

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

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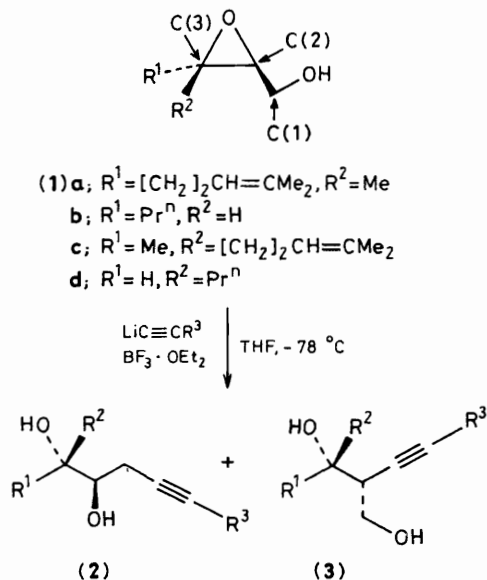
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Lithium acetylides in the presence of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ react with epoxy alcohols derived from (*E*)-allylic alcohols to give *erythro*-1,2-diols, a reaction used successfully in the stereoselective synthesis of *erythro*-hexadecan-5-olide.

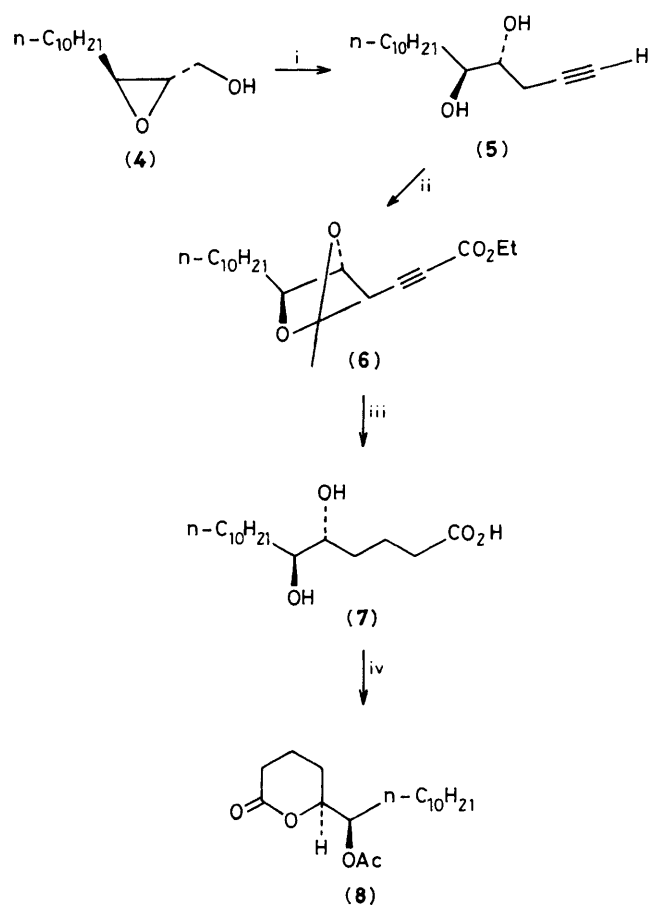
The regioselective ring cleavage of the epoxy alcohols (**1**) with various nucleophiles has received much attention and many examples of substitution at the C(2) or C(3) positions of (**1**) have been reported.¹ Conversely, only a few examples of reactions at the C(1) position, which involve rearrangement 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

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 ₅ H 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 ₅ H ₁₁	81:19 ^d	81	83.4, 76.1, 73.2 72.8, 34.2, 31.1
(1c)	n-C ₅ H 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 atmosphere, (**1**) (0.5 mmol) was added to a THF solution of lithium acetylide (2.0 mmol) at -78°C . Then, $\text{BF}_3 \cdot \text{OEt}_2$ (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 ¹³C 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 ¹³C 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, $\text{LiC}\equiv\text{CH}$, $\text{BF}_3\cdot\text{OEt}_2$, THF, -78°C , 57%; ii, $\text{Me}_2\text{C}=\text{O}$, HClO_4 , molecular sieves (4 Å), room temperature (r.t.), 30 min, 71%; $\text{Bu}^\text{t}\text{Li}$, 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 ether³ 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 , ^1H 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 - $[\text{D}_6]\text{Me}_2\text{SO}$) δ 174.8, 74.1, and 73.8 p.p.m. The lactonization was performed as described previously⁵ and the synthetic lactone (8) gave identical spectral data (^1H and ^{13}C n.m.r., i.r.) to those of an authentic sample.

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