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Formation of Allenes by Reaction of Lithium Diorganocuprates on Propargylic Acetates - A Mechanistic Approach[1]

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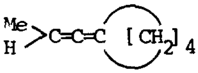
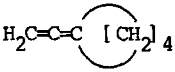
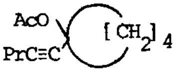
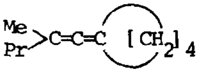
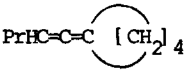
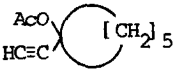
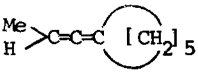
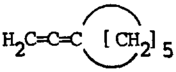
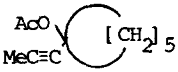
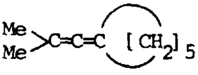
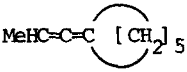
In the past, we reported an efficient synthesis of substituted allenes by reaction of lithium dimethylcopper with acetylenic acetates[2]. Numerous other preparations of allenes through the use of organometallic reagents (1) on propargylic esters (2) have been reported[3-6]. Besides the expected propadiene (3), a non-alkylated allene (4) has sometimes been isolated, the origin of which remained obscure.

As shown in the Table, the reaction appears to be general, applicable to primary, secondary and tertiary acetates of non-substituted as well as substituted propargylic compounds. One of the particular facets of this reaction is that there seems to be no simple relationship between the structure of the ester and the ratio of alkylated (3) and non-alkylated (4) material.

The experimental data listed in the Table induced us to re-examine the reaction mechanism, since the free-radical approach mentioned earlier[2] did not account for all observations. Instead, the results of some recent experiments seem to imply the intervention of an organometallic intermediate such as the allenic copper derivative (5).

Reaction of lithium dimethylcopper on the acetate (6) under the usual conditions (see Table), was followed by acid hydrolysis with 10% DBr in a D_2O solution. Vapor phase chromatography (V.P.C.) and mass spectrometry indicated 22% of deuterated allene (7a) and 78% of the methylated allene (8a). Significantly, treatment of the acetate (6) with $Li(CD_3)_2Cu$ followed by HCl hydrolysis afforded the trideuteromethyl allene (8b) and the non-deuterated allene (7b) in 79% and 21% yield respectively, thus establishing that the entering hydrogen in (7b) did not originate from the organocuprate reagent.

TABLE

Esters	R_2CuLi[a] R=	Conversion in %[b]	Allenes	
			3	4
$HC\equiv C-CH_2OAc$	Me[c]	70	$MeHC=C=CH_2$	not isolated
	n-Bu[c]	75	$BuHC=C=CH_2$	not isolated
$HC\equiv C-\underset{OAc}{C}HAm$[c]	Me	80	MeCH=C=CHAm(75%)	$H_2C=C=CHAm$(25%)
	n-Bu	40	BuCH=C=CHAm(50%)	$H_2C=C=CHAm$(50%)
	Ph	50	PhCH=C=CHAm(100%)	——
$MeC\equiv C-\underset{OAc}{C}HAm$	Me	80	$Me_2C=C=CHAm$(60%)	MeCH=C=CHAm(traces)
$MeC\equiv C-\underset{OAc}{C}HPh$[c]	Me	73	$Me_2C=C=CHPh$(96%)	MeCH=C=CHPh(4%)
	Me	93	 (93%)	 (7%)
	Me	99	 (99%)	 (traces)
	Me	85	 (98%)	 (2%)
	Me	62	 (95%)[d]	 (5%)[d]

a. One equiv. ester added into an ether soln. of n equiv. R_2CuLi (n=1.2 for R=Me ; n=2 for R=nBu and Ph) cooled to -10° (-30° for R=nBu). After stirring for 2 hrs. at same temp., hydrolysis with sat. NH_4Cl, extraction with ether, the compounds were isolated. b. Purification and estimation by V.P.C. (Carlo Erba Fractovap, 4 m. 20% Carbowax 20 M column, F.I.D.). c. Me=methyl Bu=butyl ; Am=amyl ; Ph=phenyl. d. Estimated by mass spectrometry, since these tri- and tetra-substituted allenes could not be separated by V.P.C.

An organometallic intermediate of type (5), formed by dimethylcopper anion attack on the acetylene carbon and acetate expulsion, would constitute a reasonable precursor for the allene (7b). The intermediate (5) may lead to the methyl-allene (8a) by alkyl migration from the copper to the sp^2 carbon atom, while its hydrolysis would produce the corresponding non-alkylated allene (7b). Thus, direct distillation of the reaction mixture of the ester (6) with lithium dimethylcopper before hydrolysis yielded 98% of alkylated allene (8a) and only 2% of (7b) (the origin of the latter is attributed to traces of moisture in the medium). It is worth to emphasize that acid treatment (HCl, DBr) gave a higher proportion of allene (7b) than hydrolysis with NH_4Cl. Additionally, a longer reaction time increased the proportion of alkylated allene (8a), by favouring alkyl migration from the organometallic intermediate (5). So, whereas addition of lithium dimethylcopper to the ester (6) for 2 hrs. at -10°, followed by 1.2N HCl hydrolysis, afforded 78% of (8a) and 22% of (7b), this ratio was modified to 91:9% of propadienes (8a) and (7b) respectively when the reaction time was 2 hrs. at -10°, followed by 21 hrs. at room temperature. A higher yield of (8a) (98%) has been obtained under slightly different conditions. Conversely, the addition of cumene or α-methylstyrene, as free radical scavengers, to the reaction medium did not affect the alkylated : non-alkylated allene ratio.

It was also anticipated that the steric course of the reaction should cast some light on its mechanism. Hence, a lithium dimethylcopper reaction was performed on an optically active propargylic acetate. (S)-(-)-3-Hydroxy-1-octyne acetate $[\alpha]_D$ -69.5° (9)[7], obtained after esterification of the known (S)-(-) alcohol[8], was treated with lithium dimethylcopper under the usual conditions (at -10°). The allene (10) exhibited a specific rotation $[\alpha]_D$ -10°. Application of the Brewster-Lowe rule[9] leads to the (R)-(-) absolute configuration for compound (10). Hence the approach of the cuprate reagent and the formation of the carbon-copper bond seem to take place preferentially in an anti-relationship with respect to the carbon-oxygen bond which is cleaved. This stereospecificity was increased when the reaction was performed at lower temperature (-30°), thus affording the optically active allene (10), showing $[\alpha]_D$ -18°[10]. The above results would appear to rule out a free-radical mechanism or a cationic mechanism.

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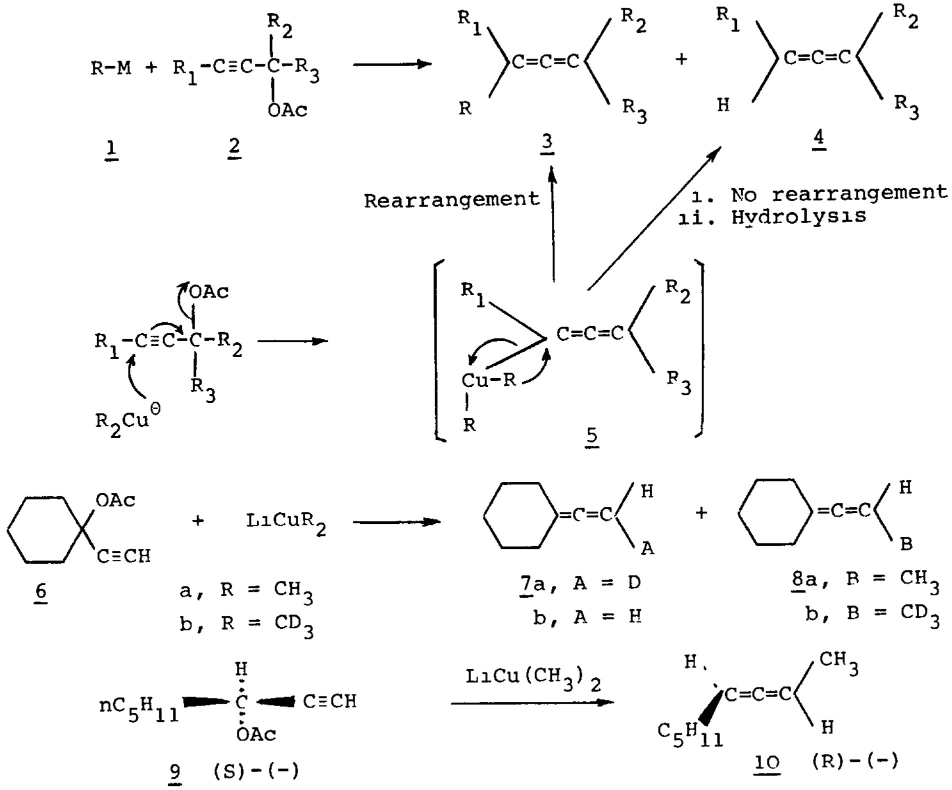

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