Carbohydrate Research, 139 (1985) C1–C3
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Preliminary communication

A new approach to the synthesis of β-glycosidically linked oligosaccharides containing 2-acetamido-2-deoxy-D-mannose residues

EMILIO MICHELI, FRANCESCO NICOTRA, LUIGI PANZA†, FIAMMA RONCHETTI*, and L. TOMA

Dipartimento di Chimica Organica e Industriale and Centro di Studio per le Sostanze Organiche Naturali del C.N.R., Via Venezian 21, 20133 Milano (Italy)

(Received December 31st, 1984; accepted for publication, February 11th, 1985)

The synthesis of the repeating units of bacterial capsular polysaccharides is important because of their potential use as vaccines[1]. The structures of several such polysaccharides have been elucidated[1] and frequently they contain a 2-acetamido-2-deoxy-β-D-mannose residue. The introduction of this unit into an oligosaccharide chain is not easy, because of the difficulty in obtaining a 1,2-*cis*-β-D-mannopyranosidic linkage[2].

We now describe a synthetic approach to such β-glycosidic linkages which utilises the well-known[2] Koenigs–Knorr reaction; this leads easily and with high stereoselectivity to a β-D-glucopyranosyl glycopyranoside from an α-D-glucopyranosyl bromide with an equatorial participating-group at C-2. Selective exposure of HO-2 of the glucopyranosyl moiety, followed by oxidation, oximation, stereoselective reduction, and acetylation, yields the axially oriented *N*-acetylamino group. The inversion of configuration at C-2 of β-D-glucopyranosides has already been employed to obtain β-D-mannopyranosides[3], as well as the catalytic reduction of the 2-oximino function to obtain 2-amino-2-deoxy-α-D-glucosides[4].

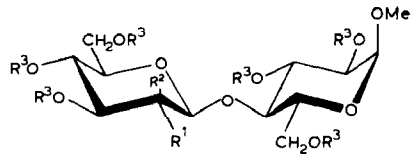
Thus, reaction of methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside[5] (**2**, 0.57 mmol) with 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-glucopyranosyl bromide[6] (**3**, 1.14 mmol) was performed[7] in the presence of silver triflate (1.14 mmol), 2,4,6-trimethylpyridine (0.14 mL), and molecular sieves Type 3A under argon in CH_2Cl_2 (at 0° for 2 h, and then room temperature overnight) to yield methyl 4-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside** (**1**, 75% after purification by SiO_2 column chromatography using hexane–ethyl acetate, 7:3), m.p. 86–87° (from ethanol–hexane), $[\alpha]_D$ +17° (*c* 0.9, chloroform). ^{1}H-N.m.r. data (200 MHz, $CDCl_3$): δ 1.87 (s, 3 H, OAc), 3.36 (s, 3 H, OMe), 3.3–3.9 (m, 11 H), 4.48 (d, 1 H, $J_{1',2'}$ 8.5 Hz, H-1'), 4.62 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.95 (dd, 1 H, $J_{2',3'}$ 9.5 Hz, H-2'), 4.3–5.1 (6 ABq, 12 H, 6 CH_2Ph), 7.1–7.5 (m, 30 H, 6 Ph). *O*-Deacetylation of **1** yielded **4** (85%), $[\alpha]_D$ +14.5° (*c* 1, chloroform). ^{1}H-N.m.r. data: δ 3.35 (s, 3 H, OMe), 3.1–4.0 (m, 12 H), 4.3–5.1 (m, 14 H, H-1,1' and 6 CH_2Ph), 7.1–7.5 (m, 30 H, 6 Ph).

†Fondazione "Guido Donegani" Fellow, June 1984–May 1985.

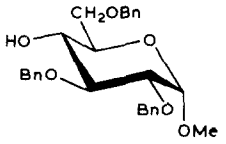
*To whom enquiries should be addressed.

**All the new compounds exhibited elemental analyses consistent with the theoretical ones.

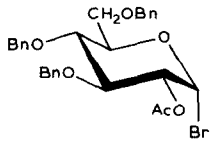
0008-6215/85/$03.30



1 R^1 = OAc, R^2 = H, R^3 = Bn
4 R^1 = OH, R^2 = H, R^3 = Bn
5 R^1 = R^2 = OH, R^3 = Bn
6 R^1, R^2 = NOH, R^3 = Bn
7 R^1 = H, R^2 = NH_2, R^3 = Bn
8 R^1 = H, R^2 = NHAc, R^3 = Bn
9 R^1 = R^3 = H, R^2 = NHAc



2



3

Oxidation of **4** with acetic anhydride–dimethyl sulfoxide[3] (room temperature, overnight) gave the glyculose **5** mainly as the hydrate[8] (77% after purification by column chromatography using hexane–ethyl acetate, 6:4), $[\alpha]_D$ +9° (*c* 2.8, chloroform); $\nu_{max}^{CHCl_3}$ 1750 cm^{-1}. ^{1}H-N.m.r. data: δ 3.36 and 3.37 (s, 3 H, OMe), 3.3–5.3 (m, 25 H), 7.1–7.5 (m, 30 H, 6 Ph). Treatment[4] of **5** with hydroxylamine hydrochloride gave the oxime **6** as a mixture of *E* and *Z* isomers (80% after purification by column chromatography using hexane–ethyl acetate, 6:4). ^{1}H-N.m.r. data (80 MHz): δ 3.36 and 3.38 (s, 3 H, OMe), 3.3–5.3 (m, 24 H), 5.50 and 5.90 (s, 1 H, H-1′), 7.1–7.5 (m, 30 H, 6 Ph). Reduction of **6** with $LiAlH_4$ in tetrahydrofuran yielded the 2′-axial amine **7**, $[\alpha]_D$ +9° (*c* 1.5, chloroform). ^{1}H-N.m.r. data: δ 3.35 (s, 3 H, OMe), 2.9–4.0 (m, 12 H), 4.3–5.1 (m, 14 H, H-1,1′ and 6 CH_2Ph), 7.1–7.5 (m, 30 H, 6 Ph). Acetylation of **7** then gave methyl 4-*O*-(2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-mannopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (**8**), $[\alpha]_D$ −1° (*c* 0.9, chloroform). ^{1}H-N.m.r. data: δ 1.83 (s, 3 H, NAc), 3.35 (s, 3 H, OMe), 3.1–4.0 (m, 11 H), 4.2–5.0 (m, 15 H, H-1,1′,2′ and 6 CH_2Ph), 5.75 (d, $J_{2',NH}$ 10 Hz, NH), 7.1–7.5 (m, 30 H, 6 Ph).

That **7** and **8** have an axially oriented substituent at C-2′ is evident from the $J_{1',2'}$ and $J_{2',3'}$ values (1.5 and 4.5 Hz, respectively) obtained from the 300-MHz ^{1}H-n.m.r. spectrum (D_2O) of methyl 4-*O*-(2-acetamido-2-deoxy-β-D-mannopyranosyl)-α-D-glucopyranoside **9**, obtained by catalytic hydrogenation of **8** over Pd/C, which contained signals for H-1′ and H-2′ at δ 4.879 and 4.546, respectively.

ACKNOWLEDGMENTS

We thank Professor G. Russo for helpful discussions. Professor G. Ricca for the 200-MHz spectra, and Dr. D. Monti for the 300-MHz spectrum. This contribution is part of the "Progetto finalizzato Chimica fine e secondaria".

REFERENCES

1 H. J. Jennings, *Adv. Carbohydr. Chem. Biochem.*, 41 (1983) 155–208.
2 H. Paulsen, *Angew. Chem. Int. Ed. Engl.*, 21 (1982) 155–224,
3 G. Ekborg, B. Lindberg, and J. Lonngren, *Acta Chem. Scand.*, 26 (1972) 3287–3292.
4 H. B. Boren, G. Ekborg, and J. Lonngren, *Acta Chem. Scand., Ser. B*, 29 (1975) 1085–1088.
5 P. J. Garegg, H. Hultberg, and S. Wallin, *Carbohydr. Res.*, 108 (1982) 97–101.
6 M. A. E. Shaban and R.W. Jeanloz, *Carbohydr. Res.*, 52 (1976) 103–114.
7 C. D. Warren, C. Augé, M. L. Laver, S. Suzuki, D. Power, and R. W. Jeanloz, *Carbohydr. Res.*, 82 (1980) 71–82.
8 D. C. Baker, D. Horton, and C. G. Tindall, Jr., *Carbohydr. Res.*, 24 (1972) 192–197.