PARTIAL METHYLATION OF METHYL 4,6-DIDEOXY-α- AND -β-L--*ribo*-HEXOPYRANOSIDES

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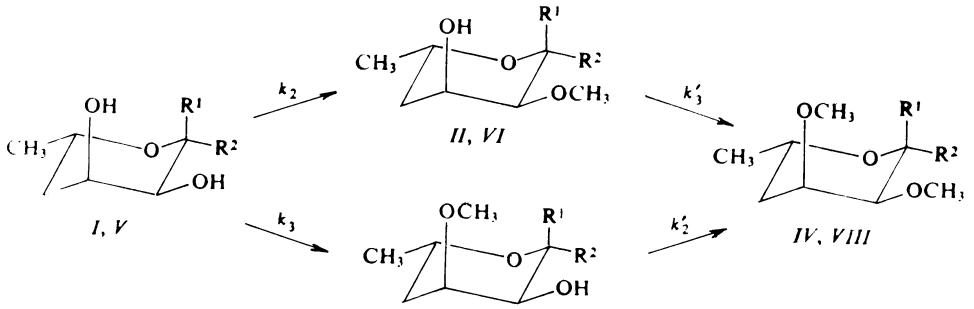
Anomeric methyl 4,6-dideoxy-L-*ribo*-hexopyranosides *I* and *V*, prepared from aldose *IX*, were etherified with methyl iodide in acetonitrile in the presence of sodium hydroxide. From the products of partial methylation methyl 4,6-dideoxy-2-O-methyl-α-L-*ribo*-hexopyranoside (*II*) and methyl 4,6-dideoxy-2,3-di-O-methyl-α-L-*ribo*-hexopyranoside (*IV*), or methyl 4,6-dideoxy--2-O-methyl-β-D-*ribo*-hexopyranoside (*VI*) and methyl 4,6-dideoxy-2,3-O-methyl-β-L-*ribo*-hexopyranoside (*VIII*), respectively, were isolated. The substances were identified by ^{1}H NMR, mass and IR spectra and comparison with standards. The course of etherification of glycosides *I* and *V* was checked by gas chromatography and the reactivity of the hydroxyl groups was evaluated by determining the rate constants or their ratios. The observed values were compared with analogous data for other isomers of methyl 4,6-dideoxyhexopyranosides and discussed from the view-point of sterical and polar influence on the reactivity of both their hydroxyl groups.

In the preceding papers of this series[1,2] the course and the relative kinetics of the O-methylation of methyl 4,6-dideoxy-D-*xylo*-, L-*lyxo*- and D-*arabino*-hexopyranosides with methyl iodide in acetonitrile in the presence of sodium hydroxide has been described. In this paper the same etherification of methyl 4,6-dideoxy-α- and -β-L-*ribo*--hexopyranosides (*I* and *V*) is investigated, which, theoretically, should afford methyl 4,6-dideoxy-2-O-methyl-α- and β-L-*ribo*-hexopyranosides (*II* and *VI*), methyl 4,6-dideoxy-3-O-methyl-α- and β-L-*ribo*-hexopyranosides (*III* and *VII*) and methyl 4,6-dideoxy-2,3-di-O-methyl-α- and β-L-*ribo*-hexopyranosides (*IV* and *VIII*, Scheme 1).

The starting glycosides *I* and *V* were prepared from 4,6-dideoxy-L-*ribo*-hexose (*IX*, ref.[3]) on reaction with methanolic hydrogen chloride. The mixture of α and β anomers obtained (in an approximately 1 : 2 ratio) was separated in the form of 2,3--di-O-acetyl derivatives *X* and *XI* by preparative gas chromatography. Deacetylation of derivatives *X* and *XI* gave glycosides *I* and *V* the structure and the prevailing ^{1}C$_4$ L-configuration of which was confirmed by ^{1}H NMR and IR spectra. For the identification of substances in the product of methylation of glycoside *I* a sample for comparison was prepared, *i.e.* methyl 4,6-dideoxy-2-O-methyl-α-D-*ribo*-hexopyranoside (*XII*), by oxidation of methyl 4,6-dideoxy-2-O-methyl-α-D-*xylo*-hexopyranoside (*XIII*, ref.[4]) with ruthenium (*VIII*) oxide and subsequent reduction of the 3-oxo

derivative *XIV* obtained with sodium borohydride. The structure of glycoside *XII* was confirmed by spectral measurements in three ways: *1*) In the mass spectrum of derivative *XII* an abundant peak of *m/z* 88 was observed, assigned to the CH_3O—$\overset{+}{C}H$—$CH{=}\overset{+}{O}CH_3$ ion formed by H_1^1-fragmentation[5] of the molecular ion of com-



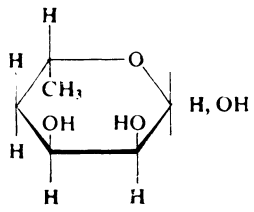
I, II, III, IV, $R^1 = OCH_3$, $R^2 = H$; *V, VI, VII, VIII*, $R^1 = H$, $R^2 = OCH_3$

SCHEME 1

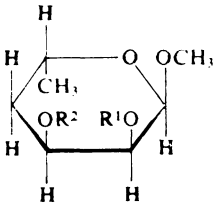
pound *XII*. Since the cleavage of 3-O-methyl derivatives cannot give such an ion this fact indicates the assumed position of the methoxy group on the atom $C_{(2)}$. *2*) In the ^1H NMR spectrum of compound *XII* the small values for $J_{2,3}$, $J_{4a,3}$ and $J_{4e,3}$ agree with the mutual ax-eq-ax arrangement of the atoms $H_{(2)}$, $H_{(3)}$ and $H_{(4a)}$ and eq-eq position of the atoms $H_{(3)}$ and $H_{(4e)}$ in the $^4C_1$ (D) conformation. *3*) The infrared spectrum of compound *XII* (0·001 mol l^{-1}, tetrachloromethane) displays an intensive band at ν 3 558 cm^{-1} in the region of absorption of the OH bonds; such an important shift, with respect to the wave-number of a free OH bond (ν 3 629 cm^{-1}), can evidently be attributed[6] to the strong intramolecular hydrogen bond in the six-membered ring $C_{(3)}$—O—H···O—$C_{(1)}$, which can be formed only in the $^4C_1$ (D) conformation of compound *XII*.

For the identification of the compounds in the product of methylation of glycoside *V* a sample was prepared for comparison, *i.e.* 3-O-methyl derivative *VII*, by partial esterification of glycoside *V* with 1 molar equivalent of benzoyl chloride in pyridine, methylation of methyl 2-O-benzoyl-4,6-dideoxy-β-L-*ribo*-hexopyranoside (*XV*) with diazomethane, and debenzoylation of methyl 2-O-benzoyl-4,6-dideoxy-3-O-methyl-β-L-*ribo*-hexopyranoside (*XVI*). In the mass spectrum of the substance *VII* obtained in this manner the base peak of *m/z* 74 was assigned to the ion $(CH_3O{-}CH{=}CH{-}OH)^{\cdot +}$, formed by H_1^1 and H_1^2 fragmentation[5] of the molecular ion of compound *VII*; in contrast to this the presence of the ion *m/z* 88 could not be detected. These facts confirm the assumed position of the methoxy group

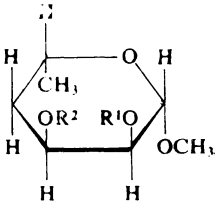
on $C_{(3)}$ in the molecule of glycoside *VII*. The chemical shifts of the signals $H_{(2)}$ and $H_{(3)}$ in the ^1H NMR spectra of compounds *XV*, *XVI* and *XVII* are adequate to the substitutions on the hydroxyl groups on $C_{(2)}$ and $C_{(3)}$, and together with other spectral data they confirm the assumed structure with the prevailing $^1C_4$ (L) conformation of these compounds.



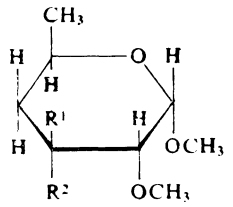
IX



X, $R^1, R^2 = CH_3CO$



XI, $R^1 = R^2 = CH_3CO$
XV, $R^1 = C_6H_5CO$, $R^2 = H$
XVI, $R^1 = C_6H_5CO$, $R^2 = CH_3$



XII, $R^1 = H$, $R^2 = OH$
XIII, $R^1 = OH$, $R^2 = H$
XIV, $R^1 - R^2 = =O$

Partial methylation of glycosides *I* and *V* was carried out at room temperature with an excess of methyl iodide in acetonitrile in the presence of maximally two molar equivalents of sodium hydroxide, with respect to the amount of the applied glycoside. The course of the etherification was checked by gas chromatography in order to determine the percentual content of the compounds in the reaction mixture. A larger number of data (78 in the case of glycoside *I*, 89 in the case of glycoside *V*) concerning the composition of the reaction mixtures at various degrees of substitution was collected from several experiments, a part of them is given in Table I. From the observed values it is evident that the main products of partial methylation of both anomers are 2-O-methyl derivatives *II* or *VI*, respectively. In the methylation course of the α-anomer *I* the presence of 3-O-methyl derivative *III* could not be detected at all. In the product of the methylation of glycoside *V* the 3-O-methyl derivative was detected, but its content did not exceed 6%. However,

we were unable to isolate it by preparative gas chromatography. The assignment of the peak in the chromatographic record to *VII* is based on the identity of its R_F value with that of a standard substance *VII* and on their identical mass spectra. Compounds *II*, *IV*, *VI* and *VIII* were isolated by preparative gas chromatography and their structure was proved by ^{1}H NMR spectra. The structure of monomethyl derivative *II* was also confirmed by comparison of its mass and infrared spectrum and the absolute value of specific rotation with those of its D-enantiomer *XII*.

The knowledge of the data concerning the reaction mixtures at various degrees of substitution of glycoside *V* permitted the use of a known[7,8] mathematical approach for the calculation of the ratios of rate constants. For glycoside *I* the value of the ratio of constants k_2/k_3' could thus be calculated (with respect to the exclusive substitution in the position 2 in the first reaction stage) and, using the data of the experiment observed in time (Table II), the absolute values of both rate constants $k_2 = 9{\cdot}69 \cdot 10^{-4}\ s^{-1}$ and $k_3' = 8{\cdot}19 \cdot 10^{-5}\ s^{-1}$ calculated by means of the relations[9] for two consecutive reactions. The constants calculated from the data obtained from individual time intervals (Table II) do not display dependence on time and thus support the assumption of 1st order kinetics. The ratios of the rate constants, comparison the reaction rate of the methylation of hydroxyl groups of compounds, *I*, *II*, *V*, *VI* and *VII* are given together with the earlier[1,2] data for other methyl

TABLE I

Partial methylation of methyl 4,6-dideoxy-α- and β-L-*ribo*-hexopyranosides *I* and *V*. Composition of the reaction mixtures at various stages of substitution (mol %)

I	*II*	*IV*	*V*	*VI*	*VII*	*VIII*
97·77	2·23	0	95·70	4·30	0	0
82·62	17·38	0	85·08	13·24	1·68	0
78·70	20·90	0·40	75·30	21·61	2·88	0·20
67·56	31·71	0·73	67·27	29·63	2·56	0·54
50·87	47·38	1·75	55·33	40·41	3·05	1·20
25·07	70·98	7·30	45·28	47·50	5·48	1·74
16·97	73·43	9·61	34·52	59·20	3·01	3·27
16·54	73·66	9·80	25·36	67·38	2·66	4·61
15·42	74·24	10·34	15·40	72·93	5·99	5·66
3·89	77·96	18·15	6·34	83·52	1·10	9·04
2·23	76·29	21·48	0	84·53	0	15·47
1·45	75·07	23·47	0	60·05	0	39·95
1·12	74·24	24·64	0	40·39	0	59·61
1·00	73·80	25·17	0	25·09	0	74·91
0·64	72·42	26·93	0	15·20	0	84·80

4,6-dideoxy hexopyranosides in Table III. From the mentioned data the prevailing reactivity of the hydroxyl group on $C_{(2)}$ is also evident for glycoside *V* and both mono-substituted derivatives *VI* and *VII* (ratio k'_2/k'_3).

TABLE II

Course of methylation of glycoside *I* in time

Time s	Composition of the reaction mixture mol %[a]			Rate constants[b,c], s^{-1}	
	I	*II*	*IV*	$k_2 . 10^4$	$k'_3 . 10^5$
170	85·48	14·52	0	9·2	8·8
1 020	35·41	59·88	2·26	10·2	7·4
1 920	17·57	73·42	8·98	9·1	9·0
2 460	8·07	78·95	12·97	10·2	7·4
3 180	4·41	78·59	16·99	9·8	7·9
3 900	2·25	76·28	21·50	9·7	8·0
4 620	1·42	75·32	23·23	9·6	8·8

[a] A solution of 70·1 mg (0·432 mmol) of glycoside *I* in 9 ml of acetonitrile was stirred at 20°C with 1·5 ml of methyl iodide and 32·8 mg (0·82 mmol) of sodium hydroxide. The reaction mixture was analysed by gas chromatography at the given time intervals; [b] the values of the constants were calculated from the relationships; $k_2 = t^{-1} . \ln c_{I_0}/c_I$; $k'_3 = k_2 . c_{I_0}/c_{IImax} . e^{-k_2 t} c_{IImax}$ for graphically read values $tc_{IImax} = 2\,796$ s and $c_{IImax} = 79{\cdot}69\%$; [c] Mean value of the constants: $k_2 = 9{\cdot}7 . 10^{-4}\ s^{-1}$, $k'_3 = 8{\cdot}2 . 10^{-5}\ s^{-1}$.

TABLE III

Ratios of the rate constants of the methylation of methyl 4,6-dideoxyhexopyranosides

Configuration	Ratio						Ref.
	k_2/k_3	k'_2/k'_3	k_2/k'_3	k'_2/k_3	k'_2/k_2	k'_3/k_3	
α-*xylo*[a,b]	2·8	7·0	8·1	2·5	0·9	0·4	1
α-*lyxo*[a,b]	0·9	4·5	2·7	1·5	1·6	0·3	1
α-*arabino*	2·9	6·6	5·6	3·4	1·18	0·5	2
α-*ribo*	—	—	12·05[d]	—	—	—	c
β-*ribo*	10·1	37·7	53·5	7·2	0·7	0·19	c

[a] Average values of the data given in ref.[1]; [b] ratio of the reaction constants $k_2(xylo)/k_2(lyxo) = 3{\cdot}5$; $k_3(xylo)/k_3(lyxo) = 1{\cdot}3$ (ref.[1]); [c] values determined in this study; [d] ratio calculated from average values for k_2 and k'_3 from Table II: $k_2/k'_3 = 11{\cdot}83$.

When considering possible reasons for the differing reactivity of the hydroxyl groups in methyl 4,6-dideoxy-α- and β-L-*ribo*-hexopyranosides, it is useful to evaluate all the isomers of methyl 4,6-dideoxyhexopyranosides investigated so far together (Table III). It seems that in this group of substances the induction effect of the semiacetal grouping plays a decisive role in the first stage of the reaction, increasing the methylation on the hydroxyl group in the position 2 about three times with respect to the hydroxyl group on $C_{(3)}$; a further role is played by the steric effect which enhances etherification on the equatorial hydroxyl group three times with respect to the axial hydroxyl group. In isomers with diequatorially or diaxially arranged OH groups in $C_{(2)}$ and $C_{(3)}$ (*xylo* and *arabino* configuration) the steric effect on both hydroxyl groups is equal and the value of the ratio $k_2/k_3 \sim 3$ is a result of the induction effect. In the methyl glycoside of *lyxo* configuration the induction effect accelerating the reaction of the axial $C_{(2)}$—OH group is balanced by the steric effect increasing the reaction on the equatorial hydroxyl group on $C_{(3)}$, so that the resulting value of k_2/k_3 is close to one. This is in agreement with the results of the experiments[1] in which the relative rate was measured on a hydroxyl group of two pairs of 3-O-methyl derivatives and 2-O-methyl derivatives of *xylo* and *lyxo* configuration equally affected by polar effect. The ratio of the rate constants was found to be $k_2(xylo)/k_2(lyxo) = 3{\cdot}5$ (in the derivative of *xylo* configuration the steric effect of the equatorial $C_{(2)}$—OH group is effective), while $k_3(xylo)/k_3(lyxo) = 1{\cdot}3$ (the compared hydroxyl groups are in the equatorial position in both isomers). In the methyl glycoside of β-*ribo* configuration the steric and inductive effects multiply the reactivity of the hydroxyl group on $C_{(2)}$ to the value $k_2/k_3 \sim 10$. In the isomer of α-*ribo* configuration the reactivity of the axially placed hydroxyl group on $C_{(3)}$ is further hindered by the steric interaction with the methoxyl group on $C_{(1)}$. The substitution of $C_{(2)}$ probably induces a smaller conformational change in derivative *II* (this is evidenced by the different value of the intramolecular hydrogen bond $C_{(3)}$—OH···O—$C_{(1)}$ in the IR spectra of compounds *I* and *II* and the somewhat different values of the coupling constants $J_{1,2}$, $J_{4e,5}$, $J_{4a,5}$ in the ^{1}H NMR spectra of these compounds). This change probably leads to the deviation of the $C_{(1)}$—O and $C_{(3)}$—O bonds from the eclipsed position and facilitates the etherification of the 2-O-methyl derivative *II* to the second stage.

The originally considered[1] effect of the intramolecular hydrogen bonds on the reactivity of the hydroxyl groups is not of decisive importance for the reactivity of the hydroxyl groups in the series of 4,6-dideoxyhexopyranosides. This is evident from the values of the ratios k_2/k_3 of the *arabino* and α-*ribo* isomers in which very strong intramolecular hydrogen bonds $C_{(3)}$—OH···O—$C_{(1)}$ were observed, but without an observable accelerating effect on the reactivity of the donor group. The effect of the vicinal substitution on the reactivity is interesting. While the reactivity of the OH groups in the position 2 is only negligibly affected by substitution on the hydroxyl group in the position 3 (the values k'_2/k_2 in Table III are close to *1*), in the

opposite case a considerable slowing down of the reaction on the hydroxyl group in the position 3 may be observed (the values k'_3/k_3 0·2–0·5), and that without respect to mutual steric constellation of the two groups.

EXPERIMENTAL

The melting points were determined on a Kofler block and their values are not corrected. Optical rotation was measured on an Opton instrument at 20°C in chloroform (subjective reading). The infrared spectra were measured on a Perkin–Elmer 325 instrument, for the wave-number region 4 000–600 cm^{-1} in a KBr pellet or chloroform solution, for the region of the hydroxyl bonds absorption in an approximately 0·001 mol l^{-1} solution in tetrachloromethane in a 20 mm quartz cell, at a slit width of 1·2 cm at 3 400 cm^{-1}. The ^1H NMR spectra were measured on a Varian XL-100-15 or Tesla BS 567 instrument in deuteriochloroform at 37°C, using tetramethylsilane as an internal reference; the chemical shifts are given in δ-scale. The mass spectra were measured on a GCMS LKB 9000 apparatus, with a chromatographic column 1 500 × 2·5 mm, packed with 10% Versamide on Chromaton N, at 135°C, temperature of the ion source 290°C, accelerating voltage 3·5 kV and ionizing energy 70 eV. Analytical gas chromatography was carried out on a Varian Aerograph 2100 instrument with a 900 × 2 mm column, filled with 5% poly(propylene sebacate) on Chromosorb G (80–100 mesh), heated at 130°C (partial methylation of glycoside *I*), or a 1 800 × 2 mm column filled with 5% Versamide on Chromosorb I (40–60 mesh), heated at 150°C; the carrier gas was helium in both instances, with flow rate 20 ml/min; the signals from the FID detector were recorded and evaluated automatically on a Hewlett–Packard 3380 A integrator. Preparative gas chromatography was carried out on a Chrom 3 apparatus, using detection with a catharometer, under the conditions given in the text.

Methyl 2,3-Di-O-acetyl-4,6-dideoxy-α- and β-D-*ribo*-hexopyranoside (*X*, *XI*)

A solution of 2·0 g (1·35 mmol) of aldose *IX* (ref.[3]) in 20 ml methanol containing 2·5% of hydrogen chloride was refluxed for 4 h. After neutralization with lead carbonate the filtrate was evaporated and the residue dissolved in 10 ml of pyridine and then esterified with acetic anhydride (10 ml) at room temperature for 24 h. Distillation of the esterification product at 120°C (bath temperature) and 2·7 Pa pressure gave 3·5 g of a syrupy mixture of *X* and *XI* which was separated by preparative gas chromatography on a 900 × 12 cm column filled with 10% poly(propylene sebacate) on Silocel 22 and eluted with 90 ml/min of hydrogen gas at 140°C. In addition to 291 mg of a mixed fraction methyl 2,3-di-O-acetyl-4,6-dideoxy-α-L-*ribo*-hexopyranoside (*X*) (650 mg) was obtained, b.p. 102°C/1·3 Pa (bath temperature 120°C), $[\alpha]_D$ −53·8 ± 2·5° (*c* 0·9). For $C_{11}H_{18}O_6$ (246·3) calculated: 53·65% C, 7·36% H; found: 53·28% C, 7·65% H. Further methyl 2,3-di-O-acetyl-4,6-dideoxy-β-L-*ribo*-hexopyranoside (*XI*) was also obtained (1 470 mg), b.p. 98°C/1·3 Pa (bath temperature 120°C), $[\alpha]_D$ +107·5° ± 2° (*c* 1·5). For $C_{11}H_{18}O_6$ (246·3) calculated: 53·65% C, 7·35% H; found: 53·70% C, 7·41% H.

Methyl 4,6-Dideoxy-α-L-*ribo*-hexopyranoside (*I*)

Diacetyl ester *X* (908 mg, 3·7 mmol) was deacetylated in ethanol with sodium methoxide. After evaporation the product was chromatographed on a column of 10 g of silica gel, using chloroform for elution. The syrup obtained was distilled at 100°C (bath temperature) and 6·7 Pa pressure. Yield, 575 mg (97%) of glycoside *I*, $[\alpha]_D$ −116·6 ± 2·5° (*c* 1). ^1H NMR spectrum: 4·22 (1 H, d, $J_{1,2}$ = 3·5 Hz, H-1); 4·02 (1 H, m, H-5); 3·97 (1 H, m, ΣJ = 9·5 Hz, H-3); 3·57 (1 H, dd, $J_{2,1}$ = 3·5 Hz, $J_{2,3}$ = 3·5 Hz, H-2); 3·45 (3 H, s, OCH_3); 2·89/37°C, 2·80/60°C (2 H, s,

2 × OH); 1·96 (1 H, m, $J_{4e,3}$ = 3 Hz, $J_{4e,5}$ = 3·5 Hz, $J_{4e,4a}$ = 13·5 Hz, H-4e); 1·58 (1 H, m, $J_{4a,3}$ = 3 Hz, $J_{4a,5}$ = 11·5 Hz, $J_{4a,4e}$ = 13·5 Hz, H-4a); 1·21 (3 H, d, $J_{6,5}$ = 6·5 Hz, H-6). IR spectrum: $\tilde{\nu}$(OH) 3 623 cm^{-1}, 3 594 cm^{-1}, 3 542 cm^{-1}. For $C_7H_{14}O_4$ (162·2) calculated: 51·84% C, 8·70% H; found: 51·98% C, 8·94% H.

Methyl 4,6-Didoexy-β-L-*ribo*-hexopyranoside (*V*)

Using an analogous procedure deacetylation of 1·82 g of ester *XI* gave 1·24 g of glycoside *V*, which when purified by vacuum sublimation had m.p. 61°C, $[\alpha]_D$ +104·5 ± 1° (*c* 1·3). ^{1}H NMR spectrum: 4·51 (1 H, d, $J_{1,2}$ = 8 Hz, H-1); 4·01 (1 H, m, $J_{5,4e}$ = 2·5 Hz, $J_{5,4a}$ = 10 Hz, $J_{5,6}$ = = 6·5 Hz, H-5); 4·14 (1 H, m, ΣJ = 10 Hz, H-3); 3·53 (3 H, s, OCH_3); 3·37 (1 H, dd, $J_{2,1}$ = = 8 Hz, $J_{2,3}$ = 3 Hz, H-2); 2·96 (2 H, s, 2 × OH); 1·89 (1 H, m, $J_{4e,3}$ = 3 Hz, $J_{4e,5}$ = 2·5 Hz, $J_{4e,4a}$ = 14·5 Hz, H-4e); 1·49 (1 H, m, $J_{4a,3}$ = 4 Hz, $J_{4a,5}$ = 10 Hz, $J_{4a,4e}$ = 14·5 Hz, H-4a); 1·23 (3 H, d, $J_{6,5}$ = 6·5 Hz, H-6). IR spectrum: $\tilde{\nu}$(OH) 3 614 cm^{-1}, 3 603 cm^{-1}. For $C_7J_{14}O_4$ (162·2) calculated: 51·84% C, 8·70% H; found: 51·75% C, 8·81% H.

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

Glycoside *XIII* (ref.[5]) (584· mg, 3·32 mmol) was oxidized in a mixture of 2·7 ml of chloroform and 2·7 ml of water with 35 mg of ruthenium dioxide and 1·3 g of potassium periodate in the presence of 160 mg of potassium carbonate (the oxidizing reagent was introduced into the reaction mixture in two portions after 8 h). The oxidation course was checked by thin layer chromatography on silica gel G in chloroform–methanol 10 : 1, R_F of the starting compound 0·4, R_F of the product 0·5. After the disappearance of the spot of the starting compound the mixture was decomposed with 10 ml of 2-propanol, the catalyst and the remaining salts were filtered off and the filtrate partitioned between water and chloroform. The chloroform extract was dried and evaporated and the residue distilled in a vacuum. The distillate (401 mg, 69%, b.p. 65°C/13 Pa, bath temperature 100°C) displayed in its IR spectrum a distinct band (C=O) 1 730 cm^{-1}. Sodium borohydride (126 mg; 3·3 mmol) was then added to the cooled solution of 387·5 mg (2·22 mmol) of the product of oxidation *XIV* in 10 ml of water and the mixture allowed to stand for 21 h at room temperature. The mixture was decomposed with 100 μl of acetic acid and evaporated. The residue was extracted with chloroform, the extract was dried and evaporated and the residue was distilled in a vacuum. According to gas chromatography the distillate (265 mg, 68%, b.p. 46°C/13 Pa, bath temperature 100—120°C) was a mixture of glycoside *XIII* and 74% of glycoside *XII*. The mixture was decomposed by preparative gas chromatography on a column (1 800 × 12 mm) packed with Chromosorb T impregnated with 5% of Versamide, at 140°C, flow rate 20 ml of hydrogen per minute. Distillation of the chromatographically pure fraction gave 153 mg of glycoside *XII*, b.p. 43°C/6·7 Pa (bath temperature 70—80°C), $[\alpha]_D$ +76·2 ± 1·5° (*c* 1·03). ^{1}H NMR spectrum: 4·81 (1 H, d, $J_{1,2}$ = 3·5—4 Hz, H-1); 3·90—4·36 (2 H, m, H-3, H-5); 3·44—3·46 (2 × 3 H, s, 2 × OCH_3); 3·28 (1 H, dd, $J_{2,1}$ = 3·5—4 Hz, $J_{2,3}$ = 3·5 Hz, H-2); 3·27/37°C, 3·22/60°C (1 H, s, OH); 1·98 (1 H, m, $J_{4e,3}$ = 3 Hz, $J_{4e,5}$ = = 2·5 Hz, $J_{4e,4a}$ = 14·5 Hz, H-4e); 1·46 (1 H, m, $J_{4a,3}$ = 3 Hz, $J_{4a,5}$ = 11·5—12 Hz, $J_{4a,4e}$ = 14.5, H-4a); 1·21 (3 H, d, $J_{6,5}$ = 6·5, H-6). IR spectrum: $\tilde{\nu}$(OH) 3 622 cm^{-1}, 3 558 cm^{-1}; in the 4 000—600 cm^{-1} region the spectrum was identical with that of compound *II*. For C_8H_{16}·.O_4 (176·2 calculated: 54·53% C, 9·15% H; found: 54·24% C, 9·31% H.

Methyl 2-O-Benzoyl-4,6-dideoxy-β-L-*ribo*-hexopyranoside (*XV*)

Benzoyl chloride (150 μl; 1·3 mmol) was added under stirring at 0°C to a solution of 190 mg (1·17 mmol) of glycoside *V* in a mixture of 5 ml of chloroform and 5 ml of pyridine and the mix-

ture was allowed to stand at room temperature for 15 h. It was then decomposed with icy water and extracted with chloroform. The dried extract was evaporated to give 300 mg of a syrupy residue which was chromatographed on 12 g of silica gel with benzene containing 1% of ethanol. Yield, 244 mg (79%) of derivative *XV*, m.p. 74–75°C (ether–light petroleum), $[\alpha]_D^{20}$ +58·9 ± 1° (*c* 1·0). IR spectrum (KBr): ($\tilde{\nu}$OH), 3 540 cm^{-1}, $\tilde{\nu}$(CH) 3 000–2 850 cm^{-1}, $\tilde{\nu}$(C=O) 1 703 cm^{-1}. ^{1}H NMR spectrum: 8·12 (2 H, m, arom); 7·5 (3 H, m, arom).; 5·03–4·80 (2 H, m, H-2, H-1); 4·38 (1 H, m, H-3); 4·18 (1 H, m, $J_{5,6}$ = 6·7 Hz, $J_{5,4a}$ = 10 Hz, $J_{5,4e}$ = 2·5 Hz, H-5); 3·53 (3 H, s, OCH_3); 2·25/25°C, 2·15/60°C (1 H, s, OH); 1·95 (1 H, m, $J_{4e,5}$ = 2·5 Hz, $J_{4e,3}$ = 4 Hz, $J_{4e,4a}$ = 15 Hz, H-4e); 1·68 (1 H, m, $J_{4a,5}$ = 10 Hz, $J_{4a,3}$ = 3 Hz, $J_{4a,4e}$ = 15 Hz, H-4a); 1·28 (3 H, d, $J_{6,5}$ = 6·7 Hz, H-6). For $C_{14}H_{18}O_5$ (266·2) calculated: 63·18% C, 6·76% H; found: 62·92% C, 6·92% H.

Methyl 2-O-Benzoyl-4,6-dideoxy-3-O-methyl-β-L-*ribo*-hexopyranoside (*XVI*)

Boron trifluoride etherate (5 µl) was added at 0°C to a solution of 180 mg (0·67 mmol) of benzoyl derivative *XV* in 3 ml of dichloromethane, followed in 50 min by 20 ml of a diazomethane solution in dichloromethane (ref.[10,11]) and the mixture was stirred for another 30 min. After filtration the filtrate was shaken with two 10 ml portions of a saturated sodium hydrogen carbonate solution and two 10 ml portions of water and dried. After evaporation the syrupy product (216 mg) was analysed by thin-layer chromatography on silica gel G (benzene–5% ethanol), which indicated the presence of two substances, with the starting substance predominating. Methylation was repeated, giving 210 mg of a mixture, where the required substance predominated. Chromatography on a column packed with 12 g of silica gel, using benzene–1% ethanol for elution, gave 120 mg (62%) of chromatographically pure syrupy derivative *XVI*. ^{1}H NMR spectrum: 8·12 (2 H, m, arom).: 7·5 (3 H, m, arom.); 5·0–4·8 (2 H, m, H-2, H-1); 4·08 (1 H, m, $J_{5,6}$ = 6·7 Hz, $J_{5,4e}$ = 2·5 Hz, $J_{5,4a}$ = 10 Hz, H-5); 3·97 (1 H, m, ΣJ = 9 Hz, H-3); 3·54 (3 H, s, OCH_3); 3·47 (3 H, s, OCH_3); 2·02 (1 H, m, $J_{4e,5}$ = 2·3 Hz, $J_{4e,3}$ = 4·4 Hz, $J_{4e,4a}$ = 14·5 Hz, H-4e); 1·58 (1 H, m, $J_{4a,5}$ = 10·5 Hz, $J_{4a,3}$ = 3 Hz, $J_{4a,4e}$ = 14·5 Hz, H-4a); 1·30 (3 H, d, $J_{6,5}$ = 6·7 Hz, H-6).

Methyl 4,6-Dideoxy-3-O-methyl-β-L-*ribo*-hexopyranoside (*VII*)

Sodium (30 mg) was added to a solution of 346 mg (1·2 mmol) of compound *XVI* in 5 ml of methanol and the mixture was analysed at room temperature by thin-layer chromatography on silica gel G in benzene–5% ethanol. After 2 h the mixture was neutralized by introducing carbon dioxide and evaporated. The residue was dissolved in 2 ml of water and heated with 1 ml 1M-NaOH. After cooling and neutralization with CO_2 gas the reaction mixture was extracted with chloroform. After evaporation of the solvent the residue (239 mg) was distilled in a vacuum (oil pump). Yield, 130 mg (61%) of an oil, b.p. 44–45°C/25 Pa; $[\alpha]_D^{20}$ +129·2° (*c* 0·62). IR spectrum: $\tilde{\nu}$(OH): 3 630 cm^{-1}, 3 593 cm^{-1}; KBr pellet: $\tilde{\nu}$(OH): 3 600 cm^{-1}, $\tilde{\nu}$(CH): 3 010 to 2 840 cm^{-1}; ^{1}H NMR spectrum: 4·42 (1 H, d, $J_{1,2}$ = 8 Hz, H-1); 3·86 (1 H, m, $J_{5,6}$ = 6·5 Hz, $J_{5,4e}$ = 2·5 Hz, $J_{5,4a}$ = 10 Hz, H-5); 3·68 (1 H, m, $J_{3,2}$ = 3·5 Hz, $J_{3,4e}$ = 3 Hz, $J_{3,4a}$ = 2·5 Hz, H-3); 3·43 (1 H, H-2); 3·51 (3 H, s, OCH_3); 3·40 (3 H, s, OCH_3); 2·41/35°C, 2·34/60°C (1 H, s, OH); 1·98 (1 H, m, $J_{4e,5}$ = 3 Hz, $J_{4e,3}$ = 2·5 Hz, $J_{4e,4a}$ = 14·5 Hz, H-4e); 1·37 (1 H, m, $J_{4a,5}$ = 10 Hz, $J_{4a,3}$ = 2·5 Hz, $J_{4a,4e}$ = 14·5 Hz, H-4a); 1·22 (3 H, d, $J_{6,5}$ = 6·5 Hz, H-6). For $C_8H_{16}O_4$ (176·2) calculated: 54·53% C, 9·15% H; found: 54·62% C, 9·11% H.

Partial Methylation of Methyl 4,6-Dideoxy-α-L-*ribo*-hexopyranoside

A solution of 83·7 mg (0·52 mmol) of glycoside *I* in 10 ml of acetonitrile was stirred at 20°C with 1·5 ml of methyl iodide and 33 mg (0·82 mmol) of powdered sodium hydroxide which was

added in three portions over 3 h. The composition of the reaction mixture at various stages of substitution was analysed by gas chromatography (Table I). After the termination of the reaction acetonitrile was evaporated and the residue extracted with chloroform. The combined chloroform extracts from several experiments were extracted with a solution of sodium thiosulphate, dried and evaporated. The residue (250 mg) was separated by gas chromatography on a 900 × 12 mm column packed with 20% poly(propylene sebacate) on Silocel 22, giving two fractions: *1)* Methyl 4,6-dideoxy-2-O-methyl-α-L-*ribo*-hexopyranoside (*II*), b.p. 45°C/7 Pa (60 to 70°C bath temperature); $[\alpha]_D$ −75·8 ± 1·5° (*c* 1·03). Its IR spectrum in a KBr pellet was identical with the spectrum of the D-enantiomer *XII* within the 4 000−600 cm^{-1} region. *2)* Methyl 4,6-dideoxy-2,3-di-O-methyl-α-L-*ribo*-hexopyranoside (*IV*), b.p. 50°C/6·7 Pa (80−90°C bath temperature); $[\alpha]_D^{20}$ −67·3° ± 1·5° (*c* 1). ^{1}H NMR spectrum: 4·75 (1 H, d, $J_{1,2}$ = 3·7 Hz, H-1); 4·12 (1 H, m, $J_{5,4e}$ = 2·5 Hz, $J_{5,4a}$ = 11·5 Hz, $J_{5,6}$ = 6·5 Hz, H-5); 3·71 (1 H, dd, ΣJ = = 10 Hz, H-3); 3·43, 3·41, 3·39 (3 × 3 H, s, 3 × OCH_3); 3·28 (1 H, dd, $J_{2,1} = J_{2,3}$ = 3·75 Hz, H-2); 1·98 (1 H, m, $J_{4e,3}$ = 3·5 Hz, $J_{4e,5}$ = 2·5 Hz, $J_{4e,4a}$ = 14·5 Hz, H-4e); 1·37 (1 H, m, $J_{4a,3}$ = 3·5 Hz, $J_{4a,5}$ = 11 Hz, $J_{4a,4e}$ = 14·5 Hz, H-4a); 1·12 (3 H, d, $J_{6,5}$ = 6·5 Hz, H-6). For $C_9H_{18}O_4$ (190·2) calculated: 56·82% C, 9·53% H; found: 56·53% C, 9·58% H.

Partial Methylation of Methyl 4,6-Dideoxy-β-L-*ribo*-hexopyranoside

A mixture of 80·5 mg (0·5 mmol) of glycoside *V* and 1·5 ml of methyl iodide in 10 ml of acetonitrile was stirred at room temperature with 26 mg (0·65 mmol) of powdered sodium hydroxide, which was added to the mixture in four portions in 2 h intervals. In other experiments a larger amount of sodium hydroxide was used, up to the molar ratio of glycoside/NaOH 1 : 2. The composition of the mixture was determined by gas chromatography. A part of the data is given in Table I. After evaporation of the solvent the residue was extracted with chloroform, the chloroform extract was dried and evaporated. The combined fractions of several such experiments (294 mg) were separated by preparative gas chromatography on a 5000 × 8 mm column filled with 5% of Versamide on Chromaton N at 180°C, flow rate of hydrogen 80 ml/min. Distillation of chromatographically pure fractions gave:

Methyl 4,6-dideoxy-2-O-methyl-β-L-*ribo*-hexopyranoside (*VI*) (160 mg), boiling at 60°C (bath temperature) and 6·7 Pa pressure, $[\alpha]_D^{20}$ +101·8 ± 2° (*c* 0·86). ^{1}H NMR spectrum: 4·55 (1 H, d, $J_{1,2}$ = 8 Hz, H-1); 4·23 (1 H, m, $J_{3,2}$ = 3·5 Hz, $J_{3,4e} = J_{3,4a}$ = 3 Hz, H-3); 4·01 (1 H, m, $J_{5,4a}$ = 10 Hz, $J_{5,4e}$ = 2·5 Hz, $J_{5,6}$ = 6·5 Hz, H-5); 3·53, 3·51 (2 × 3 H, s, 2 × OCH_3); 2·99 (1 H, dd, $J_{2,1}$ = 8 Hz, $J_{2,3}$ = 3·5 Hz, H-2); 2·73/37°C, 2·66/60°C (1 H, s, OH); 1·82 (1 H, m, $J_{4e,3}$ = 3 Hz, $J_{4e,5}$ = 2·5 Hz, $J_{4e,4a}$ = 14·5 Hz, H-4e); 1·45 (1 H, m, $J_{4a,3}$ = 3 Hz, $J_{4a,5}$ = = 10 Hz, $J_{4a,4e}$ = 14·5 Hz, H-4a); 1·22 (3 H, d, $J_{6,5}$ = 6·5 Hz, H-6). IR spectrum: $\tilde{\nu}$(OH) 3 620 cm^{-1}, 3 591 cm^{-1}. For $C_8H_{16}O_4$ (176·2) calculated: 54·53% C, 9·15% H, 35·22% OCH_3; found: 54·20% C, 9·02% H, 35·74% OCH_3.

Methyl 4,6-dideoxy-2,3-di-O-methyl-β-L-*ribo*-hexopyranoside (*VIII*), (45 mg), boiling at 50°C of bath temperature and 6·7 Pa, $[\alpha]_D^{20}$ +89·3 ± 1·2° (*c* 1·1). ^{1}H NMR spectrum: 4·59 (1 H, d, $J_{1,2}$ = 8 Hz, H-1); 3·73−4·08 (2 H, m, H-3, H-5); 3·54, 3·51, 3·43 (3 × 3 H, s, 3 × OCH_3); 3·02 (1 H, dd, $J_{2,1}$ = 8 Hz, $J_{2,3}$ = 3·5 Hz, H-2); 2·0 (1 H, m, $J_{4e,3}$ = 4·5 Hz, $J_{4e,5}$ = 2·5 Hz, $J_{4e,4a}$ = 13·5 Hz, H-4e); 1·33 (1 H, m, $J_{4a,3}$ = 2·5 Hz, $J_{4a,5}$ = 10 Hz, $J_{4a,4e}$ = 13·5 Hz, H-4a); 1·22 (3 H, d, $J_{6,5}$ = 6·5 Hz, H-6). For $C_9H_{18}O_4$ (190·2) calculated: 56·82% C, 9·53% H, 48·94% OCH_3; found: 56·86% C, 9·61% H, 49·63% OCH_3.

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