Carbohydrate Research, 75 (1979) 322–324

Note

Synthesis of methyl 3-*O*-α-D-mannopyranosyl-α-D-mannopyranoside

ELIZABETH E. LEE AND JOHN O. WOOD
Chemistry Department, University College, Galway (Ireland)
(Received December 19th, 1978; accepted for publication, January 15th, 1979)

As part of a study of the application of lanthanide shift-reagents in ^{1}H- and ^{13}C-n.m.r. spectroscopy of some carbohydrate derivatives[1], methyl 4,6-*O*-benzylidene-3-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**1**) has been synthesised.

Condensation of methyl 4,6-*O*-benzylidene-α-D-mannopyranoside[2] (**2**) with tetra-*O*-acetyl-α-D-mannopyranosyl bromide[3], using the Helferich[4] modification of the Koenigs–Knorr reaction, afforded crystalline **1** (24%). Complete assignment of the p.m.r. spectrum of **1** was made by using the shift reagent[1] Eu(fod)$_3$, which was added in small quantities to a solution of **1** in deuteriochloroform. Spectra were recorded after each addition; individual proton resonances were identified by consideration of coupling constants, and by spin-decoupling whenever possible. Good straight-line plots of induced shift *vs.* molar ratio [Eu(fod)$_3$/substrate] were obtained for protons having well-resolved resonances, and relative shift gradients (*G*, p.p.m. per mol of Eu(fod)$_3$ per mol of substrate) were calculated (Table I). The ring proton having the highest *G*-value (*i.e.*, that which was shifted most under the influence of the shift reagent) was H-2, indicating that the free hydroxyl group (the co-ordination site of the Eu ion) was HO-2, and therefore that compound **1** was a (1→3)-linked disaccharide. Further evidence was obtained by a computer search procedure[1], using the shift data, to locate the co-ordination site of the Eu ion; this showed that the lanthanide was indeed co-ordinated to HO-2.

The α-D configuration of **1** was indicated by comparison of its $[M]_D$ value (+412°) with the sum of the $[M]_D$ values of **2** (+169°) and methyl tetra-*O*-acetyl-α-D-mannopyranoside (+177°). In contrast, the sum of the $[M]_D$ values of **2** (+169°) and methyl tetra-*O*-acetyl-β-D-mannopyranoside (−181°) is −12°.

Hydrogenation of **1** and acetylation of the product afforded the syrupy hepta-acetate **4** which, on Zemplén deacetylation, gave syrupy methyl 3-*O*-α-D-mannopyranosyl-α-D-mannopyranoside (**5**), in 72% overall yield from **1**.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage and are uncorrected. Solutions were concentrated under reduced pressure below 50°. Optical rotations were measured with a Perkin–Elmer Model 241 polarimeter. T.l.c. was performed on silica gel F_{254} (Merck) with benzene–methanol (9:1), and detection with ferric hydroxamate or by charring with sulphuric acid. Column chromatography was performed on silica gel (Grace, 50–100 mesh). ^{1}H-N.m.r. spectra were recorded on a Jeol JNM-MH-100 spectrometer at normal operating temperatures.

Methyl 4,6-O-benzylidene-3-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**1**). — A solution of **2** (0.6 g, 2.13 mmol) and mercuric cyanide (0.6 g) in acetonitrile (8 ml, distilled over calcium hydride) was treated with a solution of tetra-*O*-acetyl-α-D-mannopyranosyl bromide[3] (1.4 g, 3.4 mmol) in acetonitrile (3 ml). The mixture was stirred for 20 h in the dark at room temperature and then concentrated. The residue was extracted with chloroform, and the combined extracts were washed with M potassium bromide, saturated, aqueous sodium hydrogen carbonate, and water, dried ($MgSO_4$), and concentrated. The syrupy residue (1.2 g) contained (t.l.c.), *inter alia*, a major (R_F 0.32) and a minor (R_F 0.44) component. Crystallisation from ethanol gave **1** (0.3 g), m.p. 210–213°, $[\alpha]_D$ +67° (*c* 0.47, chloroform), R_F 0.32. P.m.r. data ($CDCl_3$): δ 7.2–7.5 (m, 5 H, Ph), 5.6 (s, 1 H, PhC*H*), 5.18–5.5 (m, 4 H, H-1′,2′,3′,4′), 4.76 (d, 1 H, $J_{1,2}$ 1 Hz, H-1′), 3.96–4.4 (m, 7 H, H-2,3,4,6eq,5′,6′a,6′b), 3.7–3.9 (m, 2 H, H-5,6ax), 3.4 (s, 3 H, OMe), 2.85 (bs, 1 H, OH), and 1.98–2.1 (12 H, 4 AcO).

Anal. Calc. for $C_{28}H_{36}O_{15}$: C, 54.9; H, 5.9. Found: C, 55.2; H, 6.0.

Methyl 3-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**3**). — A solution of **1** (0.2 g) in ethanol–chloroform (9:1, 50 ml) was hydrogenolysed in the presence of 10% palladium-on-charcoal (0.2 g). The reaction was monitored by t.l.c. and, when complete, the solution was filtered and concentrated *in vacuo* to give **3** as a foam (168 mg), $[\alpha]_D$ +70° (*c* 0.43, ethanol).

Anal. Calc. for $C_{21}H_{32}O_{15}$: C, 48.1; H, 6.1. Found: C, 47.3; H, 6.25.

Methyl 2,4,6-tri-O-acetyl-3-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**4**). — Conventional treatment of **3** (0.16 g) with acetic anhydride (5 ml) and anhydrous sodium acetate (0.1 g) gave **4** as a chromatographically homogeneous syrup (0.19 g), $[\alpha]_D$ +39° (*c* 0.9, chloroform). P.m.r. data ($CDCl_3$): δ 4.7 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 3.32 (s, 3 H, OMe), and 2.16–1.94 (21 H, 7 AcO).

Anal. Calc. for $C_{27}H_{38}O_{18}$: C, 49.8; H, 5.8. Found: C, 48.6; H, 5.7.

TABLE I

^{1}H RELATIVE SHIFT GRADIENTS[a] (*G*) FOR DISACCHARIDE **1**

Proton	H-1	H-2	H-3	H-4	H-5	H-6ax	H-6eq
G	3.80	6.70	3.40	5.20	2.30	1.20	0.94

[a]P.p.m. per mol of Eu(fod)$_3$ per mol of substrate.

Methyl 3-O-α-D-mannopyranosyl-α-D-mannopyranoside (**5**). — A solution of **4** (0.17 g) in dry methanol (10 ml) was treated with a catalytic amount of 0.2M methanolic sodium methoxide for 2 h, and then neutralised with Amberlite IR-120(H^+) resin, filtered, and concentrated to give **5** as a chromatographically homogeneous syrup (83 mg), $[\alpha]_D$ +91° (*c* 0.8, water).

Anal. Calc. for $C_{13}H_{24}O_{11}$: C, 41.0; H, 6.7. Found: C, 40.6; H, 6.5.

ACKNOWLEDGMENT

The authors thank the Irish National Board for Science and Technology for financial support.

REFERENCES

1 P. McArdle, J. O. Wood, E. E. Lee, and M. J. Conneely, *Carbohydr. Res.*, 69 (1979) 39–46.
2 J. G. Buchanan and J. C. P. Schwarz, *J. Chem. Soc.*, (1962) 4770–4776.
3 P. A. Levene and R. S. Tipson, *J. Biol. Chem.*, 90 (1931) 89–98; W. A. Bonner, *J. Am. Chem. Soc.*, 80 (1958) 3372–3379.
4 B. Helferich and J. Zirner, *Chem. Ber.*, 95 (1962) 2604–2610.