alkynes with dialkylboranes, particularly when the alkyl group is primary, is often complicated by competing dihydroboration. This can be suppressed by using a large excess of 1-alkyne. But such use of a large excess of 1-alkyne is not practical for

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(2) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975.
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Table I. Synthesis of Cis-Disubstituted Alkenes from Alkyldibromoboranes and 1-Alkynes[a]

alkene for $R^1BBr_2 \cdot SMe_2$	1-alkyne	product[b,c]	yield,[d] %	bp/mm	n^{20}_D	amounts of vinyl iodide formation,[e] %
cyclohexene	1-pentyne	3A	74	77-79/12	1.4612	3
cis-3-hexene	1-pentyne	3B	69	70-71/12	1.4319	6
cyclopentene	1-pentyne	3C	62	66-68/12	1.4565	10
2-methyl-1-pentene	1-pentyne	3D	67[f]	71-72/12	1.4321	14
1-octene	1-pentyne	3E	61	82-83/2.5	1.4357	15
1-hexene	1-octyne	3F	68[f]	76-77/0.8 [lit.[3] 75-76/0.8]	1.4392 [lit.[3] 1.4399]	15
1-tridecene	1-decyne	4	59	140-142/0.01 [lit.[9] 157-158/0.1]	1.4559 [lit.[9] n^{26}_D 1.4517]	16

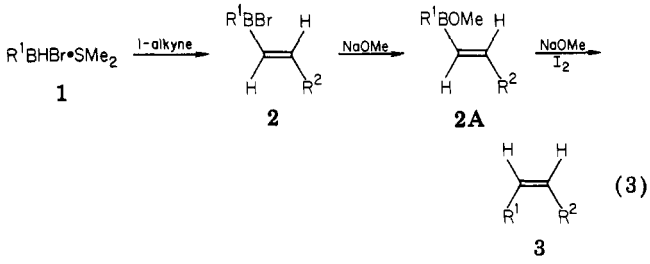
[a] All reactions were carried out in 30-mmol scale (except 3D and 3F). [b] Chemical purities of all distilled compounds are >98% by GC analysis on a 6-ft SE-30 column. [c] Isomeric purities are >99% by ^{13}C NMR analysis.[12] [d] Yields of pure products isolated by distillation (except 3D and 3F). [e] GC yields of vinyl iodides determined by separate experiments. [f] GC yields of the alkenes.

cases where the alkyne has a high boiling point. (2) There is a loss of one of the two alkyl groups, a serious loss when the alkyl group is derived from an expensive or difficultly synthesized alkene. Now we herein report a novel, general, stereospecific synthesis of cis-disubstituted alkenes that surmounts these two problems.

Recently we developed a general synthesis of mixed trialkylboranes and mixed dialkylhaloboranes via the controlled hydridation of alkyldibromoboranes with $LiAlH_4$ in Et_2O[5] (eq 2).

$$R^1BBr_2 \cdot SMe_2 \xrightarrow[Et_2O]{0.25LiAlH_4} \underset{\mathbf{1}}{R^1BHBr \cdot SMe_2} \xrightarrow{1\text{-alkene}} R^1R^2BBr \cdot SMe_2 \rightarrow \rightarrow R^1R^2R^3B \quad (2)$$

It appeared to us that the vinylboranes 2, obtained via hydroboration of 1-alkynes with alkylbromoboranes 1, on treatment with iodine in the presence of base, might provide the desired cis-alkene 3 (eq 3). Consequently, we examined this reaction sequence as a potential route for the stereospecific synthesis of cis-disubstituted alkenes.

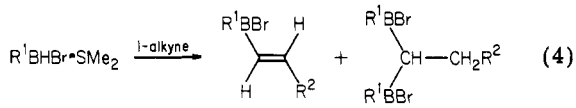


1 2 2A

3 (3)

Monohydroboration of 1-alkynes with a variety of alkylbromoboranes was first examined. It was established that there is no dihydroboration for a secondary alkyl group and only 2% dihydroboration for a primary[6] (eq 4). Thus, this new hydroborating agent, $R^1BHBr \cdot SMe_2$, solves the problem of dihydroboration and cleanly provides the monohydroborated vinylborane 2.

We encountered one difficulty in the iodination reaction. Iodination of the vinylborane **2A** produced considerable amounts of vinyl iodides (≈40%) along with the desired cis alkenes. The formation of such vinyl iodides presumably arises from a reaction similar to that involved in

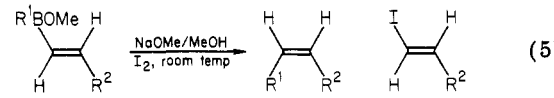


2 (4)

100% (for R^1 secondary) 0% (for R^1 secondary)

96% (for R^1 primary) 2% (for R^1 primary)

converting vinylboronic acids into the corresponding vinyl iodides.[7] The best results were obtained when the iodination was carried out at room temperature with sodium methoxide as base and methanol as solvent, reducing the amount of vinyl iodides to 15% (eq 5). Similar results were realized in the related prostaglandin synthesis with MeOH·THF as solvent.[8]



2A 3 15% (5)

We observed that the formation of vinyl iodide varies inversely with the steric bulk of the alkyl group on boron, sterically more hindered alkyl groups leading to decreased amounts of vinyl iodides. Thus, the relatively hindered cyclohexyl group forms only 3% vinyl iodides, whereas the less hindered *n*-hexyl group provides 15% vinyl iodide (Table I). Attempts to further decrease the formation of vinyl iodides by lowering the reaction temperature caused only minor changes in the formation of vinyl iodides. However, at −78 °C, the formation of vinyl iodides was diminished to 6–7%, but the reaction becomes very slow, requiring 18 h to achieve 70% completion.

A representative selection of cis-disubstituted alkenes (**3A–3F**) were prepared by this procedure (Table I).

This procedure has been successfully extended to the synthesis of muscalure[9] (4), a sex pheromone of the housefly (*Musca domestica*), from 1-tridecene and 1-decyne (eq 6).

The following procedure for the synthesis of *cis*-6-ethyl-4-nonene (**3B**) is representative. To 30 mmol of 3-hexyldibromoborane–dimethyl sulfide,[10] prepared from

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

(6) In the present experiments, only 5–10% of 1-octyne remained unreacted, corresponding to the amount of ether cleaved product $R^1B(OEt)_2$ formed during the hydridation step (estimated from the ^{11}B NMR spectrum of 1). The amount of dihydroboration was estimated from the amount of 1-octanol formed after the oxidation. Reference: Brown, H. C.; Basavaiah, D.; Kulkarni, S. U. *J. Organometal. Chem.* **1982**, *225*, 63.

(7) Brown, H. C.; Hamaoka, T.; Ravindran, N. *J. Am. Chem. Soc.* **1973**, *95*, 5786.

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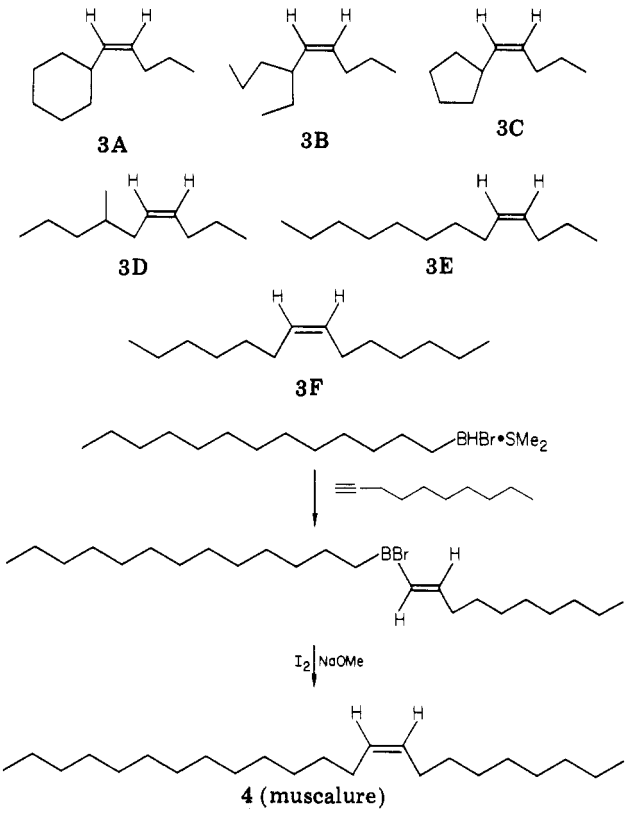
(9) Carlson, D. A.; Mayer, M. S.; Silhacek, D. L.; James, J. D.; Beroza, M.; Bierl, B. A. *Science* **1971**, *174*, 76.



(6)

cis-3-hexene and dibromoborane–dimethyl sulfide, were added at 0 °C 3 mL of SMe_2 and 25 mL of Et_2O, followed by a slow addition of $LiAlH_4$ in Et_2O (7.5 mmol), with stirring under nitrogen. The reaction was allowed to proceed 3 h at 0 °C and 1 h at room temperature. The resulting alkylbromoborane was slowly transferred to a solution of 1-pentyne (30 mmol) in Et_2O at 0 °C. The reaction mixture was stirred 1 h at 0 °C and 1 h at room temperature. Then the resulting vinylbromoborane was added to the solution of NaOMe (150 mmol) in MeOH at 0 °C. After 0.5 h at room temperature, the solvent ether was removed under vacuum and 30 mL of MeOH was added. Iodine (30 mmol, 7.6 g) was added to this vinylborane solution in MeOH at 0 °C and the solution was stirred at room temperature for 3 h. Aqueous $Na_2S_2O_3$ solution was now added and the reaction mixture was extracted with pentane and the extract dried over anhydrous $MgSO_4$. The crude product showed ≈6% 1-pentenyl iodide. This could be separated by careful distillation to yield pure *cis*-6-ethyl-4-nonene (**3B**; 3.18 g, 69%) bp 70–71 (12 mm), n^{20}_D 1.4319 GC analysis indicated >99% chemical purity. **3B**: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.69–1.68 (m, 17 H), 1.78–2.38 (m, 3 H), 4.84–5.61 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 11.18, 13.19, 13.67, 20.14, 22.71, 28.41, 29.54, 37.86, 38.50 (alkyl C); 129.16, 134.34 (C=C).

This procedure solves the two major problems associated with the earlier procedure,[3] thus providing a general, one-pot, stereospecific synthesis of cis-disubstituted alkenes. We are presently exploring the possibilities of employing this procedure for the stereodefined synthesis of trisubstituted alkenes. The application of alkylbromoboranes for the stereospecific synthesis of trans-disubstituted alkenes has been also established.[11]

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(11) Brown, H. C.; Basavaiah, D.; Kulkarni, S. U. *J. Org. Chem.*; following paper in this issue.
(12) In a mixture of isomers, the vinylic carbons of cis alkenes can be distinguished from the corresponding carbons of trans alkenes. Dorman, D. E.; Jautelat, M.; Roberts, J. D.; *J. Org. Chem.* **1971**, *36*, 2757.
(13) Postdoctoral research associate on Grant GM 10937 from the National Institutes of Health.

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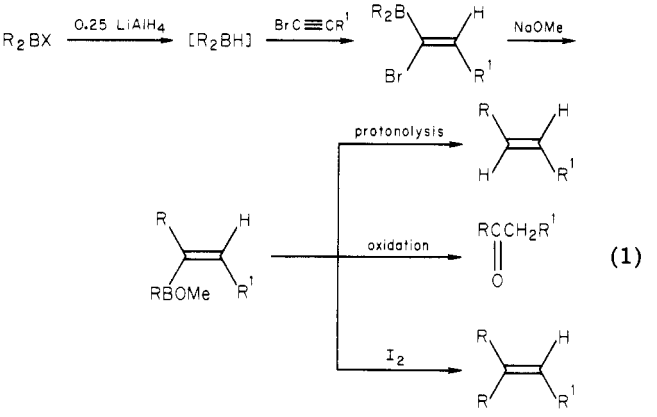
A General and Stereospecific Synthesis of Trans Alkenes and Regiospecific Synthesis of Ketones via Stepwise Hydroboration

Summary: The hydroboration of 1-bromo-1-alkynes with alkylbromoboranes ($RBHBr\cdot SMe_2$), conveniently obtained via the controlled hydridation of alkyldibromoboranes ($RBBr_2\cdot SMe_2$), followed by treatment with sodium methoxide produces *B*-(*trans*-1-alkyl-1-alkenyl)boronate esters that provide the corresponding trans alkenes on protonolysis and ketones on oxidation.

Sir: Recently we reported[1] a general synthesis of ketones, trans alkenes, and trisubstituted alkenes via the hydroboration of 1-bromo-1-alkynes, thus expanding the scope of the original Zweifel[2] procedure (eq 1).



(1)

In the preparation of trans alkenes and ketones, this procedure has a disadvantage in that one of the two alkyl groups on boron is lost, rendering it less practical for alkyl groups derived from expensive or synthesized alkenes. This difficulty was surmounted by using thexylborane[3] or thexylchloroborane.[4] These modified methods are satisfactory for the synthesis of ketones and trans alkenes, although the blocking group (thexyl moiety) does not permit application of this approach for the preparation of trisubstituted alkenes.

In order to expand further the scope of this approach, we undertook to examine the use of an easily replaceable blocking group on boron, a group such as halogen. Recently we reported the preparation of a new class of partially alkylated haloborane reagents, alkylbromoborane ($R^1BHX\cdot SMe_2$, 1), via controlled hydridation of the cor-

(1) Brown, H. C.; Basavaiah, D. *J. Org. Chem.* **1982**, *47*, 754.
(2) Zweifel, G.; Arzoumanian, H. *J. Am. Chem. Soc.* **1967**, *89*, 5086.
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(4) (a) Brown, H. C.; Lee, H. D.; Kulkarni, S. U. *Synthesis* **1982**, 195. (b) Kulkarni, S. U.; Lee, H. D.; Brown, H. C. *Ibid.* **1982**, 193.

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