Ministry of Education, Science and Culture in Japan (Grant No. 57218016).

Registry No. 1, 10409-46-8; 2, 39512-00-0; 3, 38043-89-9; 4a, 18424-76-5; 4b, 996-82-7; 6a, 87451-62-5; 6b, 87451-63-6; 7a, 87451-64-7; 7b, 87451-65-8; 8, 87451-66-9; *endo*-9, 87451-67-0; *exo*-9, 87451-68-1; 10, 87451-69-2; *cis*-11, 70430-75-0; *trans*-11, 70430-70-5; *endo*-12, 87451-70-5; *cis*-13, 3664-69-5; *trans*-13, 3664-70-8; dimethyl malonate, 108-59-8; diethyl malonate, 105-53-3; ethyl 1-cyclopentenecarboxylate, 10267-94-4.

Supplementary Material Available: ^{13}C NMR spectral data of compounds 8, *endo*-9, *exo*-9, and 10 (1 page). Ordering information is given on any current masthead page.

Chemistry of Substituted (α-Carbethoxyvinyl)cuprates. 2. Stereospecific Olefin Synthesis

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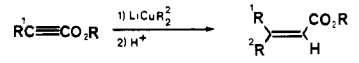
The reactivity of substituted (α-carbethoxyvinyl)cuprate reagents with various electrophiles has been studied systematically. The reaction of this type of cuprate reagent with ketones and epoxides leads to high yields of isomerically pure olefinic esters, while its condensation reaction with aldehydes produced mixtures of isomers. The stereochemistry of the condensation reaction with carbonyl compounds is explained by a steric control mechanism involving an allenoate intermediate.

Introduction

The stereospecific synthesis of substituted alkenes is a challenging problem in synthetic organic chemistry. Within the array of olefinic natural products are the insect pheromones.[1] Such compounds as the codling moth pheromone,[2] and Cecropia juvenile hormone,[3] have stimulated much of the development in the methodology for olefin synthesis. The high sensitivity of physiological activity in relation to olefin geometry mandates strict control of stereochemistry.

While many methods for the synthesis of substituted olefins are known,[4] the carbometalation of alkynes by organometallic reagents has become a highly regarded and widely used method.[5] The stereospecific cis addition of organocuprates to acetylenes has provided a versatile method for the synthesis of trisubstituted olefins.[4,5]

The regiospecific, copper-catalyzed conjugate addition of butylmagnesium bromide to esters of propiolic, tetrolic, and acetylenedicarboxylic acids was first described in 1960.[6] In the absence of a catalyst, the addition of Grignard reagents to activated acetylenes led exclusively to tertiary acetylenic alcohol products. The pioneering works of Corey and Katzenellenbogen,[7] Siddall et al.,[8] and Klein and Turkel[9] on the addition of organocuprates and copper(I) species to acetylenic esters have provided the groundwork for what has now become a general method for the preparation of β-disubstituted olefinic esters. The extension of this methodology to α,β-substituted olefinic esters has not been effectively carried out.



The addition of lithium dialkylcuprates to substituted acetylenic esters has found frequent application.[10] Vinylcuprate species also add to acetylenic esters in good yield.[11] Other functionalized cuprate reagents have been added to substituted acetylenic esters and amides, as well as to ethyl propiolate.[12] Many of these examples are not stereospecific; mixtures of cis and trans isomers are obtained upon protonolysis.

Although the organocuprate addition reaction to activated acetylenes appears to have enjoyed wide application, little attention has been given to the reactivity of the cuprate intermediate with electrophilic species. Carlson[13] has synthesized 5,6-dihydro-2*H*-pyran-2-ones by reaction of the copper intermediate with very reactive electrophiles in the presence of excess hexamethylphosphorous triamide (HMPA). All of the alkylated products were obtained as

(1) Novak, V. J. A. "Insect Hormones"; Methuen: London, 1966.
(2) (a) Bowlus, S. J.; Katzenellenbogen, J. A. *Tetrahedron Lett.* **1973**, 1277. (b) Cooke, M. P. *Ibid.* **1973**, 1281.
(3) (a) Siddall, J. B.; Marshall, J. P.; Bomers, A.; Cross, A. D.; Edward, J. A.; Fried, J. H. *J. Am. Chem. Soc.* **1966**, *88*, 379. (b) Corey, E. J.; Katzenellenbogen, J. A.; Gilman, N. W.; Roman, S.; Erickson, B. W. *Ibid.* **1968**, *90*, 5618.
(4) Marfat, A.; McGuirk, P. R.; Helquist, P. *J. Org. Chem.* **1979**, *44*, 3888 and references therein.
(5) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841.
(6) Bretting, C.; Munch-Petersen, J.; Jorgensen, P. M.; Refn, S. *Acta Chem. Scand.* **1960**, *14*, 151.
(7) Corey, E. J.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 1853.
(8) Siddall, J. B.; Biskup, M.; Fried, J. H. *J. Am. Chem. Soc.* **1969**, *91*, 1853.
(9) Klein, J.; Turkel, R. M. *J. Am. Chem. Soc.* **1969**, *91*, 6186.
(10) (a) Obayashi, M.; Utemota, K.; Nozaki, H. *Tetrahedron Lett.* **1977**, 1807. (b) Katzenellenbogen, J. A.; Bowlus, S. B. *J. Org. Chem.* **1973**, *38*, 2733. (c) Rousch, W. R.; Peseckis, S. M. *J. Am. Chem. Soc.* **1981**, *103*, 6696. (d) Pitzele, B. S.; Baran, J. S.; Steinman, D. H. *J. Org. Chem.* **1975**, *40*, 269. (e) Walba, D. M.; Edwards, P. D. *Tetrahedron Lett.* **1980**, 3531. (f) Ramsby, S. *Acta Chem. Scand.* **1971**, *25*, 1471. (g) Kluendec, H.; Bradley, C. H.; Sih, C. T.; Fawcett, P.; Abraham, E. P. *J. Am. Chem. Soc.* **1973**, *95*, 6149.
(11) (a) Naf, F.; Degen, P. *Helv. Chim. Acta* **1971**, *54*, 1939. (b) Corey, E. J.; Kim, C. U.; Chen, R. H. K.; Takeda, M. *J. Am. Chem. Soc.* **1972**, *94*, 4395. (c) Keck, G. E.; Nickell, D. G. *Ibid.* **1980**, *102*, 3632. (d) Oida, S.; Ohashi, Y.; Ohki, E. *Chem. Pharm. Bull.* **1973**, *21*, 528. (e) Alexakis, A.; Normant, J.; Villieras, J. *Tetrahedron Lett.* **1976**, 3461. (f) Alexakis, A.; Cahiez, G.; Normant, J. *Tetrahedron* **1980**, *36*, 1961.
(12) For example: *allylic*, ref 11b; *homoallylic*, Poulter C. D.; Wiggins, P. L.; Plummer, T. L. *J. Org. Chem.* **1981**, *46*, 1532; *cyclopropyl*, Marino, J. P.; Browne, L. J. *Ibid.* **1976**, *41*, 3629; *2,4-pentadienyl*, Miginiac, P.; Davidand, G.; Gerald, F. *Tetrahedron Lett.* **1979**, 1811; *allenic*, Michalot, P.; Linstrumelle, G. *Ibid.* **1976**, 275; *misc*, Alexakis, A.; Cahiez, G.; Normant, J. F.; Villieras, J. *Bull. Chim. Soc. Fr.* **1977**, 693; Semmelhack, M. F.; Stauffer, R. D. *J. Org. Chem.* **1975**, *40*, 3619; Jalander, L.; Iambolieva, K.; Sundstrom, V. *Acta Chem. Scand., Ser. B* **1980**, *34*, 715.
(13) Carlson, R. M.; Oyler, A. R.; Peterson, J. R. *J. Org. Chem.* **1975**, *40*, 1610.

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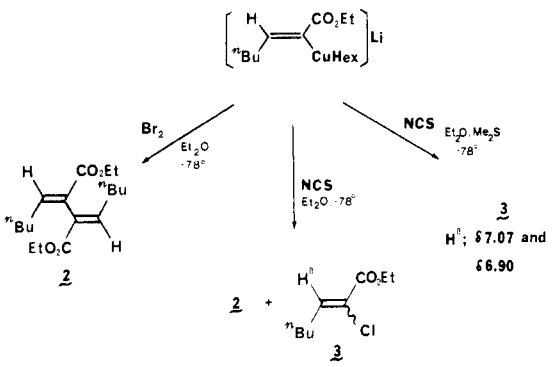
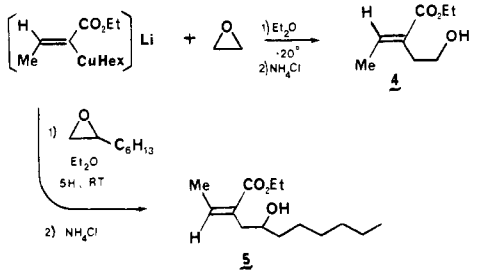
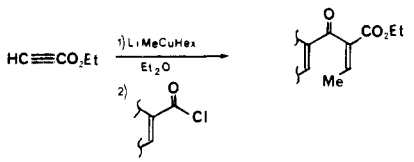
Scheme I



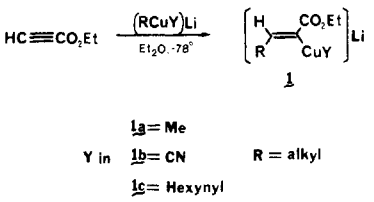
Scheme II



stereochemical mixtures in modest yield. We have previously reported[14] the stereospecific acylation of (β-monosubstituted-α-carbethoxyvinyl)cuprate reagents with unsaturated acid chlorides. We have now completed



further studies on the reactivity of β-substituted-α-acrylate cuprate reagents and describe herein the results obtained in the reaction of cuprate intermediate 1 (generated from ethyl propiolate and mixed-alkylcuprate reagents) with electrophilic halogen sources, epoxides, ketones,[15] and aldehydes. The stereochemistry of the carbonyl condensation reactions is discussed in terms of an allenoate steric control mechanism.



Reactions with Electrophiles

Our initial results[14] on acylation of the cuprate intermediate 1 indicated that a nontransferable ligand was required. Reaction of **1a** with acyl chlorides led only to transfer of the methyl ligand, while reaction of **1b** or **1c** led to high yields of acylated products. We then sought to determine if these reagents could be used as a general method for the preparation of α,β-substituted acrylate esters. We investigated the reaction of **1b** and **1c** with a variety of electrophilic species at low temperature (−78 °C). With cyclohexenone, no product of 1,4- nor 1,2-addition was observed; however, ethyl crotonate was obtained in quantitative yield (by GPC analysis). Quenching the reaction mixture with deuterium oxide gave ethyl 2-deuteriocrotonate in 98% isolated yield. Unquestionably the acetylenic addition product intermediate was formed yet at −78 °C was unreactive. Attempts to achieve successful alkylation of **1b** at higher reaction temperatures (−20 °C or higher) led to diminished yields of ethyl crotonate with no alkylated products. The same reactions carried out with **1c** were also unsuccessful at −78 °C. However, reagent **1c** proved to be thermally stable, even to 0 °C, thereby allowing for reaction with electrophiles at higher temperatures. These results are described in detail below.

From earlier work in our research group[16] on the generation of acrylate cuprate reagents from α-haloacrylate esters, we were interested in preparing isomerically pure β-substituted-α-halogenated olefinic esters. Vinylcuprate reagents generated by organocuprate addition to simple acetylenes have provided vinyl halides stereospecifically.[17] Therefore, lithium butylhexynylcuprate was added to ethyl propiolate, producing **1c** (R = Bu), which when reacted with bromine at −78 °C produced a dimerized product **2** rather than the vinyl bromide (see Scheme I). By use of *N*-chlorosuccinimide, the vinyl chloride **3** was obtained, but dimer formation was not eliminated (vinyl chloride/dimer, 1.7:1). The vinyl chloride **3** was obtained as a mixture of isomers, as evidenced by two triplets for the olefinic proton in the ^{1}H NMR. The dimer **2** was clearly a single isomer (^{1}H NMR, ^{13}C NMR, and HPLC analysis), which was assigned the *E,E* configuration. Dimer formation was eliminated in this reaction by using an excess of dimethyl sulfide (cosolvent with ether); however, the vinyl chloride product isolated was still a mixture of geometric isomers. Although this method was not suitable for the stereospecific preparation of α-haloacrylates, information regarding the reactive cuprate species **1** was obtained (see Discussion section).

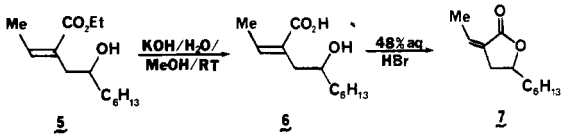
We next investigated the potential of the reagent to act as a β-substituted acrylate α-anion in carbon–carbon bond forming reactions. A nucleophilic species of this type has the potential for application toward the synthesis of α-alkylidene-γ-butyrolactones.[18] Many of these unsaturated lactones are physiologically active[19] and several natural products possess this unique structural feature. At the present time, no method has been reported for the direct alkylation of an α-acrylate anion with simple epoxides.[20] This reaction would readily lead to the alkylidene lactone via lactonization.

Reaction of **1c** (R = Me) with ethylene oxide at room temperature resulted predominantly in polymerization. Careful control of the reaction temperature (−20 °C) did produce the alkylated product **4** in moderate yield (see Scheme II). The stereochemistry of the product was assigned by ^{1}H NMR as the *E* olefin (olefinic proton δ 6.97 and the vinylogous methyl absorption at δ 1.67). The epoxide of 1-octene gave no addition product when the reaction was carried out at −20 °C. However, after the

(14) Marino, J. P.; Linderman, R. J. *J. Org. Chem.* **1981**, *46*, 3696.
(15) Preliminary results with ketones have appeared: Marino, J. P.; Linderman, R. J. in ref. 14.
(16) (a) Marino, J. P.; Floyd, D. M. *J. Am. Chem. Soc.* **1974**, *96*, 7138. (b) Marino, J. P.; Floyd, D. M. *Tetrahedron Lett.* **1975**, 3897. (c) *Ibid.* **1979**, 675.
(17) (a) Levy, A. B.; Talley, P.; Dunford, J. A. *Tetrahedron Lett.* **1977**, 3545. (b) Westmijze, H.; Meijer, J.; Vermeer, P. *Recl. Trav. Chim. Pays-Bas.* **1977**, *96*, 198.
(18) Rollinson, S. W.; Amos, R. A.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1981**, *103*, 4114.
(19) For a general discussion of physiologically active acrylate derivatives, see Fujita, E.; Nagao, Y. *Bioorg. Chem.* **1977**, *6*, 287.
(20) Our previous reagent, ref 16, was only active with allylic epoxides.

reaction mixture was allowed to warm to room temperature for 5 h prior to aqueous workup, a 61% yield of a single regio- and stereoisomeric product **5** was obtained. The regiochemistry was that anticipated for the reaction of a cuprate with an unsymmetrical epoxide.[21] More significant was the observation that the single olefin isomer obtained was assigned the *Z* configuration by virtue of the chemical shift of the methyl and olefinic protons (δ 1.87 and 6.00, respectively). Comparison of the spectral data of **5** with that of the ethylene oxide adduct **4** clearly distinguishes the isomers. Examination of the crude reaction mixture detected no *E* isomer. The *Z* olefin product corresponds to an overall trans addition of the cuprate intermediate, i.e., cis addition to the acetylenic ester followed by reaction through a second isomerized intermediate. Several other epoxides were investigated (cyclopentene and cyclohexene oxides, for example), but the results indicated that the reaction was limited to acyclic, terminal epoxides.

To illustrate the potential for α-alkylidene lactone synthesis via this method, the octene adduct **5** was cyclized to α-alkylidene lactone **7**. Acid-catalyzed ester hydrolysis



5 6 7

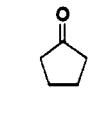
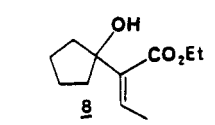
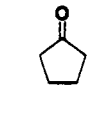
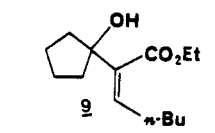
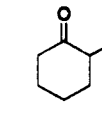
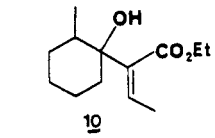
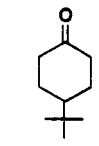
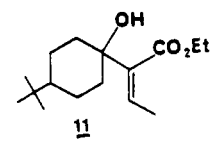
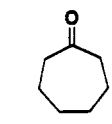
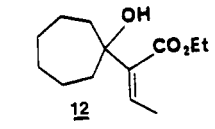
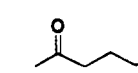
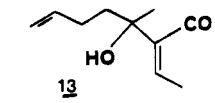
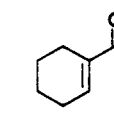
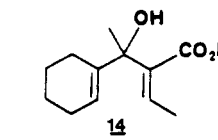
with concomitant lactonization was nonproductive, while basic hydrolysis of the hydroxy ester with Claisen's alkali[22] provided the free acid **6** in nearly quantitative yield. Dilute acid catalyzed lactonization as well as DCC-promoted[23] lactone formation from the free acid were also unsuccessful. A 44% isolated yield of the lactone was obtained by treatment of the hydroxy acid **6** with 48% HBr.

Our earlier report of anomalous 1,2 carbonyl addition to enones by the unsubstituted (α-carbalkoxyvinyl)cuprate reagent[16] led to a systematic study of the condensation reaction of **1c** with carbonyl compounds. The results obtained with ketones are presented in Table I, and the aldehyde condensation products are given in Table II.

When **1c** was combined with enones, such as acetylcyclohexene, 1,2 carbonyl addition products were obtained exclusively. More importantly, these high yield condensation reactions were completely stereoselective, producing only the *Z* trisubstituted olefinic esters with ketones.[24] Aldehyde condensation products were produced with a degree of stereoselectivity, although none of the isolated products were single isomers. In attempting to extend the reaction to unsaturated aldehydes, no carbonyl addition products could be isolated; instead, anionic polymerization of the substrate was observed.

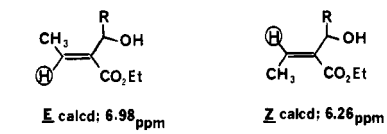
The assignment of the *Z* isomer for the ketone adducts is based on a comparison of the chemical shifts of known compounds with those obtained from the reaction. The aldehyde condensation products clearly illustrate the difference in chemical shift for the β-olefinic proteon in the *E* and *Z* isomers. Calculation[25] of the chemical shift

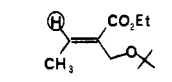
Table I. Condensation Reactions of 1c with Ketones

ketone	product[a]	% yield[b]	chemical shift,[c] δ β-CH_3	β-H
	 **8**	96	1.90	6.12
	 **9**	98		5.85
	 **10**	99	1.77	5.97
	 **11**	99[d]	1.82	6.10
	 **12**	96	1.77	5.97
	 **13**	93	1.82	6.05
	 **14**	92[e]	1.82	6.02

[a] Single isomer. [b] Yield after chromatography. [c] $CDCl_3$ solution. [d] A mixture of axial and equatorial isomers, both having *Z* olefin geometry, was obtained. [e] No 1,4-addition product was detected

of the olefinic protons also correlates well with observed *E* and *Z* olefinic absorptions. Ethyl (*E*)-2-(*tert*-butoxymethyl)-2-butenoate (**21**) is also illustrated for comparison.



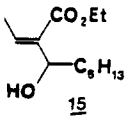
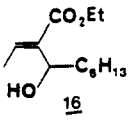
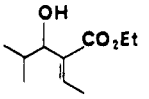
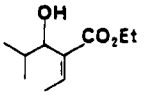
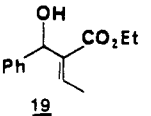
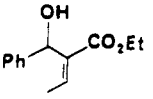


21; 6.92ppm

Further evidence for the olefin stereochemical assignment was also obtained from spectral data of the aldehyde adducts. Although the assignment of the stereochemistry of substituted olefins by allylic spin–spin coupling constants (^4J) has been the subject of controversy,[27] the gen-

(21) Johnson, C. R.; Herr, R. W.; Wieland, D. M. *J. Org. Chem.* **1973**, *38*, 4263.
(22) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; 1967; Vol. 1, p 153.
(23) Marshall, J. A.; Cohen, N. *J. Org. Chem.* **1965**, *30*, 3475.
(24) Some recent examples for nonstereoselective methods to prepare α,β-disubstituted olefinic esters are as follows: (a) Slougui, N.; Rousseau, G.; Corriu, J. M. *Synthesis* **1982**, *58*. (b) Tanikaga, R.; Miyashita, K.; Ono, N.; Kaji, A. *Ibid.* **1982**, *131*. (c) Brittelli, D. R. *J. Org. Chem.* **1981**, *46*, 2514.
(25) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. "Spectrometric Identification of Organic Compounds", 3rd ed.; Wiley: New York, 1974.
(26) Goldberg, O.; Dreiding, A. S. *Helv. Chim. Acta* **1976**, *59*, 1904.

Table II. Condensation Reactions of 1c with Aldehydes

aldehyde	products	ratio[a]	chemical shift,[b] δ β-CH_3	β-H	^4J, Hz[c]	% yield[d]
$C_6H_{13}CHO$	 15	1.6	1.95	6.19	0.73	80
	 16	1.0	1.80	6.84	0.49	
	 17	3.6	1.95	6.14	0.98	89
	 18	1.0	1.82	6.93	0.73	
PhCHO	 19	4.0	2.03	6.29	0.98	86
	 20	1.0	1.96	7.18	0.40	

[a] Determined by integration of the 360-Hz ^1H NMR β-CH_3 signal. [b] $CDCl_3$ solution. [c] Coupling of the CH(OH) with the olefinic proton. [d] Combined yield of chromatographed products.

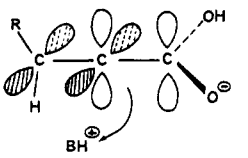
eral relationship found in isomeric acylic compounds is $^4J_{cisoid}$ is greater than $^4J_{transoid}$.[28] The allylic coupling constants for compounds **15–20** have been measured by 360-MHz ^1H NMR (see Table II) and are found to correspond to the general trend. From the spectral data presented and the correlations with known compounds, the stereochemistry of the products should be firmly assigned.

Discussion

The results obtained for the (β-substituted-α-carbalkoxyvinyl)cuprate reagents suggest that these reagents are more complex than nonfunctionalized vinylcuprate species. Henrick and co-workers[29] provided further insight into the problem. In contrast to the copper-ate complex (cuprates), polymeric copper(I) reagents produced the highest degree of stereochemical control. Complexing agents, such as TMEDA, also served to increase the stereoselectivity. Recently, Piers et al.[30] have obtained >99% selectivity using an in situ proton source method. Yamamoto et al.[31] have prepared a configurationally stable intermediate using organocopper–organoboron complexes.

Klein and Levene[32] speculated that an enolate intermediate was responsible for the stereochemical complexity of the cuprate additions to acetylenic esters. Infrared data was presented that indicated that an intermediate exhibiting absorptions at 1900–1930 cm^{-1} was observed upon the addition of excess methyllithium. We have reported[14] that an allenoate intermediate is obtained directly from the addition of alkylcuprates to ethyl propiolate, as evidenced by O-alkylation of the allenoate with trimethylsilyl chloride.

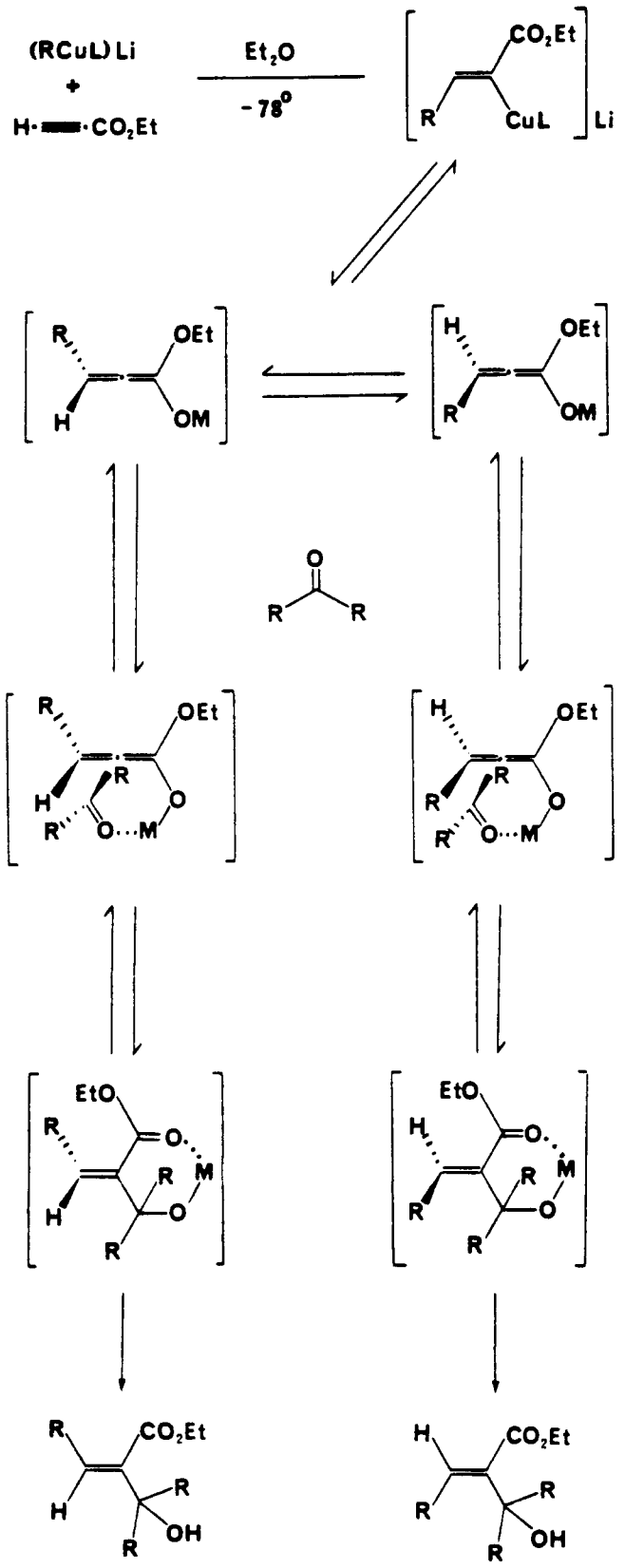
An allenoate structure has been invoked in the decarboxylation of unsaturated malonic acids by quinoline.[33] In



this case, protonolysis occurs by attack at C-2 of the allene on the π-orbital of the (C-1)–(C-2) bond. This attack must

(27) (a) Newsoroff, G. P.; Sternhell, S. *Tetrahedron Lett.* **1968**, 6117. (b) Newsoroff, G. P.; Sternhell, S. *Aust. J. Chem.* **1972**, *25*, 1669.
(28) Jackman, L. M.; Sternhell, S. "Applications of NMR Spectroscopy in Organic Chemistry"; Pergamon Press: Oxford, 1969; Chapter 4.
(29) Anderson, R. J.; Corbin, V. L.; Cotterrell, G.; Cox, G. R.; Henrick, C. A.; Schaub, F.; Siddall, J. B. *J. Am. Chem. Soc.* **1975**, *97*, 1197.
(30) Piers, E.; Chong, J. M.; Morton, H. E. *Tetrahedron Lett.* **1981**, 4905.
(31) Yamamoto, Y.; Yatagai, H.; Maruyama, K. *J. Org. Chem.* **1979**, *44*, 1744.
(32) Klein, J.; Levene, R. *J. Chem. Soc., Perkins Trans. 2* **1973**, 1971.
(33) Klein, J.; Meyer, A. Y. *J. Org. Chem.* **1964**, *29*, 1038.

Scheme III



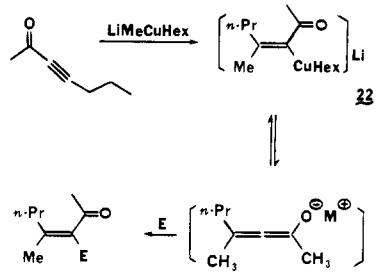
necessarily occur in the plane of the groups attached to the β-carbon and, therefore, will preferentially occur from the least hindered side of the allene.

We propose a mechanism depicted in Scheme III for the condensation reaction. After conversion of the initial *cis*-vinylcopper adduct to the allenoate intermediate, the carbonyl group is complexed to the allenoate metal atom. Kraus and Smith[34] have shown that lithium (from LiI) may compete with copper (from the cuprate) for a complexation site at the carbonyl oxygen. For an efficient condensation or alkylation reaction to occur on the allenoate, the exchange of copper for lithium may be required. Copper enolates are generally less reactive than the corresponding lithio enolate.[35] Oxygen complexation to lithium then serves to orient the carbonyl group for attack on the allenoate. At this point, the stereochemistry of the reaction is governed by steric interaction. The small degree of interaction of the allenoate R group with an aldehyde results in mixtures of isomers. As the steric bulk of the aldehyde R group increases, there is a complementary increase in the stereoselectivity of the condensation reaction. The minimum steric requirement for complete stereoselectivity is a methyl ketone. For all the ketones investigated, reaction occurred exclusively from the least hindered side of the allenoate, producing the *Z* olefin.

Reaction with electrophiles at low temperature can trap the vinylcuprate intermediate prior to equilibration to the allenoate. At or above 0 °C, extensive vinyl–allenyl equilibration occurs, then metal–metal exchange and the alkylation or condensation reaction ensues.

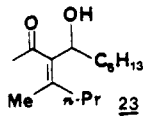
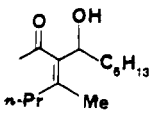
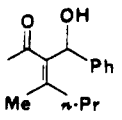
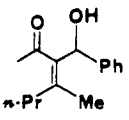
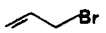
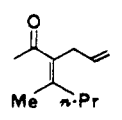
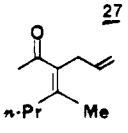
The reaction with electrophilic halogen sources does not fit this mechanism. The isolated of dimeric products indicates an electron-transfer process may be active, coupled to the Cu^{I}, $Cu^{I}I$ redox cycle.[36] This separate reaction pathway may facilitate vinyl–allene equilibration at lower temperatures, thus producing mixtures of isomers for the halogenated products. A free-radical process that may also lead to isomeric mixtures has not been ruled out.

As an extention of the methodology described herein, we sought to prepare α,β-disubstituted enones from α-acetylenic ketones. Cuprate additions to acetylenic ketones have been reported to yield mixtures of isomers upon protolytic workup.[37] This regiospecific addition reaction has been extended to α-acetylenic nitriles,[38] sulfoxides,[39] and sulfones.[40] None of these studies have attempted to trap the copper intermediate with any electrophile other than a proton source. 3-Heptyn-2-one was readily prepared on a large scale by the reaction of pentynylcopper(I) with acetyl chloride.[41] Addition of lithium methylhexynylcuprate produced an intermediate **22**, which exhibited reactivity analogous to **1c**. The results are given



(34) Krause, S. R.; Smith, S. G. *J. Am. Chem. Soc.* **1981**, *103*, 141.
(35) For general aspects of the reactivity of cuprates, see: (a) Posner, G. H. *Org. React.* **1972**, *19*, 1. (b) Posner, G. H. *Ibid.* **1975**, *22*, 253. (c) Normant, J. F. *Synthesis* **1972**, 63. (d) Normant, J. F. *Pure Appl. Chem.* **1978**, *50*, 709. (e) Jukes, A. E. *Adv. Organomet. Chem.* **1974**, *12*, 215. (f) Posner, G. H. "An Introduction to Synthesis Using Organocopper Reagents"; Wiley: New York, 1980.
(36) Cotton, F. A.; Wilkinson, G. "Advanced Inorganic Chemistry"; Interscience: New York, 1972; p 921.
(37) (a) Klein, J.; Levene, R. *J. Chem. Soc., Perkins Trans. 2* **1973**, 1971. (b) Reference 33.
(38) Westmijze, H.; Klejn, H.; Vermeer, P. *Synthesis* **1978**, 454.
(39) Truce, W. E.; Lusch, M. L. *J. Org. Chem.* **1978**, *43*, 2252.
(40) Fiandonese, V.; Marchese, G.; Naso, F. *Tetrahedron Lett.* **1978**, 5131.
(41) Normant, J. F.; Bourgain, M. *Tetrahedron Lett.* **1970**, 2659.

Table III. Reactions of an (α-Acetylvinyl)cuprate Reagent with Electrophiles

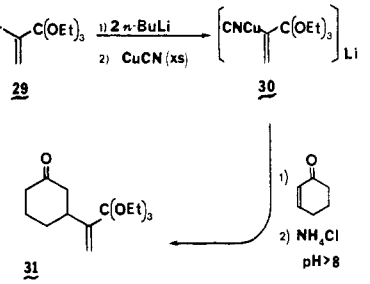
electrophile	products	ratio[a]	β-CH_3 chemical shift,[b] δ	% yield[c]
$C_6H_{13}CHO$	 23	30	1.72	89
	 24	70	1.69	
PhCHO	 25	30	1.85	94
	 26	70	1.83	
	 27	43	1.83	89
	 28	57	1.70	

[a] Determined by 360-Hz ^1H NMR integration of the β-CH_3. [b] $CDCl_3$ solution. [c] Combined yield of isomers after chromatography.

in Table III. The same allenoate steric control mechanism can be invoked to explain the selectivity observed. Indeed, the major isomer of the product results from preferential attack of the electrophilic species on the least hindered side of the allenoate. Fleming and Perry[42] have isolated an allenic enol ether by O-silylation of the complex obtained by lithium dimethylcuprate addition to a β-silyl ynone, providing chemical evidence for the allenoate intermediate.

As further chemical evidence for this mechanism, we sought to generate a functionalized vinylcuprate reagent having the same oxidation state as the ester but unable to achieve an allenoate structure. Stetter and Uerdinger[43] have reported the preparation of 2-bromo-3,3,3-trieth-oxypropene (**29**), the ethyl ortho ester of 2-bromoacrylic acid. Subsequently, Goldberg and Dreiding[26] reported metallation of this vinyl bromide with *n*-butyllithium. To our knowledge, no further reports of reactions of this vinyllithio species have appeared. We have found the metallation procedure more reproducible when 2 equiv of *n*-butyllithium is used to generate the vinyl anion (see Scheme IV). Generation of the cyanocuprate reagent **30** was accomplished in tetrahydrofuran at −40 °C. Reaction of **30** with cyclohexenone provided the 1,4-addition product

Scheme IV



31. The "normal" vinylcuprate reactivity indicated that an allenoate intermediate was not formed. Incidentally, this reagent also provided the first method for the direct conjugate addition of an unsubstituted α-acrylate anion to an enone.

In conclusion, the addition of cuprate reagents to α-acetylenic esters and ketones generates a reactive anionic intermediate. At low temperatures (−78 °C) very reactive electrophiles will react with a vinylic cuprate intermediate, producing a C-alkylated product having olefin geometry attributable to cis addition followed by alkylation with retention of configuration. In the case of alkylhexynylcuprates, the intermediate will undergo condensation reactions with carbonyl compounds at or above 0 °C. The product olefin geometry is then dependent on the steric interactions of an allenoate intermediate with the substrate. Analogous reactivity is observed with other enolizable cuprate reagents. However, if the ability to enolize is removed, as in the case of the ortho ester propenylcuprate **30**, "normal" cuprate reactivity is restored.

Experimental Section

General Procedures. Infrared spectra were obtained on a Perkin-Elmer 727B spectrophotometer. ^1H NMR spectra were obtained on a Varian T-60A or a Bruker 360 spectrometer with tetramethylsilane as the standard. ^{13}C NMR spectra were obtained on a JEOL-FX90Q spectrometer with deuteriochloroform as the standard ($CDCl_3$, 77.00 ppm).

Elemental analyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, MI. Column chromatography was carried out on EM Reagents silica gel 60 (230–400 mesh ASTM). Preparative thin-layer chromatography was carried out on EM Reagents silica gel 60 F-254 precoated (2 mm) PLC plates. Diethyl ether was freshly distilled from LAH (under N_2). Hexyne and ethyl propiolate were purchased from Farchan and used without further purification. Technical-grade cuprous cyanide was purchased from J.T. Baker. Ninety-eight percent cuprous iodide was purchased from Alfa and purified by the procedure of House et al.[44] Commercial methyllithium, low halide in ether, was obtained from Alfa and titrated[45] prior to use. All reactions were carried out in flame-dried glassware under an inert atmosphere of dry nitrogen.

Preparation of 1c (R = Me). A 0.48-mL (4.2 mmol) sample of hexyne was dissolved in 20 mL of dry ether and the solution cooled to 0 °C. A 2.53-mL (4 mmol) sample of a 1.58 M solution of methyllithium was added and the mixture stirred for 15 min. The white slurry of hexynyllithium was transferred to a second flask (via cannula) that contained 0.78 g (4.1 mmol) of ultrapure CuI suspended in 20 mL of ether at −20 °C. The bright yellow slurry was stirred for 50 min at 0 °C and then cooled to −78 °C for 30 min. A 2.53-mL (4 mmol) sample of a 1.58 M solution of methyllithium was added, and the mixture was stirred for 30 min at −78 °C. A 0.41-mL (4 mmol) sample of ethyl propiolate was added to the rapidly stirred lithium hexynylmethylcuprate, producing a bright orange heterogeneous mixture. The reagent

(42) Fleming, I.; Perry, D. A. *Tetrahedron* **1981**, *37*, 4027.
(43) Stetter, H.; Uerdinger, W. *Synthesis* **1973**, 207.
(44) House, H. O.; Chu, C. Y.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, *40*, 1860.
(45) Watson, S. C.; Eastman, J. E. *J. Organomet. Chem.* **1967**, *9*, 165.

was ready for use after stirring 45–60 min at −78 °C.

Standard Workup Conditions for Reactions of 1c with Electrophiles. After reaction was complete, the reaction mixture was filtered through a pad of Celite, and the layers were separated. The organic phase was diluted with an additional 50 mL of ether and then washed with 25 mL of NH_4Cl (saturated aqueous) and then with 25 mL of brine and dried over $MgSO_4$.

Reaction of 1c (R = Bu) with Electrophilic Halogen Sources. (*E*,*E*)-6,7-Dicarbethoxy-5,7-dodecadiene (2; 69%). Bromine (0.96 g, 6 mmol) was added to a stirred solution of 1c (R = Bu; 4 mmol in 40 mL of ether) at −78 °C. After stirring 1 h at −78 °C, the reaction mixture was quenched by the addition of 5 mL of NH_4Cl (saturated aqueous). The crude product was isolated by the standard workup conditions after warming to room temperature. The product was purified by chromatography on silica gel with 30% ethyl acetate/hexane as eluent: ^1H NMR (CCl_4) δ 6.82 (t, 2 H, J = 7 Hz), 4.10 (q, 4 H), 2.25–1.78 (4 H), 1.7–0.7 (20 H); IR (liquid film) ν_{CO} 1720, $\nu_{C=C}$ 1635 cm^{-1}; ^{13}C NMR ($CDCl_3$) 166.44, 146.18, 127.71, 60.53, 30.30, 29.33, 22.39, 14.21, 13.78 ppm.

Anal. Calcd for $C_{18}H_{30}O_4$: C, 69.69; H, 9.67. Found: C, 69.65; H, 9.78.

Ethyl 2-Chloroheptenoate (3). A suspension of *N*-chlorosuccinimide (1.06 g, 8 mmol) in 15 mL of tetrahydrofuran was added to a solution of 1c (R = Bu; 4 mmol) in 40 mL of ether at −78 °C, and the mixture was stirred for 1 h. The reaction mixture was quenched by the addition of 5 mL of NH_4Cl (saturated aqueous) and then subjected to the standard workup conditions after warming to room temperature. Two compounds were obtained by chromatography of the crude product on silica gel with 30% ethyl acetate/hexane as eluent; ethyl 2-chloroheptenoate (3) and the dimer 2 in a ratio of 1.7:1 (95% combined yield). 3: ^1H NMR (CCl_4) δ 7.07 and 6.90 (overlapping t, 1 H), 4.18 (q, 2 H), 2.6–2.1 (2 H), 1.6–0.7 (10 H); IR (liquid film) ν_{CO} 1720, $\nu_{C=C}$ 1640 cm^{-1}.

Anal. Calcd for $C_9H_{15}ClO_2$: C, 56.74; H, 7.87; Cl, 18.58. Found: C, 56.72; H, 7.85; Cl, 18.31.

Reactions with Epoxides. 3-Carbethoxypent-3-en-1-ol (4; 40%). An ether solution of ethylene oxide (0.13 g, 3 mmol; in 10 mL) was added dropwise over a period of 20 min to an ether solution of 1c at −20 °C, and the mixture was then stirred 1 h at −20 °C. The reaction mixture was quenched (at −20 °C) by the addition of 5 mL of NH_4Cl (saturated aqueous) and subjected to the standard workup after warming to room temperature. The product could not be purified for correct elemental analysis: ^1H NMR (CCl_4) δ 6.97 (q, 1 H, J = 7 Hz), 4.08 (q, 2 H), 3.3–3.0 (4 H), 1.67 (d, 3 H, J = 7 Hz), 1.23 (t, 3 H); IR (liquid film) ν_{OH} 3500, ν_{CO} 1725, $\nu_{C=C}$ 1640 cm^{-1}.

3-Carbethoxy-5-hydroxy-2-undecene (5; 61%). An ether solution of octene oxide (0.77 g, 6 mmol; in 10 mL) was added to 1c (8 mmol in 40 mL of ether) at −78 °C. The mixture was allowed to warm to room temperature for 5 h and then quenched by the addition of 5 mL of NH_4Cl (saturated aqueous) and subjected to standard workup. The product was chromatographed on silica gel with 30% ethyl acetate in hexane as eluent: ^1H NMR ($CDCl_3$) δ 6.00 (q, 1 H, J = 7 Hz), 4.27 (q, 2 H), 3.45–3.55 (m, 1 H), 1.87 (d, 3 H, J = 7 Hz), 1.55–1.65 (m, 2 H), 1.31 (t, 3 H), 1.3–1.2, 0.9–0.8 (13 H); IR (liquid film) ν_{OH} 3450, ν_{CO} 1720, $\nu_{C=C}$ 1655 cm^{-1}; ^{13}C NMR ($CDCl_3$) 169.20, 140.17, 129.12, 74.08, 60.42 ppm.

Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.44; H, 10.74. Found: C, 69.60; H, 10.84.

Basic Hydrolysis of Hydroxy Ester 5. A 160-mg sample of 5 was dissolved in 2 mL of ether under an inert atmosphere. Claisen's alkali (2 mL) was then added and the mixture was stirred at room temperature for 2 h. The solution was cooled to 0 °C and 8 mL of ether was added. The solution was acidified by gradual addition of 6 N HCl to a Congo Red endpoint (pH 3–5). Water was then added, and the layers were separated. The aqueous layer was extracted with ether (2 × 30 mL), and the combined organic phases were dried over $MgSO_4$. The solvent was removed in vacuo, affording the crude hydroxy acid 6 (98% yield). The crude acid was carried on directly to the lactone 7.

Lactonization of 6. A 250-mg sample of 6 was added to 5 mL of 48% HBr and the solution was heated to 60 °C (bath temperature) for 12 h. The mixture was cooled to room temperature and 20 mL of water was added. The aqueous phase was extracted with ether (3 × 30 mL), and the combined ether extracts were dried over $MgSO_4$. The solvent was removed in vacuo and the product chromatographed on silica gel with 10% ethyl acetate in hexane as eluent. 7: ^1H NMR (CCl_4) δ 6.92 (q, 1 H, J = 7 Hz), 3.75–3.67 (m, 1 H), 2.27–2.0 (m, 2 H), 1.78 (d, 3 H, J = 7 Hz), 1.45–0.8 (13 H); IR (liquid film) ν_{CO} 1775, $\nu_{C=C}$ 1690 cm^{-1}. For comparison to a complementary method, see ref 46.

General Conditions for 1,2-Addition Reactions with Carbonyl Compounds. The ketone or aldehyde compound was added to a solution of 1c in ether in a ratio of 1:2 (carbonyl/cuprate) at −78 °C. The mixture was then allowed to warm to room temperature and stirred an additional hour and then quenched by the addition of 10 mL of NH_4Cl (saturated aqueous) and subjected to standard workup conditions. The product allylic alcohol was chromatographed on silica gel with 40% ethyl acetate in hexane.

Ethyl (*Z*)-2-(Cyclopentanoxy)-2-butenoate (8; 96%): ^1H NMR ($CDCl_3$) δ 6.12 (q, 1 H, J = 7 Hz), 4.28 (q, 2 H), 1.90 (d, 3 H, J = 7 Hz), 1.83 (s, 8 H), 1.33 (t, 3 H); IR (liquid film) ν_{OH} 3450, ν_{CO} 1720, $\nu_{C=C}$ 1650 cm^{-1}.

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.69; H, 9.00. Found: C, 66.61; H, 8.97.

Ethyl (*Z*)-2-(Cyclopentanoxy)-2-heptenoate (9; 98%): ^1H NMR (CCl_4) δ 5.85 (t, 1 H, J = 7 Hz), 4.18 (q, 2 H), 2.5–2.0 (m, 2 H), 1.75 (br s, 8 H), 1.32 (t, 3 H), 1.5–0.7 (7 H); IR (liquid film) ν_{CO} 1720, $\nu_{C=C}$ 1660 cm^{-1}; ^{13}C NMR ($CDCl_3$) 169.31, 137.62, 135.56, 82.36, 60.42 ppm.

Anal. Calcd for $C_{14}H_{24}O_3$: C, 70.02; H, 9.99. Found: C, 70.19; H, 9.89.

Ethyl (*Z*)-2-(2-Methylcyclohexan-1-oxy)-2-butenoate (10; 99%): ^1H NMR ($CDCl_3$) δ 5.97 (q, 1 H, J = 7 Hz), 4.23 (q, 2 H), 1.95–1.15 (9 H), 1.77 (d, 3 H, J = 7 Hz), 1.32 (t, 3 H), 0.82 (d, 3 H, J = 6 Hz); IR (liquid film) ν_{OH} 3525, ν_{CO} 1720, $\nu_{C=C}$ 1660 cm^{-1}; ^{13}C NMR ($CDCl_3$) 169.31, 142.17, 126.62, 75.32, 60.36 ppm.

Anal. Calcd for $C_{13}H_{22}O_3$: C, 69.04; H, 9.73. Found: C, 69.08; H, 9.65.

Ethyl (*Z*)-2-[4-(1,1-Dimethylethyl)cyclohexan-1-oxy]-2-butenoate (11; 99%). The product obtained from 4-*tert*-butylcyclohexanone was a mixture of axial and equatorial isomers (50:50), which were clearly distinguished by the *tert*-butyl proton resonances, 0.83 ppm and 0.88 ppm. Only axial isomer was obtained pure by column chromatography. For the axial isomer: ^1H NMR ($CDCl_3$) δ 6.10 (q, 1 H, J = 7 Hz), 4.23 (q, 2 H), 2.1–1.0 (8 H), 1.82 (d, 3 H, J = 7 Hz), 1.34 (t, 3 H), 0.82 (s, 9 H); IR (liquid film) ν_{OH} 3510, ν_{CO} 1720, $\nu_{C=C}$ 1660 cm^{-1}; ^{13}C NMR ($CDCl_3$) 169.69, 137.02, 131.19, 72.83, 60.58 ppm.

Anal. Calcd for $C_{16}H_{27}O_3$: C, 71.93; H, 10.10. Found: C, 71.67; H, 10.07.

Ethyl (*Z*)-2-(Cycloheptan-1-oxy)-2-butenoate (12; 96%): ^1H NMR ($CDCl_3$) δ 5.97 (q, 1 H, J = 7 Hz), 4.27 (q, 2 H), 2.1–1.4 (12 H), 1.77 (d, 3 H, J = 7 Hz), 1.33 (t, 3 H); IR (liquid film) ν_{OH} 3500, ν_{CO} 1720, $\nu_{C=C}$ 1660 cm^{-1}; ^{13}C NMR ($CDCl_3$) 169.58, 141.79, 127.22, 76.19, 60.42 ppm.

Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.97; H, 9.82. Found: C, 68.96; H, 9.71.

3-Carbethoxy-4-hydroxy-4-methyl-2(*Z*),7-octadiene (13; 93%): ^1H NMR ($CDCl_3$) δ 6.05 (q, 1 H, J = 7 Hz), 6.0–5.5 (m, 1 H), 5.2–4.8 (m, 2 H), 4.28 (q, 2 H), 2.2–1.7 (4 H), 1.82 (d, 3 H, J = 7 Hz), 1.38 (s, 3 H), 1.33 (t, 3 H); IR (liquid film) ν_{OH} 3460, ν_{CO} 1720 cm^{-1}.

Anal. Calcd for $C_{13}H_{20}O_3$: C, 70.54; H, 9.32. Found: C, 70.48; H, 9.25.

Ethyl 2-Ethylidene-3-(1-cyclohexen-1-yl)-3-hydroxybutenoate (14; 92%): ^1H NMR ($CDCl_3$) δ 6.02 (q, 1 H, J = 7 Hz), 5.70 (m, 1 H), 4.18 (q, 2 H), 3.55 (m, 1 H), 2.2–1.1 (8 H), 1.82 (d, 3 H, J = 7 Hz), 1.42 (s, 3 H), 1.25 (t, 3 H); IR (liquid film) ν_{OH} 3460, ν_{CO} 1720 cm^{-1}.

Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.54; H, 9.32. Found: C, 70.48; H, 9.25.

Ethyl 2-Ethylidene-3-hydroxynonanoate (15/16; 80%). 15 (*Z*): ^1H NMR ($CDCl_3$) δ 6.19 (q, 1 H, J = 7 Hz), 4.24 (q, 2 H), 4.16 (m, 1 H), 1.95 (d, 3 H, J = 7 Hz), 1.4–1.2 (10 H), 1.30 (t, 3 H), 0.9–0.8 (3 H).

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16 (*E*): ^{1}H NMR ($CDDcl_3$) δ 6.84 (q, 1 H, J = 7 Hz), 4.18 (q, 2 H), 4.10 (m, 1 H), 1.80 (d, 3 H, J = 7 Hz), 1.4–1.2 (10 H), 1.28 (t, 3 H), 0.9–0.8 (3 H).

Anal. Calcd for $C_{13}H_{24}O_3$: C, 68.44; H, 10.52. Found: C, 68.32; H, 10.60.

Ethyl 2-Ethylidene-3-hydroxy-4-methylpentanoate (17/18; 89%). **17** (*Z*): ^{1}H NMR ($CDCl_3$) δ 6.14 (q, 1 H, J = 7 Hz), 4.23 (q, 2 H), 3.77 (1 H), 1.95 (d, 3 H, J = 7 Hz), 1.30 (t, 3 H), 0.96 (d, 3 H), 0.79 (d, 3 H).

18 (*E*): ^{1}H NMR ($CDCl_3$) δ 6.93 (q, 1 H, J = 7 Hz), 4.08 (q, 2 H), 4.05 (m, 1 H), 1.82 (d, 3 H, J = 7 Hz), 1.23 (t, 3 H), 1.06 (d, 3 H), 0.74 (d, 3 H).

Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.54; H, 9.67. Found: C, 64.72; H, 9.41.

Ethyl 2-Ethylidene-3-hydroxy-3-phenylpropanoate (19/20; 86%). **19** (*Z*): ^{1}H NMR ($CDCl_3$) δ 6.29 (q, 1 H, J = 7 Hz), 5.41 (br d, 1 H), 4.12 (q, 2 H), 2.03 (d, 3 H, J = 7 Hz), 1.17 (t, 3 H).

20 (*E*): ^{1}H NMR ($CDCl_3$) δ 7.18 (q, 1 H, J = 7 Hz), 5.70 (br d, 1 H), 4.15 (q, 2 H), 1.96 (d, 3 H, J = 7 Hz), 1.23 (t, 3 H).

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.93; H, 7.27. Found: C, 70.83; H, 7.29.

Preparation and Reaction of Lithium (4-Methyl-2-oxohepten-3-yl)hexynylcuprate (22). Lithium hexynylmethylcuprate (4 mmol in 20 mL of ether) was prepared as described previously, and 2-oxo-3-heptyne (0.44 g, 4 mmol) was added at −78 °C. The light orange mixture was stirred 1 h at −78 °C, and the electrophile (2 mmol) was then added. The mixture was stirred an additional hour at −78 °C and allowed to warm to room temperature before quenching with 5 mL of NH_4Cl (saturated aqueous). The layers were separated after filtering through a pad of Celite, and the organic phase was washed with brine and then dried over $MgSO_4$. The solvent was evaporated and the product chromatographed on silica gel with 25% ethyl acetate/hexane as eluent.

2-Oxo-3-(2-pentylidene)decan-3-ol (89%). A mixture of **23** and **24** was obtained in a ratio of 30:70, which were not separable by chromatography: ^{1}H NMR ($CDCl_3$) δ 4.5–4.6 (m, CH(OH)), 2.32, 2.30 (s, CH_3CO), 2.05, 1.96 (t, CH_2C=), 1.72, 1.69 (s, =C-(R)CH_3); IR (liquid film) ν_{OH} 3460, ν_{CO} 1695, $\nu_{C=C}$ 1665, ν_{COCH_3} 1380 cm^{-1}; ^{13}C NMR ($CDCl_3$) 208.70, 70.45, 70.12, 21.20, 17.14 ppm.

Anal. Calcd for $C_{15}H_{28}O_2$: C, 75.02; H, 11.66. Found: C, 75.13; H, 11.54.

3-Oxo-2-(2-pentylidene)-1-phenylbutanol (94%). A mixture of **25** and **26** was obtained in a ratio of 30:70, which were not separable by chromatography: ^{1}H NMR ($CDCl_3$) δ 7.36–7.22 (arom), 1.97 (s, CH_3CO), 1.85, 1.,3 (s, =C(R)CH_3); IR (liquid film) ν_{OH} 3440, ν_{CO} 1690, ν_{arom} 1605, 1500, ν_{COCH_3} 1380, 1460 cm^{-1}; ^{13}C NMR ($CDCl_3$) 208.10, 71.20, 70.93, 32.85, 32.69, 21.26, 17.79 ppm.

Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.60; H, 8.62. Found: C, 77.71; H, 8.73.

4-Acetyl-5-methyl-1,4-octadiene (89%). A mixture of **27** and **28** was obtained in a ratio of 43:57, which were not separable by chromatography: ^{1}H NMR ($CDCl_3$) δ 5.81–5.69, 5.05–4.98 (RCH=CH_2), 3.03–3.01, 3.00–2.97 ($CHCH_2$), 2.20, 2.19 (s, $COCH_3$), 1.83, 1.70 (=C(R)CH_3); IR (liquid film) ν_{CO} 1690, $\nu_{C=C}$ 1645, 1620, 920 cm^{-1}.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.53; H, 10.84. Found: C, 79.66; H, 10.96.

Lithium 2-(3,3,3-Triethoxypropenyl)cyanocuprate (30). A 3.2-mL sample of *n*-butyllithium (2.5 M in hexane, 8 mmol) was added to a solution of freshly distilled 2-bromo-3,3,3-triethoxy-1-propene (1.01 g, 4 mmol) in 20 mL of tetrahydrofuran at −78 °C. The solution was stirred for 1 h and then transferred (via cannula) to a suspension of curpous cyanide (0.37 g, 4.1 mmol) in 20 mL of tetrahydrofuran at −40 °C. The clear, yellow/brown colored solution of **30** was ready for use after stirring 1 h at −40 °C.

Triethyl 2-(3-Cyclohexanonyl)orthopropenoate (31; 68%). To a solution of **30** (4 mmol) in 40 mL of tetrahydrofuran was added a 0.26-g sample of cyclohexenone (2.7 mmol), and the mixture was stirred for 90 min at −50 °C. After warming to −30 °C (20 min), the reaction mixture was quenched by the addition of 5 mL of NH_4Cl (saturated aqueous) and allowed to warm to room temperature. The mixture was filtered through a pad of Celite, and the layers were separated. The aqueous layer was extracted with ether (2 × 50 mL), and the combined organic phases were dried over K_2CO_3. The solvent was removed under reduced pressure and the crude product was chromatographed on basic alumina with 4:1 petroleum ether/ether as eluent: ^{1}H NMR (CCl_4) δ 5.6–5.1 (m, 2 H), 3.42 (q, 6 H), 2.4–1.3 (9 H), 1.13 (t, 9 H); IR (liquid film) ν_{CO} 1715, $\nu_{C=C}$ 1680 cm^{-1}.

Anal. Calcd for $C_{15}H_{26}O_4$: C, 66.69; H, 9.62. Found: C, 66.41; H, 9.42.

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Registry No. **1c** (R = Me), 87351-23-3; **1c** (R = Bu), 87351-24-4; **2**, 87351-27-7; (*E*)-**3**, 87351-28-8; (*Z*)-**3**, 87351-29-9; **4**, 87351-30-2; **5**, 87351-31-3; **6**, 87351-32-4; **7**, 87351-33-5; **8**, 87351-34-6; **9**, 87351-35-7; **10**, 87351-36-8; **11** (isomer 1), 87351-37-9; **11** (isomer 2), 87419-64-5; **12**, 87351-38-0; **13**, 87351-39-1; **14**, 87351-40-4; **15**, 87351-41-5; **16**, 87351-42-6; **17**, 87351-43-7; **18**, 87351-44-8; **19**, 87351-45-9; **20**, 87351-46-0; **22**, 87351-25-5; **23**, 87351-47-1; **24**, 87351-48-2; **25**, 87351-49-3; **26**, 87351-50-6; **27**, 87351-51-7; **28**, 87351-52-8; **30**, 87351-26-6; **31**, 87351-53-9; CuI, 7681-65-4; 1-hexyne, 693-02-7; ethyl propiolate, 623-47-2; lithium hexynylmethylcuprate, 41799-09-1; bromine, 7726-95-6; *N*-chlorosuccinimide, 128-09-6; ethylene oxide, 75-21-8; octene oxide, 2984-50-1; 2-oxo-3-heptyne, 26059-43-8; 2-bromo-3,3,3-triethoxy-1-propene, 42335-47-7; cuprous cyanide, 544-92-3; cyclohexenone, 930-68-7; cyclopentanone, 120-92-3; 2-methylcyclohexanone, 583-60-8; 4-(1,1-dimethylethyl)cyclohexanone, 98-53-3; cycloheptanone, 502-42-1; hex-5-en-2-one, 109-49-9; 1-acetylcyclohexene, 932-66-1; heptanal, 111-71-7; 2-methylpropanal, 78-84-2; benzaldehyde, 100-52-7; 3-bromo-1-propene, 106-95-6.