Carbohydrate Research, 122 (1983) 165–167
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Note

Synthesis of *p*-trifluoroacetamidophenyl 4-*O*-α-D-glucopyranosyl-α-L-rhamnopyranoside*

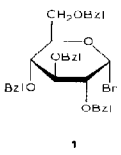
PER J. GAREGG, THOMAS NORBERG
Department of Organic Chemistry, Arrhenius Laboratory, University of Stockholm, S-106 91 Stockholm (Sweden)

PETER KONRADSSON, AND STEFAN C. T. SVENSSON
Department of Chemistry, University of Linkoping, S-581 83 Linköping (Sweden)

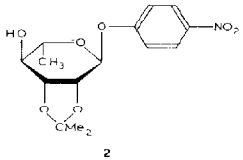
(Received February 28th, 1983; accepted for publication, March 29th, 1983)

The synthesis of the title disaccharide derivative, which contains a unit suitable, after deacylation, for attachment to proteins[1], is described as part of our programme on artificial antigens useful for the improved diagnosis of disease caused by infections with *Shigella flexneri* bacteria[2]. The disaccharide fragment corresponds to the *Shigella flexneri* O-antigenic determinant II[3].

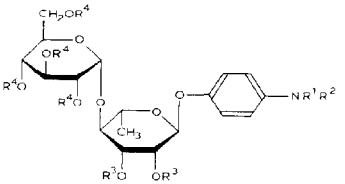
2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl bromide[4] (**1**) was condensed with *p*-nitrophenyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**2**) under halide-assistance conditions[5] to give the disaccharide derivative **3**. The nitro group of **3** was converted into a trifluoroacetamido group, and the resulting compound **4** was deblocked to give the title compound **5** in a total yield of 34% from **2**.



1



2



3 $R^1 = R^2 = O, R^3 - CMe_2, R^4 = Bzl$
4 $R^1 = H, R^2 = COCF_3, R^3 = CMe_2\ R^4 = Bzl$
5 $R^1 = R^3 = R^4 = H, R^2 = COCF_3$

*Disaccharides Related to *Shigella flexneri* O-Antigens, Part III. For Part II, see ref. 2

0008-6215/83/$ 03.00

EXPERIMENTAL

General methods. — These were the same as those previously reported[6]. N.m.r. spectra (^1H and ^{13}C) were recorded for all compounds, and accorded with the postulated structures. Only selected data are reported: ^{13}C-chemical shifts refer to proton-decoupled spectra, and ^{13}C C–H coupling-constants to undecoupled spectra.

p-*Nitrophenyl 2,3-O-isopropylidene-α-*L*-rhamnopyranoside* (**1**). — A mixture of *p*-nitrophenyl α-L-rhamnopyranoside[7,8] (5.60 g), dried Dowex 50 (H^+) resin, 2,2-dimethoxypropane (50 mL), and dried acetone (160 mL) was stirred at 0° for 5 h. Filtration through calcium oxide and concentration gave a crude material that crystallised from light petroleum, to yield **3** (5.69 g, 89%), m.p. 107–108°, $[\alpha]_D$ −128° (*c* 1.1, chloroform). N.m.r. data ($CDCl_3$): ^1H, δ 1.24 (d, 3 H, $J_{5,6}$ 5.9 Hz, H-6), 1.42 and 1.59 (2 s, each 3 H, CMe_2), and 5.84 (d, 1 H, $J_{1,2}$ 0.6 Hz, H-1); ^{13}C, δ 17.2 (C-6), 24.2 and 27.9 (CMe_2), and 95.3 (C-1).

Anal. Calc. for $C_{15}H_{19}NO_7$: C, 55.4; H, 5.89; N, 4.30. Found: C, 55.2; H, 5.94; N, 4.24.

p-*Nitrophenyl 2,3-O-isopropylidene-4-O-(2,3,4,6-tetra-O-benzyl-α-*D*-glucopyranosyl)-α-*L*-rhamnopyranoside* (**3**). — Gaseous hydrogen bromide was passed through a stirred solution of 2,3,4,6-tetra-*O*-benzyl-1-*O*-*p*-nitrobenzoyl-α-D-glucopyranose[4] (1.52 g, 2.22 mmol) in dichloromethane (10 mL) for 10 min. After 1 h at room temperature, the solution was cooled to −40° and filtered through a pad of Celite which was washed with cold dichloromethane (10 mL). The combined dichloromethane solution was concentrated to 3 mL and added to **1** (360 mg, 1.11 mmol), tetraethylammonium bromide (470 mg), and powdered 4 Å molecular sieves (2 g) in dichloromethane (10 mL). After being stirred at room temperature for 7 days, the mixture was diluted with dichloromethane, filtered, washed with M sulfuric acid, saturated aqueous sodium hydrogencarbonate, and water, dried ($MgSO_4$), filtered, and concentrated, to give a residue that was purified by chromatography on a column of silica gel[9]. Elution with toluene–ethyl acetate (30:1) afforded **3** (510 mg, 54%), $[\alpha]_D$ −29° (*c* 1.4, chloroform). N.m.r. data ($CDCl_3$): ^1H, δ 1.21 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6), 1.30 and 1.47 (2 s, each 3 H, CMe_2), and 5.77 (s, 1 H, H-1); ^{13}C, δ 17.4 (C-6), 26.3 and 27.9 (CMe_2), 95.0 ($J_{C-1',H-1'}$ 171 Hz, C-1), and 98.1 ($J_{C-1',H-1'}$ 166 Hz, C-1').

p-*Trifluoroacetamidophenyl 2,3-O-isopropylidene-4-O-(2,3,4,6-tetra-O-benzyl-α-*D*-glucopyranosyl)-α-*L*-rhamnopyranoside* (**4**). — A solution of **3** (350 mg) in ethyl acetate (50 mL) was hydrogenated over platinum oxide (Adams' catalyst, 50 mg) at atmospheric pressure until the hydrogen consumption ceased, and then filtered and concentrated. Trifluoroacetic anhydride (0.18 mL) was added dropwise with stirring at 0° to a solution of the residue in pyridine (3 mL). After 30 min at 50°, a few drops of water were added and stirring was continued for 10 min. The solution was diluted with dichloromethane, washed with water, M sulfuric acid, and saturated aqueous sodium hydrogencarbonate, dried ($MgSO_4$), filtered, and con-

centrated. Purification on a column of silica gel[9], which was eluted with toluene–ethyl acetate (8:1), gave **4** (310 mg, 82%), $[\alpha]_D$ −8° (*c* 1.2, chloroform). N.m.r. data ($CDCl_3$): ^1H, δ 1.22 (d, 3 H, $J_{5,6}$ 6.5 Hz, H-6), 1.30 and 1.47 (2 s, each 3 H, CMe_2), 5.67 (s, 1 H, H-1), and 7.90 (s, 1 H, NH); ^{13}C, δ 17.4 (C-6), 26.3 and 28.0 (CMe_2), 65.8 (C-5), 67.8 (C-6′), 94.9 (C-1), 98.1 (C-1′), 115.8 (q, $J_{C,F}$ 288 Hz, CF_3), and 155.0 (q, $J_{C,F}$ 37 Hz, C=O).

p-*Trifluoroacetamidophenyl* 4-O-α-D-*glucopyranosyl*-α-L-*rhamnopyranoside* (**5**). — A solution of **4** (150 mg) in 95% ethanol–ethyl acetate (3:1, 50 mL) was hydrogenated over palladium-on-charcoal (10%, 250 mg) at atmospheric pressure for 40 h, filtered, and concentrated. The isopropylidene group was removed by treatment of the product with 80% aqueous acetic acid at 60° for 2 h. Concentration, followed by purification on a column of silica gel that was eluted with ethyl acetate–methanol–water (16:3:1), afforded **5** (70 mg, 77%), $[\alpha]_D$ −27° (*c* 1.2, methanol). N.m.r. data: ^1H (D_2O, δ_{HDO} 5.19 p.p.m.), δ 1.64 (d, 3 H, $J_{5,6}$ 5.9 Hz, C-6), 5.40 (d, 1 H, $J_{1',2'}$ 3.4 Hz, H-1′), 5.79 (s, 1 H, H-1), 7.36 and 7.71 (2 d, each 2 H, *J* 8.8 Hz, aromatic H); ^{13}C (1,4-dioxane 67.4 p.p.m., complete data), δ 17.4 (C-6), 61.6 (C-6′), 69.4, 69.8, 70.2, 71.1, 72.5, 72.7, 73.7, 82.0 (C-2,3,4,5, C-2′,3′,4′,5′), 98.6 (C-1), 100.7 (C-1′), 118.1, 124.0, 130.4, and 154.2 (aromatic C), 116.7 (q, $J_{C,F}$ 286 Hz, CF_3), and 157.1 (q, $J_{C,F}$ 37.8, C=O).

ACKNOWLEDGMENTS

We thank Professor B. Lindberg for his interest, the Swedish Board for Technical Development and the Swedish Natural Science Research Council for financial support.

REFERENCES

1 D. H. Buss and I. J. Goldstein, *J. Chem. Soc., C*, (1968) 1457–1461.
2 P. J. Garegg, T. Norberg, P. Konradsson and S. C. T. Svensson, *Carbohydr. Res.*, 116 (1983) 308–311.
3 L. Kenne, B. Lindberg, K. Petersson, E. Katzenellenbogen, and E. Romanowska, *Eur. J. Biochem.*, 91 (1978) 279–284.
4 C. P. J. Glaudemans and H. G. Fletcher, Jr., *Methods Carbohydr. Chem.*, 6 (1972) 373–376.
5 R. U. Lemieux, K. B. Hendriks, R. V. Stick and K. James, *J. Am. Chem. Soc.*, 97 (1975) 4056–4062.
6 P. J. Garegg and T. Norberg, *J. Chem. Soc., Perkin Trans. 1*, (1982) 2973–2982.
7 O. Westphal and H. Feier, *Chem. Ber.*, 89 (1956) 582–588.
8 P. J. Garegg, H. Hultberg, and T. Iversen, *Carbohydr. Res.*, 62 (1978) 173–174.
9 W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, 43 (1978) 2923–2925.