determining. Combination of eq 4b and 3 gives eq 5.

$$(d[RH]/d[RT]) = (k_H/k_T) \times \left[([BH_4^-]/[BH_3T^-])\left(\frac{4[\alpha + 0.75 + (k_T/4k_H)]}{\alpha + 1}\right) + 3\right] \quad (5)$$

To the approximation that $([BH_4^-]/[BH_3T^-])$ is constant,[3] eq 5 can be integrated and solved for α. From the specific activities, we can calculate that $([RH]/[RT]) \simeq 7400$ and $([BH_4^-]/[BH_3T^-]) \simeq 1090$. Insertion of these into the expression for α provides eq 6, which contains two unknown quantities, α and (k_H/k_T).

$$(4\alpha/3) = [(k_H/k_T) - 1.9]/[1.7 - (k_H/k_T)] \quad (6)$$

To investigate the extent to which the observed isotope discrimination determines α, we must consider what values of k_H/k_T and α simultaneously satisfy eq 6. We note that if $k_H/k_T = 1.9$, $\alpha = 0$ and diffusion is wholly rate determining, while if $k_H/k_T = 1.7$, $\alpha = \infty$ and hydride transfer is wholly rate determining. Both 1.9 and 1.7, and any intermediate value, are physically acceptable values for k_H/k_T, so α is not determined by the observations.

The same result may be derived qualitatively from eq 1 by noting that isotope discrimination may occur intramolecularly in reaction of the $\{R^+, BH_3T^-\}$ ion pair whether it is formed reversibly (hydride transfer rate determining) or irreversibly (diffusion rate determining). The observation of Pawlowski and Sinnhuber[2] does show that for the hydride transfer process, the tritium isotope effect is in the range $k_H/k_T = 1.7$–1.9, a significant and interesting result.

Acknowledgment. We are glad to thank Professor N. E. Pawlowski for his patient help in clarifying this paper.

Registry No. Sodium borohydride, 16940-66-2; cyclopropenium ion, 19553-81-2.

(3) Commonly less than 10% of the sodium borohydride was consumed: personal communication from Professor Norman Pawlowski.

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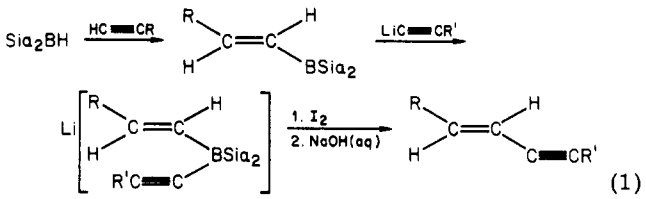
Stereospecific Synthesis of Conjugated Enynes from Alkenyldialkylboranes via Alkenylcopper Intermediates

Summary: Alkenylcopper intermediates, readily generated from alkenylboron derivatives of 9-borabicyclo[3.3.1]nonane (9-BBN), undergo coupling with 1-halo-1-alkynes to provide stereodefined conjugated enynes of high isomeric purity and in yields approaching quantitative.

Sir: Many insect sex pheromones contain a conjugated *cis,trans*-diene grouping.[1] Examples include bombykol,[2] megatomoic acid,[3] and the pheromones of the European grapevine moth[4] and the Egyptian cotton leafworm.[1b] Because conjugated *trans*-enynes are readily converted to the corresponding conjugated *cis,trans*-dienes by a simple hydroboration–protonolysis sequence,[4,5] the high-yield, stereospecific synthesis of conjugated enynes is a highly desirable goal.

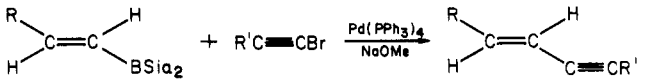
Several complex, relatively low-yield procedures have been developed for the synthesis of conjugated *trans*-enynes.[6] Some of these require a prior stereoselective synthesis of alkenyl halides.[7]

It would appear that a highly promising approach to such conjugated enynes involves alkenylborane intermediates. Thus, Negishi and co-workers developed a highly stereoselective (≥99%) synthesis of conjugated *trans*-enynes and utilized the method for the synthesis of two insect pheromones[5c,d] (eq 1). Perhaps the best synthesis to date,



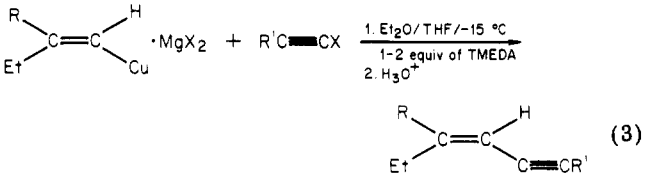
(1)

however, is that reported by Suzuki et al., utilizing the palladium-catalyzed reaction of 1-alkenylboranes with 1-halo-1-alkynes[8] (eq 2).



(2)

We were intrigued, however, by the report that alkenylcopper intermediates could be coupled to 1-halo-1-alkynes in the presence of 1–2 equiv of TMEDA to provide excellent yields of conjugated enynes[9] (eq 3).



(3)

Recently we developed a novel procedure for the conversion of alkenyldialkylboranes into the corresponding alkenylcopper compounds and reported their thermal decomposition to symmetrical 1,3-dienes[10] and their coupling to allylic halides to provide stereodefined 1,4-dienes[11] (eq 4).

(1) (a) Mayer, M. S.; McLaughlin, J. R. "An Annotated Compendium of Insect Sex Pheromones"; Florida Agricultural Experiment Stations Monograph Series No. 6, University of Florida, Gainesville, FL, Aug 1975. (b) Henrick, C. A. *Tetrahedron* **1977**, *33*, 1845.
(2) Eiter, K. *Fortchr. Chem. Forsch.* **1970**, *28*, 204 and references cited therein.
(3) Silverstein, R. M.; Rodin, J. O.; Burkholder, W. E.; Gorman, J. E. *Science* **1967**, *157*, 85.
(4) Labovitz, J. N.; Henrick, C. A.; Corbin, V. L. *Tetrahedron Lett.* **1975**, 4209 and references cited therein.
(5) (a) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 3834. (b) Zweifel, G.; Polston, N. L. *Ibid.* **1970**, *92*, 4068. (c) Negishi, E.; Lew, G.; Yoshida, T. *J. Chem. Soc., Chem. Commun.* **1973**, 874. (d) Negishi, E.; Abramovitch, A. *Tetrahedron Lett.* **1977**, 411.
(6) Descoins, C.; Samain, D. *Tetrahedron Lett.* **1976**, 745.
(7) Garwood, R. F.; Osakay, E.; Weedon, B. C. L. *Chem. Ind. (London)* **1962**, 1684.
(8) Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrahedron Lett.* **1979**, 3437.
(9) Normant, J. F.; Commercon, A.; Villieras, J. *Tetrahedron Lett.* **1975**, 1465.

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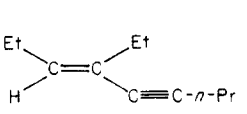
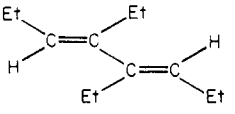
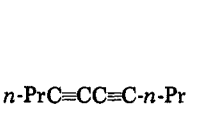
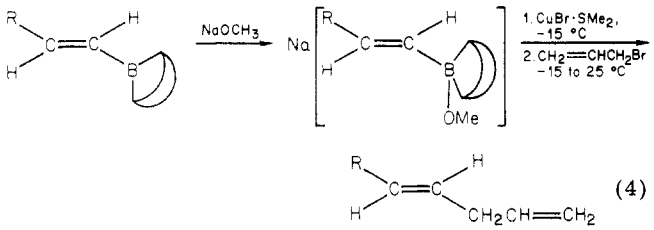
Table I. Coupling of Internal Alkenylcopper Reagents to 1-Halo-1-alkynes[a]

base	"CuX"[b]	Y	additive[c]	GC yield,[d] %		
						
NaOMe	$CuBr \cdot SMe_2$	Br	TMEDA	10	10	49
NaOMe	$CuBr \cdot SMe_2$	I	TMEDA	0	0	100
NaOMe	$CuBr \cdot SMe_2$	Br		92	1.5	0
NaOMe	$CuBr \cdot SMe_2$	I		28	9	33
NaOMe	CuI	Br		81	3	0
NaOMe	CuI	I		71	7	0
MeLi	CuI	Br		20	0	0

[a] All reactions were run in THF, utilizing the same basic procedure as described for the coupling of alkenylcopper reagents to allylic halides.[11] [b] Cuprous bromide–dimethyl sulfide was prepared according to the published procedure.[12] Cuprous iodide was extracted with THF in a Soxhlet extractor for 24 h and then dried in vacuo prior to use. [c] 2 equiv of TMEDA was utilized in each case. [d] Where the material balance is poor, many other unidentified products were formed in the reaction.



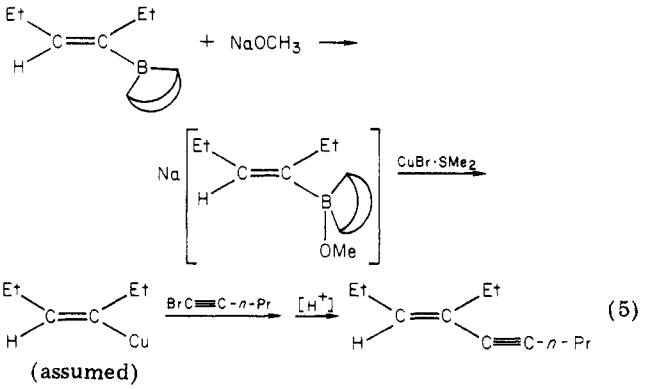
(4)

We felt that the alkenylcopper reagents generated via organoboranes might provide a stereospecific high-yield entry into conjugated enynes which could be utilized as intermediates in the synthesis of insect pheromones and other natural products of interest. The method would also be stereochemically complementary to the one developed by Normant.[9] Alkenylcopper reagents generated by the carbometalation reaction have inherently different stereochemistry and substitution patterns than those prepared from organoboranes via hydroboration. Consequently, a study of the reaction was undertaken.

Previously, Normant had determined that TMEDA was essential to promote the clean coupling of alkenylcopper reagents with 1-halo-1-alkynes.[9] In our initial attempt, we therefore used 2 equiv of TMEDA as an additive to the reaction mixture, utilizing 3-hexyne as a model internal alkyne leading to the desired internal alkenylcopper intermediate (Table I). We soon found that not only was the TMEDA *not* necessary, but it actually was detrimental to the desired process! Large amounts of conjugated diynes were formed instead, presumably as a result of metal–halogen exchange, followed by decomposition of the alkynylcopper compound.

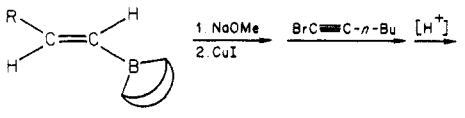
It was established that excellent results are achieved without any additive whatsoever! Both cuprous iodide and cuprous bromide–dimethyl sulfide are effective in promoting the coupling reaction, although the latter was clearly superior in terms of yield and product purity. Thus, (3*E*)-4-ethyl-3-nonen-5-yne was prepared in 92% GC yield, >98% pure (eq 5).

Attempts to apply these conditions to terminal *B*-(1-alkenyl)-9-BBN compounds gave unsatisfactory results. Although the yield of conjugated diene was quite high (~85%), it was always contaminated with ~10% of another substance, presumed to be the diene which results from thermal decomposition of the intermediate alkenylcopper compound. After a systematic search, we finally settled on the use of cuprous iodide and 1-bromo-1-alkyne as the reagents of choice for terminal *B*-(1-alkenyl)-9-BBN compounds (eq 6). As shown in Table II, the yields are



(5)

(assumed)



(6)

uniformly high. The purity of the crude product was >95% in all cases studied. This procedure is also satisfactory for the internal alkyne (Table I).

A simple workup procedure involving the precipitation of the *B*-methoxy-9-BBN byproduct as the ethanolamine adduct of 9-BBN allows ready isolation of the conjugated enyne. The following procedure is representative. To a slurry of 0.56 g (10.36 mmol) of dry sodium methoxide[13] in 10 mL of THF in a N_2-flushed 50-mL flask was added 2.00 g (9.78 mmol) of *B*-[(1*E*)-3,3-dimethyl-1-buten-1-yl]-9-BBN,[14] followed by *n*-octane as the internal standard. The reaction mixture was stirred for 0.5 h, and the resulting solution was slowly added to a suspension of 1.90 g (9.96 mmol) of cuprous iodide[15] in 5 mL of THF at −40 °C. To the golden yellow slurry was then added 1.73 g (10.76 mmol) of 1-bromo-1-hexyne. The reaction was stirred for 1 h at −40 °C and then allowed to warm to 25

(10) Brown, H. C.; Campbell, J. B., Jr. *J. Org. Chem.* **1980**, *45*, 549.
(11) Brown, H. C.; Campbell, J. B., Jr. *J. Org. Chem.* **1980**, *45*, 550.
(12) House, H. O.; Chu, C.-Y.; Wilkins, J. M.; Umer, M. J. *J. Org. Chem.* **1975**, *40*, 1460.
(13) A 5 M solution of sodium methoxide in methanol was heated at 160 °C for 2 h under high vacuum to drive off all of the methanol.
(14) Brown, H. C.; Scouten, C. G.; Liotta, R. *J. Am. Chem. Soc.* **1979**, *101*, 96.
(15) Cuprous iodide was extracted for 24 h with THF in a Soxhlet extractor and then dried in vacuo prior to use.

Table II. Synthesis of Conjugated Enynes via Terminal Alkenylcopper Coupling to 1-Bromo-1-hexyne

alkenylborane	product[a]	GC yield,[b] %
B-[(1E)-1-hexen-1-yl]-9-BBN	(5E)-5-dodecen-7-yne	93
B-[(1E)-3,3-dimethyl-1-buten-1-yl]-9-BBN	(3E)-2,2-dimethyl-3-decen-5-yne	90 (81)
B-[(1E)-1-(5-chloropenten)-1-yl]-9-BBN	(4E)-1-chloro-4-undecen-6-yne	98 (75)

[a] Satisfactory ^{1}H NMR, ^{13}C NMR, IR, and exact mass spectral analyses were obtained for all products. [b] Isolated yields in parentheses refer to analytically pure material.

°C. The reaction was quenched by the addition of 5 mL of 1 N HCl. The organic phase was then transferred via a double-ended needle to a separate flask and the remaining aqueous phase was washed with three 5-mL portions of Et_2O. The volatiles were removed in vacuo (60 mmHg) from the combined organic extracts and 25 mL of pentane was added. This was followed by the addition of 1 mL of ethanolamine, which precipitated the borane byproduct formed in the reaction. The resulting slurry was centrifuged, and an aliquot was taken from the supernatant and analyzed by GC. There was present 90% (3E)-2,2-dimethyl-3-decen-5-yne, >97% pure. The product was isolated in the following manner. After the supernatant was removed from the solid, the solution was washed with water and then dried over $MgSO_4$. The pentane was removed in vacuo and the product was distilled [bp 62–64 °C (1.7 mmHg)] to provide 1.30 g (81%) of a clear, colorless liquid, which was analytically pure by GC analysis: n^{20}_D 1.4666; ^{1}H NMR ($CDCl_3$) δ 6.09 (d, J = 16 Hz, 1 H), 5.35 (dt, J = 16, J = 2 Hz, 1 H), 2.4–2.0 (m, 2 H), 1.8–1.2 (m, 4 H), 1.01 (s, 9 H), 1.0–0.7 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 153.06, 105.90, 88.76, 79.48, 33.72, 31.25, 29.25, 22.12, 19.19, 13.63; IR (neat) 2230, 1785, 1465, 1365, 1270, 1200, 1165, 965 cm^{-1}; exact mass spectral analysis calculated for $C_{12}H_{20}$ 164.156, found 164.156.

Thus, alkenylcopper intermediates generated from B-alkenyl-9-BBN readily undergo cross-coupling with 1-halo-1-alkynes in a highly stereospecific manner. A convenient workup procedure allows the isolation of crude products, >95% pure, in nearly quantitative yields. Analytically pure products are obtained upon simple distillation. The stereochemistry of the conjugated enyne is predefined by the stereochemistry of the starting alkenylborane. The mildness of the method promises to permit the use of a variety of sensitive functional groups. At the present time, we are exploring the extension of this reaction to other, perhaps more versatile, alkenyldialkylboranes and the use of the reaction in the synthesis of various insect pheromones.

Acknowledgment. We are grateful to Albany International Chemicals Division for their financial support of this work.

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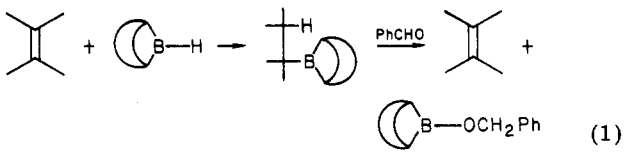
Received August 12, 1980

Synthesis of Methylenecycloalkanes from Cycloalkenes via Borane Chemistry

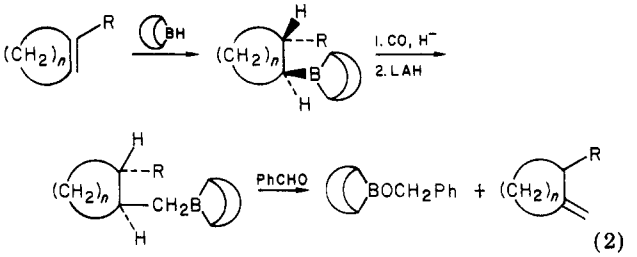
Summary: B-(Cycloalkylmethyl)-9-BBN derivatives, now readily available through the homologation reaction,[1] are convenient substrates for the synthesis of exocyclic methylene compounds. The method appears to be general. Moreover, since the synthesis proceeds from the cycloalkene, it provides a valuable alternative to the customary methylenation of carbonyl compounds by the Wittig and related procedures. The method also provides a clean synthesis of deuterium-labeled compounds without positional scrambling or loss of label.

Sir: The scope and utility of the phosphorane route to exocyclic olefins is well documented.[2] The method does have limitations, however, and several workers have proposed alternatives to overcome problems, such as steric hindrance, enolization, and epimerization.[3]

Midland and co-workers have recently shown[4] that B-alkyl-9-BBN derivatives undergo a facile reaction with aldehydes to generate olefins (eq 1). This reaction, coupled with our recently developed synthesis of B-(cycloalkylmethyl)-9-BBN derivatives[1] via carbonylation–reduction, provides an alternative method for methylenecycloalkane synthesis (eq 2).



(1)

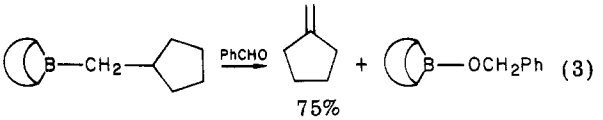


(2)

R = H, alkyl

The method is limited to those substrates which hydroborate regioselectively (or which are symmetrical), but the high stereospecificity of the reaction of 9-BBN with olefins should provide compounds unavailable by other methods.

Thus, B-(cyclopentylmethyl)-9-BBN reacts with benzaldehyde in refluxing THF with a half-life of less than 10 min to give a 75% yield of methylenecyclopentane (eq 3).



(3)

75%

(1) Brown, H. C.; Ford, T. M.; Hubbard, J. L. *J. Org. Chem.* **1980**, *45*, 4067.
(2) Maercker, A. *Org. React.* **1965**, *14*, 270. Johnson, A. W. "Ylid Chemistry"; Academic Press: New York, 1966.
(3) (a) Brady, W. T.; Patel, A. D. *Synthesis* **1972**, 565. (b) Coates, R. M.; Sowerby, R. L. *J. Am. Chem. Soc.* **1972**, *94*, 4758. (c) Johnson, C. R.; Shanklin, J. R.; Kirchhoff, R. A. *Ibid.* **1973**, *95*, 6462. (d) Hata, Y.; Wanatabe, M. *Ibid.* **1973**, *95*, 8450. (e) Hasselmann, D. *Chem. Ber.* **1974**, *107*, 3486. (f) Meyers, A. I.; Ford, M. E. *Tetrahedron Lett.* **1975**, 2861. (g) Watanabe, Y.; Shiono, M.; Mukaiyama, T. *Chem. Lett.* **1975**, 871. (h) Oshima, K.; Takai, K.; Hotta, Y.; Nozaki, H. *Tetrahedron Lett.* **1978**, 2417.
(4) Midland, M. M.; Tramontano, A.; Zderic, S. A. *J. Organomet. Chem.* **1978**, *156*, 203.

0022-3263/81/1946-0647$01.00/0