Synthetic Use of an Unusual Organocuprate Intermediate[1]

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Summary The organometallic intermediate (**3**) can be used to prepare iodo-allenes, and allenic and β-acetylenic ketones as well as ethers; the site of the reaction of an electrophile on the organometallic intermediate seems to depend on the hard or soft nature of the reagent according to Pearson's theory.

It has already been shown that the reaction of lithium dialkyl copper (**1**) with prop-2-ynylic acetates (**2**) may proceed by a two-step process, which takes place by an S_N2' mechanism.[2]

The structure of the presumed intermediate (**3**) implies the existence, at least transitorily, of a +3 oxidation state for copper, which has been postulated in other organocuprous and -cuprate reactions.[3] The usually high degree of product control and the synthetically useful yields of alkylated (**4**; X = alkyl) or reduced (**4**; X = H) allenes obtained[2] in the reactions of (**3**), prompted the investigation with some electrophiles which we now report.

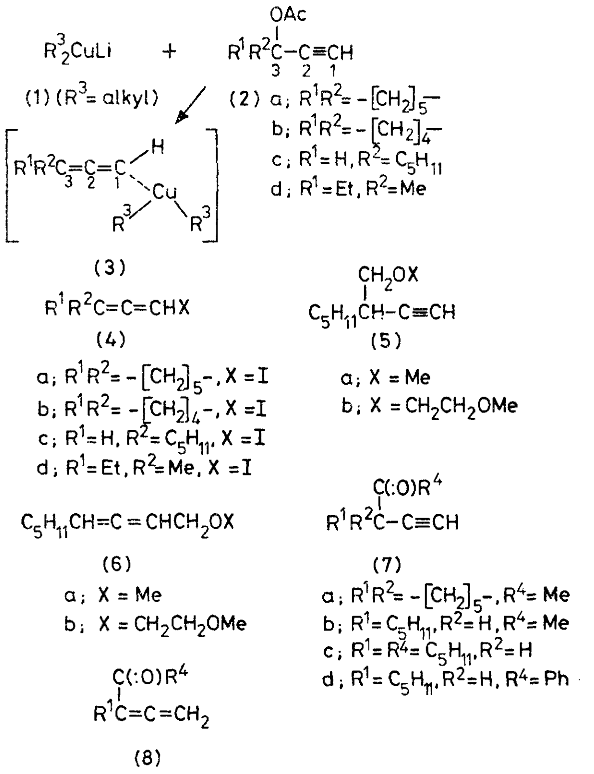

Table 1. Preparation of the iodo-allenes (**4**) from the acetylenic esters (**2**).[a]

Ester	Iodo-allene	% Yield
(**2a**)	(**4a**)	65
(**2b**)	(**4b**)	70
(**2c**), $[\alpha]_D$ −69°	(**4c**), $[\alpha]_D$ −160°	70
(**2d**), $[\alpha]_D$ −21·4	(**4d**), $[\alpha]_D$ −29·2°	60

[a] The ester (**2**) (1 equiv.) in ether was added to the lithium–copper reagent (**1**) (2 equiv.) in ether at −78 °C, and the mixture was stirred for 2 h. Iodine (8 equiv.) in DME was then added and the temperature was allowed to reach room temperature during 1 h. After hydrolysis with aqueous NH_4Cl, the iodo-allene (**4**) was isolated by t.l.c. on silica gel. Spectroscopic properties (i.r., u.v., n.m.r.) of the allenes (**4**) were consistent with the assigned structures. Mass spectra showed a weak molecular ion peak, in addition to a peak due to iodine.

Treatment of (**3**; R^3 = Me) with iodine in 1,2-dimethoxyethane (DME) at −78 °C affords the iodo-allenes (**4**; X = I) in good yields (see Table 1). The only side-products are the allenes (**4**; X = alkyl) (formed by thermal rearrangement) and/or (**4**; X = H) [formed by hydrolysis of (**3**)]. Starting from optically active prop-2-ynylic esters, this reaction affords optically active iodo-allenes, not readily available by other methods. The degree of stereospecificity of this process is currently under investigation.

In contrast treatment of the intermediates (**3**; R^3 = Me) with chloromethyl methyl ether provides the acetylenic compounds (**5**). Reaction of the copper species formed from the (*S*)(−)-octyn-3-ol acetate (**2c**), $[\alpha]_D$ −69°, with chloromethyl methyl ether furnished the acetylenic ether (**5a**), $[\alpha]_D$ −10·7°, 75% yield. No trace of the isomeric compound (**6a**) was detected. However, reaction of (**3**) with 2-methoxyethoxymethyl (MEM) chloride leads (50% yield) to a 90:10 mixture of the acetylenic MEM ether (**5b**) [attack of (**3**) at C-3] and the allenic MEM ether (**6b**) [attack of (**3**) at C-1].

Carboxylic acid anhydrides react with the organometallic intermediates (**3**) at position 3 leading to the β-acetylenic ketones (**7**) (Table 2), formally a 'retro Baeyer-Villiger' reaction of the acetates (**2**).

Table 2. Conversion of the esters (**2**) into the acetylenic ketones (**7**).[a]

Ester	% Conversion of (**2**)	Anhydride	Ketone	% Yield of ketone
(**2a**)	95	$(MeCO)_2O$	(**7a**)	45
(**2c**)	90	$(MeCO)_2O$	(**7b**)	50
(**2c**)	90	$(C_5H_{11}CO)_2O$	(**7c**)	50
(**2c**)	95	$(PhCO)_2O$	(**7d**)	60

[a] After formation of the organometallic intermediate (**3**) (see footnote to Table 1), the anhydride (4 equiv.) was added at −78 °C and the temperature was allowed to increase slowly (2 h) to room temperature. After hydrolysis with aqueous NH_4Cl and the usual work-up, the ethereal phase was evaporated to eliminate volatile side-products (allenes), and the less volatile residue was then purified by t.l.c. to provide the acetylenic ketones (**7**). Spectroscopic properties (i.r., u.v., n.m.r.) of the ketones (**7**) are consistent with the assigned structures. Mass spectra give molecular ion peaks at the required positions.

When R^2 = H, the β-acetylenic ketones (**7**) isomerise readily by prototropic rearrangement to give the α-allenic ketones (**8**). The ready formation of compounds (**8**) from (**3**) offers an attractive synthetic route to allenones.

Metallated allenes frequently exhibit ambident reactivities.[5] In the case of the intermediates (**3**), the hard or soft nature of the electrophile, according to Pearson's theory,[6] can explain our results. It is not surprising that iodine, a soft reagent, gives exclusively reaction at C-1, whereas harder reagents (chloroethers, acid anhydrides) react mostly at C-3.

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[1] For previous paper, see: A. E. Greene, J. P. Deprès, H. Nagano, and P. Crabbé, *Tetrahedon Letters*, 1977, 2365.

[2] P. Crabbé, E. Barreiro, J. M. Dollat, and J. L. Luche, *J.C.S. Chem. Comm.*, 1976, 183; J. L. Luche, E. Barreiro, J. M. Dollat, and P. Crabbé, *Tetrahedron Letters*, 1975, 4615.

[3] P. Vermeer, J. Meijer, and L. Brandsma, *Rec. Trav. chim.*, 1975, **94/5**, 112; Th. Cohen and I. Cristea, *J. Amer. Chem. Soc.*, 1976, **98**, 748; G. H. Posner, J. S. Ting, and C. M. Lentz, *Tetrahedron*, 1976, **32**, 2281, and references cited; see also W. E. Keyes, J. B. R. Dunn, and Th. M. Loehn, *J. Amer. Chem. Soc.*, 1977, **99**, 4527.

[4] C. S. L. Baker, P. D. Landor, S. R. Landor, and A. N. Patel, *J. Chem. Soc.*, 1965, 4348.

[5] M. L. Roumestant, P. Place, and J. Goré, *Tetrahedron*, 1977, **33**, 1283; G. Linstrumelle and D. Michelot, *J.C.S. Chem. Comm.*, 1975, 561; M. Saniere Karila, M. L. Capmau, and W. Chodkiewicz, *Bull. Soc. chim. France*, 1973, 3371.

[6] R. G. Pearson, *J. Amer. Chem. Soc.*, 1963, **85**, 3583; Tse Lok Ho, *Chem. Rev.*, 1975, **75**, 1.