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HIGHLY STEREOSELECTIVE SYNTHESES OF CONJUGATED E,E- AND E,Z-DIENES, E-ENYNES AND E-1,2,3-BUTATRIENES VIA ALKENYLBORANE DERIVATIVES[1,2]

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Abstract: A highly selective and potentially general methodology for the synthesis of conjugated E,E- and E,Z-dienes, E-enynes, and E-1,2,3-butatrienes via hydroboration of alkynes is reported. The observed stereoselectivity was >98-99%.

Stereodefined conjugated dienes, polyenes, and enynes represent a wide variety of natural products of biological interest, such as carotenoids, insect pheromones, and arachidonic acid metabolites.[3] Furthermore, stereodefined conjugated dienes are useful intermediates for preparing stereodefined cyclohexenes via the Diels-Alder reaction.[4] Surprisingly, there were very few satisfactory and selective procedures of reasonable generality for the synthesis of these compounds at the outset of our study in 1972.[5,6] Only a method for preparing Z,Z-dienes by partial reduction of conjugated diynes via hydroboration appeared to meet the above requirements.[7] Noting that a wide variety of E- and Z-monoenes can be stereoselectively synthesized via hydroboration of alkynes,[8] we decided to develop stereoselective procedures for preparing E,E- and E,Z-dienes as well as E-enynes and E-1,2,3-butatrienes via hydroboration of alkynes.

For the synthesis of E,Z-dienes and E-enynes, we envisioned a process shown in eq. 1 on the basis of previously developed methods for Z-monoenes.[8a] We also envisioned a process shown in eq. 2 for the synthesis of E,E-dienes. In this paper, we describe details of what appears to be the first reported methodology of some generality for preparing in a highly stereoselective manner, conjugated E,Z- and E,E-dienes as well as E-enynes and E-1,2,3-butatrienes.[2]

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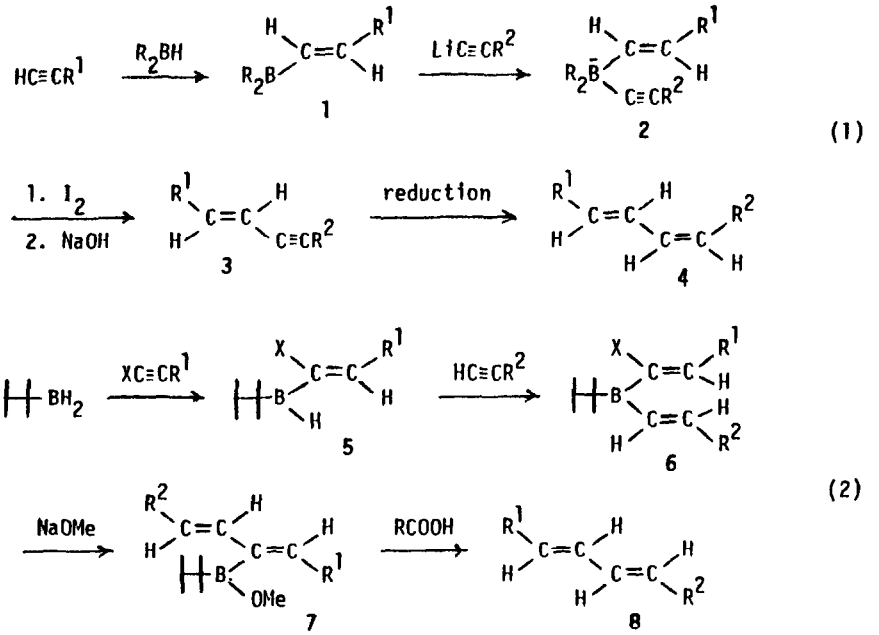

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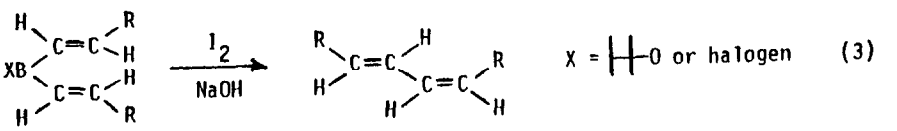
(2)

RESULTS AND DISCUSSION

Stereoselective Synthesis of Conjugated E-Enynes and E,Z-Dienes and Its Application to the Synthesis of Bombykol and a Sex Pheromone of Lobesia Botrana. Prior to our investigation, there was a procedure for the synthesis of E- and Z-enynes involving the reaction of alkynylmagnesium halides with E- or Z-alkenyl halides in the presence of a catalytic amount of $CoCl_2$.[6b] Unfortunately, the reported product yields were very low (20-30%). Although the method was reported to be stereospecific, no details were described. A totally different approach to the synthesis of E,Z-dienes reported by Zweifel[9] involves treatment of dialkenylboranes with iodine, as shown in eq. 3. Although it is high-yielding and stereoselective, its applicability as a stereoselective synthesis of conjugated E,Z-dienes appears to be limited to the synthesis of symmetrically substituted dienes.



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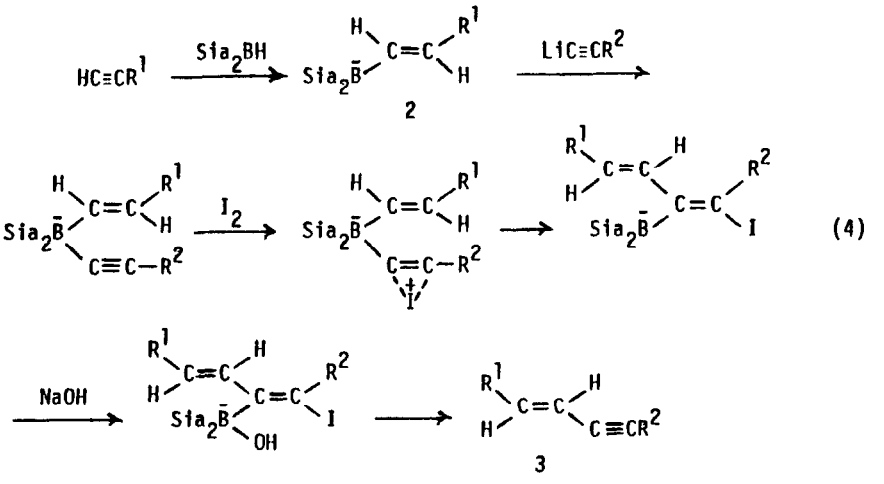
Our synthetic strategy outlined in eq. 1 called for successive treatment of E-alkenylboranes with alkynyllithiums, iodine, and a base, e.g., NaOH, to induce β elimination leading to the formation of E-enynes. Accordingly, several representative E-alkenylboranes (1) were generated by treating the corresponding alkynes with one equivalent of bis(1,2-dimethylpropyl)borane (disamylborane)[10] in THF at 0°C for 1 h. After cooling the reaction mixtures to -78°C, they were sequentially treated with alkynyllithiums (1 equiv, -78 to -50°C, 1-2 h), iodine (1 equiv, -78 to 0°C, 2-3 h), and NaOAc or 3N NaOH (1 equiv, 0 to 25°C, 0.5 h). The reaction mixtures thus obtained were treated with 30% H_2O_2 and NaOAc (or 3N NaOH) to destroy B-containing byproducts, which otherwise tend to interfere with the product isolation procedure, and analyzed by GLC (SE-30 columns) using appropriate saturated hydrocarbon internal standards.

The experimental results of the preparation of conjugated E-enynes are summarized in Table I. In all cases, the desired E-enynes were obtained in acceptable yields (60-75% by GLC and 51-70% by isolation). The stereoselectivity in each case was >98-99%, as judged by capillary GLC analysis and NMR. In the case of 5-dodecen-7-yne, the absence (<1%) of the Z isomer was established by coinjection of an authentic sample prepared by partial reduction of 5,7-dodecadiyne.[7] The E and Z enynes can also be readily distinguished by their discrete coupling constants between the two alkenyl protons. Those for the E isomers are ca. 16 Hz. In some select cases, the isomeric purity was further confirmed by ^{13}C NMR. The nearly exclusive E geometry is consistent with selective attack of the alkynyl bond by iodine accompanied by migration of the E alkenyl group with retention (eq. 4). Indeed, treatment of alkynylborates with iodine can give alkynes via migration-elimination.[11] On the other hand, attack of the alkenyl group by iodine accompanied by migration of the alkynyl group would have produced the Z isomer[8] in the presence of an excess of sodium hydroxide.

Table I. Preparation of Conjugated E-Enynes via Organoboranes

R^1 of $R^1C{=}C(H)BSia_2$ (2)	R^2 of $LiC{\equiv}CR^2$	Yield[a], %	$R^1C{=}C(H)C{\equiv}CR^2$ (3) Isomeric purity, %	$SiaC{\equiv}CR^2$ Yield, %
n-Bu	n-Bu	74(60)	>99	7
	n-Bu	71(53)	>99	7
n-Bu		60(51)	>99	4
$Me_3SiO(CH_2)_9$	n-Pr	-(63)	>99	6
$AcO(CH_2)_2$	n-Bu	75(70)	>98	7
$AcO(CH_2)_6$	Et	70(60)	>98	7

[a] GLC yields. The number in parentheses is the isolated yield.

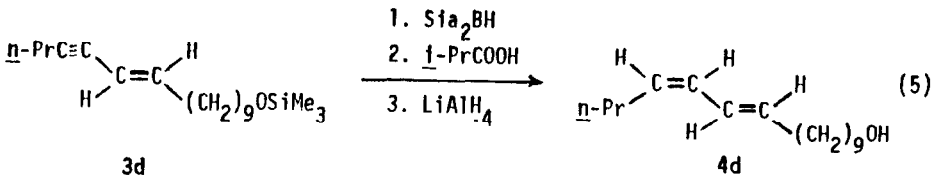


(4)

Sia = $(CH_3)_2CHC(CH_3)H$-

It is noteworthy that, in the cases of acetoxy derivatives, alkynyllithiums attack selectively the boron atom with no sign of attack at the acetoxy group. Although the number of examples in Table I is somewhat limited, we believe that this procedure first reported by us in 1973[2b] provided, for the first time, a potentially general method for the highly stereoselective synthesis of both unsymmetrically and symmetrically 1,4-disubstituted conjugated E enynes in high yields.

Conversion of alkynes into Z-alkenes can, in principle, be achieved by various methods including catalytic hydrogenation over Lindlar's catalyst[12] and hydroboration-protonolysis.[13] Although the latter method had not been applied to the conversion of conjugated E-enynes into E,Z-dienes prior to this study, it had been applied to the conversion of conjugated diynes into Z-enynes and their subsequent conversion into Z,Z-dienes.[7]



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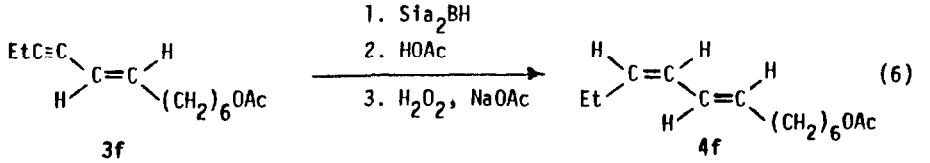
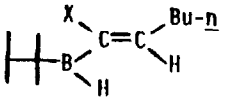


(6)

Hydroboration of enyne 3d with disiamylborane (1 equiv) followed by evaporation of THF and protonolysis in refluxing isobutyric acid for 1 h gave, after workup, a mixture containing bombykol (4d) and its isobutyrate ester. The ester was reduced with $LiAlH_4$ in THF, and pure bombykol[14] was obtained in 69% yield (eq. 5). After further purification by GLC (Carbowax 20 M), its identity was established by comparing its NMR and IR data, GLC retention time, and refractive index ($n_D^{26.5}$ 1.4800) with those of an authentic sample.[14] The stereochemical purity was >98%. For the conversion of 3f into a sex pheromone of lobesia botrana 4f,[15] protonolysis of the hydroboration mixture was carried out in HOAc, which was followed by oxidation with 30% H_2O_2 and NaOAc to destroy the organoborane byproducts (eq. 6). ^{13}C NMR examination of the reaction mixture indicated that the isomeric purity of the dienic product was ≥98%. After column chromatography (neutral alumina, activity 4), pure 4f, ≥98% isomeric purity, was obtained in 93% yield. The spectral data and GLC behavior of 4f were indistinguishable from those of an authentic sample.[15] The overall yield of 4f based on 1-butyne and 1-heptyne is approximately 40%.

Stereoselective Synthesis of Conjugated E,E-Dienes and E-Alkenyl Ketones. Stereoselective synthesis of conjugated E,E-dienes according to eq. 2 requires that single-stage hydroboration of 1-halo-1-alkynes with a monosubstituted borane, such as thexylborane, proceed selectively to give the desired (Z)-(1-halo-1-alkenyl)hydridoboranes, e.g., 5, in high yields. Since no such hydroboration reaction had been developed, we chose thexylborane as a convenient and potentially satisfactory hydroborating agent and examined its reaction with 1-halo-1-hexynes containing Cl, Br, and I. The reaction of thexylborane with 1-chloro-1-hexyne in a 1:1 ratio at -25°C for 1 h gave 5a in 75% yield, as judged by ^1H NMR analysis of its methanolysis product as well as residual hydride analysis using $MeSO_3H$ as a quenching agent. The ^1H NMR signals for the alkenyl and methoxy protons appeared at 5.72 (t, J = 7 Hz) and 3.72 (s) ppm. In fact, the reaction of 5a with the second equivalent of 1-chloro-1-hexyne was very sluggish, and the yields of 6a obtained from the reaction of thexylborane with 2 equiv of 1-chloro-1-hexyne at 0°C were 10 and 22% after 0.5 and 3 h, respectively. 1-Bromo-1-hexyne reacted analogously. Thus, the yields of 5b from the 1:1 reaction and 6b from the 1:2 reaction were 70 and 35%, respectively. On the other hand, the corresponding reactions of 1-iodo-1-hexyne gave 5c and 6c in 30 and 70% yields, respectively. In summary, 1-chloro- and 1-bromo-1-alkynes are suited for preparing 5, whereas 6 can be prepared in high yields only from 1-iodo-1-alkynes. It is also worth mentioning here that hydroboration of 1-hexyne with 1 molar equiv of thexylborane gives only ca. 20% yield of thexyl(E-1-hexenyl)borane.



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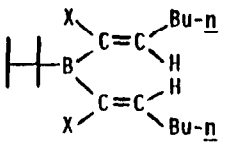

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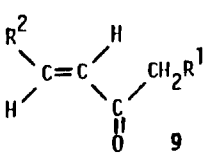
a: X = Cl
b: X = Br
c: X = I

Treatment of 5a or 5b with 1-alkynes (1 equiv) and then with NaOMe produced 7, which were protonolyzed with refluxing isobutyric acid to give 8 in 53-63% yields by GLC based on 1-alkynes and 1-halo-1-alkynes. Isomerically ≥98% pure samples were isolated by distillation in 45-55% yields. Oxidation of 7 with 30% H_2O_2 and NaOAc provided 9 in ca. 50% yields (55-60% by GLC). The use of a stronger base, such as NaOH, in place of NaOAc caused isomerization of the products, and the excess of NaOMe was neutralized with acetic acid before oxidation. These results are summarized in Table II.

Table II. Preparation of Conjugated E,E-Dienes and E-Alkenyl Ketones

R^1	$R^1C{=}CX$ X	R^2 of $R^2C{=}CH$	Yield (%) of (E,E)-$R^1CH{=}CHCH{=}CHR^2$ GLC	Isolated	Isomeric purity (%)
n-Bu	Cl	n-Pent	63	45	99
n-Bu	Br	n-Pent	51		98
n-Bu	I	n-Pent	21		85
n-Bu	Br	n-Bu	56		99
n-Bu	Cl	c-C_6H_{11}	59	55	98
c-C_6H_{11}	Cl	n-Bu	53		98
n-Bu	Cl	n-Pent	58[a]	48[a]	99[a]
n-Bu	Cl	c-C_6H_{11}	54[a]	48[a]	99[a]

[a]The product was 9.



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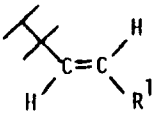

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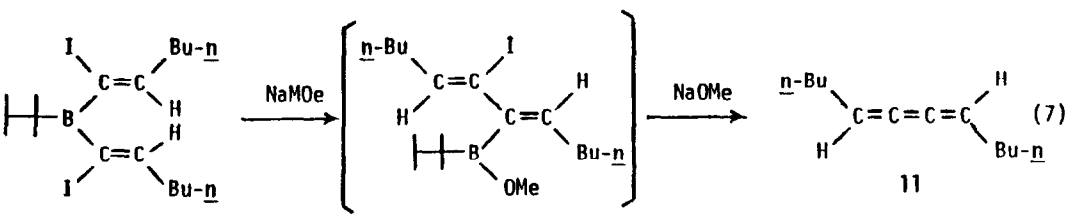
It should be noted that this method for the synthesis of conjugated E,E-dienes is applicable to the preparation of both symmetrically and unsymmetrically substituted dienes, as is the method for the synthesis of conjugated E,Z-dienes described earlier. Examination

by GLC (SE-30) revealed that, except for a minor amount (ca. 5%) of the side product arising from the migration of the thexyl group (10) and a few other unidentified peaks with considerably longer retention times, the desired product appeared, in each case where either a 1-chloro- or a 1-bromo-1-alkyne was used, as an essentially single peak in the expected region of the GLC trace. The E,E geometry of the products was indicated by ^{1}H NMR and IR. In the case of 5,7-dodecadiene, the essential absence (<1%) of the E,Z- and Z,Z-isomers was further established by GLC coinjection with authentic samples of these isomers.[7]

Stereoselective Synthesis of 1,2,3-Butatrienes. The high-yield formation of 6c (X = I) suggested to us that its treatment with 1 equiv of NaOMe might produce (E)-5,6,7-dodecatriene (11) via 12 in a stereospecific manner according to eq. 7. To our knowledge, there had been no report on the stereoselective synthesis of 1,2,3-butatriene derivatives prior to our study. Our interest was further aroused by predictions[16] that, although the energy barrier to the E-Z isomerization of hexapentaenes is too low to permit separation of the two stereoisomers at room temperature, 1,2,3-butatrienes would be stable to stereochemical isomerization at room temperature.



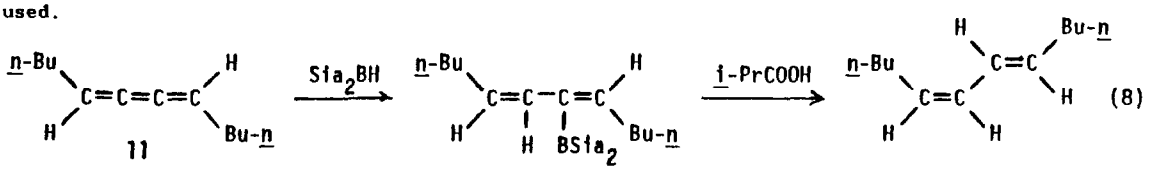
6c 12 11 (7)

Indeed, treatment of 6c with 2 molar equiv of NaOMe at 0°C readily produced 11 in 47% yield by GLC. The product was stable in solution (hexane, benzene, or THF) for at least 72 h at 25°C. On evaporation of the solvent, however, an initially clear oil gradually turned gelatinous. Various attempts to prevent the formation of the gelatinous substance, including (i) addition of antioxidants, such as hydroquinone and 4-methyl-2,6-di-tert-butylphenol, and (ii) exclusion of oxygen and light, failed. The gelatinous substance did not redissolve in any of the organic solvents tested, including those mentioned above. The thermal instability of 11 precluded its purification by distillation or preparative GLC. Fortunately, a highly pure sample of 11 was obtained by column chromatography (Florisil F-101, 100-200 mesh, Fisher, petroleum ether). The first compound eluted was essentially pure 11 (ca. 99% by GLC). Although its elemental analysis wa not performed, it was fully characterized immediately following rapid evaporation of the solvent by ^{1}H NMR, IR, UV, and MS.

GLC examination (2 ft SE-30, column temperature 100°C) of the reaction mixture containing 11 at the injection block temperature of 125°C revealed only a single sharp peak in the region expected for the C_{12} hydrocarbons. At the injection block temperatures of ≥200°C, however, two peaks consisting of the original peak and a new peak with a slightly shorter

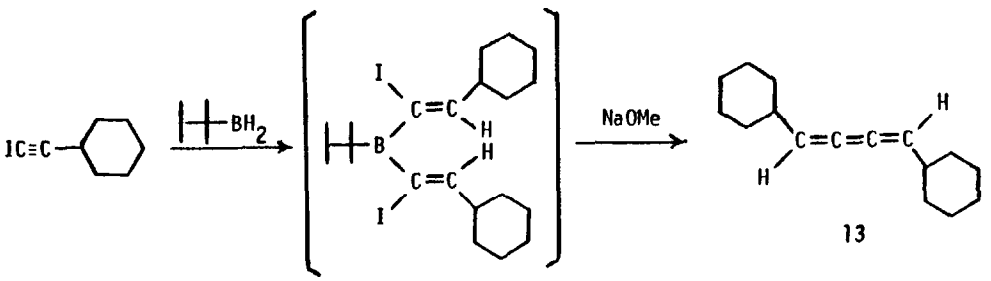
retention time were observed, indicating a rapid isomerization of 11. When the injection block temperature was 400°C, the two peaks were comparable in size. This isomerization was markedly catalyzed by a trace amount of iodine. Thus, when 0.3 mol % of iodine was added to 11, a nearly 1:1 mixture of 11 and its isomer was obtained within 10 min at 25°C. That the new peak corresponded to the stereoisomer of 11 was established by the ^{1}H NMR spectrum of the 1:1 mixture which was virtually identical with that of the initially obtained 11. All these results firmly established that the initial product which exhibited a sharp single GLC peak was indeed stereoisomerically pure (>99%).

The E geometry of 11 was established by its conversion into essentially pure (E,Z)-5,7-dodecadiene in 71% yield by hydroboration with disiamylborane followed by protonolysis with isobutyric acid (eq. 8). The results are in agreement with the exclusive cis addition of the B-H bond to the central double bond of 11 followed by protonolysis proceeding with retention of configuration. Hydroboration-protonolysis of the Z-isomer is expected to produce a mixture of E,E- and Z,Z-5,7-dodecadienes. Indeed, the 1:1 mixture of 11 and its stereoisomer yielded, after hydroboration-protonolysis, E,E- and/or Z,Z-5,7-dodecadienes in addition to the E,Z-isomer. The E,E- and Z,Z-isomers were not seen separately under the GLC conditions used.



(8)

The preparation of 1,4-dicyclohexyl-1,2,3-butatriene (13) in 29% yield and its structural determination were performed analogously (eq. 9).



(9)

CONCLUSION

A highly selective and potentially general methodology for the synthesis of conjugated E,E- and E,Z-dienes, E-enynes, and E-1,2,3-butatrienes via hydroboration of alkynes has been developed. To our knowledge, the approach reported in our preliminary communications[2] and described herein in full detail provided, for the first time, a highly selective methodology of potential generality for preparing the above-mentioned classes of compounds. Partial

reduction of conjugated diynes developed by Zweifel[7] is still a viable route to Z,Z-dienes, while the Pd-catalyzed cross-coupling route[5] initially reported by us and further developed by others appears to be the method of choice for preparing various types of conjugated dienes, especially the E,E-isomers. Nonetheless, we believe the procedure for preparing conjugated E-enynes and E,Z-dienes herein described is highly competitive and will prove to be the method of choice in many instances.

EXPERIMENTAL SECTION

General Methods. All operations involving organoboron compounds were performed under an inert atmosphere of nitrogen. Unless otherwise mentioned, commercial chemicals were used as received. Organolithiums were titrated with either menthol/2,2'-bipyridyl or 2-butanol/1,10-phenanthroline.[17] Borane in tetrahydrofuran (THF) was generated from $NaBH_4$ and BF_3-OEt_2, as reported in the literature.[13] It may also be purchased from commercial sources. As needed, boron hydrides were titrated by measuring the amount of hydrogen evolved.[13] As needed, benzene and hexane were distilled from $LiAlH_4$. Diethyl ether and THF were distilled from sodium benzophenone ketyl.

Preparation of Conjugated (E)-Enynes. (a) (E)-7-Dodecen-9-yn-1-yl Acetate (3f): Representative Procedure. To 7.25 mL of 2.76[18] M borane in THF (20 mmol) was added at 0°C 2.80 g (40 mmol, 4.2 mL) of 2-methyl-2-butene.[18] The reaction mixture was stirred at 0°C for 1 h. After it was diluted with 20 mL of THF and cooled to -30°C, 3.36 g (20 mmol) of 7-octyn-1-yl acetate was slowly added. The reaction mixture was stirred at 0°C for 1 h. In a separate flask an excess of 1-butyne (>20 mmol) was dissolved in 30 mL of THF and treated with 8.5 mL 920 mmol) of 2.35 M n-BuLi in hexane at 0°C, and the resultant mixture was slowly added at -78°C to the organoborane mixture prepared above. The combined mixture was stirred for 1-2 h at -50°C to complete "ate" complexation and then cooled to -78°C. To this was added 5.4 g (20 mmol) of I_2 in 30 mL of THF. In cases where the intense iodine color started persisting near the end of the addition of I_2, no more I_2 was added. After the mixture was warmed to 0°C over 2-3 h, it was treated with 6.7 mL (20 mmol) of 3N NaOH, and then with 8 mL each of 3N NaOAc and 30% H_2O_2. The oxidized mixture was extracted with ether, washed with water, aqueous $Na_2S_2O_3$, and $NaHCO_3$, dried over $MgSO_4$, filtered, concentrated, and chromatographed (neutral Al_2O_3, activity 4) to give 2.64 g (60% of 97% pure (E)-7-dodecen-9-yl acetate: n_D^{20} 1.4763; ^1H NMR ($CDCl_3$, Me_4Si) 1.12 (t, J = 7 Hz, 3H), 0.8-1.8 (m, 10H), 2.02 (s, 3H), 1.8-2.5 (m, 2H), 4.05 (t, J = 6 Hz, 2H), 5.42 (d, J = 16 Hz, 1H), 6.05 (dt, J = 16 and 6 Hz, 1H; ^{13}C NMR ($CDCl_3$, Me_4Si) 13.05, 14.05, 20.87, 25.88 (2C), 28.69, 28.32, 64.46, 78.85, 89.91, 110.33, 142.73, 170.85; IR (neat) 2210 (w), 1735 (s), 1235 (s), 1035 (s), 955 (m) cm^{-1}. Anal Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.98. Found: C, 75.37; H, 9.76. The Z-isomer exhibited the olefinic ^{13}C NMR signals at 109.6 and 141.8 ppm. In a separate run, GLC examination of the reaction mixture indicated that the title compound and 5,5-dimethyl-3-heptyne were formed in 70 and 7% yields, respectively.

(b) (E)-5-Dodecen-7-yne (3a). This compound was prepared in 60% yields (74% by GLC) from 1-hexyne. Its isomeric purity was >99%, as judged by GLC analysis using an authentic sample of the Z-isomer. The title compound yielded the following data: ^1H NMR ($CDCl_3$, Me_4Si) 0.92 (t, J = 7 Hz, 6H), 1.1-1.8 (m, 8H), 1.8-2.5 (m, 4H), 5.45 (bd, J = 16 Hz, 1H), 6.10 (dt, J = 16 and 7 Hz, 1H); IR ($CDCl_3$) 2220 (w), 1550 (m), 955 (s) cm^{-1}. Anal Calcd for $C_{12}H_{20}$: C, 87.73; H, 12.27. Found: C, 87.91; H, 12.09.

(c) (E)-1-Cyclohexyl-1-octen-3-yne (3b). The title compound was prepared in 53% yield (71% by GLC) from cyclohexylethyne and 1-hexyne: isomeric purity >99%; n_D^{25} 1.4902; ^1H NMR ($CDCl_3$, Me_4Si) 0.7-2.05 (m with a triplet at 0.92, 17H), 2.05-2.5 (m, 3H), 5.41 (bd, J = 16 Hz, 1H), 6.05 (dd, J = 16 and 6 Hz, 1H); IR (neat) 1440 (m), 955 (s) cm^{-1}. Anal Calcd for $C_{14}H_{22}$: C, 88.35; H, 11.65. Found: C, 88.14; H, 11.81.

(d) (E)-1-Cyclohexyl-3-octen-1-yne (3c). The title compound was prepared in 51% yield (60% by GLC) from cyclohexylethyne and 1-hexyne: isomeric purity >99%; ^1H NMR ($CDCl_3$, Me_4Si)

0.90 (t, J = 6 Hz, 3H), 1.1-2.7 (m, 17H), 5.46 (bd, J = 16 Hz, 1H), 6.11 (dt, J = 16 and 7 Hz, 1H); IR (neat) 1440 (m), 955 (m) cm^{-1}. Anal Calcd for $C_{14}H_{22}$: C, 88.35; H, 11.65. Found: C, 87.98; H, 11.52.

(e) (E)-1-Trimethylsiloxy-10-hexadecen-12-yne (3d). This compound was prepared in 63% yield from 20 mmol each of 1-pentyne and 10-undecynyl trimethylsilyl ether; bp 127-133°C (0.2 mm Hg); n_D^{27} 1.4585; ^1H NMR ($CDCl_3$, Me_4Si) 0.11 (s, 9H), 0.99 (t, J = 7 Hz, 3H), 1.2-1.8 (m, 16H), 1.8-2.5 (m, 4H), 3.57 (t, J = 6 Hz, 2H), 5.45 (d, J = 16 Hz, 1H), 6.09 (dt, J = 16 and 6 Hz, 1H); IR (neat) 1725 (w), 1245 (s), 1095 (s), 955 (s), 875 (s), 840 (s) cm^{-1}. This compound was used for the preparation of bombykol without further purification.

(f) (E)-3-Decen-5-yn-1-yl Acetate (3e). This compound was prepared from 1-hexyne and 3-butyn-1-yl acetate in 70% yield (75% by GLC) and used for the preparation of (3E,5Z)-3,5-decadien-1-yl acetate without further purification.

(Z)-5-Dodecen-7-yne. This compound was prepared by a literature method:[7] ^1H NMR ($CDCl_3$, Me_4Si) δ 0.92 (t, J = 6 Hz, 6H), 1.1-1.7 (m, 8H), 1.9-2.6 (m, 4H), 5.44 (bd, J = 11 Hz, 1H), 5.87 (dt, J = 11 and 7 Hz, 1H); IR (neat) 2200 (w), 1680 (w), 1620 (w), 1450 (m), 730 (m) cm^{-1}.

7-Octyn-1-yl Acetate. This preparation was achieved through the use of a literature method.[19] To 10.0 g (250 mmol) of dry KH (obtained by washing with pentane under nitrogen a 35% suspension of KH in mineral oil followed by drying) was added 180 mL of 1,3-diaminopropane. A slow reaction occurred and 200 mL of hydrogen evolved in 4 h at room temperature. 2-Octyn-1-ol (10.7 g, 25 mmol) prepared by a literature procedure,[20] was then added at 0°C. The reaction mixture was allowed to warm up to 25°C and kept at this temperature for 5 h. The resultant mixture was cooled to 0°C, quenched with H_2O (300 mL), extracted with ether, washed sequentially with cold 10% HCl, saturated $NaHCO_3$, and then dried over $MgSO_4$. Evaporation of the volatiles provided 10.7 g (85 mmol, 100%) of crude 7-octyn-1-ol, which was essentially pure by GLC. This was slowly added at 0°C to a solution containing 9.5 mL of Ac_2O and 7.5 mL of pyridine. The reaction mixture was stirred at room temperature overnight, poured into ice water (250 mL), extracted with ether, washed with 10% HCl and saturated $NaHCO_3$, and dried over $MgSO_4$. Filtration and distillation provided 11.4 g (68 mmol, 80% yield based on 2-octyn-1-ol) of the title compound: bp 66-67°C (0.9 mm Hg); n_D^{20} 1.4401; ^1H NMR ($CDCl_3$) δ 1.1-1.8 (m, 6H), 1.85 (t, J = 2.5 Hz, 1H), 1.9-2.3 (m, 2H), 1.98 (s, 3H), and 4.0 (t, J = 6 Hz, 2H) ppm; IR (neat) 3280 (m), 2930 (s), 2850 (m), 2120 (w), 1740 (s), 1460 (w), 1430 (w), 1390 (m), 1360 (m), 1240 (s), 1070 (m), 1050 (m), 1035 (m) cm^{-1}. This compound was used without further purification.

2-Butyn-1-yl Acetate. 2-Butyn-1-ol obtained from a commercial source was acetylated as above and used directly.

1-(Trimethylsiloxy)-10-undecyne. 10-Undecyn-1-ol, obtained from a commercial source, was silylated with Me_3SiCl and NEt_3 and used directly without purification: 82% yield by isolation; bp 60-62°C (0.05 mm Hg); $n_D^{25.5}$ 1.4352; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.10 (s, 9H), 1.2-1.7 (m, 7H), 1.90 (t, J = 2.5 Hz, 1H), 2.0-2.3 (m, 2H), 3.57 (t, J = 6 Hz, 2H) ppm; IR (neat) 3300 (m), 2900 (s), 2850 (s), 2120 (w), 1250 (s), 1095 (s), 875 (s), 840 (s) cm^{-1}.

Preparation of Conjugated E,Z-Dienes from E-Enynes. (7E,9Z)-7,9-Dodecadien-yl Acetate (4f): Representative Procedure Using HOAc. To 270 mg (1.25 mmol) of (E)-7-dodecen-9-yn-1-yl acetate dissolved in 3 mL of THF was added at 0°C 0.65 mL (1.233 mmol) of disiamylborane in THF. The reaction mixture was kept at 0°C for 1 h, and then 3 mL of glacial HOAc was added. The mixture was kept at 40°C overnight, evaporated under reduced pressure, and sequentially treated with NEt_3 (2 mL), 3N NaOAc (0.5 mL), and 30% H_2O_2 (0.5 mL). Extraction with petroleum ether (30-60°C), washing with water and $NaHCO_3$, drying over $MgSO_4$, and concentration gave 250 mg (1.15 mmol, 93%) of 98% isomerically pure (7E,9Z)-7,9-dodecadien-1-yl acetate: ^1H NMR ($CDCl_3$) δ 0.99 (t, J = 7 Hz, 3H), 1.1-1.9 (m, 8H), 1.9-2.5 (m, 4H), 2.03 (s, 3H), 4.07 (t, J = 6 Hz, 2H), and 5.05-6.65 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$) δ 14.33, 21.04, 25.85, 28.63, 28.86, 29.31, 32.80, 64.55, 125.77, 128.08, 131.68, 134.29, 171.04 ppm; IR (neat) 2950 (s), 2850 (m), 1740 (s), 1360 (m), 1235 (s), 990 (s), 950 (m) cm^{-1}. The GLC

behavior and spectral properties of the compound were indistinguishable from those of an authentic sample.[15] The E,Z- and E,E-isomers were readily distinguishable by ^{13}C NMR. The E,E-isomer exhibits the olefinic signals at δ 129.48, 130.65, 132.06, and 133.95 ppm.

(10E,12Z)-10,12-Hexadecadien-1-ol (Bombikol). To 0.616 g (2 mmol) of 3d in 4 mL of THF was added at 0°C 1.24 mL (2 mmol) of 1.61 M disiamylborane in THF. After 1 h, the solvents were removed in vacuo (25°C, 1 h, >5 mm Hg), and isobutyric acid (4 mL) was added. The reaction mixture was refluxed for 1 h, extracted with ether, washed with water and $NaHCO_3$, dried over $MgSO_4$, and concentrated. The concentrated mixture was redissolved in THF and treated with 0.63 mL (1.2 mmol) of 1.9 M $LiAlH_4$ in THF, first at 0°C and then at 25°C for 1 h. The mixture was extracted with ether, washed with water and $NaHCO_3$, dried over $MgSO_4$, and concentrated to give 0.33 g (69%) of isomerically >98% pure bombykol, which was further purified by GLC (Carbonex 20 M): n_D^{26} 1.4800 (lit.[14] n_D^{20} 1.4835); ^1H NMR ($CDCl_3$, Me_4Si) δ 0.93 (t, J = 6 Hz, 3H), 1.1-1.8 (m, 16H), 1.8-2.4 (m, 4H), 3.6 (m, 3H), 5.5-6.6 (m, 4H) ppm; IR (neat) 3300 (s), 2900 (s), 2820 (s), 1460 (s), 1050 (s). 985 (s), 950 (s), 720 (w) cm^{-1}. The isomeric purity by GLC was >98%. This product was indistinguishable from an authentic sample of bombykol.[14] In this experiment, the need for the use of isobutyric acid in place of HOAc was not established, and the use of HOAc may well be satisfactory.

(3E,5Z)-3,5-Decadien-1-yl Acetate (4e). (E)-3-Decen-5-yn-1-yl acetate (3e) obtained as a crude product from 5 mmol of 3-butyn-1-yl acetate was mixed with 20 mL each of ethanol and water. To this was added 20 g of zinc powder[21] from a freshly opened container. The reaction mixture was refluxed overnight. GLC analysis indicated complete conversion of (3e) into (4e) in 95% yield. The reaction mixture was cooled, filtered, and extracted with 30-60 petroleum ether, washed with $NaHCO_3$, and dried over $MgSO_4$. Concentration under reduced pressure, after chromatography (silica gel) gave isomerically >98% pure 4e: ^1H NMR ($CDCl_3$, Me_4Si) 0.7-1.1 (t, J = 6 Hz, 3H), 1.1-1.8 (m, 4H), 1.9-2.7 (m, 4H), 1.99 (s, 3H), 4.07 (t, J = 6 Hz, 2H), 5.05-6.65 (m, 4H) ppm; IR (neat) 2940 (s), 2.20 (w), 1735 (s), 1235 (s), 1035 (s), 955 (s) cm^{-1}. Anal Calcd for $C_{12}H_{20}O_2$: C, 79.94; H, 11.18. Found: C, 79.68; H, 11.35.

Preparation of 1-Chloro-1-alkynes. (a) 1-Chloro-1-hexeyne. The following literature procedure[22] is representative. To 8.2 g (100 mmol, 11.5 mL) of 1-hexyne dissolved in 75 mL of THF was added 52.5 mL (100 mmol) of 1.9 M n-BuLi in hexane at -50°C. After the mixture had been stirred for 1 h at -50°C, a solution of 19.1 g (100 mmol) of p-toluenesulfonyl chloride in 40 mL of THF was added dropwise at -50°C. The mixture was stirred for 6 h at -50 to -40°C, poured into 500 mL of water, extracted with pentane (200 mL), washed with water, dried over $MgSO_4$, and distilled to give 7.5 g (64%) of 1-chloro-1-hexyne:[22] bp 65-67°C (125 mm Hg). (b) 1-Chloro-2-cyclohexylethyne. This compound[22] was prepared analogously.

1-Bromo-1-hexyne. This compound was prepared according to a literature procedure[23] by addition of 1-hexyne to a mixture of KOH (6 equiv) and bromine (1 equiv) at 0°C: 90% yield; n_D^{21} 1.4652.

1-Iodo-1-alkynes. (a) 1-Iodo-1-hexyne. The following literature procedure[24] is representative. To 16.9 g (200 mmol, 22.9 mL) of 1-hexyne in 500 mL of ether was added 94.9 mL (200 mmol) of 2.67 M n-BuLi in hexane at -50°C. After 1 h, the mixture was warmed to 0°C, and 50.8 g (200 mmol) of I_2 dissolved in 150 mL of ether was added. After having been stirred for 1 h at 0°C, the mixture was washed with water and saturated $Na_2S_2O_3$ until the iodine color no longer persisted. Drying over $MgSO_4$ and distillation gave 1-iodo-1-hexyne in 85% yield: bp 91°C (23 mm Hg). (b) 1-Iodo-2-cyclohexylethyne. This compound was prepared analogously: bp 82-85°C (3 mm Hg).

Reaction of 1-Halo-1-alkynes with 1,1,2-Trimethylpropylborane(Thexylborane). (a) 1-Chloro-1-hexyne. Thexylborane was generated in situ by adding 1 equiv of 2,3-dimethyl-2-butene to borane-THF.[13] To a 10 mmol aliquot of thexylborane generated above was added at -25°C 1-chloro-1-hexyne (10 mmol). After 1 h, addition of CH_3SO_3H induced evolution of ca. 9 mmol of H_2. Addition of an excess of dry MeOH produced a species showing a triplet at 5.72 (J = 7 Hz) ppm and a singlet at 3.72 ppm. Their integrations indicated that 5a was formed in ca. 75% yield. The reaction of thexylborane with 2 equiv of 1-chloro-1-hexyne at 0°C

produced 6b in 10 and 22% after 0.5 and 3 h, respectively, by ^{1}H NMR analysis. (b) 1-Bromo-1-hexyne. The corresponding 1:1 and 1:2 reactions gave 5b and 6b in 70 and 35% yields, respectively. (c) 1-Iodo-1-hexyne. The corresponding 1:1 and 1:2 reactions gave 5c and 6c in 30 and 70% yields, respectively. (d) 1-Hexyne. The 1:1 reaction of thexylborane and 1-hexyne gave a ca. 20% yield of thexyl[(E)-1-hexenyl]borane.

Preparation of Conjugated E,E-Dienes. (a) (1E,3E)-1-Cyclohexyl-1,3-octadiene: Representative Procedure. To 0.58 g (5 mmol) of 1-chloro-1-hexyne in 4 mL of THF was added at -25°C 5 mL (5 mmol) of 1.0 M thexylborane in THF. After 1 h at -25°C, 0.54 g (5 mmol, 0.65 mL) of cyclohexylethyne was added, and the mixture was stirred for 1 h at -25°C and then treated with 0.41 g (7.5 mmol) of NaOMe in 7.5 mL of MeOH at -25°C. The mixture was stirred for 1 h at room temperature and evaporated to remove all the volatiles at 1 mm Hg. To this was added 7.5 mL of isobutyric acid. The reaction mixture was refluxed for 1 h, poured into 20 mL of water, extracted with ether, washed with aq. Na_2CO_3, and oxidized with 1.7 mL each of 3N NaOH and 30% H_2O_2. Extraction with ether, washing with water, drying over $MgSO_4$, distillation, and chromatography (Florisil, petroleum ether) provided 0.53 g (55% yield) of the title compound which was isomerically 98% pure: bp 112-115°C (3 mm Hg); n_D^{20} 1.4905; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, J = 6 Hz, 3H), 1.1-2.4 (m, 17H), 5.3-6.2 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.01, 22.38, 26.19, 26.33, 31.77, 32.47, 33.12, 40.85, 128.23, 131.05, 132.85, 138.57; IR (neat) 990 (s), 965 (m), 890 (m) cm^{-1}. Anal Calcd for $C_{14}H_{24}$: C, 87.42; H, 12.58. Found: C, 87.29; H, 12.62.

(b) (5E,7E)-5,7-Tridecadiene. The title compound[5a] was prepared from 1-chloro-1-hexyne and 1-heptyne in 63% GLC yield (45% by isolation) as a 99% isomerically pure compound, following the representative procedure. The use of 1-bromo-1-hexyne and 1-iodo-1-hexyne in place of 1-chloro-1-hexyne led to 51 and 21% yields, respectively: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, J = 6 Hz, 6H), 1.1-1.7 (m, 10H), 1.7-2.4 (m, 4H), 5.2-6.6 (m, 4H) ppm; IR (neat) 1660 (w), 1630 (w), 1460 (m), 1370 (m), 985 (s) cm^{-1}.

(c) (5E,7E)-5,7-Dodecadiene. This compound was also prepared analogously in 56% GLC yield (99% isomerically pure) and identified by GLC coinjection with authentic samples of the (E,E), (E,Z), and (Z,Z) isomers available in our laboratories.

Preparation of α,β-Unsaturated Ketones. (a) (E)-1-Cyclohexyl-3-oxo-1-octene: Representative Procedure. The reaction of thexylborane with 1-chloro-1-hexyne and then with cyclohexylethyne was carried out as described above for the preparation of (1E,3E)-1-cyclohexyl-1,3-octadiene on the same scale. Without evaporation of the solvents, the reaction mixture was oxidized with 2 mL each of 3N NaOAc and 30% H_2O_2, extracted with ether, washed with water, dried over $MgSO_4$, and distilled to give 0.50 g (48% yield) of the title compound as a 99% isomerically pure compound: bp 91-92°C (0.2 mm Hg); ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, J = 6 Hz, 3H), 1.1-2.3 (m, 17H), 2.55 (t, J = 7 Hz, 2H), 6.07 (d, J = 16 Hz, 1H), 6.83 (dd, J = 16 and 6 Hz, 1H) ppm; IR (neat) 1700 (s), 1680 (s), 1630 (s), 1450 (s), 985 (s) cm^{-1}.

(b) (5E)-7-Oxo-5-tridecene. This compound was prepared analogously from 1-chloro-1-hexyne and 1-heptyne in 48% yield (58% by GLC) as a 99% isomerically pure substance: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.89 (t, J = 6 Hz, 3H), 0.92 (t, J = 6 Hz, 3H), 1.2-1.7 (m, 10H), 2.15-2.3 (m, 2H), 2.53 (t, J = 7 Hz, 2H), 6.10 (dt, J = 16 and 1 Hz, 1H), 6.84 (dt, J = 16 and 7 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.89, 14.00, 22.37, 22.61, 24.15, 30.39, 31.66, 32.28, 40.19, 130.77, 147.73, 201.53 ppm; IR (neat) 1700 (s), 1675 (s), 1630 (s), 980 (s) cm^{-1}.

Preparation of (E)-1,3-Dialkyl-1,2,3-butatrienes. (a) (E)-5,6,7-Dodecatriene (11): Representative Procedure. To 10.4 g (6.75 mL, 50 mmol) of freshly distilled 1-iodo-1-hexyne in 20 mL of THF placed in a dry 200-mL flask was added at 0°C 14.3 mL of 1.75 M (25 mmol) thexylborane in THF. Two hours later a solution of 2.7 g (50 mmol) of NaOMe in 50 mL of methanol was added at 0°C, and this mixture was stirred for 3 h at 25°C. GLC analysis of a quenched aliquot indicated a 47% yield of 11, the stereoisomeric purity of which was >99% by GLC (2f SE-30, 100°C). The reaction mixture was concentrated to a quarter of its original volume, extracted with petroleum ether (50 mL) to remove methanol and other insoluble materials. The extract was concentrated to 20 mL under vacuum and promptly chromatographed

(Florisil, F-101, 100-200 mesh, Fisher, petroleum ether) under nitrogen at or below 0°C. The product thus obtained was ≥99% pure and stable at room temperature in THF, hexane, and benzene for at least 72 h. Upon concentration, however, it decomposed to an apparently polymeric unidentified species within 24 h at 25°C. Immediately following rapid evaporation of the solvent, the compound yielded the following spectroscopic data: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.92 (t, J = 6 Hz, 6H), 1.1-1.8 (m, 8H), 1.9-2.5 (m, 4H), 5.54 (t, J = 5 Hz, 2H) ppm; IR (neat) 1660 (w), 1480 (m), 1390 (m), 825 (m) cm^{-1}; UV_{max} (hexane) 255 (ϵ 28,600), 266 (ϵ 11,700) nm.

GLC analysis at injection block temperatures higher than 100-120°C caused extensive E-Z isomerization. Similarly, 0.26 mol% if I_2 isomerized 99% pure 11 to a 57:43 mixture of the E and Z isomers within 1 h at room temperature. No essential loss of 5,6,7-dodecatriene was detected by GLC. That the two species are isomeric was indicated by the ^{1}H NMR spectrum of the mixture which was very similar to that of the isomerically pure 11.

(b) (E)-1,3-Dicyclohexyl-1,2,3-butatriene (13). This compound was prepared in 29% GLC yield from 5.92 g (25.4 mmol) of 1-iodo-2-cyclohexylethyne, 6.32 mL (12.7 mmol) of 2.01 M thexylborane in THF and 1.37 g (25.4 mmol) of NaOMe in 25 mL of MeOH: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.75-2.5 (m, 22H), 5.43 (d, J = 4 Hz, 2H) ppm.

Conversion of (E)-5,6,7-Dodecatriene with (5E,7Z)-5,7-Dodecadiene. Disiamylborane (1.04 M, 20 mL, 2.08 mmol) in THF was added to a solution of 11 (2.0 mmol) in 3 mL of THF at -30 to -25°C. Two hours later, the solvent was removed in vacuo, and isobutyric acid (1 mL) was added. This mixture was refluxed for 1 h, and quenched with aqueous Na_2CO_3. GLC examination of the organic layer (SE-30) using n-decane as an internal standard indicated that (5E,7Z)-5,7-dodecadiene was formed in 71% yield as a >95% isomerically pure species. Its identity and isomeric purity were established by coinjection with authentic samples of the (E,E), (E,Z) and (Z,Z) isomers available in our laboratories.

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