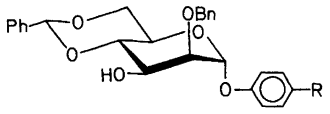
Synthesis of *p*-Trifluoroacetamidophenyl 3-*O*-(α-D-Glucopyranosyl)-α-D-mannopyranoside

PER J. GAREGG and THOMAS NORBERG

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

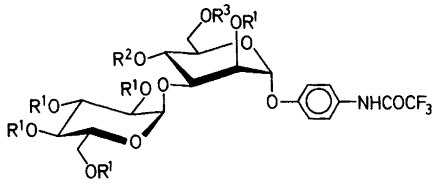
In our continuing programme of synthesis of artificial *Salmonella* antigens, oligosaccharides linked to a moiety suitable for attachment to proteins corresponding to O-antigens [1] 2,4,8 and 9 have been made.[2-6] We now report the synthesis of the title substance, required for immunological studies. The disaccharide moiety has been suggested to be the immunodominant part of O-antigen 14 occurring in *Salmonella* bacteria belonging to serogroup C_1.[7]

p-Nitrophenyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside[6,8] (*1*) was converted into the corresponding *p*-trifluoroacetamido mannoside[9] (*2*). This was allowed to react with 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl bromide[10] under halide-ion assisting conditions using molecular sieves as acid acceptor.[11] The resulting α-linked disaccharide *3* was obtained in a 44% yield. Hydrogenation over palladium on carbon afforded the title compound *4*. The conversion of *4* into the corresponding isothiocyanate and the subsequent coupling to bovine serum albumin were carried out as previously described.[6,12]



1 R=NO_2

2 R=$NHCOCF_3$



3 R^1=CH_2Ph; R^2+R^3=>CHPh

4 R^1=R^2=R^3=H

0302-4369/81/040305-02$02.50

Experimental. General methods were the same as those described before.[13]

p-*Trifluoroacetamidophenyl 2-O-benzyl-3-O-(2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl)-4,6-O-benzylidene-α-D-mannopyranoside (3).* 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl bromide[10] (prepared from the corresponding 1-*O*-*p*-nitrobenzoate (1.60 g, 2.32 mmol and used directly) in dichloromethane (2 ml) was added to a solution of *p*-trifluoroacetamidophenyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (*2*)[6,8] (1.0 g, 2.32 mmol) in dichloromethane (9 ml) and *N,N*-dimethylformamide (1 ml) containing tetraethylammonium bromide (0.42 g) and powdered 4 Å molecular sieves. After stirring at 35 °C overnight, when TLC indicated that most of the bromide had reacted, the mixture was filtered, the filtrate was washed with water and aqueous sodium hydrogencarbonate, dried ($MgSO_4$), filtered and concentrated to syrupy crude *3* which was purified by silica gel column chromatography[14] (toluene – ethyl acetate 9:1) Syrupy *3* (0.85 g, 44 %) $[\alpha]_D$ +113° (*c* 0.5, $CHCl_3$) was obtained.

p-*Trifluoroacetamidophenyl 3-O-(α-D-glucopyranosyl)-α-D-mannopyranoside (4).* *3* (0.85 g) in 95% aqueous ethanol was hydrogenated with 10% palladium on carbon (0.4 g) at 400 kPa. After filtration, concentration, partitioning between water and diethyl ether and lyophilization of the aqueous phase, chromatographically (TLC, ethyl acetate – methanol – acetic acid – water, 20:3:3:2) pure *4* was obtained (0.40 g, 96 %), $[\alpha]_D$ +108° (*c* 0.5, H_2O). 25 MHz ^{13}C NMR (D_2O, external TMS): δ 61.8 (glucose and mannose C-6), 66.9, 70.9, 73.0, 73.6, 74.1, 74.6, 79.8 (pyranose ring carbons), 99.3 (mannose C-1), 101.8 (glucose C-1), 118.5, 124.5, 130.8, 154.7 (aromatic C). 100 MHz ^1H NMR (D_2O, external TMS): δ 5.28 (d, 1 H, $J_{1,2}$ 3.7 Hz, glucose H-1), 5.57 (d, 1 H, $J_{1,2}$ 2.0 Hz, mannose H-1).

Acknowledgements. We are indebted to Professor Bengt Lindberg for his interest and to the Swedish Natural Science Research Council for financial support.

1. Kauffmann, F. *Die Bacteriologie der Salmonella Species*, Munksgaard, Copenhagen 1961.
2. Garegg, P. J. and Gotthammar, B. *Carbohydr. Res. 58* (1977) 345.
3. Ekborg, G., Garegg, P. J. and Josephson, S. *Carbohydr. Res. 65* (1978) 301.
4. Eklind, K., Garegg, P. J. and Gotthammar, B. *Acta Chem. Scand. B 30* (1976) 305.
5. Garegg, P. J. and Hultberg, H. *Carbohydr. Res. 72* (1979) 276.

6. Ekborg, G., Garegg, P. J. and Gotthammar, B. *Acta Chem. Scand. B 29* (1975) 765.
7. Fuller, N. A. and Staub, A. M. *Eur. J. Biochem. 4* (1968) 286.
8. Iversen, T. *Chem. Commun. Univ. Stockholm* (1979) No. 5.
9. Garegg, P. J. and Norberg, T. *Carbohydr. Res. In press.*
10. Lemieux, R. U., Hendricks, K. B., Stick, R. V. and James, K. *J. Am. Chem. Soc. 97* (1975) 4056.
11. Lemieux, R. U. and Driguez, H. *J. Am. Chem. Soc. 97* (1975) 4069.
12. Buss, D. H. and Goldstein, I. J. *J. Chem. Soc. C* (1968) 1457.
13. Garegg, P. J., Hultberg, H. and Lindberg, C. *Carbohydr. Res. 83* (1980) 157.
14. Still, W. C., Kahn, M. and Mitra, A. *J. Org. Chem. 43* (1978) 2923.

Received March 24, 1981.