

EXPERIMENTS IN THE FURAN SERIES. XV.*
SYNTHESIS OF RACEMIC 4-KETOPENTOSE

J.ŠROGL, M.JANDA, I.STIBOR and J.KUČERA

Department of Organic Chemistry,
Institute of Chemical Technology, Prague 6

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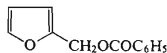
Racemic *erythro*-pentopyranos-4-ulose (*VII*) has been prepared from *trans*-2,5-dimethoxy-2-benzoyloxymethyl-2,5-dihydrofuran (*IIIa*) by the route of its *cis*-hydroxylation, debenzoylation, and cleavage of the acetal bonds.

The use of five-membered cyclic acetals *i.e.* the methoxylation products of furan compounds¹, for the synthesis of sugar derivatives has been the subject of some earlier papers from us²⁻⁴ as well as from other authors⁵. For the synthesis of five-membered racemic sugars we regarded as the most suitable of these compounds *trans*-2,5-dimethoxy-2-benzoyloxymethyl-2,5-dihydrofuran prepared earlier in contrast to our electrolytic methoxylation by the brominating methoxylation of furyl benzoate⁶ (*I*). Compound *IIIa* is a derivative of a primary alcohol, and can be used as such for the direct synthesis of derivatives of pentoses. Configurational uniformity on the carbon atoms 2 and 5 is in respect to our synthetic purpose without any significance as both isomers would after hydrolysis afford the same product.

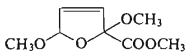
The methoxylation of the ester *I* was performed by the electrolytic method^{2,7}, where part of the *trans*-acetal *IIIa* crystallised directly in the electrolyser. The remaining product was then separated by distillation *in vacuo* into the starting compound *I*, the mixture of the isomers *IIIa* and *IIIb*, and the pure isomer *IIIb*. The NMR spectra of both isomers are different but on the basis of its spectrum it is not possible to confirm the earlier suggested configuration⁶ of the crystalline isomer *IIIa*. By treatment the ester *IIIa* with sodium methoxide in methanol⁸ was prepared *trans*-2,5-dimethoxy-2-hydroxymethyl-2,5-dihydrofuran (*IVa*). The mixture of both isomers *IV* was obtained by reduction of methyl 2,5-dimethoxy-2,5-dihydro-2-furoate (*II*) with lithium aluminium hydride. *cis*-Hydroxylation of the esters *IIIa* and *IIIb* with potassium permanganate in aqueous methanolic solution in the presence of magnesium sulphate afforded the isomeric 2,5-dimethoxy-3,4-dihydroxy-2-benzoyloxymethyltetrahydrofurans (*Va* and *Vb*). Their constitution was proved

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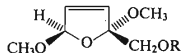
by elemental analysis and spectral data. From these data the position of the *cis*-hydroxyl groups with respect to the benzoyloxymethyl group cannot be determined.



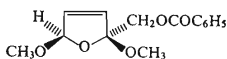
I



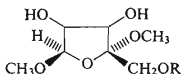
II



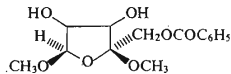
IIIa, R = COC₆H₅
IVa, R = H



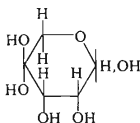
IIIb



Va, R = COC₆H₅
VI, R = H



Vb



VII

The compounds *Va* and *Vb* were chromatographically uniform. Debenzylation of product *Va* was carried out with sodium methoxide in methanol⁸ giving in 71% yield 2,5-dimethoxy-3,4-dihydroxy-2-hydroxymethyltetrahydrofuran (*VI*) with *trans*-configuration of the methoxy groups at C₍₂₎ and C₍₅₎, the constitution of which was proved both by analysis and spectral data. Cleavage of the acetal bonds of the triol *VI* in a 1 : 1 dioxane–water mixture on Dowex W-50 affords in 95% yield *erythro*-pentopyranos-4-ulose (*VII*) in the form of the relatively stable hydrate. Its infrared spectrum is devoid of a carbonyl band; in the rather complex NMR spectrum it can be reliably identified the singlet $\delta = 6.52$ (26°C), 5.92 (60°C) due to the hydroxyl groups.

EXPERIMENTAL

The temperature data are uncorrected. Infrared spectra were taken in thin layer on a Zeiss UR-10 spectrophotometer. NMR spectra were measured in deuteriochloroform on a BS 477 Tesla, Brno instrument using tetrachlormethylsilane as internal standard. The NMR shifts are recorded in delta units.

2,5-Dimethoxy-2-benzoyloxymethyl-2,5-dihydrofuran (*IIIa*, *IIIb*)

A solution of 60.6 g (0.3 mol) of furfuryl benzoate (*I*) and 6 g of ammonium bromide in 300 ml of methanol was electrolysed² at -20°C (electric current 25 V, 4 A). After 4 hours the mixture was cooled to -50°C , and the electrolysis continued for another hour. The liquid was then poured into a solution of sodium methoxide prepared from sodium (1.5 g) and methanol (30 ml). In the electrolyser remained the crystals of the *trans*-isomer *IIIa* which were recrystallised from methanol; yield 21 g (26.3%). The isomer *IIIa* melts at 73°C (lit.⁶ gives m.p. $76-77^{\circ}\text{C}$). IR spectrum: 832, 913, 981, 1028, 1061, 1115, 1180, 1198, 1282, 1318, 1345, 1378, 1460, 1615, 1739, 2838, 2885, 2910, 2937, 2965, 2998, 3035, 3070, 3090 cm^{-1} . NMR spectrum: 3.23, 3.53 (s, altogether 6 H, OCH_3), 4.72, 4.54, 4.40, 4.22 (2 H, CH_2), 5.55 (1 H, 5-position), 6.22, 6.10, 6.04, 5.92 (2 H, 3- and 4-position), 8.00 and 7.50 (multiplet, altogether 5 H, phenyl). From the methanolic solution were after neutralisation evaporated ammonia and methanol, and the product taken up in ether. The deposited salts were filtered off with suction, and the ethereal solution was dried over sodium sulphate and the solvent then distilled off. On vacuum distillation was collected besides the fraction containing the starting product and the mixture of both isomers, the fraction with b.p. $125-135^{\circ}\text{C}/0.5\text{ Torr}$ which is the *cis*-isomer *IIIb* (lit.⁶ gives b.p. $152-153^{\circ}\text{C}/2.5\text{ Torr}$). NMR spectrum: 3.18, 3.36 (s, altogether 6 H, OCH_3), 4.68, 4.48, 4.45, 4.25 (2 H, CH_2), 5.77 (s, 1 H, 5-position), 6.20, 6.10, 6.04, 5.94 (2 H, 3- and 4-position), 8.05, 7.45 (multiplet, 5 H, phenyl).

2,5-Dimethoxy-2-hydroxymethyl-2,5-dihydrofuran (*IV*)

To a solution of 47 g (0.25 mol) of the methyl ester *II* in 100 ml of ether was added lithium aluminium hydride (12 g; 0.3 mol) in ether (100 ml). After boiling for three hours, the reaction mixture was decomposed with water and 15% NaOH. The product was distilled *in vacuo* through a column to afford compound *IV* in a yield of 5 g (12.5%); b.p. $110-114^{\circ}\text{C}/12\text{ Torr}$ (lit.⁹ gives b.p. $106-110^{\circ}\text{C}/10\text{ Torr}$).

trans-Isomer *IVa*: A solution of 20 g (0.076 mol) of ester *IIIa* in 1000 ml of methanol was treated with sodium methoxide (27 g; 0.5 mol) and the reaction mixture left at room temperature for 48 hours. The excess of sodium methoxide was then decomposed with gaseous carbon dioxide, the solvent evaporated, the residue dissolved in ether, and the solution dried over sodium sulphate. The ether was removed by distillation, and the residue was distilled through a column to yield 17 g (76%) of compound *IVa* with b.p. $114^{\circ}\text{C}/14\text{ Torr}$. IR spectrum: 890, 982, 1030, 1072, 1088, 1104, 1135, 1180, 1200, 1252, 1352, 1378, 1460, 1640, 2832, 2879, 2935, 2956, 2993, $3495, 3600\text{ cm}^{-1}$. NMR spectrum: 2.90 (1 H, OH), 3.21, 2.48 (s, altogether 6 H, OCH_3), 3.55 (2 H, CH_2), 5.49 (1 H, 5-position), 6.17, 6.07, 6.01, 5.91 (3- and 4-position, 2 H). For $\text{C}_7\text{H}_{12}\text{O}_4$ (160.1) calculated: 52.49% C, 7.55% H, 38.75% OCH_3 ; found: 52.55% C, 7.40% H, 38.31% OCH_3 .

Hydroxylation of the Acetals *IIIa* and *IIIb*

To a solution of 28 g (0.106 mol) of the acetal *IIIa* (or *IIIb*) in 400 ml of methanol a solution of 0.1 mol of potassium permanganate and 0.1 mol of magnesium sulphate in 400 ml of water was added during 1.5 h at -15°C , and the mixture was left at room temperature overnight. The manganese dioxide was then filtered off with suction and washed with methanol. Isolation of product *Va*: The filtrate was freed from methanol, the residue extracted with 300 ml of dichloromethane, the solvent evaporated, and the residue was again dissolved in 30 ml of methanol. From this solution crystallised at -70°C the starting compound *IIIa*. From the residue was then obtained product *Va* (8.4 g; 26.7%). For $\text{C}_{14}\text{H}_{18}\text{O}_7$ (298.1) calculated: 56.37% C, 6.08% H, 20.81% OCH_3 ; found: 56.54% C, 6.45% H, 20.78% OCH_3 . Isolation of product *Vb*: The filtrate was three times extracted by shaking with 100 ml of light petroleum, and the aqueous solution

was then evaporated to dryness. The residue was extracted with dichloromethane and the extract evaporated affording product *Vb* (6.65 g; 22.3%). For $C_{14}H_{18}O_7$ (298.1) calculated: 56.37% C, 6.08% H, 20.81% OCH_3 ; found: 56.45% C, 6.51% H, 20.57% OCH_3 .

2,5-Dimethoxy-3,4-dihydroxy-2-hydroxymethyltetrahydrofuran (*VI*)

To a solution of 2.98 g (0.01 mol) of compound *Vb* in 100 ml of methanol was added 1 g of sodium methoxide, and the mixture was set aside at room temperature for 48 hours. Then was the mixture neutralised with gaseous CO_2 , methanol distilled off, and the residue was dissolved in water and extracted with light petroleum. The aqueous solution was saturated with potash and extracted for 100 hours with ether. Evaporation of the ether gave 1.2 g (71%) of compound *VI*. IR spectrum: 830, 875, 890, 918, 986, 1020, 1030, 1070, 1130, 1200, 1245, 1355, 1378, 2837, 2945, 3005, 3420, 3600 cm^{-1} . NMR spectrum: 3.30 and 3.42 (s, altogether 6 H, OCH_3), 3.73 (s, 2 H, CH_2), 4.19 (2 H, 3- and 4-position), 4.91 (s, 1 H, 5-position), and 4.44 (3 H, OH). For $C_7H_{14}O_5$ (178.2) calculated: 47.17% C, 7.92% H; found: 47.35% C, 7.85% H.

erythro-Pentopyranos-4-ulose Hydrate (*VII*)

A solution of 1.78 g (0.01 mol) of compound *VI* in 100 ml of 1 : 1 water-dioxan mixture was stirred for 48 hours with Dowex W-50, whereupon the ion exchanger was separated and washed. Evaporation of the solvent gave the viscous compound *VII* (1.58 g; 95%). For $C_5H_{10}O_6$ (166.1) calculated: 36.15% C, 6.07% H; found: 36.16% C, 6.15% H.

Elemental analyses and spectral measurements were performed in the Central Laboratories, Institute of Chemical Technology, Prague.

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