SYNTHESIS OF 4,6-DIDEOXY-D-*arabino*-HEXOSE, 3,4,6-TRIDEOXY-D-*erythro*- AND *threo*-HEXOSES, 2,4,6-TRIDEOXY-D-*erythro*-HEXOSE, AND THEIR DERIVATIVES

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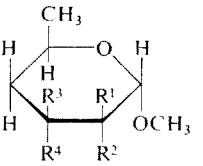
When reacting methyl 4,6-dideoxy-α-D-*xylo*-hexopyranoside (*I*) with one equivalent of methanesulfonyl chloride in pyridine, 2-O-methanesulfonyl- and 3-O-methanesulfonyl derivatives *II* and *III* were obtained in a 4 : 1 ratio in addition to the disubstituted derivative *IV*. Reaction of ester *II* with sodium methoxide gave methyl 2,3-anhydro-4,6-dideoxy-α-D-*lyxo*-hexopyranoside (*V*); analogous reaction of derivatives *III* and *IV* led to methyl 2,3-anhydro-4,6-dideoxy-α-D--*ribo*-hexopyranoside (*VI*). Reaction of anhydro derivative *V* with sodium hydroxide, sodium methoxide, or lithium aluminum hydride leads to an opening of the anhydro ring on the third carbon exclusively, giving rise to methyl 4,6-dideoxy-α-D-*arabino*-hexopyranoside (*VII*) or its 3-O-methyl ether *VIII*, or methyl 3,4,6-trideoxy-α-D-*threo*-hexopyranoside (*XI*), respectively. Analogous reactions of anhydro derivative *VI* with sodium methoxide or lithium aluminium hydride always lead to mixtures of both possible products *i. e.* methyl 4,6-dideoxy-2-O-methyl--α-D-*arabino*-hexopyranoside (*IX*) and methyl 4,6-dideoxy-3-O-methyl -α-D-*xylo*-hexopyranoside (*X*), or methyl 2,4,6-trideoxy-α-D-*erythro*-hexopyranoside (*XII*) and methyl 3,4,6-trideoxy--α-D-*erythro*-hexopyranoside (*XIII*). On hydrolysis of glycosides free hexoses *XIV*—*XIX* were obtained. The structure and the prevailing conformation of all newly prepared substances was demonstrated on the basis of the analysis of their NMR and IR spectra.

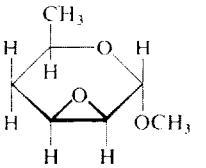
Trideoxyhexoses represent a very incomplete group in the systematics of sugars. Disregarding the types on the chain of which an additional non-oxygen functional group (for example amino-, dimethylamino, *etc.*) is bound in addition to the hydroxy group, we can find the reports only on 2,3,6-trideoxy-L-*threo*-hexose (rhodinose)[1] and 2,3,6-trideoxy-D-*erythro*-hexose (amicetose)[2] which were isolated from natural material. All synthetic studies in this group of substances[2–9] aimed at the preparation of these compounds or their enantiomers.

The present paper describes the synthesis of methyl 3,4,6-trideoxy-α-D-*threo*-hexopyranoside (*XI*), methyl 3,4,6-trideoxy-α-D-*erythro*-hexopyranoside (*XIII*), methyl 2,4,6-trideoxy-α-D-*erythro*-hexopyranoside (*XII*) and methyl 4,6-dideoxy-α-D-*arabino*-hexopyranoside (*VII*). As starting material methyl 4,6-dideoxy-α-D-*xylo*-hexopyranoside[10] (*I*) was used. Its reaction with methanesulfonyl chloride in pyridine (molar ratio 1 : 1) and in the cold gave a mixture from which 2-O-methanesulfonyl

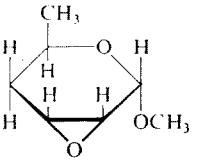
derivative *II*, 3-O-methanesulfonyl derivative *III*, and 2,3-di-O-methanesulfonyl derivative *IV* were isolated in addition to the starting glycoside *I* by preparative chromatography on silica gel. The ratio of the substances isolated was approximately *I* : *II* : *III* : *IV* = 1 : 6·5 : 1·6 : 2·8. The dominant reaction product, the methyl 4,6-dideoxy-2-O-methanesulfonyl-α-D-*xylo*-hexopyranoside (*II*) already described[11] was converted on reaction with sodium methoxide to the known[11] methyl 2,3-anhydro-4,6-dideoxy-α-D-*lyxo*-hexopyranoside (*V*). The isomeric methyl 2,3-anhydro-4,6-dideoxy-α-D-*ribo*-hexopyranoside (*VI*) was obtained either as the sole product of the reaction of the as yet undescribed 3-O-methanesulfonyl derivative *III* with sodium methoxide, or, using a described procedure[11], as the main product of the same reaction of 2,3-di-O-methanesulfonyl derivative *IV*. The reaction of the oxiran ring of anhydro derivatives *V* and *VI* with nucleophilic reagents took place in agreement with the known results of their amonolyses[12,13], as well as in agreement with analogous reactions of their racemates[14]. During the reaction of anhydro derivative *V* with sodium hydroxide or sodium methoxide an exclusive attack on $C_{(3)}$ takes place under formation of methyl 4,6-dideoxy-α-D-*arabino*-hexopyranoside (*VII*) or methyl



I; $R^1 = R^4 = H$, $R^2 = R^3 = OH$
II; $R^1 = R^4 = H$, $R^2 = OSO_2CH_3$, $R^3 = OH$
III; $R^1 = R^4 = H$, $R^2 = OH$, $R^3 = OSO_2CH_3$
IV; $R^1 = R^4 = H$, $R^2 = R^3 = OSO_2CH_3$
VII; $R^1 = R^4 = OH$, $R^2 = R^3 = H$
VIII; $R^1 = OH$, $R^2 = R^3 = H$, $R^4 = OCH_3$
IX; $R^1 = OCH_3$, $R^2 = R^3 = H$, $R^4 = OH$
X; $R^1 = R^4 = H$, $R^2 = OH$, $R^4 = OCH_3$
XI; $R^1 = OH$, $R^2 = R^3 = R^4 = H$
XII; $R^1 = R^2 = R^3 = H$, $R^4 = OH$
XIII; $R^1 = R^3 = R^4 = H$, $R^2 = OH$



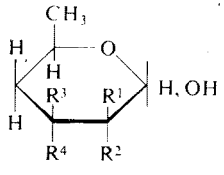
V



VI

4,6-dideoxy-3-O-methyl-α-D-*arabino*-hexopyranoside (*VIII*). Methyl ether *VIII* was also prepared directly from 2-O-methanesulfonyl derivative *II* on reaction with excess sodium methoxide, without the isolation of anhydro derivative *V*. Alkaline methanolysis of anhydro derivative *VI* led to a mixture of products formed on cleavage of the oxiran ring at $C_{(2)}$ and $C_{(3)}$, *i.e.* methyl 4,6-dideoxy-2-O-methyl-α-D-*arabino*-hexopyranoside (*IX*) and methyl 4,6-dideoxy-3-O-methyl-α-D-*xylo*-hexopyranoside (*X*) present in an approximate 2 : 3 ratio. Both monomethyl derivatives were isolated from the mixture by preparative gas chromatography. Reduction of anhydro derivative *V* with lithium aluminum hydride gave methyl 3,4,6-trideoxy-α-D-*threo*-hexopyranoside (*XI*) exclusively, while the isomeric anhydro derivative *VI* was reduced to a mixture of methyl 2,4,6-trideoxy-α-D-*erythro*-hexopyranoside (*XII*) and methyl 3,4,6-trideoxy-α-D-*erythro*-hexopyranoside (*XIII*) in a 1·6 : 1 ratio. They were isolated by preparative gas chromatography. All the newly prepared methyl glycosides, *i.e. VII*, *VIII*, *IX*, *XI*, *XII* and *XIII* were hydrolysed to corresponding aldoses, of which 4,6-dideoxy-D-*arabino*-hexose (*XIV*), 4,6-dideoxy-2-O-methyl-D-*arabino*-hexose (*XVI*), and 2,4,6-trideoxy-D-*erythro*-hexose (*XVIII*) were syrupy, and 4,6-dideoxy-3-O-methyl-D-*arabino*-hexose (*XV*), 3,4,6-trideoxy-α-D-*threo*-hexose (*XVII*) and 3,4,6-trideoxy-α-D-*erythro*-hexose (*XIX*) crystalline.

The structure assignment to the products of cleavage of anhydro derivatives *V* and *VI* partly followed from the chemical relationships and it could also be inferred from comparison with analogous reactions of structurally close anhydro derivatives, for example methyl 2,3-anhydro-4,6-benzylidene-α-D-mannopyranoside and methyl 2,3-anhydro-4,6-benzylidene-α-D-allopyranoside. An unambiguous proof was obtained from NMR and IR data. The structure of glycoside *VII* is confirmed by the coupling constant values, $J_{1,2}$ and $J_{2,3}$ (2.0 and 4·0 Hz respectively) and mutually equal values of the constants $J_{3,4a}$ and $J_{3,4e}$ (3·0 Hz) which are in good agreement with the supposed values of these constants of compound *VII* in $^4C_1$ conformation. Very



XIV, $R^1 = R^4 = OH$, $R^2 = R^3 = H$
XV; $R^1 = OH$, $R^2 = R^3 = H$, $R^4 = OCH_3$
XVI; $R^1 = OCH_3$, $R^2 = R^3 = H$, $R^4 = OH$
XVII; $R^1 = OH$, $R^2 = R^3 = R^4 = H$
XVIII; $R^1 = R^2 = R^3 = H$, $R^4 = OH$
XIX; $R^1 = R^3 = R^4 = H$, $R^2 = OH$

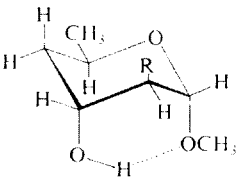
close constants were also obtained for monomethyl derivatives *VIII* and *IX*. The position of the methoxyl group became evident from the upfield shift of the signal of the proton bound to the carbon carrying this group. The coupling constant values in the spectra of compounds *VII*–*IX* agree, within the limits of error of their determination, with the described values of their racemic analogues[14]. In the spectrum of trideoxy derivative *XI* the relatively low value of $J_{1,2}$, and equal values of $J_{2,3e}$ and $J_{2,3a}$ indicate that this substance exists in the mentioned structure and $^4C_1$ conformation. For the assignment of the structure to the products of reduction of anhydro derivative *VI* the splitting of the signal of $H_{(1)}$ in their NMR spectra was most important; trideoxy derivative *XII* was split to a quartet of approximately equal J_{vic} values (approx. 2 Hz), and derivative *XIII* gave a doublet with the value $J_{1,2} = 3{\cdot}5$ Hz. The NMR data are in good agreement with the IR data in the region of OH-band absorption (Table I) which was measured in a 0·002–0·003M tetrachloromethane solution, *i.e.* under conditions when the presence of absorption bands of a free hydroxyl group and an intramolecularly hydrogen-bonded (to another oxygen atom) group; could be expected. The assignment of single absorption bands to various types of intramolecular hydrogen bonds was possible both on the basis of mutual comparison of the spectra of all substances investigated, and on the basis of comparison with the

TABLE I

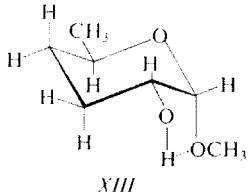
IR Spectra (frequencies, cm^{-1}) of Compounds *VII*–*IX*, *XI*–*XIII*, and *XX*–*XXIII* in the Region of O–H Bonds Absorption[a]

Compound	(OH) free	$C_{(2)}$—O—H→ →$O_{(1)}CH_3$	$C_{(2)}$—O—H→ →$O_{(r)}$	$C_{(3)}$—O—H→ →$O_{(1)}CH_3$
VII	3 634	—	3 598	3 552
VIII	3 630	—	3 603	—
IX	—	—	—	3 545[b]
XI[d]	3 629	—	3 596	—
XII	—	—	—	3 545
XIII[d]	—	3 584	—	—
XX	—	—	—	3 542[c]
XXI[d]	3 630	—	3 604	—
XXII[d]	—	3 585	—	—

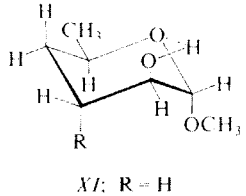
[a] Measured in a 0·002–0·003M solution in tetrachloromethane; accuracy of the reading of the band position ±2 cm^{-1}, [b] an additional small band is also present in the spectrum, of $\nu =$ = 3 596 cm^{-1} (compound *X* as impurity); [c] an additional smaller band of $\nu = 3\,590$ cm^{-1} was present in the spectrum, belonging probably to the $C_{(3)}$—O—H→$O_{(4)}$ bridge; [d] the presented data have been obtained in connection with another study[19].



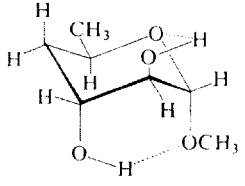
XII: R = H
IX: R = OCH_3



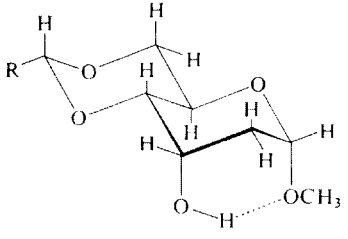
XIII



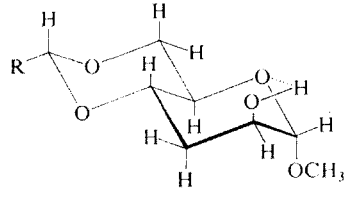
XI: R = H
VIII: R = OCH_3



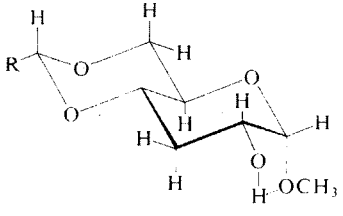
VII



XX: R = C_6H_5



XXI: R = C_6H_5



XXII: R = C_6H_5

spectra of substances with known structure and rigid conformation, *XX*–*XXII*. The observed $\Delta\nu$-shifts (with respect to the position of the free sec-hydroxyl group; when this band was absent in the spectrum, the shift was referred to the value $\nu = 3630\ cm^{-1}$) range within the values given[15] for the supposed types of hydrogen bonds. The position of the hydroxyl in trideoxyhexoside *XII* is confirmed by the formation of a strong hydrogen bond ($\Delta\nu$ 85 cm^{-1}) with the anomeric methoxyl group, which by the magnitude of the absorption band shift agrees with the bridge found in the spectrum of methyl 4,6-benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside (*XX*). Trideoxyhexoside *XIII* forms under the same conditions a somewhat weaker but nevertheless a complete bridge $C_{(2)}—O—H\rightarrow O_{(1)}CH_3$ with a shift of approximately 45 cm^{-1}, which agrees well with the value found in the spectrum of methyl 4,6-benzylidene-3-deoxy-α-D-*ribo*-hexopyranoside (*XXII*). In the spectrum of trideoxy derivative *XI* a band $\Delta\nu$ 33 cm^{-1} was observed in addition to the band of the free hydroxy group, due to a weak bridge directed to the pyranose oxygen, as evident from the comparison with similar values found in the spectrum of methyl 4,6-benzylidene-3-deoxy-α-D-*arabino*-hexopyranoside (*XXI*). In the spectrum of glycoside *VII* three bands were found, due both to the strong bridge $C_{(3)}—O—H\rightarrow O_{(1)}CH_3$,

to the weak bridge $C_{(2)}$—O—H→$O_{(r)}$, and to the free hydroxy group. The band of the strong bridge also appeared, as expected, in the spectrum of 2-O-methyl derivative *IX*, while the bands of the weaker bond and the free hydroxy group were found in the spectrum of 3-O-methyl derivative *VIII*. An appreciable agreement of the values of the absorption band positions with the values found in the spectra of reference substances with rigid conformation, *XX*–*XXII*, and the absence of other bands confirms that in agreement with the NMR data the substances investigated have preferentially the $^4C_1$ conformation.

EXPERIMENTAL

The melting points of solid substances were measured on a Kofler block and they are not corrected. Optical rotations were measured on an Opton apparatus, subjective readings. The solvents were distilled off on rotatory evaporators at 15–20 Torr and a temperature not exceeding 40°C. The following of the reaction courses by thin-layer chromatography was carried out on plates 2·5 × × 7·5 cm with a silica gel G (Merck) layer 0·2 mm thick, using the systems chloroform–methanol 100 : 2 (S_1) and chloroform–methanol 100 : 5 (S_2) for development. Preparative and analytical gas chromatographies were carried out on a CHROM III apparatus (Laboratorní přístroje, Prague) under the conditions given in the text. The NMR spectra were measured on a Varian XL-100-15 instrument in $CDCl_3$ solutions at 37°C; the assignment of the signals was carried out on the basis of decoupling experiments. The indicated values of the chemical shifts (δ-scale, tetramethylsilane as internal reference) and of the coupling constants are from first-order analysis. The infrared spectra were measured on apparatuses Perkin-Elmer 325 and Beckmann IR 20 A under the conditions indicated in the text.

Mesylation of Methyl 4,6-Dideoxy-α-D-*xylo*-hexopyranoside

To a solution of glycoside *I* (2·0 g, 12 mmol, ref.[10]) in 20 ml of pyridine 1·06 ml (1·60 g, 14 mmol) of methanesulfonyl chloride were added at −40°C and the mixture was allowed to stand at −15°C for three days. Thin-layer chromatography control in S_2 indicated that in addition to the starting substance (R_F 0·26) further substances were present in the mixture, of R_F 0·41, 0·49 and 0·66. The reaction mixture was decomposed with crushed ice and extracted with chloroform. The chloroform extract was washed with 10% sulfuric acid, water, saturated potassium hydrogen carbonate and water, and dried over magnesium sulfate. After evaporation of the solvent 3·05 g of a syrupy mixture were obtained which was separated by preparative column chromatography on 280 g of silica gel CH. Elution with chloroform gave consecutively: 900 mg (23%) of methyl 4,6-dideoxy-2,3-di-O-methanesulfonyl-α-D-*xylo*-hexopyranoside (*IV*), m.p. 167–168°C (ethanol), lit.[16] gives m.p. 164–165°C; 411 mg (13·5%) of methyl 4,6-dideoxy-3-O-methanesulfonyl--α-D-*xylo*-hexopyranoside (*III*), syrup, $[\alpha]_D^{22}$ +157 ± 1° (*c* 0·95, chloroform), for $C_8H_{16}O_6S$ (240·3) calculated: 39·99% C, 6·71% H, 13·55% S; found: 39·96% C, 6·92% H, 13·17% S; 1 570 mg (53%) of methyl 4,6-dideoxy-2-O-methanesulfonyl-α-D-*xylo*-hexopyranoside (*II*), syrup, $[\alpha]_D^{19}$ +112 ± 1° (*c* 1·2, chloroform), lit.[11] gives $[\alpha]_D^{23}$ +114·5 ± 1·5° (*c* 1·5, chloroform).

Methyl 2,3-Anhydro-4,6-dideoxy-α-D-*lyxo*-hexopyranoside (*V*)

This was prepared in a 87% yield from 2-O-methanesulfonyl derivative *II* according to a described procedure[11]. B.p. 69°C/10 Torr, $[\alpha]_D^{23}$ +52 ± 1° (*c* 1·4, chloroform); lit.[11] gives $[\alpha]_D^{25}$ +55 ± 1° (*c* 2·7, chloroform).

Methyl 2,3-Anhydro-4,6-dideoxy-α-D-*ribo*-hexopyranoside (*VI*)

A. A solution of 1M-$NaOCH_3$ in methanol (6 ml) was added to a solution of 1·29 g (5·38 mmol) of methanesulfonyl ester *III* in 20 ml of benzene and the mixture was mildly refluxed for one hour. After filtration off of the precipitated salts the filtrate was neutralized with carbon dioxide gas and the precipitated salts were filtered off. The residue after evaporation of the solvents was distilled in a vacuum to give 610 mg (79%) of an oil, b.p. 80°C/10 Torr (110°C bath temperature), $[\alpha]_D^{23}$ +77 ± 1° (*c* 1·3, chloroform); lit.[11] gives $[\alpha]_D^{23}$ +75 ± 2° (*c* 1, chloroform).

B. From 2,3-di-O-methanesulfonyl derivative *IV* anhydro derivative *VI* was prepared in the described manner[11]. The preparation contained approximately 5% of the isomer *V*. For further reactions in repeated experiments this mixture was used without further separation.

Methyl 4,6-Dideoxy-α-D-*arabino*-hexopyranoside (*VII*)

A solution of anhydro derivative *V* (1·50 g, 10·4 mmol) in 10 ml of 1M-NaOH was heated at 95–100°C for 3·5 hours under simultaneous control of the reaction course by thin-layer chromatography in system S_1; R_F of the starting compound was 0·46, R_F of the product 0·11. After complete disappearance of the starting compound from the reaction mixture the alkali was neutralized with carbon dioxide, the solution evaporated and the residue extracted with chloroform. The colourless syrup, obtained after evaporation of the chloroform solution, weighed 1·55 g and it was purified by chromatography on a column of 80 g of silica gel CH, using chloroform with a increasing amount of methanol (0–1%) for elution. The syrupy product was vacuum distilled for analysis, using a finger condenser, at 90–100°C bath temperature and 0·2 Torr. $[\alpha]_D^{20}$ +94 ± 1° (*c* 1, chloroform); NMR: $H_{(1)}$: 4·62 p.p.m., $J_{1,2}$ = 2·0 Hz; $H_{(2)}$: 3·54 p.p.m., $J_{2,1}$ = 2·0 Hz, $J_{2,3}$ = 4 Hz; $H_{(3)}$: 3·81 p.p.m., $J_{3,2}$ = 4 Hz, $J_{3,4e}$ = $J_{3,4a}$ = 3·0 Hz, 2 $H_{(4)}$: 1·48–2·0 p.p.m. (multiplet), $H_{(5)}$: 4·06 p.p.m., $J_{5,4a}$ = 9·5 Hz, $J_{5,4e}$ = 4 Hz, $J_{5,6}$ = 6·5 Hz, $H_{(6)}$: 1·21 p.p.m., $J_{6,5}$ = 6·5 Hz; OCH_3: 3·40 p.p.m.;. For $C_7H_{14}O_4$ (162·2) calculated: 51·84% C, 8·70% H; found: 52·14% C, 8·97% H. Lit.[14] gives for racemate $J_{6,5}$ = 6·3 Hz.

Methyl 4,6-Dideoxy-3-O-methyl-α-D-*arabino*-hexopyranoside (*VIII*)

A. To a solution of 430 mg of anhydro derivative *V* in 10 ml of toluene 3 ml of approximately 1M-$NaOCH_3$ in methanol were added and the mixture refluxed under control by thin-layer chromatography (in system S_1; R_F of the starting compound 0·46, R_F of product 0·27). After 15 hours refluxing the mixture was cooled and neutralized with carbon dioxide. After evaporation of toluene the residue was diluted with 5 ml of water and extracted with chloroform. The oil obtained after evaporation of chloroform (473 mg, 90%) had b.p. 68°C/0·05 Torr (bath temperature 90–100°C), $[\alpha]_D^{23}$ +83·4 ± 1° (*c* 1·8, chloroform), NMR: $H_{(1)}$: 4·57 p.p.m., $J_{1,2}$ = 3·0 Hz; $H_{(2)}$: 3·64 p.p.m., $J_{2,1}$ = 3·0 Hz, $J_{2,3}$ = 4·5 Hz; $H_{(3)}$: 3·4–3·55 p.p.m. (multiplet); $H_{(4)}$: 1·55–1·99 p.p.m. (multiplet):, $H_{(5)}$: 4·17 p.p.m., $J_{5,4a}$ = 8·5 Hz, $J_{5,4e}$ = 4·5 Hz, $J_{5,6}$ = 6·5 Hz; $H_{(6)}$: 1·24 p.p.m., $J_{6,5}$ = 6·5 Hz; OCH_3: 3·40 p.p.m., 3·45 p.p.m.. For $C_8H_{16}O_4$ (176·2) calculated: 54·53% C, 9·15% H; found: 54·52% C, 9·28% H. Lit.[14] gives for the corresponding racemate b.p. 60–70°C at 0·04 Torr.

B. A solution of 1M-$NaOCH_3$ in methanol (15 ml) was added to a solution of 1·48 g (6·16 mmol) of methane sulfonyl ester *II* in 20 ml of toluene and the mixture was stirred at 75°C (bath temp.) for 36 hours, under simultaneous control by thin-layer chromatography. After separation of the precipitated salts by filtration the filtrate was neutralized with carbon dioxide and evaporated,

The residue was extracted with boiling ether; after evaporation of the solvent the residue was distilled to afford 919·5 mg (86%) of an oil, b.p. 74°C/0·1 Torr, identical with the substance prepared by procedure *A*.

Methyl 4,6-Dideoxy-2-O-methyl-α-D-*arabino*-hexopyranoside (*IX*) and Methyl 4,6-Dideoxy-3-O-methyl-α-D-*xylo*-hexopyranoside (*X*)

A solution of 1·1 g (7·65 mmol) of anhydro derivative *VI* in 20 ml of toluene and 10·5 ml of 1M-$NaOCH_3$ in methanol was refluxed for 32 hours. A thin-layer chromatogram (in S_1) indicated the presence of substances of R_F 0·43, 0·27 and 0·14 in the reaction mixture. After neutralization with carbon dioxide and evaporation of the solvents the residue was extracted with chloroform. The product from the extract was distilled (b.p. 52—55°C/0·1 Torr, 70—100°C bath temperature), yielding 1·06 g of a material which was separated by preparative gas chromatography on a 400 × × 0·6 cm column packed with Versamide 900 (10% on Chromaton H), at 200°C working temperature and a 40 ml/min of carrier gas (hydrogen) flow. The following fractions were obtained: 317 mg (24%) of 2-O-methyl derivative *IX*, b.p. 51°C/0·1 Torr (bath 80°C), $[\alpha]_D^{21}$ +82·4 ± 1° (*c* 1·5, chloroform); NMR: $H_{(1)}$: 4·76 p.p.m., $J_{1,2}$ = 2·0 Hz; $H_{(2)}$: 3·17 p.p.m., $J_{2,1}$ = 2·0 Hz. $J_{2,3}$ = 3·5 Hz; $H_{(3)}$: 3·97 p.p.m. (multiplet), $H_{(4)}$: 1·5—1·96 p.p.m. (multiplet); $H_{(5)}$: 4·03 p.p.m., $J_{5,4a}$ = 10 Hz, $J_{5,4e}$ = 3·5 Hz, $J_{5,6}$ = 6·5 Hz; $H_{(6)}$: 1·23 p.p.m., $J_{6,5}$ = 6·5 Hz; OCH_3: 3·41 p.p.m. and 3·45 p.p.m., for $C_8H_{16}O_4$ (176·2) calculated: 54·53% C, 9·15% H; found: 54·81% C, 9·25% H; and 439 mg (33%) of 3-O-methyl derivative *X*, b.p. 56°C/0·2 Torr (bath temp. 80 to 90°C), $[\alpha]_D^{23}$ +192 ± 1° (*c* 1·2, chloroform), identical according to its IR spectrum with an authentic sample[17].

Methyl 3,4,6-Trideoxy-α-D-*threo*-hexopyranoside (*XI*)

An ethereal solution of 1010 mg (6·9 mmol) of anhydro derivative *V* was added dropwise to a suspension of 464 mg (12 mmol) of lithium aluminum hydride in 15 ml of ether and the mixture was stirred under reflux, controlling the reaction course by thin-layer chromatography in S_1 (R_F of the starting compound 0·64, R_F of product 0·43). Already after 15 minutes the reaction mixture did not contain the starting material. After decomposition with water and sodium hydroxide[18], filtration off and washing of the precipitated salts, the ethereal solution was evaporated and the residue distilled *in vacuo*. Yield 811 mg (79%) of an oil distilling at 100—120°C (bath temperature) and 20 Torr; $[\alpha]_D^{22}$ +108·5 ± 1° (*c* 1·0, chloroform), NMR: $H_{(1)}$: 4·03 p.p.m., $J_{1,2}$ = 2 Hz; $H_{(2)}$: 3·60 p.p.m., $J_{2,1}$ = 2 Hz, $J_{2,3a}$ = $J_{2,3e}$ = 3 Hz; $H_{(3)}$ and $H_{(4)}$: 1·35—2·05: p.p.m. (multiplet); $H_{(5)}$: 3·85 p.p.m., $J_{5,4a}$ = 8·5 Hz, $J_{5,4e}$ = 4·5 Hz, $J_{5,6}$ = 6·5 Hz; $H_{(6)}$, 1·18 p.p.m., $J_{6,5}$ = 6·5 Hz; OCH_3: 3·40 p.p.m.. For $C_7H_{14}O_4$ (146·2) calculated: 57·51% C 9·65% H; found: 57·36% C, 9·74% H.

Methyl 2,4,6-Trideoxy-α-D-*erythro*-hexopyranoside (*XII*) and Methyl 3,4,6-Trideoxy-α-D--*erythro*-hexopyranoside (*XIII*)

Anhydro derivative *VI* (2·3 g, 16 mmol) dissolved in 20 ml of ether was added dropwise to a suspension of 1 g (26 mmol) of lithium aluminum hydride in 30 ml of ether and the mixture was refluxed under stirring and control by thin-layer chromatography in system S_1. After two hours the presence of the starting material (R_F 0·68), in the mixture could no longer be detected but two substances of R_F 0·53 and 0·33 appeared. After decomposition of the reducing agent with water and sodium hydroxide[18] the ethereal solution was filtered, dried and evaporated. The residue (2 g of an oil) was distilled to yield 1·7 g (73%) of a mixture of trideoxyhexosides *XII* and *XIII*.

The mixture of both substances (ratio 1·64 : 1) was separated by preparative gas chromatography on a 240 × 0·6 cm column containing 10% of Tween 60 on Chromaton N as packing. Operation temperature was 110°C and the carrier gas (hydrogen) flow 60 ml/min. Distillation of the fraction with the shorter retention time gave 550 mg (32%) of pyranoside *XII*, b.p. 29°C/0·3 Torr (bath 40—45°C); $[\alpha]_D^{22}$ +149·0 ± 1° (*c* 1·9, chloroform); NMR: $H_{(1)}$: 4·83 p.p.m., $J_{1,2e} = 1·6$ Hz, $J_{1,2a} = 2·4$ Hz; 2 $H_{(2)}$:1·30—2·00 p.p.m. (multiplet together with 2 $H_{(4)}$); $H_{(3)}$: 3·90—4·35 p.p.m. (together with H_5); $J_{5,4e} = 2·5$ Hz; $J_{5,4a} = 9$ Hz; $H_{(6)}$: 1·20 p.p.m., $J_{6,5} = 6·5$ Hz; OCH_3: 3·48 p.p.m.. For $C_7H_{14}O_3$ (146·2) calculated: 57·51% C, 9·65% H; found: 57·79% C, 9·77% H. Distillation of the fraction with the longer retention time gave 320 mg (19%) of pyranoside *XIII*, b.p. 37—38°C/0·3 Torr (bath 50—55°C), $[\alpha]_D^{22}$ +154·5° ± 1° (*c* 1·1, chloroform); NMR: $H_{(1)}$: 4·63 p.p.m., $J_{1,2} = 3·5$ Hz; $H_{(2)}$ and $H_{(5)}$: 3·45—3·95 p.p.m.; $H_{(3)}$ and $H_{(4)}$: 1·30—2·0 p.p.m.; $H_{(6)}$: 1·15 p.p.m., $J_{6,5} = 6·5$ Hz; OCH_3: 3·48 p.p.m.. For $C_7H_{14}O_3$ (146·2) calculated: 57·51% C, 9·65% H; found: 57·62% C, 9·67% H.

The Preparation of Free Aldoses *XIV*—*XIX*

A solution of 0·6 to 0·9 mmol of glycoside in 2—4 ml of 0·25M H_2SO_4 was heated at 90°C for 1—2 hours under control by thin-layer chromatography. After cooling the reaction mixture was filtered through a column of Amberlite IR-4-B (OH^-). After evaporation of the neutral solution the syrupy residue was distilled at 90—100°C bath temperature and 0·1 to 0·2 Torr pressure, and the crystalline product was sublimated at 50—60°C bath temperature and 0·1—0·2 Torr. In this manner 4,6-dideoxy-D-*arabino*-hexose (*XIV*), 4,6-dideoxy-3-O-methyl-D-*arabino*-hexose (*XV*), 4,6-dideoxy-2-O-methyl-D-*arabino*-hexose (*XVI*), 3,4,6-trideoxy-D-*threo*-hexose (*XVII*) and 3,4,6-trideoxy-D-*erythro*-hexose (*XIX*) were obtained.

TABLE II

Physical Constants and Elemental Analyses of Aldoses *XIV*—*XIX*

Aldose (yield, %)	M.p. °C	$[\alpha]_D^{23}$ (equil.) (conc., solvent)	Calculated/Found	
			% C	% H
XIV	—	−2·1 ± 0·5°	48·64	8·16
(92)		(*c* 1·5, water)	48·34	8·30
XV	93—95	−15·9 ± 1·5°	51·84	8·70
(86)		(*c* 0·8, $CHCl_3$)	51·72	8·70
XVI	—	+24·8 ± 2°	51·84	8·70
(90)		(*c* 1·5, $CHCl_3$)	51·79	8·81
XVII	92—95	+42·7° ± 1°	54·53	9·15
(86)		(*c* 1·4, $CHCl_3$)	54·24	8·95
XVIII	—	+57·3° ± 1·5°	54·53	9·15
(66)		(*c* 2·0, $CHCl_3$)	54·85	9·21
XIX	56—58	+23·6 ± 1·5°	54·53	9·15
(90)		(*c* 1·7, $CHCl_3$)	54·23	8·86

2,4,6-Trideoxy-D-*erythro*-hexose (*XVIII*) was liberated from glycoside *XII* in the following manner: A solution of 84·5 mg (0·58 mmol) of glycoside *XII* in 2 ml of 60% acetic acid was heated at 60°C. After 30 minutes the reaction mixture did not contain according to thin-layer analysis in S_2 any starting material (R_F 0·32), but only the product of its hydrolysis (R_F 0·13). The reaction mixture was diluted with water and evaporated. The syrupy residue (75 mg) was purified by chromatography on a column of 2·5 g of silica gel using chloroform and chloroform–methanol (1%) mixture for elution. The chromatographically pure syrup was distilled in a vacuum (rotary oil pump; finger-shape condenser). The review of yields, basic constants and elemental analyses of single aldoses are listed in Table II.

Elemental analyses were carried out in the laboratory of organic analysis (head Dr L. Helešic) at the Department of Organic Chemistry, Institute of Chemical Technology, Prague, and in the analytical department (head Dr J. Horáček) of the Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague. The spectra were measured in the laboratory of NMR spectroscopy (head Dr P. Trška) at the Department of Organic Chemistry, Institute of Chemical Technology, Prague, in the laboratory of absorption spectroscopy (head Prof. B. Hájek) of the same Institute, and in the spectral department (head Dr F. Hanousek) of the Institute of Inorganic Chemistry, Czechoslovak Academy of Sciences, Řež - Prague. — We thank the staff of these departments for their effective collaboration. We further thank Mrs J. Červená for technical assistance during the preparation of the starting compound and Mr V. Ineman for the analysis and the separation of substances by gas chromatography.

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