Highly Stereoselective Synthesis of Trisubstituted Olefins via Addition of Alkylcopper Complexes to Acetylenes[1]

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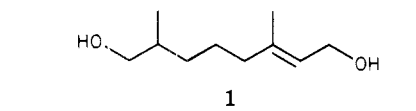
Alkylcopper reagents prepared from the reaction of Grignard reagents with the dimethyl sulfide complex of cuprous bromide undergo efficient addition to terminal acetylenes to generate 2,2-disubstituted alkenylcopper intermediates. The addition also occurs very efficiently with a methylcopper complex despite earlier reports in the literature of difficulty in effecting this reaction. Among the electrophilic species with which the alkenylcopper species react are various organic halides, α,β-unsaturated carbonyl compounds, and epoxides. The overall sequence provides a convenient one-flask route to trisubstituted olefins from simple starting materials. The types of products available include 5-keto olefins and homoallylic alcohols which contain useful functionalities for further transformations. The reactions may be applied iteratively to construct systems containing multiple trisubstituted olefin units arranged in 1,5 relationships as seen in large numbers of naturally occurring compounds. ^{1}H NMR, ^{13}C NMR, lanthanide shift reagent, and GLPC studies reveal that these reactions proceed with ≥99.6% stereoselectivity to give the products of syn addition to the acetylenes.

Trisubstituted olefins are of widespread occurrence among natural products. Included among these naturally occurring olefins are a rich array of structural types. Some examples are the secretion (**1**) of the African Monarch (*Danaus chrysippus*),[2] geraniol (**2**), the sex attractant propylure (**3**) of the pink bollworm moth (*Pectinophora gossypiella*),[3] farnesylacetone (**4**), which is an inhibitor of amino acid incorporation in a crab (*Carcinus maenas*),[4] a constituent (**5**) of the codling moth (*Laspeyresia pomonella*),[5] the antibiotic conocandin (**6**) from a strain of *Hormococcus conorum*,[6] the antibiotic grifolin (**7**) from the mushroom *Albatrellus confluens*,[7] and caulerpol (**8**) which is a constituent of a marine alga (*Caulerpa brownii*).[8] In addition to their importance in nature, trisubstituted olefins are often used as key intermediates in the synthesis of other compounds. For example, the diene **9** is a precursor of the antibiotic lasalocid A,[9] and triene **10** is the final intermediate in a synthesis of the *Cecropia* juvenile hormone.[10]



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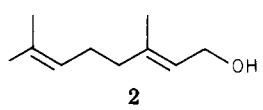

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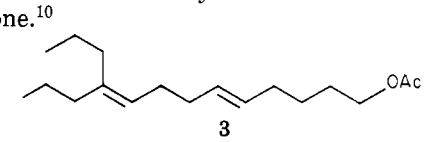

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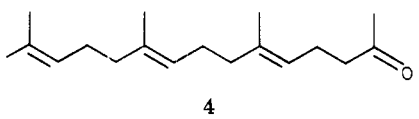

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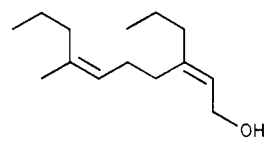

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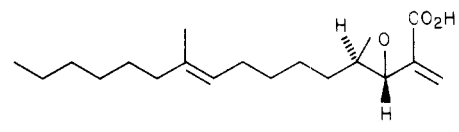

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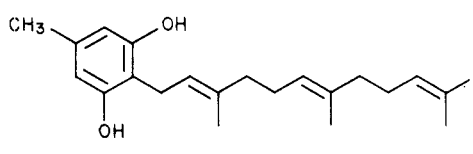

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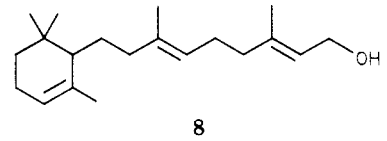

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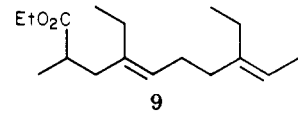

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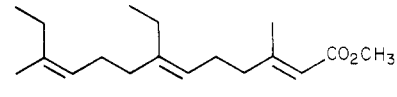

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Among the naturally occurring trisubstituted olefins, the most common olefinic substituent is simply the methyl group. This statement is particularly applicable to olefinic terpenes (e.g., geraniol, **2**). Also, individual natural products often contain several trisubstituted olefin moieties, usually arranged in a 1,5 relationship, within a single structure. Furthermore, the physiological activity of the natural substances is often highly sensitive to the geometry of the olefinic units. On the basis of these observations, some important criteria may therefore be listed for methods for the synthesis of trisubstituted olefins: (1) the methods should permit the introduction of various functional groups which either may be present

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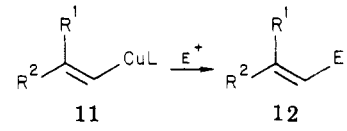
in natural products or may be useful in further transformations leading to natural products; (2) the methods should permit the introduction of a variety of olefinic substituents, including the simple methyl group; (3) iterative application of the methods should be possible in order to permit the construction of polyolefinic structures as seen frequently in nature; (4) good control of olefin stereochemistry must be possible.

Large numbers of methods for the synthesis of trisubstituted olefins have been developed previously and have been discussed in review articles.[11] More recent progress in this area has been made through the development of methods involving the following approaches: (1) elimination or cleavage reactions of organic halides,[12] alcohol derivatives and other C–O-bonded compounds,[13] amine derivatives and other C–N-bonded compounds,[14] sulfur- and selenium-containing compounds,[15] silanes,[16] β-lactones,[17] and boranes;[18] (2) carbonyl condensation reactions of phosphonium ylides and other phosphorus reagents,[19] organosilicon compounds,[20] sulfur- and selenium-containing reagents,[21] enolates and related species,[22] imines,[23] and isocyanides;[24] (3) addition of various reagents to acetylenes,[25] 1,3-dienes,[26] and allenes;[27] (4) reactions of various alkenylmetal species;[28] (5) substitution reactions of alkenyl halides and related compounds;[29] (6) reactions of various allylmetal[30] and other allylic systems;[31] (7) cleavage and rearrangements of other carbon frameworks.[32]

In recent years, the reactions of various types of alkenylcopper complexes **11** (L = ligand) with electrophilic reagents (E^+) have been employed frequently in routes to olefins **12** (eq 1).[33,34] Among the most commonly used



(1)

11 **12**

a, R^1 = H
b, R^1 = alkyl, etc.

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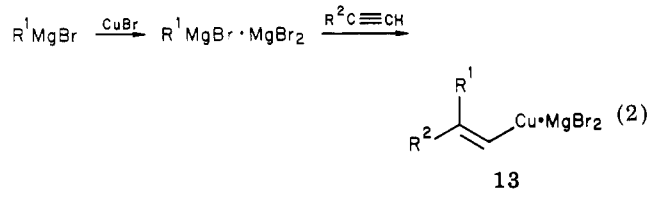
electrophiles are organic halides and α,β-unsaturated carbonyl compounds, the latter undergoing conjugate addition reactions to give olefins containing carbonyl groups that are useful in subsequent transformations. Whereas these reactions have been applied frequently to the synthesis of disubstituted olefins (**12a**), these approaches have not been widely practical for trisubstituted olefins (**12b**) because the requisite disubstituted alkenylcopper complexes (**11b**) were not as readily available as the monosubstituted species (**11a**) until recently. However, in 1971 Normant reported a prospective solution to this problem; alkylcopper complexes derived from Grignard reagents were found to undergo addition to simple terminal acetylenes to give disubstituted alkenylcopper complexes **13** (eq 2).[35] This reaction and subsequent reactions of the intermediates **13** with various electrophiles have been the subjects of further extensive studies by the groups of Normant,[36] Vermeer,[37] and others.[38]



(2)

13

(34) For some recent examples of preparations and reactions of alkenylcopper complexes see: (a) Yamamoto, Y.; Yatagai, H.; Sonoda, A.; Murahashi, S.-I. *J. Chem. Soc., Chem. Commun.* **1976**, 452–3. (b) Clark, R. D.; Heathcock, C. H. *J. Org. Chem.* **1976**, *41*, 1396–1403. (c) Posner, G. H.; Ting, J.-S.; Lentz, C. M. *Tetrahedron* **1976**, *32*, 2281–7. (d) Still, W. C.; MacDonald, T. L. *Tetrahedron Lett.* **1976**, 2659–62. (e) Corey, E. J.; Wollenberg, R. H. *Ibid.* **1976**, 4705–8. (f) Yamamoto, Y.; Yatagai, H.; Maruyama, K.; Sonoda, A.; Murahashi, S.-I. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 3427–28. (g) Stork, G.; Takahashi, T. *J. Am. Chem. Soc.* **1977**, *99*, 1275–6. (h) Yamamoto, Y.; Yatagai, H.; Maruyama, K.; Sonoda, A.; Murahashi, S.-I. *Ibid.* **1977**, *99*, 5652–6. (i) Raynolds, P. W.; Manning, M. J.; Swenton, J. S. *J. Chem. Soc., Chem. Commun.* **1977**, 499–500. (j) Dimsdale, M. J.; Newton, R. F.; Rainey, D. K.; Webb, C. F.; Lee, T. V.; Roberts, S. M. *Ibid.* **1977**, 716; (k) Gordon-Gray, C. G.; Whiteley, C. G. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2040–6. (l) Kubota, M.; Miyashita, A.; Komiya, S.; Yamamoto, A. *J. Organomet. Chem.* **1977**, *139*, 111–20. (m) Tanaka, T.; Kurozumi, S.; Toru, T.; Kobayashi, M.; Miura, S.; Ishimoto, S. *Tetrahedron* **1977**, *33*, 1105–12. (n) Yoshifuji, M.; Loots, M. J.; Schwartz, J. *Tetrahedron Lett.* **1977**, 1303–6. (o) Baudouy R.; Crabbé, P.; Greene, A. E.; Le Drian, C.; Orr, A. E. *Ibid.* **1977**, 2973–6. (p) Boeckman, R. K.; Bruza, K. J. *Ibid.* **1977**, 4187–90. (q) Trost, B. M.; Timko, J. M.; Stanton, J. L. *J. Chem. Soc., Chem. Commun.* **1978**, 436–8. (r) Lee, T. V.; Roberts, S. M.; Dimsdale, M. J.; Newton, R. J.; Rainey, D. K.; Webb, C. F. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1176–8. (s) Corey, E. J.; Floyd, D.; Lipshutz, B. H. *J. Org. Chem.* **1978**, *43*, 3418–20. (t) Drouin, J.; Leyendecker, F.; Conia, J.-M. *Nouv. J. Chem.* **1978**, *2*, 267–70. (u) Dang, H. P.; Linstrumelle, G. *Tetrahedron Lett.* **1978**, 191–4. (v) Corey, E. J.; Bock, M. G.; Kozikowski, A. P.; Rama Rao, A. V.; Floyd, D.; Lipshutz, B. *Ibid.* **1978**, 1051–4.

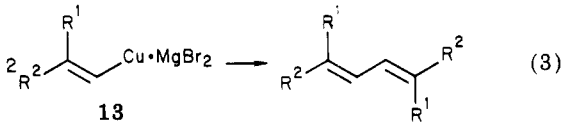
(35) Normant, J. F.; Bourgain, M. *Tetrahedron Lett.* **1971**, 2583–6.

(36) (a) Normant, J. F.; Cahiez, G.; Chuit, C.; Alexakis, A.; Villieras, J. *J. Organomet. Chem.* **1972**, *40*, C49–C52. (b) Normant, J. F.; Cahiez, G.; Chuit, C.; Villieras, J. *Tetrahedron Lett.* **1973**, 2407–8. (c) Normant, J. F.; Cahiez, G.; Bourgain, M.; Chuit, C.; Villieras, J. *Bull. Soc. Chim. Fr.* **1974**, 1656–60. (d) Normant, J. F.; Cahiez, G.; Chuit, C.; Villieras, J. *J. Organomet. Chem.* **1974**, *77*, 269–79, 281–7. (e) Alexakis, A.; Normant, J. F.; Villieras, J. *J. Mol. Catal.* **1975/76**, *1*, 43–58. (f) *J. Organomet. Chem.* **1975**, *96*, 471–85. (g) Normant, J. F.; Commercon, A.; Villieras, J. *Tetrahedron Lett.* **1975**, 1465–8. (h) Chuit, C.; Cahiez, G.; Normant, J.; Villieras, J. *Tetrahedron* **1976**, *32*, 1675–80. (i) Alexakis, A.; Commercon, A.; Villieras, J.; Normant, J. F. *Tetrahedron Lett.* **1976**, 2313–6. (j) Alexakis, A.; Normant, J.; Villieras, J. *Ibid.* **1976**, 3461–2. (k) Alexakis, A.; Cahiez, G.; Normant, J. F.; Villieras, J. *Bull. Soc. Chim. Fr.* **1977**, 693–8. (l) Duboudin, J. G.; Jousseaume, B.; Alexakis, A.; Cahiez, G.; Villieras, J.; Normant, J. F. *C. R. Hebd. Seances Acad. Sci.* **1977**, *285*, 29–31. (m) Scott, F.; Cahiez, G.; Normant, J. F.; Villieras, J. *J. Organomet. Chem.* **1978**, *144*, 13–16. (n) Alexakis, A.; Cahiez, G.; Normant, J. F. *Tetrahedron Lett.* **1978**, 2027–30.

(37) (a) Westmijze, H.; Meijer, J.; Bos, H. J. T.; Vermeer, P. *Recl. Trav. Chim. Pays-Bas* **1976**, *95*, 299–303, 304–7. (b) Westmijze, H.; Meijer, J.; Vermeer, P. *Ibid.* **1977**, *96*, 168–71, 194–6. (c) Westmijze, H.; Vermeer, P. *Synthesis* **1977**, 784–5. (d) Westmijze, H.; Kleijn, H.; Meijer, J.; Vermeer, P. *Tetrahedron Lett.* **1977**, 869–72. (e) Westmijze, H.; Kleijn, H.; Vermeer, P. *Ibid.* **1977**, 2023–6. (f) *Ibid.* **1978**, 3125–6. (g) Tadema, G.; Everhardus, R. H.; Westmijze, H.; Vermeer, P. *Ibid.* 1978, 3935–6.

Results and Discussion

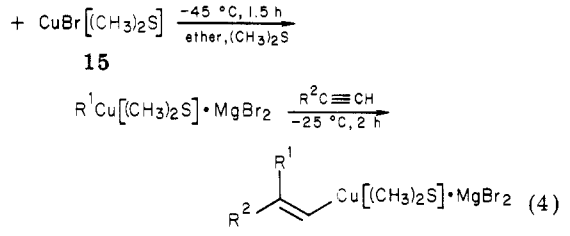
Addition of Alkylcopper Complexes to Acetylenes. Because the addition of alkylcopper complexes to acetylenes (eq 2) appeared to be a very promising approach to trisubstituted olefins, we were interested in applying this reaction to the synthesis of various olefinic natural products. However, in our initial efforts to employ the addition reaction, we found that substantial amounts (ca. 5–20% yields) of 1,3-dienes **14** are formed as byproducts. These dienes apparently arise by coupling of the alkenylcopper intermediates **13** (eq 3), a reaction which is



(3)

13 **14**

well-known to be induced either thermally or by various oxidizing agents, including some transition-metal ions.[33,39] We believe that in our studies the coupling is promoted by impurities (e.g., Cu^{2+}) present in the cuprous halides that are commercially available in this country.[40] The dienes are formed whether the cuprous halides are purified by the commonly used precipitation procedure[41] or by extraction in a Soxhlet apparatus.[42] Also, the dienes are obtained even though the addition reactions are performed under a rigorously maintained inert atmosphere. Fortunately, during the course of our work, House[43] reported a method for preparing the dimethyl sulfide–cuprous bromide complex **15** in a highly pure form as a white, crystalline solid free of the contaminants (especially Cu^{2+} salts) that induce decomposition of organocopper compounds. We have found that when **15** is employed in reactions with Grignard reagents, the resulting alkylcopper complexes undergo addition to terminal acetylenes to give high yields of products derived from the disubstituted alkenylcopper intermediates **16** (eq 4)[44] and only trace



(4)

16

amounts (typically 0–2%) of the dienes. For example, when the intermediate **16** with $R^1 = C_2H_5$ and $R^2 = n$-

(38) (a) Crandall, J. K.; Battioni, P.; Wehlacz, J. T.; Bindra, R. *J. Am. Chem. Soc.* **1975**, *97*, 7171–2. (b) Jousseaume, B.; Duboudin, J.-G. *J. Organomet. Chem.* **1975**, *91*, C1–C3; (c) Crandall, J. K.; Collonges, F. *J. Org. Chem.* **1976**, *41*, 4089–92. (d) Boutet, G.; Mornet, R.; Gouin, L. *J. Organomet. Chem.* **1977**, *135*, 151–9. (e) Levy, A. B.; Talley, P.; Dunford, J. A. *Tetrahedron Lett.* **1977**, 3545–8. (f) LaLima, N. J.; Levy, A. B. *J. Org. Chem.* **1978**, *43*, 1279–81.

(39) Whitesides, G. M.; Casey, C. P.; Krieger, J. K. *J. Am. Chem. Soc.* **1971**, *93*, 1379–89.

(40) In a personal communication, Professor J. F. Normant has reported the same difficulty with cuprous halides obtained in the United States but not with material obtained from Prolabo in France.

(41) Kauffman, G. B.; Teter, L. A. *Inorg. Synth.* **1963**, *7*, 9–12.

(42) (a) Posner, G. H.; Sterling, J. J. *J. Am. Chem. Soc.* **1973**, *95*, 3076–7 ref 6. (b) Posner, G. H.; Whitten, C. E.; Sterling, J. J. *Ibid.* **1973**, *95*, 7788–800.

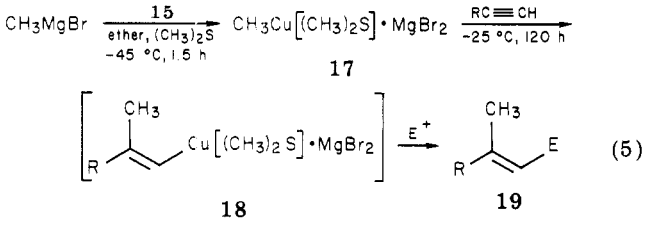
(43) House, H. O.; Chu, C.-Y.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, *40*, 1460–9.

(44) We do not intend to imply any specific structures for the organocopper species such as **16** involved in these studies.

C_6H_{13} is treated with aqueous ammonium chloride, 2-ethyl-1-octene is obtained in 90% yield; only a 2% yield of the corresponding diene **14** ($R^1 = C_2H_5$, $R^2 = n\text{-}C_6H_{13}$) is obtained. After our initial development of this improved procedure for the addition reaction,[1a] essentially the same procedure was employed by Levy and his co-workers.[38e,f] We cannot fully exclude the possibility that the observed improvements are due, at least in part, to stabilization of the intermediates **16** by the coordination of dimethyl sulfide rather than the absence of impurities. A relevant observation, though, is that these clean results are obtained consistently only if the starting sulfide complex **15** is white and its solutions are colorless; if either the solid **15** or its solutions develop a pink color (indicative of Cu^{2+} salts[43]), larger amounts of dienes are obtained. For this reason, we generally store **15** under a nitrogen atmosphere to prevent oxidation of the cuprous species, although all manipulations of this material may be performed routinely in the presence of air without noticeable changes in the appearance of the solid or its solutions.

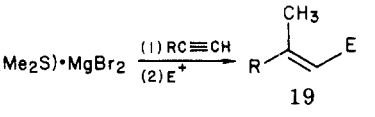
As may be seen by studying the structures of many of the naturally occurring trisubstituted olefins (e.g., **1**, **2**, **4**, **6–8**), most of these natural products bear a methyl group as at least one of the olefinic substituents. Therefore, the addition reaction of alkylcopper complexes with acetylenes would be most generally useful if it could be accomplished with methylcopper. Unfortunately, earlier attempts to effect this reaction with simple, unactivated acetylenes[45] have had only limited success. A factor which is likely to contribute to this difficulty is that methylcopper is a very insoluble, polymeric solid that is less reactive than many other alkylcopper complexes.[46] Normant reported that methylcopper adds to acetylenes only under conditions (+13 °C) that promote rapid thermal decomposition of the resulting alkenylcopper complexes to give 1,3-dienes (**14**, $R^1 = CH_3$). More recently, Vermeer reported the addition of a soluble and much more reactive dimethylcuprate complex to a terminal acetylene, but a very large excess (5 equiv) of the copper reagent is used.[37a]

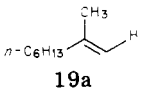
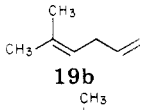
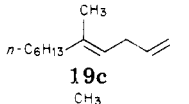
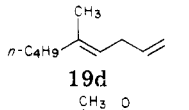
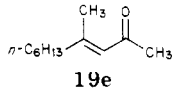
Because of the limitations presented by these earlier findings, we undertook an investigation of more suitable means for performing the desired addition reaction. We found that our approach employing the dimethyl sulfide complex **15** provides a solution to this problem. Reaction of methylmagnesium bromide with **15** generates a methylcopper complex **17**[44] which undergoes addition to terminal acetylenes to afford the corresponding methyl-substituted alkenylcopper complexes **18** (eq 5). The



reaction proceeds very efficiently with *only a stoichiometric amount or a small excess* (10–15%) of the copper reagent. The high efficiency of this reaction is indicated by the 90% yield of olefin (**19a**) obtained upon hydrolysis of the reaction mixture with aqueous ammonium chloride. The major disadvantage of our method is that the addition reaction is rather slow (**17** has poor solubility in the reaction medium); in our preliminary report,[1b] we had indicated a reaction period of 60–70 h, but upon optimizing our reaction conditions, we have found that 120 h is required for the best results.

Table I. Synthesis of Methyl-Substituted Olefins



run	R	E^+ [a]	product	% yield[b]
1	$n\text{-}C_6H_{13}$	NH_4Cl	 **19a**	90
2	CH_3		 **19b**	70[c]
3	$n\text{-}C_6H_{13}$		 **19c**	81
4	$n\text{-}C_4H_9$		 **19d**	84
5	$n\text{-}C_6H_{13}$		 **19e**	65

[a] Electrophile. [b] Unless otherwise indicated, the yields were determined by GLPC with an internal standard after calibration of the instrument with a pure sample of the product. [c] Isolated yield.

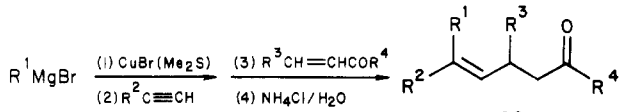
The reactions of **18** with a variety of electrophilic reagents, usually in the presence of hexamethylphosphoric triamide, produce trisubstituted olefins **19** (eq 5). Some typical results are shown in Table I; a few special cases involving reactions with α,β-unsaturated carbonyl compounds and epoxides are discussed in later sections. Careful control of temperature and maintenance of an inert atmosphere throughout the reaction sequence are necessary to avoid formation of substantial amounts of 1,3-dienes (**14**, $R^1 = CH_3$) as side products. If these precautions are taken, only very small amounts (≤3% yields) of the dienes are produced. Although the yields of the final products (**19**) shown here are high, further work has shown that simple alkyl halides as electrophiles provide, at best, only moderate yields of the trisubstituted olefins.

Recently, the addition reactions of other methylmetal species to acetylenes have been reported. Negishi[47] employed zirconium-promoted addition of trimethylaluminum to simple acetylenes, whereas Snider[48] investigated nickel-catalyzed addition of methylmagnesium bromide to silylacetylenes. The latter procedure gives mixtures of geometrically isomeric olefins.

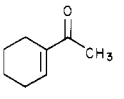
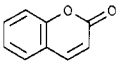
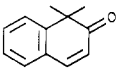
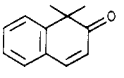
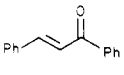
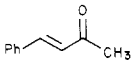
Conjugate Addition Reactions. As discussed earlier, the conjugate or 1,4-addition reactions of alkenylcopper complexes with α,β-unsaturated carbonyl compounds are good sources of functionalized olefins. The use of disubstituted alkenylcopper complexes **13** would provide functionalized trisubstituted olefins, but, prior to our work, the only reported conjugate additions of **13** were those of a highly reactive acetylenic carbonyl compound.[36i] We have found that the alkenylcopper species **16** obtained through use of the dimethyl sulfide–cuprous bromide complex **15** readily undergo conjugate addition to a

(45) The addition of methylcopper complexes occurs with acetylenes bearing various activating groups. For an example, see ref 36i.
(46) Gilman, H.; Jones, R. G.; Woods, L. A. *J. Org. Chem.* **1952**, *17*, 1630–4.
(47) Van Horn, D. E.; Negishi, E. *J. Am. Chem. Soc.* **1978**, *100*, 2252–4.
(48) Snider, B. B.; Karras, M.; Conn, R. S. E. *J. Am. Chem. Soc.* **1978**, *100*, 4624–6.

Table II. Formation of Conjugate Addition Products

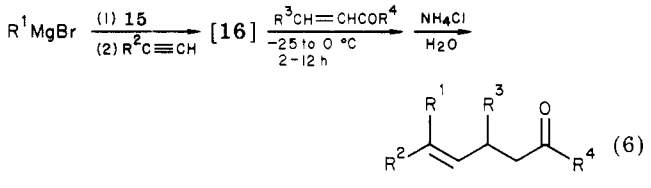


20

run	R^1	R^2	$R^3CH{=}CHCOR^4$	product	% yield[a]
1	C_2H_5	n-C_6H_{13}		**20a**	70
2	n-C_6H_{13}	C_2H_5		**20b**	(68)
3	n-C_4H_9	n-C_6H_{13}		**20c**	(64)
4	CH_3	n-C_6H_{13}		**20d**	(63)
5	n-C_6H_{13}	CH_3		**20e**	73
6	C_2H_5	n-C_6H_{13}		**20f**	69[b]
7	C_2H_5	n-C_6H_{13}		**20g**	(0), (62)[b,c]
8	C_2H_5	n-C_3H_7		**20h**	50
9	n-C_3H_7	C_2H_5		**20i**	50
10	C_2H_5	n-C_6H_{13}		**20j**	(10), (30)[b,d]
11	C_2H_5	n-C_6H_{13}		**20k**	52
12	C_2H_5	n-C_6H_{13}		**20l**	(35), 53[b]
13	CH_3	CH_3		**20m**	(25)[b]
14	C_2H_5	n-C_6H_{13}		**20n**	(31)[b]

[a] The values in parentheses were determined by GLPC with an internal standard after calibration of the instrument with a pure sample of the product. The other values are isolated yields. [b] In this run, the intermediate alkenylcopper complex was allowed to react with 1-lithio-1-pentyne before the α,β-unsaturated carbonyl compound was added. [c] This conjugate addition was performed at 4 °C for 60 h. [d] This conjugate addition was performed at −78 °C for 4 h.

number of α,β-unsaturated carbonyl compounds to give the desired trisubstituted olefins **20** (eq 6). Some typical



(6)

20

results are given in Table II. The reported yields are for the overall route starting with the Grignard reagent and using nearly equimolar quantities of all reactants. Therefore, unlike many reports in which large excesses of organocopper species are used in various types of reactions, the yields reported here are very representative of the efficiency of the overall multistep process. The yields are also quite acceptably high in consideration of the fact that this pathway provides the rather complex products in a convenient, one-flask procedure by using simple, readily available starting materials. In addition to the desired olefins **20** and traces (0–3%) of the dienes **14**, some of the other compounds present in the product mixtures are small amounts of the 2-alkyl olefins ($R^1R^2C{=}CH_2$) and the starting acetylenes ($R^2C{\equiv}CH$). The yield of the desired product from the reaction of cyclopenten-3-one (run 10) is relatively low but is typical of reported conjugate additions of alkenylcopper species to this enone.[42b]

In some cases, mixed cuprates (**21**), as compared to the simpler alkylcopper complexes (RCu), have been reported to be superior reagents for conjugate additions. The mixed cuprates are obtained from the reactions of alkyllithiums with copper(I) acetylides, thiolates, or alkoxides (eq 7).[42b,49]

$$RLi + CuZ \rightarrow [RCuZ]^-Li^+ \quad (7)$$

21

$$Z = C{\equiv}CR', SR', OR'$$

Attempted improvement of the yields of the trisubstituted olefins **20** was therefore made in our work by trying to

(49) Corey, E. J.; Beames, D. J. *J. Am. Chem. Soc.* **1972**, *94*, 7210–1.

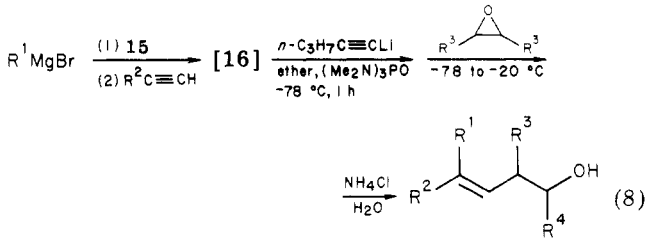
convert the alkenylcopper intermediates **16** into mixed cuprates by reaction with 1-lithio-1-pentyne before the α,β-unsaturated carbonyl compounds were added to the reaction mixtures. However, improvements in yields were observed in only a limited number of cases (Table II, runs 6, 7, 10, 12–14). One substrate which failed to give useful quantities of product under any conditions is ethyl acrylate. In addition to the acetylide, lithium thiophenoxide and lithium *tert*-butoxide were used to generate the corresponding mixed cuprates in a few cases, but no improvements resulted. In performing these studies, we realize that we have attempted to prepare mixed cuprates by addition of ligands to copper in the reverse of the usual fashion; with only a few exceptions,[50] mixed cuprates are normally prepared by allowing the lithio derivative of the transferable organic group (the group that is to undergo the conjugate addition) to react with the cuprous derivative of the second ligand. Therefore, the species that we have generated may be structurally different from the usual mixed cuprates. Furthermore, the initial alkenylcopper complexes **16** and similar species used by earlier workers[51] may actually exist as mixed cuprates of the type $[R^1R^2C{=}CHCuBr]^-M^+$. Related halocuprates have been employed previously in conjugate additions.[52]

The products of the conjugate-addition reactions should prove to be very useful in natural-products synthesis. For example, compound **4** from a crab species (vide supra) contains precisely the same functionality and type of carbon skeleton that is generated in our reaction sequence. Furthermore, Wittig-type olefination or related reactions of the carbonyl groups of the conjugate-addition products (**20**) would lead to several of the compounds (**2–5**, **7–10**) discussed above that contain 1,5-diene moieties. In a later section, we describe a synthesis of the insect pheromone sulcatol which was obtained by a further reaction of one of the conjugate-addition products.

Synthesis of Homoallylic Alcohols. Homoallylic alcohols and their derivatives such as the corresponding halides and sulfonates are very useful compounds for the synthesis of natural products, especially various terpenoids. Among the applications of these homoallylic systems have been syntheses of *Cecropia* juvenile hormone[53] and steroids.[54] Several methods have previously been reported for the preparation of homoallylic alcohols and their derivatives.[55] Among the more recent methods are the use of alkenyllithium reagents,[56] alkenylaluminum compounds,[57] allylmetal species,[30d,58] organoselenium compounds,[59] 2-thiazolines,[60] rearrangement of cyclopropylcarbinols,[61] and other methods.[26b,62] Many of the natural products that are derivable from homoallylic alcohols contain trisubstituted olefinic units. Therefore, especially important are those methods which permit the stereoselective synthesis of homoallylic systems in which the olefinic portions exist as trisubstituted alkenes. Unfortunately, many of the methods above do not permit the synthesis of these types of systems with high stereoselectivity.

Conceivably, the alkenylcopper species **16** obtained from the addition of alkylcopper complexes to acetylenes may be useful in the synthesis of homoallylic alcohols. On the basis of the known reactions of various organocopper complexes with epoxides,[63] the alkylation of **16** with epoxides would produce the desired alcohols containing stereospecifically trisubstituted olefinic units. However, the alkenylcopper complexes obtained from the acetylene addition reaction exhibit low reactivity in alkylation reactions.[56] Indeed, we have found that the reaction of **16** with epoxides proceeds rather sluggishly, as would be expected on the basis of the only moderate activity of epoxides as alkylating agents.

On the basis of work described in the previous section, we have investigated the possibility of increasing the reactivity of the alkenylcopper complexes **16** toward epoxides by adding a lithium acetylide to the reaction mixtures for the purpose of perhaps generating more reactive mixed cuprates. This approach, as outlined in eq 8, has been quite successful.[64] Earlier, Normant had reported a related route which provided only disubstituted homoallylic alcohols.[36j]



(8)

22

The results summarized in Table III demonstrate that this one-flask reaction sequence is a very efficient method for the synthesis of the desired homoallylic alcohols **22**. High regioselectivity is observed in the case of monoalkylated epoxides (runs 5 and 6); the only products that are detected are those resulting from reaction at the less substituted position. Styrene oxide (run 7), as expected, gives a mixture of two products. Cyclohexene oxide (run 8), an epoxide of relatively low reactivity, gives a low yield of product under our conditions.

This new method for the synthesis of homoallylic alcohols should conceivably be applicable to the synthesis of many naturally occurring compounds. For example, the product of run 2 contains a key portion of the carbon skeleton of compound **5** from the codling moth, and indeed we have converted this product (run 2) into **5** in three simple steps.[65] Also, the products of runs 3 and 4 contain

(50) For some exceptions see: (a) Yamamoto, Y.; Yatagai, H.; Sonoda, A.; Murahashi, S.-I. *J. Chem. Soc., Chem. Commun.* **1976**, 452–3. (b) Bergbreiter, D. E.; Whitesides, G. M. *J. Org. Chem.* **1975**, *40*, 779–82. (c) Nilsson, M.; Rahman, M. T.; Ullenius, C. *Acta Chem. Scand., Ser. B* **1977**, *31*, 514–8. (d) Gustafsson, B. *Tetrahedron* **1978**, *34*, 3023–6.

(51) Corey, E. J.; Kim, C. U.; Chen, R. H. K.; Takeda, M. *J. Am. Chem. Soc.* **1972**, *94*, 4395–6.

(52) Luong-Thi, N.-T.; Riviere, H. *Tetrahedron Lett.* **1970**, 1583–6. See also ref 33a, p 66, and ref 33b, pp 11–12.

(53) (a)Johnson, W. S.; Li, T-T.; Faulkner, D. J.; Campbell, S. F. *J. Am. Chem. Soc.* **1968**, *90*, 6225–6 (b) Anderson, R. J.; Corbin, V. L.; Cotterrell, G.; Cox, C. R.; Henrick, C. A.; Schaub, F.; Siddall, J. B. *Ibid.* **1975**, *97*, 1197–1204.

(54) Johnson, W. S.; Semmelhack, M. F.; Sultanbawa, M. U. S.; Dolak, L. A. *Ibid.* **1968**, *90*, 2994–6.

(55) Partial discussions of homoallylic systems are included in ref 11.

(56) Cahiez, G.; Bernard, D.; Normant, J. F. *Synthesis* **1976**, 245–8.

(57) (a) Negishi, E.; Baba, S.; King, A. O. *J. Chem. Soc., Chem. Commun.* **1976**, 17–8. (b) Malpass, D. B.; Watson, S. C.; Yeargin, G. S. *J. Org. Chem.* **1977**, *42*, 2712–5.

(58) (a) Hegedus, L. S.; Wagner, S. D.; Waterman, E. L.; Siirala-Hansen, K. *J. Org. Chem.* **1975**, *40*, 593–8. (b) Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 3179–81. (c) Hosomi, A.; Shirahata, A.; Sakurai, H. *Tetrahedron Lett.* **1978**, 3043–6.

(59) Sevrin, M.; Krief, A. *Tetrahedron Lett.* **1978**, 187–90.

(60) Meyers, A. I.; Durandetta, J. L.; Munavu, R. *J. Org. Chem.* **1975**, *40*, 2025–9.

(61) McCormick, J. P.; Barton, D. L. *J. Chem. Soc., Chem. Commun.* **1975**, 303–4.

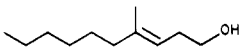
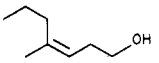
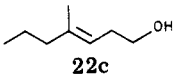
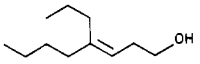
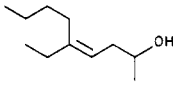
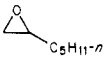
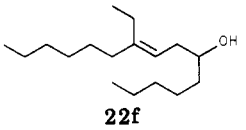
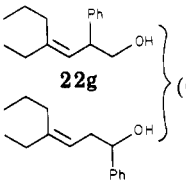
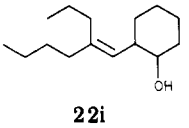
(62) Lipton, M. F.; Shapiro, R. H. *J. Org. Chem.* **1978**, *43*, 1409–13.

(63) Johnson, C. R.; Herr, R. W.; Wieland, D. M. *J. Org. Chem.* **1973**, *38*, 4263–8.

(64) The addition of LiBr in place of the acetylide did not effect a similar increase in reactivity of the alkenylcopper species.

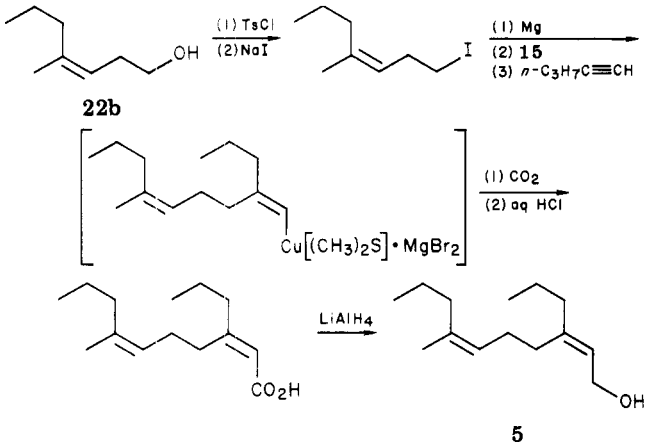
(65) Marfat, A.; McGuirk, P. R.; Helquist, P. *J. Org. Chem.* **1979**, *44*, 1345–7.

Table III. Synthesis of Homoallylic Alcohols (22)

run	R^1	R^2	epoxide	product(s)	% yield[a]
1	CH_3[b]	n-C_6H_{13}		 **22a**	75[c]
2	n-C_3H_7	CH_3		 **22b**	95, 89[c]
3	CH_3[b]	n-C_3H_7		 **22c**	78[c]
4	n-C_3H_7	n-C_4H_9		 **22d**	95
5	n-C_4H_9	C_2H_5		 **22e**	82
6	C_2H_5	n-C_6H_{13}		 **22f**	94
7	n-C_3H_7	C_2H_5		 **22g** (63:37) **22h**	75
8	n-C_3H_7	n-C_4H_9		 **22i**	26

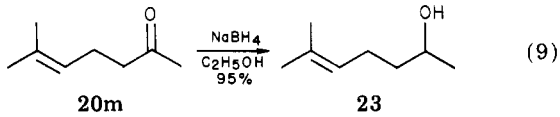
[a] Unless otherwise noted, the yields were determined by GLPC with an internal standard. [b] The addition of the methylcopper complex required 120 h at -23 °C, whereas the other alkylcopper complexes required only 2 h. [c] Isolated yield.

Scheme I

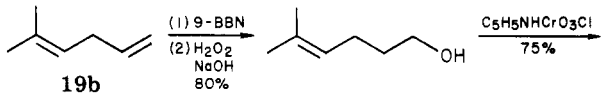


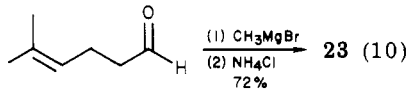
a type of methyl-substituted olefinic unit commonly found in terpenoids.

Applications. In order to illustrate the applicability of our methodology to the synthesis of natural products, we have performed two simple, initial syntheses. In the first of these, sulcatol (**23**), an aggregation pheromone of an ambrosia beetle (*Gnathotricus sulcatus*),[66] was obtained through the use of two routes. Simple reduction of 6-methyl-5-hepten-2-one (**20m**), the product of one of the earlier conjugate additions (Table II, run 13), gives sulcatol directly (eq 9). Interesting, **20m**, which is commercially available, is itself an alarm pheromone of an ant (*Iridomyrmex detectus*).[67] An alternative synthesis of sulcatol employs 5-methyl-1,4-hexadiene (**19b**), an earlier alkylation product (Table I, run 2), as a key intermediate (eq 10).



(9)





(10)

We have also performed a very short synthesis of the codling moth constituent **5**[5] through the use of (*Z*)-4-methyl-3-hepten-1-ol (**22b**), one of the homoallylic alcohols prepared earlier (Table III, run 2). Because this synthesis has been described in detail elsewhere,[65] we present here only the basic outline (Scheme I) of our route. Including the preparation of **22b** this route provides **5** in an overall yield of 37% in only four steps from 1-propyne. To be

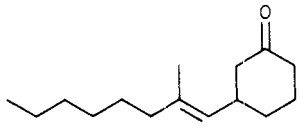
(66) (a) Byrne, K. J.; Swigar, A. A.; Silverstein, R. M.; Borden, J. H.; Stokkink, E. *J. Insect Physiol.* **1974**, *20*, 1895-1900. (b) Mori, K. *Tetrahedron* **1975**, *31*, 3011-2. (c) Borden, J. H.; Chong, L.; McLean, J. A.; Slessor, K. N.; Mori, K. *Science* **1976**, *192*, 894-6.

(67) Cavill, G. W. K.; Ford, D. L. *Chem. Ind. (London)* **1953**, 351.

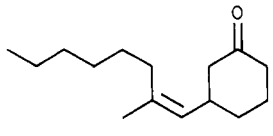
emphasized is that this synthesis illustrates the iterative nature of our approach to trisubstituted olefins which permits the construction of the very commonly occurring 1,5-diene system in which both double bonds are trisubstituted. Normant[36h] and Vermeer[37g] have described alternative approaches which lead to products in which the secondly introduced olefinic double bond has stereochemistry opposite to that of our products.

Stereochemical Studies. Because of the importance of preparing olefins of carefully defined configuration, the stereochemistry of our routes was investigated. The assignment of olefin stereochemistry that has been shown in the previous sections is based upon two precedents: (1) Normant had shown that alkylcopper complexes undergo cis addition to acetylenes,[35,36b,h] and (2) others have shown that alkenylcopper complexes retain their olefinic configurations during various reactions, including conjugate addition.[68] However, we wished to provide stronger evidence for the stereochemistry of our pathways.

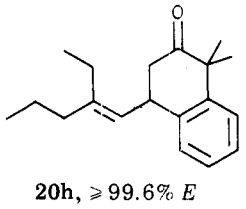
First of all, we chose to investigate the stereospecificity of the reactions. A point to be emphasized about our methods is that either member of a pair of *E* and *Z* isomers may be prepared simply by the appropriate choice of starting Grignard reagent and acetylene. For our stereochemical studies, we therefore prepared and carefully investigated two pairs of *E* and *Z* isomers (**20d** and **20e**, **20h** and **20i**; see Table II) through use of the conjugate-addition reaction. When mixed together, **20d** is cleanly separable from **20e**, and **20h** is cleanly separable from **20i** by GLPC. Analysis (GLPC) of the crude reaction mixtures of each of these four compounds reveals no detectable amount of the opposite isomer in each case. The minimum detectable quantity, or the GLPC baseline noise level, was 0.04% for the first pair and 0.4% for the second pair of compounds. Therefore, we are able to list the following *lower* limits of isomeric purity for the four compounds:



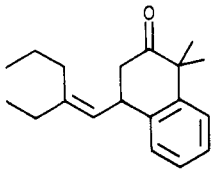
20d, ⩾99.96% *E*



20e, ⩾99.96% *Z*



20h, ⩾99.6% *E*

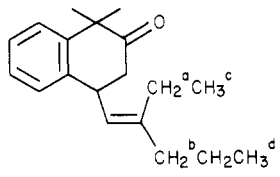


20i, ⩾99.6% *Z*

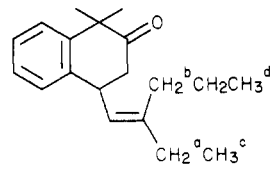
Of these results, the value for **20d** is especially important because the preparation of this compound involved the crucial methylcopper addition reaction. All of these results indicate that our approach to trisubstituted olefins possesses unusually high stereoselectivity.[69]

To determine the actual configuration of some of our olefinic products rather than simply relying upon the earlier precedents, we first examined the ^{1}H NMR spectra of the four methyl-substituted compounds **20d**, **20e**, **22b**, and **22c** (Tables II and III). The vinyl methyl protons of these compounds appear at δ 1.59, 1.66, 1.67, and 1.60, respectively. These values are in excellent agreement with earlier observations that vinyl methyl groups of *E*-trisubstituted olefins resonate at δ 1.57–1.61 in the ^{1}H NMR spectrum whereas those of *Z* olefins resonate at δ 1.67–1.71.[70] Also consistent with the assigned structures are the positions of resonances of the vinyl methyl groups in the ^{13}C NMR spectra; for **22b** and **22c**, these signals appear at δ 23.49 and 16.05, respectively, as compared to literature values of δ 23–24 for *Z* olefins and δ 15–16 for *E* olefins.[71,72] Furthermore, the heteronuclear coupling constant between the vinyl methyl group and the vinyl proton in **22b** is $J_{C\text{-}H}^{cis}$ = 6.8 Hz, and the corresponding value for **22c** is $J_{C\text{-}H}^{trans}$ = 8.3 Hz; the literature values for related compounds are $J_{C\text{-}H}^{cis} \simeq 7$ Hz and $J_{C\text{-}H}^{trans} \simeq 8$ Hz.[73]

Table IV. Lanthanide NMR Shift Reagent Studies of **20h**, **20i**, **22b**, and **22c**



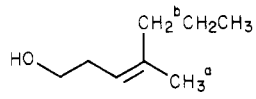
20h



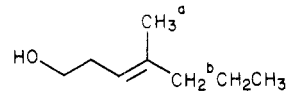
20i

mol of Eu(fod)$_3$/mol of **20h**, $\delta(H^a)$, $\delta(H^b)$: 0.00, 2.16, 2.09; 0.20, 2.31, 2.15; 0.33, 2,42, 2.22; 0.47, 2.49, 2.25; 0.60, 2.58, 2.38; 0.73, 2.63, 2.33; 0.86, 2.66, 2.34

mol of Eu(fod)$_3$/mol of **20i**, $\delta(H^a)$, $\delta(H^b)$: 0.00, 2.00, 2.13; 0.26, 2.19, 2.29; 0.32, 2.20, 2.33; 0.38, 2.25, 2.43; 0.48, 2.26, 2.45; 0.64, 2.30, 2.50; 0.74, 2.32, 2.56; 0.83, 2.33, 2.60; 0.96, 2.33, 2.61



22b



22c

mol of Eu(fod)$_3$/mol of **22b**, $\delta(H^a)$, $\delta(H^b)$: 0.00, 1.70, 2.04; 0.08, 1.85, 2.30; 0.17, 2.01, 2.56; 0.25, 2.19, 2.86; 0.42, 2.50, 3.43; 0.58, 2.80, 3.95; 0.75, 2.99, 4.33; 0.91, 3.24, 4.71; 1.08, 3.32, 4.87

mol of Eu(fod)$_3$/mol of **22c**, $\delta(H^a)$, $\delta(H^b)$: 0.00, 1.62, 2.00; 0.08, 1.88, 2.16; 0.21, 2.41, 2.51; 0.35, 2.92, 2.84; 0.49, 3.39, 3.15; 0.63, 3.75, 3.39; 0.78, 4.04, 3.58; 0.92, 4.20, 3.70

In order to obtain more convincing stereochemical evidence, we decided to investigate compounds **20h** and **20i** in more detail. We believed that this isomeric pair would serve as suitable substrates for lanthanide NMR shift investigations. Related studies have been reported by others.[25j,36h,68a] Study of molecular models indicates that the methylene groups CH_2^a and CH_2^b (Table IV) in several conformations of these compounds are located at significantly different distances from the carbonyl groups, the sites of coordination of a shift reagent. Also, the methylene groups are potentially distinguishable by ^{1}H NMR because the protons H^a are expected to appear principally as quartets and H^b as triplets. Furthermore, in decoupling experiments, if the upfield regions of the spectra in which the resonances of H^c and H^d (Table IV) appear were irradiated, the signals for H^a would collapse to singlets, but the signals for H^b would remain essentially unchanged. Therefore, a lanthanide shift experiment would consist of observing the relative shifts of H^a and H^b as the shift

(68) (a) Casey, C. P.; Boggs, R. A. *Tetrahedron Lett.* **1971**, 2455–8. (b) Naf, F.; Degan, P. *Helv. Chim. Acta* **1971**, *54*, 1939–49. (c) Naf, F.; Degen, P.; Ohloff, G. *Ibid.* **1972**, *55*, 82–5.

(69) The isomeric pair of **20a** and **20b** was analyzed earlier by using less sensitive GLPC instrumentation. The minimum purities were 99.5% and 99.0%, respectively.

(70) (a) Bowlus, S. B.; Katzenellenbogen, J. A. *J. Org. Chem.* **1973**, *38*, 2733–4. (b) Cooke, M. P. *Tetrahedron Lett.* **1973**, 1281–4.

(71) Couperus, P. A.; Clague, A. D. H.; van Dongen, J. P. C. M. *Org. Magn. Reson.* **1976**, *8*, 426–31.

(72) For **20d** and **20e**, the ^{13}C NMR signals were not assigned unambiguously because of the much greater complexity of these spectra.

(73) (a) von Philipsborn, W. *Pure Appl. Chem.* **1974**, *40*, 159–80. (b) Vogeli, U.; von Philipsborn, W. *Org. Magn. Reson.* **1975**, *7*, 617–27.

reagent is added to samples of **20h** and **20i**. For compound **20h**, the signal for H^a would be shifted to a larger extent than for H^b, and the reverse would be true for **20i**. Further reasons for the choice of **20h** and **20i** are that their ^1H NMR spectra have somewhat simplified aliphatic regions, in contrast with adducts of other α,β-unsaturated compounds that we have studied, and the two methyl substituents adjacent to the carbonyl group may possibly direct the coordination of the lanthanide reagent to a position which would maximize the difference in shifts of H^a and H^b.

The magnitude of shifts of NMR peak positions induced by lanthanide reagents is given by the simplified expression shown in eq 11

$$\Delta(\delta) = K\left\langle \frac{(3\cos^2\theta - 1)}{r^3} \right\rangle_{\text{time}} \quad (11)$$

in which θ is the angle between the principal magnetic axis of the lanthanide–substrate complex and the vector of length r joining the lanthanide ion and the nuclei under consideration (H^a and H^b in our case).[74] By inspection of molecular models of lanthanide complexes of **20h** and **20i**, θ may be estimated to possess a range of values ($\leq 37°$) which will ensure that only downfield shifts are observed for H^a and H^b. Also, through use of eq 11, the differences in downfield shifts of H^a and H^b should lie within the range of 0.21–0.53 ppm, depending mainly upon conformations resulting from rotation about the single bonds joining the vinyl groups to the alicyclic rings of **20h** and **20i**. These estimates of θ and $\Delta(\delta)$ are made with the simplifying assumption that the principle magnetic axis is collinear with the Ln–O bond of the complex and, in turn, collinear with the C=O bond.[74] Deflection of the lanthanide to the side of the carbonyl group away from the *gem*-dimethyl groups would not alter the qualitative results of the work described below.

Samples of **20h** and **20i** were dissolved in dry $CHCl_3$, and spectra were recorded after addition of incremental amounts of $Eu(fod)_3$.[75] The triplet and quartet signals of H^a and H^b progressively became further separated from each other. The spin-decoupling experiments described above were performed to identify these peaks unambiguously. Plots of the chemical shifts of H^a and H^b vs. mol of $Eu(fod)_3$/mol of **20h** and **20i** are very nearly linear. According to a linear least-squares analysis, the H^a plot for **20h** has a slope of 0.59, and the H^b plot has a slope of 0.30. The values for H^a and H^b in **20i** are 0.26 and 0.51, respectively. The observed differences in shifts of H^a and H^b are 0.38 and 0.31 ppm (extrapolated to mol of $Eu(fod)_3$/mol of substrate = 1.0) for **20h** and **20i**, respectively. These values agree with those predicted on the basis of eq 11. The greater shifts of H^a in **20h** and H^b in **20i** are therefore consistent with the given olefin configurations of these compounds.

A similar lanthanide shift reagent study was also performed on the pair of isomers **22b** and **22c**, on which the detailed ^1H and ^{13}C NMR studies were done as described above. These lanthanide shift studies, as summarized in Table IV, are again wholly consistent with the assigned structures of these compounds. For this pair of compounds, the assignment of the relevant NMR signals is especially straightforward; the protons H^a of the vinyl methyl groups appear essentially as singlets whereas the protons H^b of the appropriate methylene groups appear as triplets.

Finally, our synthesis of the codling moth constituent **5** as discussed above has provided chemical evidence for the stereochemistry of our pathways to trisubstituted olefins. Our synthetic material is identical with an authentic sample and is easily separable by GLPC from samples of isomers having the other olefinic configurations.[65] Therefore, our route to **5** must have proceeded to generate both olefinic units with the stereochemistry assigned for these pathways.

Overall, there now is no doubt that the addition of alkylcopper complexes to simple terminal acetylenes followed by reactions of the alkenylcopper intermediates with various organic electrophiles occurs with syn addition of the two organic groups to the acetylenes and with a very high degree of stereoselectivity.

Conclusion

The studies described in this paper have resulted in the development of highly stereoselective and direct routes to various types of trisubstituted olefins, including those bearing methyl groups as olefinic substituents. Especially noteworthy is that many of the products bear functionalities such as carbonyl and hydroxy groups that are useful in further elaboration of complex structures. Also, the methods are amenable to the construction of carbon frameworks containing repetitive trisubstituted olefin units. These methods have high potential for applications in natural products synthesis, especially in the area of olefinic terpenoids.

Experimental Section

General Procedures. All reactions of air- and water-sensitive materials were performed in flame-dried glassware under nitrogen by using double-manifold techniques.[75] Air-sensitive solutions or liquids were transferred with hypodermic syringes or double-ended needles. Tetrahydrofuran (THF) and ether were distilled from dark blue or dark purple solutions of sodium benzophenone radical anion or dianion under nitrogen. Hexamethylphosphoric triamide (HMPT) was distilled under vacuum from calcium hydride. The Grignard reagents either were obtained commercially from Alfa or were prepared directly from alkyl halides.[76] *n*-Butyllithium was obtained as a hexane solution from Alfa. All Grignard and organolithium reagents were stored at 0 °C under nitrogen and were titrated prior to use by the method of Watson and Eastham[77] or Kofron and Baclawski.[78] Lithium thiophenoxide was prepared immediately before use according to the procedure of Posner.[42b] Cuprous iodide either was continuously extracted[42] with refluxing THF in a Soxhlet apparatus for 12 h under nitrogen followed by drying in vacuo at 25 °C or was precipitated[41] from an aqueous potassium iodide solution. The dimethyl sulfide complex of cuprous bromide (**15**) was prepared by the method of House[43] and remained as a white crystalline solid indefinitely when stored at 25 °C under nitrogen, although it was handled routinely in the air. The commercially obtained acetylenes, dimethyl sulfide, α,β-unsaturated ketones, and various alkylating agents were generally distilled or recrystallized prior to use and stored under nitrogen. All other materials were used without purification but were usually checked for purity by ^1H NMR, IR, and GLPC.

Constant temperatures were maintained by using dry ice–acetone (−78 °C), dry ice–acetone–carbon tetrachloride (−45 °C), or dry ice–carbon tetrachloride (−23 °C) baths or through use of a bath equipped with a Neslab CryoCool Model CC-100F low-temperature unit, a Cole-Parmer Versa-Therm Model 2158

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(77) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165–8.

(78) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879–80.

temperature controller, and a 500-W immersible heating coil. The ^{1}H NMR spectra were recorded at 60 MHz with a Varian EM-360 spectrometer or at 80 MHz with a Varian HFT-80 spectrometer. The ^{13}C NMR spectra were recorded at 20 MHz with a Varian CFT-20 spectrometer. The NMR spectra were obtained from $CDCl_3$ solutions containing tetramethylsilane (Me_4Si) as the internal standard. The chemical shifts are expressed in parts per million (δ) downfield from Me_4Si, and the ^{1}H NMR peak areas are expressed as the number of hydrogen atoms (H). Mass spectra were recorded with Hewlett-Packard Model 5982A and AEI Model MS-30 mass spectrometers by using electron impact ionization at 70 eV. The IR spectra were obtained with a Pye-Unicam Model SP-1000 or a Perkin-Elmer Model 727 spectrophotometer as neat liquid films or solutions in chloroform and were calibrated with a polystyrene standard. Elemental analyses were performed by Galbraith Laboratories, Inc., or by Schwarzkopf Microanalytical Laboratory. In general, though, the products were oils for which accurate analyses were difficult to obtain. Therefore, the analytical results are given only when they agree with the calculated values within ±0.3%. In all other cases, the homogeneity of the compounds was demonstrated by careful GLPC and TLC, and molecular formulas were determined by high-resolution mass spectroscopy. Preparative GLPC was performed with a Varian Aerograph Model 900 gas chromatograph using a 6 ft × $^1/_2$ in. 5% SE-30 column. Analytical GLPC was performed with a Hewlett-Packard Model 5711 gas chromatograph equipped with a flame ionization detector, a linear temperature programmer, and a Hewlett-Packard Model 3380A electronic integrator, and the following columns were used: A, 6 ft × $^1/_8$ in. 5% OV-1; B, 12 ft × $^1/_8$ in. 5% OV-1; C, 12 ft × $^1/_8$ in. 10% Carbowax 20M; D, 6 ft × $^1/_8$ in. 10% DEGS; E, 12 ft × $^1/_8$ in. 5% SE-30; F, 6 ft × $^1/_8$ in. 5% OV-17. For separations by high-performance liquid chromatography, a Waters dual-pump chromatograph equipped with a Model 660 linear solvent programmer and a 1 ft × $^1/_4$ in. μ-Porasil column was employed. Crude products were generally prepurified by bulb-to-bulb distillation at reduced pressure before use of any of the chromatographic purification techniques.

General Procedure for Addition of Alkylcopper Complexes to Terminal Acetylenes. 2-Ethyl-1-octene. A solution of the dimethyl sulfide complex of cuprous bromide (**15**; 0.82 g, 4.0 mmol), ether (5 mL), and dimethyl sulfide (4 mL) under nitrogen was cooled to −45 °C at which temperature a white solid formed, and a 3.04 M solution of ethylmagnesium bromide (1.32 mL, 4.0 mmol) was added dropwise over a period of 2 min. After the resulting suspension of yellow solid was stirred at −45 °C for 2 h, 1-octyne (0.52 mL, 3.5 mmol) was added over a 1-min period, and the mixture was stirred at −25 °C for 2 h. The mixture was then quenched with a saturated aqueous ammonium chloride solution (5.0 mL) adjusted to pH 8 with ammonia. After the mixture was stirred at 25 °C for 1.5 h in the air, it was partitioned between ether and water. The ether layer was washed with additional aqueous ammonium chloride, water, and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and concentrated in vacuo to give 0.442 g (90%) of a very light yellow liquid. The crude product (>95% pure by GLPC) was further purified by preparative GLPC to give 100% pure final product according to analytical GLPC (column A, 110–240 °C at 16 °C/min): IR (neat) 2900, 1642, 1460, 1375, 910, 890, 740 cm^{-1}; ^{1}H NMR 4.6 (s, 2 H), 1.7–2.3 (m, 4 H), 0.6–1.6 (m, 14 H); MS m/e 140.1630 (M^+; calcd for $C_{10}H_{20}$, 140.1564). After combination of the products from several experiments, the final product was distilled to yield 2-ethyl-1-octene as a clear, colorless liquid: bp 167–168 °C (760 torr); n^{25}_D 1.4232 [lit.[79] bp 167.0–167.6 °C (760 torr); n^{25}_D 1.4231].

Procedure for Addition of a Methylcopper Complex to Terminal Acetylenes. 2-Methyl-1-octene (19a). A mixture of **15** (0.82 g, 4.0 mmol), ether (5 mL), and dimethyl sulfide (4 mL) under nitrogen was cooled to −45 °C, and 2.9 M solution of methylmagnesium bromide (1.38 mL, 4.0 mmol) was added dropwise over a 2-min period. After the resulting suspension of yellow solid was stirred at −45 °C for 2 h, 1-octyne (0.52 mL, 3.5 mmol) was added over a 1-min period, and the mixture was stirred at −25 °C for 120 h. The dark green reaction mixture was quenched with 2 mL of saturated aqueous ammonium chloride (buffered at pH 8 with ammonia). A yield of 0.41 g (91%) of **19a** was determined by GLPC analysis (column A, 80 °C) with *n*-decane as an internal standard. A pure sample of **19a** was obtained by preparative GLPC (180 °C). The purity of the isolated product was shown to be 100% by GLPC (column B, 80–240 °C at 15 °C/min). The IR and ^{1}H NMR spectra of the product were identical with published spectra,[80] and the product exhibited a GLPC retention time identical with that of a commercial sample (Chemical Samples Co.).

5-Methyl-1,4-hexadiene (19b). A mixture of **15** (6.15 g, 30 mmol), ether (35 mL), and dimethyl sulfide (30 mL) under nitrogen was cooled to −45 °C, and a 2.95 M solution of methylmagnesium bromide (10.35 mL, 30 mmol) was added dropwise. After the resulting suspension of yellow solid was stirred at −45 °C for 2 h, propyne (2.0 mL, 35 mmol) which had been condensed at −50 °C under nitrogen was added with a dry ice cooled syringe over a 1-min period. The reaction mixture was stirred at −23 °C for 120 h. After the resulting dark green solution was cooled to −78 °C, HMPT (10.4 mL, 60 mmol) and allyl bromide (3.0 mL, 34 mmol) were added separately. The mixture was then stirred at −30 °C for 12 h, warmed to 0 °C, quenched with a saturated aqueous ammonium chloride solution (adjusted to pH 8 with ammonia), and partitioned between additional ether and water. The ether layer was washed with additional aqueous ammonium chloride, water, and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and partially concentrated in vacuo. The crude reaction product was distilled to give 2.0 g (70%) of 100% pure (GLPC, column E, 80–240 °C at 15 °C/min) **19b**: bp 88–89 °C (760 torr); ^{1}H NMR 5.50–6.15 (m, 1 H), 4.75–5.40 (m, 3 H), 2.75 (t, J = 6.5 Hz, 2 H), 1.75 (s, 3 H), 1.67 (s, 3 H); IR (neat) 3080, 2950, 1668, 1638, 994, 842 cm^{-1}; MS m/e 96.0928 (M^+; calcd for C_7H_{12}, 96.0938).

(4*E*)-5-Methyl-1,4-undecadiene (19c). The same procedure as for **19a** was followed except that after the addition reaction was complete, the resulting dark green solution was cooled to −78 °C, and HMPT (1.4 mL, 8.0 mmol) and allyl bromide (0.40 mL, 4.6 mmol) were added separately. The mixture was then stirred at −30 °C for 12 h, warmed to 0 °C, quenched with a saturated aqueous ammonium chloride solution (adjusted to pH 8 with ammonia), and partitioned between additional ether and water. The product was isolated in crude form from the ether solution, and analysis by GLPC (column E, 110–240 °C at 16 °C/min) with *n*-pentadecane as the internal standard indicated the presence of 0.47 g (81%) of **19c**. Bulb-to-bulb distillation and preparative GLPC (150 °C) provided a 100% pure sample (GLPC, column E, 110–240 °C at 15 °C/min) of **19c**: ^{1}H NMR 5.48–6.05 (m, 1 H), 4.87–5.30 (m, 3 H), 2.74 (t, J = 6.5 Hz, 2 H), 0.65–2.12 (several overlapping multiplets and a sharp singlet at 1.59, C=CCH$_3$, total area 16 H); IR (neat film) 3076, 2910, 1666, 1638, 992, 846 cm^{-1}; MS m/e 166.1750 (M^+; calcd for $C_{12}H_{22}$, 166.1722).

(4*E*)-5-Methyl-1,4-nonadiene (19d). Through the same procedure as above but with 1-hexyne (0.45 mL, 4.0 mmol) in place of 1-octyne, 0.41 g (84%) of **19d** was obtained according to GLPC (column A, 110–240 °C at 16 °C/min) with *n*-dodecane as an internal standard. The spectral data of a sample purified by preparative GLPC were as follows: ^{1}H NMR 5.50–6.06 (m, 1 H), 4.75–5.31 (m, 3 H), 2.74 (t, J = 6.5 Hz, 2 H), 0.71–2.15 (several overlapping multiplets and a sharp singlet at 1.60, total area 12 H); IR (neat) 3080, 2930, 1666, 1638, 994, 912, 842 cm^{-1}; MS m/e 138.1433 (M^+; calcd for $C_{10}H_{18}$, 138.1404).

(*E*)-4-Methyl-3-decen-2-one (19e). The standard procedure was employed with 1-octyne and with acetyl chloride (0.57 mL, 8.0 mmol) in place of allyl bromide. The yield of **19e** was 0.38 g (65%) according to GLPC (column A, 110–220 °C at 16 °C/min) with *n*-pentadecane as the internal standard. For GLPC calibration, a 100% pure sample was obtained by preparative GLPC (150 °C): ^{1}H NMR 6.06 (s, 1 H), 2.16 (s, 3 H), 2.12 (s, 3 H), 0.89–2.3 (several overlapping multiplets, 13 H); IR (neat) 2930, 1692, 1628 cm^{-1}; MS m/e 168.1543 (M^+; calcd for $C_{11}H_{19}O$, 168.1431).

Procedure for Conjugate Additions. 3-[(*E*)-2-Ethyl-1-octenyl]cyclohexanone (20a). Into a 25-mL flask was placed

(79) Perry, E.; Ory, H. A. *J. Org. Chem.* **1960**, *25*, 1685–6.

(80) (a) "Sadtler IR Spectra"; Sadtler Research Laboratories: Philadelphia, PA, 1970; no. 37072. (b) "Sadtler NMR Spectra"; Sadtler Research Laboratories: Philadelphia, PA, 1969; no. 7730.

15 (0.820 g, 4.00 mmol), and the flask was placed under nitrogen. Dimethyl sulfide (4.0 mL) and ether (5.0 mL) were added separately, and the resulting solution was cooled to −45 °C, at which temperature a white solid formed. To the mixture was added a 3.12 M solution of ethylmagnesium bromide in ether (1.32 mL, 4.0 mmol) over a period of 3 min. After 1.5 h, 1-octyne (0.52 mL, 3.5 mmol) was added to the orange-yellow mixture over a 1-min period. The mixture was allowed to warm to −23 °C over a 30-min period and was stirred at −23 °C for 2.25 h. To the resulting dark green solution, contained in a flask which had some brown solid on its walls, was added 2-cyclohexen-1-one (0.39 mL, 4.0 mmol) over a period of 2 min. The mixture was then stirred at −23 °C for 2 h and at 0 °C for 12 h. To the green-brown solution containing some finely divided dark solid was added saturated aqueous ammonium chloride (5 mL) adjusted to pH 8 with aqueous ammonia. After the mixture was stirred at 25 °C for 1.5 h in the air, it was partitioned between ether and water. The ether layer was washed with additional aqueous ammonium chloride, 1% aqueous sulfuric acid, water, and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and concentrated in vacuo to give 0.9655 g of yellow oil. Isolation by high-pressure LC with methylene chloride as the solvent afforded 0.59 g (70%) of **20a** as a clear, colorless oil: IR (neat) 2950, 1715, 865 cm^{-1}; ^1H NMR 4.95 (d, J = 9 Hz, 1 H), 0.7–2.6 (several overlapping multiplets, 27 H); MS m/e 236.2140 (M^+; calcd for $C_{16}H_{28}O$, 236.2138; ^{13}C NMR 181.26, 141.58, 127.78 48.26, 41.25, 37.97, 36.32, 32.36, 31.82, 29.04, 28.11, 25.43, 23.32, 22.69, 14.13, 13.61.

3-[(*Z*)-2-Ethyl-1-octenyl]cyclohexanone (20b). The same procedure was followed as for **20a** except for the choice of Grignard reagent and acetylene. A 1.92 M solution (2.08 mL, 4.00 mmol) of n-hexylmagnesium bromide in ether was added to the suspension of **15**. 1-Butyne was condensed at −78 °C in a separate flask under nitrogen, and a portion (0.7 mL, 9 mmol) was added with a dry ice cooled syringe over a period of 1 min to the reaction mixture at −78 °C. The mixture was warmed to −23 °C, and the remainder of the experiment was done as previously. Evaporation of the crude reaction mixture in vacuo yielded 0.9655 g of light yellow oil. The actual yield of **20b** was determined to be 0.64 g (68%) by GLPC (column B, 110–240 °C at 16 °C/min) with eicosane as an internal standard. A pure sample was obtained by preparative GLPC (240 °C): IR (neat) 2960, 1720, 1460, 1320, 1265, 1125, 1050, 865 cm^{-1}; ^1H NMR 5.10 (d, J = 9 Hz, 1 H), 0.3–2.51 (m, 27 H); ^{13}C NMR 181.58, 141.79, 126.29, 48.61, 41.29, 37.98, 32.40, 31.84, 30.60, 29.50, 28.81, 25.39, 22.66, 14.02, 12.91, 3.71; MS m/e 236.2140 (M^+; calcd for $C_{16}H_{28}O$, 236.2138).

3-[(*E*)-2-*n*-Butyl-1-octenyl]cyclohexanone (20c). The procedure was identical with the synthesis of compound **20a** except for the use of a 1.02 M solution (2.42 mL, 4.0 mmol) of n-butylmagnesium bromide in ether. After the usual workup 0.9100 g of crude yellow oil was obtained. The yield was determined to be 0.5873 g (64%) by GLPC (column B, 110–240 °C at 160 °C/min) with n-hexadecane as an internal standard. For GLPC calibration, a 100% pure sample was obtained by preparative GLPC (240 °C): IR (neat) 2920, 1720, 1460, 1315, 1225, 805 cm^{-1}; ^1H NMR 5.00 (d, J = 9.0 Hz, 1 H), 2.27–0.88 (m, 31 H); MS m/e 246.2457 (M^+; calcd for $C_{18}H_{32}O$, 246.2445).

3-[(*E*)-2-Methyl-1-octenyl]cyclohexanone (20d). The first part of the experimental procedure was identical with that for the synthesis of **19c**. After the alkenylcopper intermediate was formed, 2-cyclohexen-1-one (0.39 mL, 4.0 mmol) was added over a period of 2 min. Then, the remainder of the usual procedure for conjugate addition was followed as outlined in detail for compound **20a**. A yield of 0.4908 g (63%) of **20d** was determined by GLPC (column D, 100–220 °C at 16 °C/min) with biphenyl as an internal standard. A 100% pure (GLPC, column D, 110–220 °C at 16 °C/min) sample was obtained by preparative GLPC (6 ft × $^1/_2$ in. 10% DEGS column): ^1H NMR 4.99 (d, J = 8.8 Hz, 1 H), 0.65–2.95 (several multiplets overlapping a doublet at 1.59, J = 1.2 Hz, overall area 25 H); IR (neat) 2930, 1715, 865 cm^{-1}; MS m/e 222.2009 (M^+; calcd for $C_{15}H_{26}O$, 222.1982).

3-[(*Z*)-2-Methyl-1-octenyl]cyclohexanone (20e). The standard procedure was followed, using a 2.5 M solution (1.6 mL, 4.0 mmol) of n-hexylmagnesium bromide in ether and then excess propyne (1.0 mL). The crude product (80% pure by GLPC) was purified by column chromatography (methylene chloride/silica gel) to give 0.651 g (73%) of **20e** as a colorless oil: IR (neat) 2920, 1715, 1450, 865 cm^{-1}; ^1H NMR 4.99 (d, J = 8.8 Hz, 1 H), 0.88–2.79 (several multiplets overlapping a doublet at 1.66, J = 1.4 Hz, overall area 25 H); high-resolution MS m/e 222.1982 (M^+; calcd for $C_{11}H_{22}O$, 222.2009). The purity of the final product was >99% according to GLPC (column F, 110–240 at 16 °C/min).

2-[(*E*)-2-Ethyl-1-octenyl]-1-acetylcyclohexane (20f). The procedure was modified to employ a mixed-cuprate intermediate. A solution of 1-lithio-1-pentyne was prepared by the reaction of a solution of 1-pentyne (0.4 mL, 4 mmol) and HMPT (0.7 mL, 4 mmol) in ether (5 mL) at −78 °C with a 2.64 M solution (1.5 mL, 4.0 mmol) of n-butyllithium in hexane. This solution was then added to a solution at −78 °C of the alkenylcopper species generated in the usual manner from ethylmagnesium bromide (4.0 mmol) and 1-octyne (3.5 mmol). The mixture was warmed to −23 °C for 45 min and again cooled to −78 °C before 1-acetylcyclohexene (0.52 mL, 4.0 mmol) was added dropwise over a period of 2 min. The reaction was then allowed to proceed in the usual manner at −23 °C for 12 h. The crude product was purified by column chromatography (1:1 pentane–methylene chloride (v/v) on silica gel) to give 0.73 g (69%) of **20f** as a clear, colorless oil: IR (neat) 3060, 2950, 1715, 1660, 1460, 1350, 1160, 960, 850, 720 cm^{-1}; ^1H NMR 5.5 (d, J = 9 Hz, 0.5 H), 4.9 (d, J = 9 Hz, 0.5 H), 2.8–0.6 (m, overlapping a singlet at 2.05, 31 H); MS m/e 264.2432 (M^+; calcd for $C_{18}H_{32}O$, 264.2445). Analysis by GLPC (column F, 110–240 °C at 16 °C/min) revealed that the product was >99.5% pure but that it existed as an ~1:1 mixture of two components assumed to be cis and trans isomers.

(*E*)-[2-Ethyl-1-octenyl]-3,4-dihydrocoumarin (20g). The mixed alkenylcuprate was generated as in the previous procedure followed by addition of a solution of coumarin (0.548 g, 4.00 mmol) in THF (5 mL) and ether (3 mL) over a period of 7 min. The reaction mixture was then warmed from −78 to −45 °C for 1 h, to −23 °C for 2 h, and to +4 °C for 60 h. After the usual workup, 1.0 g of dark brown oil was obtained. The yield of **20g** was determined to be 0.620 g (62.0%) by GLPC (column B, 110–240 °C at 16 °C/min) with eicosane as an internal standard. For GLPC calibration, a pure sample was obtained by preparative GLPC (240 °C): IR (neat) 3080, 3050, 2980, 2940, 1690, 1590, 1615, 1490, 1470, 1230, 1150, 920, 760 cm^{-1}; ^1H NMR 6.68–7.41 (m, 4 H), 5.01 (d, J = 9.3 Hz, 1 H), 3.96 (d of d, J = 15.8, 10.7 Hz, 1 H), 2.82 (dd, J = 19.7, 5.5 Hz, 1 H), 2.49 (dd, J = 15.8, 10.7 Hz, 1 H), 1.92–2.25 (m, 5 H), 0.68–1.81 (m, 13 H); MS m/e 286 (M^+).

Anal. Calcd for $C_{19}H_{26}O_2$: C, 79.67; H, 9.15. Found: C, 79.67; H, 9.34.

1,1-Dimethyl-4-[(*E*)-2-ethyl-1-pentenyl]-2-tetralone (20h). The procedure was similar to that for compound **20a**. The reagents employed were as follows: **15** (1.64 g, 8.00 mmol), ethylmagnesium bromide (2.56 mL, 3.12 M, 8.00 mmol), 1-pentyne (0.97 mL, 8.0 mmol), ether (10 mL), dimethyl sulfide (8 mL), and 1,1-dimethyl-(2*H*)-napthalenone[81] (1.38 g, 8.00 mmol). The crude product was obtained as 2 g of yellow oil which was distilled to give 1.08 g (50%) of **20h** as a 100% pure (GLPC, column B, 110–240 °C at 16 °C/min), clear, colorless oil: bp 110 °C (0.005 torr); IR (neat) 2900, 1714, 1665, 1600, 1485, 1463, 1444, 846 cm^{-1}; ^1H NMR 7.08–7.50 (m, 4 H), 5.05 (d, J = 9.7 Hz, 1 H), 4.05 (m, 1 H), 2.42–2.92 (m, 2 H), 1.85–2.32 (m, 4 H), 0.72–1.77 (several overlapping peaks, 14 H); MS m/e 270.1981 (M^+; calcd for $C_{19}H_{26}O$, 270.1984.

1,1-Dimethyl-4-[(*Z*)-2-ethyl-1-pentenyl]-2-tetralone (20i). The previous procedure was employed but with the following different reagents: 1-butyne (0.68 mL, 8.0 mmol, condensed at −45 °C and transferred with a dry ice cooled syringe) and n-propylmagnesium bromide (4.4 mL, 1.82 M, 8.0 mmol). The crude product was obtained as 1.65 g of yellow oil which was distilled to give 1.0 g (50%) of 100% pure (column B, 110–240 °C at 16 °C/min), clear, colorless oil: bp 105–105.5 °C (0.005 torr). The spectral data were essentially identical with those of its isomer, **20h**.

3-[(*E*)-2-Ethyl-1-octenyl]cyclopentanone (20j). The mixed alkenylcuprate was prepared in a manner identical with that for compound **20f**. To the reaction mixture at −78 °C was added neat

(81) Wenkert, E.; Youssefyeh, R. D.; Lewis, R. G. *J. Am. Chem. Soc.* **1960**, *82*, 4675–80.

2-cyclopenten-1-one (0.355 mL, 4.00 mmol) over a period of 1 min, and the reaction mixture was stirred at −78 °C for 4.5 h before it was quenched with saturated aqueous ammonium chloride (buffered at pH 8 with ammonia). After the usual workup, 0.88 g of a cloudy oil was obtained. The yield of **20j** was 0.232 g (30%) according to GLPC (column A, 110–240 °C at 16 °C/min) with *n*-tridecane as the internal standard. For GLPC calibration, a pure sample was obtained by preparative GLPC (110–240 °C): IR (neat) 2980, 1750, 1663, 808 cm^{-1}; ^1H NMR 5.70 (d, J = 9 Hz, 1 H), 3.0 (br m, 1 H), 0.5–2.3 (m, 24 H); MS m/e 222.1983 (M^+; calcd for $C_{15}H_{26}O$, 222.1982).

(*E*)-5-Ethyl-1,3-diphenyl-4-undecen-1-one (20k). The same alkenylcopper complex was generated as for **20a** but on a scale of 14.0 mmol. To the reaction mixture at −78 °C was then added a solution of chalcone (0.833 g, 14.0 mmol) in ether (5 mL) over a 5-min period. After the addition, the reaction mixture was warmed to −45 °C for 1 h, then to −23 °C for 2 h, and finally to +4 °C for 12 h. After the usual workup, 1.1155 g of yellow oil was obtained. The yield of **20k** was determined to be 0.6292 g (52%) by high-pressure LC (25% methylene chloride, 75% hexane, flow rate 1.5 mL/min) isolation. The purity of the isolated product was >99% according to GLPC (column A, 110–240 °C at 16 °C/min): IR (neat) 3070, 3040, 2960, 1690, 1610, 1500, 1460, 750, 700 cm^{-1}; ^1H NMR 7.7–8.2 (m, 2 H), 6.8–7.52 (m, 8 H), 5.30 (d, J = 9 Hz, 1 H), 4.3 (dt, J = 9, 7 Hz, 1 H), 3.30 (d, J = 7 Hz, 2 H), 1.60–2.25 (m, 4 H), 0.4–1.60 (m, 14 H); MS m/e 348.2463 (M^+; calcd for $C_{25}H_{22}O$, 348.2453).

(*E*)-6-Ethyl-4-phenyl-5-dodecen-2-one (20l). The mixed alkenylcuprate was generated by the same procedure as for **20f**, using either 1-lithio-1-pentyne or 1-lithio-1-hexyne. To the reaction mixture at −78 °C was added a solution of benzalacetone (0.58 g, 4.0 mmol) and ether (5 mL) over a period of 5 min. The mixture was then stirred at −23 °C for 2 h and at +4 °C for 12 h. After the usual quenching and work-up procedure, the crude product was obtained as 0.986 g of yellow oil. The yield of **20l** was 0.527 g (53%) as determined by high-pressure LC (methylene chloride, flow rate 1.1 mL/min) isolation. The purity of the isolated product was 100% according to GLPC (column B, 110–240 °C at 16 °C/min): IR (neat) 3062, 3032, 2960, 1717, 1660, 1600, 1588, 1449, 750, 694 cm^{-1}; ^1H NMR 7.23 (s, 5 H), 5.25 (d, J = 9 Hz, 1 H), 4.2 (dt, J = 9, 7 Hz, 1 H), 2.81 (d, J = 7 Hz, 2 H), 1.8–2.4 (m, overlapping a singlet at 2.07, 7 H), 0.6–1.7 (m, 14 H); MS m/e 286.2343 (M^+; calcd for $C_{20}H_{30}O$, 286.2296); ^{13}C NMR ($CDCl_3$) 172.76, 132.75, 130.00, 116.24, 114.88, 140.00, 113.82, 39.04, 27.29, 24.07, 19.49, 18.44, 16.79, 14.81, 11.08, 10.39, 1.76, 0.66.

6-Methyl-5-hepten-2-one (20m). The procedure was based upon that for **20f**, but the following reagents were employed to generate the mixed alkenylcuprate: **15** (6.15 g, 30 mmol), ether (30 mL), dimethyl sulfide (30 mL), methylmagnesium bromide (10.2 mL, 2.9 M, 30 mmol), propyne (2.0 mL, 35 mmol, condensed at low temperature and transferred with a dry ice cooled syringe), 1-lithio-1-pentyne (30 mmol), and HMPT (10 mL, 60 mmol). As usual, the addition reaction of methylcopper required an extended period (6 days at −31 °C). To the solution of the mixed cuprate at −78 °C was added neat methyl vinyl ketone (2.8 mL, 35 mmol) over a 2-min period. The mixture was stirred at −78 °C for 4 h and at −23 °C for 12 h before being warmed to +25 °C and then quenched with saturated aqueous ammonium chloride (20 mL, adjusted to pH 8 with ammonia). The usual workup afforded 5.6 g of a light yellow oil which was purified by preparative GLPC to give 100% pure (GLPC, TLC) **20m** which was identical with an authentic sample (Aldrich) in all respects: ^1H NMR 5.05 (m, 1 H), 2.2–2.7 (m, 4 H), 2.15 (s, 3 H), 1.70 (s, 3 H), 1.60 (s, 3 H); IR (neat) 2950, 1710, 1360, 1190, 880 cm^{-1}; MS m/e 126.1072 (M^+; calcd for $C_8H_{14}O$, 126.1043); bp 164–165 °C (760 torr); n^{20}_D 1.4392. The yield was determined to be 0.96 g (25%) by GLPC (column B, 110–240 °C at 16 °C/min), using *n*-tridecane as an internal standard.

(*E*)-6-Ethyl-5-dodecen-2-one (20n). The mixed alkenylcuprate was generated by a procedure identical with that for **20f**, but this intermediate was allowed to react with excess methyl vinyl ketone (0.66 mL, 8.0 mmol) according to the previous procedure for **20m**. The yield of **20n** was 0.2627 g (31%) according to GLPC (column F, 110–240 °C at 16 °C/min) with *n*-tetradecane as the internal standard. A 99% pure (GLPC) sample was obtained by preparative GLPC (100–240 °C): IR (neat) 2960, 2940, 2860, 1720, 1460, 1160 cm^{-1}; ^1H NMR 5.0 (t, J = 7 Hz, 1 H), 1.6–2.5 (m, overlapping a singlet at 2.1, 11 H), 0.6–1.5 (m, 14 H); MS m/e 210.2015 (M^+; calcd for $C_{14}H_{26}O$, 210.1982).

Procedure for Homoallylic Alcohols. (*E*)-4-Methyl-3-decen-1-ol (22a). To a mixture of **15** (0.82 g, 4.0 mmol), ether (5 mL), and dimethyl sulfide (4 mL) at −45 °C under nitrogen was added a 2.90 M solution (1.39 mL, 4.0 mmol) of methylmagnesium bromide in ether over a 2-min period. After 2 h, 1-octyne (0.52 mL, 3.5 mmol) was added over 1 min to the yellow-orange suspension. The mixture was stirred at −23 °C for 120 h, and then the resulting dark green solution was cooled to −78 °C. A solution of 1-lithio-1-pentyne (prepared from 4.0 mmol of *n*-butyllithium and 4.0 mmol of 1-pentyne), ether (5 mL), and HMPT (1.4 mL, 8.0 mmol) was transferred to the green solution. After 1 h, ethylene oxide (0.21 mL, 4.0 mmol), which had been condensed at −45 °C, was added with a dry ice cooled syringe over a 0.5-min period. The resulting mixture was stirred at −78 °C for 2 h, allowed to stand at −25 °C for 24 h, quenched at 0 °C by addition of an aqueous solution (5 mL) of ammonium chloride (adjusted to pH 8 with ammonia), and then partitioned between ether and water. The crude product (90% pure by GLPC) was purified by column chromatography (CH_2Cl_2/silica gel) to give 0.44 g (75%) of **22a** as a colorless liquid: IR (neat) 3300, 1669, 874 cm^{-1}; ^1H NMR 5.05 (t, J = 7 Hz, 1 H), 3.55 (t, J = 7 Hz, 2 H), 1.58 (s, 3 H, overlapping a series of multiplets at 0.65–2.40, 16 H); MS m/e 170.1691 (M^+; calcd for $C_{11}H_{22}O$, 170.1667). Careful GLPC analysis (column A, 110–240 °C/min) indicated >99% purity, and TLC on silica gel (methylene chloride) showed only one spot.

(*Z*)-4-Methyl-3-hepten-1-ol (22b). To a mixture of **15** (18.4 g, 90 mmol), ether (110 mL), and dimethyl sulfide (88 mL) at −45 °C was added a 2.55 M solution (33 mL, 90 mmol) of *n*-propylmagnesium bromide in ether over a 10-min period. After 2 h, propyne (5.1 mL, 90 mmol), which had been condensed at −45 °C, was added with a dry ice cooled syringe over 5 min to the yellow-orange suspension. The mixture was stirred at −23 °C for 2.5 h, and the resulting dark green solution was cooled to −78 °C. A solution of 1-lithio-1-pentyne (prepared from 90 mmol of *n*-butyllithium and 90 mmol of 1-pentyne), ether (110 mL), and HMPT (15.7 mL, 90 mmol) was transferred to the green solution. After 1 h, ethylene oxide (4.5 mL, 90 mmol) was added with a dry ice cooled syringe over a 5-min period. The resulting mixture was stirred at −78 °C for 3 h and at −33 °C for 24 h, quenched at 0 °C by addition of a solution (25 mL) of saturated aqueous ammonium chloride (adjusted to pH 8 with aqueous ammonia), and partitioned between water and ether. The crude product was purified by column chromatography on silica gel (methylene chloride) to give 10.30 g (89%) of **22b** as a clear colorless oil: bp 44.5–45 °C (77 torr); IR 3300, 2900, 1640, 824 cm^{-1}; ^1H NMR 5.06 (t, J = 7.2 Hz, 1 H), 3.52 (t, J = 6.6 Hz, 2 H), 0.54–2.44 (several multiplets overlapping a doublet at 1.67, J = 1.1 Hz, 11 H overall); ^{13}C NMR 138.95, 120.69, 62.69, 34.02, 31.51, 23.49, 21.28, 14.00; MS m/e 128.1221 (M^+; calcd for $C_8H_{16}O$, 128.1200). The long-range coupling constant between the vinyl methyl group and the vinyl proton (J_{C-H}^{cis}) was measured by a gated decoupling experiment[73] on the Varian CFT-20 spectrometer with an acquisition time of 1.023 s and a pulse delay of 1.0 s at maximum broad-band decoupler power. The value thus obtained was J_{C-H}^{cis} = 6.8 Hz. Careful GLPC analysis (column A, 110–240 °C/min) of **22b** indicated >99% purity, and TLC on silica gel (methylene chloride) showed only one spot. Further confirmation of the identity of **22b** was given by its subsequent conversion into the codling moth constituent **5**.[65] The yield of **22b** was 95% according to GLPC analysis (column A, 110–220 °C at 16 °C/min) of the crude product mixture with *n*-heptadecane as the internal standard.

The same procedure as outlined above for compounds **22a** and **22b** was employed for the synthesis of the following homoallylic alcohols from the starting materials indicated in Table III. Acetylene with low boiling points was condensed at low temperature and added via dry ice cooled syringes. In some cases, a slight excess (5–10%) of these acetylenes was added due to the difficulty involved in transferring liquids at −78 °C.

(*E*)-4-Methyl-3-hepten-1-ol (22c). The reaction was performed as for **22a** but with 1-pentyne (0.39 mL, 4.0 mmol) in place of 1-octyne. The crude product was purified by column chro-

matography on silica gel (methylene chloride followed by 19:1 chloroform–acetone (v/v)) to give 0.40 g (78%) of **22c** as a clear, colorless liquid: IR (neat) 3400, 2900, 1650, 1380, 860 cm^{-1}; ^1H NMR 5.06 (t, J = 7.1 Hz, 1 H), 3.61 (t, J = 6.7 Hz, 2 H), 0.75–2.41 (several multiplets overlapping a singlet at 1.60, 11 H overall); MS m/e 128.1219 (M^+; calcd for $C_8H_{16}O$, 128.1200); ^{13}C NMR 138.75, 119.89, 62.54, 41.92, 31.61, 21.03, 16.05, 13.69. By the same procedure as for **22b**, the long-range coupling constant between the vinyl methyl group and the vinyl proton was found to be $J_{C\text{-}H}^{trans}$ = 8.3 Hz. Careful GLPC analysis of **22c** (column A, 110–240 °C at 16 °C/min) indicated >99% purity, and TLC on silica gel (methylene chloride) showed only one spot.

(*E*)-4-*n*-Propyl-3-octen-1-ol (22d). The procedure for **22b** was employed on a 4.0-mmol scale with 1-hexyne (0.46 mL, 4.0 mmol) in place of propyne. According to GLPC analysis (column A, 110–240 °C at 16 °C/min) with *n*-pentadecane as the internal standard, the yield of **22d** was 95%. A 100% pure sample (GLPC) was isolated by preparative GLPC (200 °C): IR (neat) 3360, 2940, 1638, 845 cm^{-1}; ^1H NMR 5.09 (t, J = 7 Hz, 1 H), 3.61 (t, J = 6.5 Hz, 2 H), 0.68–2.48 (several multiplets, 18 H); MS m/e 170.1652 (M^+; calcd for $C_{11}H_{22}O$, 170.1673).

(*Z*)-5-Ethyl-4-nonen-2-ol (22e). The reaction was performed by the procedure for **22b** on a 4.0-mmol scale, using *n*-butylmagnesium bromide (2.47 mL, 1.02 M, 4.0 mmol), 1-butyne (0.34 mL, 4.0 mmol), and 1,2-epoxypropane (0.28 mL, 4.0 mmol). The yield of **22e** was 82% according to GLPC (column A, 110–240 °C at 16 °C/min). A pure sample was isolated by preparative GLPC (150–240 °C): IR (neat) 3350, 2960, 1665; ^1H NMR 5.13 (t, J = 7 Hz, 1 H), 3.79 (m, 1 H), 0.70–2.39 (several multiplets overlapping a doublet at 0.94, J = 7.5 Hz, 20 H overall); MS m/e 170.1684 (M^+; calcd for $C_{11}H_{22}O$, 170.1669).

(*E*)-9-Ethyl-8-pentadecen-6-ol (22f). The reaction was performed by the procedure for **22b** on a 4-mmol scale, using ethylmagnesium bromide (1.3 mL, 3.0 M, 4.0 mmol), 1-octyne (0.59 mL, 4.0 mmol), and 1,2-epoxyheptane (0.55 mL, 4.0 mmol). With *n*-tetradecane as an internal standard, GLPC (column A, 110–220 °C at 16 °C/min) indicated a yield of **22f** of 94%. A pure sample was isolated by preparative GLPC (6 ft × $^1/_2$ in. 10% Carbowax 20 M): IR (neat) 3320, 2910, 1652 cm^{-1}; ^1H NMR 5.08 (t, J = 6.9 Hz, 1 H), 3.56 (m, 1 H), 0.60–2.46 (several multiplets, 32 H); MS m/e 254.2681 (M^+; calcd for $C_{12}H_{34}O$, 254.2609).

Anal. Calcd for $C_{12}H_{34}O$: C, 80.24; H, 13.47. Found: C, 80.44; H, 13.22.

(*Z*)-4-Ethyl-2-phenyl-3-hepten-1-ol (22g) and (*Z*)-4-Ethyl-1-phenyl-3-hepten-1-ol (22h). The reaction was performed by the procedure for **22b** on a 4-mmol scale, using *n*-propylmagnesium bromide (1.7 mL, 2.4 M, 4.0 mmol), 1-butyne (0.34 mL, 4.0 mmol), and styrene oxide (0.46 mL, 4.0 mmol). The product consisted of a 63:37 mixture of **22g** and **22h** in a combined yield of 75% according to GLPC (column A, 110–220 °C at 16 °C/min) with eicosane as the internal standard. A 100% pure sample of a mixture of the two isomers was obtained by preparative GLPC (200 °C): IR (neat) 3360, 3050, 3032, 2950, 1655, 1598, 1490, 1451, 750, 692 cm^{-1}; ^1H NMR 7.10–7.50 (m, 5 H), 5.26 (m, 1 H), 4.66 (t J = 6.5 Hz, 0.3 H, PhC**H**OH), 3.70 (m, 0.7 H, PhC**H**(C=C)CH_2OH), 2.46 (t, J = 7 Hz, 0.7 H, C=CHC**H**$_2$CHOH), 0.68–2.30 (several overlapping multiplets, 14 H).

Anal. Calcd for $C_{15}H_{22}O$: C, 82.75; H, 10.16. Found: C, 82.75; H, 10.06.

2-[(*E*)-2-*n*-Propyl-1-hexenyl]cyclohexanol (22i). The reaction was performed as for **22b** but on a 4-mmol scale, using *n*-propylmagnesium bromide (1.7 mL, 2.4 M, 4.0 mmol), 1-hexyne (0.46 mL, 4.0 mmol), and cyclohexene oxide (0.41 mL, 4.0 mmol). The yield of **22i** was 26% according to GLPC (column A, 110–220 °C at 16 °C/min) with eicosane as an internal standard. A pure sample was isolated by preparative GLPC and was found to be >99% pure (GLPC): IR (neat) 3420, 2910, 1053 cm^{-1}; ^1H NMR 4.92 (d, J = 9.8 Hz, 1 H), 3.16 (m, 1 H), 0.66–2.62 (several overlapping multiplets, 26 H); MS m/e 222.2122 (M^+; calcd for $C_{15}H_{28}O$, 222.2138).

Procedure for Synthesis of Sulcatol (23). A. From 6-Methyl-5-hepten-2-one (20m).[66a] A solution of **20m** (0.60 g, 4.7 mmol), obtained by the conjugate-addition pathway, and sodium borohydride (0.18 g, 4.7 mmol) in 95% ethanol (80 mL) was stirred at room temperature for 4 h. The excess hydride reagent was destroyed by the addition of 1 N hydrochloric acid (5 mL), and the solution was concentrated in vacuo, diluted with water, and extracted thoroughly with ether. The ether layer was washed with saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and concentrated in vacuo, yielding 0.57 g (95%) of **23** as a colorless oil which was >98% pure by GLPC (column E, 80–240 °C at 15 °C/min): IR (neat) 3400, 2980, 2940, 2880, 1455, 1385, 1315, 1180, 1135, 1080, 995, 860, 830 cm^{-1}; ^1H NMR 5.09 (br t, 1 H), 3.4–3.95 (m, 1 H), 3.17 (s, 1 H), 1.8–2.3 (m, 2 H), 1.69 (s, 3 H), 1.62 (s, 3 H), 1.3–1.7 (m, 2 H), 1.15 (d, J = 6 Hz, 3 H); MS m/e 128.1200 (M^+; calcd for $C_8H_{16}O$, 128.1200); bp 178–180 °C (760 torr); n^{20}_D 1.4465 [lit.[66] bp 176–181 °C; n^{20}_D 1.4463]. All spectral and physical data were in excellent agreement with the literature values.[66]

B. From 5-Methyl-1,4-hexadiene (19b). A dry 50-mL flask equipped with a septum inlet, dropping funnel, condenser, magnetic stirring bar, and mercury bubbler was evacuated and placed under nitrogen, and a steady flow of nitrogen was maintained throughout the reaction. Into the flask was placed **19b** (1.00 g, 10.4 mmol). Then a solution (20.8 mL, 0.5 M, 10.4 mmol) of 9-BBN (Aldrich) in tetrahydrofuran was added over a period of 1.5 h at 25 °C, and the reaction mixture was stirred for 2 h. To the mixture was added 5.0 mL of 3 M sodium hydroxide solution rapidly, followed by slow dropwise addition of 5.0 mL of 30% hydrogen peroxide at a rate such that the temperature did not rise above 50 °C. The aqueous phase was saturated with sodium chloride, and the organic layer was separated and diluted with 50 mL of ether and 50 mL of distilled water. The organic layer was then washed with water and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and concentrated in vacuo to yield 0.91 g (80%) of 5-methyl-4-hexen-1-ol which was >95% pure according to GLPC (column E, 80–240 °C at 15 °C/min): IR (neat) 3250, 2950, 1660, 1460, 1060 cm^{-1}; ^1H NMR 5.51 (t, J = 7 Hz, 1 H), 3.6 (t, J = 7 Hz, 2 H), 2.5 (s, 1 H), 1.95 (t, J = 7 Hz, 2 H), 1.70 (s, 3 H), 1.65 (s, 3 H), 1.60 (m, 2 H); MS m/e 114.1080 (M^+; calcd for $C_7H_{14}O$, 114.1043).

In a 50-mL round-bottomed flask fitted with a reflux condenser was suspended pyridinium chlorochromate (1.42 g, 6.57 mmol)[82] in anhydrous methylene chloride (10 mL). A portion of the previous product (0.50 g, 4.3 mmol) dissolved in 3 mL of methylene chloride was added in one portion to the magnetically stirred suspension at room temperature. After 2 h, dry ether (15 mL) was added and the supernatant liquid was decanted from the resulting black gum. The insoluble residue was washed thoroughly with ether (3 × 5.0 mL) whereupon it became a black granular solid. The combined organic solutions were passed through a short pad of Florisil, and the solvent was removed in vacuo, leaving 0.365 g (75%) of 5-methyl-4-hexenal as a clear, colorless liquid. Analysis of the crude product by GLPC (column E, 80–240 °C at 16 °C/min) indicated the final product to be >95% pure: IR (neat) 2950, 2720, 1722, 1258, 1108, 860 cm^{-1}; ^1H NMR 9.9 (s, 1 H), 4.97–5.38 (m, 1 H), 2.46 (br s, 4 H), 1.73 (s, overlapping another singlet at 1.69, 6 H overall); MS m/e 112.0906 (M^+; calcd for $C_7H_{12}O$, 112.0887).

A solution of methylmagnesium bromide (5 drops, 2.95 M) in ether was added to a portion of the previous product (0.0106 g, 0.094 mmol) in 0.5 mL of anhydrous ether at 0 °C. After 1 h at 0 °C, the reaction mixture was warmed to room temperature and stirred for an additional 1 h. The reaction mixture was then treated with 1.0 mL of saturated aqueous ammonium chloride (pH adjusted to 8 with aqueous ammonia) and partitioned between ether and water. The ether layer was separated, washed with water and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and concentrated in vacuo to give 0.008 g (70%) of **23** as a clear, colorless liquid which was 100% pure according to GLPC (column E, 80–240 °C at 15 °C/min) and which exhibited spectral and physical properties identical with those of the product obtained from reduction of **20m**.

Lanthanide Shift Reagent Studies. The isomeric tetralone derivatives **20h** and **20i** were purified by distillation [bp 110 °C (0.005 torr)] and then by preparative GLPC. Their isomeric purities were determined by GLPC (column C, 250 °C); neither sample contained any detectable amount (<0.4%) of its isomer

(82) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647–50.

either before or after preparative GLPC. The $CDCl_3$ for the NMR studies was purified by elution through a column of silica gel and was stored over Linde 4A molecular sieves. The $Eu(fod)_3$ shift reagent was handled in a nitrogen-filled glovebox and was dissolved in the purified $CDCl_3$ to form a 0.54 M solution. The NMR samples of **20h** and **20i** were placed in nitrogen-filled sample tubes sealed with small serum stoppers, and aliquots of the $Eu(fod)_3$ solution were added with a 50-μL syringe. The NMR spectra were recorded on a Varian HFT-80 spectrometer, and the decoupling experiments were performed with a Hewlett-Packard Model 3320A frequency synthesizer. The data from the shift reagent studies are shown in Table IV. The isomeric heptenols **22b** and **22c** were studied by the same procedure, and the corresponding data for these compounds are also given in Table IV. The isomeric purities of these two compounds could not be determined by GLPC because the two isomers were not separable with any of the several columns that were employed.

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Registry No. 15, 54678-23-8; **19a**, 4588-18-5; **19b**, 763-88-2; **19c**, 67356-84-7; **19d**, 67356-85-8; **19e**, 67356-86-9; **20a**, 71360-09-3; **20b**, 71360-10-6; **20c**, 71360-11-7; **20d**, 67356-87-0; **20e**, 71360-12-8; *cis*-**20f**, 71360-13-9; *trans*-**20f**, 71392-87-5; **20g**, 71360-14-0; **20h**, 69417-95-4; **20i**, 69417-96-5; **20j**, 71360-15-1; **20k**, 71360-16-2; **20l**, 71360-17-3; **20m**, 110-93-0; **20n**, 71360-18-4; **22a**, 67356-88-1; **22b**, 13679-01-1; **22c**, 13679-00-0; **22d**, 71360-19-5; **22e**, 71360-20-8; **22f**, 71360-21-9; **22g**, 71360-22-0; **22h**, 71360-23-1; **22i**, 68705-77-1; **23**, 4630-06-2; 1-octyne, 629-05-0; 1-propyne, 74-99-7; 1-hexyne, 693-02-7; ammonium chloride, 12125-02-9; allyl bromide, 106-95-6; acetyl chloride, 75-36-5; ethyl bromide, 74-96-4; hexyl bromide, 111-25-1; butyl bromide, 109-65-9; methyl bromide, 74-83-9; propyl bromide, 106-94-5; 1-butyne, 107-00-6; 1-pentyne, 627-19-0; 2-cyclohexen-1-one, 930-68-7; 1-acetylcyclohexene, 932-66-1; coumarin, 91-64-5; 1,1-dimethyl-(2*H*)-naphthalenone, 23230-52-6; 2-cyclopenten-1-one, 930-30-3; chalcone, 94-41-7; benzalacetone, 122-57-6; methyl vinyl ketone, 78-94-4; ethylene oxide, 75-21-8; 1,2-epoxypropane, 75-56-9; 1,2-epoxyheptane, 5063-65-0; styrene oxide, 96-09-3; cyclohexene oxide, 286-20-4; 2-ethyl-1-octene, 51655-64-2.

Active Metal Slurries by Metal Vapor Techniques. Reactions with Alkyl and Aryl Halides[1]

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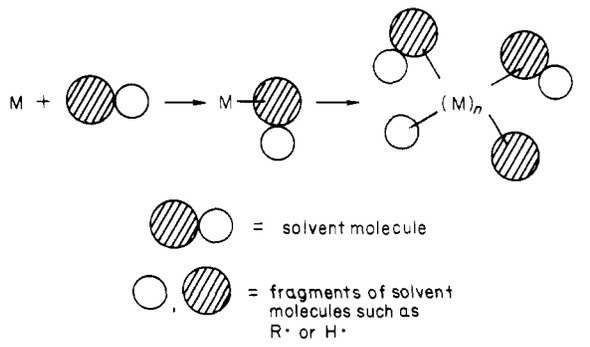
The low-temperature codesposition of metal vapors with solvents in high excess, followed by warming and subsequent partial reclustering of metal atoms, allows preparation of very active metal particles in slurry form. Thus, slurries of Al, In, Zn, Cd, Sn, Pb, and Ni were prepared in either xylene, toluene, hexane, tetrahydrofuran, or diglyme. These metal–organic dispersions were allowed to react with alkyl and aryl halides: $(Al)_n$/solvent with ArX yielded Ar_xAlX_{3-x}; $(In)_n$/solvent with RX yielded R_xInI_{3-x}; $(Zn)_n$/solvent with RX yielded R_2Zn, which could readily be isolated in nonsolvated form, and $(Zn)_n$/solvent with CH_2X_2/olefin yielded Simmons–Smith chemistry in fair to poor yields; $(Cd)_n$/solvent with RX yielded RCdX, in some cases in nonsolvated form; $(Sn)_n$/solvent with RX yielded R_xSnI_{4-x}; $(Pb)_n$/solvent with RX yielded R_3PbX; and $(Ni)_n$/solvent with RX yielded organic products resulting from R or RNiX intermediates. The active powders prepared from the slurries by solvent evaporation were storable for many months without significant loss in activity, as measured by RX reaction rates after readdition of pure solvent.

When metal atoms are codeposited at −196 °C with high excesses of solvents, unexpected reactions often take place.[3,4] These reactions usually occur during matrix warmup, and with Ni even C–C cleavage in alkanes can occur efficiently as low as −130 °C. Also during matrix warmup, M–M clustering takes place, and this can occur quite rapidly (even below −196 °C)[5] if the solvent possesses no available complexing π or nonbonding electrons, such as with alkanes.[6] Therefore, in all such systems where metal atoms and weakly complexing solvents (considering the metal atom in question) are codeposited, upon warmup



a competition exists between M–M *bond reformation* (clustering) and *reaction* of the atoms and/or clusters with

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