A New Reaction of 1-Bromoalk-1-ynes; Synthesis of 3-Alkylalk-1-ynes from Terminal Acetylenes

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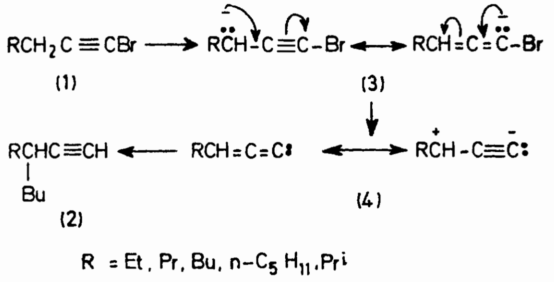
Summary The reaction of 1-bromoalk-1-ynes with two equivalents of butyl-lithium in hexane gives 3-butylalk-1-ynes; the reactive intermediate is a dilithioalkyne which can also be directly prepared from terminal acetylenes, and selective reaction with alkyl halides in hexane occurs at the propargylic site to provide a general synthesis of 3-alkylalk-1-ynes.

We report a new synthesis of 3-butylalk-1-ynes from 1-bromoalk-1-ynes and butyl-lithium, and a general synthesis of 3-alkylalk-1-ynes which were inaccessible by direct synthesis from acetylene.[1] Previous work on the reactions of 1-bromoalk-1-ynes with basic reagents has shown that the nature of the base can direct the course of reaction. Thus with organo-metallic reagents in the absence of catalysts, metal-halogen exchange occurs to give the metal acetylide,[2] whereas reaction with potassium t-butoxide gives an allene-carbene.[3] Nitrogen and sulphur bases lead to substitution and adducts.[4]

Reaction of the 1-bromoalk-1-ynes (**1**) with at least two equivalents of butyl-lithium in hexane gave in each case the 3-butylalk-1-ynes (**2**) in excellent yields.† ^{13}C n.m.r. spectroscopy showed the structures[5] of the products since there is a specific signal for each different carbon atom along the hydrocarbon chain.[6]

Attempts to introduce methyl or propyl groups into 1-bromohept-1-yne (**1**; R = Bu) by reaction with the less basic methyl-lithium in ether or with ethereal propylmagnesium bromide in the presence of butyl-lithium led only to hept-1-yne from a metal–halogen exchange reaction. However butylation occurs in ether with 1-bromopropyne (**1**; R = H) and with 1-bromohept-1-yne (**1**; R = Bu) on reaction with butyl-lithium to give respectively hept-1-yne and 3-butylhept-1-yne (**2**; R = Bu).



Scheme 1

Two mechanisms were considered for the formation of the 3-butylalk-1-ynes (**2**). One pathway based on the work of Cymerman-Craig[3] necessitates the formation of an allene-carbenoid (**3**) or zwitterion (**4**) intermediate from the abstraction of a proton at C-3 by butyl-lithium, expulsion of bromide at C-1 and butylation at C-3 with butyl-lithium (Scheme 1).

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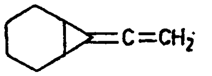
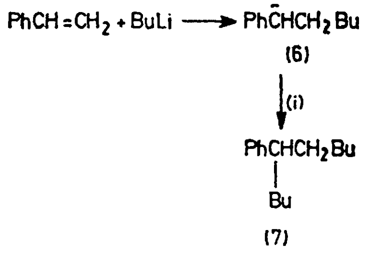
† Satisfactory analytical data were obtained for all new compounds. The reaction mixture was stirred under nitrogen at −20° to ambient temperatures from 6 h to 2 days in concentrated hexane, and the acetylene was isolated after addition of hydrochloric acid.

The reactive intermediates were trapped with cyclohexene and styrene. Allenecarbene (**4**; R = H), generated from propargyl bromide and butyl-lithium forms the allenylcyclopropane (**5**) with cyclohexene, but 1-bromopropyne does not form this adduct under similar conditions and instead gives butyl bromide. Styrene is reported to be a better trap for allene-carbenes (**4**) but reaction of 1-bromohept-1-yne (**1**; R = Bu) and two equivalents of butyl-lithium gave only 5-phenyldecane (**7**). Formation of the product (**7**) is rationalised by Scheme 2 which requires the formation of butyl bromide, from metal-halogen exchange, for reaction with the anion (**6**)[7] formed from addition of butyl-lithium to styrene.



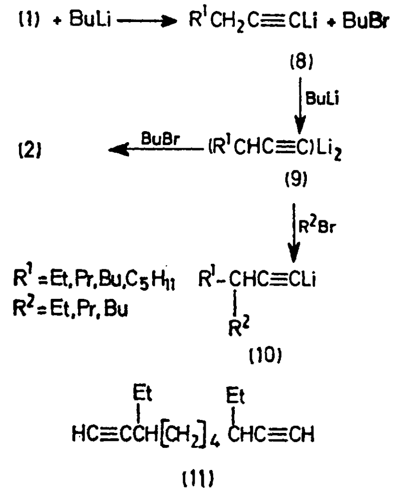
(5)



(i) BuBr from $C_5H_{11}C\equiv CBr$ + BuLi

Scheme 2

The favoured mechanism (Scheme 3) for the conversion of 1-bromoalk-1-ynes into 3-butylalk-1-ynes requires metal-halogen exchange first to give butyl bromide and the lithium acetylide (**8**). Further reaction with butyl-lithium forms the dilithio-derivative (**9**) which selectively alkylates with butyl bromide in hexane only at the propargylic site; alkylation at the terminal acetylide carbon does not occur unless a suitable dipolar aprotic solvent is present. In support of this mechanism it was demonstrated that 1-bromohept-1-yne (**1**; R = Bu) with one equivalent of butyl-lithium, undergoes quantitative metal-halogen exchange within one hour at −33° in hexane and that no further reaction occurs. These results and the related work of Klein *et al.*[8] lead to a simpler and more versatile method of preparing branched acetylenes (**10**). Thus reaction of pent-, hex-, hept- and oct-1-ynes with two equivalents of butyl-lithium gives, in each case, hexane-soluble, yellow dilithio acetylides (**9**) which alkylate at the 3-position with ethyl, propyl and butyl bromides.† An extension of this reaction with 1,4-dibromobutane and the dilithioderivative of pent-1-yne gives 3,8-diethyldeca-1,9-diyne (**11**).



Scheme 3

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