Reaction of Propargylic Substrates with Organocopper Species. Synthetic Aspects

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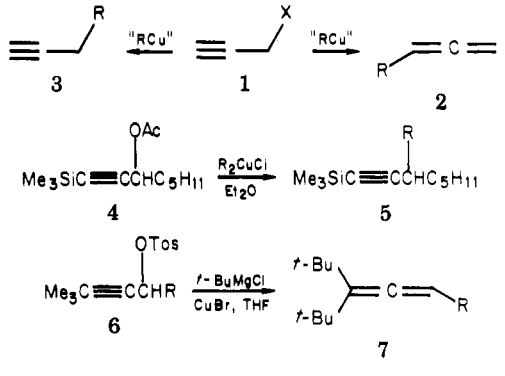
Received December 20, 1979

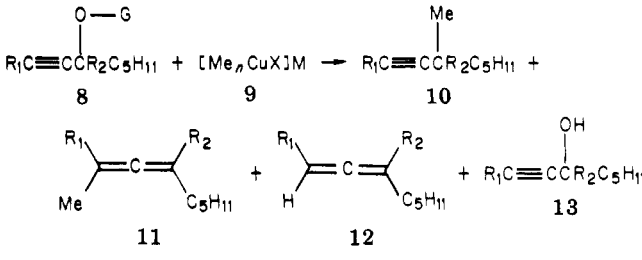
The reaction of propargylic substrates with organocopper species can yield two major products, a substituted allene or a new acetylene. This paper is a study of the factors which influence the distribution of these products in this displacement (e.g., 1 → 2 + 3). Those factors are (1) organocopper reagent stochiometry (R_3CuLi_2, R_2Cu^-, RCu metal salt), (2) organocopper species concomitant salt or counterion (Mg^{2+}, Li^+), (3) acetylenic site substitution and, to a limited extent, propargylic site substitution, (4) temperature, (5) solvent (ether, THF), and (6) leaving group (OAc, OTos, OCO_2Me). The most dominant factor in determining the site of displacement leading to either substituted acetylenes or substituted allenes is the nature of the organocopper reagent. The complex organocopper species [MeCu·LiBr·MgBrI] favors predominantly allene formation, whereas di- or trialkyl organocopper species tend to generate the α-substituted acetylenic system. A second factor intimately associated with product distribution is the leaving group. Of the leaving groups examined, the methyl carbonate moiety appears to be the most versatile and efficacious leaving group available for obtaining either desired displacement product. Relative steric hindrance at the reacting sites of the propargylic skeleton exerts a prominent influence in formation of the acetylenic product 3. Solvent plays a definite and synthetically important role for the reactivity pattern of the monoalkyl-bound species [MeCu·LiBr·MgBrI] and [MeCu·MgBrI] and a nominal role on the product distribution derived from the di- and trialkyl bound copper species. Tetrahydrofuran, the solvent with enhanced donicity, was required for reactivity of the complex, allene-generating organocopper species [MeCu·LiBr·MgBr] and improved the ratio of the alkyne/allene products with the copper "ate" species. Temperature appears to have a nominal impact on the distribution of products. The synthetic goals of these studies have been realized by the establishment of specific reaction conditions to obtain exclusively the coupled allenic product 2 or to maximize formation of the acetylenic product 3.

The reaction of organocopper species (R_3CuLi_2, R_2CuLi, RCu) with prop-2-ynylic halides, esters, tosylates, and ethers can proceed to generate either substituted allenes via 1,3-substitution [Scheme I, 1 → 2][1,2] or alkylated acetylenes via direct substitution [Scheme I, 1 → 3].[2o] Despite the extensive synthetic use of these transformations, the factors which control the position of organocopper nucleophilic attack in prop-2-ynylic substrates have not been clearly delineated. For example, we recently reported the displacement of propargylic acetate 4 with a variety of lithium dialkylcuprate agents to give the α,α-dialkylacetylenes 5 via direct substitution.[2o] Earlier, Vermeer had described the exclusive 1,3-substitution of the structurally related propargylic tosylates 6 with the

Scheme I



Scheme II



complex organocopper agents *t*-BuMgCl (10 equiv)/CuBr (1 equiv) to yield substituted alllenes 7.[2h]

In an attempt to elucidate those factors which influence the product distribution and thereby enhance the predictive capability and synthetic utility of this coupling reaction, we have examined the effects of several substrate and reaction condition parameters on the composition of products in standardized displacement processes. The effects on product distribution of the following substrate

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(2) (a) Rona, P.; Crabbe, P. *J. Am. Chem. Soc.* **1968**, *90*, 4733. (b) Rona, P.; Crabbe, P. *Ibid.* **1969**, *91*, 3289. (c) Van Dijck, L. A.; Lankwerde, B. J.; Vermeer, J. G. C. M.; Weber, A. J. M. *Recl. Trav. Chim. Pays-Bas* **1971**, *90*, 801. (d) Crabbe, P.; Carpie, H. *J. Chem. Soc., Chem. Commun.* **1972**, 904. (e) Kalli, M.; Landor, P. D.; Landor, S. R. *Ibid.* **1972**, 593. (f) Descoins, C.; Henrick, C. A.; Siddal, J. B. *Tetrahedron Lett.* **1972**, 3777. (g) Kalli, M.; Landor, P. D.; Landor, S. R. *J. Chem. Soc., Perkin Trans 1* **1973**, 1347. (h) Vermeer, P.; Meijer, J.; Brandsma, L. *Recl. Trav. Chim. Pays-Bas* **1975**, *94*, 66. (i) Tadema, G.; Vermeer, P.; Meijer, J.; Brandsma, L. *Ibid.* **1976**, *95*, 112. (j) Crabbe, P.; Barreiro, E.; Collat, J.-M.; Luche, J.-M. *J. Chem. Soc., Chem. Commun.* **1976**, 183. (k) Moreau, J. L.; Gandemar, M. *J. Organomet. Chem.* **1976**, *108*, 159. (l) Luche, J. L.; Barreiro, E.; Dollat, J.-M.; Crabbe, P. *Tetrahedron Lett.* **1975**, 4615. (m) Vermeer, P.; Westmyze, H.; Kleijn, H.; van Dijck, L. A. *Recl. Trav. Chim. Pays-Bas* **1978**, *97*, 56. (n) Pasto, D. J.; Chou, S.-K.; Fritzen, E.; Shults, R. H.; Waterhouse, A.; Hennion, G. F. *J. Org. Chem.* **1978**, *43*, 1389. (o) Brinkmeyer, R. S.; Macdonald, T. L. *J. Chem. Soc., Chem. Commun.* **1978**, 876. (p) Klein, H.; Westmijze, H.; Krinthof, K.; Vermeer, R. *Recl. Trav. Chim. Pays-Bas* **1979**, *98*, 27. (q) Westmijze, H.; Vermeer, P. *Synthesis* **1979**, 390. (r) Duboudin, J. C. *J. Organomet. Chem.* **1979**, *108*, 1.

0022-3263/80/1945-4740$01.00/0

Table I. Factors Analyzed in the Displacement of Propargylic Substrates 8[a]

	substrate 8			conditions				% products[b]				
expt	R_1[f]	R_2[f]	leaving group	equiv of agent	organocopper agent[c]	solvent	temp, °C	10	11	12	13	ratio of 10/(11 + 12)
1	*t*-Bu	H	OAc	2	[Me_2CuLi]	Et_2O	0	98	0	0	2	100/0
2	$(Me)_3Si$	H	OAc	2	[Me_2CuLi]	Et_2O	0	91	4	0	5	95/5
3	C_6H_{11}	H	OAc	2	[Me_2CuLi]	Et_2O	0	26	21	0	53	55/45
4[d]	C_6H_5	H	OAc	2	[Me_2CuLi]	Et_2O	0	33	63	4	0	33/67
5	*n*-Bu	H	OAc	2	[Me_2CuLi]	Et_2O	0	10	90	0	0	10/90
6[d]	C_6H_{11}	CH_3	OAc	2	[Me_2CuLi]	Et_2O	0	16	50	0	34	24/76
7	C_6H_{11}	H	OTos	2	[Me_2CuLi]	Et_2O	0	63	37	0	0	63/37
8	C_6H_{11}	H	OCO_2Me	2	[Me_2CuLi]	Et_2O	0	63	37	0	0	63/37
9[e]	C_6H_{11}	H	OAc	6	[MeCu·LiBr·MgBrI]	Et_2O	0					
10	C_6H_{11}	H	OAc	6	[MeCu·LiBr·MgBrI]	THF	0	0	100	0	0	0/100
11[e]	C_6H_{11}	H	OAc	2	[MeCu·LiI]	Et_2O or THF	0					
12	C_6H_{11}	H	OAc	2	[MeCu·MgBrI]	Et_2O	0	58	42	0	0	58/42
13	C_6H_{11}	H	OAc	2	[$Me_2CuMgI·MgBrI$]	Et_2O	0	41	21	0	38	66/34
14	C_6H_{11}	H	OAc	2	[Me_3CuLi_2]	Et_2O	0	15	8	0	77	66/34
15	C_6H_{11}	H	OTos	2	[MeCu·LiBr·MgBrI]	THF	0	12	74	0	14	13/87
16	C_6H_{11}	H	OCO_2Me	6	[MeCu·LiBr·MgBrI]	THF	0	0	100	0	0	0/100
17	C_6H_{11}	H	OTos	2	[Me_3CuLi_2]	Et_2O	0	46	28	0	26	62/38
18	C_6H_{11}	H	OCO_2Me	2	[Me_3CuLi_2]	Et_2O	0	40	21	0	39	65/35
19	C_6H_{11}	H	OAc	2	[MeCu·MgBrI]	THF	0	72	17	0	11	81/19
20	C_6H_{11}	H	OAc	2	[Me_2CuLi]	THF	0	27	20	0	52	57/43
21	C_6H_{11}	H	OAc	2	[$Me_2CuMgI·MgBr_2$]	THF	0	56	24	0	20	70/30
22	C_6H_{11}	H	OAc	2	[Me_2CuLi]	Et_2O	−70	24	32	0	44	42/68
23	C_6H_{11}	H	OAc	2	[Me_2CuLi]	Et_2O	−40	22	27	0	51	45/55
24	C_6H_{11}	H	OAc	2	[Me_2CuLi]	Et_2O	−20	36	35	0	29	51/49
25	C_6H_{11}	H	OAc	2	[Me_2CuLi]	Et_2O	20	24	18	0	58	57/43
26	*t*-Bu	H	OCO_2Me	6	[MeCu·LiBr·MgBrI]	THF	0	0	100	0	0	0/100
27	C_6H_5	H	OAc	6	[MeCu·LiBr·MgBrI]	THF	0	4	96	0	0	4/96
28	C_6H_{11}	H	OCO_2Me	2	[$Me_2CuMgI·MgBr_2$]	THF	20	66	33	0	0	66/33
29	*n*-Bu	H	OCO_2Me	2	[$Me_2CuMgI·MgBr_2$]	THF	20	52	48	0	0	52/48
30[d]	C_6H_{11}	CH_3	OAc	2	[$Me_2CuMgI·MgBr_2$]	THF	20	29	67	0	4	30/70
31	C_6H_{11}	H	OCO_2Me	2	[MeCu·MgBrI]	THF	0	75	25	0	0	75/25
32	*n*-Bu	H	OCO_2Me	2	[MeCu·MgBrI]	THF	0	68	32	0	0	68/32
33[d]	C_6H_{11}	CH_3	OAc	2	[MeCu·MgBrI]	THF	20	32	69	0	0	46/54

[a] All data presented represent the average of a minimum of two trials. [b] All experiments proceeded to complete conversion in 1 h or less under the designated reaction conditions and produced a volatile mass balance (Kugelrohr distribution, 87–95% of theoretical). [c] The bracketed organocopper species refers to methyl organometallic stoichiometry and not to be characterized organocopper agents. Thus, [Me_2CuLi] refers to the agent generated from 2 MeLi + CuI, and [MeCu·MgBrI] refers to the agent generated from MeMgBr + CuI. When methyllithium was employed as the methyl organometallic, 1 equiv of LiBr may or may not be "complexed" with this reagent. The LiBr concurrently present in the reaction mixture did not influence the distribution of products and was therefore omitted from the table. In contrast to these findings see ref 6 and the text. [d] In these instances, the C_5H_{11} propargylic substituent was substituted by C_4H_9. [e] No reaction. [f] See Scheme I for the structures.

and reaction condition variables have been examined: (1) organocopper reagent stoichiometry (R_3CuLi_2, R_2Cu^-, RCu metal salt); (2) organocopper species concomitant salt or counterion (Mg^{2+}, Li^+); (3) acetylenic site substitution and, to a limited extent, propargylic site substitution; (4) temperature; (5) solvent (ether, THF); (6) leaving group (OAc, OTos, OCO_2Me). These studies have established specific reaction conditions for maximizing the formation of either allenic or acetylenic products for a given propargylic substrate and have developed the methyl carbonate moiety as the most versatile leaving group available for obtaining either desired displacement product.

Results

The reactions of propargyl substrates 8 with organocopper species 9 can lead to the formation of four products: substituted acetylenes **10**, allenes **11**, reduced allenes **12**, and propargylic alcohols **13** (Scheme II). To facilitate the study of this formal displacement process, the distribution of these products was analyzed as a function of two greatly simplified factors—the relative steric interactions for displacement at the acetylenic and propargylic sites and the intrinsic propensities for 1,3 and direct substitution of the alkylcopper nucleophiles and propargylic leaving groups.[3,4] Both parameters (steric and intrinsic nucleophile or electrophile reactivity) could be temperature and solvent dependent. An additional factor, the nature of the copper-bound alkyl ligand, was not examined since studies of propargylic and related displacements by alkylcopper species have demonstrated that the alkyl ligand normally has a nominal impact on the distribution of products.[1] Consequently, methyl was employed as the copper-bound alkyl nucleophile in our investigations due to the ease of product structure determination and to the commercial availability of methyl organometallics in both halide-free and halide-complexed states. We have approached the evaluation of these two factors, steric considerations and intrinsic displacement propensities, by attempting initially to separate their possible influences and to analyze them independently. Our final analysis concerning the importance of steric and intrinsic reactivity parameters was derived from a relative evaluation scheme.

(a) Steric Effects. The effect of relative steric bulk at the acetylenic and propargylic sites on product distri-

(3) For a molecular orbital treatment of the factors associated with attack on propargylic ↔ allenic cations, see: Mirejovsky, D.; Drenth, W. *J. Org. Chem.* **1978**, *43*, 763.

(4) For factors associated with approach to acetylenic sites, see: (a) Dykstra, C. E.; Schaefer, H. F. *J. Am. Chem. Soc.* **1978**, *100*, 1378. (b) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

bution was examined by employing uniform reaction conditions (Me_2CuLi, Et_2O, 0 °C) and propargylic site substitution ($CHOAcC_5H_{11}$), while changing the size of the acetylene-bound substituent (8, R_1 = variable) (Table I, expt 1–5). A smooth continuum of alkyne/allene product ratios is observed as the acetylenic substituent of 8 (R_1) was varied from a sterically congested, tertiary atom ($C(CH_3)_3$, $Si(CH_3)_3$; ~100/0) through a secondary carbon (phenyl, cyclohexyl; ~1/1) to a primary carbon (*n*-butyl, 10/90). The converse relationship also appears to hold. Additional steric bulk at the propargylic site inhibits displacement at that site relative to the acetylenic position (expt 3 vs. 6). In addition, the formation of reduced allenic, **12**, and alcoholic, **13**, products is related, although not in an obvious fashion, to the substitution pattern at the acetylenic and carbonyl electrophilic sites. For example, under these reaction conditions, only phenyl substitution (8, R_1 = phenyl) afforded an appreciable amount of reduced allenic **12** (4%, expt 4), and only cyclohexyl substitution (8, R_1 = cyclohexyl) generated a substantial amount of alcohol **13** (53%, expt 3).

(b) Leaving-Group Effects. The effect of the leaving group was examined by maintaining constant substrate structural features (8, R_1 = cyclohexyl) and reaction conditions (Me_2CuLi, Et_2O, 0 °C) while varying the nature of the oxygen-bound leaving group of 8 (OG = variable). A relationship between the leaving group and mode of direct or 1,3 displacement had been observed previously.[2p,5] The effect on the mode of displacement by the leaving capability of the group, as determined to a first-order approximation by the pK_a of the conjugate acid, was examined. A range of leaving-group capabilities was investigated: tosylate (TsOH; pK_a = −6.5), acetate (AcOH; pK_a = 4.78), and methyl carbonate ($MeOCO_2H$, $pK_a \simeq 6.35$). Under these reaction conditions, the leaving group possessed an unpredictable influence on the distribution of products (Table I, expt 3, 7, 8). Both the most (TsO^-) and least ($MeOCO_2^-$) effective leaving groups on the basis of this crude conjugate acid pK_a analysis generated identical alkyne **10**/allene **11** ratios (63/37). In addition, these functions did not produce detectable amounts of either reduced allene **12** or alcohol **13**. In contrast, the acetate moiety, intermediate in ability to depart, produced principally alcohol **13**, no reduced allene **12**, and a diminished alkyne **10**/allene **11** ratio (55/45).

(c) Organocopper Agent Stoichiometry and Counterion Effects. Several organocopper species have been employed in displacement processes.[1,2n,p] We have examined six organocopper agents which differ in the number of alkyl ligands bound to copper and the nature of two metal ions or salts (Li^+ or $MgBr^+$), either acting as counterion to the copper "ate" complex or concurrently present in the methylcopper solution as a consequence of the transmetalation process. The organocopper species examined include (1) MeCu·LiBr·MgBrI (expt 10), (2) MeCu·LiI (expt 11), (3) MeCu·MgBrI (expt 12), (4) Me_2CuLi (expt 8), (5) $Me_2CuMgBr$ (expt 13), and (6) Me_3CuLi_2 (expt 14). The substitution of commercial halide-free methyllithium (MeLi) as the methyl organometallic source for organocopper species generation did not cause a significant deviation from the reactivity pattern observed for the commercial halide-complexed methyllithium (MeLi·LiBr; vide infra). Consequently, lithium bromide, which can be present in an equivalent proportion to the methyllithium employed in these experiments, has been omitted in the column describing the lithium organocopper species in Table I.

Lithium bromide does have a dramatic impact on the reactivity pattern of methylcopper species which concomitantly possess a magnesium salt (e.g., MeCu·MgBrI; cf. ref 6a). Vermeer has employed these complex lithium salt–magnesium salt organocopper agents extensively in studies of propargylic and related displacements and has termed this phenomenon the "lithium effect".[2p,6] Effects attributable to lithium salts on reaction rates or product distribution have been noted by others in nucleophilic addition processes.[7]

The complex organocopper agent [MeCu·LiBr·MgBrI], prepared via equivalent addition of MeMgBr, LiBr, and CuI or MeLi·LiBr, CuI, and $MgBr_2$ in THF, produced exclusively 1,3-displacement, generating the substituted allene **11** (expt 10). This complex organocopper reagent was extremely sensitive to solvent. No detectable reaction occurred when the reagent was generated in diethyl ether even under prolonged reaction periods (expt 9). These alkylcopper species in THF are clearly the agents of choice in selective synthesis of substituted allenes from propargylic substrates. Although displacement is rapid (<30 min at 0 °C) with these organocopper agents in THF, the ratio of organocopper agent required to effect complete displacement is dependent upon the substrate leaving group. Two equivalents of the complex agent [MeCu·LiBr·MgBrI] effect complete displacement of the tosylate leaving group (expt 15), whereas 6 equiv of the reagent effect conversion of the carbonate and acetate substrates (expt 10 and 16).

That both magnesium and lithium salts must be present in this methylcopper agent to selectively produce substituted allenes was demonstrated by studying the corresponding specific salt-deficient organocopper species [MeCu·LiI] and [MeCu·MgBrI]. The reagent prepared from 1 equiv of methyllithium (or the LiBr complex) and cuprous iodide was unreactive, effecting no propargylic displacement over substantial reaction periods in either Et_2O or THF (expt 11). The "lithium effect" noted above is not simply a salt effect and is critically dependent upon the presence of a magnesium salt in these solutions, since the addition of lithium bromide to the [MeCu·LiI] complex had no impact on initiation of propargylic displacement by this alkylcopper species.

The alternate magnesium halide complexed methylcopper species [MeCu·MgBrI] generated via equivalent addition of MeMgBr and CuI in ether demonstrated a high alkyne **10** to allene **11** product preference for the substrate examined (expt 12). The similarity in alkyne **10** to allene **11** product ratio observed for [MeCu·MgBr] with those ratios observed for established organocopper "ate" complexes suggests that this organocopper species acts as a heterocuprate agent (e.g., $[MeCuI^-MgBr^+]$). This heterocuprate appears to have substantial preparative utility when compared with the lithium dimethylcuprate reagent, since the magnesium heterocuprate agent yielded a higher alkyne **10** to allene **11** ratio and no detectable side product (alcohol **13**) and was capable of effective utilization of the equivalents of methylmagnesium bromide employed in the generation of the reagent. In addition, the presence of excess magnesium salts in the reaction mixture had no effect upon the allene/acetylene product distribution, reinforcing the necessity of incorporating both lithium and magnesium salts in the generation of the complex

(5) Garllina, C.; Ciattini, P. G. *J. Am. Chem. Soc.* **1979**, *101*, 1036.

(6) (a) Westmijze, H.; Kleijn, H.; Vermeer, P. *Tetrahedron Lett.* **1977**, 2023. (b) Westmijze, H.; Kleijn, H.; Bos, H. J. T.; Vermeer, P. *Recl. Trav. Chim. Pays-Bas* **1976**, *95*, 299.

(7) (a) Ashby, E. C.; Lin, J. J.; Watkins, J. J. *Tetrahedron Lett.* **1977**, 1709. (b) Lafour, J. M.; Loupy, A. *Tetrahedron* **1978**, *34*, 2597 and references therein.

methylcopper species [MeCu·LiBr·MgBrI].

Two dimethylcuprate species differing only in gegenion [Me_2Cu^-(Li^+ or $MgBr^+$)] were examined with respect to their impact on product distribution. These organocopper agents have been suggested to possess a nucleophilicity which is enhanced over that of the monoalkyl-bound organocopper species [MeCu·salts] and to be the reagents of choice in displacement processes.[1,8] With the reference substrate **8** (R_1 = cyclohexyl) these dimethylcuprate agents produced a distribution of products favoring alkyne **10** over allene **11**, with the magnesium counterion (expt 13) producing a slightly superior selectivity in alkyne product formation over the lithium counterion (expt 3). These dimethylcuprate species generated a characteristic product distribution (65 ± 10% alkyne **10**) with the reference substrate **8** (R_1 = cyclohexyl) which was dramatically altered from that observed for the complex methylcopper species [MeCu·LiBr·MgBrI].

Dilithium trialkylcuprate agents **16** have been shown to be appreciably more nucleophilic than either mono- or dialkyl copper species in displacement reactions.[9] These agents, unlike their mono- or dialkyl copper counterparts, are not stoichiometric species but instead are in equilibrium with their dialkylcuprate, **14**, and alkyllithium, **15**, precursors (e.g., **14** + **15** ⇌ **16**).[8a,b] We have studied these

$$\underset{\mathbf{14}}{R_2CuLi} + \underset{\mathbf{15}}{RLi} \rightleftharpoons \underset{\mathbf{16}}{R_3CuLi_2}$$

species in an attempt to determine whether a relationship exists between the nucleophilicity of the organocopper species and the formation of alkyne product. Only limited insight into this question can be obtained from our data (e.g., expt 14). Although it is not of preparative significance, the dilithium trimethylcuprate reagent did generate a slightly improved alkyne **10** to allene **11** product ratio when compared with the lithium dimethylcuprate agent. However, the principal product, alcohol **13**, was formed in a substantially higher relative percentage, which could be a consequence of either Me_3CuLi_2 or of equilibrium quantities of MeLi.

In principle, formation of the alkyne product could be a simultaneous function of organocopper nucleophilicity and substrate electrophilicity, as crudely determined by leaving-group capability. This issue was studied by examining the product ratios for reaction of the tosylate, acetate, and methyl carbonate leaving groups with a monomethyl-ligated copper species [MeCu·LiBr·MgBrI] in THF (expt 10, 15, 16), lithium dimethylcuprate ([Me_2CuLi], expt 3, 7, 8), and the dilithium trimethylcuprate reagent ([Me_3CuLi_2], expt 14, 17, 18). The ratio of alkyne **10** to allene **11** displacement products for this substrate with both the Me_2CuLi and Me_3CuLi_2 species is relatively constant (60 ± 5/40 ± 5) regardless of the leaving group employed and despite a great variation in the percentage (0–77%) of alcohol **13** generated. The complexed methylcopper species [MeCu·LiBr·MgBrI] produced a distribution of products which followed no obvious pattern. The most effective leaving group, tosylate, was the only group to engender the acetylenic product **10** (expt 15). In addition, the acetate function generated substantial alcohol with this organocopper species. The methyl carbonate leaving group eliminated the formation of the undesired alcohol **13** product with both the complex methylcopper and dimethylcuprate species and appeared to be the most efficacious leaving group in generating high yields of either the allenic product **11** (when coupled with the complex methylcopper agent) or the acetylenic product **10** (when coupled with a methylcuprate reagent).

(d) Solvent Effects. Displacement reactions of organocopper species have been executed at a variety of reaction temperatures and in several solvent systems. In particular, solvent has been established by House to have a dramatic impact on the coupling reactions of lithium dimethylcuprate.[10] We have examined the influence on product distribution of two solvents commonly employed in organocuprate reactions, which are ethers with differing capabilities as donating solvents (THF and diethyl ether). Our data with three cuprate species, MeCu·MgBrI, Me_2CuLi, and $Me_2CuMgBr$, demonstrate that solvent played a variable role and the organocopper species a specific role in the determination of products in these cuprate-mediated displacements. As noted earlier, the use of THF as the reaction solvent was critical to the reactivity of the complex organocopper agent [MeCu·LiBr·MgBrI]. With the monomethyl-ligated copper species, [MeCu·MgBrI], solvent played a demonstrable and synthetically useful role in alkyne product selection. These organocopper species in THF provided the highest alkyne/allene ratio observed with the reference substrate **8** (81/19 expt 19), a substantially greater ratio than that observed with ether as solvent (58/42, expt 12). The acetylene/allene/alcohol product distributions were nearly constant for both the lithium cuprate reagent in ether (26/21/53; expt 3) and THF (27/20/52; expt 20) and the magnesium reagent in ether (41/21/38; expt 12) and THF (56/24/20; expt 21).

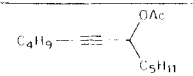
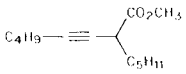
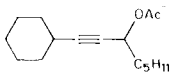
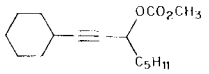
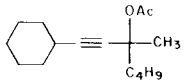
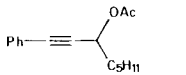
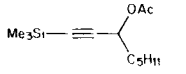
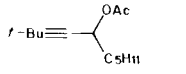
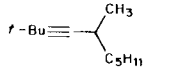
(e) Temperature Effects. No temperature-related trend in product selectivity for displacement reactions had been firmly established which was separate and distinct from the temperature-dependent destruction of the organocopper species.[1] Our data (expt 3, 22–25) demonstrate that for the cuprate-mediated propargylic displacement examined here, increased temperature enhanced the production of alkyne **10** relative to allene **11** in a slight but definite and monotonic fashion. Thus, the alkyne to allene product ratio increased with temperature from 0.75 (42/68) at −70 °C to 1.33 (57/43) at 20 °C.

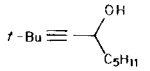
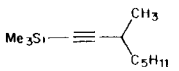
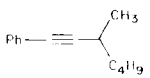
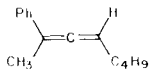
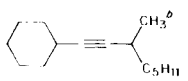
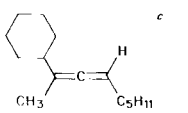
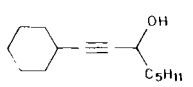
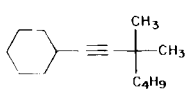
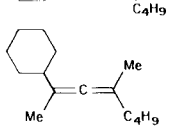
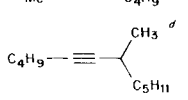
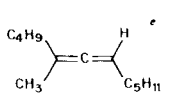
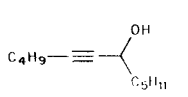
Discussion

Our data demonstrate that the distribution of products resulting from reaction of a progargylic substrate with an organocopper species is a consequence of the interplay of a variety of factors. Clearly, the most dominant factor in determining the site of displacement leading to either substituted acetylenes or substituted allenes is the nature of the organocopper reagent. The complex organocopper species [MeCu·LiBr·MgBrI] overwhelmingly favors allene formation, whereas di- or trialkyl organocopper species tend to generate the α-substituted acetylenic system. Indeed, the complex [Mg^{2+}, Li^+] salt–methylcopper species produced such a dramatic effect on the product distribution that a fundamental distinction must be suspected between the character and intrinsic reactivity of the other organocopper species examined and the complex methylcopper agent undergoing this allene-specific displacement process. The nature of this distinct organocopper species is unclear at present but may be a consequence of a free, neutral organocopper agent ["MeCu"] in contrast to the established "ate" complexes of copper(I)

(8) House, H. O. *Acc. Chem. Res.* **1976**, *9*, 59.
(9) (a) Ashby, E. C.; Watkins, J. J. *J. Am. Chem. Soc.* **1977**, *99*, 5312. (b) Ashby, E. C.; Lin, J. J. *J. Org. Chem.* **1977**, *42*, 2805. (c) Macdonald, T. L.; Still, W. C. *J. Am. Chem. Soc.* **1975**, *97*, 5280.
(10) House, H. O.; Lee, T. V. *J. Org. Chem.* **1978**, *43*, 4369 and references therein.

Table II. Physical and Spectral Characteristics of Isolated Products

compd	physical characteristics	mass spec, *m/e* (rel intens)	NMR ($CDCl_3$, Me_4Si), δ	IR (neat), cm^{-1}
	clear, light oil	224 (1), 209 (1), 195 (1), 182 (23), 182 (27), 167 (38), 153 (38), 139 (31), 126 (100), 125 (62)	5.40 (t, J = 7, 1 Hz, 1 H), 2.24 (br t, J = 7 Hz, 2 H), 2.04 (s, 3 H), 1.4 (br m, 12 H), 0.92 (br t, J = 7 Hz, 6 H)	2960, 2937, 2865, 2230 (w), 1745, 1458, 1370, 1230, 1014
	clear, light oil	240 (1), 211 (2), 197 (4), 183 (8), 169 (7), 164 (8), 135 (23), 108 (67), 93 (100)	5.20 (t, J = 7, 1 Hz, 1 H), 3.84 (s, 3 H), 1.24 (t, J = 7, 1 Hz, 2 H), 1.5 (br m, 12 H), 0.90 (br t, J = 7 Hz, 6 H)	2960, 2937, 2865, 2240, 1755, 1440, 1260, 935, 783
	clear, light oil	250 (4), 208 (26), 193 (26), 179 (19), 152 (100), 155 (54), 125 (46)	5.40 (t, J = 7, 1 Hz, 1 H), 2.40 (m, 1 H), 2.06 (s, 3H), 1.5 (br m, 18 H), 0.90 (br t, J = 7 Hz, 3 H)	2920, 2850, 2230, 1740, 1446, 1360, 1230, 1010
	clear, light oil	266 (1), 237 (1), 223 (1), 209 (5), 190 (12), 161 (18), 134 (100), 91 (88)	5.34 (t, J = 7, 1 Hz, 1 H), 3.90 (s, 3 H), 2.50 (m, 1 H), 1.5 (br m, 18 H), 0.92 (br t, J = 7 Hz, 3 H)	2935, 2860, 2232, 1752, 1440, 1255, 934, 782
	needlelike crystals at room temp, thermally unstable	362 (1), 306 (5), 291 (2), 277 (5), 191 (15), 190 (23), 155 (29), 137 (84), 91 (100)	7.76 (d, J = 8 Hz, 2 H), 7.25 (d, J = 8 Hz, 2 H), 5.00 (t, J = 7, 1 Hz, 1 H), 2.45 (s, 3 H), 2.20 (m, 1 H), 1.4 (br m, 18 H), 0.90 (br t, J = 7 Hz, 3 H)	2930, 2860, 2232, 1447, 1365, 1183, 1172, 890, 660
	clear, light oil	250 (6), 208 (18), 207 (20), 193 (22), 166 (100), 151 (100), 125 (96)	2.42 (m, 1 H), 1.98 (s, 3 H), 1.64 (s, 3 H), 1.5 (br m, 18 H), 0.92 (br t, J = 7 Hz, 3 H)	2930, 2860, 2235, 1748, 1446, 1362, 1230, 1037, 1006, 940
	yellow, medium oil	230 (9), 215 (5), 188 (25), 187 (13), 155 (22), 146 (100)	7.36 (m, 5 H), 5.61 (t, J = 7 Hz, 1 H), 2.06 (s, 3 H), 1.80 (br t, J = 7 Hz, 2 H), 1.44 (m, 4 H), 0.92 (br t, J = 7 Hz, 3 H)	2970, 2930, 2870, 2230, 1743, 1370, 1225, 1012, 750, 685
	clear, yellow oil	240 (2), 225 (2), 211 (5), 197 (38), 165 (56), 127 (35), 117 (100)	5.20 (t, J = 7 Hz, 1 H), 1.90 (s, 3 H), 1.56 (m, 2 H), 1.25 (m, 6 H), 0.80 (br t, J = 7 Hz, 3 H), 0.00 (s, 9 H)	2960, 2865, 2180, 1750, 1368, 1225, 1015, 835, 755
	clear, light oil	225 (2), 209 (13), 182 (11), 167 (30), 149 (21), 126 (100), 125 (57)	5.36 (t, J = 7 Hz, 1 H), 2.00 (s, 3 H), 1.6 (m, 2 H), 1.2 (m, 6 H), 1.12 (s, 9 H), 0.82 (br t, J = 7 Hz, 3 H)	2960, 2920, 2860, 2235, 1735, 1450, 1360, 1220, 1010
	clear oil	180 (5), 165 (11), 151 (4), 137 (16), 123 (48), 109 (100), 95 (93)	2.4 (m, 2 H), 1.36 (m, 6 H), 1.18 (s, 9 H), 1.10 (d, J = 7 Hz, 3 H), 0.90 (br t, J = 7 Hz, 3 H)	2230 (w)

	clear oil	182 (1), 181 (1), 167 (2), 149 (2), 139 (4), 125 (13), 111 (100), 43 (91)	4.52 (m, 1 H), 1.93 (br t, J = 7 Hz, 2 H), 1.5 (br m, 6 H), 1.22 (s, 9 H), 0.90 (br t, J = 7 Hz, 3 H)	3340 (br), 2960, 2935, 2865, 2230, 1457, 1360, 1260, 1030
	yellow oil	196 (1), 181 (100), 168 (5), 153 (2), 140 (5), 139 (4), 126 (12), 125 (8), 122 (17), 109 (12)	2.20 (br t, J = 7 Hz, 2 H), 1.10 (m, 6 H), 0.90 (d, J = 7 Hz, 3 H), 0.66 (br t, J = 7 Hz, 3 H), 0.00 (s, 9 H)	2180 (m)
	yellow oil	186 (20), 171 (15), 157 (20), 143 (17), 129 (100)	7.20 (m, 9 H), 2.60 (m, 1 H), 1.40 (m, 6 H), 1.20 (d, J = 7 Hz, 3 H), 0.90 (br t, J = 7 Hz, 3 H)	2230 (w)
	thermally unstable yellow oil	186 (1), 171 (1), 157 (3), 144 (60), 129 (100)	7.20 (m, 5 H), 5.45 (tq, J = 7, 3 Hz, 1 H), 2.10 (d, J = 3 Hz, 3 H), 1.40 (m, 6 H), 0.90 (br t, J = 7 Hz, 3 H)	1955 (w)
	clear oil	206 (14), 191 (5), 117 (17), 163 (21), 149 (34), 136 (70), 135 (69), 123 (83), 107 (100)	2.36 (m, 2 H), 1.70 (m, 2 H), 1.32 (br m, 16 H), 1.10 (d, J = 7 Hz, 3 H), 0.90 (br t, J = 7 Hz, 3 H)	2940, 2860, 2220 (w), 1450, 1370, 1330, 882
	thermally unstable clear oil	206 (4), 191 (3), 177 (2), 163 (3), 150 (74), 135 (100)	5.15 (m, J = 3 Hz, 1 H), 1.8 (m, 3 H), 1.66 (d, J = 3 Hz, 3 H), 1.36 (m, 16 H), 0.90 (br t, J = 7 Hz, 3 H)	2930, 2855, 1965, 1448, 1365, 1020, 885
	clear oil	208 (2), 207 (1), 190 (1), 179 (2), 165 (3), 152 (4), 137 (100)	4.30 (t, J = 7 Hz, 1 H), 3.58 (m, 1 H), 1.20 (m, 1 H), 1.2–1.8 (br m, 18 H), 0.90 (br t, J = 7 Hz, 3 H)	3350 (br), 2920, 2850, 2200, 1665, 1445, 1010
	clear oil	206 (7), 191 (13), 187 (1), 163 (5), 149 (100)	2.35 (m, 1 H), 1.4 (br m, 16 H), 1.15 (s, 6 H), 0.90 (br t, J = 7 Hz, 3 H)	2230 (w)
	thermally unstable clear oil	206 (10), 191 (8), 187 (2), 164 (44), 149 (100)	1.8 (br m, 3 H), 1.70 (s, 6 H), 1.4 (br m, 14 H), 0.90 (br t, J = 7 Hz, 3 H)	1965 (w)
	clear oil		2.40 (m, 1 H), 2.20 (br t, J = 7 Hz, 2 H), 1.35 (m, 12 H), 1.11 (d, J = 7 Hz, 3 H), 0.90 (br t, J = 7 Hz, 3 H)	2205 (w)
	thermally unstable clear oil		5.04 (m, J = 3 Hz, 1 H), 1.96 (m, 4 H), 1.70 (d, J = 3 Hz, 3 H), 1.36 (m, 10 H), 0.92 (br t, J = 7 Hz, 6 H)	C=C=C str too weak to observe
	clear oil	182 (1), 181 (1), 167 (1), 164 (1), 153 (2), 139 (4), 125 (12), 111 (100), 43 (24)	4.36 (m, 1 H), 2.24 (br t, 2 H), 1.2–1.8 (br m, 13 H), 0.90 (br t, 6 H)	3360 (br), 2930, 2860, 2220 (w), 1455, 1010

[a] ^{13}C NMR ($CDCl_3$, ppm): 169.9, 90.0, 77.7, 64.6, 35.1, 32.4, 31.2, 28.9, 25.8, 24.6, 22.4, 21.9, 13.8. [b] ^{13}C NMR ($CDCl_3$, ppm): 85.0, 84.6, 37.5, 33.3, 31.7, 29.2, 27.1, 26.1, 26.0, 24.9, 22.6, 21.6, 14.1. [c] ^{13}C NMR ($CDCl_3$, ppm): 200.8, 104.4, 90.9, 41.8, 32.1, 31.4, 29.4, 29.1, 26.6, 22.6, 17.6, 14.0. [d] ^{13}C NMR ($CDCl_3$, ppm): 84.9, 80.1. [e] ^{13}C NMR ($CDCl_3$, ppm): 201.3, 99.1, 90.1.

[e.g., $Me_nCuX_m^-$] in which the central copper(I) atom possesses a formal negative charge.

A second factor intimately associated with product distribution is the leaving group. The leaving group appears not to dramatically alter the distribution of displacement products generated via attack on the propargylic framework but instead to influence the relative portion of side product **13** formed in the reaction. The ability of the leaving group to depart, intuitively based on the relative pK_a differences of the corresponding conjugate acid, does not related in any obvious fashion to product distribution. By this crude analysis of leaving group capability, both the most effective (tosylate) and least effective (methyl carbonate) functions appear to produce coupled products at the expense of alcoholic products for the substrates examined here. Acetate, the leaving group intermediate in ability to depart, in our hands generates the largest amount of side product **13**, while maintaining a similar distribution of propargylic displacement products.

Relative steric hindrance at the reacting sites of the propargylic skeleton exerts a prominent role in formation of the acetylenic product **10**. Although the allenic product **11** may be selected by proper choice of the organocopper species, acetylenic product formation is reliant upon features of both the organocopper species and the relative steric access to the propargyic site. Displacement at the propargylic site of the substrate leading to the acetylenic product **10** is critically dependent upon the employment of either the magnesium salt of the monoalkyl-bound copper species [MeCu·MgBrI] or a higher order homocuprate. These organocopper species are sensitive to the steric considerations at the electrophilic sites of the propargylic substrate. Qualitatively, as access to the propargylic site is sterically inhibited, allenic product formation is preferentially selected. In addition, the converse relationship holds: increasing acetylenic-site steric hindrance causes enhanced propargylic-site substitution. These data enable one to predict the approximate acetylene/allene product ratio for an anticipated propargylic substrate 8.

Solvent plays a definite and synthetically important role for the reactivity pattern of the monoalkyl-bound copper species [MeCu·LiBr·MgBrI] and [MeCu·MgBrI] and a nominal role on the product distribution derived from the di- and trialkyl-bound copper species. Tetrahydrofuran, the solvent with enhanced donicity, was required for reactivity of the complex, allene-generating organocopper species [MeCu·LiBr·MgBr] and substantially improved the ratio of alkyne/allene products with the species [MeCu·MgBrI]. For the di- and trimethylcopper "ate" species, THF appeared to slightly enhance alkyne generation although the impact was small. In addition, elevated reaction temperatures (0–20 °C) promoted alkyne **10** formation with lithium dimethylcuprate although the differences in product ratio noted from one extreme position (−70 °C) to the other (20 °C) may be a consequence of a relative energy term favoring the formation of the alkyne **10** on the order of 0.15 kcal/mol.

The principal thrust of our work has been to develop a sufficient understanding of the parameters associated with this coupling process to allow some predictive capability concerning the distribution of reaction products. These synthetic goals have been realized by the establishment of specific reaction conditions to obtain exclusively the coupled allenic product **2** or to maximize the formation of the acetylenic product **3**.

Specific preparation of substituted allene **10** via this displacement process requires the use of the complex organocopper species [MeCu·LiBr·MgBrI] in THF. This organocopper agent will effect displacement exclusively at the acetylenic carbon site, providing the allenic product regardless of the nature of the steric considerations and even under severly adverse steric constraints (expt 26). This complex methylcopper species, particularly when coupled with the methyl carbonate leaving group on the propargylic substrate, generated none of the alcohol **13**, acetylene **10**, or reduced allene **12** products which were observed with alternate reaction conditions. The complex organocopper agent also appeared to inhibit formation of the reduced allene **12** side product (cf. expt 27 vs. 4).

Selective preparation of the α-substituted acetylenic product **10** is not straightforward and is a consequence of the interplay of all the factors analyzed. Either of the magnesium salt containing organocopper "ate" species [MeCu·MgBrI] or [Me_2CuMgBr·MgBrI] appeared to maximize the relative formation of α-substituted acetylene **10**. In addition, elevated temperatures (0–20 °C) and THF as solvent improved the ratio of alkyne **10** to allene **11**, and the methyl carbonate leaving group appeared to minimize or completely eliminate alcohol **13** side product formation. Clearly a dominant factor in alkyne **10** generation is the nature of the relative steric interactions at the sites on the propargylic framework. The impact of these steric concerns was evaluated empirically by utilizing reaction conditions demonstrated to maximize alkyne formation on substrates with different relative steric situations (expt 28–33). The nature of the alkyl substitution at the acetylenic carbon of the substrate would appear to be of principal importance in directing the organocopper nucleophile to the direct-substitution process. However, these data demonstrate that appreciable quantities of the alkyne **10** can be generated regardless of substrate substitution pattern via employment of the described reaction conditions. For example, in the substrate studied here (**8**; R_1 = *n*-Bu, R_2 = H), which would be analyzed a priori to be sterically adverse to alkyne **10** (R_1 = *n*-Bu, R_2 = H) generation, a 68% yield of alkyne **10** was obtained (cf. expt 5, 32).

This research has led to the empirical determination of product-selective processes for organocopper species mediated propargylic coupling reactions. The mechanistic implications of the chemistry of the organocopper species and propargylic electrophiles noted in this research are currently being pursued as well as continued synthetic applications.

Experimental Section

General Methods. Proton magnetic resonance spectra were recorded at 100 MHz with a JEOL JNM-NH-100 spectrometer using tetramethylsilane as an internal standard. ^{13}C magnetic resonance spectra were recorded at 22.50 MHz by employing a JEOL FX-90Q Fourier transform spectrometer with deuteriochloroform as internal standard. Low-resolution mass spectra were obtained by direct insertion or GC methods with an LKB 9000 spectrometer at 70 eV. The parent ion and the most intense peaks are reported. Infrared spectra were recorded by using a Perkin-Elmer 621 grating spectrometer. Short-column chromatography with E. Merck (type 60) silica gel and thin-layer chromatography with E. Merck silica gel 60, F-254 precoated (0.25-mm thickness) plates were employed. Product percentages were determined on the crude reaction mixture by using a Varian 940 FID gas chromatograph with a $5 \times {}^1/_8$ in. 107.0V-1 column at 200 °C and are reproducible within ±3%. Magnesium sulfate was used throughout as the drying agent. Constant-temperature control for the reactions between 0 and −60 °C was obtained through the use of a Haake EK-51 isothermal bath. All reactions were carried out under an atmosphere of nitrogen. Methyllithium (1.3 M in Et_2O), methylmagnesium bromide (3.0 M in Et_2O), and copper iodide were obtained from the Alfa Division of the Ventron

Corp. The copper iodide was purified by an established procedure.[11] Monosubstituted acetylenes were purchased from the Farchan Division of Chemsampco, Inc. Fisher anhydrous ether was used without purification, and Fisher tetrahydrofuran was distilled from benzophenone ketyl radical prior to use. Physical data on all compounds synthesized have been compiled in Table II. All experiments executed had volatile mass balances (Kugelrohr distillation, 0.5 mm) which were 87–95% of the theoretical values. Isolated yields of displacement products were approximately 10% less than the value reported in Table I.

Preparation of Propargylic Acetates (8, OG = OAc). To a solution of alkylacetylene (20 mmol) in THF (50 mL) was added *n*-butyllithium (9.17 mL of a 2.4 M solution in hexane, 22 mol) dropwise at −40 °C. After 1 h, *n*-hexanal (3.6 mL, 30 mmol) was added (5 min) and the reaction allowed to come to room temperature (1 h). Acetic anhydride (4.08 g, 40 mmol) was then added and the reaction followed by TLC (2% ethyl acetate in pentane) to completion (~$^1/_2$ h). The white suspension was partitioned between ether (50 mL) and saturated aqueous ammonium chloride (100 mL), washed with saturated aqueous sodium bicarbonate (50 mL), and then dried, and the solvent was removed in vacuo. Chromatography (1% ethyl acetate in pentane eluant) yielded the pure propargylic acetate (70–85% yield).

Acetylenic alcohols were prepared either by the standard workup of the reaction mixture after the addition of the aldehyde or by hydrolysis (10% sodium hydroxide, methanol, ~1 h) of the corresponding acetate.

Preparation of Propargylic Methyl Carbonates (8, OG = OCO_2Me). Propargylic carbonates 8 (OG = OCO_2Me) were obtained in the manner described for propargylic acetates 8 (OG = OAc) (see above) except that methyl chloroformate (3.78 g, 40 mmol) was substituted for acetic anhydride and the sodium bicarbonate wash was omitted. Chromatography (2% ethyl acetate in pentane) yielded the pure propargylic carbonate (70–85%).

Preparation of Propargylic Tosylates (8, OG = Tos). To a solution of the propargylic alcohol (5.8 mmol) and tosyl chloride (1.24 g, 6.50 mmol) in diethyl ether (15 mL) at −50 °C was added potassium hydroxide (2.16 g, 38.0 mmol, finely powdered). The reaction was allowed to come to room temperature within 15 min. After an additional 0.5 h, the mixture was extracted with water (2 × 50 mL), the organic phase dried, and the solvent removed in vacuo, yielding the propargylic tosylate (95%).

General Reaction of the [Me_2CuLi] Organocopper Species with Propargylic Substrates 8. To a flame-dried flask (25 mL, two necked) were added copper iodide (0.190 g, 1.00 mmol) and Et_2O (4.0 mL). The resulting suspension was cooled to the desired temperature (e.g., 0 °C for expt 1), and methyllithium (1.54 mL of a 1.3 M ethereal solution of MeLi, 2.00 mmol) was added dropwise. After the mixture was stirred for 15 min, the propargylic substrate 8 (0.5 mmol) in Et_2O (1.0 mL) was added over a period of 5 min. The progress of the reaction was followed by TLC until completion (5 min to 1 h). The mixture was then poured into a saturated aqueous solution of ammonium chloride, the organic layer dried, and the solvent removed in vacuo.

General Reaction of the [Me_3CuLi_2] or [MeCu·LiI] Organocopper Species with Propargylic Substrates 8. These organocopper species were prepared and allowed to react in the manner described for the [Me_2CuLi] species with one exception: methyllithium (2.31 mL of a 1.3 M solution of MeLi in hexane, 1.50 mmol) was used with the [Me_3CuLi_2] species, and methyl lithium (0.77 mL of a 1.3 M solution of MeLi in hexane, 0.50 mmol) was used with the [MeCu·LiI] species. Identical reaction workup and purification (see above) gave the products listed in Table II.

General Reaction of the [$Me_2CuMgI·MgBr_2$] or [MeCu·MgBrI] Organocopper Species with Propargylic Substrates 8. To a flame-dried flask (25 mL, two necked) were added copper iodide (0.190 g, 1.00 mmol) and THF (4 mL). The suspension was cooled to the desired temperature (e.g., 0 °C for expt 12 and 13), and MeMgBr [0.66 mL of a 3.0 M ethereal solution (2.00 mmol) for the [$Me_2CuMgI·MgBr_2$] species or 0.33 mL (1.00 mmol) for the [MeCu·MgBrI] species] was introduced via syringe. After the mixture was stirred 15 min, the propargylic substrate 8 in THF (1 mL) was added over 5 min. The progress of the reaction was followed by TLC until completion (5 min to 1 h). The reaction was worked up as described for the [Me_2CuLi] species (see above).

General Reaction of the [MeMgBr·LiBr·CuI] Organocopper Species with Propargylic Substrates 8. To a well-stirred mixture of lithium bromide (0.078 g, 1.00 mmol) and copper iodide (0.190 g, 1.00 mmol) in THF (5 mL) at 0 °C was added methylmagnesium bromide (0.66 mL of a 3 M ethereal solution, 1.00 mmol), and the solution was stirred for 15 min. The propargylic substrate 8 (0.50 mmol) in THF (1 mL) was added dropwise, and product formation was followed by TLC. At the completion of the reaction (~0.5 h) a workup as described for the [Me_2CuLi] species yielded the products (e.g., expt 26).

Acknowledgment. We are grateful for support of these studies by the Vanderbilt University Research Council and Natural Science Committee and of the FT NMR facility by a Biomedical Research Support Grant (RR05424-17; DHEW).

Registry No. 8 (R_1 = ±-Bu; R_2 = H; OG = OAc), 74835-41-9; 8 (R_1 = $(Me)_3Si$; R_2 = H; OG = OAc), 69498-70-0; 8 (R_1 = C_6H_{11}; R_2 = H; OG = OAc), 74835-42-0; 8 (R_1 = C_6H_5; R_2 = H; OG = OAc; C_5H_{11} substituted by C_4H_9), 74835-43-1; 8 (R_1 = *n*-Bu; R_2 = H; OG = OAc), 74835-44-2; 8 (R_1 = C_6H_{11}; R_2 = CH_3; OG = OAc; C_5H_{11} substituted by C_4H_9), 74835-45-3; 8 (R_1 = C_6H_{11}; R_2 = H; OG = OTos), 74835-46-4; 8 (R_1 = C_6H_{11}; R_2 = OG = OCO_2Me), 74835-47-5; 8 (R_1 = *t*-Bu; R_2 = H; OG = OCO_2Me), 74843-73-5; 8 (R_1 = *n*-Bu; R_2 = H; OG = OCO_2Me), 74835-48-6; 8 (R = C_6H_{11}; R_2 = H; OG = OH), 74835-49-7; 10 (R_1 = *t*-Bu; R_2 = H), 74835-50-0; 10 (R_1 = $(Me)_3Si$; R_2 = H), 40276-96-8; 10 (R_1 = C_6H_{11}; R_2 = H), 74835-51-1; 10 (R_1 = C_6H_5; R_2 = H; C_5H_{11} substituted by C_4H_9), 74835-52-2; 10 (R_1 = *n*-Bu; R_2 = H), 74835-53-3; 10 (R_1 = C_6H_{11}; R_2 = CH_3; C_5H_{11} substituted by C_4H_9), 74835-54-4; 11 (R_1 = $(Me)_3Si$; R_2 = H), 25909-12-0; 11 (R_1 = C_6H_{11}; R_2 = H), 74835-55-5; 11 (R_1 = C_6H_5; R_2 = H; C_5H_{11} substituted by C_4H_9), 74835-56-6; 11 (R_1 = *n*-Bu; R_2 = H), 74835-57-7; 11 (R_1 = C_6H_{11}; R_2 = CH_3; C_5H_{11} substituted by C_4H_9), 74835-58-8; 11 (R_1 = *t*-Bu; R_2 = H), 74835-59-9; 12 (R_1 = C_6H_5; R_2 = H; C_5H_{11} substituted by C_4H_9), 13633-28-8; 13 (R_1 = *t*-Bu; R_2 = H), 74835-60-2; 13 (R_1 = $(Me)_3Si$; R_2 = H), 69498-66-4; 13 (R_1 = C_6H_{11}; R_2 = H), 74835-49-7; 13 (R_1 = C_6H_{11}; R_2 = CH_3; C_5H_{11} substituted by C_4H_9), 74835-61-3; 13 (R_1 = *n*-Bu; R_2 = H), 74835-62-4; *n*-hexanal, 66-25-1; *t*-BuC≡Ch, 917-92-0; $Me_3SiC{\equiv}CH$, 1066-54-2; $C_6H_{11}C{\equiv}CH$, 931-48-6; $C_6H_5C{\equiv}CH$, 536-74-3; *n*-BuC≡CH, 693-02-7; CuI, 7681-65-4; MeLi, 917-54-4; MeMgBr, 75-16-1; LiBr, 7550-35-8.

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