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The Chemistry of Carbanions. XXVII. A Convenient Precursor for the Generation of Lithium Organocuprates[1]

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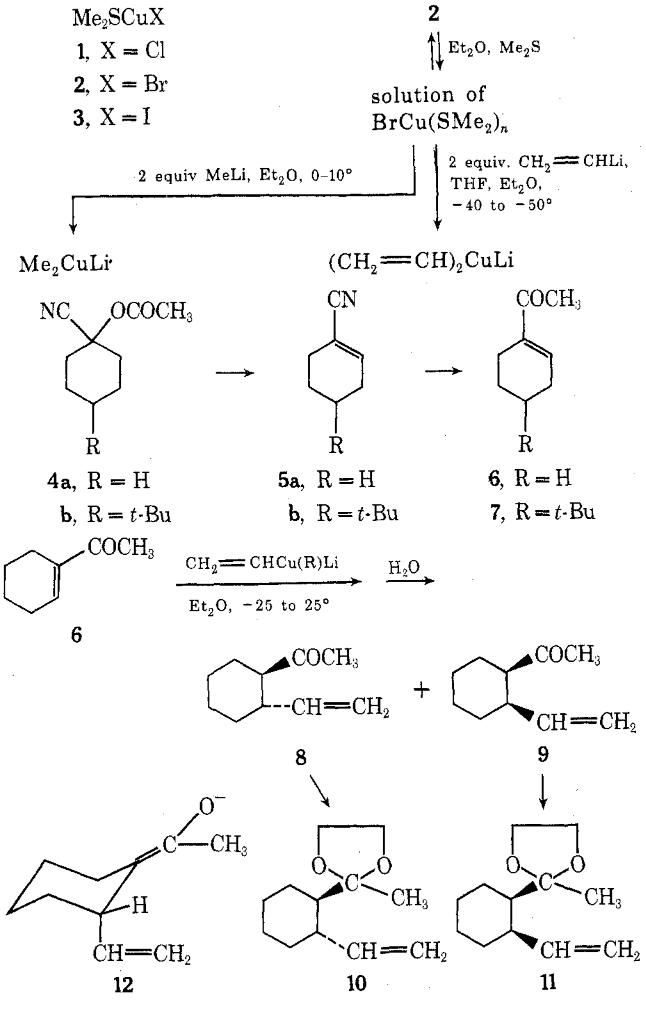
To avoid side reactions resulting from the presence of Cu(II) compounds and other metal salt impurities in the Cu(I) salts used to form lithium organocuprate reagents, use of the easily prepared, crystalline complex, Me_2S-CuBr(**2**), is recommended. This complex **2** is readily soluble in mixtures of Me_2S and ethereal solvents, and the sulfide ligand, Me_2S (bp 37°), is easily separated from reaction products. This procedure is illustrated with several additional reactions involving the cuprate reagents, Me_2CuLi and $(CH_2{=}CH)_2CuLi$. The difficultly reduced enone **22** and the moderately acidic saturated ketones **32** and **37** undergo a relatively slow reaction with Me_2CuLi at 25° to form enolate anions that are inert to further reaction with the cuprate. The saturated ketones **32**, **37**, and **40** are also slowly converted to alcohol products by a solution of Me_2CuLi at 25°; this latter reaction may involve a small concentration of MeLi present in equilibrium with the cuprate reagent.

From various studies of the preparation and use of lithium organocuprate reagents,[2] it has become apparent that two practical problems complicating the general use of these reagents are inadvertent thermal decomposition[3] and inadvertent oxidation leading to coupling of the organic residues.[4] Both of these initial side reactions often lead to the formation of Cu(0), which usually appears as a black colloidal suspension in the reaction mixture and is believed to catalyze the decomposition of still more copper reagent.[5]

The most common preparative procedure for lithium dialkylcuprates consists of addition of 2 molar equiv of an alkyllithium solution to an ethereal slurry of one of the commercially available Cu(I) salts, CuI, CuBr, or CuCl. As noted previously,[6] use of this procedure may be accompanied by partial decomposition, especially if the reagent is one of the relatively thermally unstable cuprates, such as a vinyl derivative or a derivative with alkyl substituents that have β H atoms. Among the causes of this decomposition are the presence of other transition metal impurities in the commercial Cu(I) salts and the occurrence of local overheating during the exothermic reaction of alkyllithium with insoluble Cu(I) salts.[6] Another cause of decomposition is the presence of significant amounts of Cu(II) salts, which are effective oxidants for cuprates,[4,6b] in many commercial samples of Cu(I) halides. Other Cu(I) compounds that have been used to form cuprate reagents include the insoluble derivatives CuCN[7] and n-$C_3H_7C{\equiv}CCu$[8] and the more soluble derivatives t-BuOCu,[9] PhSCu,[9] and t-BuC$\equiv$CCu.[6a] The latter, soluble Cu(I) acetylide offers the advantage of being a scavenger for oxidizing agents such as Cu(II) salts, undergoing oxidation to form the volatile diyne, t-BuC$\equiv$CC$\equiv$CBu-t.[6] Unfortunately, the advantages of ether solubility and "protection" from oxidants offered by t-BuC$\equiv$CCu are offset by the fact that the precursor, t-BuC$\equiv$CH, is not presently available commercially at a reasonable cost. This fact has led us to examine other possible Cu(I) derivatives that might offer the advantages of both ether solubility and easy purification to separate unwanted Cu(II) impurities. In earlier work,[6,10] we have noted the solubility advantages offered by several Cu(I) halide complexes such as n-Bu_3PCuI, $(MeO)_3PCuI$,$(MeO)_3PCuBr$, and especially, the *liquid complexes* $(n\text{-}Bu_2S)_2CuI$ and $(n\text{-}Bu_2S)_2CuBr$. The use of these complexes in synthetic work is made less attractive by the relatively high boiling points of the ligands, n-Bu_2S (bp 189°), n-Bu_3P [bp 150° (50 mm)], and $(MeO)_3P$ (bp 112°) that complicate their removal from reaction products and by the persistent disagreeable odor associated with phosphine and phosphite ligands. We were attracted by reports indicating that complexes of certain Cu(I) salts with the ligand Me_2S (bp 37°) were both soluble in ether[11] and could be obtained as crystalline solids.[12] Upon exploring the reaction of Me_2S with Cu(I) halides, we found that each of the 1:1 complexes **1**, **2**, and **3** (Scheme I) could easily be obtained as a *colorless*, crystalline solid that was readily separated from Cu(II) contaminants. Since Cu(II) salts form solutions of highly colored complexes with Me_2S (dark green solution with $CuCl_2$ and dark red solution with $CuBr_2$), the absence of these Cu(II) impurities in the colorless Cu(I) complexes is readily discerned. Although the iodide complex **3** spontaneously lost Me_2S on standing, the bromide complex **2** proved to be both convenient to prepare in pure form and stable to storage. Thus, by conversion to the complex **2**, commercial samples of CuBr are readily purified to remove Cu(II) salts and other impurities.

Although none of the complexes **1–3** was soluble in ether, solutions were readily obtained when additional Me_2S was added. The bromide complex **2** could be dissolved in Et_2O, PhH, or $CHCl_3$ when Me_2S was added, suggesting the reversible formation of complexes such as $(Me_2S)_2CuBr$ or $(Me_2S)_3CuBr$ in these solutions. Treatment of solutions of the complex **2** in Et_2O–Me_2S with 2 molar equiv of either MeLi (at 0–10°) or $CH_2{=}CHLi$ (at −40 to −50°) produced solutions of the corresponding cuprate reagents, Me_2CuLi and $(CH_2{=}CH)_2CuLi$.

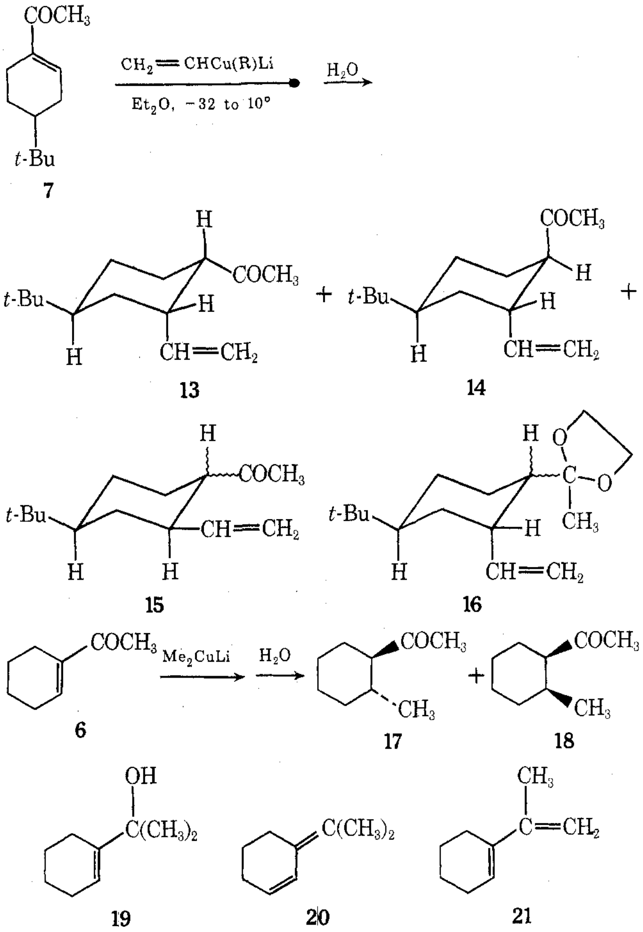
Scheme I



The effectiveness of various cuprate preparations was initially studied for the conjugate addition of vinyl groups to the unsaturated ketones **6** and **7**. From reactions of the enone **6** with $(CH_2{=}CH)(t\text{-}BuC{\equiv}C)CuLi$,[6] $(CH_2{=}CH)_2CuLi$ (from a *solution* of Me_2SCuBr), and $(CH_2{=}CH)_2CuLi$ (from a *suspension* of CuI), the yields of adducts **8** and **9** were 64, 78, and 69%, respectively. The product obtained from reaction with $(CH_2{=}CH)_2CuLi$ (from a *suspension* of CuI) was contaminated with an alcohol by-product believed to be the 1,2 adduct of the ketone **6** with $CH_2{=}CHLi$. This same type of by-product was also evident when the $(CH_2{=}CH)_2CuLi$ was generated from a *suspension* of Me_2SCuBr in Et_2O (containing no excess Me_2S). The initial mixture of ketones formed in the reactions contained ca. 80% of the cis ketone **9** and ca. 20% of the trans ketone **8** as expected from the kinetically controlled protonation of the intermediate enolate **12**.[13] After equilibration, the mixture of ketones contained ca. 15% of the cis isomer **9** and ca. 85% of the trans isomer **8** (the isomer allowing both substituents to be equatorial). Each of the ketone products was also characterized as the corresponding ketal **10** or **11**.

Reaction of the enone **7** (Scheme II) with $(CH_2{=}CH)(t\text{-}BuC{\equiv}C)CuLi$[6] or with $(CH_2{=}CH)_2CuLi$ (from a solution of Me_2SCuBr) formed a mixture of stereoisomeric adducts **13–15** in yields of 88 and 86%, respectively. The product mixture contained ca. 80% of the ketone **13**, ca. 15% of the epimeric ketone **14**, and ca. 5% of the stereoisomeric ketones **15** with equatorial vinyl substituents. Thus, the conjugate addition of a vinyl group, like the previously described[6] conjugate addition of a methyl group, to the enone **7** occurs predominantly from the direction that introduces an axial substituent.

Scheme II

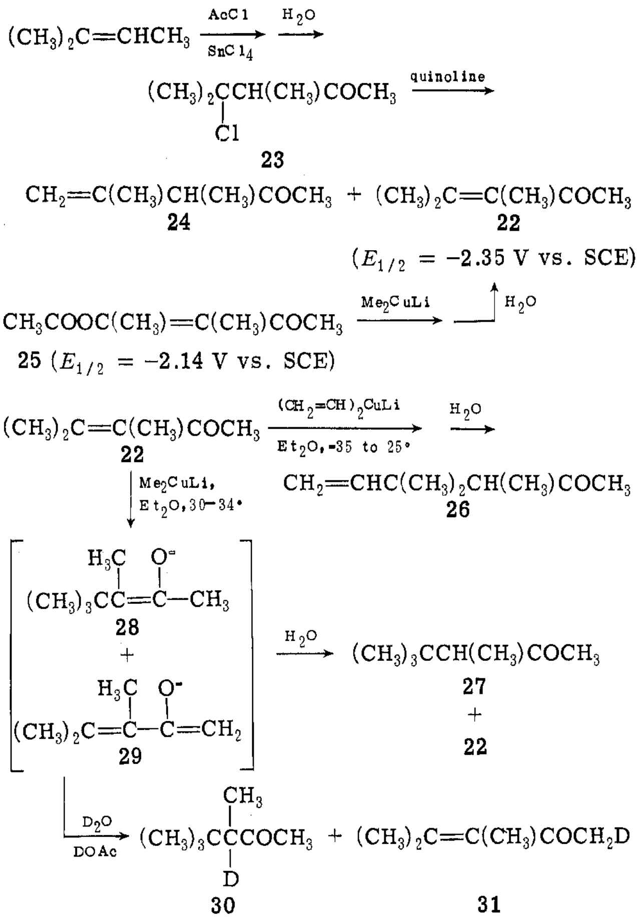


Reaction of the enone **6** with Me_2CuLi (from a *solution* of Me_2SCuBr) at 20–25° afforded a mixture of the stereoisomeric ketones **17** (21% of the mixture) and **18** (79% of the mixture) in 86% yield. Prompted by a recent report[14a] suggesting that Me_2CuLi adds in a 1,2 manner to enones at −78°, we also performed several reactions in which Me_2CuLi (*preformed at 25°*) was cooled to −78° and then treated with the enone **6**. In each of these experiments we observed the separation of only very small amounts of $(MeCu)_n$ while the reaction solutions were kept at −60 to −78° for 60–80 min. When the reaction solution was warmed to 20° before hydrolysis with aqueous NH_4Cl, an abundant precipitate of $(MeCu)_n$ separated as the solution was warmed above −20 to −10° and the adducts **17** and **18** were obtained in 70% yield. In another experiment where aqueous NH_4Cl was added to the cold (−60 to −70°) solution, the temperature rose to −20° during the hydrolysis and the adducts **17** and **18** were obtained in 11% yield. Finally, when the cold reaction solution was kept below −60° throughout the dropwise addition of a precooled mixture of MeOH and HOAc, the yield of adducts **17** and **18** was 1.3%. In each of these experiments the only other component detected in the crude product was the unchanged enone **6** and we found no indication that the alcohol **19** (or its dehydration products **20** or **21**) was present. When we attempted to prepare the Me_2CuLi by addition of MeLi to a cold (−50 to −60°) partial solution of Me_2SCuBr, formation of the cuprate reagent was clearly incomplete, since the yellow precipitate of $(MeCu)_n$ did not dissolve as excess MeLi was added. Reaction of this reagent [presumably a mixture of Me_2CuLi, $(MeCu)_n$, and MeLi] with the enone **6** at −45 to −25° resulted in the formation of the alcohol **19** (71% yield, isolated after GLC separation as the olefins **20** and **21**) accompanied by a 16% yield of the ketones **17** and **18** and 2% recovery of the enone **16.** Thus, with the enone **6**, we see no evidence that 1,2 addition of *preformed* Me_2CuLi occurs at low temperatures. Furthermore, a preformed solution of Me_2CuLi reacts only very slowly with the enone **6** to give conjugate addition products provided that the reaction temperature is maintained in the range −60 to −78° during both the reaction period *and during subsequent hydrolysis.* In view of these results, we are somewhat uncertain about how to interpret earlier reports of reactions of substituted cyclohexenone derivatives with Me_2CuLi at −78 to −80° in which both rapid conjugate addition[2a,14b] and failure of conjugate addition accompanied by partial 1,2 addition[14a] have been reported.

A recent report[15a] of the use of the mixed cuprate, $(CH_3)(CH_2{=}CH)CuLi$, for the selective conjugate addition of a vinyl unit to a cyclopentenone derivative also prompted us to examine this reaction with the enone **6.** When a preformed ethereal suspension of $(MeCu)_n$ was cooled to −20 to −30° and treated with $CH_2{=}CHLi$, reaction clearly occurred to dissolve the polymeric $(MeCu)_n$. Reaction of this mixture with the enone **6** at −20° for 20 min followed by warming produced a mixture of the methyl ketone **18** (4% yield) and the vinyl ketones **8** and **9** (73%). Our efforts to effect the same reaction by adding MeLi to a cold (−20 to −35°) ethereal slurry of $CH_2{=}CHCu$ followed by addition of the enone **6** resulted in the formation of a complex mixture in which the alcohol **19** (isolated after GLC separation as olefins **20** and **21**) was the major product. Thus, we concluded that addition of MeLi to ethereal $CH_2{=}CHCu$ at −20 to −35° did not result in complete conversion of $CH_2{=}CHCu$ to a cuprate reagent. These results indicated that, provided formation of the cuprate reagent $(CH_3)(CH_2{=}CH)CuLi$ is complete, the transfer of a vinyl group from the mixed cuprate to the enone **6** is somewhat more rapid than the transfer of a methyl group. However, the fact that some methyl transfer is observed (to form **17** and **18**) indicates that the difference in ease of transfer of methyl and vinyl groups is much less than the difference in ease of transfer of a methyl and an alkynyl group from a mixed cuprate such as $(Me)(t\text{-}BuC{\equiv}C)CuLi$ where no alkynyl group transfer was observed.[6a]

To probe further the question of relative reactivities of vinyl and methyl groups in a mixed cuprate, we synthesized (Scheme III) the trisubstituted enone **22** that was expected[16] to have a sufficiently negative reduction potential that its reaction with Me_2CuLi would be questionable.[6a] This enone **22** was prepared either by reaction of Me_2CuLi with the enol acetate **25**[17] or more simply by the acetylation of 2-methyl-2-butene.[18] Reaction of this enone **22** with $(CH_2{=}CH)_2CuLi$ (from a *solution* of Me_2SCuBr at −25 to 25°) produced, after hydrolysis, a mixture of the conjugate adduct **26** (55% yield) and the recovered enone **22** (17% recovery). Reaction of the enone **22** with the mixed reagent,

Scheme III

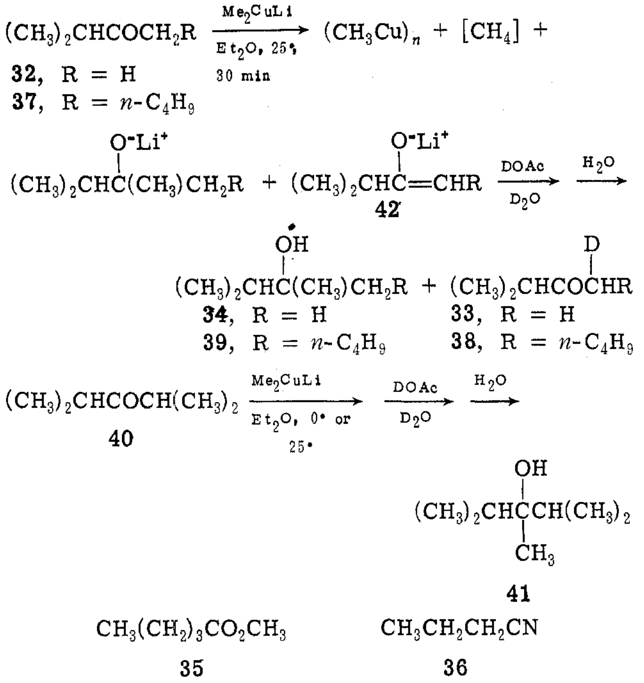


$(CH_2{=}CH)(CH_3)CuLi$, at −30 to 25° yielded a mixture of the ketones **26** (58%), **27** (2%), and **22** (13% recovery). Thus, with this acyclic enone **22**, as with the enone **6** and the previously described[15a] cyclopentenone derivatives, there is some preference for transfer of a vinyl group rather than a methyl group from the mixed cuprate, $(CH_3)(CH_2{=}CH)CuLi$. This apparent order of ease of transfer of organic ligands from mixed cuprates (vinyl > methyl ≫ alkynyl) is not what we would have expected based on an earlier study of conjugate additions of several mixed cuprates to two acyclic enones, methyl vinyl ketone and mesityl oxide, where the order alkyl > phenyl > alkynyl was suggested.[15b]

Our initial study of reaction of the enone **22** with Me_2CuLi (from either a *suspension* of CuI or a *solution* of Me_2SCuBr) led to a seemingly curious result. After an initial rapid reaction which produced, upon hydrolysis, the conjugate adduct **27** (20–35% yield) accompanied by the recovered enone **22**, no further reaction occurred even after prolonged reaction at 30–40° with excess Me_2CuLi. Further examination revealed that the initial rapid reaction was accompanied by gas evolution (presumably CH_4) to form a mixture of the adduct enolate **28** and the enolate **29** of the starting enone. Quenching this mixture with a mixture of D_2O and DOAc afforded the monodeuterated ketones **30** and **31.** Thus, with this difficultly reduced enone **22** [$E_{1/2}$ = −2.35 V (vs. SCE)] where an initial electron transfer is not energetically favorable,[19] reaction of the ketone **22** with Me_2CuLi to form an enolate **29** has clearly become a competitive reaction.[20]

Earlier studies had indicated that Me_2CuLi added only very slowly to methyl isobutyl ketone at 25° [21a] and that more than 85% of the di-*n*-butyl ketone mixed with Me_2CuLi at −10° was recovered when the reaction mixture was

Scheme IV



hydrolyzed after 15 min.[21b] The present results obtained with the enone **22** and Me_2CuLi suggested that the above results might be interpreted as conversions of saturated ketones to their enolates rather than the absence of any reaction. This idea was explored (Scheme IV) by treating Me_2CuLi solutions with several compounds having moderately acidic C–H bonds. The relatively acidic ketones **32** and **37**, having an α-methyl or an α-methylene group, clearly reacted [gas evolution and precipitation of $(MeCu)_n$] slowly during a period of 30 min with a Me_2CuLi solution at 25° to form mixtures of a lithium enolate **42** and an alkoxide. Quenching these reaction mixtures in a D_2O–DOAc mixture produced the alcohols **34** or **39** and deuterated ketones **33** or **38**. Under the same conditions, the less reactive and less acidic ester **35** and the nitrile **36** did not react in any way with a Me_2CuLi solution at 25° and were recovered unchanged after 30 min. The ketone **40**, which is less acidic than ketones **32** and **37**, reacted slowly at 25° [precipitation of $(MeCu)_n$ but no gas evolution] and, after quenching the mixture with D_2O–DOAc, the alcohol **41** (41% yield) and the nondeuterated ketone **40** were obtained. At 0° this addition reaction was much slower so that only 7–9% of the ketone **40** was converted to alcohol **41** after a 15-min reaction period.

Thus, we concluded that reaction mixtures containing saturated ketones and Me_2CuLi will undergo a slow reaction, especially if this reaction is run at 25° or is warmed to 25° before hydrolysis. With relatively acidic ketones of the types $RCOCH_3$ and $RCOCH_2R$, two competing reactions may be observed, one forming an enolate (cf. ref 14a) that is inert to further reaction and the other reaction forming an alcohol. With less acidic ketones only a slow addition to form an alcohol is observed. It should be noted that at 0° both of these reactions are very much slower than the conjugate addition of lithium organocuprate reagents to unsaturated carbonyl compounds. Thus, it is clearly possible to achieve selective addition of a cuprate reagent to an unsaturated carbonyl compound in the presence of an unconjugated carbonyl group provided one takes the precautions of not using a large excess of the cuprate reagent and of hydrolyzing the reaction mixture before it is warmed to room temperature. Finally, it should be noted that the slow conversion of relatively acidic ketones to enolate anions is apparently a reaction that is characteristic of lithium organocuprate reagents. Whether this enolate formation is facilitated by prior coordination of the carbonyl oxygen atom to the cuprate reagent is not known. However, the relatively slow reaction leading to saturated alcohol products may result, not from the slow addition of a cuprate reagent, but rather from the addition of a small concentration of an alkyllithium reagent present as a result of an equilibrium such as the following: $R_4Cu_2Li_2 \rightleftharpoons R_3Cu_2Li + RLi$.

Experimental Section[22]

Preparation of Starting Materials. Previously described procedures were used to prepare *tert*-butylacetylene[6] and to convert[6,23] 4-*tert*-butylcyclohexanone to its crude cyanohydrin (a mixture of epimers); the bulk of the material melted at 53–55° with a small amount of remaining material that melted at 63–65°. A mixture of 197.1 g (1.089 mol) of this cyanohydrin, 180 g of Ac_2O, and 12 ml of AcCl was refluxed for 5 hr, at which time TLC analysis (silica gel coating, CH_2Cl_2–Et_2O mixture as eluent) indicated complete conversion of the cyanohydrin (R_f 0.22) to its acetate **4b** (R_f 0.62). A small portion of the crude reaction mixture was partitioned between Et_2O and aqueous NaCl and the Et_2O solution was washed successively with aqueous $NaHCO_3$ and H_2O and then dried and concentrated. The crude acetate **4b**, which crystallized on standing, exhibited GLC peaks (silicone SE-52 on Chromosorb P) corresponding to 4-*tert*-butylcyclohexanone (retention time 3.9 min, ca. 2%) and the acetate **4b** (19.2 min, ca. 98%). The bulk of the crude acetate **4b** in Ac_2O solution was added dropwise to a tube packed with glass beads and heated to 550–570°.[24] A slow stream of N_2 was used to sweep the products into a cooled flask. The crude pyrolysis mixture contained (GLC, silicone SE-30 on Chromosorb P) primarily the unsaturated nitrile **5b** (retention time 7.8 min) accompanied by small amounts of 4-*tert*-butylcyclohexanone (4.2 min) and the unchanged acetate **4b** (10.9 min) as well as HOAc and Ac_2O. After the bulk of the HOAc had been removed by distillation (42–46° at 73 mm), the residue was partitioned between Et_2O and aqueous NaCl and the Et_2O solution was washed with aqueous $NaHCO_3$, dried, and concentrated. The residual unsaturated nitrile, a brown solid, was recrystallized from EtOH to separate 108 g (61%) of the nitrile **5b** as white plates, mp 45–46° (lit.[23] mp 45–46°), with ir and NMR spectra corresponding to those previously reported.[6] Reaction of nitrile **5b** with ethereal MeLi[6] yielded 65% of the ketone **7**, bp 67–81° (0.14 mm), $n^{25}D$ 1.4838–1.4842 [lit.[6] bp 141–143° (19 mm), $n^{25}D$ 1.4844], that exhibited a single GLC peak (retention time 12.8 min) on a column (silicone SE-30 on Chromosorb P) where the retention time of the starting nitrile **5b** was 9.4 min. The ir and NMR spectra of the product **7** corresponded to those previously reported.[6] Similarly, the cyanohydrin of cyclohexanone[25] was acetylated with refluxing Ac_2O containing a catalytic amount of AcCl and the crude acetate **4a** was pyrolyzed[24] by passing it through a tube heated to 575° along with a stream of N_2. An Et_2O solution of the crude pyrolysate was washed with aqueous $NaHCO_3$, dried, and distilled to separate the nitrile **5a**, bp 81–85° (14 mm), $n^{25}D$ 1.4810 [lit.[25] bp 86° (18 mm), $n^{20}D$ 1.4818].[26] After reaction of 9.54 g (89 mmol) of the nitrile **5a** with 184 mmol of MeLi in 140 ml of Et_2O for 20 min at 0–10°, the reaction mixture was poured into 500 ml of aqueous 1 *M* HCl and extracted with Et_2O. A mixture of the aqueous phase and 300 ml of hexane was refluxed for 17 hr to complete hydrolysis of the imine and then the hexane layer was separated and the aqueous phase was extracted with Et_2O. The combined organic layers were dried, concentrated, and distilled to separate 7.98 g (71%) of the ketone **6** as colorless liquid fractions, bp 88–93° (17 mm), $n^{25}D$ 1.4880–1.4894 [lit.[27] bp 63–65° (5 mm), $n^{20}D$ 1.4913]. Except for a minor low-boiling impurity in the first fraction, the product **6** exhibited a single GLC peak (retention time 8.9 min) on a column (silicone SE-30 on Chromosorb P) where the retention time for the starting nitrile **5a** was 7.4 min: ir (CCl_4) 1670 (conjugated C=O) and 1639 cm^{-1} (conjugated C=C); uv max (95% EtOH) 232 mμ (ϵ 13,900); NMR (CCl_4) δ 6.3–6.5 (1 H, m, vinyl CH) and 1.0–2.0 (11 H, m, aliphatic CH including a CH_3 singlet at 1.71).

Commercial Et_2O solutions containing about 1.6 *M* MeLi (halide free, Foote Mineral Co.) and THF solutions containing 1.6–2.1 *M* CH_2=CHLi (Lithium Corp. of America) were standardized by a double titration procedure[28] in which aliquots of the reagent, both before and after reaction with 1,2-dibromoethane, were titrated with standard aqueous acid. All of the commercial THF solutions of $CH_2{=}CHLi$ (Lithium Corp. of America) were contaminated with substantial amounts of mineral oil (presumably from the Li dispersion used) that contaminated the final product and had to be separated by fractional distillation. Commercial CuI (Fisher Scientific) was purified by solution in aqueous KI and reprecipitation.[29]

Preparation of the Me_2S Complexes of Copper(I) Halides. A. Me_2SCuBr (2).[12] To 40.0 g (279 mmol) of pulverized CuBr (Fisher Scientific) was added 50 ml (42.4 g, 682 mmol) of Me_2S (Eastman, bp 36–38°). The resulting mixture, which warmed during dissolution, was stirred vigorously and then filtered through a glass wool plug. The residual solid was stirred with an additional 30 ml (25 g, 409 mmol) of Me_2S to dissolve the bulk of the remaining solid and this mixture was filtered. The combined red solutions were diluted with 200 ml of hexane. The white crystals that separated were filtered with suction and washed with hexane until the washings were colorless. The residual solid was dried under nitrogen to leave 51.6 g (90%) of the complex **2** as white prisms that dissolved in an Et_2O–Me_2S mixture to give a *colorless* solution. For recrystallization, a solution of 1.02 g of the complex in 5 ml of Me_2S was slowly diluted with 20 ml of hexane to give 0.96 g of the pure complex **2** as colorless prisms, mp 124–129° dec. The complex **2** is essentially insoluble in hexane, Et_2O, acetone, $CHCl_3$, CCl_4, MeOH, EtOH, and H_2O. Although the complex **2** does dissolve in DMF and in DMSO, the facts that heat is evolved and the resulting solutions are green colored suggests that the complex has dissociated and that some oxidation (or disproportionation) to give Cu(II) species has occurred. A solution prepared from the complex **2** and DMSO-d_6 exhibited an NMR peak at δ 2.17 (CH_3S); a solution of Me_2S in the same solvent exhibited a peak at δ 2.05. The complex **2** would dissolve to give a colorless solution in PhH, Et_2O, MeOH, or $CHCl_3$ when excess Me_2S was added to the mixture, suggesting the reversible formation of a more soluble complex such as $(Me_2S)_2CuBr$ or $(Me_2S)_3CuBr$.

Anal. Calcd for C_2H_6BrCuS: C, 11.68; H, 2.94; Br, 38.87; S, 15.60. Found: C, 11.50; H, 2.91; Br, 38.75; S, 15.51.

B. Me_2SCuCl (1). Following the same procedure, 20 ml of Me_2S was added to a slurry of 5.00 g (50.5 mmol) of CuCl (Fisher Scientific) in 20 ml of Et_2O and the mixture was stirred for 20 min while warming to 25°. After filtration of the dark green solution, it was mixed with 50 ml of hexane and then filtered with suction and washed with hexane to leave 2.2 g (27%) of the complex **1** as a white solid. A 1.30-g portion of the material was recrystallized by dissolving it in 8 ml of Me_2S and then slowly diluting the solution with 20 ml of hexane to precipitate the complex **1** as 1.14 g of white plates, mp 118–124° dec. The complex **1** was essentially insoluble in hexane, Et_2O, acetone, $CHCl_3$, CCl_4, MeOH, EtOH, and H_2O but it did dissolve (probably with dissociation) in either DMSO or DMF to give green solutions.

Anal. Calcd for C_2H_6ClCuS: C, 14.91; H, 3.75; Cl, 22.00; S, 19.90. Found: C, 14.73; H, 3.69; Cl, 21.77; S, 19.66.

Our attempt to prepare and isolate the stable complex **3** involved a comparable reaction of 20 ml of Me_2S with a slurry of 5.00 g (26.3 mmol) of CuI (Fisher Scientific) in 15 ml of Et_2O to give a deep red solution that was filtered and diluted with 50 ml of hexane. The resulting crystalline material that separated was filtered with suction and washed with hexane to leave 5.65 g (ca. 85%) of the complex **3** as white prisms. On standing, the crystals of the complex **3** collapsed to a white powder and the sample steadily lost weight, indicating loss of Me_2S from the sample at room temperature. The sample also apparently lost Me_2S when it was heated in an attempt to obtain a melting point. When a partially decomposed sample of 1.12 g of the complex **3** was again recrystallized from 4 ml of Me_2S and 20 ml of hexane, the freshly recrystallized complex **3** (1.13 g) gained in weight and was again obtained as white prisms. The composition of a sample of the material (Anal. Found: C, 7.16; H, 1.83; S, 9.51; I, 54.14) also indicated partial loss of Me_2S from the complex **3** (Anal. Calcd for C_2H_6CuIS: C, 9.51; H, 2.39; S, 12.69; I, 50.24) even at room temperature. Like the previously described complexes **1** and **2**, the complex **3** was essentially insoluble in Et_2O, hexane, acetone, $CHCl_3$, CCl_4, H_2O, MeOH, and EtOH. It was also insoluble in DMF but did dissolve (probably with dissociation) in DMSO.

Reactions of the Enone 6. A. Addition of a Vinyl Group. A colorless solution of 3.0 g (14.6 mmol) of Me_2SCuBr (**2**), 15 ml of Me_2S, and 20 ml of Et_2O was cooled to −57° (during this cooling part of the complex **2** crystallized from the solution) and then 14.5 ml of a THF solution containing 30.5 mmol of $CH_2{=}CHLi$ (Lithium Corp. of America, this reagent also contained mineral oil), was added, dropwise and with stirring, during 20 min while the temperature of the reaction mixture was maintained at −50 and −57°. To the resulting cold, light-gray solution, containing some undissolved solid, was added, dropwise and with stirring during 2 min, a solution of 1.66 g (13.4 mmol) of the enone **6** in 10 ml of Et_2O. The mixture, which warmed to −25° during the addition, was cooled to maintain the temperature in the range −25 to −40° and stirred for 10 min, and then the mixture was allowed to warm to 25° with continuous stirring during 30 min. As the temperature of the mixture rose to −25° and warmer, the reaction mixture became a dark brown or black color. The reaction mixture was diluted with Et_2O and aqueous NH_4Cl and filtered to remove suspended solids. The Et_2O extract was then separated, washed with aqueous NH_3, dried, treated with decolorizing carbon, and concentrated. An aliquot of the residual pale yellow liquid (3.51 g) containing the ketones **8** and **9** and mineral oil (from the $CH_2{=}CHLi$) was mixed with a known weight of internal standard n-$C_{15}H_{32}$ and analyzed by GLC (Carbowax 20M on Chromosorb P, apparatus calibrated with known mixtures of authentic samples). The mixture contained ketone **8** (retention time 7.4 min, 14% yield), ketone **9** (8.2 min, 64% yield), and n-$C_{15}H_{32}$ (6.6 min); the high-boiling mineral oil was not eluted. The crude product was distilled in a short-path still to separate 1.37 g (67%) of a mixture of ketones **8** and **9** as a colorless liquid, bp 80–95° (20 mm). A collected (GLC) sample of ketone **8** was obtained as a colorless liquid: n^{25}D 1.4650; ir (CCl_4), 1713 (C=O), 1639 (C=C), 994, and 920 cm^{-1} ($CH{=}CH_2$); uv max (95% EtOH) 282 mμ (ϵ 64); NMR (CCl_4) δ 4.6–6.0 (3 H, m, vinyl CH) and 0.9–2.4 (13 H, m, aliphatic CH including a CH_3 singlet at 1.97); mass spectrum m/e (rel intensity) 152 (M^+, 20), 109 (100), 95 (32), 67 (85), 55 (28), 43 (87), and 41 (26).

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.85; H, 10.61.

A collected (GLC) sample of the ketone **9** was obtained as a colorless liquid: n^{25}D 1.4707; ir (CCl_4) 1712 (C=O), 1638 (C=C), 995, and 922 cm^{-1} ($CH{=}CH_2$); uv max (95% EtOH) 282 mμ (ϵ 83); NMR (CCl_4) δ 4.7–6.3 (3 H, m, vinyl CH) and 0.9–2.9 (13 H, m, aliphatic CH including a CH_3 singlet at 1.98); mass spectrum m/e (rel intensity) 152 (M^+, 21), 109 (85), 94 (33), 79 (24), 67 (87), 55 (28), 43 (100), and 41 (28).

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.86; H, 10.62.

The reaction was repeated employing a smaller proportion of Me_2S, the quantities being 20.0 g (97.3 mmol) of Me_2SCuBr, 2 ml of Me_2S, 120 ml of Et_2O, 100 ml of a THF solution containing 210 mmol of $CH_2{=}CHLi$, and 11.0 g (88.7 mmol) of the enone **6** in 20 ml of Et_2O. Analysis (GLC) of the crude liquid product (25.4 g, a mixture of ketones **8** and **9** and mineral oil) indicated the proportions of the ketones to be ca. 15% of **8** and 85% of **9**. Short-path distillation separated 9.15 g (68%) of the mixture of ketones **8** and **9** as a colorless liquid, bp 90–110° (20 mm), n^{25}D 1.4691–1.4706. A second distillation separated 8.72 g (65%) of fractions, bp 53–55° (1.2 mm), containing (GLC) only the ketones **8** and **9**.

The reaction was also performed with no added Me_2S employing 3.00 g (14.6 mmol) of Me_2SCuBr, 25 ml of Et_2O, 14.5 ml of THF solution containing 30.5 mmol of $CH_2{=}CHLi$, and a solution of 1.66 g (13.4 mmol) of the enone **6** in 3 ml of Et_2O. The yields of the ketones (GLC analysis with added n-$C_{15}H_{32}$) were 8% of **8** and 56% of **9**. The ir spectrum (CCl_4) of this crude product exhibited substantial absorption at 3590 and 3480 cm^{-1} (OH) suggesting that the crude product, unlike the materials formed in the previous experiments, contained some alcohol derived from 1,2 addition of $CH_2{=}CHLi$ to the enone **6**.

A solution of t-BuC≡CLi, from 12.1 g (147 mmol) of t-BuC≡CH and 1.48 mmol of MeLi in 106 ml of Et_2O, was added to a cold (5°) slurry of 28.0 g (147 mmol) of purified[29] CuI in 180 ml of Et_2O. The resulting orange solution of t-BuC≡CCu was cooled (during which time part of the t-BuC≡CCu separated as an orange solid) and then 63 ml of a THF solution containing 132 mmol of $CH_2{=}CHLi$ was added, dropwise and with stirring, while the temperature of the mixture was maintained at −50 to −60°. The resulting dark-colored solution of the cuprate reagent was warmed to −40° and stirred for 5 min, and then a solution of 5.00 g (40.7 mmol) of the enone **6** in 100 ml of Et_2O was added, dropwise and with stirring, while the temperature was maintained at −40°. The resulting mixture was warmed to 0–10°, stirred for 90 min, and then poured into 150 ml of ethanolic 1 M HOAc. After this mixture had been neutralized with aqueous $NaHCO_3$, it was extracted with Et_2O and the Et_2O extract was washed successively with aqueous 28% NH_3[30] and with H_2O. The organic solution was dried, treated with decolorizing carbon, and then concentrated to leave 11.2 g of red liquid containing the ketone product and mineral oil. Analysis (GLC of an aliquot with added n-$C_{16}H_{32}$) indicated the yields of ketone to be 30% of **8** and 34% of **9**. To examine the outcome of a reaction with no solubilizing ligand for the copper salt, a cold (−33°) slurry of 2.65 g (14.6 mmol) of purified[29] CuI in 15 ml of Et_2O was treated, dropwise and with stirring, with 14.5 ml of a THF solution containing 30.5 mmol of $CH_2{=}CHLi$ while the temperature of the mixture was kept at −25 to −33°. During this addition a black precipitate formed in the reaction mixture. To the cold (ca. −30°) solution was added, dropwise and with stirring, 1.535 g (12.4 mmol) of the enone **6**. As soon as the addition was complete, the temperature of the reaction mixture was raised to −5° and the mixture was stirred at −5 to 8° for 10 min and then poured into aqueous NH_4Cl and NH_3 (pH 8). The Et_2O layer was separated and combined with the Et_2O extract of the aqueous phase. The ethereal solution was washed with aqueous $Na_2S_2O_3$, dried, and concentrated to leave 3.63 g of yellow liquid containing the ketones **8** and **9**, mineral oil, and other products. The ir (peaks at 3590 and 3490 cm^{-1}) and NMR (singlet at δ 1.30) spectra of the crude product suggested that it was contaminated with the alcohol formed by 1,2 addition of $CH_2{=}CHLi$ to the enone **6**. Analysis (GLC with added n-$C_{15}H_{32}$) indicated the yield of ketone products to be 11% of **8** and 58% of **9**.

A solution of 382 mg (2.51 mmol) of a mixture of epimeric ketones (54% of **9** and 46% of **8**) and 102 mg of p-TsOH in 10 ml of $CHCl_3$ was refluxed for 2 hr and then cooled and washed with aqueous $NaHCO_3$. After the organic solution had been dried and concentrated, analysis (GLC with added n-$C_{15}H_{32}$) indicated that the total recovery of the ketones was 88% and the mixture contained 21% of **9** and 79% of **8**. A collected (GLC) sample of ketone **8** was identified with an authentic sample by comparison of GLC retention times and NMR spectra. In a similar experiment, 544 mg (3.85 mmol) of a mixture of ketones (87% of **9** and 13% of **8**) was chromatographed on 11 g of basic alumina employing a hexane–Et_2O mixture as the eluent. The combined eluted fractions of ketone (quantitative recovery) contained (GLC) 11% of the cis ketone **9** and 89% of the trans ketone **8**. A sample of the eluted product was identified with ketone **8** by comparison of GLC retention times and ir and NMR spectra.

B. Reaction with Me_2CuLi. To a colorless solution of 3.00 g (14.6 mmol) of Me_2SCuBr in 20 ml of Me_2S and 20 ml of Et_2O was added, dropwise and with stirring while maintaining the temperature at 20–25°, 16.2 ml of an Et_2O solution containing 26.7 mmol of MeLi. The addition of MeLi was stopped at the point when the last of initially formed yellow precipitate of $(MeCu)_n$ just dissolved to form a pale yellow solution. To this solution was added 1.33 g (10.7 mmol) of the enone **6** and the resulting mixture, from which a yellow precipitate of $(MeCu)_n$ separated, was stirred at 25° for 40 min and then partitioned between Et_2O and an aqueous solution (pH 8) of NH_4Cl and NH_3. The ethereal layer was dried and concentrated to leave 1.49 g of a pale yellow liquid that contained (GLC, Carbowax 20M on Chromosorb P, n-$C_{14}H_{30}$ added as an internal standard and apparatus calibrated with known mixtures) n-$C_{14}H_{30}$ (retention time 4.9 mm), the trans ketone **17** (5.8 min, 18% yield), and the cis ketone **18** (6.8 min, 68% yield). A collected (GLC) sample of the trans ketone **17** was obtained as a colorless liquid: $n^{25}D$ 1.4471 [lit.[31] bp 64–65° (10 mm), $n^{25}D$ 1.4464]; ir (CCl_4) 1705 cm^{-1} (C=O); NMR (CCl_4) δ 2.01 (3 H, s, CH_3CO), 0.9–2.0 (10 H, m, aliphatic CH), and 0.80 (3 H, d, J = 5 Hz, CH_3); mass spectrum m/e (rel intensity) 140 (M^+, 23), 97 (45), 85 (22), 82 (22), 71 (29), 55 (100), and 43 (48). A collected (GLC) sample of the cis ketone **18** was obtained as a colorless liquid: $n^{25}D$ 1.4552 [lit.[31] bp 67–68° (10 mm), $n^{25}D$ 1.4532]; ir (CCl_4) 1710 cm^{-1} (C=O); NMR (CCl_4) δ 1.0–2.7 (13 H, m, aliphatic CH including a $COCH_3$ singlet at δ 2.00) and 0.82 (3 H, d, J = 6.5 Hz, CH_3); mass spectrum m/e (rel intensity) 140 (M^+, 18), 97 (45), 55 (100), and 43 (41).

In several additional experiments the Me_2CuLi solution was formed at 25°, and then cooled to −78° before the enone **6** was added. When the reaction mixture was stirred at −78° for 80 min (during which time no reaction was apparent) and then allowed to warm to 20° with stirring during 25 min [during which time a copious precipitate of $(MeCu)_n$ separated], the crude product contained (GLC) n-$C_{14}H_{30}$ (5.0 min), the trans ketone **17** (5.9 min, 16% yield), the cis ketone **18** (6.9 min, 54% yield), and the starting enone **6** (10.6 min, 10% recovery). In a comparable experiment, the reaction solution was stirred at −60 to −70° for 1 hr and then hydrolyzed by addition of aqueous NH_4Cl and NH_3 (pH 8). After this hydrolysis procedure (which warmed the reaction mixture to −20°), the crude product contained (GLC and NMR analyses) adducts **17** (3% yield) and **18** (8% yield) accompanied by the starting enone **6** (65% recovery). The same reaction was repeated and the cold (−60 to −70°) reaction solution was hydrolyzed by the dropwise addition of a precooled mixture of MeOH and HOAc (5:1 v/v) so that the temperature of the reaction solution was kept below −60°. In this case the crude product contained (GLC and NMR analyses) only minor amounts of the adducts **17** (0.8% yield) and **18** (0.5% yield) accompanied by the unchanged enone **6** (82% recovery). When we attempted to form the cuprate reagent by adding MeLi to the Me_2SCuBr solution in Et_2O and Me_2S at −50 to −60°, formation of Me_2CuLi was clearly incomplete, since most of the yellow $(MeCu)_n$ did not dissolve when the second equivalent of MeLi was added. Addition of the enone **6** to this cold mixture was followed by reaction at −45 to −25° for 5 min and subsequent warming of the mixture to 25° during 30 min; then the usual isolation and analysis procedures were used. In this case the crude product contained (GLC, Carbowax 20M on Chromosorb P) the olefin **21** (retention time 2.8 min, 43% yield), the olefin **20** (3.3 min, 28% yield), n-$C_{14}H_{30}$ (4.6 min), the trans ketone **17** (5.4 min, 5% yield), the cis ketone **18** (6.4 min, 11% yield), and the starting enone **6** (9.6 min, 2% recovery). The two olefins **20** and **21** are presumably formed from the alcohol **19** during GLC analysis, since the ir spectrum of the crude product (CCl_4) has strong bands at 3590 and 3470 cm^{-1} (OH). A collected (GLC) sample of the olefin **21** [lit.[32a,b] bp 49–50° (7 mm)] has ir absorption at 1630, 1605 (C=C), and 885 cm^{-1} ($C{=}CH_2$) and NMR (CCl_4) peaks at δ 5.79 (1 H, broad, vinyl CH), 4.6–4.9 (2 H, m, vinyl CH), and 1.1–2.6 (11 H, m, aliphatic CH including a broad singlet at δ 1.83 attributable to an allylic CH_3 group). A collected (GLC) sample of the olefin **20** (lit.[32b,c] bp 164–165°) exhibited ir (CCl_4) weak absorption at 1672, 1638, and 1605 cm^{-1} (C=C) with NMR absorption (CCl_4) at δ 6.1–6.6, 5.4–5.8 (2 H, two multiplets, vinyl CH), and 1.1–2.4 (12 H, m, aliphatic CH including a broad singlet at δ 1.67 attributable to two allylic CH_3 groups).

C. Reaction with $Me(CH_2{=}CH)CuLi$. A solution of 3.00 g (14.6 mmol) of Me_2SCuBr in 20 ml of Me_2S and 20 ml of Et_2O was treated at 25° with 8.1 ml of an Et_2O solution containing 13.4 mmol of MeLi. The resulting slurry of yellow $(MeCu)_n$ was cooled to −30° and then 8.2 ml of a THF solution containing 13.4 mmol of $CH_2{=}CHLi$ was added, dropwise and with stirring, while the temperature was maintained at −20 to −30°. To the resulting cold mixture was added, dropwise and with stirring while the temperature was maintained at −20 to −30°, a solution of 372 mg (3.00 mmol) of the enone **6** in 2 ml of Et_2O. The reaction mixture was stirred at −20° for 10 min and at 25° for 90 min and then subjected to the usual isolation and analysis procedures. The crude liquid product (1.26 g of yellow liquid) contained (GLC, Carbowax 20M on Chromosorb P, n-$C_{15}H_{32}$ added as an internal standard) ketone **18** (6.7 min, 4% yield), n-$C_{15}H_{32}$ (7.2 min), ketone **8** (9.0 min, 10% yield), and ketone **9** (10.3 min, 63% yield). Collected (GLC) samples of ketones **8** and **9** were identified with previously described samples by comparison of GLC retention time and NMR spectra and a collected (GLC) sample of ketone **18** was identified with a previously described sample by comparison of GLC retention times and mass spectra.

An attempt to form the mixed cuprate by treating a cold (−20 to −35°) solution of Me_2SCuBr in Me_2S and Et_2O, first with 1 equiv of $CH_2{=}CHLi$ and then with 1 equiv of MeLi, failed to form the cuprate. After the addition of the enone **6**, the major products formed after GLC analysis were the previously described olefins **20** and **21**, indicating that the unchanged MeLi in the original reaction mixture had reacted with the enone **6** to form the alcohol **19**.

Preparation of the Ketals 10 and 11. A solution of 1.50 g (9.87 mmol) of a mixture of ketones (46% of **8** and 54% of **9**), 35 mg of p-TsOH, 20 ml of $HOCH_2CH_2OH$, and 100 ml of PhH was refluxed for 48 hr with continous separation of H_2O and then cooled and partitioned between Et_2O and aqueous $NaHCO_3$. The organic solution was dried and concentrated to leave 2.189 g of the crude product as a yellow liquid containing [GLC, Carbowax 20M on Chromosorb P, internal standard (n-$C_{15}H_{32}$) added and the apparatus was calibrated with known mixtures of authentic samples] n-$C_{15}H_{32}$ (retention time 6.0 min), the cis ketal **11** (15.6 min, 21% yield), and the trans ketal **10** (13.9 min, 57% yield).

A collected sample of the trans ketal **10** was obtained as a colorless liquid: $n^{25}D$ 1.4773; ir (CCl_4) 1632 (C=C), 991, and 903 cm^{-1} ($CH{=}CH_2$); uv (95% EtOH) end absorption with ϵ 96 at 210 mμ; NMR (CCl_4) δ 4.7–6.2 (3 H, m, vinyl CH), 3.6–3.9 (4 H, m, CH_2O), and 0.9–2.1 (13 H, m, aliphatic CH including a CH_3 singlet at 1.12); mass spectrum m/e (rel intensity) 196 (M^+, <1), 87 (100), 55 (22), and 43 (27).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.40; H, 10.28.

A solution of 27.3 mg of the ketal **10** and 1.5 ml of aqueous 1 *M* HCl in 5 ml of dioxane was stirred at 25° for 5 hr and then partitioned between Et_2O and H_2O. The Et_2O layer was washed with aqueous $NaHCO_3$, dried, and concentrated to leave a colorless liquid identified as the trans ketone **8** by comparison of GLC retention times and NMR spectra.

A collected (GLC) sample of the cis ketal **11** was obtained as a colorless liquid: n^{25}D 1.4791; ir (CCl_4) 1629 (C=C), 991, and 910 cm^{-1} ($CH{=}CH_2$); uv (95% EtOH) end absorption with ϵ 247 at 210 mμ; NMR (CCl_4) δ 4.8–6.6 (3 H, m, vinyl CH), 3.6–3.9 (4 H, broad, CH_2O), and 1.0–2.8 (13 H, m, aliphatic CH including a CH_3 singlet at 1.13); mass spectrum *m/e* (rel intensity) 196 (M^+, <1), 181 (8), 87 (100), and 43 (10).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.45; H, 10.28.

A solution of 10 mg of the cis ketal **11** and 0.5 ml of aqueous 1 *M* HCl in 2 ml of dioxane was subjected to the previously described reaction and isolation procedures to yield a liquid product identified as the cis ketone **9** by comparison of GLC retention times and NMR spectra.

Preparation of the Vinyl Ketones 13 and 14. To a cold (0°) solution of 0.139 mol of MeLi in 80 ml of Et_2O was added 11.6 g (0.142 mol) of *t*-BuC≡CH. The resulting solution of *t*-BuC≡CLi was added to a cold (5°) slurry of 26.5 g (0.139 mol) of purified[29] CuI in 160 ml of Et_2O and the resulting mixture was warmed to 29° with stirring during 15 min to give a red-orange solution of *t*-BuC≡CCu. This solution was cooled to −50° and the resulting orange suspension was treated with a solution of 0.129 mol of $CH_2{=}CHLi$[33] in 68 ml of Et_2O while the temperature was maintained at −45 to −50°. The resulting solution, whose color changed progressively from orange to red to green, was warmed to −32° with stirring during 10 min and then treated with a solution of 7.2 g (40 mmol) of the ketone **7** in 80 ml of Et_2O. The resulting mixture was stirred at 0–10° for 1 hr and then added to 150 ml of ethanolic 1 *M* HOAc. The resulting mixture was neutralized with aqueous $NaHCO_3$ and extracted with Et_2O. After the Et_2O extract had been washed successively with aqueous 28% NH_3[30] and with H_2O, it was dried and concentrated to leave 7.94 g of liquid containing (GLC, silicone fluid QF_1 on Chromosorb P) a mixture of a component believed to be one epimer of ketone **15** (retention time 10.1 min, ca. 4%), ketone **14** (12.8 min, ca. 15%), a component believed to be the second epimer of ketone **15** (15.4 min, ca. 3%), and ketone **13** (17.5 min, ca. 78%). A 5.69-g aliquot of this crude product was distilled to separate 4.745 g of fractions, bp 69–91° (0.1–0.7 mm), containing various mixtures of the ketones **13**, **14**, and **15**. A collected (GLC) sample of the major product **13** was obtained as a colorless liquid: n^{25}D 1.4728; ir (CCl_4) 1710 (C=O), 1635 (C=C), and 920 cm^{-1} ($CH{=}CH_2$); uv max (95% EtOH) 278 mμ (ϵ 35); NMR (CCl_4) δ 4.8–6.2 (3 H, m, vinyl CH), 2.8–3.2 (1 H, m, allylic CH), 2.38 [1 H, d (J_{aa} = 10.8 Hz) of t (J_{ae} = 4.4 Hz), axial H of CHCO, exchanged with NaOMe in MeOD], 1.99 (3 H, s, CH_3CO, exchanged with NaOMe in MeOD), 0.9–1.9 (7 H, m, aliphatic CH), and 0.85 (9 H, s, *t*-Bu); the signal at δ 2.38 exhibited the same splitting pattern and *J* values when the spectrum was determined at 100 MHz with a Jeol NMR spectrometer; mass spectrum *m/e* (rel intensity) 208 (1, M^+), 152 (8), 151 (6), 109 (17), 58 (30), 57 (30), and 43 (100); calcd for $C_{14}H_{24}O$, 208.1827; found, 208.1847.

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.91; H, 11.78.

A solution of 59 mg (0.28 mmol) of the pure (GLC) ketone **13** and 23 mg (0.42 mmol) of NaOMe in 3 ml of MeOH was refluxed for 38.5 hr and then partitioned between Et_2O and aqueous 1 *M* HCl. The Et_2O solution was dried and concentrated to leave 53 mg of yellow liquid containing (GLC) the ketones **14** (ca. 31%) and **13** (ca. 69%). Collected (GLC) samples of the ketone **14** from this equilibration and from the original cuprate addition reaction were identified by comparison of GLC retention times and ir and mass spectra: ir (CCl_4) 1705 (C=O), 1635 (C=C), and 920 cm^{-1} ($CH{=}CH_2$); mass spectrum *m/e* (rel intensity) 208 (M^+, <1), 152 (21), 109 (45), 57 (88), 43 (100), and 41 (26).

In a larger scale reaction the mixed cuprate, from 27.0 g (329 mmol) of *t*-BuC≡CH, 329 mmol of MeLi, 62.5 g (329 mmol) of purified[29] CuI, 308 mmol of $CH_2{=}CHLi$,[33] and 773 ml of Et_2O, was treated with a solution of 17.1 g (95 mmol) of the ketone **7** in 150 ml of Et_2O. After the previously described reaction and isolation procedures were followed, distillation afforded 15.70 g (88%) of colorless liquid product, bp 82–100° (0.4 mm), containing (GLC) the ketones **13** (ca. 80%) and **14** (ca. 11%) as well as two minor components (ca. 2 and 5%) believed to be the epimers of ketone **15** and a minor unidentified component (ca. 2%).

In another experiment in which the mixed cuprate was generated from ethereal $CH_2{=}CHLi$ and a solution prepared from pure[6] *t*-BuC≡CCu, the same reaction and isolation procedures were followed. The crude liquid reaction product contained (GLC) the same mixture of ketones **13**, **14**, and **15** formed in the previously described experiment.

A solution of 15.0 g (73.0 mmol) of Me_2SCuBr (**2**) in 75 ml of Me_2S and 100 ml of Et_2O was cooled to −50 to −57° (accompanied by partial crystallization of the complex **2**) and then 93.2 ml of a THF solution containing 153 mmol of $CH_2{=}CHLi$ was added, dropwise with stirring. The resulting reddish-brown solution was warmed to −35° and a solution of 12.06 g (67.0 mmol) of the ketone **7** in 50 ml of Et_2O was added dropwise with stirring. The resulting mixture was stirred at −30 to −35° for 10 min and then allowed to warm to 25° with stirring during 1 hr. As the solution warmed from −30 to 25°, it became dark brown to black in color. The reaction mixture was partitioned between ether and aqueous NH_4Cl and NH_3 and then the ether solution was washed successively with aqueous 10% $Na_2S_2O_3$ and with aqueous 28% NH_3. The organic solution was then decolorized with carbon, dried, and concentrated to leave a pale yellow liquid (59.89 g, containing mineral oil from the $CH_2{=}CHLi$). The crude mixture contained (GLC, Carbowax 20M on Chromosorb P) the ketone **13** (retention time 17.1 min, ca. 80% of the mixture) as well as a partially resolved mixture of ketones **14** and **15** (9.9 and 12.4 min, ca. 20% of the mixture). A collected (GLC) sample of the major product, ketone **13**, was identified with the previously described sample by comparison of GLC retention times and ir and NMR spectra. Distillation of the crude product separated 11.94 g (85.7%) of a mixture of ketones **13**, **14**, and **15** as fractions of colorless liquid, bp 83–87° (1.5 mm), n^{25}D 1.4724–1.4730, and left the higher boiling mineral oil (from the $CH_2{=}CHLi$) in the still pot.

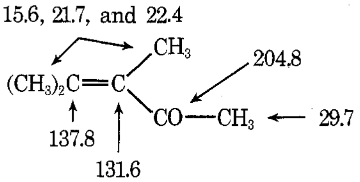
Preparation of the Ketal 16. A solution of 13.16 g (63.5 mmol) of the previously described mixtures of ketones **13** (ca. 80%) and **14** (ca. 11% plus minor amounts of ketones **15**), 306 mg of *p*-TsOH·H_2O, and 170 ml of ethylene glycol in 950 ml of PhH was refluxed for 68 hr with continuous separation of H_2O and then partitioned between Et_2O and aqueous $NaHCO_3$. The organic layer was dried and concentrated to leave 16.14 g of the crude ketal **16** as a pale yellow liquid containing (ir analysis) only a very minor amount of the starting ketones **13–15** and containing (GLC, silicone fluid QF_1 on Chromosorb P) two major components, the epimeric ketals **16** [retention times 13.3 (ca. 20%) and 15.1 min (ca. 80%)]. A collected (GLC) sample of the mixture of epimers **16** was obtained as a colorless liquid: n^{25}D 1.4790; ir (CCl_4) 1630 (C=C) and 910 cm^{-1} ($CH{=}CH_2$); uv (95% EtOH) end absorption with ϵ 66 at 210 mμ; NMR (CCl_4) δ 5.8–6.2 and 4.7–5.2 (3 H, m, vinyl CH), 3.7–4.0 (4 H, m, CH_2O), 1.0–3.0 [12 H, m including two singlets at 1.23 (minor) and 1.15 (major), 3 H, CH_3 of epimers], and 0.82 (9 H, s, *t*-Bu)]; mass spectrum *m/e* (rel intensity) 252 (<1, M^+), 237 (1), 87 (100), and 43 (18).

Anal. Calcd for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 76.24; H, 11.20.

To demonstrate the absence of C=C migration during ketalization, a 234-mg portion of the crude ketal **16** was stirred at 25° for 12.5 hr with a solution of 3 ml of aqueous 0.01 *M* HCl in 7 ml of dioxane and for 6.5 hr with 3 ml of aqueous 1 *M* HCl in 7 ml of dioxane and then partitioned between Et_2O and aqueous $NaHCO_3$. The Et_2O layer was dried and concentrated to leave 140 mg of crude product that contained (GLC, ir, and NMR analysis) the same mixture of ketones **13–15** that was used to form the ketal **16**.

Preparation of the Unsaturated Ketone 22. To a cold (4°) mixture of 20.01 g (285 mmol) of 2-methyl-2-butene and 2.55 g (9.8 mmol) of freshly distilled $SnCl_4$ (bp 114°) was added, dropwise and with stirring, 26.8 g (341 mmol) of AcCl.[18] After the addition was complete, the yellow reaction solution was allowed to warm to 25° (accompanied by formation of a red-brown color) and then the mixture was stirred at 25–27° for 3.5 hr. After the reaction mixture had been poured onto ice and extracted with Et_2O, the ethereal solution was washed successively with aqueous $NaHCO_3$ and with H_2O and then dried and concentrated. The crude residual liquid was distilled to separate 19.05 g of fractions, bp 43–80° (44 mm), n^{25}D 1.4401–1.4449, that contained (ir and NMR analysis) a mixture of the unsaturated ketones **22** and **24** and the chloro ketone **23**. A mixture of this crude product (12.05 g) with 16.53 g (128 mmol) of freshly distilled quinoline [bp 87–91° (0.35 mm)] was heated under reflux (ca. 140°) for 2.5 hr and then cooled and partitioned between Et_2O and H_2O. The ethereal layer was dried and concentrated and the residual liquid was distilled to separate 12.15 g (38%) of fractions, bp 73.5–75.5° (20 mm), that contained (GLC, TCEP on Chromosorb P) ca. 12–33% of the unconjugated ketone **24** (retention time 4.5 min) and 67–88% of the conjugated ketone **22** (9.1 min). A mixture of these ketones **22** and **24** (12.15 g) and 120 mg of *p*-TsOH was heated to 140° for 20 min and then cooled and partitioned between Et_2O and aqueous $NaHCO_3$. The ethereal solution was dried and concentrated to leave a ketone mixture containing (GLC) ca. 19% of ketone **24** and ca. 81% of ketone **22**.

The mixture was fractionally distilled at atmospheric pressure with a 55-cm Teflon spinning-band column to separate the pure ketone **24**, bp 125°, $n^{25}D$ 1.4201, followed by fractions containing (GLC) mixtures of ketones **22** and **24**, and finally the pure ketone **22**, bp 146°, $n^{25}D$ 1.4500 (lit. bp 146°,[34] 149.5°,[18] $n^{24}D$ 1.4473[15]). The ketone **24** exhibited ir peaks (CCl_4) at 1718 (C=O), 1641 (C=C), and 890 cm^{-1} ($C{=}CH_2$) with NMR peaks (CCl_4) at δ 4.7–5.0 (2 H, m, vinyl CH), 3.15 (1 H, q, J = 7 Hz, allylic CH), 2.01 (3 H, s, CH_3CO), 1.65 (3 H, partially resolved multiplet, allylic CH_3), and 1.10 (3 H, d, J = 7 Hz, CH_3). The ketone **22** has the following spectroscopic properties: ir (CCl_4) 1684 (conjugated C=O) and 1615 cm^{-1} (conjugated C=C); uv max (95% EtOH) 247 mμ (ϵ 6000); NMR (CCl_4) δ 2.12 (3 H, s, $COCH_3$), 1.80 (6 H, s, CH_3), and 1.73 (3 H, s, CH_3); mass spectrum *m/e* (rel intensity) 112 (M^+, 100), 97 (64), 69 (93), 53 (22), 43 (63), 41 (81), and 39 (30). A 0.017 *M* solution of the enone **17** in DMF containing 0.5 *M* n-$Bu_4N^+BF_4^-$ at 25° exhibited a polarographic[35] $E_{1/2}$ value of −2.35 V (vs. SCE), n = 1.1. Measurement by cyclic voltammetry[35] indicated a half-life of ca. 0.01 sec for the anion radical derived from the enone **22**. The natural-abundance ^{13}C NMR spectrum of the enone **22**, measured in $CDCl_3$ with added Me_4Si, is summarized in the following formula.



$(CH_3)_2C{=}C(CH_3)CO{-}CH_3$

In an alternative preparation,[36] 130.4 g (1.30 mol) of 2,4-pentanedione was methylated with 228 g (1.61 mol) of CH_3I and 168 g (1.22 mol) of anhydrous K_2CO_3 in 500 ml of acetone to yield 100.4 g (68%) of 3-methyl-2,4-pentanedione: bp 75.5–76.5° (25 mm); $n^{25}D$ 1.4375 [lit. bp 60–65° (13 mm),[37] 75° (30 mm),[38] $n^{20}D$ 1.4443[37]]; ir (CCl_4) 1725 and 1695 cm^{-1} (C=O); NMR (CCl_4) δ 16.75 (ca. 0.35 H, s, enol OH), 3.70 (ca. 0.65 H, q, J = 7 Hz, CH_3 of keto form), 2.13, 2.07 (6 H, two singlets, CH_3CO of enol and keto forms). This product contained (GLC, silicone QF_1 on Chromosorb P) about 95% of the monomethylated product (retention time 5.3 min) accompanied by a minor component thought to be the dialkylated product (6.1 min). A solution of 5.71 g (50 mmol) of this diketone, 27.6 g (270 mmol) of Ac_2O, and 0.034 ml of aqueous 70% $HClO_4$ in 60 ml of CCl_4 was allowed to stand at 25° for 3 hr and then partitioned between pentane and aqueous $NaHCO_3$. The organic layer was dried, concentrated, and distilled to separate 6.05 g (77%) of the crude enol acetates **25**, bp 85.5–86.5° (10 mm) [lit.[39] bp 115–117° (30 mm)], which contained (GLC, silicone QF_1 on Chromosorb P) the stereoisomeric enol acetates **25** [retention times 13.3 (ca. 67%) and 16.1 min (ca. 33%)] as well as a small amount of the starting diketone (5.4 min). A collected (GLC) sample of the more rapidly eluted (13.3 min) isomer **25a** was obtained as a colorless liquid: $n^{25}D$ 1.4518; ir (CCl_4) 1755 (enol ester C=O), 1697 (conjugated C=O), and 1626 cm^{-1} (C=C); mass spectrum *m/e* (rel intensity) 156 (M^+, <1), 114 ($M - CH_2{=}C{=}O$, 17), 99 (47), and 43 (100); NMR (CCl_4) δ 2.22 (3 H, s, CH_3CO_2), 2.12 (3 H, s, CH_3CO), 2.07 (3 H, q, J = 1.5 Hz, allylic CH_3), and 1.77 (3 H, q, J = 1.5 Hz, allylic CH_3); uv max (95% EtOH) 237 mμ (ϵ 7630) with a shoulder at 290 mμ (ϵ 185). A 0.009 *M* solution of this enol acetate **25a** in DMF containing 0.5 *M* n-$Bu_4N^+BF_4^-$ at 24° exhibited a polarographic[35] $E_{1/2}$ value of −2.14 V (vs. SCE), n = 1.2.

A collected (GLC) sample of the more slowly eluted (16.1 min) enol acetate **25b** was obtained as a colorless liquid: $n^{25}D$ 1.4559; ir (CCl_4) 1757 (enol ester C=O), 1695 (conjugated C=O), 1665, and 1647 cm^{-1} (C=C); mass spectrum *m/e* (rel intensity) 114 ($M - CH_2{=}C{=}O$, 3), 99 (7), and 43 (100); NMR (CCl_4) δ 2.12 (6 H, s, CH_3CO and CH_3CO_2), ca. 2.07 (3 H, broad, allylic CH_3), and 1.80 (3 H, broad, allylic CH_3); uv max (95% EtOH) 234.5 mμ (ϵ 8330) with a shoulder at 286 mμ (ϵ 160). A 0.0088 *M* solution of this enol acetate **25b** in DMF containing 0.5 *M* n-$Bu_4N^+BF_4^-$ at 26° exhibited a polarographic[35] $E_{1/2}$ value of −2.13 V (vs. SCE), n = 1.1.

Following a previously described general procedure,[17] a cold (−40°) solution of Me_2CuLi, from 2.99 g (15.7 mmol) of purified[29] CuI and 31.5 mmol of MeLi in 30 ml of Et_2O, was added to a cold (−75°) solution of 2.46 g (15.7 mmol) of the enol acetate **25** in 10 ml of Et_2O. The reaction mixture, from which a red-brown precipitate separated, was allowed to stand for 30 min and then partitioned between Et_2O and aqueous NH_4Cl and NH_3 (pH 8). The organic layer was washed with aqueous $Na_2S_2O_3$, dried, and concentrated to leave 1.00 g of crude liquid product. Distillation in a short-path still separated 0.61 g (35%) of the crude enone **22** as a yellow liquid containing (GLC, silicone QF_1 on Chromosorb P) primarily the enone **22** (retention time 6.2 min) accompanied by a small amount of unchanged enol acetates **25** (13.3 and 16.1 min). A collected (GLC) sample of the enone **22** was identified with the previously described material by comparison of ir and NMR spectra and GLC retention times.

Reactions with the Enone 22. A. Addition of Me_2CuLi. To a solution of Me_2CuLi, prepared by the addition of 17 ml of an Et_2O solution containing 28.1 mmol of MeLi to a solution of 3.0 g (14.6 mmol) of Me_2SCuBr in 15 ml of Me_2S and 15 ml of Et_2O, was added 1.12 g (10.0 mmol) of the enone **22**. The resulting solution, from which $(MeCu)_n$ separated, was stirred at 30–34° for 1.7 hr and then partitioned between Et_2O and aqueous (pH 8) NH_4Cl and NH_3. The ethereal layer was washed successively with aqueous 28% NH_3 and with aqueous NaCl and then dried and concentrated to leave 1.10 g of residual yellow liquid containing (GLC, Carbowax 20M on Chromosorb P) the ketone **27** (retention time 5.1 min, ca. 23% of the mixture) and the starting enone **22** (8.7 min, ca. 77% of the mixture). A collected (GLC) sample of the enone **22** was identified with an authentic sample by comparison of GLC retention times and ir and NMR spectra. A collected (GLC) sample of the pure ketone **27** was obtained as a colorless liquid: $n^{25}D$ 1.4162 [lit. bp 148–154° (760 mm),[40] 78–79.5° (77 mm),[41] $n^{25}D$ 1.4161[41]]; ir (CCl_4) 1711 cm^{-1} (C=O); NMR (CCl_4) δ 2.42 (1 H, q, J = 7 Hz, CHCO), 2.15 (3 H, s, CH_3CO), and 0.9–1.1 (12 H, CH_3 including a singlet at δ 0.96 attributable to *t*-Bu); mass spectrum *m/e* (rel intensity) 128 (M^+, 2), 97 (12), 85 (29), 72 (81), 57 (70), 43 (100), 41 (64), and 39 (26).

In various similar experiments at other concentrations, temperatures, and reaction times, the composition of crude product remained within the ranges 15–30% of the ketone **27** and 70–85% of the recovered enone **22**. The composition of the reaction mixture was established in less than 5 min and did vary with longer reaction periods; during this intial 5-min reaction period, gas evolution (presumably CH_4) was evident in the reaction mixture. The reaction was repeated with 10.0 mmol of the enone **22** employing a reaction time of 50 min at 25° and then a solution of 58 mmol of DOAc in 10 ml of D_2O was added and the mixture was extracted with hexane. The hexane extract was washed successively with aqueous $NaHCO_3$, aqueous 28% NH_3, and aqueous NaCl and then dried and concentrated to leave 1.48 g of colorless liquid containing (GLC) ca. 25% of the ketone **30** and ca. 75% of the enone **31**. A collected (GLC) sample of the ketone **30** contained (mass spectral analysis) 12% d_0 species, 85% d_1 species, and 3% d_2 species; NMR (CCl_4) differs from the spectrum of ketone **27** in lacking CHCO absorption centered at δ 2.42 and in a collapse of the partially resolved CH_3 doublet at ca. δ 0.98 to a signal partially resolved from the *t*-Bu singlet at δ 0.96. A collected sample of the enone **31** contained (mass spectral analysis) 12% d_0 species, 74% d_1 species, 13% d_2 species, and 1% d_3 species; NMR (CCl_4) differs from the spectrum of the enone **22** in that the CH_3CO singlet at δ 2.12 appears as a three-line signal ($J_{H\text{-}D}$ = 1.1 Hz) of diminished intensity.

B. Addition of $(CH_2{=}CH)_2CuLi$. A solution of 3.00 g (14.6 mmol) of Me_2SCuBr in 15 ml of Me_2S and 20 ml of Et_2O was cooled to −57° and then 17 ml of a THF solution containing 27.6 mmol of $CH_2{=}CHLi$ was added, dropwise and with stirring, while the temperature was kept at −49 to −59°. The resulting mixture was warmed to −40° and a solution of 1.25 g (11.1 mmol) of the enone **22** in 2 ml of Et_2O was added. After the resulting mixture had been stirred for 10 min at −35 to −25°, it was warmed to 25°, stirred for 50 min, and then partitioned between Et_2O and aqueous NH_4Cl and NH_3. The ethereal layer was washed successively with aqueous 28% NH_3 and with aqueous NaCl and then dried and concentrated. The residual yellow liquid (3.72 g, contained mineral oil) was mixed with an internal standard (n-$C_{11}H_{24}$) and analyzed by GLC (silicone SE-30 on Chromosorb P). The mixture contained the starting enone **22** (retention time 3.4 min, 17% recovery, collected sample identified by comparison of NMR spectra and GLC retention times), the ketone **26** (4.9 min, 55% yield), and n-$C_{11}H_{24}$ (10.7 min). A collected (GLC) sample of the ketone **26** was obtained as a colorless liquid: n^{25}D 1.4371; ir (CCl_4) 1711 (C═O), 1635 (C═C), and 910 cm^{-1} ($CH═CH_2$); NMR (CCl_4) δ 4.7–6.2 (3 H, m, vinyl CH), 2.45 (1 H, q, J = 7 Hz, CHCO), 2.04 (3 H, s, CH_3CO), and 0.9–1.1 [9 H, two lines corresponding to a doublet (J = 7 Hz) at δ 0.96 superimposed on a singlet at δ 1.01]; mass spectrum m/e (rel intensity) 140 (M^+, 2), 125 (30), 97 (31), 72 (66), 69 (100), 55 (59), 53 (24), 43 (63), 41 (78), and 39 (39).

Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.06; H, 11.52.

To examine the reaction with the mixed cuprate, (CH_2═CH)(CH_3)CuLi, a solution of 3.00 g (14.6 mmol) of Me_2SCuBr in 10 ml of Me_2S was treated with 8.0 ml of an ether solution containing 14.3 ml of MeLi and the resulting slurry was cooled to −30 to −40° and treated with 8.8 ml of a THF solution containing 14.3 mmol of CH_2═CHLi. To the resulting cold (−22 to −30°) mixture was added, dropwise and with stirring, 1.12 g (10.0 mmol) of the enone **22**. The reaction mixture was then allowed to warm to 25° with stirring during 30 min and then subjected to the usual isolation and analysis procedures. The crude product contained (GLC, silicone SE-30 Chromosorb P) the ketone **27** (retention time 4.1 min, 2% yield), the enone **22** (4.5 min, 13% recovery), the ketone **26** (6.3 min, 58% yield), and n-$C_{11}H_{24}$ (13.6 min, internal standard). A collected (GLC) sample of the enone **22** was identified by comparison of NMR spectra and GLC retention times and a collected (GLC) sample of the ketone **26** was identified by comparison of ir and NMR spectra and GLC retention times.

Reaction of Me_2CuLi with Some Nonconjugated Compounds. To a 25° solution of Me_2CuLi, prepared from 3.00 g (14.6 mmol) of Me_2SCuBr, 28.6 mmol of MeLi, 16 ml of Et_2O, and 10 ml of Me_2S, was added 1.00 g (11.6 mmol) of the ketone **32**. An immediate reaction occurred as indicated by the evolution of gas and the separation of a yellow precipitate. The reaction mixture was stirred at 25° for 30 min and then poured into a solution of 59 mmol of DOAc in D_2O. The resulting mixture was extracted with Et_2O and the ethereal extract was washed successively with aqueous $NaHCO_3$, aqueous 28% NH_3, and aqueous NaCl and then dried and concentrated by fractional distillation. The crude liquid product (0.94 g) contained (GLC, Carbowax 20M on Chromosorb P) n-C_8H_{18} (retention time 2.2 min, internal standard), the ketone **33** (3.9 min, 49% yield), and the alcohol **34** (8.4 min, 16% yield). A collected (GLC) sample of the alcohol **34** was identified with an authentic sample by comparison of ir and NMR spectra and GLC retention times. A collected (GLC) sample of ketone **33** exhibited NMR absorption (CCl_4) at δ 2.53 (1 H, m, CH), 2.03 (ca. 2 H, $COCH_2D$), and 1.06 (6 H, d, J = 7 Hz, CH_3); mass spectrum 45% d_0 species, 34% d_1 species, 20% d_2 species, and 1% d_3 species.

When comparable cold (−2 to 2°) solutions containing 14 mmol of Me_2CuLi were treated with either 1.16 g (10 mmol) of the ester **35** or 0.69 g (10 mmol) of the nitrile **36**, no evidence of reaction was observed. Each solution was warmed to 25° and stirred for 30 min with no evidence of reaction. After each reaction solution had been quenched in a mixture of DOAc and D_2O, the crude organic products were recovered and found to contain (GLC) only the starting material **35** or **36**. Collected samples (GLC) of each compound were identified and shown to contain no appreciable quantity of deuterium by NMR analysis. When a solution of 14.3 mmol of Me_2CuLi was treated with 1.42 g (10 mmol) of the ketone **37** at 25°, a reaction was evident (gas evolution, temperature rise, separation of a yellow precipitate). The mixture was stirred for 30 min at 25–32° and then quenched in a mixture of DOAc and D_2O and subjected to the usual isolation procedure. The crude neutral product (1.46 g of yellow liquid) contained (GLC, silicone SE-30 on Chromosorb P) n-C_9H_{20} (2.2 min, added internal standard), the ketone **38** (3.8 min, 21% yield), and the alcohol **39** (5.9 min, 55% yield). A collected (GLC) sample of the ketone **38** contained (mass spectral analysis) 25% d_0 species and 75% d_1 species and exhibited a 2 H NMR (CCl_4) multiplet in the region δ 2.0–2.8 where the starting ketone **37** has a 3 H multiplet (>$CHCOCH_2$–). The mass spectrum of the ketone **38** exhibited an abundant fragment peak at m/e 100 (n-$C_4H_9CHDC{\equiv}O^+$) rather than the peak at m/e 99 (n-$C_4H_9CH_2C{\equiv}O^+$) found in the mass spectrum of the starting ketone **37**. A collected (GLC) sample of the alcohol **39** was identified with an authentic sample by comparison of GLC retention times and ir and NMR spectra. An authentic sample of the alcohol **39**, obtained by reaction of the ketone **37** with MeLi, was obtained as a colorless liquid: bp 104–105° (15 mm); n^{25}D 1.4371 [lit.[42] bp 69–70° (5 mm), n^{25}D 1.4380]; ir (CCl_4) 3580 and 3470 cm^{-1} (OH).

When 1.14 g (10 mmol) of the ketone **40** was added to 21 ml of an Et_2O solution containing 14.3 mmol of Me_2CuLi at 25–27°, no gas evolution was observed but a yellow precipitate of $(MeCu)_n$ began to separate after about 2 min. After this mixture had been stirred at 25–27° for 30 min, it was quenched in a DOAc–D_2O mixture and then subjected to the usual isolation procedure. The crude product contained (GLC, Carbowax 20M on Chromosorb P, n-$C_{11}H_{24}$ added as internal standard) the unchanged ketone **40** (retention time 2.2 min, 34% recovery), n-$C_{11}H_{24}$ (3.3 min), and the alcohol **41** (5.6 min, 41% yield). Collected (GLC) samples of each component **40** and **41** were identified with authentic samples by comparison of GLC retention times and ir and NMR spectra. The recovered ketone **40** contained (NMR analysis) no appreciable amount of deuterium. An authentic sample of the alcohol **41**, prepared by reaction of the ketone **40** with ethereal MeLi, was obtained as a colorless liquid, n^{25}D 1.4336 (lit.[43] n^{25}D 1.4326). In additional experiments cold (0°) ethereal solutions of 2.9 mmol of Me_2CuLi (prepared either from a solution of Me_2SCuBr and Me_2S or from a slurry of CuI) were treated with 2.0-mmol samples of the ketone **40**. After these solutions had been stirred for 15 min at 0°, aliquots were removed and subjected to the usual isolation and analysis procedures. These mixtures contained 91–93% of the unchanged ketone **40** and 7–9% of the alcohol **41**. When one of these reaction solutions was allowed to warm to 25° with stirring during 15 min [during which time separation of $(MeCu)_n$ indicated that a slow reaction was occurring], the resulting crude product contained 52% of the unchanged ketone **40** and 48% of the alcohol **41**.

Registry No.—**1**, 54678-22-7; **2**, 54678-23-8; **3**, 54678-24-9; **4a**, 32379-37-6; **4b**, 54678-03-4; **5a**, 1855-63-6; **5b**, 7370-14-1; **6**, 932-66-1; **7**, 37881-09-7; **8**, 54678-07-8; **9**, 54678-08-9; **10**, 54678-09-0; **11**, 54678-10-3; **13**, 54678-11-4; **14**, 54678-12-5; **15** epimer 1, 54678-13-6; **15** epimer 2, 54678-14-7; **16** epimer 1, 54678-15-8; **16** epimer 2, 54678-16-9; **17**, 5222-61-7; **18**, 5222-62-8; **20**, 6248-81-3; **21**, 6252-18-2; **22**, 684-94-6; **24**, 54678-04-5; **25a**, 54678-17-0; **25b**, 54678-18-1; **26**, 54678-05-6; **27**, 5340-45-4; **32**, 563-80-4; **33**, 54678-06-7; **35**, 624-24-8; **36**, 104-74-0; **37**, 923-28-4; **38**, 54678-19-2; **40**, 565-80-0; 4-*tert*-butylcyclohexanone, 98-53-3; CuBr, 7787-70-4; Me_2S, 75-18-3; CuCl, 7758-89-6; CuI, 7681-65-4; CH_2═CHLi, 917-57-7; t-BuC≡CLi, 37892-71-0; Me_2CuLi, 15681-48-8; Me(CH_2═CH)CuLi, 54678-20-5; $HOCH_2CH_2OH$, 107-21-1; 2-methyl-2-butene, 513-35-9; 2,4-pentanedione, 123-54-6; 3-methyl-2,4-pentanedione, 815-57-6; $(CH_2{=}CH)_2CuLi$, 22903-99-7.

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Stereoselective Organometallic Alkylation Reactions. IV. Organolithium and Organoaluminum Addition to Trimethyl-, Triphenyl-, and Trichloroaluminum Complexes of 4-*tert*-Butylcyclohexanone and 2-Methylcyclopentanone[1]

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Reaction of (C$_2$H$_5$)$_3$Al with 4-*tert*-butylcyclohexanone–Al(CH$_3$)$_3$ complex gave significant percentages of ethylation, methylation, and reduction. The similarity between this reaction and the addition of (CH$_3$)$_3$Al and (C$_2$H$_5$)$_3$Al in 1:1 ratio to 4-*tert*-butylcyclohexanone as well as the similarity of the predominant isomer (equatorial alcohol) arising from methylation and ethylation in both cases indicates that in the first case redistribution of the alkyl groups between (C$_2$H$_5$)$_3$Al and ketone–Al(CH$_3$)$_3$ is much faster than alkylation. Triethylaluminum addition to ketone–AlCl$_3$ complex leads to ethyl entry predominantly from the axial side (compression effect) accompanied by a much larger percentage of reduction than (C$_2$H$_5$)$_3$Al addition to uncomplexed ketone. Compounds of the type (C$_2$H$_5$)$_n$AlX$_{3-n}$ give larger ethylation:reduction ratios than (C$_2$H$_5$)$_3$Al when X is electron donating (CH$_3$) and smaller ratios when X is electron withdrawing (Cl). Attempts to introduce n-butyl groups into 4-*tert*-butylcyclohexanone and 2-methylcyclopentanone from the more hindered side by reaction of n-butyllithium with ketone–AlR$_3$ and ketone–AlCl$_3$ complexes were not successful. Alkylation of these complexes gave about the same ratio of isomeric alcohols as did n-butyllithium. Analysis of the results of these latter reactions indicates that the reactions did not occur via the corresponding ate complexes, LiAl(CH$_3$)$_3$C$_4$H$_9$-n and LiAl(C$_6$H$_5$)$_3$C$_4$H$_9$-n, since the latter gave a significantly larger percentage of methylation and reduction, respectively.

One of the more potentially fruitful recent developments in the area of stereoselective alkylation of ketones has been the discovery that reaction of (CH$_3$)$_3$Al with alicyclic ketones in 2:1 ratio in hydrocarbon solvent causes attachment of the methyl group at the carbonyl site predominantly (90%) from the most hindered side.[3,4] Unfortunately, the method is limited in those cases where the organoaluminum reagent possesses β hydrogens in that reduction products are formed.

The present work involves a study of reactions of (C$_2$H$_5$)$_3$Al and n-C$_4$H$_9$Li with aluminum alkyl and aluminum chloride complexes of 4-*tert*-butylcyclohexanone and 2-methylcyclopentanone (ketones displaying a large compression effect)[3c] in order to investigate the possibility of bonding groups other than methyl or phenyl, particularly those that possess a β hydrogen, to the more hindered side of the ketones in high yield. The object of adding the RLi or R$_3$Al compounds to a complexed ketone was not only to direct the R group to the most hindered side of the carbonyl group (compression effect), but also to hinder the possibility of reduction by the ethyl or butyl group via β-hydrogen transfer. In addition, the potential of compounds such as (CH$_3$)$_n$Al(C$_2$H$_5$)$_{3-n}$, (CH$_3$)$_n$AlCl$_{3-n}$, and (C$_2$H$_5$)$_n$AlCl$_{3-n}$ were investigated as stereoselective alkylating agents. In each case, special attention was given to the total percentages of the various possible alkylation–reduction products as well as to the ratio of isomeric alcohols obtained from alkylation and reduction.