

## ALKYNYLATION OF ALICYCLIC EPOXIDES WITH ALKYNYLDIETHYL ALANES

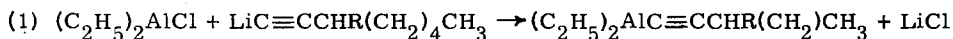
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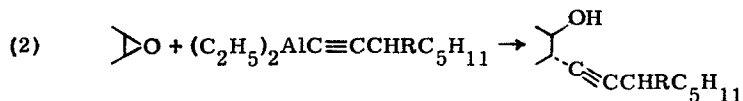
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The reaction of epoxides with alkali acetylides to form  $\beta$ -hydroxyacetylenes, a potentially important synthetic tool, suffers from low yields and becomes inapplicable as the degree of substitution of the epoxide is increased.<sup>1,2,3</sup> In a recently reported synthesis of  $(\pm)$ -7-oxa-prostaglandin F<sub>1 $\alpha$</sub> <sup>4</sup> this reaction could be made to perform in respectable yields and in a stereospecific manner by employing a diethylalkynyl alane in place of the alkali acetylide. In that report the alane was generated in situ according to Binger,<sup>5</sup> which involves substituting one of the ethyl groups of triethyl alane with the acetylenic moiety in the presence of triethylamine.

We now wish to report reaction conditions, which will result in quantitative yields with straight chain alkynes, viz. 1-octyne, and which will, moreover, permit extension of this reaction to more highly substituted and complex acetylenes. The diethylalkynyl alane reagents were prepared at room temperature according to equation (1),<sup>6,7</sup> where R = H benzyloxy<sup>8</sup> or tetrahydropyranyloxy (OTHP).<sup>8</sup>



Thus, a toluene solution of the alkyne was converted into the lithium derivative with *n*-butyl lithium in hexane. Addition of 20% diethylchloro alane in toluene (Texas Alkyls, Inc.) led to the formation of the reagent with precipitation of LiCl.<sup>9</sup> The supernatant containing the alane reagent (2 equiv.) was reacted with the requisite epoxide (1 equiv.) (equation (2))





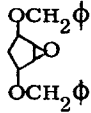


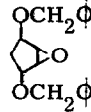


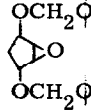
under the conditions and with the results shown in Table 1.<sup>10</sup> Experiments ranged in scale from 0.5 to 500 mmoles with essentially identical results. All reactions with 1-octyne were essentially quantitative. 3-Benzoyloxy-1-octyne and 3-tetrahydropyranyloxy-1-octyne gave lower yields. This latter statement should, however, be viewed in light of the fact that under our previously published conditions<sup>4</sup> the alanes prepared from the latter two compounds gave infinitesimally small or no yields at all.

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#### REFERENCES

1. R. A. Raphael, *Acetylenic Compounds in Organic Synthesis*, Butterworth, London, 1955, page 13.
2. H. H. Inhoffen, K. Weissermel, G. Quinkert and D. Bartling, *Ber.*, 89, 853 (1956).
3. R. T. Arnold and G. Smolinsky, *J. Am. Chem. Soc.*, 82, 4918 (1960).
4. J. Fried, S. Heim, S. J. Etheredge, P. Sunder-Plassmann, T. S. Santhanakrishnan, J. Himizu and C. H. Lin, *Chem. Comm.* 634 (1968).
5. P. Binger, *Angew. Chem.*, 75, 918 (1963).
6. G. Wilke and H. Müller, *Ann.*, 629, 222 (1960).
7. H. Demarne, *Compt. Rend.*, 261, 1992 (1965).
8. 3-Benzoyloxy-1-octyne, was prepared from 3-hydroxy-1-octyne (Farchan Chemicals) with 1 equiv. each of NaH and benzyl chloride in DMF. B. p. 83-84°<sub>3 mm</sub>. The THP ether was prepared according to Parham and Anderson, *J. Am. Chem. Soc.*, 70, 4187 (1948). B. p. 74-75°<sub>3 mm</sub>.
9. In the case of R = OCH<sub>2</sub>ϕ no precipitate formed at 25° but only after heating at 70-90° for 4-6 hours.
10. All new products gave the expected analytical values and n. m. r. spectra.

Table 1  
Results of Reaction of Epoxides with Alane Reagents

Alane	Epoxide	Temp.	Time h.	Isolated Yield %	Isolation Procedure
$\text{Et}_2\text{AlC}\equiv\text{CC}_6\text{H}_{13}$ <sup>b</sup>		25°	18	77 <sup>a</sup>	dist. over trace $\text{Na}_2\text{CO}_3$ , b. p. 80-90° <sup>3,4</sup> 0.05
"		25°	18	98 <sup>a</sup>	no further purification <sup>3,4</sup>
"		25°	20	78 <sup>a</sup>	column chromat. ( $\text{Al}_2\text{O}_3$ I) <sup>4</sup>
$\text{Et}_2\text{AlC}\equiv\text{CCHC}_5\text{H}_{11}$   $\text{OCH}_2\phi$		85°	72	30 <sup>c</sup>	one t. l. c. ( $\text{SiO}_2$ )
"		90°	72	38 <sup>c</sup>	two t. l. c. ( $\text{SiO}_2$ ) <sup>d</sup>
"		85°	72	59	two t. l. c. ( $\text{SiO}_2$ )
$\text{Et}_2\text{AlC}\equiv\text{CCHC}_5\text{H}_{11}$   $\text{OTHP}$		reflux	18	27 <sup>c</sup>	two t. l. c. ( $\text{SiO}_2$ )
"		"	18	20 <sup>c</sup>	two t. l. c. ( $\text{SiO}_2$ ), $\text{Al}_2\text{O}_3$ V)
"		"	140	28	two t. l. c. ( $\text{SiO}_2$ , $\text{Al}_2\text{O}_3$ V)

a) Crude yield 95-100% as determined by g. l. c. and n. m. r. spectra. b) A smaller than 2:1 ratio of alane-epoxide ratio gave lower yields. c) There was some loss of epoxide by evaporation at the higher temperatures. d) Prepared by Mr. Paul Dalven.