PARTIAL METHYLATION OF METHYL 2,6-DIDEOXY-α-D-*ribo*-HEXOPYRANOSIDE*

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On the basis of substituent distribution in partial etherification of the glycoside *I* with methyl iodide and solid sodium hydroxide in acetonitrile, the relative rate constants of side and consecutive reactions have been calculated. Differences in methylation rates of the particular hydroxylic functions are explained by the influence of internal hydrogen bonds and the steric effect of the vicinal methoxyl group.

In the preceding paper[1] of this Series, partial methylation of methyl 4,6-dideoxyhexosides has been examined. In connection with detailed investigations on partial alkylation of monosaccharides, attention has been now focussed on a further set of model compounds with another position of deoxy groups. Of a special interest in this respect appear the methyl 2,6-dideoxyhexosides, the both hydroxylic functions of which are out of the reach of the polar effect of the hemiacetal grouping. In the present paper, the partial methylation of methyl 2,6-dideoxy-α-D-*ribo*-hexopyranoside (*I*) is examined with the aim to determine a quantitative relationship between the particular rate constants and to present a theoretical motivation of the results.

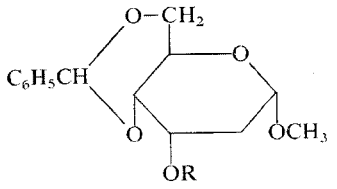
In the methylation of the glycoside *I* (prepared according to Haga and coworkers[2]), methyl 2,6-dideoxy-3-O-methyl-α-D-*ribo*-hexopyranoside (*II*) and methyl 2,6-dideoxy-4-O-methyl-α-D-*ribo*-hexopyranoside (*III*) are formed in the first stage. In the subsequent stage, the monomethyl ethers *II* and *III* afford the same product, namely, methyl 2,6-dideoxy-3,4-di-O-methyl-α-D-*ribo*-hexopyranoside (*IV*), see Scheme 1.

From the qualitative standpoint, the reaction mixture was examined by means of gas chromatography in combination with mass spectrometry. The mass spectrometry allowed to identify the dihydroxy derivative *I* and the di-O-methyl derivative *IV* but was not operative in determination of the substituent position in monomethyl ethers *II* and *III*. In the latter respect, comparison of retention times with those of standard compounds obtained by another route was successful.

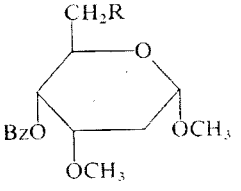
The 3-O-methyl ether[3,4] *II* was synthesized from methyl 4,6-O-benzylidene-2-de-

* Part III in the series Partial Alkylations of Dideoxy Sugars; Part II: This Journal *40*, 300 (1975).

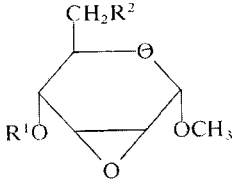
oxy-α-D-*ribo*-hexopyranoside[5-7] (*V*). Methylation of compound *V* with methyl iodide and sodium hydride afforded methyl 4,6-O-benzylidene-2-deoxy-3-O-methyl--α-D-*ribo*-hexopyranoside[8,9] (*VI*), the reaction of which with N-bromosuccinimide yielded methyl 4-O-benzoyl-6-bromo-2,6-dideoxy-3-O-methyl-α-D-*ribo*-hexopyranoside (*VII*). By hydrogenolysis under catalysis of Raney nickel, compound *VII* was converted to methyl 4-O-benzoyl-2,6-dideoxy-3-O-methyl-α-D-*ribo*-hexopyranoside (*VIII*), the catalytic debenzoylation of which yielded the derivative *II*.



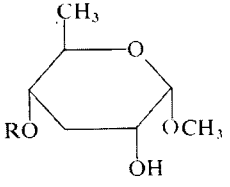
V, R = H
VI, R = CH_3



VII, R = Br
VIII, R = H



IX, R^1 = H, R^2 = H
X, R^1 = H, R^2 = OTs
XI, R^1 = H, R^2 = I
XII, R^1 = CH_3, R^2 = H



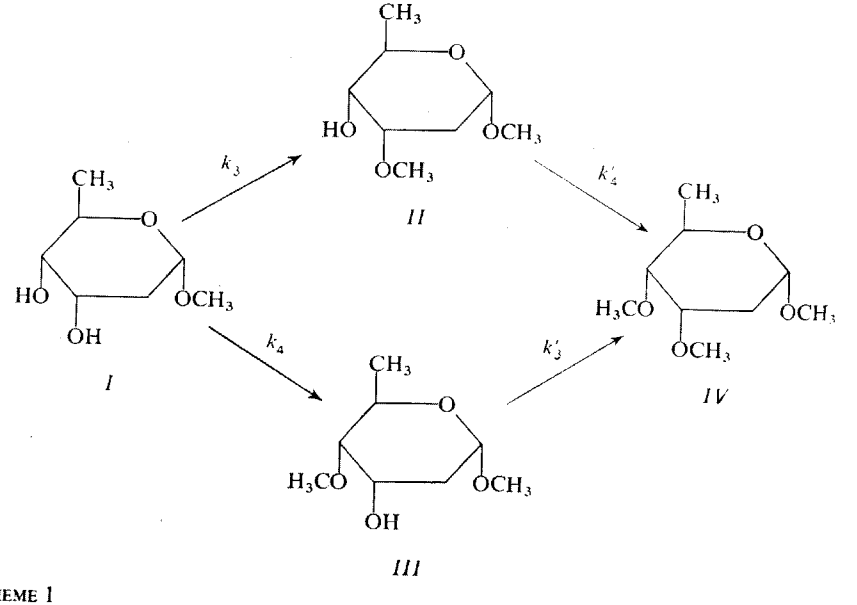
XIII, R = CH_3
XIV, R = H
Bz = benzoyl
Ts = *p*-toluenesulphonyl

The 4-O-methyl ether[10] *III* was prepared from methyl 2,3-anhydro-6-deoxy--α-D-allopyranoside (*IX*) obtained from methyl 2,3-anhydro-6-O-*p*-toluenesulfonyl--α-D-allopyranoside[11] (*X*) in the usual manner *via* methyl 2,3-anhydro-6-deoxy--6-iodo-α-D-allopyranoside (*XI*). Methylation of compound *IX* with methyl iodide and sodium hydride afforded methyl 2,3-anhydro-6-deoxy-4-O-methyl-α-D-allopyranoside (*XII*). When reduced with sodium bis(2-methoxyethoxy)aluminium hydride (Synhydride) or lithium aluminium hydride, compound *XII* afforded a mixture of two substances, namely, methyl 2,6-dideoxy-4-O-methyl-α-D-*ribo*-hexopyranoside (*III*) and methyl 3,6-dideoxy-4-O-methyl-α-D-*ribo*-hexopyranoside (*XIII*). Compound *XIII* was not isolated by preparative gas chromatography in pure state but its structure is in accord with the retention time identical with that of the partial methylation product of methyl 3,6-dideoxy-α-D-*ribo*-hexopyranoside[12] (*XIV*); the structure also corresponds to the ^{1}H-NMR spectrum of the crude substance *XIII*.

The ratio of compounds *III* and *XIII* was 1 : 1 in the Synhydride reduction and 2 : 1 in the lithium aluminium hydride reduction. On a larger scale, the monomethyl ethers *II* and *III* were prepared by partial methylation of the glycoside *I*. Compounds *I*–*IV* were isolated from the reaction mixture by preparative gas chromatography. The di-O-methyl ether *IV* was also prepared by a complete methylation of compound *I* with methyl iodide and sodium hydride in formaldehyde dimethylacetal.

The partial methylation (Scheme 1) of the dihydroxy derivative *I* was performed with methyl iodide and sodium hydroxide in acetonitrile. In the particular assays, the molar ratio of sodium hydroxide to the starting diol was gradually varied from 0·5 to 1·8. The mixture containing the unreacted starting compound *I* and its etherification products, namely, the monomethyl ethers *II* and *III*, and the di-O-methyl ether *IV*, was quantitatively analysed by means of gas chromatography (Table I).

As stated earlier[1,13], no conclusions on the reactivity of the $C_{(3)}$—OH and $C_{(4)}$—OH hydroxylic functions in the first stage can be drawn from the percentual content of components of the reaction mixture after the partial methylation of the diol *I*. The known mixtures of monomethyl ethers *II* and *III* were, therefore, subjected to an additional treatment with methyl iodide in acetonitrile in the presence of 0·5 equivalent of sodium hydroxide. The resulting reaction mixtures were then analysed by means of gas chromatography and the thus-obtained data were used in calculation[13] of the *K* value, $K = k'_3/k'_4 = 5{\cdot}77$. This value and data shown in Table I were used to solve equations[13] (*1*) and (*2*) describing kinetics of side and consecutive reactions in Scheme 1.



SCHEME 1

$$C_{II} = \frac{p}{q-1}\left(C_I - C_{I_0}^{(1-q)} \cdot C_I^q\right) \qquad (1)$$

$$C_{III} = \frac{1-p}{K \cdot q - 1}\left(C_I - C_{I_0}^{(1-K.q)} \cdot C_I^{K.q}\right) \quad C_{I_0} = 100\% \qquad (2)$$

By means of equations (*1*) and (*2*), the q and p values were determined, namely, $q = 0{\cdot}11$ and $p = 0{\cdot}497$, and then the relative rate constants $k_4/k_3 = 1{\cdot}01$, $k'_3/k_3 = 1{\cdot}28$, and $k_4/k'_4 = 4{\cdot}57$ were calculated.

On the basis of relative rate constant values in Scheme 1, the following conclusions can be drawn: *1*) In methylation of the pyranoside *I* with methyl iodide and sodium hydroxide in acetonitrile, the monomethyl ethers *II* and *III* are formed by an almost equal rate ($k_4/k_3 = 1{\cdot}01$). *2*) In the subsequent methylation step, the 4-O-methyl ether *III* reacts with the formation of the di-O-methyl ether *IV* almost six times as fast as the 3-O-methyl derivative *II* ($k'_3/k'_4 = 5{\cdot}77$). *3*) Let us now compare the etherification rate of the same hydroxylic function in an unsubstituted and in a monosubstituted derivative. Thus, the hydroxylic function at position 4 of the pyranose ring reacts in the glycoside *I* 4·57 times as fast as in the case of the 3-O-methyl derivative *II* ($k_4/k'_4 = 4{\cdot}57$). On the other hand, the etherification of the hydroxylic function on the $C_{(3)}$ carbon atom is somewhat slower in the case of the glycoside *I* than with the 4-O-methyl derivative *III* ($k_3/k'_3 = 0{\cdot}78$).

TABLE I

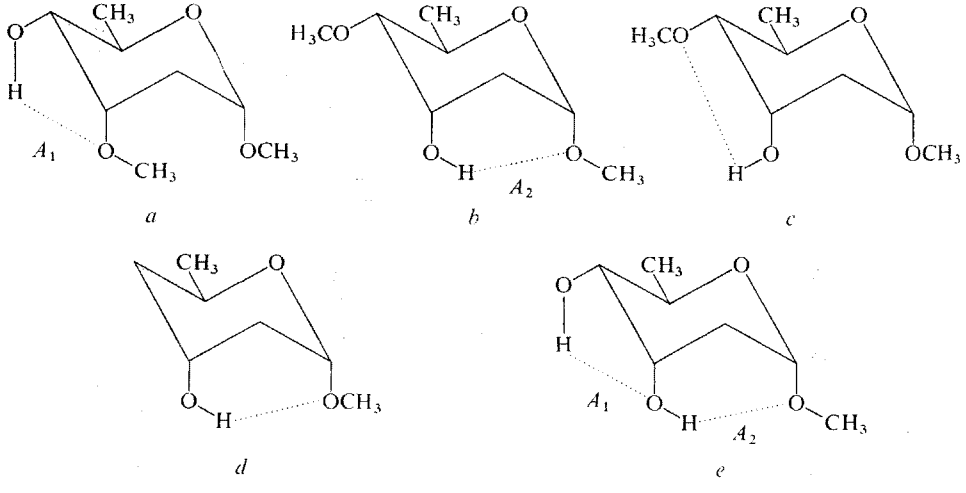
Content (%) of Reaction Mixtures in Partial Methylations of the Glycoside *I*

For the reaction conditions see the Experimental. The content of mixtures was read from integration records of three determinations and calculated from each record by means of the relative response of the detector. The response was determined by analysis of mixtures containing known amounts of standard compounds. The data refer to the glycoside *I*.

Molar ratio NaOH/*I*	Glycoside *I*	3-O-Methyl ether *II*	4-O-Methyl ether *III*	Di-O-methyl ether *IV*
0·5	87·4	5·8	6·3	0·5
0·7	64·7	16·5	15·7	3·1
1·0	60·2	19·3	17·6	2·9
1·2	47·3	25·8	20·6	6·3
1·3	44·1	26·5	21·0	8·4
1·4	30·1	32·9	22·5	14·5
1·5	20·4	35·3	21·0	23·3
1·6	7·8	37·9	14·6	39·7
1·8	2·6	34·9	9·0	53·5

As shown by ^{1}H-NMR spectra, all of the above discussed compounds exist in the $^4C_1$ conformation ($J_{1,2ax} = 4{\cdot}5$ Hz, $J_{1,2eq} < 2$ Hz), in which the $C_{(3)}$—OH group is axial and the $C_{(4)}$—OH equatorial. Consequently, a different rate of etherification may be *a priori* expected in favour of the more accessible equatorial hydroxylic function. However, this assumption *per se* is not sufficient for a satisfactory explanation of the above results (*cf.* the methylation of methyl 4,6-dideoxyglycosides[1]). To our opinion, the reactivity of hydroxylic functions in the present methylation of glycosides *I*, *II*, and *III* is markedly affected by the different nucleophilicity of oxygen atoms in hydroxylic functions due to the formation of intramolecular hydrogen bonds[1]. The existence of these bonds was established by measurement of IR spectra of compounds *I*–*III* (*c* 2 . 10^{-3}M solutions in tetrachloromethane) in the 3000 to 3800 cm^{-1} region. (The intramolecular hydrogen bonds may exist[14] even in the medium of acetonitrile which is a relatively weak acceptor of hydrogen bonds despite the considerably high dielectric constant[15]).

In the IR spectrum of the 3-O-methyl derivative *II*, the intensive absorption band $\nu(OH) = 3561$ cm^{-1} corresponds to the intramolecular hydrogen bond A_1 (Scheme 2, *a*). The intensive absorption band $\nu(OH) = 3545$ cm^{-1} of the 4-O-methyl derivative *III* apparently corresponds to a hydrogen bond in the six membered ring (Scheme 2, *b*) since the other possible bond (Scheme 2, *c*) with an almost identical steric arrangement to that of A_1 should exhibit the $\nu(OH)$ value equal to about 3 560 cm^{-1}. The assignement A_2 is supported by the same $\nu(OH)$ value (3545 cm^{-1}) in the case of methyl 2,4,6-trideoxy-α-D-*erythro*-hexopyranoside[16] (Scheme 2, *d*).



SCHEME 2

The two intensive absorption bands $\nu(OH) = 3521\ cm^{-1}$ and $\nu(OH) = 3546\ cm^{-1}$ in the spectrum of the dihydroxy compound *I* can be explained by the formation of a "double bridge" (*cf.*[17]). Its existence may be inferred from comparison of band positions in the spectrum of compound *I* with those in spectra of compounds *II* and *III*. The strong hydrogen bond A_2 (Scheme 2, *e*) increases the electron density of the oxygen atom at $C_{(3)}$ and thus the strength of the hydrogen bond A_1 (Scheme 2, *e*). This effect manifests itself by a shift of the hydrogen bond A_1 vibration to lower wavenumber values with respect to the 3-O-methyl ether *II* (from $3561\ cm^{-1}$ to $3546\ cm^{-1}$). Simultaneously, due to the formation of the hydrogen bond A_1 which involves the oxygen atom of the hydroxylic function at the $C_{(3)}$ carbon atom as the donor of the electron pair, the strength of the hydrogen bond A_2 is increased; this effect results in a shift of the vibration from $3545\ cm^{-1}$ to $3521\ cm^{-1}$. An opposite assignment of the observed absorption bands in the spectrum of the dihydroxy derivative *I* would require a shift by about $40\ cm^{-1}$ in the case of bond A_1 and an almost unchanged vibration value of bond A_2. Such an alternative appears farly less probable.

On the basis of IR spectra, the experimental observations might be explained as follows: *1*) Concerning the reactivity of hydroxylic functions in monomethyl ethers *II* and *III*, the higher reactivity of the sterically less accessible axial $C_{(3)}$—OH hydroxylic function may be explained on the basis of a different nucleophilicity of oxygen atoms of these groups. The stronger intramolecular hydrogen bond in the case of the 4-O-methyl derivative *III* (Scheme 2, *b*) results in a higher nucleophilicity of the $C_{(3)}$—OH group oxygen atom and consequently, a markedly higher reactivity of the 4-O-methyl ether *III* when compared with that of the 3-O-methyl derivative *II* ($k'_3/k'_4 = 5{\cdot}77$). *2*) The $C_{(4)}$—OH hydroxylic function is more fastly etherified in the glycoside *I* than in the 3-O-methyl derivative *II*, probably due to the existence of a "double bridge" (*cf.*[1,17]) which enhances the strength of the A_1 bond and thus the nucleophilicity of the oxygen atom on the $C_{(4)}$ carbon atom when compared with the nucleophilicity of the oxygen atom of the hydroxylic function in the 4-O-methyl derivative *II*. The observed k_4/k'_4 value (4·57) apparently comprises the steric effect of the vicinal methoxyl group which may somewhat lower[1] the reactivity of the hydroxylic function in the 3-O-methyl ether *II*. Concerning the methylation of the $C_{(3)}$—OH hydroxylic function, the reaction is somewhat slower in the case of the glycoside *I* than with the 4-O-methyl derivative *III* ($k_3/k'_3 = 0{\cdot}78$). When compared with the nucleophilicity of the oxygen atom at $C_{(3)}$ in the 4-O-methyl ether *III*, the nucleophilicity of oxygen on the same hydroxylic function of the glycoside *I* is lowered because of the existence of the "double bridge". The reactivity decrease is probably partly compensated by the retarding steric effect of the vicinal methoxyl group in the 4-O-methyl derivative *III*. *3*) The almost identical reactivity of the two hydroxylic functions ($k_4/k_3 = 1{\cdot}01$) determined in the case of the dihydroxy derivative *I* might be due to the enhanced nucleophilicity of the oxygen

atom at $C_{(4)}$ by the action of the "double bridge" as well as to the lowered nucleophilicity of the oxygen atom at $C_{(3)}$ owing to the A_1 bond. These effects along with the efffect of the disadvantageous position of the axial hydroxylic function at the $C_{(3)}$ carbon atom appear to contribute to equalisation of the reactivity of the $C_{(3)}$ and $C_{(4)}$ hydroxylic functions in the glycoside *I* despite the markedly different reactivity of these functions in glycosides *II* and *III*.

EXPERIMENTAL

Melting points (uncorrected) were taken on a heated microscope stage (Kofler block). Optical rotations were measured on an Opton polarimeter at 20°C. Solvents were taken down on a rotatory evaporator at 40°C under diminished pressure of a water pump. Liquids were distilled under diminished pressure of an oil pump (1·33 Pa). Thin-layer chromatography was performed on the Stahl silica gel G (particle size, 10—40 μm; Merck, Darmstadt), on 25 × 75 mm layers, 0·2—0·3 mm thick. Spots were detected by a spray with conc. sulfuric acid and the subsequent carbonisation. Analytical samples were dried (except for distilled liquids or sublimed solids) at 20°C/2·66 Pa.

The IR spectra were measured in tetrachloromethane in 20 mm quartz cells on a Perkin Elmer 325 apparatus (slit width 1·2 cm^{-1} at 3400 cm^{-1}). Mass spectra were recorded on a Varian MAT-311 apparatus. The ^{1}H-NMR spectra (tetramethylsilane as internal standard) were taken on a Varian XL-100-15 apparatus; chemical shifts in the δ scale (p.p.m.), coupling constants in Hz. Gas chromatography was performed on a Chrom 3 apparatus (Laboratorní přístroje, Prague, Czechoslovakia); flame-ionisation detection; nitrogen as carrier gas. Preparative runs were carried out on the same apparatus with hydrogen as carrier gas (catarometer as detector).

Methyl 4,6-O-Benzylidene-2-deoxy-3-O-methyl-α-D-*ribo*-hexopyranoside (*VI*)

Compound *V* (0·5 g; 1·88 mmol) in benzene (100 ml) was stirred with sodium hydride (120 mg; 5·2 mmol) for 1 h and the mixture treated dropwise with methyl iodide (5 ml). The reaction course was checked by thin-layer chromatography in 94 : 6 benzene–acetone. When the starting compound *V* disappeared, the excess sodium hydride was decomposed with methanol (50 ml) and the mixture evaporated. The residue was extracted with chloroform, the extracts washed with water, dried over anhydrous magnesium sulfate, filtered, and the filtrate evaporated. The residue was crystallised from ether and light petroleum to afford 510 mg (97%) of compound *VI*, m.p. 101—102°C, $[\alpha]_D$ +125° (*c* 0·8; chloroform). Reported[8], m.p. 88—90° and $[\alpha]_D^{25}$ +111° (*c* 1·05; chloroform), and[9] m.p. 99—100°C, $[\alpha]_D$ +125°.

Methyl 4-O-Benzoyl-6-bromo-2,6-dideoxy-3-O-methyl-α-D-*ribo*-hexopyranoside (*VII*)

Compound *VI* (1·14 g; 4·08 mmol) in tetrachloromethane (50 ml) was treated with barium carbonate (1·6 g) and N-bromosuccinimide (0·8 g) and the whole mixture was refluxed. The reaction course was checked by thin-layer chromatography in 94 : 6 benzene–acetone. When the reaction was complete, the mixture was filtered and the material on the filter washed with boiling tetrachloromethane (100 ml). The filtrate and washings were combined and evaporated. The residue was taken up into chloroform (150 ml), the solution washed with water, dried over anhydrous magnesium sulfate, filtered, and the filtrate evaporated. The residual sirup (1·2 g) was chromatographed on silica gel to afford 394 mg (26%) of compound *VII*, m.p. 67—70°C, $[\alpha]_D$ +137° (*c* 0·7; chloroform). For $C_{15}H_{19}BrO_5$ (359·2) calculated: 50·15% C, 5·33% H, 22·23% Br; found:

50·36% C, 5·45% H, 21·67% Br. The ^{1}H-NMR spectrum ($CDCl_3$): 1·94 (1 H, dt, $J_{2eq,2ax} = 15$, $J_{1,2ax} = 3{\cdot}4$, $J_{2ax,3} = 3{\cdot}4$, H-2ax); 2·28 (1 H, dq, $J_{2eq,2ax} = 15$, $J_{1,2eq} < 2$, $J_{2eq,3} = 3{\cdot}1$, H-2 eq); 3·40 (3 H, s, OCH_3); 3·46 (3 H, s, OCH_3); 3·46—3·70 (2 H, m, CH_2Br); 3·94 (1 H, m, $J_{2ax,3} = 3{\cdot}4$, $J_{2eq,3} = 3{\cdot}1$, $J_{3,4} = 3{\cdot}1$, H-3); 4·52 (1 H, dq, $J_{4,5} = 9{\cdot}5$, $J_{5,6} = 3{\cdot}0$, $J_{5,6'} = 5{\cdot}8$, H-5); 4·82 (1 H, d, $J_{1,2ax} = 3{\cdot}4$, $J_{1,2eq} < 2$, H-1); 5·06 (1 H, q, $J_{4,5} = 9{\cdot}5$, $J_{3,4} = 3{\cdot}1$, H-4); 7·3—7·6 (3 H—Ar); 8·0—8·12 (2 H—Ar).

Methyl 4-O-Benzoyl-2,6-dideoxy-3-O-methyl-α-D-*ribo*-hexopyranoside (*VIII*)

A solution of compound *VII* (392 mg; 1·14 mmol) in methanol (100 ml) was treated with Raney nickel W-6 (10 ml) and 20% diethylamine in methanol (0·3 ml), and the whole mixture was stirred under hydrogen at atmospheric pressure for 5 h at 20°C. When the reaction was complete (as determined by thin-layer chromatography in 94 : 6 benzene–acetone), the mixture was filtered, the filtrate evaporated, the residue diluted with water (1·5 ml), and extracted with chloroform. The extracts were combined, washed with water, dried over anhydrous magnesium sulfate, filtered, and the filtrate evaporated. Yield, 297 mg (97·5%) of compound *VIII* as a sirup, $[\alpha]_D$ +163° (*c* 0·6; chloroform). For $C_{15}H_{20}O_5$ (280·3) calculated: 64·27% C, 7·19% H; found: 64·49% C, 7·51% H. The ^{1}H-NMR spectrum ($CDCl_3$): 1·26 (3 H, d, $J_{5,6} = 6{\cdot}0$, CH_3—CH); 1·92 (1 H, dt, $J_{2ax,3} = 4{\cdot}0$, $J_{1,2ax} = 4{\cdot}0$, $J_{2eq,2ax} = 15{\cdot}0$, H-2 ax); 2·24 (1 H, dq, $J_{2ax,2eq} = 15$, $J_{2eq,3} = 4{\cdot}0$, $J_{1,2eq} = 2{\cdot}0$, H-2 eq), 3·40 (6 H, s, 2 × OCH_3); 3·85 (1 H, m, $J_{3,4} = 3{\cdot}0$, $J_{2eq,3} = 4{\cdot}0$, $J_{2ax,3} = 4{\cdot}0$, H-3); 4·39 (1 H, o, $J_{4,5} = 9{\cdot}0$, $J_{5,6} = 6{\cdot}0$, H-5); 4·70 (1 H, q, $J_{1,2eq} = 2{\cdot}0$, $J_{1,2ax} = 4{\cdot}0$, H-1); 4·88 (1 H, q, $J_{3,4} = 3{\cdot}0$, $J_{4,5} = 9{\cdot}0$, H-4); 7·3—7·6 (3 H—Ar); 8·0—8·12 (2 H—Ar).

Methyl 2,6-Dideoxy-3-O-methyl-α-D-*ribo*-hexopyranoside (*II*)

A solution of compound *VIII* (110 mg; 0·39 mmol) in methanol (50 ml) was treated with sodium (about 5 mg) and the solution was heated at 40°C for 4 h, *i.e.*, until the reaction was complete (thin-layer chromatography). The solution was then saturated with carbon dioxide to the loss of alkalinity and evaporated. A suspension of the residue in water (1 ml) was extracted with two 0·6 ml portions of ether in order to remove methyl benzoate. Methyl benzoate can also be removed by coevaporation with water. The aqueous layer was evaporated and the residue extracted with ethyl acetate. The extracts were combined, dried over anhydrous magnesium sulfate, filtered, and evaporated. Yield, 46 mg (66·6%) of compound *II*, m.p. 40—43°C, $[\alpha]_D$ +214° (*c* 0·7; methanol); reported[3], m.p. 35°C, $[\alpha]_D^{14}$ +210° (*c* 1·263; methanol), and [4] m.p. 41—44°C, $[\alpha]_D^{17}$ +212° (*c* 1·21; methanol). MS data, *m/e* (%): 145 (23), 127 (25), 113 (33), 101 (16), 99 (18), 95 (23), 87 (31), 86 (22), 75 (26), 74 (100), 72 (25), 71 (44), 69 (33), 59 (77).

Methyl 2,3-Anhydro-6-deoxy-6-iodo-α-D-allopyranoside (*XI*)

A mixture of compound *X* (2 g), sodium iodide (1 g), and acetone (20 ml) was heated (steam bath) in a sealed glass tube for 2 h, cooled down, and filtered. The filtrate was evaporated, the residue diluted with chloroform, the chloroform solution washed with water, dried over anhydrous magnesium sulfate, filtered, and the filtrate evaporated. Crystallisation of the residue (1·7 g) from ethyl acetate yielded 1·34 g (77·4%) of compound *XI*, m.p. 130—132°C, $[\alpha]_D$ +107° (*c* 0·7; chloroform). For $C_7H_{11}IO_4$ (286·1) calculated: 29·39% C, 3·88% H, 44·36% I; found: 29·47% C, 3·89% H, 44·32% I.

Methyl 2,3-Anhydro-6-deoxy-α-D-allopyranoside (*IX*)

A mixture of compound *XI* (1·02 g), methanol (10 ml), 5% palladium on alumina (0·5 g), and triethylamine (0·5 ml) was stirred under hydrogen at 20°C (atmospheric pressure) until the reaction was complete. The mixture was then filtered, the filtrate evaporated, the residue diluted with chloroform, the chloroform solution washed with water, dried over anhydrous magnesium sulfate, filtered, and the filtrate evaporated. The residue was sublimed under diminished pressure (water pump) at 70—80°C. Yield, 270 mg (47·3%) of compound *IX*, m.p. 100—101°C, $[\alpha]_D$ +168° (*c* 0·7; chloroform). For $C_7H_{12}O_4$ (160·2) calculated: 52·48% C, 7·55% H; found: 52·59% C 7·72% H.

Methyl 2,3-Anhydro-6-deoxy-4-O-methyl-α-D-allopyranoside (*XII*)

Sodium hydride (80 mg) was added portionwise to compound *IX* (330 mg; 2·06 mmol) in benzene (80 ml), the mixture stirred at room temperature for 1 h, and then treated dropwise with methyl iodide (5 ml). The stirring was continued until the reaction was complete (as determined by thin-layer chromatography in 9 : 1 benzene–acetone). The excess hydride was decomposed with methanol, the solvents were evaporated, and the residue was extracted with chloroform. The extracts were combined, washed with water, dried over anhydrous magnesium sulfate, filtered, the filtrate evaporated, and the residue crystallised from ether and light petroleum. Yield, 341 mg (95·5%) of compound *XII*, m.p. 82—83°C, $[\alpha]_D$ +194° (*c* 0·5; chloroform). For $C_8H_{14}O_4$ (174·2) calculated: 55·16% C, 8·05% H; found: 55·00% C, 8·02% H.

Reduction of Compound *XII*

A. Compound *XII* (80 mg; 0·46 mmol) in benzene (50 ml) was treated dropwise under stirring with sodium bis(2-methoxyethoxy)aluminium hydride (2 ml of a 70% solution in benzene) and then refluxed until the reaction was complete (thin-layer chromatography). The mixture was decomposed with 15% aqueous sodium potassium tartrate (Seignette salt), the benzene layer washed with water, dried over anhydrous magnesium sulfate, filtered, and the filtrate evaporated to afford 70 mg of a sirup representing (gas chromatography) an approximately 1 : 1 mixture of compounds *III* and *XIII*.

B. A solution of compound *XII* (341 mg; 1·94 mmol) in ether (50 ml) was added dropwise with stirring into a suspension of lithium aluminium hydride (270 mg) in ether (50 ml). When the reaction was complete (thin-layer chromatography in 9 : 1 benzene–acetone), the mixture was decomposed successively with water (0·27 ml), 15% aqueous sodium hydroxide (0·27 ml), and water again (0·81 ml). The precipitate was filtered off and the filtrate was evaporated. Yield, 255 mg of a sirup representing an approximately 2 : 1 mixture of compounds *III* and *XIII*. Compound *III* was isolated by means of preparative gas chromatography on a 500 × 1 cm column packed with 10% Versamide 900 on Chromaton N-AW at 180°C and the hydrogen flow rate of 1 ml per second. Yield, 89 mg (25·8%) of the sirupous methyl 2,6-dideoxy-4-O-methyl-α-D-*ribo*-hexopyranoside (*III*), the optical rotation of which, $[\alpha]_D$ +210° (*c* 0·35; chloroform), markedly differs from the reported value[10], $[\alpha]_D$ +121° (*c* 0·5; chloroform). For $C_8H_{16}O_4$ (176·2) calculated: 54·53% C, 9·15% H; found: 54,87% C, 9·49% H, ^{1}H-NMR spectrum ($CDCl_3$): 1·31 (3 H, d, $J_{5,6}$ = 6·0, CH_3—CH); 1·83 (1 H, dt, $J_{2eq,2ax}$ = 15, $J_{1,2ax}$ = 3·5, $J_{2ax,3}$ = 3·5, H-2 ax); 2·18 (1 H, m, $J_{2eq,2ax}$ = 15, $J_{1,2eq}$ < 1·5, $J_{2eq,3}$ = 1·5, H-2 eq); 2·83 (1 H, q, $J_{3,4}$ = 3·0, $J_{4,5}$ = 9·5, H-4); 3·3 (1 H, OH); 3·38 (3 H, s, OCH_3); 3·44 (3 H, s, OCH_3); 3·95 (1 H, o, $J_{4,5}$ = 9·5, $J_{5,6}$ = 6·0, H-5); 4·14—4·26 (1 H, m, H-3); 4·74 (1 H, q, $J_{1,2ax}$ = 3·5, $J_{1,2eq}$ < < 1·5, H-1). MS data, *m/e* (%): 176 (1), 145 (2), 127 (11), 118 (8), 100 (7), 74 (100), 73 (11), 72 (35), 71 (24), 59 (29).

Partial Methylation of the 3,6-Dideoxy Derivative *XIV*

Powdered sodium hydroxide (about 5 mg) was added to a solution containing compound[12] *XIV* (20 mg), acetonitrile (25 ml), and methyl iodide (0·5 ml). The mixture was stirred at 20°C for 24 h, evaporated, and the residue extracted with a mixture of chloroform and acetone. Gas chromatography on a 360 × 0·2 cm column packed with 10% Versamide 900 on Varaport 30 at 190°C and the helium flow rate of 18 ml per second indicated the presence of four compounds with retention times 269 s, 314 s, 493 s (compound *XIII*, obtained as by-product in reduction of compound *XII*), and 1 690 s (compound *XIV*). The ^{1}H-NMR spectrum ($CDCl_3$) of compound *XIII*: 1·14 (3 H, d, $J_{5,6}$ = 6·0, CH_3—CH); 1·36 (1 H, q, $J_{3eq,3ax}$ = 11·5, $J_{2,3ax}$ = 11·5, $J_{3ax,4}$ = = 11·5, H-3 ax); 1·67 (1 H, OH); 2·23 (1 H, dt, $J_{3,3ax}$ = 11·5, $J_{2,3eq}$ = 4·5, $J_{3eq,4}$ = 4·5, H-3 eq); 2·73 (1 H, m, $J_{3eq,4}$ = 11·5, $J_{4,5}$ = 9·0, H-4); 3·30 (3 H, s, OCH_3); 3·41 (3 H, s, OCH_3); 3·25—3·45 (2 H, m, H-5, H-2); 4·43 (1 H, d, $J_{1,2}$ = 3·5, H-1).

Methyl 2,6-Dideoxy-3,4-di-O-methyl-α-D-*ribo*-hexopyranoside (*IV*)

Sodium hydride (80 mg) was added to the dihydroxy derivative *I* (80 mg; 0·49 mmol) in formaldehyde dimethylacetal (50 ml), the mixture stirred at room temperature for 1 h, and then treated dropwise with methyl iodide (3 ml). When the reaction of compound *I* and intermediates *II* and *III* with methyl iodide was complete (thin-layer chromatography), the excess sodium hydride was decomposed by the addition of methanol. The mixture was evaporated, extracted with chloroform, the extracts combined, washed with water, dried over anhydrous magnesium sulfate, filtered, and the filtrate evaporated. Yield, 85 mg (90·6%) of compound *IV* as a sirup, $[\alpha]_D$ +174° (*c* 0·8; chloroform). For $C_9H_{18}O_4$ (190·2) calculated: 56·80% C, 9·48% H; found: 56·74% C, 9·51% H. The ^{1}H-NMR spectrum ($CDCl_3$): 1·25 (3 H, d, $J_{5,6}$ = 6, CH_3—CH); 1·70 (1 H, m, $J_{1,2ax}$ = 4·5, $J_{2eq,2ax}$ = 15·0, H-2 ax); 2·24 (1 H, dq, $J_{1,2eq}$ = 1·5, $J_{2eq,2ax}$ = 15, $J_{2eq,3}$ = 4·0, H-2 eq); 2·93 (1 H, q, $J_{3,4}$ = 3·0, $J_{4,5}$ = 9·0, H-4); 3·34 (3 H, s, OCH_3); 3·42 (3 H, s, OCH_3); 3·45 (3 H, s, OCH_3); 3·77 (1 H, m, $J_{2eq,3}$ = 4·0, $J_{2ax,3}$ = 3·5, $J_{3,4}$ = 3·0, H-3); 4·11 (1 H, o, $J_{4,5}$ = 9·0, $J_{5,6}$ = 6·0, H-5); 4·63 (1 H, q, $J_{1,2eq}$ = 1·5, $J_{1,2ax}$ = 4·5, H-1). MS data, *m/e* (%): 159 (1), 146 (1), 127 (17), 115 (8), 114 (100), 99 (69), 95 (9), 88 (73), 75 (18), 73 (13), 72 (22), 71 (42), 67 (10), 59 (39).

Methyl 2,6-Dideoxy-α-D-*ribo*-hexopyranoside (*I*)

The title compound *I* was prepared according to the procedure of Haga and coworkers[2] in the form of a sirup, $[\alpha]_D$ +180° (*c* 0·8; chloroform). MS data, *m/e* (%): 131 (6), 118 (6), 113 (6), 104 (23), 73 (6), 71 (7), 69 (10), 61 (12), 60 (100), 59 (94).

Partial Methylation of the Dihydroxy Derivative *I*

Powdered sodium hydroxide was added with stirring in the molecular ratio 0·5—1·8 (referred to compound *I*) to a solution containing the dihydroxy derivative *I* (200 mg; 1·23 mmol), acetonitrile (50 ml), and methyl iodide (1 ml; 16 mmol). The mixture was stirred at 20°C for 24 h, evaporated, and the residue extracted with a mixture of chloroform and acetone. The analysis was performed by means of gas chromatography on a 400 × 0·6 cm column packed with 10% Versamide 900 on Chromaton N-AW at 180°C and the nitrogen flow rate of 6 ml per second. Retention time (s): *IV* 204, *II* 240, *III* 300, and *I* 348. Preparative runs were performed under analogous conditions on a 500 × 1 cm column with the hydrogen flow rate of 1 ml per second.

Partial Methylation of the Mixture of Monomethyl Ethers *II* and *III*

Powdered sodium hydroxide (about 5 mg) was added with stirring to a mixture of compound *II* (23 mg), compound *III* (30 mg), acetonitrile (25 ml), and methyl iodide (0·5 ml). The stirring was continued at 20°C for 24 h. The solvent was then evaporated and the residue taken up into chloroform. As shown by gas chromatography of the crude product (55 mg), the resulting dimethyl ether *IV* was accompanied by the unreacted compounds *II* (85·65% of the original amount) and *III* (41·00% of the original amount).

In another partial methylation of compounds *II* (21 mg) and *III* (29 mg), a mixture (52 mg) was obtained containing according to gas chromatography 83·33% of the original amount of compound *II* and 35·86% of the original amount of compound *III*.

Elemental analyses were performed in the Department of Organic Analysis (Dr L. Helešic, Head) of this Institute. The ^{1}H-NMR *spectra were measured in the Department of* NMR *spectrometry (Professor Dr V. Dědek, Head). The authors also wish to thank Mr V. Ineman for the assistance in the analysis and preparative separation of reaction mixtures by gas chromatography and Dr P. Sedmera for measurement of mass spectra.*

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