Carbohydrate Research, 107 (1982) 296–299
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

Note

Synthesis of 3-*O*-methyl-L-xylose, a component of lipopolysaccharides of Gram-negative bacteria

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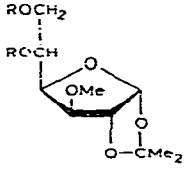
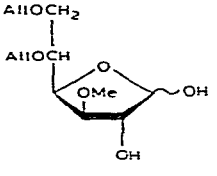
(Received December 7th, 1981; accepted for publication, February 2nd, 1982)

Cell-wall lipopolysaccharides of Gram-negative bacteria contain various sugars, including partially methylated pentoses and hexoses that rarely occur elsewhere in Nature[1]. Recently, 3-*O*-methyl-L-xylose was detected in the lipopolysaccharide of *Rhodopseudomonas viridis*[2] and *Pseudomonas maltophilia*[3,4] N.C.T.C. 10257, and a synthesis of this sugar is now reported.

1,2-*O*-Isopropylidene-3-*O*-methyl-α-D-glucofuranose[5] (**1**) was treated with allyl bromide in the presence of potassium hydroxide, and the resulting 5,6-di-*O*-allyl derivative **2** was hydrolysed with sulfuric acid in water–1,4-dioxane–ethanol, to give a mixture of mainly 5,6-di-*O*-allyl-3-*O*-methyl-α-D-glucofuranose (**3**) together with the α- and β-D-glucofuranoside derivatives **4** and **5**. The formation of **4** and **5**



1 R = H
2 R = Allyl



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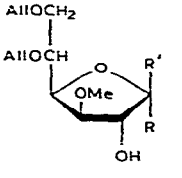
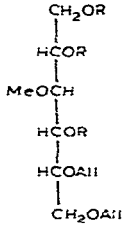
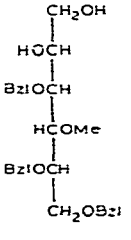


4 R = OEt, R' = H
5 R = H, R' = OEt



6 R = H
7 R = Bzl



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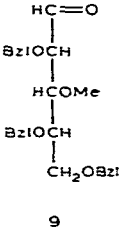

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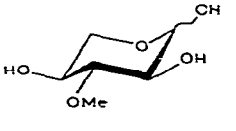

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TABLE I

^{13}C-N.M.R. DATA FOR SOLUTIONS OF 3-*O*-METHYL-α- AND -β-L-XYLOPYRANOSE IN D_2O

Atom	*Chemical shifts (δ)*					
	α Anomers			*β Anomers*		
	D-*Xyl*	**10**	*Δδ*	D-*Xyl*	**10**	*Δδ*
C-1	92.3	92.16	−0.14	96.7	96.52	−0.18
C-2	71.6	70.84	−0.76	74.1	73.30	−0.80
C-3	73.0	82.59	+9.59	75.9	85.24	+9.34
C-4	69.55	68.73	−0.82	69.35	68.58	−0.77
C-5	61.05	60.96	−0.09	65.25	64.94	−0.31
OMe		59.88			59.66	

in a reaction mixture containing water was unexpected, and they were present even after prolonged hydrolysis.

Borohydride reduction of **3** and benzylation[6] of the product **6** afforded 5,6-di-*O*-allyl-1,2,4-tri-*O*-benzyl-3-*O*-methyl-D-glucitol (**7**). The allyl groups were removed from **7** (→**8**) by the Ogawa procedure[7]; one of the allyl groups was easily cleaved, but the second required prolonged heating.

Periodate oxidation of 1,2,4-tri-*O*-benzyl-3-*O*-methyl-D-glucitol (**8**) was complete within 20 min and gave 2,4,5-tri-*O*-benzyl-3-*O*-methyl-L-xylose (**9**). Catalytic hydrogenolysis of **9** occurred smoothly, to give 3-*O*-methyl-L-xylose (**10**) and no traces of the alditol derivative.

The assignments for α- and β-D-xylopyranose[8] were used to interpret the ^{13}C-n.m.r. spectrum of 3-*O*-methyl-L-xylose (Table I). Methylation at position 3 results in the well-known downfield shift of the C-3 signal, and the *Δδ* values are similar. Surprisingly, the values of the negative β-shifts are low.

EXPERIMENTAL

Melting points were determined on a Kofler apparatus and are uncorrected. A Perkin–Elmer 241 polarimeter was used for measurement of optical rotations at 22°. ^{13}C-N.m.r. spectra were recorded with a Bruker WP-200 spectrometer at room temperature. ^{1}H-N.m.r. spectra were recorded with a Jeol MH-100 instrument. T.l.c. was performed on Silica Gel F_{254} (Merck). G.l.c. was performed with a Hewlett–Packard 5840A instrument fitted with a nickel column (1.2 m × 2 mm i.d.) packed with 10% of UCW 982 on Gas Chrom Q (80–100 mesh). Nitrogen was used as carrier gas at 20 mL/min. The temperature programmes were *A*, 170° isothermal; *B*, from 150° at 5°/min; and *C*, 250° isothermal.

5,6-Di-O-allyl-1,2-O-isopropylidene-3-O-methyl-α-D-glucofuranose (**2**). — A solution of **1** (18.8 g, prepared from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose

by treatment[9] with MeI–KOH–Me_2SO followed by partial hydrolysis with H_2O–MeOH–H_2SO_4) in methyl sulfoxide (50 mL) was treated with allyl bromide (38.9 g) in the presence of powdered potassium hydroxide (36 g) for 50 min and then diluted with dichloromethane (300 mL), filtered, washed with water (8 × 50 mL), dried (Na_2SO_4), and concentrated. The syrupy residue (23.0 g, 91.2%) contained (g.l.c., programme *A*) two components with *T* 5.77 (95.2%) and 4.51 min (4.8%).

The crude product (580 mg) was purified by column chromatography, to give **2**, $[\alpha]_D$ −33° (*c* 0.9, chloroform), R_F 0.87 (dichloromethane–acetone, 8:2).

Anal. Calc. for $C_{16}H_{26}O_6$: C, 61.12; H, 8.33. Found: C, 61.40; H, 8.28.

5,6-Di-O-allyl-3-O-methyl-D-glucofuranose (**3**). — A mixture of **2** (22.3 g), 0.05M sulfuric acid (100 mL), ethanol (50 mL), and 1,4-dioxane (50 mL) was stirred and boiled under reflux. After 30 h, **2** had disappeared and three components were detected by t.l.c. The mixture was neutralised with $BaCO_3$, filtered, and concentrated. The syrupy residue (19.1 g) was eluted from a column of silica gel (500 g) with dichloromethane–acetone (8:2) to give, first, ethyl 5,6-di-*O*-allyl-3-*O*-methyl-α-D-glucofuranoside (**4**; 1.13 g, 5.3%), $[\alpha]_D$ +51° (*c* 0.66, chloroform), R_F 0.77. ^{1}H-N.m.r. data ($CDCl_3$): δ 6.20–5.72 (m, 2 H, 2 CH_2-CH=CH_2), 5.40–5.12 (m, 4 H, 2 CH_2=CH-CH_2), 5.08 (s, 1 H, H-1), 4.30–3.50 (m, 12 H, H-2,3,4,5,6,6′, CH_2-CH_3 and 2 CH_2-CH=CH_2), 3.46 (s, 3 H, MeO-3), 3.02 (d, 1 H, HO-2), and 1.26 (t, 3 H, CH_2-CH_3).

Eluted second was ethyl 5,6-di-*O*-allyl-3-*O*-methyl-β-D-glucofuranoside (**5**; 2.05 g, 9.5%), $[\alpha]_D$ −77° (*c* 1.1, chloroform), R_F 0.58. ^{1}H-N.m.r. data ($CDCl_3$): δ 6.18–5.72 (m, 2 H, 2 CH_2-CH=CH_2), 5.40–5.08 (m, 4 H, 2 CH_2=CH-CH_2), 4.88 (s, 1 H, H-1), 4.40–3.50 (m, 13 H, H-2,3,4,5,6,6′, HO-2 and CH_2-CH_3), 3.42 (s, 3 H, MeO-3), and 1.24 (t, 3 H, CH_2-CH_3).

Eluted third was **3** (11.82 g, 60.9%), $[\alpha]_D$ −17° (*c* 1, chloroform), R_F 0.38. ^{1}H-N.m.r. data ($CDCl_3$): δ 6.05–5.70 (m, 2 H, CH_2-CH=CH_2), 5.50–5.00 (m, 4 H, 2 CH_2=CH-CH_2), 4.90 and 4.54 (2 d, 1 H, H-1), and 3.36 (s, 3 H, MeO-3).

Anal. Calc. for $C_{13}H_{22}O_6$: C, 56.91; H, 8.08. Found: C, 57.10; H, 8.16.

5,6-Di-O-allyl-3-O-methyl-D-glucitol (**6**). — To a solution of **3** (11 g) in ethanol (50 mL) was added sodium borohydride (3.78 g). After 36 h at room temperature, more sodium borohydride (1.9 g) was added, and the solution was kept at room temperature for an additional 24 h, neutralised with Amberlite IR-120 (H^+) resin, filtered, and concentrated. Methanol (3 × 20 mL) was evaporated from the residue to remove boric acid. The syrupy residue **6** (10.72 g, 96.7%) was pure enough for the next step, but a portion (650 mg) was eluted from silica gel (40 g) with dichloromethane–methanol (9:1), to give syrupy **6**, $[\alpha]_D$ −24° (*c* 1.5, chloroform), R_F 0.25.

Anal. Calc. for $C_{13}H_{24}O_6$: C, 56.50; H, 8.75. Found: C, 56.80; H, 9.01.

5,6-Di-O-allyl-1,2,4-tri-O-benzyl-3-O-methyl-D-glucitol (**7**). — Compound **6** (10 g) was treated with benzyl chloride (55 mL) and powdered KOH (25 g) at 105° for 16 h. The mixture was cooled, filtered, washed with dichloromethane, and steam-distilled. The residue of the steam distillation was extracted with dichloromethane (3 × 100 mL), dried (Na_2SO_4), and concentrated. The syrupy residue was eluted

from silica gel (500 g) with dichloromethane–ethyl acetate (9:1), to give **7** (17.9 g, 90.5%), $[\alpha]_D$ −3° (*c* 2.5, chloroform), R_F 0.75, *T* 30.74 min (programme *B*).

Anal. Calc. for $C_{34}H_{42}O_6$: C, 74.71; H, 7.74. Found: C, 75.10; H, 7.83.

*1,2,4-Tri-O-benzyl-3-O-methyl-*D*-glucitol* (**8**). — A solution of **7** (17 g) in ethanol (100 mL), acetic acid (50 mL), and water (50 mL) was treated with 10% Pd/C (1.1 g) at 70°. After 4 h, one allyl group had been removed, but the removal of the second one required 30 h. The mixture was filtered and concentrated, and the residue was eluted from silica gel (500 g) with dichloromethane–acetone (85:15), to give syrupy **8** (8.6 g, 59.3%), $[\alpha]_D$ +13° (*c* 0.56, chloroform), R_F 0.47. ^{1}H-N.m.r. data ($CDCl_3$): δ 7.45–7.20 (m, 15 H, 3 Ph), 4.70 (q, 2 H, CH_2-Ph), 4.62 (s, 2 H, CH_2-Ph), 4.50 (s, 2 H, CH_2-Ph), 3.46 (s, 3 H, OMe), 2.66 and 2.10 (2 b, 2 H, HO-5,6).

Anal. Calc. for $C_{28}H_{34}O_6$: C, 72.07; H, 7.34. Found: C, 72.45; H, 7.34.

*2,4,5-Tri-O-benzyl-3-O-methyl-*L*-xylose* (**9**). — A well-stirred solution of **8** (3.62 g) in ethanol (250 mL) and water (150 mL) was treated with $NaIO_4$ (2 g, 1.2 mol) at room temperature. T.l.c. then showed the absence of **8** after 15 min, and only one product could be detected. The solution was concentrated to 180 mL, and the aqueous phase was extracted with dichloromethane (2 × 50 mL). The combined extracts were concentrated, to give syrupy **9** (3.08 g, 91.3%), $[\alpha]_D$ +3° (*c* 2.5, chloroform), R_F 0.89 (dichloromethane–acetone, 95:5). G.l.c. showed its purity to be 99.7%; *T* 8.01 min (programme *C*).

Anal. Calc. for $C_{27}H_{30}O_5$: C, 74.62; H, 6.96. Found: C, 75.02; H, 7.02.

*3-O-Methyl-*L*-xylose* (**10**). — A solution of **9** (2.88 g) in ethanol (150 mL) and acetic acid (150 mL) was hydrogenated in the presence of 10% Pd/C (0.9 g) for 18 h, to give **10** (0.92 g, 84.5%), m.p. 102–103°, $[\alpha]_D$ −57→−18° (*c* 1, water); lit.[2] $[\alpha]_D$ −18°; lit.[10] for the D isomer, m.p. 103–104°, $[\alpha]_D$ +55→+17° (water).

Anal. Calc. for $C_6H_{12}O_5$: C, 43.90; H, 7.36; OMe, 18.90. Found: C, 44.08; H, 7.42; OMe, 18.76.

ACKNOWLEDGMENTS

The author thanks Professor P. Nánási for his interest, and Dr. J. Harangi for recording the n.m.r. spectra.

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