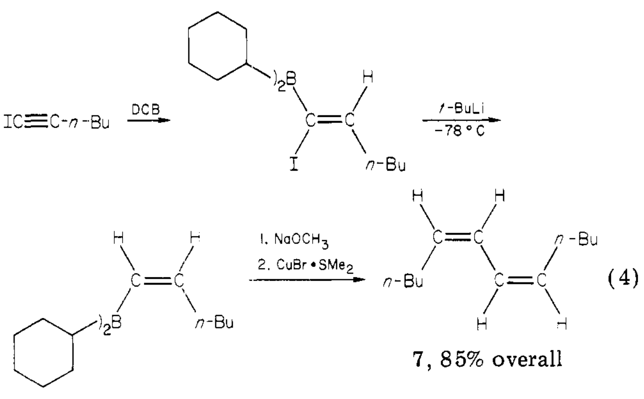
Table I. Preparation of Symmetrical Conjugated Dienes

alkyne	hydroborating reagent	product	yield,[c] %
1-hexyne	9-BBN[a]	(5*E*,7*E*)-5,7-dodecadiene (2)	95
	DCB[b]	(5*E*,7*E*)-5,7-dodecadiene (2)	97
3-hexyne	DCB	(3*E*,5*E*)-4,5-diethyl-3,5-octadiene	99 (91)
3,3-dimethyl-1-butyne	9-BBN	(3*E*,5*E*)-2,2,7,7-tetramethyl-3,5-octadiene	98
4-acetoxy-1-butyne	DCB	(3*E*,5*E*)-1,8-diacetoxy-3,5-octadiene	80
phenylethyne	DCB	(1*E*,3*E*)-1,4-diphenyl-1,3-butadiene	(79)
5-chloro-1-pentyne	DCB	(4*E*,6*E*)-1,10-dichloro-4,6-decadiene	95
1-iodo-1-hexyne	DCB[d]	(5*Z*,7*Z*)-5,7-dodecadiene (7)	85

[a] 9-Borabicyclo[3.3.1]nonane. [b] Dicyclohexylborane. [c] Yields are by GC analysis. Numbers in parentheses are yields by isolation. [d] The intermediate, (1-iodo-1-hexenyl)dicyclohexylborane, was treated with *t*-BuLi to provide (1*Z*)-1-hexen-1-yldicyclohexylborane.



(4)

7, 85% overall

6

tolerated by the reaction procedure.

The following procedure for the preparation of (3*E*,5*E*)-4,5-diethyl-3,5-octadiene is representative. To a freshly prepared suspension of dicyclohexylborane[8] (50.0 mmol) in THF at 0 °C is added 5.81 mL (51.0 mmol) of 3-hexyne over a period of 3–5 min. The cold-bath temperature is adjusted to 5–10 °C and the reaction stirred until the precipitate of the dicyclohexylborane completely disappears (ca. 1.5 h). The cooling bath is then removed and the reaction stirred an additional 30 min to ensure complete hydroboration. The solution is decanted onto a suspension of $NaOCH_3$ (53.0 mmol) in THF at 25 °C.[9] After being stirred for 30 min, the resultant solution is decanted dropwise via cannula onto a 0 °C suspension of $CuBr{\cdot}SMe_2$[10] (10.5 g, 51.0 mmol) in THF. The reaction is stirred 1 h each at 0 and 25 °C, followed by quenching with 10 mL of 3 N HCl. The clear organic layer is separated from the copper sediments, with the residue being washed with pentane (3 × 30 mL). Ethanolamine (3.06 mL, 51.0 mmol) is added, resulting in immediate precipitation of the ethanolamine–dicyclohexylborinate adduct. The precipitate is removed by centrifugation and washed with fresh pentane (2 × 30 mL). The clear organic phase is dried ($MgSO_4$) and concentrated to give a slightly yellow oil. Distillation affords 3.77 g (22.7 mmol) or 91% of the diene [bp 86–87 °C (18 mm Hg)]. The product was analytically pure by GC analysis and a single stereoisomer by ^1H and ^{13}C NMR.

The exact nature of the reactive species generated in the reaction is uncertain. The intermediacy of a copper(I) borate complex formed by cation exchange with sodium appears likely. Such borate complexes have been previously suggested as intermediates in reactions involving trialkylboranes and copper(I) complexes.[11] However, whether this intermediate decomposes directly to give a diene or dissociates to yield an alkenylcopper compound remains to be established. The cleanly defined stereospecificity of the hydroboration of alkynes, usually with very high regiospecificity, permits accurate prediction of the stereochemistry of the ultimate product. The tolerance for reactive functional groups is also promising for the scope and versatility of this synthesis.

Registry No. 1, 69322-45-8; 2, 30651-68-4; 3, 38050-71-4; 5, 37609-12-4; 6, 56962-83-5; 7, 6108-62-9; 1-hexyne, 693-02-7; 3-hexyne, 928-49-4; 3,3-dimethyl-1-butyne, 917-92-0; 4-acetoxy-1-butyne, 56703-55-0; phenylethyne, 536-74-3; 5-chloro-1-pentyne, 14267-92-6; 1-iodo-1-hexyne, 1119-67-1; (3*E*,5*E*)-4,5-diethyl-3,5-octadiene, 30651-70-8; (3*E*,5*E*)-2,2,7,7-tetramethyl-3,5-octadiene, 22430-49-5; (3*E*,5*E*)-1,8-diacetoxy-3,5-octadiene, 72161-00-3; (1*E*,3*E*)-1,4-diphenyl-1,3-butadiene, 538-81-8; (4*E*,6*E*)-1,10-dichloro-4,6-decadiene, 57404-73-6; 9-BBN, 280-64-8; DCB, 1568-65-6.

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

[9] The $NaOCH_3$ must be free of any CH_3OH. Typically, a standard aliquot of $NaOCH_3$ in CH_3OH was "dried" by heating at 150 °C for 2 h under high vacuum (ca. 0.1 torr).

[10] House, H. O.; Chu, C. Y.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, *40*, 1460.

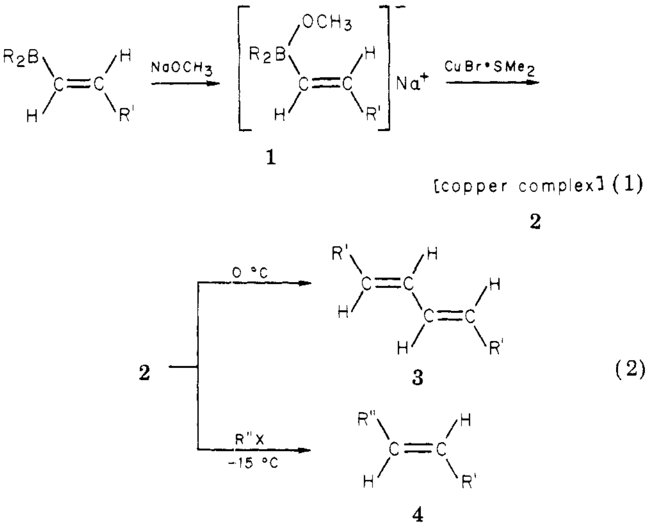
[11] (a) Miyaura, N.; Itoh, M.; Suzuki, A. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2199. (b) Miyaura, W.; Itoh, M.; Suzuki, A. *Tetrahedron Lett.* **1976**, 255.

[12] Graduate research assistant on Grant No. CHE 76-20846 provided by the National Science Foundation.

Stereospecific Synthesis of 1,4-Dienes by Cross-Coupling of Allyl Halides with Alkenylcopper Intermediates from Alkenyldialkylboranes

Summary: Alkenylcopper intermediates, generated from alkenyldialkylborane derivatives of 9-borabicyclo[3.3.1]nonane (9-BBN) and dicyclohexylborane (DCB), undergo stereospecific cross-coupling with allylic halides to yield stereodefined 1,4-dienes.

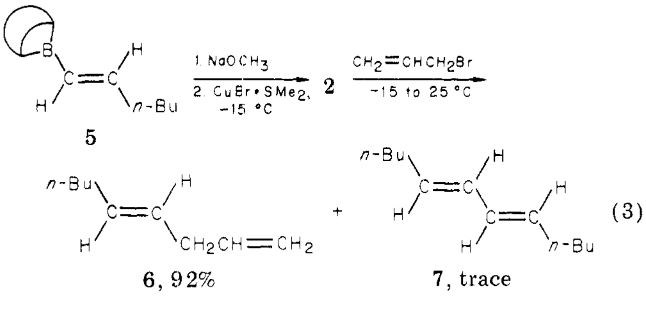
Sir: In the preceding communication, a stereospecific synthesis of (*E*,*E*)- and (*Z*,*Z*)-1,3-dienes was described on the basis of alkenyldialkylborane precursors readily synthesized via hydroboration.[1] Treatment of such sterically defined alkenylboranes with sodium methoxide and $CuBr{\cdot}SMe_2$ provides excellent yields of dienes with defined stereochemistry. These dienes are postulated to be formed through the intermediacy of an alkenylcopper complex.



The possibility of intercepting the proposed alkenylcopper intermediate with allylic halides was explored as a possible synthesis of sterically defined 1,4-dienes.

Addition of such sodium methoxide–alkenylborane complexes (1) to $CuBr{\cdot}SMe_2$ at −15 °C immediately gives dark blue-black suspensions (eq 1). At this temperature, the production of the symmetrical conjugated diene **3** is quite slow (eq 2), with only traces detected after several hours. In contrast, a nearly quantitative yield of the diene **3** is produced within 2 h at 0 °C. Conceivably, then, a reaction mixture at −15 °C containing the postulated reactive alkenylcopper species **2** and the added reactive allylic halide could be diverted to participate in cross-coupling which would then afford the corresponding 1,4-diene **4** stereospecifically (eq 2).[2]

To test this possibility, *B*-(1*E*)-1-hexen-1-yl-9-borabicyclo[3.3.1]nonane (**5**), prepared by the hydroboration of 1-hexyne with 9-BBN, was treated with sodium methoxide to form the methoxyalkenylborate complex. Addition of this adduct to $CuBr{\cdot}SMe_2$ at −15 °C was followed after 10 min by the addition of 1.1 equiv of allyl bromide. After being stirred for 1 h at −15 °C, the reaction was allowed to warm slowly to 25 °C and then quenched. Analysis of the reaction mixture by GC revealed a 92% yield of (4*E*)-1,4-nonadiene (**6**), with only a trace of the symmetrical 1,3-diene **7** detected (eq 3).[3,4] The 1,4-diene **6** proved to be exclusively the *E* isomer, establishing that the coupling had occurred with complete preservation of the original alkenylborane stereochemistry.



6, 92%   **7**, trace

Table I. Preparation of 1,4-Dienes from Allyl Bromide

alkyne	product	yield,[c] %
1-hexyne[a]	(4*E*)-1,4-nonadiene (**6**)	92
1-hexyne[b]	(4*E*)-1,4-nonadiene (**6**)	93
3-hexyne[a]	(4*E*)-4-ethyl-1,4-heptadiene	95
3-hexyne[b]	(4*E*)-4-ethyl-1,4-heptadiene	96
4-acetoxy-1-butyne[b]	(4*E*)-7-acetoxy-1,4-heptadiene (**8**)	(73)
1-iodo-1-hexyne[b,d]	(4*Z*)-1,4-nonadiene	76
1-(trimethylsilyl)-1-nonyne[b]	(4*Z*)-4-(trimethylsilyl)-1,4-dodecadiene	(83)

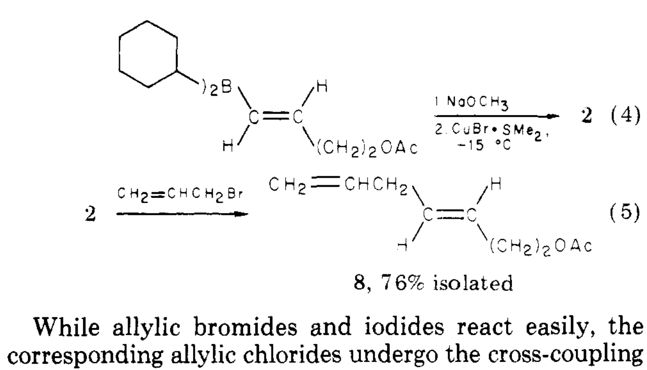
[a] 9-BBN as hydroborating reagent. [b] Dicyclohexylborane as hydroborating reagent. [c] GC analysis, isolated yields in parentheses. [d] The intermediate (1-iodo-1-hexenyl)dicyclohexylborane was treated with *t*-BuLi to provide (1*Z*)-1-hexen-1-yldicyclohexylborane.[5]

Alkenyldicyclohexylboranes are also useful precursors to such 1,4-dienes. Thus hydroboration of 1-hexyne with dicyclohexylborane, followed by sequential treatment of the resulting alkenylborane with $NaOCH_3$, $CuBr{\cdot}SMe_2$, and allyl bromide at −15 °C, gives a 93% yield of diene **6**. Also detected in the reaction mixture is a trace of the dimerized diene **7** and <1% allylcyclohexane. The latter product presumably arises from a small amount of competing alkyl-group transfer from boron with subsequent coupling to allyl bromide.

The readily available (1*Z*)-1-hexen-1-yldicyclohexylborane[5] reacts in an analogous manner to yield exclusively (4*Z*)-1,4-nonadiene in a yield of 76%.[3]

The sole boron byproducts appear to be the corresponding methyl dialkylborinates. These may be conveniently removed from the reaction mixture by precipitation as the air-stable ethanolamine adducts, greatly facilitating isolation of the dienes.

The procedure is quite general and can accommodate a wide variety of both internal and terminal alkynes as precursors (Table I). The mild nature of both the hydroboration and the subsequent cross-coupling reaction can also accommodate many functional groups, such as ether, halogen, nitrile, and ester. This is illustrated by the tolerance of the acetate group (eq 4 and 5).



8, 76% isolated

While allylic bromides and iodides react easily, the corresponding allylic chlorides undergo the cross-coupling only very sluggishly. For example, reaction of the copper intermediate derived from alkenylborane **5** affords only 6% of the desired 1,4-diene **6** accompanied by 86% of the thermal decomposition product **7**. However, the difficulty

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[1] Campbell, J. B., Jr.; Brown, H. C. *J. Org. Chem.*, preceding paper in this issue.

[2] Alkenylcopper reagents have been known to react with allylic halides to yield 1,4-dienes. See, for example: (a) Corey, E. J.; Mann, J. *J. Am. Chem. Soc.* **1972**, *94*, 4395. (b) Normant, J. F.; Cahiez, G.; Chuit, C.; Villieras, J. *J. Organomet. Chem.* **1974**, *77*, 269. (c) Normant, J. F.; Alexakis, A.; Cahiez, C. *Synthesis* **1978**, 528. (d) Van Mourik, G. L.; Pabon, H. J. J. *Tetrahedron Lett.* **1978**, 2705.

[3] All compounds show satisfactory ^{1}H and ^{13}C NMR, mass, and IR spectra, in accord with the assigned structure.

[4] Under analogous reaction conditions, allyl bromide fails to react with the sodium methoxyalkenylborate complex. Thus the copper(I) salt is essential to achieve the coupling.

[5] Campbell, J. B., Jr.; Molander, G. A. *J. Organomet. Chem.* **1978**, *156*, 71.

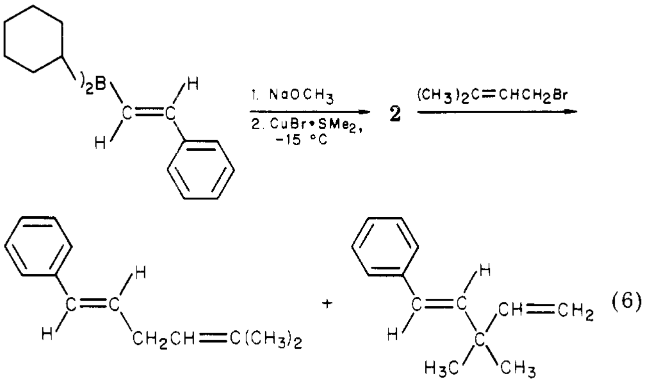
Table II. Preparation of 1,4-Dienes from Allylic Chlorides

alkyne	allylic chloride[a]	product	yield,[b] %
1-hexyne	allyl chloride	(4*E*)-1,4-nonadiene (6)	90
3-hexyne	allyl chloride	(4*E*)-4-ethyl-1,4-heptadiene	93
cyclohexylacetylene	3-chloro-2-methylpropene	(1*E*)-1-cyclohexyl-4-methyl-1,4-pentadiene	(89)
5-chloro-1-pentyne	2,3-dichloropropene	(4*E*)-2,8-dichloro-1,4-octadiene	(83)

[a] In each case, the allylic chloride was converted into the corresponding allylic iodide by treatment with 1.5 equiv of sodium iodide in THF at 25 °C. The halide was used in 10% excess. [b] GC analysis, isolated yields in parentheses.

may be circumvented easily by conversion of the allylic chlorides in situ to the more reactive iodides. Thus, stirring allyl chloride with excess sodium iodide in THF at 25 °C results in a quantitative conversion to the iodide within 20 h. Simple decantation of the solution of allyl iodide into a second flask containing the copper reagent derived from **5** provides the diene **6** in a yield of 91%. This technique proved to be generally applicable with comparable efficiency to other allylic chlorides (Table II).

To determine whether or not allylic transposition accompanies the coupling reaction, we treated the intermediate copper complex from (1*E*)-β-styryldicyclohexylborane with prenyl bromide (eq 6). A mixture of two isomeric 1,4-dienes is obtained in a combined yield of 90% with the predominant product resulting from a direct S_N2 attack. Although the S_N2' product appears highly sterically disfavored, its presence indicates the reaction can proceed by both pathways.



3:1 ratio
90% overall yield

In summary, the reactive alkenylcopper complexes generated from alkenyldialkylboranes easily undergo cross-coupling with allylic halides in excellent yield, with very high stereospecificity. In addition, there are several advantages of the method over related 1,4-diene syntheses employing other alkenylmetallic reagents.[6] First, there is no need to isolate or to purify the reactive intermediate. Second, only stoichiometric amounts of both the alkenylborane and allylic halide are required for efficient coupling. Finally, many reactive functional groups, not tolerated by the harsher reaction conditions required by many of the other procedures, are readily accommodated.

We are presently examining reactions of the copper complexes from such alkenylboranes with other electrophiles, including nonactivated alkyl halides. The mechanism and exact nature of the reactive copper intermediate are also under active investigation.

Registry No. **1**, 72161-18-3; **3**, 72161-19-4; **5**, 69322-45-8; **6**, 60835-96-3; **7**, 30651-68-4; **8**, 72161-20-7; 1-hexyne, 693-02-7; 9-BBN, 280-64-8; allyl bromide, 106-95-6; (*Z*)-1-hexen-1-yldicyclohexylborane, 56962-83-5; (*Z*)-1,4-nonadiene, 54068-77-8; (*E*)-β-styryldicyclohexylborane, 62072-25-7; prenyl bromide, 870-63-3; 3-hexyne, 928-49-4; (*E*)-4-ethyl-1,4-heptadiene, 72161-21-8; 4-acetoxy-1-butyne, 56703-55-0; 1-iodo-1-hexyne, 1119-67-1; 1-nonyne, 3452-09-3; (*Z*)-4-(trimethylsilyl)-1,4-dodecadiene, 72175-02-1; allyl chloride, 107-05-1; cyclohexylacetylene, 931-48-6; 3-chloro-2-methylpropene, 563-47-3; 5-chloro-1-pentyne, 14267-92-6; 2,3-dichloropropene, 78-88-6; (*E*)-1-cyclohexyl-4-methyl-1,4-pentadiene, 72161-22-9; (*E*)-2,8-dichloro-1,4-octadiene, 72161-23-0.

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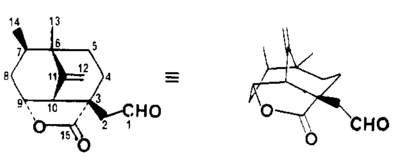
[6] Aluminum: (a) Lynd, R. A.; Zweifel, G. *Synthesis* **1974**, 658. (b) Baba, S.; Van Horn, D. E.; Negishi, E. *Tetrahedron Lett.* **1976**, 1927. Boron: (c) Yamamoto, Y.; Yatagai, H.; Sonoda, A.; Murahashi, S. I. *J. Chem. Soc., Chem. Commun.* **1976**, 452. Mercury: (d) Larock, R. C.; Bernhardt, J. C.; Driggs, R. J. *J. Organomet. Chem.* **1978**, *156*, 45. Copper: ref 2.

Upial, a Sesquiterpenoid Bicyclo[3.3.1]nonane Aldehyde Lactone from the Marine Sponge *Dysidea fragilis*

Summary: The structure of upial (1), a sesquiterpenoid marine natural product, is deduced from spectral correlations and chemical transformations.

Sir: The marine sponge genus *Dysidea* has become noted for a broad spectrum of metabolites which include bromophenols, sesquiterpenoids, and thiazole derivatives.[1] We wish to report the structure and properties of upial[2] (1), a nonisoprenoid sesquiterpene aldehyde lactone with



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the rare bicyclo[3.3.1]nonane skeleton, isolated from the Kaneohe Bay, Oahu, sponge *Dysidea fragilis*.[3] Fresh sponge was freeze-dried (1 kg) and consecutively extracted with petroleum ether and dichloromethane. The latter extract after chromatography on BioBeads SX-8[4] (C_6H_6), followed by reversed-phase chromatography on BioBeads SX-12[4] (THF/CH_2Cl_2, 3:2) and high-pressure LC on μ-

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[1] (a) Minale, L.; Cimino, G.; DeStefano, S.; Sodano, G. *Fortsch. Chem. Org. Naturst.* **1976**, *33*, 1–72 and references therein. (b) Kazlauskas, R.; Murphy, P. T.; Wells, R. J. *Tetrahedron Lett.* **1978**, 4949–50, 4951–2. (c) Charles, C.; Braekman, J. C.; Daloze, D.; Tursch, B.; Declercq, J. P.; Germain, G.; Van Meerssche, M. *Bull. Soc. Chim. Belg.* **1978**, *87*, 481–6.

[2] Pronounced o͞opeăl, after the Hawaiian 'ūpī = sponge.

[3] Identified by Dr. P. R. Bergquist.

[4] BioRad Laboratories, Richmond, CA.

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