The First Synthesis of a '*C*-Disaccharide'

Dominique Rouzaud and Pierre Sinaÿ*

Laboratoire de Biochimie Structurale, E.R.A. 739, E.U.R. de Sciences Fondamentales et Appliquées, 45046 Orleans Cedex, France

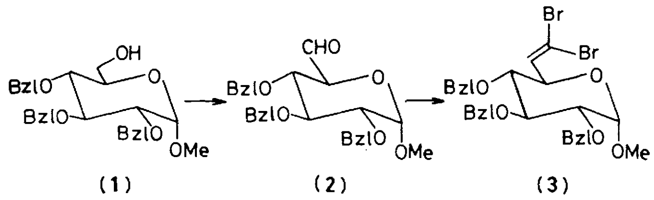
Condensation of 2,3,4,6-tetrabenzylglucopyranolactone with the anion of methyl 6,7-dideoxy-2,3,4-tri-*O*-benzyl-α-D-gluco-hept-6-ynopyranoside followed by triethylsilane reduction provided, after hydrogenolysis, the first example of a synthetic β(1 → 6')-'*C*-disaccharide.'

Although there is currently intense synthetic activity in the field of *C*-glycopyranosides,[1] 'C-disaccharides' are still elusive compounds. We now report the first, to the best of our knowledge, stereospecific synthesis of a '*C*-disaccharide,' that is a disaccharide in which a methylene group takes the place of the inter-unit oxygen atom. We took advantage of a methodology recently used by us[2] for the preparation of *C*-(alkynyl)-β-D-glucopyranosides. *C*-Linked oligosaccharides are now highly in demand for studies of sugar metabolism,[3] and as enzyme inhibitors.[4]

Oxidation of methyl 2,3,4-*O*-benzyl-α-D-glucopyranoside (**1**)[5] according to the method of Swern *et al.*[6] provided the aldehyde (**2**), which was immediately converted into the dibromo-olefin (**3**) [70% from (**1**)], m.p. 70—71 °C (from hexane), $[\alpha]_D$ +32.5°.† Treatment of 2,3,4,6-tetrabenzylglucopyranolactone[7] (tetrahydrofuran THF, 1 h, −50 °C) with the *in situ*-generated acetylenic anion (BuLi, THF, −50 °C) derived from (**3**) gave the hemiacetal (**4**) (92%), which was stereospecifically reduced (Et_3SiH, BF_3–Et_2O in MeCN–CH_2Cl_2, 17:3 v/v, 15 min, 0 °C) into the β-*C*-disaccharide (**5**) (67%), m.p. 106 °C (from hexane), $[\alpha]_D$ + 12°. No stereoisomer was detected by chromatography.

---

† All new compounds had satisfactory microanalytical and spectral properties. Optical rotations were measured for solutions in chloroform at 20 °C.



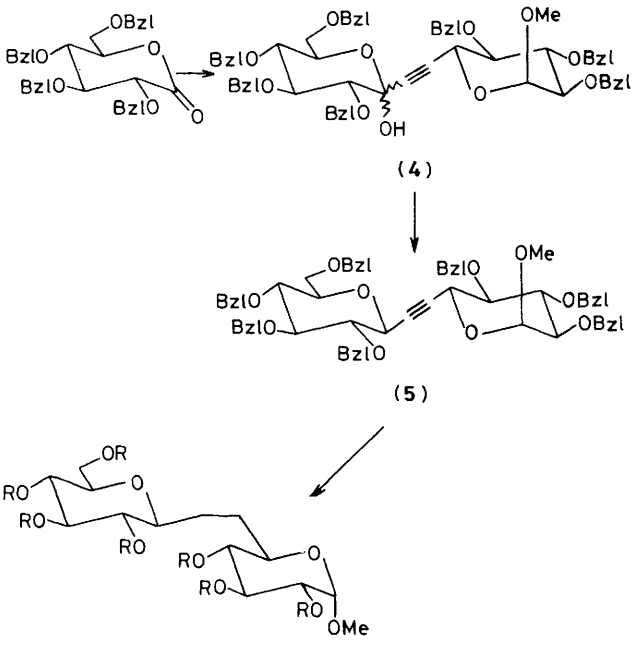
Bzl = benzyl

Catalytic hydrogenolysis (H_2, 10%, Pd/C, AcOH, 24 h) gave the *C*-disaccharide (**6**) (78%), m.p. 200—202 °C (from ethanol), $[\alpha]_D$ +88° (MeOH), which was transformed (Ac_2O, pyridine) into the peracetate (**7**) (95%), m.p. 172 °C, $[\alpha]_D$ +55°. The ^1H n.m.r. spectrum (90 MHz; $CDCl_3$) of (**7**) showed a signal for H-1′ at δ 3.7, with $J_{1,2}$ 9.5 Hz. The magnitude of this coupling constant confirms the β-D linkage.

This novel sequence, which provides the first entry to a '*C*-disaccharide', should be of general utility for the preparation of *C*-analogues of β(1 → 6′)di- or oligo-saccharides.

We thank the Centre National de la Recherche Scientifique and the Ministère de la Recherche et de l'Industrie (fellowship to D. R.) for financial support.

Received, 22nd July 1983; Com. 987



(6) R = H

(7) R = Ac

References

1 S. Hanessian and A. G. Pernet, *Adv. Carbohydr. Chem. Biochem.*, 1976, **33**, 111; M. D. Lewis, J. K. Cha, and Y. Kishi, *J. Am. Chem. Soc.*, 1982, **104**, 4976 and references cited therein; R. M. Williams and A. O. Stewart, *Tetrahedron Lett.*, 1983, **24**, 2715 and references cited therein.
2 J.-M. Lancelin, P. H. Amvam Zollo, and P. Sinaÿ, *Tetrahedron Lett.*, in the press.
3 Quotation from L. A. Reed III, I. Ito, S. Masamune, and K. B. Sharpless, *J. Am. Chem. Soc.*, 1982, **104**, 6468.
4 M. L. Shulman, S. D. Shiyan, and A. Y. Khorlin, *Carbohydr. Res.*, 1974, **33**, 229; D. Cerretti, *ibid.*, 1981, **94**, C10.
5 P. Kováč, J. Alföldi, and B. Kosik, *Chem. Zvesti*, 1974, **28**, 820; A. Lipták, I. Jodál, and P. Nánási, *Carbohydr. Res.*, 1975, **44**, 1.
6 A. J. Mancuso, S. L. Huang, and D. Swern, *J. Org. Chem.*, 1978, **43**, 2480.
7 H. Kuzuhara and H. G. Fletcher, *J. Org. Chem.*, 1967, **32**, 2531.