NSF Northeast Regional NMR Facility at Yale University. We also thank Dr. T. Wachs of Cornell University for supplying mass spectral data.

Registry No. **1a**, 106-95-6; **1b**, 513-31-5; **1c**, 78-88-6; **1d**, 107-05-1; **2a**, 762-72-1; **2b**, 81790-10-5; **2c**, 18187-38-7; **4a**, 21964-44-3; **4c**, 17642-48-7; **4d**, 4352-44-7; **4e**, 4048-42-4; **5a**, 67242-74-4; **5b**, 21087-29-6; **5c**, 91899-45-5; **5d**, 58649-21-1; **5e**, 71518-12-2; **6a**, 35329-43-2; **6b**, 26146-77-0; **7a**, 65689-00-1; **8a**, 87976-83-8; **8b**, 35802-50-7; **8c**, 91899-29-5; **8d**, 91899-32-0; **8e**, 91899-34-2; **9a**, 63922-74-7; **9b**, 40595-34-4; **9c**, 91899-30-8; **9d**, 91899-33-1; **9e**, 91899-35-3; **10a**, 63922-75-8; **10c**, 91899-31-9; **10e**, 91899-36-4; **11**, 5389-87-7; **12a**, 85956-58-7; **12b**, 78055-70-6; **13**, 24626-27-5; **14**, 83438-57-7; **15**, 42886-46-4; **17a**, 91899-47-7; **17c**, 91899-48-8; **17d**, 91899-49-9; **17e**, 91899-50-2; **18**, 1940-19-8; **19**, 91899-51-3; **20**, 63922-76-9; **21a**, 91899-37-5; **21b**, 91899-40-0; **21c**, 91899-43-3; **22a**, 91899-38-6; **22b**, 91899-42-2; **23a**, 91899-39-7; **23b**, 91899-41-1; **23c**, 91899-44-4; **24a**, 91899-46-6; **24b**, 58649-14-2; **24c**, 51666-96-7; 25a, 91899-52-4; **25b**, 58649-17-5; **25c**, 58844-31-8; **26a**, 91899-53-5; Me_3SiLi, 18000-27-6; Me_3SiCu, 91899-54-6; geraniol, 106-24-1.

Supplementary Material Available: Full spectroscopic data (^1H NMR, IR, low and high resolution mass spectra) for allyltrimethylsilanes **8b–e**, **9c–e**, **10c–e**, and **14** and 2,3-bis(trimethylsilyl)alk-1-enes **21b,c**, **22b**, and **23b,c** may be obtained (6 pages). Ordering information is given on any current masthead page.

Allenes and Acetylenes. 28.[1] On the Mechanism of Reduction of Propargylic Ethers and Acetates with Organocuprates

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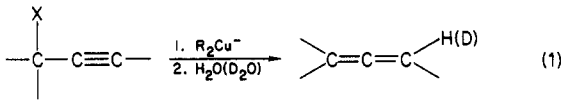
The amounts of substitution and reduction products from the reactions of two types of propargylic methyl ethers and acetates with organocuprates were determined. The methyl ethers give rise to more of the reduction products than the acetates. It is shown that "reduced" allenes are formed by hydrolysis of an organometallic intermediate whereas "reduced" acetylenes are formed mainly by another mechanistic pathway. The mechanisms of these reduction reactions are discussed in terms of stabilized, transient Cu(III)-intermediates and concerted β-hydride transfer in the formation of the acetylene.

In a number of cases, reductions of acetylenic compounds with various organocopper reagents have been reported. Thus, propargylic acetates,[2,3] tosylates,[4] chlorides,[5] oxiranes,[6] and methyl ethers[7,8] have all been found to give varying amounts of allenes in which a hydrogen has been introduced instead of the expected alkyl group (eq 1). The reduction has found application in the synthesis



(1)

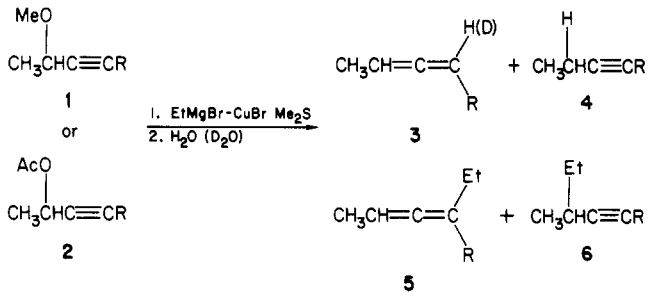
of, for example, allenic prostaglandins[2a,3] and amines.[8] A mechanistic interpretation of an analogous reaction of allylic ethers has been reported.[9]

The present study is an attempt to further elucidate the mechanism of the above reaction and the factors which affect the apparent competition between reduction and substitution in the reactions of organocuprates with propargylic compounds.

Results

The propargylic methyl ethers **1a** and **1b** and acetates **2a** and **2b** were allowed to react with an ethylcuprate, derived from EtMgBr and $CuBr{\cdot}Me_2S$, in tetrahydrofuran (THF) at −30 °C. As is shown in Scheme I, the reactions give four products (**3**, **4**, **5**, and **6**) in addition to butane and ethene, which are postulated to be formed in an amount equivalent to the sum of the reduction products.[9] The relative amounts of reduction (**3** and **4**) and substitution products (**5** and **6**) are listed in Table I. In the case

Scheme I[a]



[a] 1-6a, R = C_6H_{13}; 1-6b, R = $CH_2N(CH_3)CH_2Ph$.

Table I. Reactions of Compounds 1 and 2 with EtMgBr–CuBr•Me_2S (4:1) in THF at −30 °C

compd	reacn time, h	redn prod, percent of total (%3; %4)	substn prod, percent of total (%5; %6)	total GC yield of 3–6, %
1a	22	79[a] (23; 56)	21[a] (17; 4)	>75
1a	20	78[b] (22; 56)	22[b] (17; 5)	>95
1b	20	91 (71; 20)	9 (9; –)	>95
2a	1.5	30 (22; 8)	70 (58; 12)	75
2b	5	45 (42; 3)	55 (31; 24)	45
2b	2[c]	37 (37; –)	63 (37; 26)	80

[a] Mean of two runs giving reduction products 85% and 72% and substitution products 15% and 28%, respectively. [b] Run with 10% $CuBr{\cdot}Me_2S$. [c] Run with 40% $CuBr{\cdot}Me_2S$.

(1) Part 27: *Acta Pharm. Suec.* **1983**, *20*, 233.
(2) (a) Crabbé, P.; Carpio, H. *J. Chem. Soc., Chem. Commun.* **1972**, 904. (b) Luche, J.-L.; Barreiro E., Dollat, J.-M.; Crabbé, P. *Tetrahedron Lett.* **1975**, 4615. (c) Dollat, J.-M.; Luche, J.-L.; Crabbé, P. *J. Chem. Soc., Chem. Commun.* **1977**, 761. (d) Crabbé, P.; Barreiro, E.; Dollat, J.-M.; Luche, J.-L. *J. Chem. Soc., Chem. Commun.* **1976**, 183.
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(7) Claesson, A.; Tämnefors, I.; Olsson, L.-I. *Tetrahedron Lett.* **1975**, 1509.
(8) Sahlberg, C.; Claesson, A. *Acta Chem. Scand., Ser. B* **1982**, *36*, 179.
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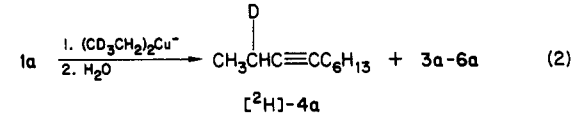
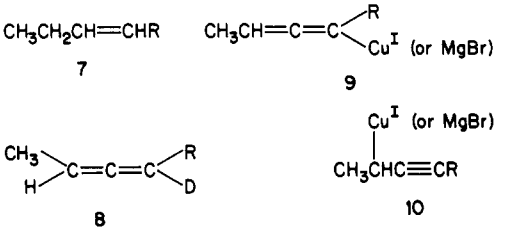
of the acetates **2**, competing cleavage of the ester function occurred resulting in lower yields of products **3–6** than from the methyl ethers. A slow rise in the reaction tem-



(2)

perature (−30 °C → 20 °C) and a reaction time of 20 h when reacting the ethers **1a** and **1b** with the cuprate led to the formation of alkenes **7** in a yield of about 10–15% and a decrease in the yield of "reduced" acetylenes **4** was observed. On the other hand, a quick rise in the temperature (−30 °C → 20 °C) and a short reaction time (2–3 h) gave only a few percent of alkenes **7** and had negligible influence on the reduction–substitution ratio.

Deuteriolysis with D_2O of the reaction mixtures from **1a** and **1b** showed that the "reduced" allenes **3** incorporate one deuterium per molecule, giving the deuterated allenes **8a** and **8b**. In the experiment with **1b** it was established



by NMR and by MS that the "reduced" acetylene **4b** did not contain any deuterium (<5%). The nonalkylated acetylene **4a** from **1a**, in contrast, contained substantial amounts of deuterium, estimated by NMR (200 MHz) to be around 45% (estimated accuracy of the order ±10%). In excellent agreement with this result, the reaction of the acetylene **1a** with CD_3CH_2MgBr–$CuBr{\cdot}Me_2S$ (4:1) in THF at −30 °C → 20 °C for 3 h gave partial incorporation of deuterium (estimated to 50–70% by 200-MHz NMR) in the "reduced" acetylene **4a** but none (<5%) in the allene **3a** (eq 2).

Discussion

The present experiments were designed to investigate the possible influence of the leaving group on the ratio of reduction and substitution products in the reactions of propargylic derivatives with organocuprates. The influence of solvent was not examined since its importance has already been established; reduction products are seldom formed in the reaction of propargylic methyl ethers with RMgX–CuX when diethyl ether is the solvent.[7,8,10] On the other hand, reduction products are reported to be formed from propargylic acetates,[2] chlorides,[5] and oxiranes[6] in diethyl ether when the more reactive lithium dialkylcuprates are used. The use of lower temperatures is another factor known to increase the reduction–substitution product ratio.[2a,4,9] This influence was not tested on the present reactions since the reaction rates were too slow at lower temperatures. A quick rise in the reaction temperature from −30 °C to 20 °C, however, only had a negligible influence on the reduction–substitution ratio.

As shown in Table I the methyl ethers **1a** and **1b**, in contrast to the acetates **2a** and **2b**, give reduction products (**3** + **4**) as the main products. Furthermore, the amino ether **1b** is reduced to a slightly greater extent than the decynyl ether **1a**. One can also note that the two ethers give different relative proportions of allenic and acetylenic reduction products; an allene (**3b**) is formed in a synthetically useful[8] yield (71%) from **1b** whereas an acetylene (**4a**) is the main product (56%) from **1a**. This relative product distribution is not, as we thought earlier,[8] determined solely by the site of protonation of an allenyl–propargyl organometallic intermediate (**9** and/or **10**), the presence of which was indicated by the incorporation of deuterium from D_2O. Instead, the acetylene **4a** must be formed to a considerable extent in the reaction mixture prior to hydrolysis as shown by the fact that a deuterated diethylcuprate gives rise to a partly deuterated product (eq 2) and that deuteriolysis only gives partial incorporation of deuterium. Furthermore, the amino acetylene **4b** appears to be formed exclusively by a route different from protonation of an anionic intermediate since it does not incorporate any deuterium from D_2O. This difference in mode of formation between the hydrocarbon **4a** and the amine **4b** might be largely explained by different regioselectivities in the protonation of the organometallic intermediate, in turn, possibly due to different concentrations of the isomers **9** and **10**. This hypothesis would also be able to explain the different ratios of allene to acetylene among the reduction products from **1a** and **1b** (Table I). Plausible mechanisms for the reduction reaction will be discussed below. The observation that the acetylenes **4** are reduced to olefins **7** by the organocuprate in a known reaction[11] also support the deuteration experiment in that only preformed acetylenes, and not **9** or **10**, would be expected to undergo further reduction.

In order to explain why certain allylic ethers are reduced to a greater extent than the corresponding acetates by the same organocuprate used in the present experiments, a copper(III) intermediate was invoked which somehow is affected by the expelled methoxide.[9] It was furthermore observed that for this reduction to occur, the allyl group should be a highly delocalized (stable) species such as the cinnamyl group and that the solvent should be THF. The central theme of the explanation delivered was that reductive elimination of the hypothetic, transient copper(III)-intermediate was slowed down to such an extent that side reactions, such as electron acceptance from other cuprate molecules, or rearrangements within the complex could intervene, leading to the observed reduction process.

We believe that it is possible to apply this concept of a copper(III) or similar intermediate,[12] which decomposes by other routes than normal coupling, to the present acetylene reduction. The difference in extent of reduction between the present methyl ethers and acetates is not, however, as pronounced as in the allyl case.[9] The present reduction process probably reflects the generally low tendency, at least in comparison with alkyl anions, of certain carbanions such as aryl and in particular 1-alkynyl to couple in organocuprate reactions either as ligands in the cuprate or as they are formed from a halide substrate in the oxidative addition.[13]

An interesting and probably relevant analogy to the present findings is provided by the reactions of 4-cyclooctenyl bromide and tosylate with lithium dimethylcuprate.[14] Only the bromide gives rise to bicyclic products

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(11) Crandall, J. K.; Colonges, F. *J. Org. Chem.* **1976**, *41*, 4089.

(12) By using the term Cu(III)-intermediate and also picturing it in formula **11** we do not mean to suggest any detailed structure for a likely transient intermediate nor do we believe that our cuprate has the structure shown in eq 1 and 2. The structures of magnesium organocuprates are quite variable and complex (Ashby, E. C.; Goel, A. B. *J. Org. Chem.* **1983**, *48*, 2125) which suggests that a transient intermediate formed by electron transfer or oxidative addition has an even less predictable structure which might involve copper clusters.

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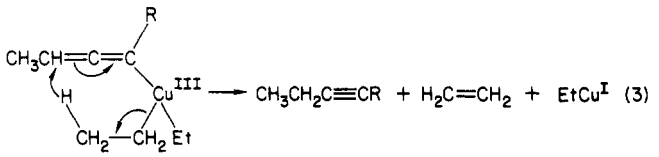
(14) Posner, G. H.; Ting, J. S. *Tetrahedron Lett.* **1974**, 683. We thank Professor Posner for calling our attention to this analogy.

formed by participation of the double bond. One of these products was formed in an overall reduction process (54% of total).

The facts that the acetylenic reaction product **4a** becomes partly deuterated in reaction of **1a** with a deuterated organocuprate (eq 2) and that **4a** and **4b** incorporate deuterium from D_2O in an incomplete manner point, however, to a more complex reaction mechanism than the one discussed above. On the basis of its shown formation in a β-elimination reaction of alkylcopper(I) compounds,[15] copper hydride has been claimed[16] to be the reducing species in other reduction processes involving organocuprates.

An explanation of the present results based on the involvement of copper(I) hydride (deuteride) should however include answers to the following questions: (i) why would copper hydride only give rise to reduction products which are acetylenes and not allenes and (ii) why would copper hydride reduce the methyl ethers **1** faster than the corresponding acetates **2**? Due to the difficulties in finding satisfactory answers to these questions we have considered the possibility that β-elimination of metal hydride is somehow coupled to the reduction in a concerted reaction. A tentative formulation of such a mechanism is outlined in eq 3.[12] We can for the moment offer no explanation



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why deuterated allenes are not formed in eq 2. The suggested mechanism is, however, compatible with the observed results and therefore preferable to the hypothesis of reduction with preformed copper hydride or other unlikely suggestions that reduced products are formed by hydrolysis of Cu(III) intermediates.[2b,c,4]

Reduction by β-hydride transfer, which of course is a well-known process for other organometallic species especially Grignard reagents, might also explain the facile formation of *cis*-alkenes from acetylenes and Grignard reagents in the presence of copper(I) salts.[11] We have shown that reduction of diphenylacetylene with the deuterated cuprate reagent shown in eq 2 results in monodeuterated *cis*-stilbene.[17]

Experimental Section

^1H NMR spectra were recorded at 60 MHz with a Perkin-Elmer R-12 spectrometer or at 90 and 200 MHz with JEOL FX 90 Q and FX200 spectrometers, using $CDCl_3$ as the solvent and Me_4Si as an internal standard. GC–MS was performed on a LKB 9000 mass spectrometer connected to a 1.0-m 3% OV-17 column. GC analyses were run on a Varian 1700 chromatograph equipped with a 2.7-m-long 5% OV-25 column or, for preparative use, a 3.0-m-long 20% OV-25 column. All reactions were carried out in an atmosphere of argon or nitrogen.

General Procedure for the Reactions of Propargylic Methyl Ethers and Acetates with Ethylcuprate. To a suspension of 2.5 mmol of $CuBr{\cdot}Me_2S$ in 5 mL of THF at −30 °C was added 10 mmol (about 10 mL) of a EtMgBr solution in THF. The reaction mixture was stirred for 15 min and then 2.5 mmol of an appropriate propargylic compound (**1** or **2**) was added over a 3-min period. The reaction mixture was stirred at −30 °C for 1.5–24 h and hydrolyzed with 10 mL of 0.1 M aqueous NH_3. The mixture was extracted with ether (3 × 25 mL). The combined extracts were washed with additional aqueous NH_3 and water, dried over K_2CO_3–Na_2SO_4, and concentrated in vacuo. The reaction mixtures were analyzed by GC, and the products were separated by preparative GC and characterized by NMR and GC–MS. Products, yields, and reaction times are given in Table I.

Deuteriolysis of the Reaction Mixture from Reaction of 1a with Ethylcuprate. The general procedure was followed except that the reaction mixture was hydrolyzed with 5 mL of D_2O and stirred for an additional period of 15 min. The reduction reactions products were isolated by preparative GC and characterized by NMR and MS. The allene had structure **8a**: NMR a doublet at 1.6 ppm (**3a** has a double doublet at 1.6 ppm); MS $M^+ = 139$ m/e ($M^+ = 138$ for **3a**). NMR of the acetylene showed it to consist of approximately equal amounts of deuterated ([^2H]-**4a**) and nondeuterated acetylene **4a**. The methylene protons resonate at 2–2.2 ppm.

Deuteriolysis Following Reaction of 1b with Ethylcuprate. The reaction was allowed to slowly reach room temperature and after 2 h it was hydrolyzed with 5 mL of D_2O. The reduction products were isolated by preparative GC and characterized. The structure of the allene was confirmed to be that of **8b**: ^1H NMR showed a doublet at 1.65 ppm (**3b** has a double doublet at 1.65 ppm); MS $M^+ = 188$ m/e ($M^+ = 187$ for **3b**). The ^1H NMR spectrum and MS of the acetylenic amine were identical with those of **3b**, i.e., no deuterium was incorporated.

Reactions of 1a with 2,2,2-Trideuterioethylcuprate. A Grignard reagent derived from Mg (10 mmol) and 10 mmol of Cd_3CH_2Br, prepared from CD_3COOD by standard methods, in 15 mL of THF was cooled to −30 °C. $CuBr{\cdot}Me_2S$ (2.5 mmol) was then added over a 5-min period. The mixture was stirred for 15 min and **1a** (2.5 mmol) was added. The temperature was allowed to reach room temperature. After standard workup the products were isolated and characterized. The NMR spectrum of the nonalkylated allene was identical with that of compound **3a**, i.e., no deuterium incorporation occurred. On the other hand, deuterium incorporation was observed in the reduced acetylene. NMR showed that 60% (±10) of the acetylene was deuterated ([^2H]-**4a** in eq 2). MS (at 20 eV) showed peaks at m/e 138 (1.8%) and 139 (2.6%).

Registry No. **1a**, 91948-34-4; **1b**, 67280-39-1; **2a**, 91948-35-5; **2b**, 91948-36-6; **3a**, 84328-70-1; **3b**, 67280-45-9; **4a**, 2384-85-2; [^2H]-**4a**, 91948-37-7; **4b**, 91948-38-8; **5a**, 91948-39-9; **5b**, 91948-40-2; **6a**, 91948-41-3; **6b**, 91948-42-4; **8a**, 91948-43-5; EtBr, 74-96-4; CD_3CH_2Br, 7439-86-3; Me_2S, 75-18-3; CuBr, 7787-70-4.

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(16) House, H. O.; DuBose, J. C. *J. Org. Chem.* **1975**, *40*, 788.

(17) PhC≡CPh + $(CD_3CH_2)CuMgBr \rightarrow$ PhCD=CHPh (cis). Sahlberg, C.; Olsson, L.-I.; Claesson, A., unpublished results.