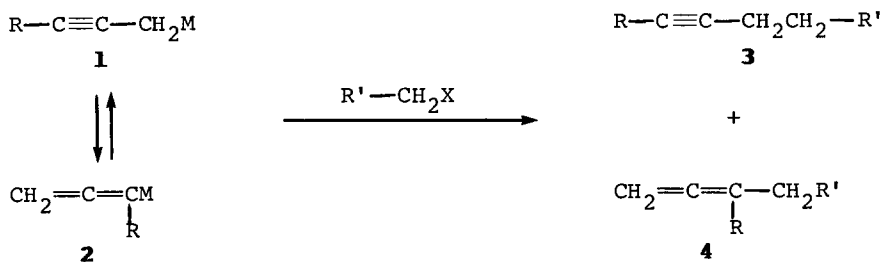


AN EFFICIENT COUPLING REACTION OF ANIONIC PROPARGYL
AND ORGANIC HALIDES

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Summary: The organometallic produced by controlled lithiation of allene functions as an efficient propargylic anion equivalent in coupling reactions with alkyl and allyl halides.

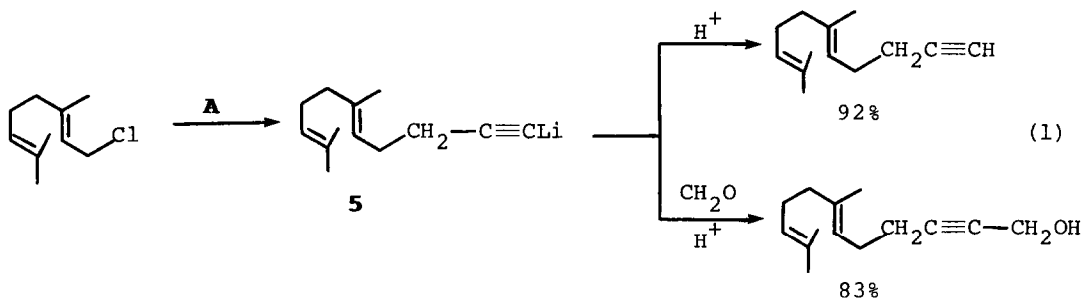
Addition and substitution reactions employing anionic propargyl equivalents provide a potentially valuable route to acetylenic derivatives. Their general applicability in coupling processes, however, is frequently hampered by the tendency of such ambident nucleophiles to produce troublesome mixtures^{1,2,3} of acetylenic and allenic products, viz.



Several indirect methods (varying the metal M, solvent, etc.) have been explored^{4,5,6} to control the regiochemical outcome, and in addition, 1,3-dilithiopropyne **1** (R = M = Li) in tetramethylenediamine has been shown to couple with simple halides⁸ to form acetylenes **3** in moderate yield, although it reportedly fails to couple cleanly with allylic halides.⁹

We now wish to report a simple direct solution to this problem based on the controlled lithiation of allene.¹⁰ Under appropriate conditions the active species produced, **A**, behaves as a highly effective operational equivalent of the propargyl dianion (C₃H₂Li₂), and couples with excellent positional selectivity and in high isolated yields to produce the acetylene **3** (Table). In none of the cases examined was there detectable evidence (nmr, glpc) of isomeric allene formation.

Propargyl-allyl cross-coupling also proceeded efficiently, as illustrated for geranyl chloride (eq. 1). An additional advantage is that the initially formed lithium acetylide intermediates (i.e., 5) can be further transformed in situ to other useful functional derivatives by treatment with suitably reactive electrophiles (CH_2O , ClCOOEt), thereby providing a convenient and experimentally abbreviated "one-pot" approach.



A typical procedure for the preparation of A and its reaction with an alkyl or allyl halide (15 mmol scale) is as follows. To a cooled (-78°) magnetically stirred solution of allene (4.5 ml., Matheson) in 35 ml ether is added 34.5 ml of 1.52 M *n*-butyllithium (52.4 mmol) in hexane (Foote). It is important that a 1:1 ether/hexane solvent mixture be employed (see below). The reaction mixture is allowed to gradually warm (ca 30 min) to -15° , and the white precipitate of propargylating reagent A that forms is stirred an additional 10 min at that temperature. A solution of the alkyl or allyl halide (15 mmol) in 10 ml ether is added dropwise (ca 15 min) and the mixture allowed to warm to room temperature (ca 1 h for allyl and 7 h for alkyl halide). We find that higher yields are conveniently achieved using an excess of the reagent (typically a ratio of ca. 1.7 for allylic/-benzylic halides and ca. 2.4 for simple primary halides). If the terminal acetylene is required, the mixture is poured into ice water, saturated with sodium chloride and extracted with ether. Removal of solvent from the dried ether extracts followed by distillation affords the corresponding acetylene. The hydroxymethylene derivative is prepared by adding paraformaldehyde (66 mmol, dried over P_2O_5) all at once (exothermic), stirring the mixture overnight, and isolation in the manner usual.

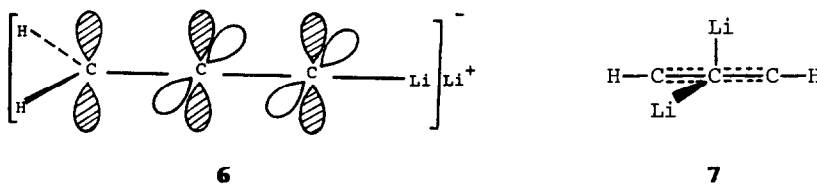
It should be noted that the regiochemical selectivity is strongly dependent on solvation characteristics - the presence of more effective Lewis base donors leading to higher allene:acetylene ratios. For example, metalation of allene with *n*-BuLi (THF, -50°) or with *n*-BuLi \cdot TMEDA (ether) at -50° and coupling with *n*-heptyl iodide produced a 1,2-decadiene:1-decyne ratio of 1.3.

Table. Propargylation of Organic Halides by Reagent A.

Electrophile	Product ^a	% Yield
CH ₃ (CH ₂) ₆ I	CH ₃ (CH ₂) ₇ C≡CH	88 ^b
C ₆ H ₅ CH ₂ Cl	C ₆ H ₅ CH ₂ C≡CH	93 ^c
C ₆ H ₅ CH ₂ Cl	C ₆ H ₅ CH ₂ C≡C—CH ₂ OH	80 ^b
C ₆ H ₅ CH ₂ Cl	C ₆ H ₅ CH ₂ C≡C—CO ₂ Et	80 ^b
CH ₃ C(=CH)CH ₂ Cl Cl	CH ₃ C(=CH)CH ₂ CH ₂ C≡CH Cl	80 ^c

^aAll compounds were fully characterized by acceptable compositional analysis and/or precise mass measurement and compatible spectral (nmr, ir) data. ^bIsolated yield. ^cDetermined by glpc analysis.

Structural designations for C₃H₂Li₂ have included the "propargylide" (1,3-dilithiopropyne) form **6** on the basis of comparative infrared spectroscopy studies,¹¹ as well as a "sesquiacetylene" form **7** (with both lithiums close to the central carbon atom) based on CNDO/2 calculations.¹²



We have dilithiated propyne (2 equiv. *n*-BuLi·TMEDA)⁸ labelled with ¹³C at the methyl group. Reaction with benzyl chloride afforded 4-phenyl-1-butyne in which the only peak displaying enhancement in the ¹³C NMR spectrum (CDCl₃) corresponded to the CH₂ (C-3, 20.6 ppm) derived from the methyl group of propyne. The character and chemical behavior of reagent A and the corresponding propyne-derived reagent is thus aptly described as a propargylide.¹³



References and Notes

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