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CARBOHYDRATES AS A PRACTICAL SOURCE OF CHIRAL POLYHYDROXY ACETYLENES

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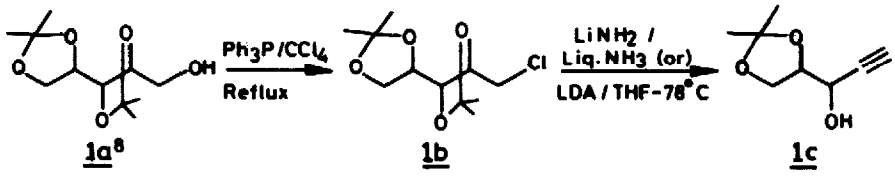
Syntheses of chiral polyhydroxy propargyl alcohols by employing double elimination of β-alkoxy chlorides with strong bases have been described.

The concept of deriving undisputedly valuable chiral precursors with wide assortment of applications for natural product synthesis from carbohydrates has been relentlessly pursued in recent years[1]. Some of the meticulously designed syntheses of biologically active polyhydroxylated unsaturated fatty acids such as leukotrienes[2], lipoxins[2] and others[3,4] particularly from carbohydrates have been developed[5] efficiently. However we reasoned that these syntheses could be further simplified if carbohydrates are rendered effectively into hydroxy intermediates endowed with terminal carbon-carbon triple bond[6]. By the attachment of suitable alkyl chain onto these precursors, their total syntheses would become greatly simplified and effective. We have recently demonstrated[7] that β-alkoxy chloride obtained from tartaric acid undergoes facile elimination in the presence of a base to chiral acetylenic alcohols. Influenced by this reaction it became imperative for us to extend the scope of this reaction to cheap and readily available carbohydrate precursors.

1-Chloro-1-deoxy-2,3:4,5-O-isopropylidene-DL-xylitol (**1b**) prepared from **1a**[8] was treated with $LiNH_2$ (6 eq.) in liq. NH_3 at -33° to give rise to the acetylenic alcohol (**1c**) as a single product in 92% yield (Scheme 1). Later it was observed that the elimination reaction of **1b**

Scheme 1



1a[8] **1b** **1c**

could also be effected with LDA (5 eq.) in THF at -78° in almost similar yield. In order to test the efficacy of this approach various chiral chloride derivatives (**2b-7b**) were prepared[9] from the corresponding alcohols[10] by treatment with triphenylphosphine and carbon tetrachloride

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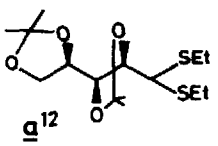
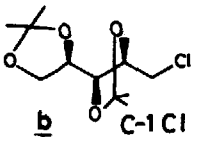
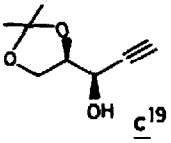
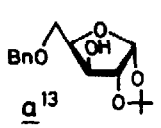
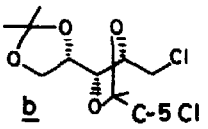
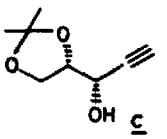
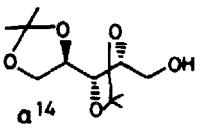
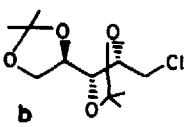
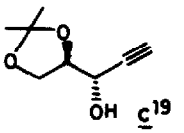
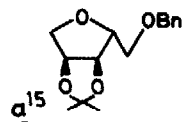
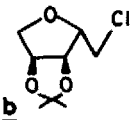
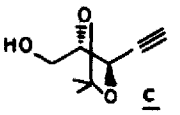
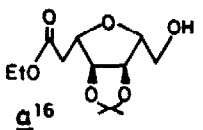
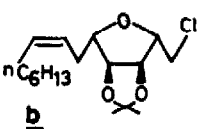
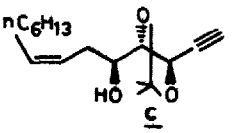
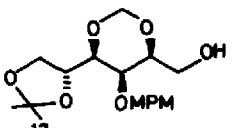
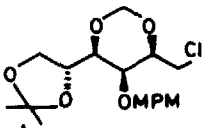
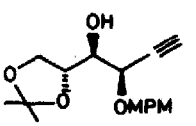
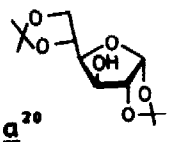
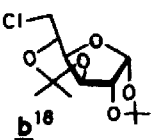
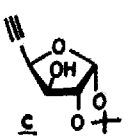
Table 1 : CHIRAL ACETYLENIC ALCOHOLS PREPARED

Compd. No.	Carbo-hydrate source	Precursor	Chlorocompds.	Products	$[\alpha]_D^\circ$	Yield %
2	D-Xylose	 a[12]	 b C-1 Cl	 c[19]	12.8 (1.7)	98
3	D-Xylose	 a[13]	 b C-5 Cl	 c	-12.8 (1.5)	96
4	D-Arabinitol	 a[14]	 b	 c[19]	21.9 (2.3)	98
5	D-Ribose	 a[15]	 b	 c	-4.3 (1.2)	89
6	D-Ribose	 a[16]	 b	 c	35.2 (3.1)	86
7	D-Sorbitol	 a[17]	 b	 c	-81.6 (4.0)	76
8	D-Glucose	 a[20]	 b[18]	 c	-18.2 (4.5)	81

2a → 2b (OH): (i) HgO-$HgCl_2$ (ii) $NaBH_4$; 3a → 3b (OH): (i) 80% aq. AcOH, (ii) $NaBH_4$, (iii) acetone, H_2SO_4 (iv) Ni, H_2; 5a → 5b (OH): (i) Li/ Liq. NH_3; 6a → 6b (OH): (i) DIBAL-H, (ii) $n\text{-}C_6H_{13}CH_2\overset{+}{P}Ph_3\bar{B}r$, $NaNH_2$; 8a $\xrightarrow{\text{ref. 10}}$ 8b : $Me_2\overset{+}{N}{=}CHCl^-$, 1,1',2,2'-Tetrachloroethane

Rotations were taken in chloroform.

2b (OH), 3b (OH) etc. refer to the alcohols corresponding to chlorides 2b, 3b etc.

in 85-90% yield. When these chlorides (**2b-8b**) were subjected to the base induced elimination reaction as described above, the enantiomerically pure propargyl alcohols (**2c-8c**) were isolated in 76-98% yield.

One of the advantages of this protocol is that the isomeric propargyl alcohols could be synthesised depending upon the position of the chloride being present at C-1 or C-5 (C-6) of pentose (hexose) derivatives. For instance, the C-1 chloride (**2b**) and the C-5 chloride (**3b**) prepared from D-xylose undergo facile elimination to afford enantiomeric derivatives **2c** and **3c** respectively. Apparently (Table 1), the heavily substituted tetrahydrofurfuryl chlorides (**5b** and **6b**) have also undergone facile elimination reaction[11] in high yields. Similarly the chlorides (**7b** and **8b**) derived from D-hexoses have been converted into propargyl alcohol derivatives (**7c** and **8c**) in good yield.

It is pertinent to mention that the elimination reaction is highly chemoselective because other isopropylidene group present in the substrate remains unaffected. Thus it could be concluded that the protocol reported above to obtain chiral acetylenic compounds from simple carbohydrate precursors is undoubtedly a general and efficient method and indeed will find a great deal of applications in the asymmetric synthesis.

References and Notes

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