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Note

Synthesis of 3,4-dideoxy-DL-hex-3-enopyranosides from 5-hydroxymethyl-2-furaldehyde*

REZSÖ BOGNÁR, PÁL HERCZEGH, MARTINA ZSÉLY,
Research Group of Antibiotics, Hungarian Academy of Sciences, Debrecen 4010 (Hungary)

AND GYULA BATTA
Department of Organic Chemistry, L. Kossuth University, Debrecen 4010 (Hungary)

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Some years ago, we elaborated a method for the short conversion of 2-furaldehyde and its derivatives into various racemic monosaccharides[1,2], using the formyl group of furaldehyde as the reducing end of the sugar to be synthesised. Recently, a simple preparation of 5-hydroxymethyl-2-furaldehyde (**1**) has been described[3] which made the compound available for the synthesis of the title compounds.

Isomeric methyl 3,4-dideoxy-DL-hex-3-enopyranosides have been synthesised[4] in five steps from the butyl ester of *cis,trans*-5,6-dihydro-2-methoxy-2*H*-pyrancarboxylic acid.

The hydroxyl group of **1** was protected by benzoylation (→**2**) and the formyl group by transformation into a tetramethyldioxolane derivative[1,2] (**3**), which was stable under the acidic conditions necessary for the oxidative ring opening of the furan nucleus with bromine water at pH 3–4 to give **4**. Reduction of **4** with sodium borohydride gave a 6:5 mixture of **6** and **7**, which was fractionated by chromatography. Alternatively, the furan ring in **3** was oxidised with singlet oxygen and the resulting hydroperoxide **5** was reduced with methyl sulfide and sodium borohydride successively to give **6** and **7**.

Treatment of **6** and **7** with methanolic sodium methoxide gave **8** and **9**, respectively, which were methanolysed to give methyl 3,4-dideoxy-α-DL-*threo*-hex-3-enopyranoside (**10**) and methyl 3,4-dideoxy-α,β-DL-*erythro*-hex-3-enopyranosides (**11ab**), respectively. The structures of these products were elucidated by ^{1}H- and ^{13}C-n.m.r. spectroscopy (see Table I).

The chemical shifts and $J_{1,2}$ values for **10**, **11a**, and **11b** accorded with pub-

*Dedicated to the memory of Karl Freudenberg on the centenary of his birth.

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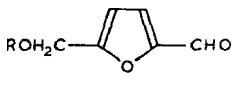

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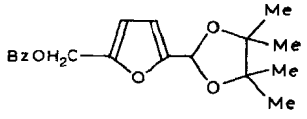

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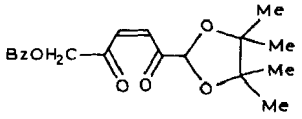

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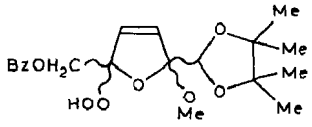

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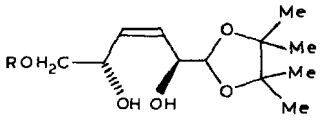

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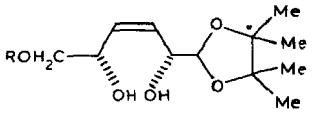

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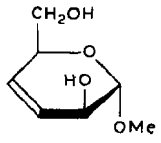

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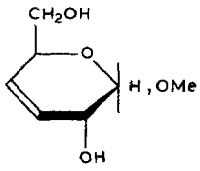

11 a,b

lished data[4]. The preponderant conformer for each compound must be $^{o}H_1$, as demonstrated by the $J_{4,5}$ and $J_{2,5}$ values of 1.5 and 2.0 Hz. Calculated[5] $J_{1,2}$ constants are also in agreement those observed (see Table I). The $J_{C\text{-}1,H\text{-}1}$ value is 168 Hz for the α anomers and 163 Hz for the *β-erythro* derivative. The ^{13}C signals for C-1,5 are shifted downfield for the β anomer **11b** as compared to those of the α anomers **10** and **11a**.

TABLE I

N.M.R. DATA FOR THE METHYL 3,4-DIDEOXY-DL-HEX-3-ENOPYRANOSIDES

Atom	α-threo (**10**)		α-erythro (**11a**)		β-erythro (**11b**)	
	δ (p.p.m.)	J *(Hz)*	δ	J *(Hz)*	δ	J *(Hz)*
H-1	4.79	$J_{1,2}$ 1.5 (0.4)[a]	4.86	$J_{1,2}$ 4.0 (4.3)[a]	4.43	$J_{1,2}$ 6.0 (8.5)[a]
H-2	3.78	$J_{1,3}$ 1.2	4.20	$J_{3,4}$ 11.0	4.09	$J_{2,3}$ 1.7
H-3	6.04[b]	$J_{2,3}$ 5.0	5.62[b]	$J_{5,6a}$ 3.5	5.74	$J_{2,4}$ 2.2
H-4	5.87[b]	$J_{3,4}$ 10.5	5.75[b]	$J_{5,6b}$ 6.0	5.87	$J_{3,4}$ 10.5
H-5	4.22	$J_{3,5}$ 2.0	4.20	$J_{6a,6b}$ 12.0	4.40	$J_{3,5}$ 1.7
H-6a	3.85	$J_{4,5}$ 1.7	3.68		3.77	$J_{4,5}$ 2.2
H-6b	3.66	$J_{2,5}$ 2.0	3.57		3.65	$J_{5,6a}$ 3.5
OH	1.72; 2.7	$J_{5,6a}$ 2.7	1.67; 2.55		1.71; 2.2	$J_{5,6b}$ 6.0
OMe	3.47	$J_{5,6b}$ 3.5	3.48		3.58	$J_{6a,6b}$ 11.5
		$J_{6a,6b}$ 11.7				
C-1	101.6		98.0		103.5	
C-2	63.2		64.2		66.4	
C-3	125.8		126.4[b]		127.5[b]	
C-4	129.5		128.4[b]		128.5[b]	
C-5	68.6		69.0		75.3	
C-6	63.6		64.6		64.5	
OMe	55.7		55.9		56.4	
$^{1}J_{C,H}$		168 Hz		169 Hz		163 Hz

[a]Calculated value for the $^{o}H_1$ conformation. [b]Interchangeable assignments.

EXPERIMENTAL

General. — Column chromatography was performed on Kieselgel 60. ^{1}H- and ^{13}C-n.m.r. spectra were recorded with a Bruker WP-200-SY instrument.

5-Benzoyloxymethyl-2-furaldehyde (**2**). — A stirred solution of **1** (6.45 g, 51 mmol) in pyridine (25 mL) was treated with benzoyl chloride (5.9 mL, 51 mmol) at 0° and then stored at room temperature for 16 h. The solvent was evaporated under diminished pressure and a solution of the residue in chloroform was washed successively with cold dilute sulphuric acid and aqueous $NaHCO_3$, then dried $MgSO_4$, and concentrated. The residue crystallised from ether–light petroleum, to give **2** (2.7 g, 84.2%), m.p. 51–52°.

Anal. Calc. for $C_{13}H_{10}O_4$: C, 67.83; H, 4.38. Found: C, 67.48; H, 4.70.

2-(5-Benzoyloxymethyl-2-furyl)-4,4,5,5-tetramethyl-1,3-dioxolane (**3**). — A mixture of **2** (1.05 g, 46 mmol), 2,3-dimethylbutane-2,3-diol (0.7 g, 59 mmol), toluene-*p*-sulphonic acid (50 mg), and benzene (100 mL) was boiled under reflux with azeotropic distillation of the water formed. After the end of the reaction (t.l.c.), the mixture was washed with aqueous $NaHCO_3$, dried ($MgSO_4$), clarified with charcoal and fuller's earth, and concentrated, to give **3** (1.1 g, 73.3%), m.p. 66.5–67.6° (from light petroleum). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.28 (s, 6 H, 2 Me), 1.34 (s, 6 H, 2 Me), 5.29 (s, 2 H, CH_2), 5.90 (s, 1 H, dioxolane CH), 6.30 (s, 2 H, furan ring), 7.38–8.10 (m, 5 H, Ph).

Anal. Calc. for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.17; H, 6.86.

*2-(*DL-threo-*5-Benzoyloxy-1,4-dihydroxy-*cis-*pent-2-enyl)-4,4,5,5-tetramethyl-1,3-dioxolane* (**6**) *and its* erythro *isomer* (**7**). — (*a*) A solution of **3** (3.3 g, 10 mmol) in *tert*-butyl alcohol (130 mL) was diluted with a phosphate buffer (80 mL, pH 8; M H_3PO_4 + M NaOH). A solution of bromine (0.54 mL, 1.58 g, 10 mmol) in *tert*-butyl alcohol (20 mL) was added dropwise while the pH was maintained at 4 by continuous addition of 2M NaOH. The mixture was then neutralised and saturated with NaCl, the organic layer was separated, and the aqueous layer was extracted with *tert*-butyl alcohol. Water (50 mL) was added to the combined organic solutions, and ethanolic sodium borohydride (0.5 g, 13 mmol in 10 mL) was added dropwise with stirring. After 3 h, the mixture was acidified (pH 5) with dilute HCl, neutralised, and extracted with chloroform, and the extract was then dried and concentrated to give a mixture of **6** and **7**. Column chromatography (light petroleum–acetone, 9:1 then 8:2) gave, first, **6**, isolated as a syrup (0.90 g). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.25 (s, 12 H, 4 Me), 2.62 (bs, 1 H, OH), 3.45 (bs, 1 H, OH), 4.39 (m, 2 H, H-5'a,5'b), 4.44 (m, 1 H, $J_{1',2'}$ 8.0, $J_{1',3'}$ 1.2 Hz, H-1'), 4.73 (m, 1 H, $J_{4',5'a}$ 6.0, $J_{4',5'b}$ 5.0 Hz, H-4'), 4.87 (d, 1 H, $J_{2,1'}$ 6.2 Hz, H-2), 5.65 (ddd, 1 H, $J_{2',3'}$ 11.5, $J_{2',4'}$ 1.0 Hz, H-2'), 5.87 (ddd, 1 H, $J_{3',4'}$ 7.7 Hz, H-3'), 7.38–8.10 (m, 5 H, Ph).

Anal. Calc. for $C_{19}H_{26}O_6$: C, 64.81; H, 7.39. Found: C, 64.88; H, 7.50.

The tribenzoate of **6** was a syrup.

Anal. Calc. for $C_{33}H_{34}O_8$: C, 70.92; H, 6.09. Found: C, 70.50; H, 6.15.

Eluted second was **7**, isolated as a syrup (0.75 g). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.15 (s, 12 H, 4 Me), 3.23 (bs, 2 H, 2 OH), 4.29–4.50 (m, 3 H, H-1',5'a,5'b), 4.75 (m, 1 H, H-4'), 4.89 (d, 1 H, $J_{2,1'}$ 6.5 Hz, H-2), 5.66 (dd, 1 H, $J_{1',2'}$ 7.5, $J_{2',3'}$ 12.1 Hz, H-2'), 5.80 (dd, 1 H, $J_{3',4'}$ 7.6 Hz, H-3'), 7.35–8.10 (m, 5 H, Ph).

Anal. Found: C, 64.70; H, 7.15.

The tribenzoate of **7** had m.p. 139–140° (from ethanol).

Anal. Found: C, 71.30; H, 6.20.

(*b*) To a solution of **3** (0.50 g) in dry methanol (20 mL) was added Methylene Blue (3 mg), and oxygen was bubbled through the solution for 1.5 h whilst it was irradiated with a 1000-W lamp. Methyl sulphide (0.22 mL) was then added, the mixture was kept in a refrigerator for 12 h and then concentrated, and the residue was reduced with sodium borohydride as in (*a*), to give **6** (50 mg) and **7** (40 mg) after chromatography.

*4,4,5,5-Tetramethyl-2-(*DL-threo-*1,4,5-trihydroxy*-cis-*pent-2-enyl)-1,3-dioxolane* (**8**). — Debenzoylation of **6** with methanolic sodium methoxide gave syrupy **8** (72.6%). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.25 (s, 12 H, 4 Me), 3.00 (bs, 3 H, 3 OH), 3.57 (m, 1 H, $J_{5'a,5'b}$ 11.5 Hz, H-5'a), 3.65 (m, 1 H, H-5'b), 4.36 (m, 1 H, $J_{1',2'}$ 7.7, $J_{1',3'}$ 1.2 Hz, H-1'), 4.46 (m, 1 H, $J_{4',5'a}$ 6.0, $J_{4',5'b}$ 4.5 Hz, H-4'), 4.85 (d, 1 H, $J_{2,1'}$ 6.2 Hz, H-2), 5.61 (ddd, 1 H, $J_{2',3'}$ 11.5, $J_{2',4'}$ 1.0 Hz, H-2'), 5.76 (ddd, 1 H, $J_{3',4'}$ 7.7 Hz, H-3').

Anal. Calc. for $C_{12}H_{22}O_5$: C, 58.51; H, 8.94. Found: C, 58.55; H, 8.99.

*4,4,5,5-Tetramethyl-2-(*DL-erythro-*1,4,5-trihydroxy*-cis-*pent-2-enyl)-1,3-dioxolane* (**9**). — Debenzoylation of **7** led to **9** (67%). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.25 (s, 12 H, 4 Me), 2.25, 2.55, 3.40 (bs, 1 H, OH), 3.60 (2 dd, 2 H, H-5'a,5'b), 4.40 (m, 2 H, H-1',4'), 4.85 (d, 1 H, $J_{2,1'}$ 7.5 Hz, H-2), 5.62 (ddd, 1 H, $J_{1',2'}$ 8.0, $J_{2',3'}$ 11.5, $J_{2',4'}$ 1.0 Hz, H-2'), 5.82 (ddd, 1 H, $J_{3',4'}$ 7.6, $J_{1',3'}$ 1.0 Hz, H-3').

Anal. Calc. for $C_{12}H_{22}O_5$: C, 58.51; H, 8.94. Found: C, 58.45; H, 8.69.

Methyl 3,4-dideoxy-α-DL-threo-*hex-3-enopyranoside* (**10**). — A solution of **8** in methanolic 1% hydrogen chloride was boiled under reflux for 6 h, then neutralised, and concentrated. Column chromatography (chloroform–methanol, 9:1) of the residue gave **10** (206 mg, 63.3%). The amount of the β isomer was <5%. See Table I for the n.m.r. data.

Anal. Calc. for $C_7H_{12}O_4$: C, 52.47; H, 7.56. Found: C, 52.40; H, 7.42.

Methyl 3,4-dideoxy-α- (**11a**) *and* -β-DL-erythro-*hex-3-enopyranoside* (**11b**). — Methanolysis of **9**, as for **8**, gave a 1:4 mixture of **11a** and **11b** (150 mg, 77%). Column chromatography (chloroform–methanol, 95:5) of the mixture gave, first, the α anomer (**11a**) (30 mg) and then the β anomer (120 mg). See Table I for the n.m.r. data.

Anal. Calc. for $C_7H_{12}O_4$: C, 52.47; H, 7.56. Found: C, 52.37; H, 7.40.

ACKNOWLEDGMENTS

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