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A NEW CONVENIENT APPROACH TO HIGHER SUGAR ALLYLIC ALCOHOLS

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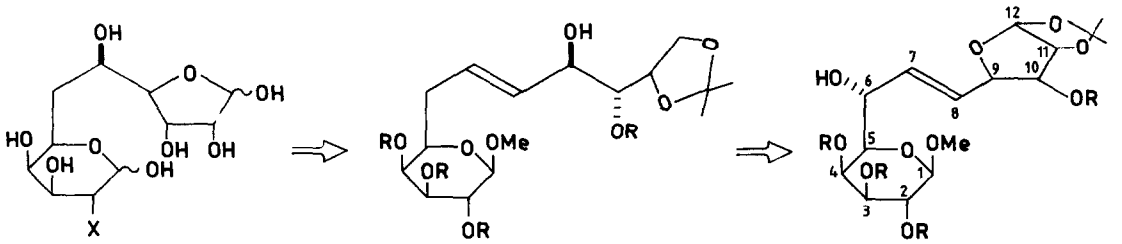
Abstract - Allylic alcohol 4, a chiral synthon for the preparation of des-aza tunicamine (2), was obtained by two independent routes starting from either D-galactose or D-ribose derivatives. The selection of the starting material depends, therefore, only on its availability. The interchangeability of the synthetic routes is especially important when rare sugars have to be used in the synthesis.

The synthesis of higher carbon sugars having ten or more carbon atoms in the chain has gained considerable attention in the past few years[1]. Although these compounds are not very common in nature, they are important components of some antibiotics such as hikizimycin[2] or tunicamycin[3]; the latter was suggested to have potential anticancer properties[4].

The main component of tunicamycin is the 11-carbon sugar, tunicamine (1). Because of the importance of this compound and of our interest in the chemistry of higher sugars, we attempted to develop a short and efficient synthesis of 1. For the model study the des-aza analogue of tunicamine (2) was chosen.

Retrosynthetic analysis of 2 revealed that this 11-carbon sugar can be prepared in a few steps from 3 (having 12 carbon atoms; the blocked diol will serve as a masked aldehyde group) which in turn can be readily prepared from 4.



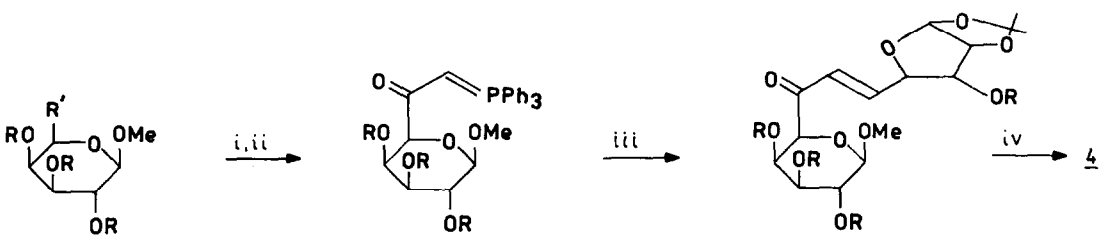
1 X = NH_2
2 X = OH

3 R = CH_2Ph

4

Compound 4 can be regarded as a higher carbon sugar arising from coupling of two monosaccharide sub-units: D-galactose (the C_1 - C_6 part) and D-ribose (the C_8 - - C_{12} part) via an additional carbon atom (C_7).

Allylic alcohol 4 was prepared in a few steps from methyl 2,3,4-tri-O-benzyl-β-D-galactopyranoside (5)[5], as shown in Scheme 1.



5 R = CH_2Ph ; R' = CH_2OH
11 R = CH_2Ph ; R' = CHO

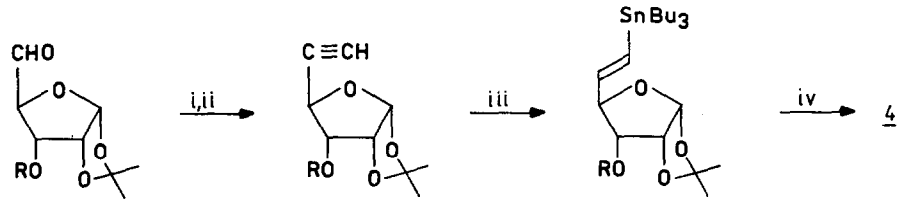
6 R = CH_2Ph

7 R = CH_2Ph

Scheme 1. i. CrO_3/H_2SO_4/acetone, 80%. ii. im_2CO, benzene, r.t., 15 min., then 2.2 equiv. $Ph_3P{=}CH_2$ in benzene, r.t., 3 h, 60%. iii. 8, r.t., 16 h, 70%. iv. $Zn(BH_4)_2$, ether, 0°, 90%.

Oxidation of 5 with Jones reagent furnished the uronic acid which was converted into phosphorane 6 according to a procedure which we have described recently[1d]. The reaction of 6 with 3-O-benzyl-1,2-O-isopropylidene-α-D-ribo-pentadialdo-1,4-furanose (8)[6] afforded enone 7 which was reduced stereoselectively to alcohol 4[7].

The above method is convenient for the synthesis of des-aza analogue of tunicamine (2), whereas it would be rather difficult to apply for the preparation of tunicamine (1), since the synthesis should be initiated with the very expensive D-galactosamine. It would be much more preferable to introduce this expensive sugar in the last step. Our recently published method for the preparation of higher sugar allylic alcohols via vinyltin intermediates[1e] helped us to solve this problem.



8 R = CH_2Ph

9 R = CH_2Ph

10 R = CH_2Ph

Scheme 2. i. $Zn/Ph_3P/CBr_4$, CH_2Cl_2, 70%. ii. 2.1 equiv. BuLi, -78°, 1 h, 65%. iii. Bu_3SnH, AIBN, xylene, reflux, 6 h, 85%. iv. 1.1 equiv. BuLi, THF, -78°, 1 h, then 11, -78° to r.t., 70%.

Aldehyde 8 was converted into acetylene 9 according to Corey et al.[8]. This compound underwent clean reduction of the triple bond with tributyltin hydride[1e], affording trans olefin 10 (J = 19.6 Hz). Replacement of the tributylstannyl moiety by lithium[1e] produced the vinyl anion which reacted with aldehyde 11[1c] to afford likewise alcohol 4[9].

Summing up, we presented here two complementary methods for preparation of higher sugar allylic alcohol substituted with two different monosaccharide sub-units. The synthesis of 4 was initiated either from D-galactose or from D-ribose derivatives, this allowing the choice of the more readily available monosaccharide as starting material. The interchangeability of the synthetic routes is especially important when rare sugars have to be used as chiral synthons.

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REFERENCES AND NOTES

1. a. J. A. Secrist, III and S.-R. Wu, J. Org. Chem., 44, 1434 (1979); J. A. Secrist, III and K. D. Barnes, ibid., 45,4526 (1980).
   b. T. Suami, H. Sasai, and K. Matsuno, Chem. Lett., 819 (1983).
   c. J. W. Krajewski, P. Gluziński, S. Jarosz, A. Zamojski, J. Bleidelis, A. Mishnyov, and A. Kemme, Carbohydr. Res., 144, 183 (1985).
   d. S. Jarosz, D. Mootoo, and B. Fraser-Reid, Carbohydr. Res., 147, 59 (1986).
   e. S. Jarosz, Carbohydr. Res., 166, 211 (1987).
   f. S. Danishefsky and C. Marig, J. Am. Chem. Soc., 107, 7762 (1985); S. Danishefsky and M. Barbachyn, ibid., 107, 7761 (1985).
   g. S. A. Babired, Y. Wang, and Y. Kishi, J. Org. Chem., 52, 1370 (1987).
2. K. Uchida, T. Ishikawa, Y. Schimauchi, T. Ishikura, and A. Ozaki, J. Antibiot., 24, 259 (1971).
3. A. Takatsuki, K. Arima, and G. Tamura, J. Antibiot., 24,215 (1971); T. Suami, H. Sasai, K. Matsuno, N. Suzuki, Y. Fukuda, and O. Sakanaka, Tetrahedron Lett., 25, 4533 (1984).
4. M. J. Morin and R. J. Bernacki, Cancer Res., 43, 819 (1983).

5. P. J. Garegg and C. G. Swanson, Acta Chem. Scand., 26, 3895 (1972).
6. R. Youssefyeh, D. Tegg, J. P. Verheyden, G. H. Jones, and J. G. Moffat, Tetrahedron Lett., 18, 435 (1978).
7. The ratio of isomers was 95:5. We assigned tentatively the configuration of the main stereoisomer at C-6 as D-glycero, consistently with our model of stereoselective reduction of higher sugar enones with zinc borohydride[10]. However, exact determination of the configuration is unnecessary, since the C-6 position will later be converted into the CH_2 group.
8. E. J. Corey, P. Ulrich, and J. M. Fitzpatrick, J. Am. Chem. Soc., 98, 222 (1976)
9. The ratio of isomers was ca 4:1; the main isomer was identical with that obtained by reduction of 7 with zinc borohydride.
10. S. Jarosz, Bull. Pol. Acad. Chem., 35, 161 (1987); S. Jarosz, to be published in Carbohydr. Res. .

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