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SYNTHESIS AND CONVERSIONS OF C-(ALKYN-1-YL)- β-D-GLUCOPYRANOSIDES

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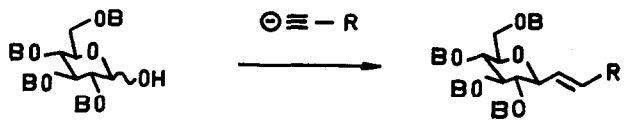
Summary: A stereospecific synthesis of C-(alkyn-1-yl)-β -D-glucopyranosides from 2,3,4,6-tetrabenzyl-glucopyranolactone is reported.

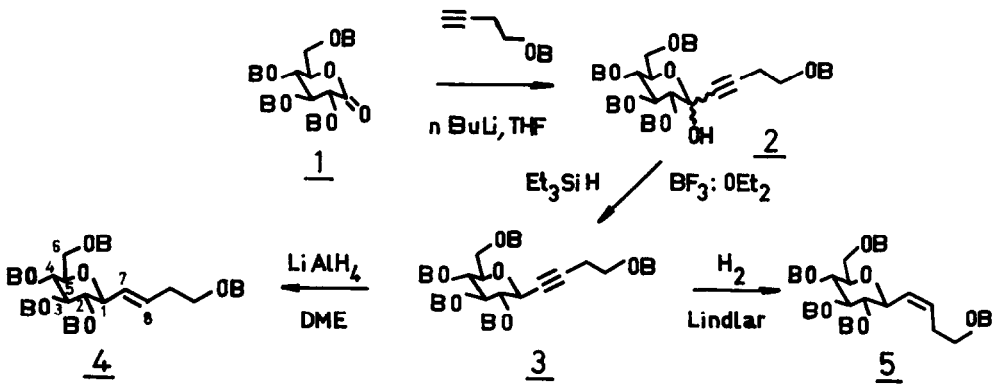
Although frantic efforts are currently devoted to the direct formation of C-C-bonds at the anomeric center of carbohydrates[1], the following stereospecific transformation has not been described to the best of our knowledge[2] :



As part of an ongoing program on the synthesis of natural products from carbohydrates, such a reaction was sought for during the study of model reactions for the construction of the "west" fragment of ambruticin [3], a unique antifungal antibiotic.We anticipated that C-(alkyn-1-yl)- β -D-glucopyranosides would be immediate precursors of substituted trans C-vinyl- β -D-glucopyranosides, and would furthermore be versatile intermediates for the preparation of a variety of β-D-C-glucopyranosides. We wish to report a stereospecific entry to such derivatives.

Ethynyl compounds have been shown to react with sugar lactones to give acetylenic lactols[4]. On the other hand, triethylsilane with a Lewis acid is known to reduce acetals[5], a property which has been used for the highly stereoselective synthesis of C-alkyl- β-D-glucopyranosides[1b].In a typical exemple,the treatment of 2,3,4,6-tetrabenzylglucopyranolactone **1**[6] with the anion (1.6 M n-BuLi, THF) of 1-benzyloxy-3-butyne[7] (THF, -78° → -40°, 1.5 h) gave a quantitative yield of the hemiketal **2**[8,9], which was stereospecifically reduced (Et_3SiH, BF_3:Et_2O in $MeCN$-CH_2Cl_2,17:3 ,v/v, -40°, 1h) into the β-D-C-glucoside **3**[10]

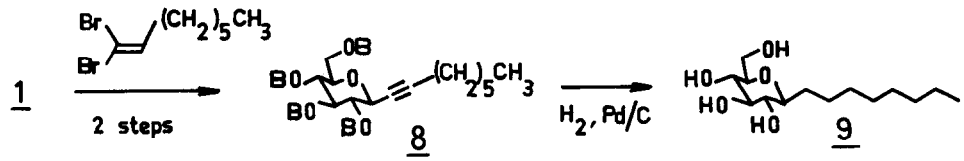
(72%), $[\alpha]_D$ 0°. No stereoisomer was detected by chromatographic means. The stereochemical control is achieved by axially oriented addition of hydride on the oxonium ion[1b]. The ethynyl derivative 3 was transformed[12] ($LiAlH_4$, DME, 90°, 12h) into the E C-vinyl-β-D-glucoside 4 (57%), m.p. 64-65°, $[\alpha]_D$0°; ^{1}H-N.M.R. (90 MHz) :$J_{7,8}$15.5Hz. For comparison purposes, 3 was reduced (H_2, Lindlar catalyst) to provide the Z isomer 5 (75%), $[\alpha]_D$ + 42°; ^{1}H-N.M.R. (90MHz): $J_{7,8}$ 10.5Hz.



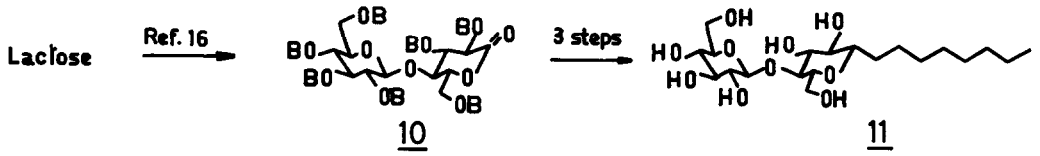
This methodology has been applied to the synthesis of a model fragment of ambruticin , as depicted in the following scheme[13]:

The racemic dibromoolefin 6 was transformed in situ into the corresponding lithioalkynyl (n-BuLi, THF, -85° for 1h,then 20° for 1h) and the three-step procedure provided compound 7 (40% from 6) as a mixture of two diastereoisomers which were not separated.

C-(Alkyn-1-yl)- β-D-glucopyranosides are immediate precursors of C-alkyl- β-D-glucopyranosides, compounds of potential utility as new forms of nonionic detergents, used for the solubilization and isolation of membrane proteins and for stabilization and activation of enzymes[14]. The analog of octyl- β-D-glucopyranoside[14] has been prepared as follows :



8 (67% from **1**), $[\alpha]_D$ 0°; **9** (93%), $[\alpha]_D$ -14°. **9** was characterized as a crystalline tetraacetate (96%), m.p. 90° (hexane), $[\alpha]_D$ -15°.Finally, the procedure is applicable to disaccharides, as exemplified by the following scheme[16]:



10 **11**

11 (50% from **10**), $[\alpha]_D$ -16°.

The reduction of the hemiketal is thus mild enough to avoid a possible reductive cleavage of the interglycosidic linkage[15]. The possibility of forming, with such C-alkyl-β-D-glycosides,monodisperse populations of micelles will be investigated.

References and Notes

1. a) S. Hanessian and A.G. Pernet, Adv.Carbohydr.Chem.Biochem.,33, 111 (1976); b) M.D. Lewis, J.K. Cha and Y.Kishi, J.Am.Chem.Soc., 104, 4976 (1982) and references cited therein; c) R.M. Williams and A.O. Stewart, Tetrahedron Lett., 24, 2715 (1983) and references cited therein.

2. We restrict ourselves in this piece of work to direct anchoring of the integrate appropriate unsaturated appendage at the anomeric center of a carbohydrate. Indirect formation of a substituted C-vinyl glycoside has been performed. See for exemple : S.S. Ko, J.M. Finan, M. Yonaga, and Y. Kishi, D. Uemura and Y. Hirata, J.Am.Chem.Soc., 104, 7364 (1982).For a low yield glucosylation of phenylacetylene, see R. Zelinski and R.E. Meyer, J.Org.Chem., 32, 810 (1958).

3. a) D.T. Connor, R.C. Greenough and M. von Strandtmann, J.Org.Chem.,42, 3664 (1977). The relative stereochemistry shown in this paper is incorrect. A correction has been submitted to the editor, J.Org.Chem., 43, 5027 (1978); b) N.J. Barnes, A.H.Davidson, L.R. Hughes, G. Procter and V. Rajcoomar, Tetrahedron Lett., 22, 1751 (1981).

4. H. Ogura, H. Takahashi, and T. Itoh, J.Org.Chem., 37, 72 (1972).

5. E. Frainnet and C. Esclamadon, C.R. Hebd.Scéances. Acad.Sci., 254, 1814 (1962).

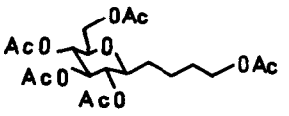
6. Prepared in 94% yield by Swern oxidation [A.J. Marcuso,S.L.Huang and D.Swern,J.Org.Chem., 43,2480(1980)] of commercially available tetrabenzylglucopyranose.See also ref. 1b.

7. W.S. Johnson, K. Wiedhaup, S.F. Brady and G.L. Olson, J.Am.Chem.Soc., 96, 3979 (1974).

8. The I.R spectrum of the anomeric mixture shows a hydroxyl band at 3350 cm^{-1} and an acetylenic band at 2250 cm^{-1}.

9. All new compounds had satisfactory microanalytical and spectral properties . Optical rotations were measured for solutions in chloroform at 20° C, unless otherwise stated.

10. The configuration at the anomeric center was best established on the pentaacetate derived from **3** (50%), $[\alpha]_D$ -12°. ^{1}H-N.M.R.(90MHz) : $J_{1,2}$ 9.7Hz.



11. For a discussion on this problem , see ref .1b.

12. E.F. Magoon and L.H. Slaugh, Tetrahedron, 23, 4509 (1967).

13. The racemic dibromoolefin **6** has been prepared from ethyl chrysanthemate (Aldrich) (1. $LiAlH_4$, Et_2O; 2. PCC, CH_2Cl_2; 3. Ph_3P-CBr_4, CH_2Cl_2).

14. Octyl- β -D-glucopyranoside and docecyl-D-maltoside are commercially available (Fluka). See the Fluka technical sheet for various references.

15. D. Rolf and G.R. Gray, J.Am.Chem.Soc., 104, 3539 (1982).

16. The lactone **10** has been prepared from acetobromolactose (1. Allyl alcohol, HgO, $HgBr_2$; 2. MeONa, MeOH; 3. $PhCH_2Br$, NaH, DMF; 4. ^{t}BuOK, DMSO; 5. HCl, acetone; 6. Swern oxidation).

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