THE SYNTHESIS OF METHYL TETROSIDES AND THEIR METHYL ETHERS

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Methyl α- and β-D-threofuranosides (*I* and *II*) and methyl α- and β-D-erythrofuranosides (*VII* and *VIII*) were prepared in a modified manner. For the preparation of monomethyl ethers of compounds *I* and *II* 1,2-O-isopropylidene-β-D-threofuranose (*IV*) was prepared as the starting compound. For the synthesis of monomethyl ethers of compounds *VII* and *VIII* partial methylation of these diols was made use of.

In connection with the preceding papers devoted to the stereochemistry of the furanoside ring[1] and the partial methylation of sugar dihydroxy derivatives[2] attention is paid in this communication to the preparation of methyl tetrosides and their methyl ethers.

Methyl α- and β-D-threofuranosides (*I* and *II*) were prepared using a procedure based on oxidative cleavage of D-galactose with lead tetraacetate[3,4]. 3,4-Di-O-formyl--D-threose (*III*) formed oxidatively was converted without previous isolation to 1,2-O-isopropylidene-β-D-threofuranose[1,5-7] (*IV*) on treatment with acetone and anhydrous copper(II) sulfate in the presence of a trace of sulfuric acid. Compound *IV* afforded on treatment with methanol in the presence of ion exchangers in H^+ cycle an anomeric mixture of methyl threosides *I* and *II* which was acetylated with acetic anhydride in pyridine to a mixture of α and β anomers of methyl 2,3-di-O-acetyl--D-threofuranoside (*V* and *VI*) in a 2·1 : 1 ratio (gas chromatography). The mixture of compounds *V* and *VI* was also obtained directly from compound *III* on treatment with ion exchangers in H^+ cycle and subsequent acetylation (in a 1·8 : 1 ratio). Pure anomers *V* and *VI* were isolated by means of preparative gas chromatography. Compound *I* was prepared from compound *V*, and similarly compound *II* from compound *VI*, on deacetylation according to Zemplén[8]. Baxter and Perlin[9] obtained a mixture of anomers *I* and *II* in a 3 : 2 ratio on treatment of compound *III* with methanolic hydrogen chloride.

For the synthesis of methyl α and β-D-erythrofuranoside (*VII* and *VIII*) oxidative

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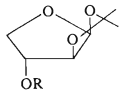
cleavage of 4,6-O-ethylidene-D-glucopyranose (*IX*) with sodium periodate according to Schaffer[10] was used. However, 2,4-O-ethylidene-D-erythrose (*X*) formed on oxidation affords on reaction with methanolic hydrogen chloride in addition to the expected methyl erythrosides *VII* and *VIII*, formed in small amount only[11], methyl 2,3-O-ethylidene-D-erythrofuranoside (*XI*). In view of the observed migration of the ethylidene group, explicable by the stability of the two connected five-membered rings[12], acid hydrolysis was carried out first during the synthesis of methyl erythrosides *VII* and *VIII* from compound *X* (in the paper by Ballou[11]), and only then the D-erythrose obtained was converted to the respective methyl glycosides. In our study the synthesis of methyl erythrosides was modified. The mixture of the anomers *VII* and *VIII* was prepared directly from compound *X*. When the methanolic solution of compound *X* was heated with ion exchangers in H^+ cycle at 60–65°C gradual transacetalation of the ethylidene group took place under formation of corresponding methyl glycosides *VII* and *VIII*. The reaction equilibrium in this synthesis was constantly disturbed by the distillation off of the acetal of acetaldehyde formed (together with methanol). The ratio of the methyl α- and β-D-erythrofuranosides *VII* and *VIII* formed was 1 : 4. Baxter and Perlin[9] obtained a 1 : 3 ratio of the α : β anomers when synthetizing methyl erythrosides on treatment of 3,4-di-O-formyl-D-erythrose with methanolic hydrogen chloride. Ballou[11] also mentions an almost exclusive formation of the β anomer for an analogous synthesis from D-erythrose, while Hockett and Maynard[13] found an approximately 6 : 4 ratio in favour of the α anomer. Acetylation of the mixture of methyl erythrosides *VII* and *VIII* with acetic anhydride in pyridine gave a mixture of methyl 2,3-di-O-acetyl-α and β-D-erythrofuranoside (*XII* and *XIII*) from which both anomers were isolated by preparative gas chromatography. Deacetylation of compound *XII* according to Zemplén[8] gave α-glycoside *VII* and compound *XIII* β-glycoside *VIII*.

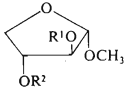
For the synthesis of monomethyl ethers of methyl threofuranosides 1,2-O-isopropylidene-β-D-threofuranose (*IV*) served as starting material. Methylation with methyl iodide and sodium hydride in formaldehyde dimethyl acetal 1,2-O-isopropylidene-3-O-methyl-β-D-threofuranose (*XIV*) was prepared which on treatment with methanol and catalysis with ion exchangers in H^+ cycle afforded a mixture of anomers of methyl 3-O-methyl-α- and β-D-threofuranoside (*XV* and *XVI*). This mixture was acetylated with acetic anhydride in pyridine to methyl 2-O-acetyl-3-O-methyl-α- and β-D-threofuranoside (*XVII* and *XVIII*). The isolation of pure anomers *XVII* and *XVIII* was carried out by preparative gas chromatography. Methyl 3-O-methyl-α-D-threofuranoside (*XV*) was obtained by deacetylation of compound *XVII* and, similarly, the pure β anomer *XVI* was obtained from compound *XVIII*.

2-O-Methyl derivatives of methyl D-threofuranoside (*XIX* and *XX*) were synthesized from 3-O-benzyl-1,2-O-isopropylidene-β-D-threofuranose[1] (*XXI*). On treatment with methanol and ion exchangers in H^+ cycle compound *XXI* gave a mixture of anomeric methyl 3-O-benzyl-D-threofuranosides (*XXII* and *XXIII*) which was

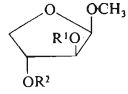
methylated with methyl iodide and sodium hydride in formaldehyde dimethyl acetal to a mixture of methyl 3-O-benzyl-2-O-methyl-α- and β-D-threofuranoside (*XXIV* and *XXV*). The isolation of pure anomers was carried out by preparative gas chromatography. Hydrogenolytic debenzylation with hydrogen of compound *XXIV*, catalyzed with palladium on charcoal, gave methyl 2-O-methyl-α-D-threofuranoside (*XIX*) while compound *XXV* gave the corresponding β anomer *XX*.



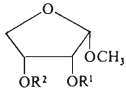
IV, R = H
XIV, R = CH_3
XXI, R = $C_6H_5CH_2$



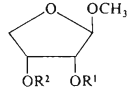
I, $R^1 = R^2 = H$
V, $R^1 = R^2 = CH_3CO$
XV, $R^1 = H$, $R^2 = CH_3$
XVII, $R^1 = CH_3CO$, $R^2 = CH_3$
XIX, $R^1 = CH_3$, $R^2 = H$
XXIV, $R^1 = CH_3$, $R^2 = C_6H_5CH_2$
XXVI, $R^1 = R^2 = CH_3$



II, $R^1 = R^2 = H$
VI, $R^1 = R^2 = CH_3CO$
XVI, $R^1 = H$, $R^2 = CH_3$
XVIII, $R^1 = CH_3CO$, $R^2 = CH_3$
XX, $R^1 = CH_3$, $R^2 = H$
XXV, $R^1 = CH_3$, $R^2 = C_6H_5CH_2$
XXVII, $R^1 = R^2 = CH_3$



VII, $R^1 = R^2 = H$
XII, $R^1 = R^2 = CH_3CO$
XXVIII, $R^1 = CH_3$, $R^2 = H$
XXIX, $R^1 = R^2 = CH_3$
XXX, $R^1 = H$, $R^2 = CH_3$



VIII, $R^1 = R^2 = H$
XIII, $R^1 = R^2 = CH_3CO$
XXXI, $R^1 = CH_3$, $R^2 = H$
XXXII, $R^1 = H$, $R^2 = CH_3$
XXXIII, $R^1 = R^2 = CH_3$

Methyl 2,3-di-O-methyl-α-D-threofuranoside (*XXVI*) was prepared by total methylation of compound *I* with methyl iodide and sodium hydride in formaldehyde dimethyl acetal. Analogously, methyl 2,3-di-O-methyl-β-D-threofuranoside (*XXVII*) was prepared from glycoside *II*.

During the synthesis of methyl ethers of methyl D-erythrofuranosides use was made of partial methylation[14] of glycoside *VII* or *VIII* with methyl iodide and sodium hydroxide in acetonitrile[15]. In the case of partial methylation of the α anomer *VII* methyl 2-O-methyl-α-D-erythrofuranoside (*XXVIII*) and methyl 2,3-di-O-methyl-α-D-erythrofuranoside (*XXIX*) were isolated from the reaction mixture by means of preparative gas chromatography. In the methylation of dihydroxy derivative *VII* 2-methyl ether *XXVIII* is formed predominantly, while methyl 3-O-methyl-α-D-erythrofuranoside (*XXX*) represents a minor component of the reaction mixture[14] over the whole span of the conversion of diol *VII*. For this reason the second monomethyl ether *XXX* was not isolated.

The characterization of these compounds was carried out by means of ^{1}H-NMR spectra (Table I). In the ^{1}H-NMR spectrum of di-O-methyl derivative *XXIX* three three-proton singlets of the methoxyl groups were detected. In the case of protons on the second (H−2) and the third (H−3) carbon a change of the chemical shifts took place in the direction of higher magnetic field in comparison with the signals of these protons in diol *VII* (in the case of H−2 from the value $\delta = 4{\cdot}08$ in compound *VII* to the value $\delta = 3{\cdot}68$; similarly, in the case of H−3 from the value $\delta = 4{\cdot}15$ in compound *VII* to the value $\delta \approx 3{\cdot}85$).

In the case of methyl ether *XXVIII* two three-proton singlets of the methoxy groups were observed in the ^{1}H-NMR spectrum. The position of the methoxy group on carbon $C_{(2)}$ in this monomethyl ether was determined on the basis of chemical shifts of protons H−2 and H−3 in compounds *VII*, *XXVIII* and *XXIX*. In monometyl ether *XXVIII* a change in the chemical shift to higher fields of the magnetic field took place for proton H−2 in comparison with the chemical shift of this proton in dihydroxy derivative *VII*. (From the value $\delta = 4{\cdot}08$ in compound *VII* to the value $\delta = 3{\cdot}68$). This value of the chemical shift of proton H−2 is simultaneously identical with the chemical shift of H−2 in dimethyl ether *XXIX*. The value of the chemical shift of the proton on the third carbon in monomethyl ether *XXVIII* is very close to the value δ for dihydroxy derivative *VII*).

Using preparative gas chromatography of the reaction mixture after partial methylation of the β anomer *VIII* both monomethyl ethers *XXXI* and *XXXII* and di-O-methyl derivative *XXXIII* were isolated in addition to the starting diol *VIII*. Methyl 2,3-di-O-methyl-β-D-erythrofuranoside (*XXXIII*) was also prepared by total methylation of diol *VIII* with methyl iodide and sodium hydride in formaldehyde dimethyl acetal. The characterization of individual substances, primarily from the point of view of the differentiation of monomethyl ethers *XXXI* and *XXXII*, was carried out using ^{1}H-NMR spectrometry. In the ^{1}H-NMR spectrum of dimethyl ether *XXXIII* three singlets were observed corresponding to nine protons of methoxyl groups. The signal of the proton on the second carbon atom (H−2) was at the same time shifted upfield from $\delta = 4{\cdot}02$ (chemical shift of H−2 in dihydroxy derivative *VIII*) to $\delta = 3{\cdot}68$. Similarly the chemical shift of the proton on the third carbon

TABLE I

^{1}H-NMR Spectra of the Derivatives of Tetroses

Compound	Chemical shifts						Coupling constants J (Hz)				
	H_1	H_2	H_3	H_4	$H_{4'}$	OCH_3	1·2	2·3	3·4	3·4′	4·4′
I[a]	s 4·87	m 4·11	m 4·11	q 3·87	q 4·31	s 3·42	<1·5	<1·5	2·0	5·0	9·8
II[b]	d 4·92	m 4·10	m 3·92—4·22	m 3·67	m 3·92—4·22	s 3·45	4·4	→0	—	—	—
V[c]	s 4·87	s 5·07	q 5·06	q 3·77	q 4·39	s 3·38	<1·5	<1·5	5·0	6·8	10·0
VI[d]	d 5·12	t 4·98	o 5·28	q 3·69	q 4·26	s 3·37	4·4	4·5	3·4	6·5	10·5
VII	d 4·83	m 4·08	m 4·15	q 3·86	m 4·08	s 3·46	4·3	—	4·7	5·5	12·0
VIII[e]	s 4·84	m 4·02	m 4·37	q 3·80	q 4·07	s 3·35	<1·5	<2·5	3·8	7·0	10·0
XII[f]	d 5·04	q 4·92	o 5·32	q 3·87	q 4·25	s 3·42	4·5	7·0	3·8	6·5	10·2
XIII[g]	d 4·92	q 5·14	m 5·41	q 3·87	q 4·20	s 3·36	1·5	5·5	4·2	5·8	10·0
XV[b,h]	s 4·82	m 3·69			4·45	—	→0	—	—	—	—
XVI[b,i]	d 4·93	d 4·12	m 3·63		4·05	—	4·4	—	—	—	—
XVII[b,j]	d 5·14	q 4·86	m 4·15	m 3·59	4·08	—	4·4	3·9	—	—	—
XXIV[b,k]	d 4·86	m 3·70			4·24	—	<1·5	—	—	—	—
XXV[b,l]	d 4·96	m 3·70			4·36	—	4·5	—	—	—	—
XXVIII[m]	d 4·91	q 3·68	m 4·24	q 3·97	d 4·16	—	4·1	5·0	1·8	<1·5	10·0
XXIX[n]	d 4·91	q 3·68	m 3·83		4·11	—	4·4	6·2	—	—	—
XXXI[o]	d 4·89	q 3·65	m 4·37	q 3·81	q 4·01	—	2·0	5·0	3·4	4·6	9·6
XXXII[p]	s 4·84	m 4·00	—4·10	q 3·89	m 4·00—4·10	—	<1·5	—	5·0	—	11·0
XXXIII[r]	d 4·91	q 3·68	m 3·80		4·08	—	2·0	4·0	—	—	—
IV[s]	d 5·91	q 4·46	m 4·23	q 3·83	q 4·07	—	3·8	<1·5	<1·5	2·6	10·0
XIV[t]	d 5·93	q 4·56	m 3·84	s 4·01	s 4·01	—	4·0	<1·5	<1·5	<1·5	—
XXI[b,u]	d 5·95	d 4·60	s 4·02	s 4·02	s 4·02	—	3·0	→0	→0	→0	→0

[a] 2 OH s 3·14; [b] 60 MHz; [c] 2 CH_3CO s 2·09; [d] CH_3CO s 2·08, s 2·11; [e] 2 OH 3·80—4·10; [f] CH_3CO s 2·11, s 2·13; [g] CH_3CO s 2·05, s 2·09; [h] OCH_3 s 3·39, s 3·41, OH s 2·70; [i] OCH_3 s 3·41, s 3·46; [j] OCH_3 s 3·36, s 3·36, CH_3CO s 2·13; [k] OCH_3 s 3·35, s 3·38, OCH_2Ar s 4·56, 5 HAr, s 7·32; [l] OCH_3 s 3·41, s 3·45, OCH_2Ar s 4·56, 5 HAr s 7·32; [m] OCH_3 s 3,44, s 3·55, OH s 2·72; [n] OCH_3 s 3·42, s 3·45, s, 3·50; [o] OCH_3 s 3·37, s 3·50, OH s 2·84; s OCH_3 s 3·34, s 3·43, OH s 2·84; [r] OCH_3 s 3·36, s 3·41, s 3·48; [s] $(CH_3)_2C$ s 1·30, 1·46, OH d 2·69; [t] $(CH_3)_2C$ s 1·34, s 1·49, OCH_3 s 3·39; [u] $(CH_3)_2C$ s 1·31, s 1·47, OCH_2Ar s 4,56, 5 HAr s 7·32.

atom (H−3) was changed from $\delta = 4{\cdot}37$ in diol *VIII* to $\delta = 4{\cdot}05$. As for monomethyl ethers *XXXI* and *XXXII* two three-proton singlets of methoxyl groups and a one-proton singlet of the hydroxyl group were found in both cases. The differentiation of compounds *XXXI* and *XXXII* was carried out on the basis of the differences in chemical shifts of proton H−2 and H−3.

In 2-O-monomethyl derivative *XXXI* the chemical shift of H−3 ($\delta = 4{\cdot}37$) is identical with that of H−3 in diol *VIII*. However, the chemical shift of H−2 was shifted upfield in comparison with compound *VIII*. The observed value $\delta = 3{\cdot}65$ corresponds to the chemical shift of H−2 in dimethyl ether *XXXIII*. In 3-O-methyl derivative *XXXII* the chemical shift of the proton on $C_{(2)}$ ($\delta \approx 4{\cdot}05$) corresponds to the δ-value for H−2 in diol *VIII*. In contrast to this, in compound *XXXII* the δ-value of the proton on $C_{(3)}$ changed from the value 4·37 belonging to H−3 in compound *VIII* to the value $\delta \approx 4{\cdot}05$ corresponding to the chemical shift of H−3 in dimethyl ether *XXXIII*.

EXPERIMENTAL

The melting points were determined on a Kofler block and they are not corrected. Optical rotations were measured on a photoelectric polarimeter of the firm Opton at 20°C. The solvents were evaporated on a rotatory evaporator in a water pump vacuum at 40°C. Samples for analysis were dried at 20°C and 2·66 Pa, liquid substances were distilled *in vacuo* (oil pump) at 1·33 Pa. Thin-layer chromatography was carried out on silica gel G according to Stahl (Merck, Darmstadt) 10—40 μm using 25 × 75 mm plates with 0·2—0·3 mm layer thickness. The substances were detected by spraying with concentrated sulfuric acid and subsequent mineralization. The ^{1}H-NMR spectra were measured in deuteriochloroform on a Varian XL-10-15 instrument or on a Jeol FX—60 one, with tetramethylsilane as internal reference. The chemical shifts are given in ppm, δ-scale, and the coupling constants in Hz. Gas chromatography was carried out on a Varian Aerograph 2100 instrument in combination with a Hewlett–Packard 3380 A integrator, using a flame-ionization detector and helium as carrier gas. Preparative gas chromatography was carried out on a Chrom 3 (Laboratorní přístroje, Prague) chromatograph, using hydrogen as carrier gas and detection with a catharometer.

1,2-O-Isopropylidene-β-D-threofuranose (*IV*)

D-Galactose was oxidized with lead tetraacetate[3,4] to 3,4-di-O-formyl-D-threose (*III*) which was not isolated but direcly converted with anhydrous cupric sulfate in acetone and trace of sulfuric acid to compound *IV*, m.p. 83—84°C, $[\alpha]_D^{20}$ −15·3° (*c* 1·5; acetone). Literature[5] gives m.p. 83°C, lit.[6] m.p. 84°C, $[\alpha]_D^{20}$ −15·27° (*c* 2·292; acetone) and lit.[7] m.p. 83—84°C, $[\alpha]_D^{20}$ −15·1° (*c* 0·8; acetone).

Methyl α- and β-D-Threofuranoside (*I* and *II*)

a) *From* 1,2-O-*isopropylidene*-β-D-*threofuranose* (IV): 20 ml of Dowex 50 W in H^+ cycle were added to a solution of 2 g (12·5 mmol) of compound *IV* in 50 ml of methanol and the reaction was followed using TLC and benzene with 10% of acetone for chromatography. When all the

starting compound *IV* had reacted the ion exchanger was filtered off and washed with methanol. The combined filtrates were evaporated and the residue was dried in a vacuum (oil pump). Yield, 1·6 g (96%) of syrupy mixture of anomeric methyl threosides *I* and *II*. Using gas chromatography* the ratio of the anomers α and β was determined to 2·1 : 1.

b) *From* 3,4-*di*-O-*formyl*-D-*threose* (III): 150 ml of Dowex 50 W in H^+ cycle were added to a solution of 39 g (0·26 mol) of compound *III* in 500 ml of methanol and the mixture was stirred at 20°C. When the reaction was terminated (by TLC) the mixture was worked up as under *a*). Yield, 29 g (82%) of a syrup in which the ratio of substances *I* and *II* was determined to be 1·8 : 1 by gas chromatography.

Methyl 2,3-Di-O-acetyl-α-D-threofuranoside (*V*) and Methyl 2,3-Di-O-acetyl-β-D-threofuranoside (*VI*)

Acetic anhydride (8·2 ml) was added to a cooled solution (at —10°C) of 1·8 g (13·4 mmol) of the mixture of methyl threosides *I* and *II* in 25 ml of pyridine and the mixture was allowed to stand at 20°C for 48 h. The solvents were then evaporated and icy water was added to the residue. Then the product was extracted with chloroform. The extract was washed with 0·5M sulfuric acid, water, saturated sodium hydrogen carbonate solution and again three times with water. The chloroform solution was dried over magnesium sulfate, filtered and evaporated. Yield, 2·8 g (96%) of a syrupy mixture of compounds *V* and *VI* which was separated by preparative gas chromatography on a 700 × 8 mm column packed with 20% polypropylene sebacate on Silocel *c* 22, at 180°C and a flow-rate of 60 ml of hydrogen per min. R_t of the β anomer *VI* was 1320 s, of the α- anomer *V* 1710 s. Preparative gas chromatography gave 0·6 g of compound *VI* and 1·1 g of compound *V*. Compound *V* was isolated in the form of a syrup, $[\alpha]_D^{20} = 36°$ (*c* 1; chloroform). For $C_9H_{14}O_6$ (218·2) calculated: 49·54% C, 6·47% H; found: 49·63% C, 6·72% H. The β anomer *VI* had m.p. 71—72·5°C (ether–light petroleum), $[\alpha]_D^{20}$ —242° (*c* 0·5; chloroform). For $C_9H_{14}O_6$ (218·2) calculated: 49·54% C, 6·47% H; found: 49·77% C, 6·60% H.

Methyl α-D-Threofuranoside (*I*)

A catalytic amount of sodium was added to a strongly cooled solution (with solid carbon dioxide) of 1·9 g (8·7 mmol) of compound *V* in 50 ml of methanol. When the temperature rose to 20°C the reaction course was monitored by TLC. When all the starting compound *V* had reacted the solution was saturated with carbon dioxide to neutrality. The solvents were evaporated and the residue extracted with chloroform. The combined extracts were dried over magnesium sulfate and filtered. After evaporation of chloroform 1·1 g (94%) of syrupy substance *I* were obtained, $[\alpha]_D^{20}$ 101° (*c* 0·9; water). For $C_5H_{10}O_4$ (134·1) calculated: 44·77% C, 7·51% H; found: 44·87% C, 7·64% H. Literature[9] gives $[\alpha]_D = 97°$ (*c* 1·6; water).

Methyl β-D-Threofuranoside (*II*)

Using an analogous procedure as in the synthesis of α anomer *I* 550 mg (90%) of syrupy *II*, $[\alpha]_D^{20}$ —191° (*c* 0·6; water) were obtained from 1 g (4·6 mmol) of compound *VI*. For $C_5H_{10}O_4$

* The analyses were carried out on a 1800 × 2 mm column packed with Versamide 900 on Chromosorb T, at 140—180°C, with a temperature gradient 4°C/min and 20 ml helium per minute flow. The temperature of the injection port was 190°C, the detector temperature 200°C. Under the given conditions the R_t value of compound *I* was 971 s and of compound *II* 625 s.

(134·1) calculated: 44·77% C, 7·51% H; found: 44·94% C, 7·76% H. Literature[9] gives $[\alpha]_D^{25}$ —193° (*c* 1·1; water).

2,4-O-Ethylidene-D-erythrose (*X*)

Oxidation of 10·3 g (0·05 mol) of 4,6-O-ethylidene-D-glucopyranose[16] (*IX*) (m.p. 179—183°C, $[\alpha]_D^{20}$ —2·4° (*c* 3·9; water)) with sodium periodate according to Schaffer[10] gave 6·7 g (92%) of compound *X*, m.p. 145—150°C, $[\alpha]_D^{20}$ —43·6° (*c* 0·8; water). Literature[10] gives m.p. 149—150°C, $[\alpha]_D^{22}$ —40 to —43·5° (water), lit.[17] m.p. 145—148°C, $[\alpha]_D^{23}$ —23·1° (*c* 1; water), lit.[18] $[\alpha]_D^{22}$ —41·36° (*c* 2·5; water), lit.[19] m.p. 149—150°C, $[\alpha]_D$ —43·5°, lit.[16] $[\alpha]_D^{20}$ —36·8° (*c* 8·25; water), lit.[20] m.p. 117—123°C, $[\alpha]_D$ 43·2°, lit.[21] m.p. 65—80°C, $[\alpha]_D^{24}$ —37·8° (*c* 3·12; water) and lit.[22] $[\alpha]_D^{22}$ —12·8° (*c* 4·08; ethanol). For 2,4-O-ethylidene-L-erythrose literature[23] gives m.p. 73—79°C, $[\alpha]_D$ +36° (*c* 2·5; water).

Methyl 2,3-Di-O-acetyl-α-D-erythrofuranoside (*XII*)
and Methyl 2,3-Di-O-acetyl-β-D-erythrofuranoside (*XIII*)

Compound *X* (7 g; 48 mmol) was dissolved in methanol, Dowex 50 W in H^+ cycle was added, and the mixture heated at 60—65°C. Methanol was slowly distilled off from the mixture together with acetaldehyde dimethyl acetal, (control by GLC). The evaporated methanol was periodically filled up. The reaction course was followed by TLC in chloroform with 10% of ethanol. After filtration off of the ion exchanger and washing with methanol the filtrate was evaporated. The residue (5 g; 78%) was a syrupy mixture of compounds *VII* and *VIII* in which the ratio of anomer α to β was 1 : 4, as determined by GLC (see note on p. 8; R_t of compound *VII* was 336 s and of compound *VIII* 960 s.) Using a procedure analogous to that used for the preparation of compounds *V* and *VI* 7·6 g (93%) of a mixture of compounds *XII* and *XIII* was obtained from 5 g (37 mmol) of a mixture of anomers *VII* and *VIII*. Half (3·8 g) of the reaction mixture was separated by preparative gas chromatography on a 4800 × 9 mm column packed with 5% of QF 1 on Chromaton N-AW at 180°C and 125 ml of hydrogen per minute flow-rate. The retention time of α anomer *XII* was 480 s and of β anomer *XIII* 720 s. Preparative gas chromatography afforded 0·55 g of compound *XII* and 2·07 g of compound *XIII*. After purification of both compounds *XII* and *XIII* under identical conditions on the same column the α anomer *XII* was obtained as a syrup with $[\alpha]_D^{20} = 100°$ (*c* 1·2; chloroform). For $C_9H_{14}O_6$ (218·2) calculated: 49·54% C, 6·47% H; found: 49·34% C, 6·62% H. β Anomer *XIII* was also isolated as a syrup, $[\alpha]_D^{20}$ —123° (*c* 0·6; chloroform). For $C_9H_{14}O_6$ (218·2) calculated: 49·54% C, 6·47% H; found: 49·58% C, 6·41% H.

Methyl α-D-Erythrofuranoside (*VII*)

Using a procedure similar to that for the preparation of *I* syrupy *VII* (167 mg; 95%) was obtained from 285 mg (2·12 mmol) of diacetyl derivative *XII*; $[\alpha]_D^{20} = 141°$ (*c* 0·6; water). For $C_5H_{10}O_4$ (134·1) calculated: 44·77% C, 7·51% H; found: 44·53% C, 7·70% H. Literature[9] gives $[\alpha]_D^{25} = 133°$ (water).

Methyl β-D-Erythrofuranoside (*VIII*)

Using a procedure analogous to that used for the synthesis of compound *I* 344 mg (2·60 mmol) of diacetyl derivative *XIII* was converted to 202 mg (96%) of syrupy compound *VIII*, $[\alpha]_D^{20}$ —139° (*c* 0·9; water). For $C_5H_{10}O_4$ (134·1) calculated: 44·77% C, 7·51% H; found: 45·08% C, 7·62% H. Literature[9] gives $[\alpha]_D^{25}$ —148° (water).

1,2-O-Isopropylidene-3-O-methyl-β-D-threofuranose (*XIV*)

Sodium hydride (0·7 g) was added to a solution of 2·76 g (17·25 mmol) of compound *IV* in 75 ml of formaldehyde dimethyl acetal and stirred for 1 h. The methyl iodide (10 ml) was added dropwise and when all the starting compound had reacted (checked by TLC in benzene with 10% of acetone) methanol was added and the solvents evaporated. The residue was extracted with chloroform and the combined extracts washed with water, dried over magnesium sulfate, filtered and evaporated. Yield 2·84 g (95%) of syrupy 3-O-methyl derivative[24] *XIV*, $[\alpha]_D^{20}$ −5° (*c* 1·2; chloroform). For $C_8H_{14}O_4$ (174·2) calculated: 55·16% C, 8·10% H; found: 55·07% C, 8·25% H.

Methyl 2-O-Acetyl-3-O-methyl-α-D-threofuranoside (*XVII*)
and Methyl 2-O-Acetyl-3-O-methyl-β-D-threofuranoside (*XVIII*)

From 2·39 g (13·7 mmol) of compound *XIV* 1·96 g (96%) of a syrupy mixture of compounds *XV* and *XVI* were obtained when proceeding as in the synthesis of the mixture of anomers *I* and *II*. Using GLC the ratio of *XV* and *XVI* was found to be 1·8 : 1 in favour of the α anomer *XV*. Acetic anhydride (4·5 ml) was then added to 1·96 g (13·2 mmol) of this mixture of *XV* and *XVI* dissolved in 25 ml of pyridine, cooled with dry ice. Analogously as in the preparation of diacetyl derivatives *V* and *VI* 2·32 g (92%) of a syrupy mixture of compounds *XVII* and *XVIII* were obtained, which was separated by preparative gas chromatography on a 700 × 8 mm column packed with 20% of polypropylene sebacate on Silocel c 22, at 185°C and 60 ml hydrogen per minute flow-rate. The retention time of the β anomer *XVIII* was 720 s and of the α anomer *XVII* 990 s. Using preparative gas chromatography 1·22 g of compound *XVII* and 0·68 g of compound *XVIII* were obtained. α-Anomer *XVII* was purified by preparative gas chromatography, giving a syrup of $[\alpha]_D^{20} = 109°$ (*c* 1·1; chloroform). For $C_8H_{14}O_5$ (190·2) calculated: 50·52% C, 7·37% H; found: 50·40% C, 7·61% H. β-Anomer *XVIII* was also obtained as a syrup, using purification by GLC, $[\alpha]_D^{20}$ −232° (*c* 0·8; chloroform). For $C_8H_{14}O_5$ (190·2) calculated: 50·52% C, 7·37% H; found: 50·73% C, 7·56% H.

Methyl 3-O-Methyl-α-D-threofuranoside (*XV*)

From 222 mg (1·2 mmol) of compound *XVII* 162 mg (94%) of syrupy monomethyl ether *XV* of $[\alpha]_D^{20} = 127°$ (*c* 0·7; chloroform) were obtained by the procedure used for the preparation of compound *I*. For $C_6H_{12}O_4$ (148·2) calculated: 48·64% C, 8·16% H; found: 48·45% C, 8·41% H.

Methyl 3-O-Methyl-β-D-threofuranoside (*XVI*)

Using an analogous procedure as in the preparation of compound *I* 113 mg (0·6 mmol) of acetyl derivative *XVIII* gave 80 mg (91%) of syrupy compound *XVI*, $[\alpha]_D^{20}$ −81° (*c* 0·4; chloroform). For $C_6H_{12}O_4$ (148·2) calculated: 48·64% C, 8·16% H; found: 48·79% C, 8·29% H.

Methyl 3-O-Benzyl-2-O-methyl-α-D-threofuranoside (*XXIV*)
and Methyl 3-O-Benzyl-2-O-methyl-β-D-threofuranoside (*XXV*)

3-O-Benzyl-1,2-O-isopropylidene-β-D-threofuranose[1] (*XXI*) (1·27 g; 5·1 mmol) was treated analogously as compound *IV* in the synthesis of the mixture of anomers *I* and *II*. A syrupy mixture (1·07 g; 94%) of benzyl derivatives *XXII* and *XXIII* was obtained; 1·06 g (4·7 mmol) of this mixture was converted to 1·08 g (96%) of a syrupy mixture of compounds *XXIV* and *XXV* using the procedure for the synthesis of compound *XIV*. The mixture was separated by preparative

gas chromatography on a 700 × 8 mm column packed with 20% polypropylene sebacate on Silocel c 22, at 185°C and using hydrogen as carrier gas. Yield 0·35 g of compound *XXIV* and 0·27 g of compound *XXV*. α-Anomer *XXIV* was isolated in the form of a syrup of $[\alpha]_D^{20} = 92°$ (*c* 0·9; chloroform). For $C_{13}H_{18}O_4$ (238·3) calculated: 65·54% C, 7·56% H; found: 65·44% C, 7·65% H. β-Anomer *XXV* was also obtained as a syrup, $[\alpha]_D^{20}$ —153° (*c* 0·5; chloroform). For $C_{13}H_{18}O_4$ (238·3) calculated: 65·54% C, 7·56% H; found: 65·60% C, 7·77% H.

Methyl 2-O-Methyl-α-D-threofuranoside (*XIX*)

A solution of 250 mg (1·05 mmol) of compound *XXIV* in methanol was hydrogenolysed by stirring it with 5%-palladium on charcoal under hydrogen at 20°C and atmospheric pressure. The reaction course was followed by TLC in benzene with 10% of acetone. After the disappearance of the starting compound *XXIV* the solution was filtered, the catalyst was washed with methanol and the combined filtrates evaporated. Yield, 145 mg (93%) of syrupy *XIX*, $[\alpha]_D^{20} = 74°$ (*c* 0·5; chloroform). For $C_6H_{12}O_4$ (148·2) calculated: 48·64% C, 8·16% H; found: 48·78% C, 8·13% H.

Methyl 2-O-Methyl-β-D-threofuranoside (*XX*)

An analogous procedure as in the synthesis of the α anomer *XIX* was applied to 200 mg (0·84 mmol) of compound *XXV*, affording 110 mg (88%) of the β anomer *XX* in the form of a syrup of $[\alpha]_D^{20}$ —145° (*c* 0·4; chloroform). For $C_6H_{12}O_4$ (148·2) calculated: 48·64% C, 8·16% H; found: 48·64% C, 8·30% H.

Methyl 2,3-Di-O-methyl-α-D-threofuranoside (*XXVI*)

Sodium hydride (about 120 mg) was added to 140 mg (1·04 mmol) of dihydroxy derivative *I* in 30 ml of formaldehyde dimethyl acetal and the mixture was stirred for 1 h. Methyl iodide (1·5 ml) was then added dropwise and the stirring continued under control of the reaction course by GLC. When the starting diol *I* and the corresponding monomethyl ethers *XV* and *XIX* disappeared, methanol was added and the solvents were evaporated. The residue was extracted with chloroform and the combined extracts washed with water, dried over magnesium sulfate, filtered and evaporated. Yield, 150 mg (89%) of liquid dimethyl ether *XXVI*, $[\alpha]_D^{20} = 105°$ (*c* 0·5; chloroform). For $C_7H_{14}O_4$ (162·2) calculated: 51·84% C, 8·70% H; found: 51·70% C, 8·87% H.

Methyl 2,3-Di-O-methyl-β-D-threofuranoside (*XXVII*)

The synthetic procedure used for the preparation of α anomer *XXVI* was applied to dihydroxy derivative *II* (120 mg; 0·89 mmol), affording 122 mg (84%) of liquid dimethyl ether *XXVII* $[\alpha]_D^{20}$ —204° (*c* 0·6; chloroform) as product. For $C_7H_{14}O_4$ (162·2) calculated: 51·84% C, 8·70% H; found: 51·68% C, 8·98% H.

Methyl 2-O-Methyl-α-D-erythrofuranoside (*XXVIII*)
and Methyl 2,3-Di-O-methyl-α-D-erythrofuranoside (*XXIX*)

Compounds *XXVIII* and *XXIX* were obtained by preparative gas chromatography of the reaction mixture after partial methylation of diol *VII* with methyl iodide and sodium hydroxide in acetonitrile[14]. The reaction mixtures of individual kinetic measurements were combined and the ob-

tained syrup was extracted with chloroform. The chloroform solution was washed with water, dried over magnesium sulfate, filtered through a small column of alumina and the filtrate evaporated. The residue was separated on a 3000 × 6 mm column packed with 5% Versamide 900 on Chromaton N-AW at 90°C using hydrogen as carrier gas. For compounds *XXVIII*—*XXX* the following retention times were found: 855 s for compound[14] *XXX*, 1 290 s for compound *XXVIII* and 1 650 s for compound *XXIX*. Preparative gas chromatography gave 9 mg of compound *XXX*, 109 mg of compound *XXVIII* and 135 mg of compound *XXIX*. In view of the fact that 2-O-methyl derivative *XXVIII* and dimethyl ether *XXIX* were not obtained sufficiently pure (nor in the case of compound *XXX* in sufficient amount), their characterization was carried out merely on the basis of their ^{1}H-NMR spectra (Table I).

Methyl 2-O-Methyl-β-D-erythrofuranoside (*XXXI*)
and Methyl 3-O-Methyl-β-D-erythrofuranoside (*XXXII*)

Preparative chromatography of the reaction mixture of partial methylation[14] of diol *VIII* on a 700 × 12 mm column packed with 20% polypropylene sebacate on Silocel c 22 at 150°C gave 2-O-methyl derivative *XXXI* as a syrup with $[\alpha]_D^{20}$ —110° (*c* 0·8; chloroform). 3-O-Methyl derivative *XXXII* were also isolated as a syrup, $[\alpha]_D^{20}$ —149° (*c* 0·7; chloroform). The structures of compounds *XXXII* and *XXXI* were proved by ^{1}H-NMR spectrometry (Table I).

Methyl 2,3-Di-O-methyl-β-D-erythrofuranoside (*XXXIII*)

Using an analogous procedure as in the case of compounds *XXVI* and *XXVII*, 90 mg (0·67 mmol) of dihydroxy derivative *VIII* was converted to 96 mg (88%) of liquid dimethyl ether *XXXIII*, $[\alpha]_D^{20}$ —110° (*c* 0·7; chloroform). For $C_7H_{14}O_4$ (162·2) calculated: 51·84% C, 8·70% H; found: 51·67% C, 9·00% H.

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