A Novel Alkynylation Reaction of Epoxy Alcohols: Use in the Synthesis of *erythro*-6-Acetoxyhexadecan-5-olide

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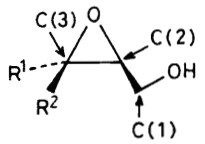
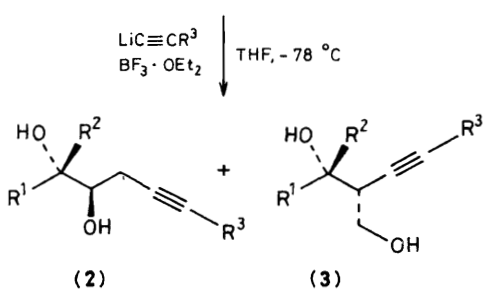
Lithium acetylides in the presence of $BF_3{\cdot}Et_2O$ react with epoxy alcohols derived from (*E*)-allylic alcohols to give *erythro*-1,2-diols, a reaction used successfully in the stereoselective synthesis of *erythro*-hexadecan-5-olide.

The regioselective ring cleavage of the epoxy alcohols (**1**) with various nucleophiles has received much attention and many examples of substitution at the C(2) or C(3) positions of (**1**) have been reported.[1] Conversely, only a few examples of reactions at the C(1) position, which involve rearrangement of the epoxy moiety, have been reported, even though this rearrangement seems to be a useful method for the stereoselective synthesis of 1,2-diols. We report herein a novel



(**1**) **a**; $R^1 = [CH_2]_2CH{=}CMe_2$, $R^2 = Me$
b; $R^1 = Pr^n$, $R^2 = H$
c; $R^1 = Me$, $R^2 = [CH_2]_2CH{=}CMe_2$
d; $R^1 = H$, $R^2 = Pr^n$

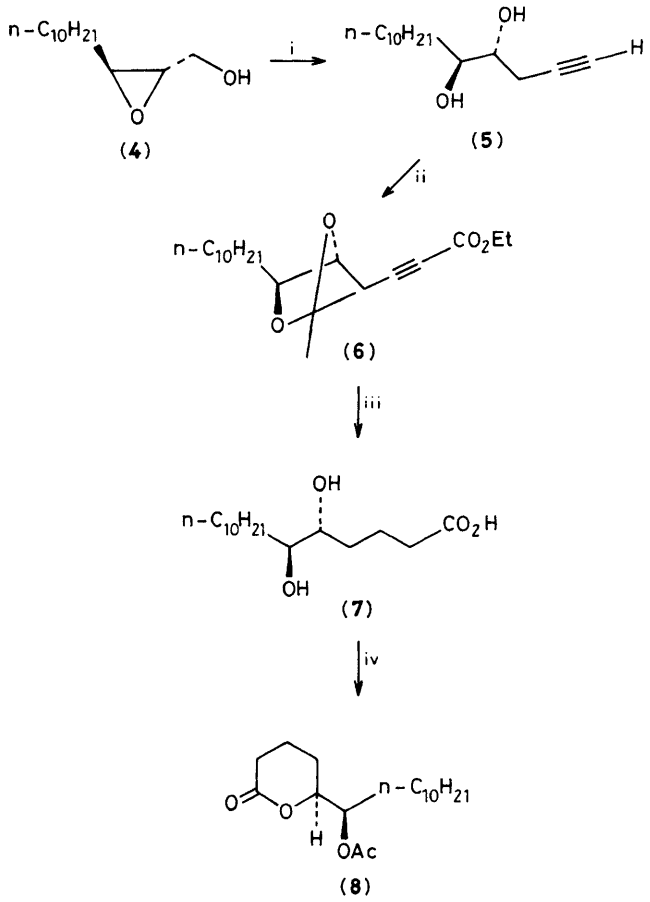


(**2**) (**3**)

Table 1. The alkynylation reaction of the epoxy alcohols (**1**).[a]

(1)	R^3	Product ratio (2) : (3)	Total yield (%)[b]	^{13}C n.m.r.[c] ($CDCl_3$, δ)
(**1a**)	Ph	55 : 45	94	86.9, 83.0, 75.5 74.2, 37.2, 25.7
	n-C_5H_{11}	80 : 20[d]	87	83.4, 76.7, 75.3 74.2, 37.3, 31.0
(**1b**)	Ph	72 : 28	77	86.4, 82.8, 73.3 72.9, 34.0, 22.9
	n-C_5H_{11}	81 : 19[d]	81	83.4, 76.1, 73.2 72.8, 34.2, 31.1
(**1c**)	n-C_5H_{11}	50 : 50	[e]	83.6, 76.6, 74.4 74.0, 39.0, 31.1
(**1d**)	Ph	42 : 58	81	86.0, 82.9, 72.9 72.5, 35.7, 25.0

[a] All the reactions were carried out as follows, under a nitrogen atomosphere, (**1**) (0.5 mmol) was added to a THF solution of lithium acetylide (2.0 mmol) at −78 °C. Then, $BF_3{\cdot}OEt_2$ (2.5 mmol) was added and the mixture was stirred for 30 min. After an aqueous work-up, the product isomers were separated by flash column chromatography on silica gel [ethyl acetate–hexane (1 : 3) for the reactions of (**1a**) or (**1c**) or ether–hexane (1 : 1) for (**1b**) and (**1d**)]. [b] All the products gave satisfactory spectral data (^1H and ^{13}C n.m.r., i.r., and/or high resolution mass). [c] Selected spectral data of 1,2-diols. [d] These compounds were identical (^1H and ^{13}C n.m.r., i.r.) with 1,3-diols obtained from the reaction of (**1a**) with the lithium acetylides in THF–hexamethylphosphoramide, which confirms the stereochemistry of (**3**). [e] Quantitative.



Scheme 1. i, LiC≡CH, BF_3·OEt_2, THF, −78 °C, 57%; ii, $Me_2C{=}O$, $HClO_4$, molecular sieves (4 Å), room temperature (r.t.), 30 min, 71%; Bu^nLi, $ClCO_2Et$, THF, −78 °C, 87%; iii, H_2-Pd/C, EtOH, r.t., 1 h; 2 M KOH, reflux, 1 h; 2 M HCl, r.t., 1 h, 50%; iv, Ac_2O, pyridine, r.t., 2 h.

reaction of acetylides with epoxy alcohols and its application in the stereoselective synthesis of *erythro*-6-acetoxy-5-hexadecanolide (**8**).

The epoxy alcohols (**1**) prepared from (*E*)-allylic alcohols reacted with lithium acetylides at −78 °C in tetrahydrofuran (THF) in the presence of boron trifluoride–diethyl ether[3] to give predominantly the acetylenic 1,2-diols (**2**), which result from attack of the nucleophile at the C(1) position of (**1**). The 1,3-diols (**3**), formed by substitution at the C(2) position, were also isolated as minor products (Table 1). The use of alcohols (**1**) derived from (*Z*)-allylic alcohols resulted in lower regioselectivity.

All of the products are stereochemically pure which indicates that the reaction is highly stereospecific. If rearrangement of (**1**) occurs with inversion of configuration at the C(2) position, then *erythro*-diols should be obtained from the original (*E*)-allylic alcohols. To confirm the stereochemistry of (**2**) and to show the use of the present reaction, we stereoselectively synthesized (**8**), the major component of a mosquito oviposition attractant pheromone.[4]

The epoxy alcohol (**4**) synthesized from (*E*)-tridec-2-en-1-ol was treated with lithium acetylide as above and the 1,2-diol (**5**) was obtained as the major product (57% yield) accompanied by the 1,3-diol (18% yield), from which (**5**) was separated by flash column chromatography [silica gel, ether–hexane (1 : 1)], (**5**); m.p. 85 °C, ^{1}H n.m.r. ($CDCl_3$) δ 2.06 (1H, t, *J* 2.7 Hz), ^{13}C n.m.r. ($CDCl_3$) δ 81.2, 73.5, 72.4, and 70.9 p.p.m. After protecting the hydroxy group, (**5**) was subjected to one-carbon homologation *via* lithium acetylide to form the acetylenic ester (**6**) (Scheme 1). Reduction of the triple bond and deprotection of the hydroxy groups yielded the dihydroxy acid (**7**), m.p. 127 °C (lit.[4] 124 °C), ^{13}C n.m.r. ($CDCl_3$–[$^2H_6$]Me_2SO) δ 174.8, 74.1, and 73.8 p.p.m. The lactonization was performed as described previously[5] and the synthetic lactone (**8**) gave identical spectral data (^{1}H and ^{13}C n.m.r., i.r.) to those of an authentic sample.

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