Carbohydrate Research, 58 (1977) 219–221

Note

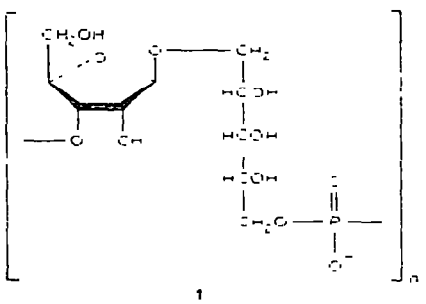
Synthesis of 1-*O*-β-D-ribofuranosyl-D-ribitol

PER J. GAREGG, BENGT LINDBERG, AND BERTIL SAMUELSSON

Department of Organic Chemistry, Arrhenius Laboratory, University of Stockholm, S-106 91 Stockholm (Sweden)

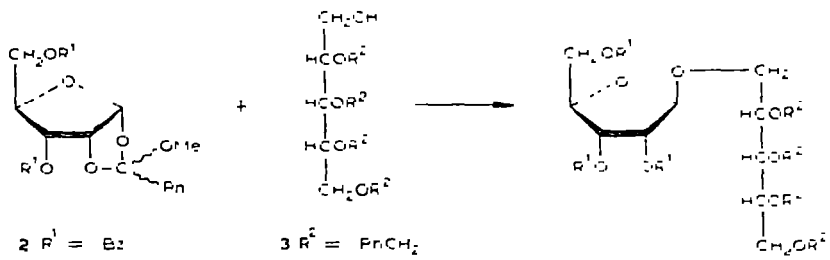
(Received November 15th, 1976; accepted for publication, November 24th, 1976)

The capsular antigen elaborated by *Haemophilus influenzae* type b is composed[1,2] of 1-*O*-β-D-ribofuranosyl-D-ribitol residues joined through phosphoric diester groups at O-3 of D-ribose and O-5 of D-ribitol (**1**). The organism causes meningitis in children, and 1-*O*-β-D-ribofuranosyl-D-ribitol (**6**) was needed for immunological studies. We now report the synthesis of **6**.



1

3,5-Di-*O*-benzoyl-α-D-ribofuranose 1,2-(methyl orthobenzoate)[3,4] (**2**) was allowed to react with 2,3,4,5-tetra-*O*-benzyl-D-ribitol[5] (**3**). Blocking groups were



2 R^1 = Bz **3** R^2 = $PhCH_2$

4 R^1 = Bz, R^2 = $PhCH_2$
5 R^1 = H, R^2 = $PhCH_2$
6 R^1 = R^2 = H

removed from the product (**4**) by debenzoylation to give **5**, followed by catalytic hydrogenation to give **6**. The disaccharide **6** was indistinguishable by ^{1}H-n.m.r. spectroscopy from the substance obtained from the *Haemophilus influenzae* antigen by dephosphorylation. The methylated disaccharides were indistinguishable by g.l.c. and gave superposable mass spectra.

EXPERIMENTAL

General. — General methods were the same as those reported in a recent paper[6].

2,3,4,5-Tetra-O-benzyl-1-O-β-D-ribofuranosyl-D-ribitol (**5**). — 3,5-Di-*O*-benzoyl-α-D-ribofuranose 1,2-(methyl orthobenzoate) (**2**), prepared from 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl bromide[3] as described by Hanessian and Banoub[4], had $[\alpha]_D$ +107° (*c* 1.0, chloroform); lit.[4] $[\alpha]_D^{25}$ +104° (chloroform). Orthoester **2** (2.34 g) and 2,3,4,5-tetra-*O*-benzyl-D-ribitol[5] (**3**, 2.09 g) were dissolved in nitromethane (25 ml). Methanol was removed by continuous distillation at constant volume with continuous addition of nitromethane for 2 h. T.l.c. (toluene–ethyl acetate, 4:1) then showed complete trans-esterification of **2**. Mercury(II) bromide (250 mg) was added, and solvent distilled off at constant volume with continuous addition of nitromethane for 3 h. T.l.c (toluene–ethyl acetate, 4:1) then showed the formation of a new product. The mixture was filtered and concentrated, and the product debenzoylated in 0.04M sodium methoxide in methanol (150 ml) for 1 h at room temperature. The solution was neutralized with Dowex 50 (H^+) resin. A little sodium hydrogen carbonate was added in order to neutralize any acid from the resin, the mixture was filtered, and the filtrate was concentrated to dryness. Chromatography on a column of silica gel (mesh size, 0.040–0.063 mm), with water-saturated ethyl acetate as eluent, yielded chromatographically pure, amorphous **5** (1.87 g, 71%), $[\alpha]_D^{29}$ −45° (*c* 1.0, chloroform).

1-O-β-D-Ribofuranosyl-D-ribitol (**6**) — A solution of **5** (1.24 g) in ethanol was hydrogenated over 10% palladium on charcoal; the measured hydrogen uptake was 180 ml (calc.: 172 ml). The mixture was then filtered through Celite and concentrated to give a chromatographically pure, amorphous product (0.58 g, 100%), $[\alpha]_D^{24}$ −38° (*c* 1.0, water). The heptabenzoate of **6** had $[\alpha]_D^{25}$ +17° (*c* 0.2, chloroform).

Anal. Calc. for $C_{59}H_{48}O_{16}$: C, 69.9; H, 4.78. Found: C, 70.1; H, 4.78.

Methylation[7] of **6** yielded the heptamethyl ether of **6**; in m.s., this gave a fragmentation pattern identical to that obtained from the presumed 1-*O*-β-D-ribofuranosyl-D-ribitol heptamethyl ether obtained from *Haemophilus influenzae*[2].

ACKNOWLEDGMENT

We thank the Swedish Natural Science Research Council for financial support.

REFERENCES

1 R. M. CRISEL, R. S. BAKER, AND D. E. DORMAN, *J. Biol. Chem.*, 250 (1975) 4926–4930.
2 P. BRANEFORS-HELANDER, C. ERBING, L. KENNE, AND B LINDBERG, *Acta Chem. Scand., Ser. B*, 30 (1976) 276–277.
3 R. K. NESS, H. G. FLETCHER, JR., AND K. W. FREER, *Carbohydr. Res.*, 19 (1971) 423–429.
4 S. HANESSIAN AND J. BANOUB, *Carbohydr. Res.*, 44 (1975) C14–C17
5 P. J. GAREGG, B. LINDBERG, K. NILSSON, AND C.-G. SWAHN, *Acta Chem. Scand.*, 27 (1973) 1595–1600.
6 P. J. GAREGG AND T. NORBERG, *Carbohydr. Res*, 52 (1976) 235–240.
7 S. HAKOMORI, *J. Biochem.* (*Tokyo*), 55 (1964) 205–208.