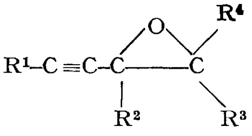
Synthesis of Allenic Alcohols

By PAUL R. ORTIZ DE MONTELLANO

(*Department of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, California* 94143)

Summary α-Hydroxyallenes are formed by the reaction of alkylcopper reagents with α-acetylenic epoxides.

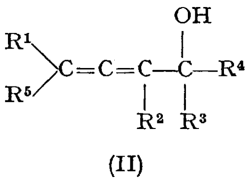
GENERAL methods for the synthesis of α-hydroxyallenes are scarce,[1] notwithstanding their presence in a number of natural substances[2] and their potential value as a replacement for allylic and acetylenic alcohols in pharmaceuticals.[3] We now report a synthesis based on the addition of dialkylcopperlithium reagents to α-acetylenic epoxides. These precursors are readily available either from the addition of metal acetylides to α-halogenocarbonyl compounds[4] or through epoxidation of conjugated acetylenic olefins.[5]



(I)

	R^1	R^2	R^3	R^4
a	Bu^n	Me	H	H
b	Bu^n	H	Et	H
c	Ph	Pr^i	Me	Me
d	H	$-CH_2CH_2CH_2CH_2-$		H

The reaction of dialkylcopperlithium with acetylenic epoxides (I) to give allenic alcohols (II) parallels the use of copper reagents to form alkylated allenes from acetylene acetates[6] and allyl alcohols from vinyl epoxides.[7] Direct addition to epoxide groups has also been reported.[8]



$$\begin{matrix}R^1\\ R^5\end{matrix}\!\!>C{=}C{=}C(R^2)-C(OH)(R^3)-R^4$$

(II)

	R^1	R^2	R^3	R^4	R^5
a	Bu^n	Me	H	H	Me
b	Bu^n	Me	H	H	Bu^n
c	Bu^n	Me	H	H	H
d	Bu^n	H	Et	H	Me
e	Ph	Pr^i	Me	Me	Me
f	H	$-CH_2CH_2CH_2CH_2-$		H	Me
g	H	$-CH_2CH_2CH_2CH_2-$		H	H
h	H	$-CH_2CH_2CH_2CH_2-$		H	Bu^n

The acyclic compounds (Ia—c) were prepared by addition of hex-1-ynyl-lithium to 1-chloropropan-2-one (Ia)and 2-chlorobutanal (Ib) and of phenylethynyl-lithium to 2-chloro-2,4-dimethylpentan-3-one (Ic).[4] The cyclic epoxide

(Id) was obtained by oxidation of 1-ethynylcyclohexene with *m*-chloroperbenzoic acid.[5] The epoxides were all obtained in > 70% yield.

TABLE

Substrate	Reagent	Products (Yields, %)
(Ia)	Me_2CuLi	(IIa) (75)
(Ia)	$Bu^n{}_2CuLi$	(IIb) (34) + (IIc) (40)
(Ib)	Me_2CuLi	(IId) (60)
(Ic)	Me_2CuLi	(IIe) (68)
(Id)	Me_2CuLi	(IIf) (40) + (IIg) (22)
(Id)	$Bu^n{}_2CuLi$	(IIh) (30) + (IIg) (22)

The reactions of the acetylenic epoxides (Ia—d) with either dimethylcopperlithium or di-n-butylcopperlithium were carried out by addition of the epoxides in Et_2O to a stirred solution of the organocopper reagent[9] (6 mol equiv) in ether at −20 to −30°. The reactions were essentially complete in 15 min. The crude oils obtained after aqueous work-up were purified by column chromatography on silica gel. The structures of the products were established by full spectroscopic and analytical characterization and in most cases by oxidation with activated manganese dioxide to the corresponding allenic carbonyl compounds.

Preliminary experiments showed that use of tetrahydrofuran or higher reaction temperatures led to increased formation of side-products, particularly as a result of direct addition to the epoxide ring. The reaction is sensitive to variations in reaction conditions. Methyl-lithium under the reaction conditions described above did not react with acetylenic epoxides.

The results obtained under the standard conditions are summarized in the Table. Essentially the only products obtained were the allene alcohols, except in the case of (Ib) where a side-product (due to direct addition at the epoxide ring) was also obtained in 10—15% yield. The main variation is the proportion of alkylated to unalkylated allene which is formed. The source of the hydrogen in the unsubstituted allenes is unknown but is presumed to be a copper-bound alkyl group.

The technical assistance of Ms. Esther Roitman and Mr. Ron Chiarello, as well as the financial support of the Academic Senate, University of California, San Francisco, is acknowledged.

(*Received*, 25*th June* 1973; *Com.* 897.)

---

[1] J. S. Cowie, P. D. Landor, and S. R. Landor, *Chem. Comm.*, 1969, 541; A. M. Foster and W. C. Agosta, *J. Org. Chem.*, 1972, **37**, 61; R. Gelin, S. Gelin, and M. Albrand, *Bull. Soc. chim. France*, 1971, 4146.

[2] J. Meinwald, K. Erickson, M. Hartshorn, Y. C. Meinwald, and T. Eisner, *Tetrahedron Letters*, 1968, 2959; R. Bonnett, A. K. Mallams, J. L. Tee, B. C. L. Weedon, and A. McCormick, *Chem. Comm.*, 1966, 515; A. Jensen, *Acta Chem. Scand.*, 1964, **18**, 2005; H. H. Strain, W. A. Svec, K. Aitzetmuller, M. C. Grandolfo, J. J. Katz, H. Kjøsen, S. Norgård, S. Liaaen-Jensen, F. T. Haxo, P. Wegfahrt, and H. Rapoport, *J. Amer. Chem. Soc.*, 1971, **93**, 1823; B. C. L. Weedon, *Chem. in Britain*, 1967, 424.

E. E. Galantay, R. V. Coombs, I. Basco, R. L. Elton, and E. Harrington, *Experientia*, 1972, **28**, 771, and references therein.

[4] H. H. Schlubach and K. Repenning, *Annalen*, 1958, **614**, 37; T. Ilometz, *Zhur. obshchei Khim.*, 1960, **30**, 194; *Chem. Abs.*, 1961, **55**, 499.

S. W. Russel and B. C. L. Weedon, *Chem. Comm.*, 1969, 85.

[6] P. Rona and P. Crabbé, *J. Amer. Chem. Soc.*, 1968, **90**, 4735.

[7] R. J. Anderson, *J. Amer. Chem. Soc.*, 1970, **92**, 4978; R. W. Herr and C. R. Johnson, *ibid.*, p. 4979.

[8] R. W. Herr, D. M. Wieland, and C. R. Johnson, *J. Amer. Chem. Soc.*, 1970, **92**, 3813.

[9] E. J. Corey and G. H. Posner, *J. Amer. Chem. Soc.*, 1968, **90**, 5615.