

## Preparation and identification of aldolization products of 1,3-dimethoxy-2-propanone

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4-Hydroxy-1,3,5-trimethoxy-4-methoxymethyl-2-pentanone (II), 4,6-dihydroxy-1,3,5,7-tetramethoxy-4,6-bis(methoxymethyl)-2-heptanone (III<sub>A</sub>), and 4,6,8-trihydroxy-1,3,5,7,9-pentamethoxy-4,6,8-tris(methoxymethyl)-2-nonanone (IV) have been prepared by aldolization of 1,3-dimethoxy-2-propanone (I) in aqueous NaOH solution at 5 °C. The components of the reaction mixture were separated by liquid chromatography and their structures were established by <sup>13</sup>C NMR spectroscopy as well as by mass spectrometry after their reduction with NaBD<sub>4</sub>.

4-Гидрокси-1,3,5-триметокси-4-метоксиметил-2-пентанон (II), 4,6-дигидрокси-1,3,5,7-тетраметокси-4,6-бис(метоксиметил)-2-гептанон (III<sub>A</sub>) и 4,6,8-тригидрокси-1,3,5,7,9-пентаметокси-4,6,8-трис(метоксиметил)-2-нонанон (IV) были получены альдолизацией 1,3-диметокси-2-пропанола (I) в водном растворе NaOH при 5 °C. Компоненты реакционной смеси были разделены с помощью жидкостной хроматографии и их структуры были установлены методом <sup>13</sup>C ЯМР спектроскопии, а также методом масс-спектрометрии после их восстановления NaBD<sub>4</sub>.

Unsubstituted trioses at suitable conditions in alkali medium undergo aldolization reaction to give higher branched and unbranched monosaccharides. Formation of a branched hexose on aldolization of 1,3-dihydroxy-2-propanone in weak alkali medium was first observed by *Utkin* [1]. Cross-aldolization of glyceraldehyde and 1,3-dihydroxy-2-propanone in alkali medium [2, 3] resulted in a mixture of branched and unbranched hexoses. It was found that the relative proportions of the compounds formed during aldolization of their mixtures depended on the basic catalyst used [4—7]. However, the branched hexoses were present in the reaction mixture always in small portions. Aldolization of substituted trioses, except 2,3-*O*-isopropylidene-*D*-glyceraldehyde [8], has not been studied so far. The significance of branched monosaccharides increased first of all due to their occurrence in antibiotics [9, 10] that contributed to development of the chemistry of branched monosaccharides in recent years.

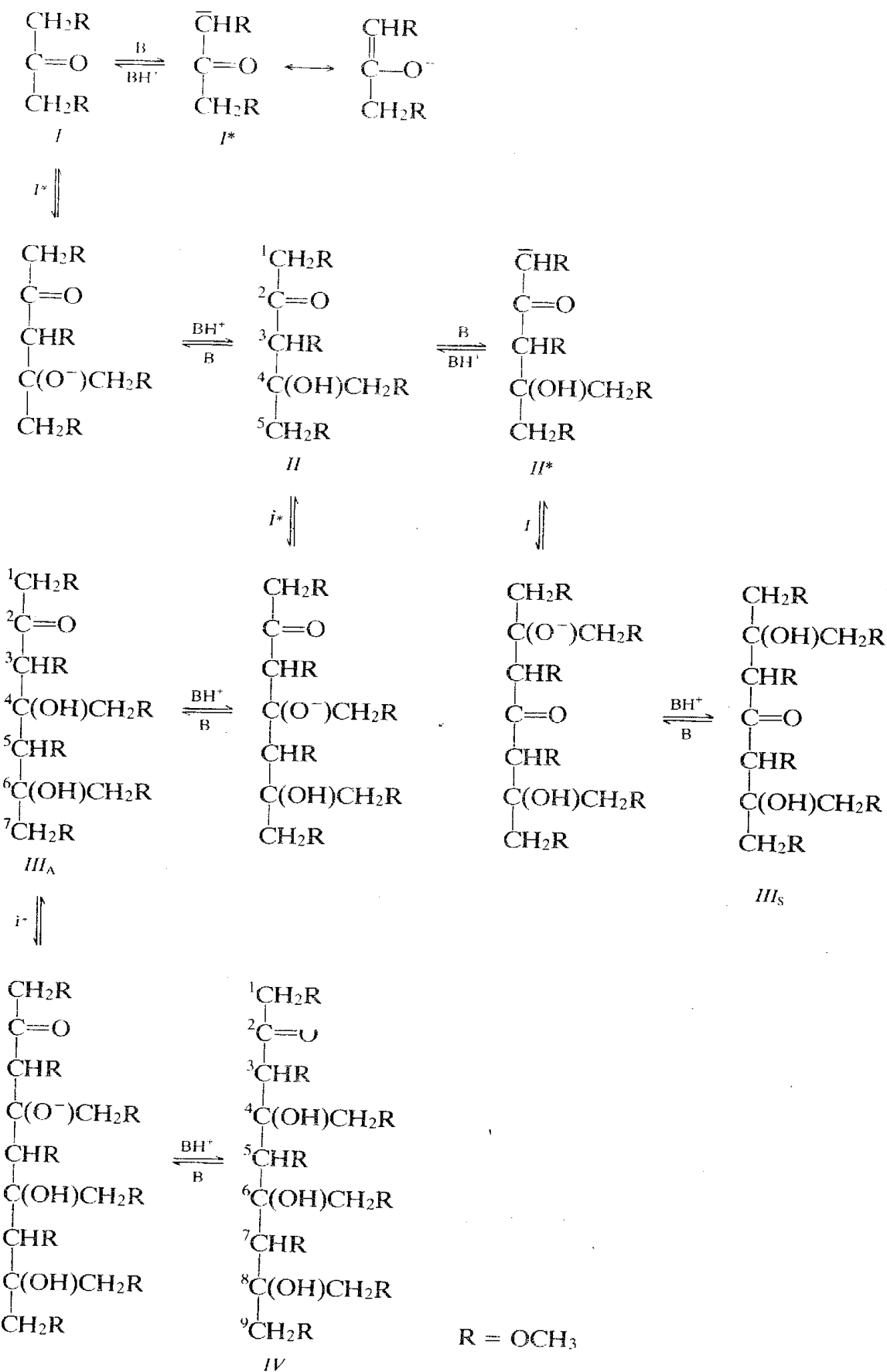
In the present paper the method for the preparation of branched partially methylated monosaccharides *II*, *III<sub>A</sub>*, and *IV* by aldolization of *I* in weak alkali medium ( $c = 0.1 \text{ mol dm}^{-3} \text{ NaOH}$ ) at  $5^\circ\text{C}$  is described (Scheme 1). At low concentration of *I* (up to  $1.0 \text{ mol dm}^{-3}$ ) an equilibrium mixture of *I* and *II* is formed, the composition of which depends on temperature considerably [11]. The structure of *II* was proved by  $^{13}\text{C}$  NMR spectrum of the compound measured in  $\text{CH}_3\text{OD}$ ,  $\delta/\text{ppm}$ : 209.7 (C-2), 87.1 (C-3), 77.6 (C-1), 77.3 (C-4), 73.9 (C-4', C-5), 60.1 and 59.3 ( $4 \times \text{OCH}_3$ ).

The mass spectrum of the compound *II* reduced with sodium borodeuteride contained signals of the primary ions of  $m/z$  (relative intensity/%) 194 (26), 119 (38) formed by splitting of the branched tetra-*O*-methylpentitol between the carbon atoms and those of secondary ions formed from these and other primary ions, not observable in the spectrum, by elimination of  $\text{H}_2\text{O}$ ,  $\text{CH}_3\text{OD}$ ,  $\text{CH}_3\text{OH}$ , and  $\cdot\text{CH}_2\text{OCH}_3$ . Those were the peaks of the ions with  $m/z$  86 (84), (163 - 45 - 32); 100 (60), (163 - 45 - 18); 101 (84), (119 - 18); 102 (100), (120 - 18); 118 (45), (163 - 45); 145 (32), (163 - 18); 161 (45), (194 - 33). The structure suggested is substantiated by the presence of the ions of  $m/z = 194$  formed by elimination of  $\cdot\text{CH}_2\text{OCH}_3$  radicals from molecular ions of tetra-*O*-methylpentitol.

Formation of higher aldolization products under suitable reaction conditions ( $c = 1\text{--}3 \text{ mol dm}^{-3} \text{ I}$ ,  $\theta = 5^\circ\text{C}$ ) became a significant reaction. As can be seen in the scheme, cross-aldolization of *I\** and *II* or *I* and *II\** led to the formation of two structurally isomeric compounds *III<sub>A</sub>* and 2,6-dihydroxy-1,3,5,7-tetramethoxy-2,6-bis(methoxymethyl)-4-heptanone, i.e. *III<sub>S</sub>*. Addition of *I\** to the carbonyl carbon of *II* would result in the asymmetric compound *III<sub>A</sub>*, while addition of the anion *II\** to the carbonyl group of *I* in the symmetric compound *III<sub>S</sub>*. The  $^{13}\text{C}$  NMR spectrum of the compound in  $(\text{CD}_3)_2\text{CO}$  revealed the following signals of chemical shifts  $\delta/\text{ppm}$ : 208.6 (C-2), 85.2 (C-3, C-5), 75.4 (C-1), 73.6 (C-7, C-4', C-6'), 77.2 (C-4, C-6), and 59.3 and 58.6 ( $6 \times \text{OCH}_3$ ). Occurrence of two signals at  $\delta = 73.6 \text{ ppm}$  and  $75.4 \text{ ppm}$ , belonging to qualitatively different methylene groups in the skeleton of the molecule, indicates that the isolated crystalline compound had the structure of *III<sub>A</sub>* because in the case of *III<sub>S</sub>* all methylene groups would show the same chemical shift.

The mass spectrum of the compound with the suggested structure showed after reduction with sodium borodeuteride signals of primary ions of  $m/z$  (relative intensity/%) 119 (40), formed by cleavage of the acyclic chain of the branched hexa-*O*-methylpentitol between the carbons, and the ions of  $m/z$  (relative intensity/%) 294 (32), 276 (17), 263 (14), 229 (34), 205 (96), 145 (72), 102 (100), 101 (85), 86 (73), formed by elimination of  $\text{H}_2\text{O}$ ,  $\text{CH}_3\text{OH}$ , and  $\text{CH}_3\text{OD}$  from primary ions. Of the ions listed the most intensive ones were those of  $m/z = 102$  arising from primary ions of  $m/z = 120$  after elimination of water. These ions proved the asymmetric structure of the crystalline compound *III<sub>A</sub>*. The

IDENTIFICATION OF ALDOLIZATION PRODUCTS



Scheme 1

compound  $III_S$  after reduction could not afford these ions. The same conclusion follows also from the presence of the ions of  $m/z = 263$ , arising from primary ions of  $m/z = 281$ . We failed to isolate the compound  $III_S$  by the procedure used for separation, however, we assume that it was the compound of  $R_f = 0.28$  moving on thin layer plates between  $II$  and  $III_A$ . When the starting concentration of  $I$  was  $3 \text{ mol dm}^{-3}$  also the compound  $IV$  appeared in the aldolization mixture. The structure of this compound, formed by cross-aldolization of  $I^*$  and  $III_A$ , was suggested on the basis of  $^{13}\text{C}$  NMR measurements and, after its reduction with sodium borodeuteride to the corresponding alditol, mass spectrometric fragmentation. The  $^{13}\text{C}$  NMR spectrum of the compound in  $\text{CDCl}_3$  revealed the signals of chemical shifts  $\delta/\text{ppm}$ : 207.6 (C-2), 79.3; 76.1 and 75.7 (C-4, C-6, C-8), 75.4 and 74.1 (C-3, C-5, C-7), 75.1; 73.7 and 70.3 (C-1, C-4', C-6', C-8', and C-9), and 61.0; 60.9; 59.2; 59.1; 59.0 and 57.9 ( $8 \times \text{OCH}_3$ ), the  $\text{OCH}_3$  groups on C-8 and C-9 being qualitatively equal. The individual signals were identified by the DEPT method. The mass spectrum of the compound  $IV$  after reduction contained signals of ions characteristic also of lower homologues, i.e. of the compounds  $II$  and  $III_A$ , which explained the mechanism of formation of the individual aldolization products. The spectrum revealed also signals of ions of  $m/z = 323$  (relative intensity = 23 %) arising from primary ions of  $m/z = 355$  after elimination of  $\text{CH}_3\text{OH}$ , proving the structure of the parent compound.

Under the given reaction conditions, neither the product of cross-aldolization of  $I$  and  $III_A^*$  nor other higher aldolization products were proved in the reaction mixture by the methods applied.

The experimental data obtained about the structure of the compounds  $II$ ,  $III_A$ , and  $IV$  confirm that aldolization of  $I$  proceeded in weak aqueous alkali medium via the mechanism generally accepted for this type of reactions, i.e. as a sequence of successive reversible reactions. In all steps of the aldolization process, hydrogen is preferentially split off from  $\alpha$ -carbon of the molecule  $I$  and the anion formed in such a way is added to the carbonyl group of the compound  $I$  or its higher homologues, i.e.  $II$  and  $III_A$ .

### Experimental

Elemental analyses were provided with a Perkin—Elmer 240 automatic analyzer. Composition of the reaction mixture and purity of the products were checked by TLC in the system: chloroform—acetone—n-hexane (volume ratio = 2 : 2 : 1) using anilinium hydrogen phthalate to visualize the compounds. Mass spectra were measured with a JMS-D 100 (Jeol) spectrometer (electron energy 12 eV, emission current 300  $\mu\text{A}$ , temperature of evaporation 60—160 °C).  $^{13}\text{C}$  NMR spectra were obtained with an FT NMR FX-100 spectrometer (Jeol) using HDMS as internal standard. Melting points were established on a Kofler block.

Liquid-chromatographic separation of the compounds *II*, *III<sub>A</sub>*, and *IV* from the aldolization mixture was achieved on a column (1000 mm × 30 mm) of silica gel (150—300 μm; Lachema, Brno) using chloroform—acetone—*n*-hexane (volume ratio = 2:2:1) as the eluent at a flow rate of 20 cm<sup>3</sup> h<sup>-1</sup>.

1,3-Dimethoxy-2-propanone (*I*) was obtained by oxidation of 1,3-dimethoxy-2-propanol with ruthenium(IV) oxide according to [12]; b.p. = 76—78 °C at 2.4 kPa (its purity was established by GLC, 1 % impurities), yield = 85 %. The procedure in [13] gives b.p. = 63.5 °C at 2.3 kPa and that in [14] gives b.p. = 78 °C at 2.4 kPa.

The compounds *II*, *III<sub>A</sub>*, and *IV* were obtained by aldolization of *I* ( $c = 3 \text{ mol dm}^{-3}$ ) in NaOH ( $c = 0.1 \text{ mol dm}^{-3}$ ) on standing at 5 °C for 2 h. The reaction progress was checked by TLC. After the reaction was complete, the mixture was neutralized with diluted hydrochloric acid at the same temperature and extracted with chloroform (7 × 25 cm<sup>3</sup>). The concentrated extract was fractionated by means of liquid chromatography.

4-Hydroxy-1,3,5-trimethoxy-4-methoxymethyl-2-pentanone (*II*) after separation ( $R_f = 0.39$ ) in 2.5 g (55 %) yield had b.p. = 124 °C at 2.6 kPa.

For (C<sub>5</sub>H<sub>10</sub>O<sub>3</sub>)<sub>2</sub>  $w_i$ (calculated): 50.83 % C, 8.53 % H, 52.55 % OCH<sub>3</sub>;  $w_i$ (found): 50.84 % C, 8.66 % H, 53.2 % OCH<sub>3</sub>.

4,6-Dihydroxy-1,3,5,7-tetramethoxy-4,6-bis(methoxymethyl)-2-heptanone (*III<sub>A</sub>*) after separation ( $R_f = 0.2$ ) was recrystallized from methanol to give 0.6 g (14 %) yield of m.p. = 100—102 °C.

For (C<sub>5</sub>H<sub>10</sub>O<sub>3</sub>)<sub>3</sub>  $w_i$ (calculated): 50.83 % C, 8.53 % H, 52.55 % OCH<sub>3</sub>;  $w_i$ (found): 50.83 % C, 8.65 % H, 52.19 % OCH<sub>3</sub>.

4,6,8-Trihydroxy-1,3,5,7,9-pentamethoxy-4,6,8-tris(methoxymethyl)-2-nonanone (*IV*) after separation ( $R_f = 0.09$ ) was purified by rechromatography to give a sirup (80 % purity) in 0.15 g (3.3 %) yield.

### *Reduction of the compounds II, III<sub>A</sub>, and IV with sodium borodeuteride*

The compounds *II*, *III<sub>A</sub>*, and *IV*, respectively (250 mg) were dissolved in methanol (10 cm<sup>3</sup>) at room temperature and NaBD<sub>4</sub> was added ( $n(\text{NaBD}_4) : n(\text{X}) = 1.1$ ). The reaction was checked by TLC. After the reaction was complete, the solution was deionized on a cation exchanger (Dowex 50W X 8, 37—74 μm), filtered and the cation exchanger was washed with methanol trice. The combined filtrates were evaporated *in vacuo* and the procedure was repeated (3 x) after adding methanol. The obtained alditols were analyzed by mass spectrometry.

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