# The Chemistry of Carbanions. XXV. The Reaction of Various Organocopper Reagents with $\alpha,\beta$ -Unsaturated Carbonyl Compounds<sup>1a</sup>

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Successful conjugate additions of lithium dimethylcuprate have been effected with the esters, methyl crotonate (15) and methyl cinnamate (17), and the ketones, benzalacetone (13), benzalacetophenone (19), 2-methoxy-3,5,5-trimethyl-2-cyclohexenone (21), and 4-tert-butyl-1-cyclohexenyl methyl ketone (6). In the latter case 6, 92% of the addition product has the added methyl group axial. The more difficultly reduced ester 12b and ketone 24 failed to react with lithium dimethylcuprate. A new mixed cuprate reagent, t-BuC $\equiv$ C(Li)CuR, is described where R, the group transferred in conjugate additions, is either methyl (36) or vinyl (37). These mixed cuprate reagents, whose preparation is especially convenient, were used in conjugate additions with isophorone 28. Other reactions studied included the reaction of lithium dimethylcuprate with the tetraester 25 to give the reduction product 26 and treatment of the unsaturated nitriles 11 and 40 with the same cuprate. No reaction was observed in these latter cases and the unchanged nitriles were recovered.

Previous studies<sup>2,3</sup> of the conjugate addition of organocopper reagents to  $\alpha,\beta$ -unsaturated carbonyl compounds have established this reaction as a useful preparative procedure for the introduction of alkyl, aryl, or alkenyl<sup>3e,4</sup> groups R from the corresponding lithium cuprate reagents R<sub>2</sub>CuLi. Several lines of evidence<sup>3a,c,e</sup> have established that a free carbon radical  $\mathbf{R} \cdot$  is not an intermediate in these reactions: particularly compelling evidence arises from the fact that alkyl and alkenyl groups R are transferred from the metal to the enone substrate with retention of configuration. In conjugate additions to unhindered cyclohexenone systems, the group R is usually introduced predominantly from the direction that will form a cyclohexanone with an axial substituent R;<sup>3b,5</sup> with more hindered cyclic enones, the group R is usually added from the less hindered side of the enone.6

Although the structures of the commonly used cuprate reagents,  $R_2CuLi$ , are uncertain, it seems probable that many of these reagents have structures such as 1a or 1b with clusters of four metal atoms bonded to the organic ligands at the faces (*e.g.*, 1a) or the edges

(3) (a) H. O. House, W. L. Respess, and G. M. Whitesides, J. Org. Chem., **31**, 3128 (1966); (b) H. O. House and W. F. Fischer, Jr., *ibid.*, **33**, 949 (1968); **34**, 3615 (1969); (c) G. M. Whitesides and P. W. Kendall, *ibid.*, **37**, 3718 (1972); (d) J. A. Marshall and R. A. Ruden, *ibid.*, **37**, 659 (1972); (e) F. Näí, and P. Degen, *Helv. Chim. Acta*, **54**, 1939 (1971); F. Näí, P. Degen, and G. Ohloff, *ibid.*, **55**, 82 (1972); (f) H. O. House and M. J. Umen, J. Amer. Chem. Soc., **94**, 5495 (1972); H. O. House, L. E. Huber, and M. J. Umen, *ibid.*, **94**, 8471 (1972); (g) J. A. Marshall, R. A. Ruden, L. K. Hirsch, and M. Phillippe, *Tetrahedron Lett.*, **No. 21**, 2455 (1971); (h) C. P. Casey, D. F. Marten, and R. A. Boggs, *ibid.*, **No. 23**, 2071 (1973). (4) (a) J. Hooz and R. B. Layton, Can. J. Chem., **48**, 1626 (1970); (b)

(4) (a) J. Hooz and R. B. Layton, Can. J. Chem., 48, 1626 (1970); (b)
E. J. Corey and R. L. Carney, J. Amer. Chem. Soc., 93, 7318 (1971); E. J.
Corey, C. U. Kim, R. H. K. Chen, and M. Takeda, *ibid.*, 94, 4395 (1972);
(c) F. S. Alvarez, D. Wren, and A. Prince, *ibid.*, 94, 7823 (1972); (d) A. F.
Kluge, K. G. Untch, and J. H. Fried, *ibid.*, 784, 7827 (1972); (e) R. Pappo and P. W. Collins, *Tetrahedron Lett.*, No. 26, 2627 (1972).

(5) (a) J. A. Marshall and N. H. Andersen, J. Org. Chem., **31**, 667 (1966);
J. A. Marshall, N. H. Andersen, and P. C. Johnson, *ibid.*, **35**, 186 (1970);
(b) H. O. House, R. W. Giese, K. Kronberger, J. P. Kaplan, and J. F. Simeone, J. Amer. Chem. Soc., **32**, 2800 (1970).

one, J. Amer. Chem. Soc., **32**, 2800 (1970).
(6) N. T. Luong-Thi and H. Rivière, C. R. Acad. Sci., Ser. C, **267**, 776 (1968); Tetrahedron Lett., **No. 19**, 1579, 1583 (1970); H. Rivière and J. Tostain, Bull. Soc. Chim. Fr., 568 (1969); (b) J. A. Marshall, W. I. Fanta, and H. Roebke, J. Org. Chem., **31**, 1016 (1966); J. A. Marshall and H. Roebke, *ibid.*, **33**, 840 (1968); (c) R. G. Carlson and E. G. Zey, *ibid.*, **37**, 2468 (1972).



(e.g., 1b) of the tetrahedron formed by the four metal atoms. Such structures (especially 1b in which all R groups are equivalent) are compatible with the structural information available for one relatively stable cuprate reagent<sup>7</sup> and are also analogous to the tetrameric structures indicated for certain stable organocopper compounds<sup>8</sup> as well as certain alkyllithium reagents.<sup>9</sup> Structures of this type 1 (*i.e.*, dimers of the usual cuprate representation  $R_2$ CuLi) serve readily to explain the oxidation of cuprates with a variety of good oxidizing agents (reduction potentials less negative than *ca.* -1.0 V vs. sce, *e.g.*, O<sub>2</sub>, Cu(II) salts, quinones, nitro compounds) to form dimers R-R (eq A) with

$$\begin{array}{ccc} R_4 Cu_2 Li_2 \xrightarrow{-e} [R_4 Cu_2 Li_2]^+ \xrightarrow{-e} (RCu)_x + R - R + 2Li^+ & (A) \\ 1 & 2 \end{array}$$

retention of stereochemistry at the group  $R^{10}$  Since it seems likely that this oxidation can occur in two stages involving an intermediate cation 2,<sup>11</sup> we have been inclined to believe that reaction of cuprates with less powerful oxidizing agents (reduction potential more negative than *ca.* -1.0 V vs. sce, *e.g.*, enones) may involve transfer of only a single electron from the cuprate cluster 1 because these less powerful oxidants are unable to remove a second electron from the intermediate cation 2. Consequently, even in reactions where initial electron transfer steps are involved, oxi-

(7) G. van Koten and J. G. Noltes, Chem. Commun., No. 16, 940 (1972).

(8) (a) G. van Koten, A. J. Leusink, and J. G. Noltes, *Chem. Commun.*,
 No. 17, 1107 (1970); J. M. Guss, R. Mason, I. Søtofte, G. van Koten, and
 J. G. Noltes, *ibid.*, No. 8, 446 (1972); (b) M. F. Lappert and R. Pearce,
 *ibid.*, No. 1, 24 (1973); (c) A. Cairneross and W. A. Sheppard, J. Amer.
 *Chem. Soc.*, 90, 2186 (1968); 93, 247 (1971); A. Cairneross, H. Omura, and
 W. A. Sheppard. *ibid.*, 93, 248 (1971).

(9) See T. L. Brown, Accounts Chem. Res., 1, 23 (1968), and references cited therein.

(10) (a) G. M. Whitesides, W. F. Fischer, Jr., J. San Filippo, Jr., R. W. Bashe, and H. O. House, J. Amer. Chem. Soc., **91**, 4871 (1969), and references cited therein; (b) G. M. Whitesides, J. San Filippo, Jr., E. R. Stredonsky, and C. P. Casey, *ibid.*, **91**, 6542 (1969).

(11) In this species there are formally both the Cu(I) and Cu(II) valence states of copper present. The spectroscopic properties of crystals containing both Cu(I) and Cu(II) species have been discussed previously: P. Day and D. W. Smith, J. Chem. Soc. A, 1045 (1967).

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<sup>(2)</sup> For recent reviews, see (a) G. H. Posner, Org. React., 19, 1 (1972);
(b) J. F. Normant, Synthesis, 63 (1972);
(c) G. Bähr and P. Burba in "Methoden der Organischen Chemie," 4th ed, Vol. 13, Part 1, E. Müller, Ed, Georg Thieme Verlag, Stuttgart, 1970, pp 731-761.

dative dimerization (eq A) need not be a competing reaction (cf. ref 3c). We hope to resolve this question with studies in progress concerning the electrochemical oxidation of organocuprate reagents.

Meanwhile, we have noted<sup>3t</sup> that reactions of Me<sub>2</sub>-CuLi with  $\alpha,\beta$ -unsaturated carbonyl compounds are normally effective for the conjugate addition of a methyl group to the  $\beta$  carbon only when the reduction potential of the unsaturated carbonyl compound in an aprotic medium is more negative than ca. -1.1 V (vs. sce) but less negative than ca. -2.4 V (vs. sce). This correlation, accompanied by a simple empirical rule<sup>3t</sup> for estimating the reduction potentials of  $\alpha,\beta$ -unsaturated carbonyl compounds, allows synthetic procedures to be designed to avoid steps where the successful conjugate addition of Me<sub>2</sub>CuLi is uncertain. The correlation with reduction potentials is, of course, compatible with (but does not prove) the mechanistic scheme (eq B) proposed<sup>3a,b,f,g</sup> for the conjugate addition of organo-



cuprates via an initial electron-transfer process to form the cation 2 and a radical anion 3. The recombination of these species followed by an intramolecular transfer of the group R as illustrated in structure 4 can account for the formation of the initial reaction product, the enolate ion 5, and the various stereochemical features of the reaction. We believe that the most reasonable alternative mechanistic path is the direct nucleophilic addition of the cuprate 1 to the enone to form the intermediate 4 is illustrated in eq C. This process, which

$$R_{4}Cu_{2}Li_{2} + CH_{3}CH = CHCOCH_{3} \xrightarrow{\text{nucleophilic}}_{\text{addition}}$$

$$4 \longrightarrow RCHCH = CCH_{3} \quad (C)$$

$$CH_{3} \quad O^{-}$$

is analogous to the oxidative addition of an alkyl halide to a cuprate suggested in the first stage of the cupratealkyl halide coupling reaction,<sup>10a</sup> differs from the twostage process (eq B) only in the timing of steps leading to intermediate 4. Although various  $\pi$  complexes of the enone and the cuprate 1 might be envisioned to precede either process, we are aware of no compelling evidence for their presence and have noted previously<sup>3a</sup> that the conjugate addition process is not retarded by the addition of reagents (e.g., trialkylphosphines or trialkyl phosphites) that would certainly compete with the enone for coordination sites on copper. In this manuscript, we will describe the details of certain reactions cited previously<sup>3f</sup> in our correlation of reactivity with reduction potential and also describe reactions involving other cuprate additions. Among these is the use of a mixed cuprate reagent which has proved to be especially useful in synthetic work.

As a background for a synthetic application of cuprate reagents to be described elsewhere,<sup>12</sup> we wished to establish that the conjugate addition of a cuprate reagent to the unhindered cyclohexenyl ketone **6** (Scheme I) would occur in the expected manner (*via* a chair-like



transition state)<sup>3b,5</sup> to form the adducts 7 and 8 with the added group in an axial conformation. As summarized in Scheme I, this expectation was realized with 92% of the conjugate addition product being the ketones 7 and 8 with axial methyl groups.<sup>13</sup> In the course of this work, we found that the more difficultly reduced unsaturated derivatives 11 and 12b failed to react with Me<sub>2</sub>CuLi and were recovered unchanged.

To show that the failure of ester 12b to react was not attributable to an inherent property of  $\alpha,\beta$ -unsaturated esters, we demonstrated the successful conjugate addition of Me<sub>2</sub>CuLi to both of the more easily reduced esters 15 and 17 (Scheme II) to form esters 16 and 18. The benzylidene ketones 13 and 19 also reacted normally to form 14 and 20. The difficultly reduced  $\beta$ alkoxy enone 24 failed to react with Me<sub>2</sub>CuLi, whereas the more easily reduced  $\alpha$ -alkoxy enone 21 did yield an adduct 22. Although the  $\beta$ -diketone enol ether 24 failed to react with Me<sub>2</sub>CuLi<sub>2</sub> and was recovered, the

(12) H. O. House and M. J. Umen, to be published.

(13) We are most grateful to Professor J. Jacques and M. Dvolaitzky for supplying us with authentic samples of ketones **7**, **8**, and **10** as well as a mixture containing ketone **9** and with nmr spectra for all of these ketones. The preparations of these ketones **7-10** are described by A. Heymes, M. Dvolaitzky, and J. Jacques, Ann. Chim. (Paris), 543 (1968).



enol acetate of the same  $\beta$ -diketone has been found to react with this reagent.<sup>3h</sup> This difference appears to be consistent with the previously noted reduction potential correlation, since the presence of an electrondonating  $\beta$ -alkoxy substituent (Hammett  $\sigma_{\text{para}} \sim -0.3$ ) is known<sup>3f</sup> to make the reduction potential of an  $\alpha,\beta$ unsaturated ketone more negative whereas an electronwithdrawing  $\beta$ -acetoxyl substituent (Hammett  $\sigma_{\text{para}}$ +0.31) would be expected to increase the ease of reduction of an enone.

In the course of the foregoing studies two observations of interest were made. Normally, the progress of a Me<sub>2</sub>CuLi reaction is easily discerned because addition of a solution of the unsaturated carbonyl compound to the initially cold  $(0^\circ)$ , colorless Et<sub>2</sub>O solution of Me<sub>2</sub>CuLi results in an immediate exothermic reaction and polymeric MeCu separates from the cold (0-10°) reaction mixture as a voluminous yellow precipitate within approximately 1 min. These reactions are usually complete within 2-5 min. Also, in many cases the initial reaction mixture exhibits a transient bright red, orange, or violet color which disappears within 15-60 sec followed by the precipitation of MeCu. However, in two of the above cases, the ester 17 and the  $\alpha$ -alkoxy ketone 21, the reaction with Me<sub>2</sub>CuLi was unusually slow and complete reaction with the excess Me<sub>2</sub>CuLi present was not obtained even after periods of 30-90 min. (Since both the reaction of ester 15 with Me<sub>2</sub>CuLi and the subsequently described reaction of ester 17 with Et<sub>2</sub>CuLi exhibited normal rapid reaction rates, the reason for the rate difference in only two cases is presently obscure.) In any event, the rather prolonged reaction of ester 17 with Me<sub>2</sub>CuLi, during which time a transient orange color persisted in the

reaction mixture, prompted us to examine these reacting solutions in the probe of an epr spectrometer. Since we were unable to resolve any well-defined signal attributable to a carbon radical, we turned to nmr techniques and examined the nmr spectra of reacting solutions for emission signals arising from CIDNP. Although our experiments with ester 17 and Me<sub>2</sub>CuLi were unrewarding, the corresponding reaction of ester 17 with Et<sub>2</sub>CuLi produced a clear emission signal in the two highest field lines of the quartet attributable to the ethyl  $CH_2$  group bound to a metal. This emission signal persisted for periods of 30 min or more at temperatures in the range -10 to  $10^{\circ}$ . However, as mentioned above, subsequent investigation revealed that reaction of the ester 17 with Et<sub>2</sub>CuLi was complete in <1 min and the prolonged CIDNP emission signal which we observed was arising from decomposition of the excess Et<sub>2</sub>CuLi in the reaction mixture. Furthermore, the CIDNP signal was observed only during the decomposition of Et<sub>2</sub>CuLi prepared from commercial CuI which was contaminated with traces of iron impurities. When these iron impurities were removed before the preparation of Et<sub>2</sub>CuLi (see Experimental Section), no CIDNP emission was observed under any of the above circumstances.<sup>14</sup> A number of pieces of circumstantial evidence have also led us to believe that the amount of iron impurities extracted from imperfectly sealed Teflon-coated magnetic stirring bars may also catalyze the decomposition of various cuprates; as a result, we believe it unwise to use any stirring device not completely encased in glass for organocuprate reactions.

In earlier synthetic studies<sup>15</sup> involving the conjugate addition of aryl Grignard reagents to the easily reduced tetraester **25** (Scheme III), a substantial fraction of the



ester 25 was reduced to ester 26 unless the Grignard reagent was prepared from triply sublimed, rather than ordinary, Grignard-grade magnesium.<sup>16</sup> These observations suggested that the tetraester 25 might be a sufficiently powerful oxidant to remove two electrons from a cuprate reagent (*cf.* eq A) forming the dianion

<sup>(14)</sup> A similar complication from the iron-catalyzed decomposition of a Grignard reagent has been observed recently: R. B. Allen, R. G. Lawler, and H. R. Ward, J. Amer. Chem. Soc., 95, 1692 (1973).

<sup>(15)</sup> H. O. House, D. G. Melillo, and F. J. Sauter, J. Org. Chem., 38, 741 (1973).

<sup>(16)</sup> The principal transition metal impurities in ordinary Grignard-grade magnesium are iron, copper, and manganese: D. O. Cowan, J. Hsu, and J. D. Roberts, J. Org. Chem., 29, 3688 (1964).

27 rather than a conjugate addition product. Reaction of the tetraester 25 with Me<sub>2</sub>CuLi confirmed this suspicion by forming, after acidification, the saturated ester 26 in 76-93% yield with no evidence for the formation of a conjugate addition product.

For a synthetic application to be described elsewhere,<sup>12</sup> we needed a reliable procedure for effecting the conjugate addition of a vinyl group in an enone. Although a number of conjugate additions with (CH<sub>2</sub>= CH)<sub>2</sub>CuLi<sup>4a,b</sup> and other dialkenylcuprates<sup>3e,4c-e</sup> have been reported, the substantial experimentation required<sup>4d</sup> to apply this reaction to preparative work suggested the need for an improved procedure. Our own experiments involving the preparation of (CH<sub>2</sub>=CH)<sub>2</sub>-CuLi from CH<sub>2</sub>=CHLi and CuI and the subsequent addition of this reagent to the model enone 28 to form adduct 29 also indicated the capricious nature of this procedure. We concluded that our problem arose because of the thermal instability of the vinvl cuprate reagents, which became especially serious as the temperature was raised from  $ca. -20^{\circ}$  to  $0^{\circ}$  or higher. This thermal instability complicated formation of the cuprate because the reaction of CH<sub>2</sub>=CHLi with the insoluble CuI was relatively slow, especially at temperatures below  $-40^{\circ}$ . Because of these problems various cuprate preparations either contained unchanged  $CH_2$ = CHLi (which added to the carbonyl group of the enone 28) or a substantial portion of the cuprate had decomposed, leading either to recovery of the enone 28 or the formation of its reduction product 30. These difficulties were partially avoided by the use of the  $Et_2O$ soluble complex (MeO)<sub>3</sub>PCuBr as a source of copper. However, neither the preparation of this complex nor the subsequent removal of (MeO)<sub>3</sub>P from the reaction mixtures was convenient and we were led to seek other soluble materials as sources of copper(I) in these reactions. Other recent approaches to this problem have utilized the reaction of CuCN,<sup>17a</sup> n-C<sub>3</sub>H<sub>7</sub>C=CCu,<sup>17b</sup> or t-BuOCu<sup>17</sup>° with an organolithium reagent RLi to form the mixed cuprates 31 and 32 (Scheme IV), which will selectively transfer the group R in conjugate addition reactions.<sup>18</sup> However, neither CuCN nor n-C<sub>3</sub>H<sub>7</sub>C= CCu have appreciable solubility in ethereal solvents; although the solubility of the acetylide precursor of cuprate 32 can be increased by the addition of the ligand, (Me<sub>2</sub>N)<sub>3</sub>P,<sup>17b</sup> use of this ligand poses the same inconveniences noted above with (MeO)<sub>3</sub>P. The mixed cuprate 31b obtained from t-BuOCu appears to be satisfactory for the conjugate addition of alkyl groups; however, use of this reagent (31b, R = vinyl)to effect conjugate addition of a vinyl group is reported<sup>17c</sup> not to be a satisfactory procedure.

In exploring other possible copper(I) sources to use for cuprate preparations, we found that copper *tert*butylacetylide (33) was an ideal reagent. This acetylide 33 was available from *tert*-butylacetylene either by reaction with a Cu(I) salt in aqueous ammonia or, preferably, by successive reaction of the acetylene 34with 1 molar equiv of an organolithium reagent and 1 molar equiv of CuI. The acetylide, an orange-red

solid melting with decomposition over the range 80- $150^{\circ}$ , could either be isolated or used in situ and, most important, the acetylide 33 is readily soluble in both ethereal solvents and in saturated hydrocarbons. Ether solutions of the acetylide 33 were conveniently hydrolyzed by shaking with aqueous  $NH_3$  and, even when some competing oxidation occurred during isolation procedures, the product diyne 35 was very volatile and easily removed from reaction products. Employing this acetylide 33, ether solutions of each of the mixed cuprates 36 (with MeLi at 0-10°) and 37 (with  $CH_2 =$ CHLi at  $-40^{\circ}$ ) could be prepared. Treatment of the cold red-orange ether solution of the acetylide 33 with the appropriate lithium reagent produced green solutions of the cuprates 36 and 37. Each cuprate reacted with isophorone (28, 0–10° for 36 and -40 to 10° for 37) to yield the corresponding adduct 29 or 38. As the reaction with the cuprate 36 progressed the green color was discharged and the reaction solution again assumed the red-orange color of the acetylide **33**. The reaction of the mixed vinyl cuprate 37 with isophorone (28) was still a relatively slow process and some competing thermal decomposition of the cuprate 37 occurred with separation of a brown or black solid (possibly metallic copper). The subsequently described<sup>12</sup> reaction of this mixed cuprate 37 with the enone 6 was more rapid than reaction with isophorone (28), and less competing thermal decomposition was observed.



An interesting by-product, the reduced ketone 30, was observed during the reaction of isophorone (28) with both  $(CH_2=\bar{C}H)_2CuLi$  and the mixed vinyl cuprate 37. The amount of the by-product formed (typically 7-13%) seemed to be greatest in those reactions where the most thermal decomposition of the vinyl cuprate 37 was occurring, suggesting that one mode of the thermal decomposition of 37 involves transfer of a  $\beta$ -hydrogen atom from the vinyl group to the metal to form a mixed hydride cuprate reagent 39 that has the ability to reduce the C==C double bond of enones. We plan to investigate the formation and possible synthetic utility of such reagents further. Itshould be noted that a thermal decomposition of the type suggested is compatible both with the pathway followed in the thermal decomposition of alkylcopper

<sup>(17) (</sup>a) J. P. Gorlier, L. Hamon, J. Levisalles, and J. Wagnon, Chem. Commun., No. 3, 88 (1973); (b) E. J. Corey and D. J. Beames, J. Amer. Chem. Soc., 94, 7210 (1972); (c) G. H. Posner and C. E. Whitten, Tetrahedron Lett., No. 21, 1815 (1973).

<sup>(18)</sup> In general, acetylide or cyanide groups are not transferred from cuprates to unsaturated carbonyl compounds (ref 3b).

derivatives<sup>10a,19</sup> and also with the enhanced thermal stability of Me<sub>3</sub>SiCH<sub>2</sub>Cu,<sup>8b</sup> a compound lacking a  $\beta$ -hydrogen atom.

The mixed methyl cuprate 36, although effective for the transfer of a methyl group to the relatively unreactive enone 28 (to form 38), appeared to be less reactive than Me<sub>2</sub>CuLi. Thus, with the  $\alpha$ -methoxy enone 21, which reacted only very slowly with Me<sub>2</sub>CuLi to form 22, none of the adduct 22 was detected after reaction of the enone 21 with the mixed cuprate 36 for 30 min at 5–18° and 73% of the unchanged enone 21 was recovered.

Finally, we have examined the reaction of the unsaturated nitrile 40 with both Me<sub>2</sub>CuLi and with the mixed cuprate 36. Although the reduction potential (-1.84 V vs. sce) of cinnamonitrile is substantially less negative than that of the unsaturated nitrile 11, in neither case was any evidence of reaction observed and both nitriles 11 and 40 were recovered unchanged. Consequently, it appears that the conjugate addition of cuprates to simple  $\alpha,\beta$ -unsaturated nitriles is not a useful procedure.

#### Experimental Section<sup>20</sup>

Starting Materials and Reagents .- Commercial ethereal solutions of MeLi (halide free, Foote Mineral Co.) were standardized by the procedure of Watson and Eastham.<sup>21</sup> An ethereal solution of EtLi, prepared from Li and EtBr, was standardized by the same procedure.<sup>21</sup> A mixture of 22.7 g (100 mmol) of tetravinyltin (M and T Corp.) and 220 mmol of n-BuLi in 135 ml of hexane was agitated for 10 min and then the solid vinyllithium was collected on a sintered glass filter.<sup>22</sup> After the solid vinvllithium had been washed with three 50-ml portions of anhydrous hexane, it was dissolved in  $Et_2O$  to give 171 ml of a pale yellow solution of ethereal 1.25 M vinyllithium (97% yield based on n-BuLi). This ethereal solution, standardized by the usual procedure, 21 had nmr absorption corresponding to the published spectrum.<sup>22</sup> Commercial solutions of vinyllithium in THF (a redbrown suspension obtained from Lithium Corporation of America) could be partially purified by removing the THF under reduced pressure followed by extraction of the residue with Et<sub>2</sub>O and centrifugation. The resulting orange ethereal solution of vinyllithium contained an extra nmr peak at  $\delta$  7.35 attributable to an unidentified impurity still present. Commercial samples of CuI and CuBr were obtained from Fisher Scientific Co. The colored impurities were removed from these salts by dissolving them in a saturated aqueous solution of the appropriate halide (KI or KBr) followed by treatment with charcoal, filtration, and dilution with water to reprecipitate the Cu(I) halide.23 Spectrographic analysis of these commercial copper salts indicated them to contain trace amounts (ca. 0.005%) of Fe salts, but other common transition metal impurities (Cr, Mn, Ni, Co) were not detected. This iron impurity could be removed by dissolving

(21) (a) S. C. Watson and J. F. Eastham, J. Organometal. Chem., 9, 165 (1967). (b) For a detailed description of the titration procedure, see M. Gall and H. O. House, Org. Syn., 52, 39 (1972).

the Cu(I) salt in at least 2 molar equiv of freshly distilled Bu<sub>2</sub>S, bp 74-75° (14 mm), to form the Et<sub>2</sub>O-soluble liquid complexes ICu(SBu<sub>2</sub>)<sub>2</sub> or BrCu(SBu<sub>2</sub>)<sub>2</sub>. These liquids were filtered through a sintered glass funnel to remove the insoluble iron-containing impurities (spectrographic analysis) and the filtrates were heated to 140-160° under 10-20-mm pressure in a rotary evaporator to leave the copper salts in which the iron-containing impurity was not detected (spectrographic analysis). The copper(I) halides purified in this fashion are subsequently designated as iron-free.

Alternatively, the iron impurity could be removed by forming and then recrystallizing the trimethyl phosphite complexes of these copper(I) halides. After a mixture of 1.897 g (10.0 mmol) of CuI and 1.230 g (9.94 mmol) of (MeO)<sub>8</sub>P in 20 ml of PhH had been refluxed for 7.8 hr, it was filtered and concentrated to separate 2.945 g (94%) of the crude phosphite complex as a white solid, mp 179.5-189.5°. Recrystallization (CHCl<sub>3</sub>-Et<sub>2</sub>O) afforded 1.066 g of pure (MeO)<sub>8</sub>PCuI as white needles, mp 192.5-194° (lit.<sup>24</sup> mp 192-193°).

A mixture of 143.5 g (1.00 mol) of CuBr and 124 g (1.00 mol) of (MeO)<sub>8</sub>P in 21. of PhH was refluxed for 8.3 hr and then filtered and concentrated. The tan solid that separated was recrystallized (CHCl<sub>3</sub>-Et<sub>2</sub>O) to separate 97.9 g (37%) of (MeO)<sub>8</sub>PCuBr as white cubes, mp 212-218° dec. Concentration of the mother liquors separated an additional 139 g (total yield 89%) of the same complex: ir (CCl<sub>4</sub>) 1450, 1180, and 1025 cm<sup>-1</sup>; nmr (CD-Cl<sub>8</sub>) 3.75 (d,  $J_{\rm PH}$  = 12.9 Hz, CH<sub>3</sub>OP); uv (CH<sub>3</sub>CN) end absorption at 230 m $\mu$  ( $\epsilon$ 10,200).

Anal. Caled for  $C_8H_9BrCuO_8P$ : C, 13.47; H, 3.39; Br, 29.87; P, 11.58. Found: C, 13.42; H, 3.26; Br, 29.82; P, 11.55.

All ethereal solvents used in organometallic reactions were distilled from LiAlH, immediately before use. Following a previously described procedure,<sup>25</sup> 200 g (1.30 mol) of 4-tert-butyl-cyclohexanone was treated with 98 g (1.9 mol) of NaCN (95%) and 3.62 mol of HCl in 380 ml of H<sub>2</sub>O and 950 ml of Et<sub>2</sub>O at 20-29° to form 236 g of the crude cyanohydrin as a pale yellow oil that solidified on standing, mp  $56-57^{\circ}$  (lit.<sup>25</sup> mp  $54-57^{\circ}$ ). Reaction of 118.5 g (0.655 mol) of this crude cyanohydrin with 200 g (1.30 mol) of POCl<sub>3</sub> in 323 ml of pyridine and 150 ml of PhH yielded 107 g (100%) of the crude nitrile 11 that crystallized on standing. Recrystallization (EtOH) afforded the pure nitrile 11 as white plates: mp  $44-45^{\circ}$  (lit.<sup>25</sup> mp  $45-46^{\circ}$ ); ir (CCl<sub>4</sub>) 2218 (conjugated C=N) and 1648 cm<sup>-1</sup> [C=C); uv (95% EtOH) end absorption at 210 m $\mu$  ( $\epsilon$  10,600); nmr (CCl<sub>4</sub>)  $\delta$  6.4–6.7 (1 H, m, vinyl CH), 1.0–2.5 (7 H, m, aliphatic CH), and 0.89 (9 H, s, t-Bu); mass spectrum m/e (rel intensity), 163 (M<sup>+</sup>, 69), 148 (63), 108 (47), 107 (100), 106 (75), 92 (63), 84 (44), 79 (38), 77 (34), 69 (50), 57 (84), and 41 (48). Hydrolysis of 32.9 g (0.202 mol) of the nitrile 11 with 41.6 g (0.64 mol) of KOH (85%) in 160 ml of refluxing ethylene glycol yielded 33.5 g (92%) of the crude solid acid 12a. Recrystallization from aqueous HOAc separated the pure acid 12a as white needles: mp 188.5–189.5° (lit.<sup>26</sup> mp 182–184°); ir (CCl<sub>4</sub>) 2850–3300 (broad, associated OH), 1688 (carboxyl C=O), and 1648 cm<sup>-1</sup> (C==C); uv max (95% EtOH) 213.5 m $\mu$  ( $\epsilon$  12,600); nmr (CF<sub>3</sub>-CO<sub>2</sub>H)  $\delta$  7.2–7.5 (1 H, m, vinyl CH), 1.1–2.6 (7 H, m, aliphatic CH), and 0.93 (9 H, s, t-Bu); mass spectrum m/e (rel intensity) 182 (M<sup>+</sup>, 30), 139 (77), 127 (60), 126 (100), 125 (38), 111 (49), 84 (36), 81 (45), 79 (50), 69 (43), 57 (70), and 41 (36). A mixture of 27.7 g (0.152 mol) of the acid 12a, 14.6 g (0.46 mol) of MeOH, 0.5 ml of concentrated H<sub>2</sub>SO<sub>4</sub>, and 75 ml of ClCH<sub>2</sub>CH<sub>2</sub>Cl was refluxed<sup>27</sup> for 15 hr and then partitioned between CH<sub>2</sub>Cl<sub>2</sub> and aqueous NaHCO3. The organic solution was concentrated and an ether solution of the residue was washed with NaHCO<sub>8</sub>, dried, and concentrated. Distillation of the residue (20.08 g) in a short-path still followed by distillation through a 60-cm spinning band column separated the pure ester 12b as a colorless liquid which exhibited a single glpc peak: bp  $62^{\circ}$  (0.3 mm);  $n^{25}$ D 1.4758; ir (CCl<sub>4</sub>), 1721, 1711 (conjugated ester C=O), and 1657 cm<sup>-1</sup> (C=C); uv max (95% EtOH) 216 m $\mu$  ( $\epsilon$  12,400); nmr (CCl<sub>4</sub>)  $\delta$  6.7–7.0 (1 H, m, vinyl CH), 3.63 (3 H, s, OCH<sub>3</sub>), 1.0– 2.5 (7 H, m, aliphatic CH), and 0.87 (9 H, s, t-Bu); mass spectrum m/e (rel intensity) 196 (M<sup>+</sup>, 11), 140 (70), 81 (21), 79 (24), 57 (100), 53 (22), and 41 (26).

<sup>(19)</sup> G. M. Whitesides, E. P. Stredronsky, C. P. Casey, and J. San Filippo, Jr., J. Amer. Chem. Soc., 92, 1426 (1970).

<sup>(20)</sup> All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated MgSO<sub>4</sub> was employed as a drying agent. The ir spectra were determined with a Perkin-Elmer Model 257 infrared recording spectrophotometer fitted with a grating. The uv spectra were determined with a Perkin-Elmer Model 202 recording spectrophotometer. The nmr spectra were determined at 60 MHz with a Varian Model A-60 or Model T-60 nmr spectrometer or at 100 MHz with a JEOL nmr spectrometer. The chemical shift values are expressed in  $\delta$  values (parts per million) relative to a MesSi internal standard. The mass spectra were obtained with an Hitachi Perkin-Elmer Model RMU-7 or a Varian Model M-66 mass spectrometer. All reactions involving strong bases or organometallic intermediates were performed under a nitrogen atmosphere.

<sup>(22)</sup> The proceedure of D. Seyferth and M. A. Weiner, J. Amer. Chem. Soc., 83, 3583 (1961); D. Seyferth, C. S. Johnson, Jr., M. A. Weiner, and J. S. Waugh, *ibid.*, 83, 1306 (1961).

<sup>(23)</sup> The procedure of G. B. Kauffman and L. A. Teter, Inorg. Syn., 7, 9 (1963).

<sup>(24)</sup> H. O. House, W. F. Fischer, Jr., M. Gall, T. McLaughlin, and N. Peet, J. Org. Chem., 36, 3429 (1971).
(25) R. A. Abramovitch and D. L. Struble, Tetrahedron, 24, 357 (1968).

<sup>(25)</sup> R. A. Abramovitch and D. L. Struble, *Tetrahedron*, 24, 357 (1968).
(26) L. Munday, J. Chem. Soc., 1413 (1964).

<sup>(27)</sup> The esterification procedure of R. O. Clinton and S. C. Laskowski, J. Amer. Chem. Soc., 70, 3135 (1948).

Anal. Calcd for  $C_{12}H_{20}O_2$ : C, 73,43; H, 10,27. Found: C. 73.32: H. 10.23.

To 110 ml of a cold (0-10°) Et<sub>2</sub>O solution containing 0.184 mol of MeLi was added 14.8 g (0.091 mol) of the nitrile 11 in 30 ml of Et2O. After the resulting red-orange solution had been stirred for 20 min, it was partitioned between  $Et_2O$  and 500 ml of aqueous 1 M HCl. The  $Et_2O$  layer was washed with aqueous NaHCO<sub>3</sub>, dried, and concentrated. The aqueous HCl layer was mixed with 300 ml of hexane and then refluxed for 18 hr to complete hydrolysis of the imine. The combined hexane layer and hexane extract of the aqueous phase were washed with aqueous NaHCO<sub>3</sub>, dried, concentrated, and combined with the earlier neutral product from  $Et_2O$  extraction. Distillation separated 12.95 g (80%) of the pure (glpc) ketone 6 as a colorless liquid: bp 141–143° (19 mm);  $n^{25}$ D 1.4844 [lit. bp 137° (18 mm),  $13^{13}$  135–137° (14 mm)<sup>28</sup>]; ir (CCl<sub>4</sub>) 1659 (conjugated C=O) and 1643 cm<sup>-1</sup> (C=C); uv max (95% EtOH) 232 mμ (ε 9150); nmr (CCl<sub>4</sub>) δ 6.7-6.9 (1 H, m, vinyl CH), 2.17 (3 H, s, COCH<sub>3</sub>), 1.0-2.7 (7 H, m, aliphatic CH), and 0.90 (9 H, s, t-Bu); mass spectrum m/e(rel intensity) 180 (M<sup>+</sup>, 100), 165 (35), 124 (77), 123 (92), 109 (89), 81 (59), 57 (91), 43 (74), and 41(43).

Preparation of Copper(I) tert-Butylacetylide (33).-tert-Butylacetylene (34) was prepared by modification<sup>29</sup> of procedures described previously.<sup>30,31</sup> To 240 g (2.4 mol) of cold (0°) pinacolone was added, portionwise with cooling and stirring during  $\mathbf{2}$ hr, 500 g (2.4 mol) of powdered PCl<sub>5</sub>. After the resulting brown suspension had been stirred in an ice bath for an additional 9 hr, it was poured onto 1.4 kg of ice and the resulting mixture was allowed to stand in a refrigerator overnight. The resulting purple mixture was extracted with Et<sub>2</sub>O and the ethereal extract was dried and concentrated cautiously under reduced pressure on a rotary evaporator until the crude product, 2,2-dimethyl-3,3dichlorobutane, just began to sublime.32 The residual yellow semisolid (237.6 g) contained (nmr analysis) ca. 60% of the dichloride and ca. 40% of 3,3-dimethyl-2-chloro-1-butene. The subsequent dehydrochlorination was effected in a flask fitted with a condenser through which warm (55°) water was circulated so that the intermediate chloro olefin (bp 97-99°)30 and EtOH would not distil from the reaction mixture. The crude mixture of dichloride and chloro olefin (239 g) was mixed with 1 kg (15 mol) of 85% KOH flakes and 120 ml of EtOH and the mixture was heated under partial reflux until distillation of the acetylene 34 was complete. The acetylene was collected as 43.9 g (ca. 20%) based on pinacolone) of a fraction, bp  $34-38^\circ$ , con-taining (nmr analysis) ca. 8% Et<sub>2</sub>O and 76.01 g (38.6%, total yield ca. 58% based on pinacolone) of the acetylene **34**, bp 36–38°. Redistillation afforded the pure acetylene 34 as a colorless liquid: bp 36-38°; n<sup>25</sup>D 1.3738 [lit. bp 36.4-37.8° (768.3 mm),<sup>30</sup> n<sup>20</sup>D 1.3736<sup>33</sup>]; ir (CCl<sub>4</sub>), 3320 (acetylenic CH) and 2110 cm<sup>-1</sup> (C=C); nmr (CCl<sub>4</sub>) § 1.88 (1 Hs, C=CH) and 1.25 (9 H, s, t-Bu).

A cold  $(0-5^{\circ})$  solution of 2.50 g (10 mmol) of CuSO<sub>4</sub>  $\cdot$  5H<sub>2</sub>O and 10 ml of aqueous 28% NH<sub>3</sub> in 40 ml of H<sub>2</sub>O was flushed with N<sub>2</sub> and then treated with 1.42 g (20.4 mmol) of HONH<sub>3</sub>Cl. The resulting solution of the copper(I) complex, under an  $N_2$  atmosphere, was treated with 0.80 g (10 mmol) of the acetylene 34 and the cold mixture was mixed vigorously with a Vibromixer. The acetylide 33 began to separate as an orange solid as soon as the mixing started. After the mixing had been maintained for 10 min, the bulk of the colorless aqueous solution was removed with a cannula and the residual orange solid copper(I) acetylide 33 was extracted from the remaining materials with 100 ml of pentane. The pentane extract was washed with H<sub>2</sub>O, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated to leave 0.77 g (54%) of the acetylide 33 as an orange liquid. A solution of this material in Et<sub>2</sub>O was concentrated under reduced pressure to deposit the pure acetylide 33 as an orange solid: mp 80-150° dec (lit.<sup>34</sup>

(28) M. S. Newman and P. H. Goble, J. Amer. Chem. Soc., 82, 4098 (1960).

(29) These modified procedures were developed in our laboratories by Dr. Norton P. Peet and Mrs. Edith F. Kinloch.

(30) P. D. Bartlett and L. J. Rosen, J. Amer. Chem. Soc., 64, 543 (1942).
(31) W. H. Puterbaugh and M. S. Newman, J. Amer. Chem. Soc., 81, 1611 (1959)

(32) It was important to remove as much Et<sub>2</sub>O as practical at this stage. since its subsequent separation from the acetylene was difficult.

(33) P. Pomerantz, A. Fookson, T. W. Mears, S. Rothberg, and F. L.
Howard, J. Res. Natl. Bur. Stand., No. 2, 52, 51 (1954).
(34) A. E. Favorskii and L. Morev, J. Russ. Phys.-Chem. Soc., 50, 571 (1920); Chem. Abstr., 18, 2496 (1924). In accord with our observations. these authors report that the yellow form of the acetylide changes to a red form when it is heated above 80°.

mp 80-140°); ir (CCl<sub>4</sub>) 2000 cm<sup>-1</sup> (C=C); uv (heptane) points of inflection at 235 m $\mu$  ( $\epsilon$  5350) and 316 (2680) with gradually diminishing absorption out to ca. 600 m $\mu$ ; nmr (CCl<sub>4</sub>)  $\delta$  1.37 (s, t-Bu).

Anal. Caled for C<sub>6</sub>H<sub>9</sub>Cu: C, 49.81; H, 6.27. Found: C, 49.88; H, 6.19.

Although this general procedure is normally very satisfactory for the synthesis of *insoluble* copper(I) acetylides, 35 in the present case the method proved to be very capricious, presumably because the acetylide 33 was soluble in the starting liquid acetylene 34 and, consequently, was not protected from hydrolysis. For example, an  $Et_2O$  solution of the acetylide 33 was rapidly hydrolyzed by shaking with aqueous NH<sub>3</sub>. For this reason, we found it more practical to generate Et<sub>2</sub>O solutions of the acetylide 33 by adding the acetylene 34 to an Et<sub>2</sub>O solution containing 1 molar equiv of MeLi. The resulting Et<sub>2</sub>O solution of t-BuC=CLi was added to a cold (5°) slurry of CuI in Et<sub>2</sub>O and the resulting mixture was stirred at 25-30° for 15 min to give an orange solution of the acetylide 33 and an equimolar amount of LiI. Apart from the presence of LiI, we have observed no difference in the physical or chemical properties between these solutions and the solutions obtained by dissolving the pure acetylide 33 in Et<sub>2</sub>O.

Employing a general procedure for the coupling of terminal acetylenes,<sup>26</sup> a mixture of 5.5 g (28 mmol) of Cu(OAc)<sub>2</sub>·H<sub>2</sub>O, 10 ml of pyridine, 10 ml of MeOH, and 1.61 g (19.6 mmol) of the acetylene 34 was refluxed with stirring for 1 hr. The resulting mixture was cooled in an ice bath, acidified with 60 ml of 9 MH<sub>2</sub>SO<sub>4</sub>, diluted with H<sub>2</sub>O, and extracted with Et<sub>2</sub>O. After the Et<sub>2</sub>O extract had been washed successively with H<sub>2</sub>O and aqueous NaHCO<sub>3</sub>, it was dried and concentrated to leave 679 mg (43%) of the crude diyne 35 as a white solid. Recrystallization (EtOH) separated 255 mg (16%) of the pure diyne 35 as white cubes: mp 129.5-131.5° (lit. mp 130-131°, <sup>37a</sup> 130-132° <sup>37b</sup>); ir (CCl<sub>4</sub>) 2160 cm<sup>-1</sup> (weak, C=C); uv max (heptane) 215 m $\mu$  ( $\epsilon$  152), 226 (245), 238 (284), and 251.5 (186); nmr (CCl<sub>4</sub>)  $\delta$  1.22 (s, *t*-Bu); mass spectrum m/e (rel intensity) 162 (M<sup>+</sup>, 100), 147 (33), 119 (50), 117 (21), 107 (24), 105 (45), 91 (45), 77 (22), 55 (29), 41(65), 40 (20), and 39 (20).

Reaction of the Enone 6 with  $LiCuMe_2$ .—To a cold (-5°) solution of Me<sub>2</sub>CuLi [from 25 mmol of MeLi and 2.37 g (12.5 mmol) of CuI] in 20 ml of Et<sub>2</sub>O was added a solution of 1.829 g (10.1 mmol) of the enone 6 in 6 ml of Et<sub>2</sub>O. The resulting mixture, from which a yellow precipitate of MeCu separated almost immediately, was stirred at -5 to  $10^{\circ}$  for 10 min and then partitioned between ether and an aqueous solution (pH 8) of  $N\hat{H_3}$  and  $NH_4Cl$ . The  $Et_2O$  solution was washed with aqueous  $Na_2S_2O_3$ , dried, and concentrated. Distillation separated 1.601 g (81%) of product as a pale yellow liquid, bp 45-59° (0.3 mm), which contained (glpc, silicone fluid  $QF_1$  on Chromosorb P) the following components: alcohol I eluted as diene II (ca. 8%, retention time 4.0 min), ketone 9 (ca. 4%, 7.6 min), ketone 7 (ca. 21%, 10.8 min), ketone 10 (ca. 4%, 12.8 min), and ketone 8 (ca. 63%, 14.9 min). The product mixture was chromatographed on silica gel with 5% EtOAc in hexane as an eluent. The latter fractions The product mixture was chromatographed on silica from the chromatograph contained the crude alcohol I. tallization from hexane and subsequent sublimation afforded the alcohol I as white needles: mp 75.3–76.3° (lit.<sup>13</sup> mp 76–78°); ir (CCl<sub>4</sub>) 3600 cm<sup>-1</sup> (OH); nmr (CCl<sub>4</sub>)  $\delta$  5.6–5.8 (1 H, m, vinyl CH), 1.0-2.3 (7 H, m, aliphatic CH), 1.37 (1 H, s, OH, exchanged with D<sub>2</sub>O), 1.23 (6 H, s, CH<sub>3</sub>), and 0.87 (9 H, s, t-Bu); mass spectrum m/e (rel intensity) 196 (M<sup>+</sup>, 11), 182 (22), 181 (100), 123 (25), 121 (27), 107 (29), 97 (22), 59 (44), 57 (61), 43 (67), and 41 (34). The early fractions from this chromatograph contained a minor liquid component believed to be the diene II: ir (CCl<sub>4</sub>) 1641 and 1610 cm<sup>-1</sup> (C=C); mass spectrum m/e (rel intensity) 178 (M<sup>+</sup>, 47), 121 (69), 107 (78), 93 (50), 79 (100), 71 (43), 57 (93), 43 (45), and 41 (53). The ketone-containing fractions were rechromatographed on silica gel with 50% PhH in hexane as the eluent to separate pure samples of the ketones 7, 8, and 9. Ketone 7 has the following spectroscopic properties: ir (CCl<sub>4</sub>) 1704 cm<sup>-1</sup> (C==0); nmr (CDCl<sub>3</sub>, 100 MHz)  $\delta$  1.0-2.8 (9, H, m, aliphatic CH), 2.10 (3 H, s, CH<sub>3</sub>CO), 1.03 (3 H, d, J = 7 Hz, CH<sub>3</sub>), and 0.78 (9 H, s, *t*-Bu); mass spectrum m/e(rel intensity) 196 (M<sup>+</sup>, 14) 140 (29), 139 (28), 97 (44), 95 (32), 85 (57), 71 (42), 69 (31), 57 (75), 55 (45), 43 (100), and 41 (51).

(35) See D. C. Owsley and C. E. Castro, Org. Syn., 52, 128 (1972), and references cited therein.

(36) I. D. Campbell and G. Eglinton, Org. Syn., 45, 39 (1965). (37) (a) H. Bock and H. Seidl, J. Chem. Soc. B, 1158 (1968); (b) F. Bohlmann, Chem. Ber., 86, 657 (1953).

The spectroscopic properties of ketone 8 are ir (CCl<sub>4</sub>) 1709 cm<sup>-1</sup> (C=O); nmr (CDCl<sub>3</sub>, 100 MHz),  $\delta$  1.0–2.7 (9 H, m, aliphatic CH), 2.06 (3 H, s, CH<sub>3</sub>CO), and 0.83 (9 H, s, t-Bu) partially resolved from an apparent 3 H doublet (CH<sub>3</sub>); mass spectrum m/e (rel intensity), 196 (M<sup>+</sup>, 40), 140 (58), 139 (79), 97 (94), 95 (46), 85 (45), 83 (40), 71 (73), 69 (57), 57 (100), 43 (90), and 40 (56). Each of these major products 7 and 8 was identified with an authentic sample<sup>13</sup> by comparison of ir and nmr spectra and glpc retention times. The spectroscopic properties of ketone 9, identified with an authentic sample<sup>13</sup> by comparison of nmr spectra and glpc retention times, are ir  $(CCl_4)$  1708 cm<sup>-1</sup> (C=O); nmr (CDCl<sub>3</sub>, 100 MHz)  $\delta$  0.9–2.8 (12 H, m, CH<sub>3</sub> and aliphatic CH), 2.06 (3 H, s, CH<sub>3</sub>CO), and 0.82 (9 H, s, *t*-Bu); mass spectrum m/e (rel intensity) 196 (M<sup>+</sup>, 44), 140 (55), 139 (51), 97 (57), 95 (33), 85 (70), 84 (34), 71 (100), 57 (89), 55 (37), 43 (92), 41 (40), and 40 (68). Treatment of 5.4 mg of ketone 9 with 3.5 mg of NaOMe in 10 ml of refluxing MeOH afforded a mixture containing primarily ketone 10, ir (CCl<sub>4</sub>) 1710 cm<sup>-1</sup> This material was identified with an authentic sample<sup>18</sup> (C=0).by comparison of ir spectra and glpc retention times.

In related experiments, a cold  $(-10 \text{ to } -5^{\circ})$  solution of Me<sub>2</sub>-CuLi [from 9.38 g (48.4 mmol) of CuI and 96.8 mmol of MeLi] in 80 ml of Et<sub>2</sub>O was treated with 6.603 g (40.5 mmol) of the nitrile 11 in 20 ml of Et<sub>2</sub>O. After a 10-min reaction period, the usual isolation procedure separated 6.033 g (92%) of the starting nitrile 11, mp 44.5-45.5° (identified by a mixture melting point and comparison of ir and nmr spectra), with no evidence for any methylated product. Similarly, treatment of Me<sub>2</sub>CuLi [from 2.26 g (11.9 mmol) of CuI and 23.6 mmol of MeLi] in 20 ml of Et<sub>2</sub>O with 1.901 g (9.70 mmol) of the ester 12b in 6 ml of Et<sub>2</sub>O resulted in recovery of 1.703 g (90%) of the starting ester 12b, bp 31-66° (0.5 mm), n<sup>25</sup>D 1.4750, identified from ir, nmr, and glpc data. Also, treatment of cold  $(-5^{\circ})$ , ethereal (28 ml) Me<sub>2</sub>CuLi [from 3.33 g (17.0 mmol) of CuI and 33.8 mmol of MeLi] with 2.695 g (13.8 mmol) of the keto enol ether 24<sup>38</sup> in 8 ml of Et<sub>2</sub>O for 10 min resulted in recovery of 2.425 g (90%) of the starting ketone 24, bp 88-92° (0.4 mm),  $n^{25}$ D 1.4782, identified from ir, nmr, and glpc data.

Reaction of the Tetraester 25 with LiCuMe2.-To a cold  $-5^{\circ}$ ) solution of LiCuMe<sub>2</sub> [from 49.0 mmol of MeLi and 4.68 g (24.6 mmol) of CuI] in 37.5 ml of Et<sub>2</sub>O was added, dropwise and with stirring during 25 min, 6.167 g (19.5 mmol) of the tetraester 25, mp  $52.5-54^\circ$  (lit.<sup>39</sup> mp  $52.5-53.5^\circ$ ), in 20 ml of Et<sub>2</sub>O. The reaction mixture, from which MeCu separated almost immediately, was maintained at -5 to  $10^{\circ}$  and stirred for an additional 10 min and then partitioned between Et<sub>2</sub>O and aqueous NH3 and NH4Cl. The organic layer was washed with aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>, dried, and concentrated to leave 4.724 g (76%) of the saturated tetraester 26, mp 71.3-72.3°. Recrystallization from EtOAc-hexane separated the pure tetraester 26 as white needles: mp 73.3–74.3° (lit. mp 75°, <sup>40b</sup> 75–76° <sup>40a</sup>); ir (CCl<sub>4</sub>), 1750 and 1740 cm<sup>-1</sup> (ester C==O); mm (CCl<sub>4</sub>)  $\delta$  4.18 (8 H, q, J = 7 Hz, ethoxyl CH<sub>2</sub>), 3.95 (2 H, s, CH), and 1.27 (12 H, t, J = 7 Hz, ethoxyl CH<sub>3</sub>); mass spectrum m/e (rel intensity) 273 (64), 245 (42), 227 (64), 199 (96), 173 (82), 171 (57), 143 (73), 127 (100), and 99 (85). When this reaction was repeated with 19.5 mmol of the unsaturated tetraester 25 and 22.7 mmol of Me<sub>2</sub>CuLi (from iron-free CuI), the yield of the saturated tetraester 26 was 93.5%.

Reaction of Benzalacetone (13) with LiCuMe<sub>2</sub>.--The addition of an  $\text{Et}_2\text{O}$  solution of 1.961 g (13.4 mmol) of the ketone 13 to a cold  $(-5^\circ)$  solution of LiCuMe<sub>2</sub> [from 32.0 mmol of MeLi and 3.10 g (16.3 mmol) of CuI in 26 ml of Et<sub>2</sub>O resulted in the immediate formation of a red color which rapidly disappeared with the simultaneous separation of MeCu. After a reaction time of 10 min at -5 to 8°, the usual isolation procedure afforded 1.767 g (ca. 82%) of liquid product, bp 64–66° (0.45 mm), which contained (glpc, silicone fluid  $\mathrm{QF_1}$  on Chromosorb P) ca. 95% of the ketone 14 (retention time 12.2 min) accompanied by ca. 5% of 1-phenyl-3-methyl-1,3-butadiene (6.0 min); no reduced product, 4-phenyl-2-butanone (retention time 11.7 min), was detected by glpc analysis and no starting ketone 13 was detected by glpc or nmr analysis. Collected (glpc) samples of the products, ketone 14, and the diene, were identified with authentic

samples<sup>41</sup> by comparison of ir spectra and glpc retention times. The ketone 14 has nmr (CCl<sub>4</sub>) peaks at  $\delta$  7.16 (5 H, m, aryl CH), 3.22 (1 H, m, benzylic CH), 2.5-2.8 (2 H, m, CH<sub>2</sub>CO), 1.95 (3 H, s,  $COCH_3$ ), and 1.23 (3 H, d, J = 6.5 Hz,  $CH_3$ ).

Reaction of Methyl Crotonate (15) with LiCuMe2.-Treatment of a cold (0°) solution of LiCuMe<sub>2</sub> [from 35 mmol of MeLi and 3.44 g (18.1 mmol) of CuI] in 30 ml of Et<sub>2</sub>O with 1.335 g (13.3 mmol) of the ester 15 in 8 ml of Et<sub>2</sub>O resulted in the rapid separation of MeCu. After a reaction time of 10 min at  $5-22^{\circ}$ , the usual isolation procedure separated 985 mg (63%) of the ester 16, bp 112-113°, n<sup>25</sup>D 1.3896, which was contaminated (glpc, silicone fluid QF1 on Chromosorb P) with a small amount of Et<sub>2</sub>O. An additional 248 mg (16%, total yield 79%) of the ester 16 was recovered from the distillation apparatus. A collected (glpc) sample of the pure ester 16 was identified with an authentic sample by comparison of ir and nmr spectra and glpc retention times. An authentic sample of the ester 16, prepared in 79% yield by esterification of isovaleric acid with MeOH, H<sub>2</sub>SO<sub>4</sub>, and CH<sub>2</sub>Cl<sub>2</sub>, was obtained as a colorless liquid: bp 115-118°;  $n^{25}$ D 1.3918 (lit. bp 115–116°, <sup>42a</sup>  $n^{25}$ D 1.3900<sup>42b</sup>); ir (CCl<sub>4</sub>), 1740 cm<sup>-1</sup> (ester C=O); nmr (CCl<sub>4</sub>)  $\delta$  3.62 (3 H, s, OCH<sub>3</sub>) and 1.9–2.3 (3 H, m, CH and CH<sub>2</sub>CO), and 0.8–1.1 (6 H, m, CH<sub>3</sub>); mass spectrum m/e (rel intensity) 116 (M<sup>+</sup>, 3), 101 (58), 88 (53), 85 (82), 74 (100), 59 (66), 57 (83), 43 (65), and 41 (49).

Reaction of Methyl Cinnamate (17) with LiCuMe2.-Addition of 2.320 g (14.3 mmol) of the ester 17 in 10 ml  $Et_2O$  to a cold -5°) solution of LiCuMe<sub>2</sub> [from 85.0 mmol of MeLi and 8.19 g (43.1 mmol) of CuI] in 63 ml of Et<sub>2</sub>O formed a yellow-orange solution which was stirred at -5 to 5° for 40 min; the precipita-tion of MeCu began after approximately 30 min. The usual isotion of MeCu began after approximately 30 min. lation procedure afforded 2.014 g (79%) of liquid product, bp  $35-75^{\circ}$  (0.5 mm), which contained (glpc, silicone fluid QF<sub>1</sub> on Chromosorb P) the ester 18 (retention time, 5.8 min) accompanied by very minor amounts of two components with the same retention times as the ketone 14 (7.4 min) and the starting ester 17 (9.4 min). A collected (glpc) sample of the ester 18 was identified with an authentic sample by comparison of ir and nmr spectra and of glpc retention times. An authentic sample of the but and a spectral s (0.5 mm);  $n^{25}$ D 1.4972 [lit. bp 133-134° (22 mm), $4^{25}$ D 1.4999<sup>48b</sup>]; ir (CCl<sub>4</sub>) 1740 cm<sup>-1</sup> (ester C=O); nmr (CCl<sub>4</sub>)  $\delta$ 7.15 (5 H, m, aryl CH), 3.47 (3 H, s, OCH<sub>3</sub>), 2.9-3.7 (1 H, m, benzylic CH), 2.4-2.7 (2 H, m, CH<sub>2</sub>CO), and 1.23 (3 H, d, J = 6.5 Hz, CH<sub>3</sub>); mass spectrum m/e (rel intensity), 178 (M<sup>+</sup>, 33), 121 (18), 118 (74), and 105 (100).

The same reaction was repeated with 36 mmol of Me<sub>2</sub>CuLi and 34.7 mmol of the ester 17 in 57 ml of Et<sub>2</sub>O at 25-40° for 30 min, to give 5.48 g of crude liquid product. After addition of a known weight of internal standard  $(n-C_{12}H_{26})$ , glpc analysis (silicone gum SE-52 on Chromosorb P) indicated the presence of *n*-dodecane (retention time 5.9 min at 133°), the saturated ester 18 (56% yield, 11.9 min at 133°), and two unidentified higher boiling components (46.4 and 52.4 min at 230°). Short-path distillation separated a sample of the pure ester 18, n<sup>25</sup>D 1.4961, that was identified with the previously described sample by comparison of ir spectra. Analysis (glpc) of the residue from this mixture established the absence of either of the diastereoisomers<sup>5b</sup> of the dihydro dimer 41 among the high-boiling byproducts.

#### PhCHCH<sub>2</sub>CO<sub>2</sub>Me

### PhCHCH2CO2Me 41

Reaction of Methyl Cinnamate (17) with Et<sub>2</sub>CuLi.-To a cold  $-30^{\circ}$ ) solution of Et<sub>2</sub>CuLi, prepared from 4.23 g (22.2 mmol) of CuI, 40.8 mmol of EtLi, and 30 ml of Et2O, was added a solution of 1.616 g (10.0 mmol) of the ester 17 in 10 ml of  $Et_2O$ . The resulting greenish-purple solution was stirred at -20 to  $2^{\circ}$  for 75 min and then subjected to the usual isolation procedure to separate 1.741 g of crude product as a yellow liquid. Shortpath distillation (100° bath and 0.3 mm) separated  $1.253 ext{ g} 65\%$ ) of the pure (glpc, silicone fluid  $QF_1$  on Chromosorb P) ester 23

<sup>(38)</sup> The preparation and properties of this enone are described elsewhere (ref 3b).

<sup>(39)</sup> B. B. Corson and W. L. Benson, "Organic Syntheses," Collect. Vol. II,

<sup>Wiley, New York, N. Y., 1943, p 273.
(40) (a) G. C. Buzby, A. J. Castro, and E. B. Reid, J. Org. Chem., 28,</sup> 1082 (1963); (b) J. Tsuji and T. Nogi, ibid., 31, 2641 (1966).

<sup>(41)</sup> H. O. House, D. D. Traficante, and R. A. Evans, J. Org. Chem., 28, 348 (1963).

<sup>(42) (</sup>a) A. Vogel, J. Chem. Soc., 624 (1948); (b) J. C. Munch, J. Amer. Chem. Soc., 48, 994 (1926).
(43) (a) G. Schroeter, Ber., 40, 1589 (1907); (b) K. Konno and S. Mitsui,

Nippon Kagaku Zasshi, 85, 497 (1964); Chem. Abstr., 62, 11728 (1965).

as a colorless liquid:  $n^{25}D$  1.4939;<sup>44</sup> ir (CCl<sub>4</sub>) 1740 cm<sup>-1</sup> (ester C==O); uv (95% EtOH) series of weak ( $\epsilon$  125–207) maxima in the region 245–265 m $\mu$ ; nmr (CCl<sub>4</sub>)  $\delta$  7.0–7.3 (5 H, m, aryl CH), 3.47 (3 H, s, OCH<sub>3</sub>), 2.7–3.2 (1 H, m, benzylic CH), 2.3–2.6 (2 H, m, CH<sub>2</sub>CO), 1.3–2.0 (2 H, m, CH<sub>2</sub>), and 0.77 (3 H, t, J = 7 Hz, CH<sub>3</sub>); mass spectrum m/e (rel intensity) 192 (M<sup>+</sup>, 8), 132 (47), 121 (82), 119 (40), 118 (38), 117 (32), 115 (25), 104 (58), 103 (51), 91 (100), 78 (52), 77 (61), 59 (26), 51 (27), 43 (28), 41 (32), and 39 (26). In a similar reaction run at  $-30^{\circ}$ , an aliquot removed after 2.5 min and subjected to glpc analysis indicated that the reaction was essentially complete after 2.5 min at  $-30^{\circ}$ . In an attempt to detect the presence of intermediates in this reaction, reaction mixtures were prepared at -30 to  $-35^{\circ}$  and allowed to warm slowly while the nmr spectra were observed.

Reaction of Benzalacetophenone (19) with LiCuMe<sub>2</sub>.--A solution of 1.799 g (8.65 mmol) of the ketone 19 in 10 ml of Et<sub>2</sub>O was added to a cold  $(-5^{\circ})$  solution of LiCuMe<sub>2</sub> [from 19.5 mmol of MeLi and 1.93 g (10.1 mmol) of CuI] in 17 ml of  $Et_2O$ . This mixing resulted in the immediate formation of a red solution from which the color faded and MeCu began to precipitate within several seconds. The mixture was stirred at -3 to  $10^{\circ}$  for 10min and then subjected to the usual isolation procedure. The crude neutral product (1.859 g, 96%, mp 67-70°) contained (glpc, silicone fluid No. 710 on Chromosorb P) the  $\beta$ -methyl ketone 20 (retention time 37.1 min); none of the reduction product, 1,3-diphenyl-1-propanone (retention time 35.2 min), was detected by glpc or nmr analysis. Recrystallization of the crude product from MeOH afforded 1.08 g (56%) of the pure ketone 20 as either white needles or white plates: mp 70.5–71° (lit.<sup>45</sup> mp 74°); ir (CCl<sub>4</sub>) 1680 cm<sup>-1</sup> (conjugated C=O); uv max (95% EtOH) 242.5 m $\mu$  ( $\epsilon$  12,600) and 278 (1190); nmr (CCl<sub>4</sub>)  $\delta$  7.0– 8.5 (10 H, m, aryl CH), 3.0-4.0 (3 H, m, aliphatic CH), and 1.47 (3 H, d, J = 6.5 Hz, CH<sub>3</sub>); mass spectrum m/e (rel intensity) 224 (83, M<sup>+</sup>), 210 (21), 209 (100), 120 (36), 106 (29), 105 (78), 91 (26), 77 (48), and 51 (21).

In another experiment in which the Me<sub>2</sub>CuLi was generated from 0.91 g (3.4 mmol) of BrCuP(OMe)<sub>3</sub> and 6.5 mmol of MeLi in 6.6 ml of Et<sub>2</sub>O and then treated with 584 mg (2.81 mmol) of the ketone 19 in 3.3 ml of Et<sub>2</sub>O, the crude product (528 mg of white solid, mp 112-153°) contained (tle analysis, SiO<sub>2</sub> with an EtOAc-hexane eluent) a mixture of the conjugate addition product 20 and the product 42 resulting from a subsequent Michael

## CH<sub>3</sub> COPh | PhCH—CHCHCH<sub>2</sub>COPh Ph 42

reaction.<sup>46</sup> Fractional crystallization of this mixture from MeOH separated samples of the ketone 20, mp 69–70°, and the Michael adduct 42: mp 161–162° (lit.<sup>46b</sup> mp 161.5–163°); ir (CCl<sub>4</sub>) 1686 and 1677 cm<sup>-1</sup> (conjugated C==O); uv max (95% EtOH) 246 m $\mu$  ( $\epsilon$  19,700) with a point of inflection at 280 (2200); mass spectrum m/e (rel intensity) 432 (M<sup>+</sup>, <1), 329 (25), 328 (100), and 223 (21).

Reactions of Isophorone (28). A. With the Methyl Cuprate 36.—A solution of t-BuC=CLi, prepared from 269 mg (3.28 mmol) of the actylene 34 and 3.06 mmol of MeLi in 2.4 ml of Et<sub>2</sub>O, was added with stirring to a cold (10–13°) slurry of 573 mg (3.02 mmol) of purified<sup>23</sup> CuI in 2.0 ml of Et<sub>2</sub>O. To the resulting cold (5–7°) red-orange solution of the acetylide 33 was added 1.7 ml of an Et<sub>2</sub>O solution containing 2.74 mmol of MeLi. This addition resulted in a progressive color change from redorange to yellow to green. To the resulting cold (5–7°) solution of the cuprate 36 was added 2 ml of an Et<sub>2</sub>O solution containing 2.08 mmol of isophorone (28). The color of the reaction mixture changed progressively from green to yellow (1–2 min) to redorange (20 min), after which the mixture was partitioned between Et<sub>2</sub>O and an aqueous solution (pH 8) of NH<sub>4</sub>Cl and NH<sub>3</sub>. The resulting orange Et<sub>2</sub>O solution was washed with three 25-ml portions of aqueous 28% NH<sub>3</sub> to complete the hydrolysis of the acetylide 33 and the remaining colorless Et<sub>2</sub>O solution was washed with H<sub>2</sub>O, dried, and concentrated. After the residual yellow liquid (288 mg) had been mixed with a known weight of n-C<sub>14</sub>H<sub>30</sub> (as an internal standard), analysis (glpc, silicone fluid QF<sub>1</sub> on Chromosorb P, apparatus calibrated with known mixtures) indicated the presence of n-C<sub>14</sub>H<sub>80</sub> (retention time 3.8 min), the tetramethyl ketone 38 (5.9 min, 76% yield), and the unchanged enone 28 (8.0 min, 12% recovery). None of the reduced ketone 30 (retention time 5.0 min) was detected. Collected samples of the ketones 28 and 38 were identified with authentic samples by comparison of glpc retention times and ir and nmr spectra.

B. With Vinylcopper Derivatives.—A solution of 1.966 g (13.6 mmol) of t-BuC≡CCu was cooled to -49° (during which time some of the acetylide 33 separated as an orange solid) and the resulting cold  $(-40 \text{ to } -49^\circ)$  orange slurry was treated, dropwise and with stirring, with 6.8 ml of an Et<sub>2</sub>O solution containing 11.6 mmol of CH<sub>2</sub>=CHLi. In the initial stages of this addition a deep red color developed and the mixture gradually changed to an orange slurry during the time required to complete the addition. The resulting mixture was stirred at -40to  $-50^{\circ}$  for 5 min, during which time it became an opaque green color, and then 7.2 ml of an  $Et_2O$  solution containing 3.65 mmol of isophorone (28) was added. The resulting solution was transferred to an ice-salt cooling bath and stirred for 90 min, during which time it slowly warmed to  $10^{\circ}$ . The resulting brownish-black mixture was added to 50 ml of cold  $(0^{\circ}) 1 M$  HOAc in EtOH and then stirred at  $25-40^{\circ}$  for 5 min and partitioned between 250 ml of saturated aqueous NaHCO<sub>8</sub> and Et<sub>2</sub>O. The Et<sub>2</sub>O layer was washed successively with aqueous 28% NH<sub>3</sub>, aqueous Na<sub>2</sub>- $S_2O_3$ , aqueous 28% NH<sub>3</sub>, and H<sub>2</sub>O, and then dried and concentrated. After the residual liquid (519 mg) had been mixed with an internal standard  $(n-C_{16}H_{34})$ , glpc analysis (silicone fluid QF<sub>1</sub> on Chromosorb P, apparatus calibrated with known mixtures) indicated the presence of the reduced ketone 30 (retention time 7.1 min, 7% yield), *n*-hexadecane (9.5 min), the vinyl ketone 29(10.6 min, 52% yield), the starting enone 28 (11.8 min, 7% re-Colcovery), and a minor unidentified component (21.2 min). lected (glpc) samples of ketones 28 and 30 were identified with authentic samples by comparison of ir spectra and glpc retention times. A collected (glpc) sample of the vinyl ketone 29 was obtained as a colorless liquid with spectral properties corresponding to those reported:<sup>4a</sup> ir (CCl<sub>4</sub>) 1710 (C=O), 1635 (C=C), and 920 cm<sup>-1</sup> (CH=CH<sub>2</sub>); nmr (CCl<sub>4</sub>) δ 4.7-6.1 (3 H, m, vinyl CH), a 2 H AB pattern with J = 14.5 Hz for signals at ca. 2.50 and 2.05 (CH<sub>2</sub>CO), 2.07 (2 H, s, CH<sub>2</sub>CO), 1.65 (2 H, s, CH<sub>2</sub>), 1.07 (3 H, s, CH<sub>3</sub>), 1.02 (3 H, s, CH<sub>3</sub>) and 0.81 (3 H, s, CH<sub>3</sub>); mass spectrum m/e (rel intensity) 166 (M<sup>+</sup>, 100), 110 (49), 109 (57), 95 (76), 83 (96), 82 (60), 81 (21), 70 (22), 69 (32), 68 (57), 67 (66), 56 (35), 55 (55), 53 (27), 41 (34), and 39 (28).

The mixed cuprate 37 could also be prepared without isolation of the copper actylide 33 by the following procedure. To 118 ml of a cold (0°) Et<sub>2</sub>O solution containing 186 mmol of MeLi was added, dropwise and with stirring during 30 min, 15.2 g (186 mmol) of the acetylene 34. The resulting solution of t-BuC CLi was added, slowly and with stirring, to a cold (8-20°) slurry of 35.42 g (186 mmol) of purified<sup>23</sup> CuI in 210 ml of Et<sub>2</sub>O. The resulting red-orange solution of the acetylide 33 was cooled to -59° and then treated, dropwise and with stirring while the solution was maintained at -42 to  $-59^{\circ}$ , with 111 ml of an Et<sub>2</sub>O solution containing 159 mmol of CH<sub>2</sub>=CHLi. The resulting opaque green mixture containing the cuprate 37 was stirred for 5 min at -38 to  $-42^{\circ}$  and then treated with a solu-The tion of 6.9 g (50 mmol) of isophorone (28) in 75 ml of  $\text{Et}_2\text{O}$ . reaction mixture was stirred for 90 min while being cooled in an ice bath and then partitioned between  $\operatorname{Et}_{\mathrm{f}}\mathrm{O}$  and aqueous (pH 8)  $\rm NH_4Cl$  and  $\rm NH_3$ . The resulting  $\rm Et_2O$  solution was washed successively with four portions of aqueous 28%  $\rm NH_3$  (to complete the hydrolysis of  ${\bf 33})$  and aqueous  $Na_2S_2O_3$  and then dried and concentrated. After a portion of the residual brown liquid (7.23 g) had been mixed with an internal standard  $(n-C_{16}H_{34})$ , analysis (glpc) showed the presence of the ketones 30 (13% yield), 29 (49% yield), and 28 (14% recovery), as well as a small amount (ca. 6%) of the ketone 43. Short-path distillation (0.5 mm,  $95^{\circ}$ bath) afforded 6.072 g of colorless liquid products containing the ketones 28 (ca. 15%), 29 (ca. 65%), 30 (ca. 15%), and 43 (ca. Returnes 28 (ca. 13%), 29 (ca. 05%), 30 (ca. 15%), and 25 (ca. 15%). Fractional distillation separated 3.70 g of a fraction, bp 104–118°,  $n^{25}p$  1.4643, containing (glpc) **30** (ca. 18%), 29 (ca. 50%), 28 (ca. 30%), and **35** (ca. 2%), and 1.51 g of a fraction, bp 118–121°,  $n^{25}p$  1.4662, containing (glpc) **30** (ca. 3%), 29

<sup>(44)</sup> This ester is reported to boil at 79-80° (0.1 mm): S. Mitsui and Y. Kudo, Chem. Ind. (London), 381 (1965).

<sup>(45)</sup> R. C. Fuson, R. E. Christ, and G. M. Whitham, J. Amer. Chem. Soc., 58, 2450 (1936).

<sup>(46)</sup> This by-product 42 has been observed previously: (a) R. A. Kretchmer, J. Org. Chem., 37, 2744, 2747 (1972); (b) W. Herz and E. Lewis, *ibid.*, 23, 1646 (1958); (c) G. Wittig and F. Wingler, Chem. Ber., 97, 2146 (1964).

(ca. 79%), 28 (ca. 16%), and 43 (ca. 2%). The residue (0.692 g) contained (glpc) 29 (ca. 31%) and 43 (ca. 69%). A collected



(glpc) sample of the major product, ketone 29, n<sup>25</sup>D 1.4678, was identified with previously described material by comparison of ir spectra and glpc retention times.

A collected (glpc) sample of the ketone 43 was obtained as a colorless liquid:  $n^{25}$ D 1.4602; ir (CCl<sub>4</sub>) 1704 cm<sup>-1</sup> (C=O); nmr (CCl<sub>4</sub>)  $\delta$  2.04 (4 H, broad, CH<sub>2</sub>CO), 1.4–1.6 (2 H, m, CH<sub>2</sub>), 1.1–2.4 (6 H, m, CH<sub>2</sub>), and 0.9–1.1 (12 H, m, including a 6 H singlet at 1.02 and a 3 H singlet at 0.98, four CH<sub>3</sub> groups); mass spectrum m/e (rel intensity) 196 (M<sup>+</sup>, <1), 181 (5), 139 (42), 83 (60), 58 (45), 55 (42), and 43 (100).

Anal. Caled for  $C_{13}H_{24}O$ : C, 79.53; H, 12.32. Found: C, 79.61; H, 12.39.

This ketone by-product 43 was evidently formed from small amounts of *n*-BuLi remaining in the CH<sub>2</sub>=CHLi [prepared from *n*-BuLi and  $(CH_2=CH)_4Sn$ ].

A cold  $(-90^{\circ})$  slurry of 1.89 g (7.05 mmol) of BrCuP(OMe)<sub>8</sub> in 3 ml of Et<sub>2</sub>O was treated with 12.8 mmol of CH<sub>2</sub>==CHLi in 10 ml of Et<sub>2</sub>O and the resulting cold  $(-65 \text{ to } -90^{\circ})$ , dark, heterogeneous mixture was then treated with 410 mg (2.97 mmol) of isophorone (28) in 1 ml of Et<sub>2</sub>O. After the mixture had been stirred at -50 to  $-60^{\circ}$  for 2.25 hr an aliquot was removed, hydrolyzed (1 *M* HOAc in EtOH at  $-60^{\circ}$ ), and found to contain (glpc) the ketones 29 (ca. 80%) and 28 (ca. 20%). Finally, the remaining solution was warmed to 23° during 30 min and then hydrolyzed. The crude product (439 mg) contained (glpc) the ketones 29 (ca. 87%) and 28 (ca. 13%).

Reaction of the Methoxy Ketone 21 with LiCuMe2.-To a cold (3-9°) mixture of 4.0 mmol of LiCuMe2 and 2.3 mmol of excess MeCu, prepared from 1.19 g (6.27 mmol) of purified<sup>23</sup> CuI and 10.3 mmol of MeLi in 7.7 ml of  $Et_2O$ , was added 329 mg (1.96 mmol) of the methoxy ketone 21 in 2 ml of Et<sub>2</sub>O. After the resulting mixture had been stirred at  $1-8^{\circ}$  for 1.3 hr, it was subjected to the usual isolation procedure. The crude product, 287 mg of a yellow liquid, was mixed with an internal standard (n- $C_{14}H_{30}$ ; it contained (glpc, silicone fluid QF<sub>1</sub> on Chromosorb P, apparatus calibrated with known mixtures of authentic samples) the internal standard  $(n-C_{14}H_{30})$ , retention time 4.0 min), the saturated ketone 22 (6.3 min, 26% yield), the starting ketone 21 (9.8 min, 37% recovery), and two or more rapidly eluted peaks (2.8 and 3.3 min) that may be olefins formed by dehydration of an alcohol product. A pure sample of the methoxy ketone product 22 was collected (glpc) as a colorless liquid: ir (CCl<sub>4</sub>) 1723 cm<sup>-1</sup> (C=O); uv max (95% EtOH) 268 m $\mu$  ( $\epsilon$  22); nmr (CCl<sub>4</sub>) § 3.28 (3 H, s, OCH<sub>3</sub>), 3.10 (1 H, s, COCH), a 2 H AB pattern with J = 12 Hz at ca. 2.36 and 2.02 (COCH<sub>2</sub>), a 2 H AB pattern with J = 15 Hz at ca. 1.70 and 1.43 (CH<sub>2</sub>), and a series of partially resolved singlets in the region 0.9-1.1 (12 H, CH<sub>3</sub>); mass spectrum m/e (rel intensity) 184 (M<sup>+</sup>, 48), 139 (31), 126 (22), 109 (28), 99 (79), 98 (31), 97 (100), 86 (23), 85 (64), 83 (65), 72 (31), 71 (25), 69 (27), 55 (40), 43 (22), and 41 (34).

Anal. Calcd for  $C_{11}H_{20}O_2$ : C, 71.69; H, 10.94. Found: C, 71.52; H, 10.85.

A variety of attempts to increase the yield of the saturated ketone 22 formed from the reaction of 21 with Me<sub>2</sub>CuLi consistent afforded mixtures of the adduct 22 and substantial quantities of the unchanged enone 21. A reaction was performed in which the mixed cuprate 36 was prepared by the successive treatment of 283 mg (3.45 mmol) of the acetylene 34 with 3.06 mmol of MeLi, 575 mg (3.02 mmol) of purified<sup>23</sup> CuI, and 2.74 mmol of MeLi. The resulting cold (5-8°) solution of the cuprate 36 in 8.7 ml of Et<sub>2</sub>O was treated with 343 mg (2.04 mmol) of the enone 21. Although color changes (green to yellow to orange) characteristic of reaction were observed during the reaction period (32 min at 5-18°), after following the usual isolation procedure, analysis (glpc) of the crude product (307 mg) indicated a 73% recovery of the unchanged enone 21 (identified by comparison of ir spectra and glpc retention times) and none of the addition product 22 was detected.

Studies with Cinnamonitrile 40.—The polarographic reductions of solutions  $(2.48 \times 10^{-3}-4.27 \times 10^{-3} M)$  of the nitrile 40 in DMF containing 0.5 M n-Bu<sub>4</sub>N<sup>+</sup>BF<sub>4</sub><sup>-</sup> were performed as previously described.<sup>3t</sup> Two reduction waves were observed at -1.84 V vs. sce ( $\alpha n = 1.3$ ,  $i_d = 13.1-17.5 \ \mu$ A) and -2.46 V vs. sce ( $\alpha n - 1.2$ ,  $i_d = 5.8-7.5 \ \mu$ A). A comparable measurement of a 2.3  $\times 10^{-3} M$  solution of isophorone (28) in DMF containing 0.5 M n-Bu<sub>4</sub>N<sup>+</sup>BF<sub>4</sub><sup>-</sup> gave the following values:  $E_{1/2} = -2.24$  V vs. sce ( $\alpha n = 1.21$ ,  $i_d = 17.4 \ \mu$ A).

To a cold  $(5-10^{\circ})$  mixture of 13.4 mmol of Me<sub>2</sub>CuLi and 4.0 mmol of excess MeCu [from 3.303 g (17.4 mmol) of purified<sup>23</sup> CuI, 30.8 mmol of MeLi, and 27 ml of Et<sub>2</sub>O] was added a solution of 1.221 g (9.47 mmol) of the nitrile 40 in 5 ml of Et<sub>2</sub>O. After a reaction period of 20 min at 0-10° (no visible evidence of reaction), the mixture was subjected to the usual isolation procedure and the crude product (1.144 g) was mixed with an internal standard  $(n-C_{14}H_{30})$ . The crude product contained (glpc, silicone fluid QF<sub>1</sub> on Chromosorb P, apparatus calibrated with known mixtures)  $n-C_{14}H_{30}$  (retention time 3.7 min) and the nitrile 40 (11.7 min, 77% recovery, identified by comparison of ir and nmr spectra and glpc retention times).

A comparable result was obtained when a solution of 15.7 mmol of the mixed cuprate 36 and 1.635 g (12.6 mmol) of the nitrile 40 in 43 ml of  $Et_2O$  was stirred at 5–10° for 20 min. The recovered nitrile 40 amounted to 85% and no other product was detected (glpc, ir, and nmr analysis).

**Registry No.**—6, 37881-09-7; 7, 22643-00-1; 8, 22642-99-5; 9, 22643-02-3; 11, 7370-14-1; 12a, 31845-19-9; 12b, 22173-19-9; I (Scheme I), 41601-70-1; 13 (Scheme II), 1896-62-4; II (Scheme I), 41601-72-3; 14 (Scheme II), 17913-10-9; 15, 623-43-8; 16, 556-24-1; 17, 103-26-4; 18, 3461-39-0; 19, 614-47-1; 20, 1533-20-6; 21, 5682-76-8; 22, 41601-77-8; 23, 30368-22-0; 24, 15466-96-3; 25, 6174-95-4; 26, 632-56-4; 28, 78-59-1; 29, 27749-07-1; 33, 40575-23-3; 34, 917-92-0; 35, 6130-98-9; 36, 41602-02-2; 37, 41602-03-3; 40, 1885-38-7; 42, 41601-83-6; 43, 41601-84-7; CuBr, 7787-70-4; (MeO)<sub>8</sub>P, 121-45-9; (MeO)<sub>8</sub>P-CuBr, 34836-54-9; *t*-BuC==CLi, 37892-71-0; MeLi, 917-54-4; CuI, 7681-65-4; CH<sub>4</sub>==CHLi, 917-57-7.