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SYNTHESIS AND SELECTIVE ALCOHOLYSIS OF D-HEXOPYRANOSIDE-URONOLACTONES

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A characteristic property of hexuronic acids with D-gluco- and D-manno-configurations is the formation of D-hexofuranurono-6,3-lactones, also known in the form of methylglycosides [1, 2]. The formation and the properties of lactones of the pyranose forms of uronic acids have been studied to a much lesser extent [3-5]. We have recently shown [6] that the lactonization of β-glycopyranosides of D-glucuronic and cellobiouronic acids leads smoothly to the acetylated 6,3-lactones (I) and (Ia). By selective methanolysis of the lactone ring in (I) and (Ia), derivatives of type (V) were obtained with a free OH group at the 3 and 3'-positions, respectively, which were used in the synthesis of the capsular polysaccharide *Streptococcus pneumoniae* type 3 [6], containing residues of glucopyranuronic acid substituted at the 3-position.

In the present work we describe the preparation of acetylated lactones of D-hexopyranosideuronic acids with D-galacto- and D-manno-configurations, (II)-(IV) and studied the possibility of the subsequent opening of the lactone ring by alcohols (MeOH, $PhCH_2OH$ and $CH_2{=}CHCH_2OH$). The choice of the alcohols used for the alcoholysis was determined by the possibilities of the transformations of uronic acid esters into free acids. Thus, the methyl esters can be saponified by an alkali, the benzyl esters can be subjected to hydrogenolysis, and the allyl esters can be split in a weakly acidic medium in the presence of Pd/C [7], or under nearly neutral conditions in a THF–morpholine mixture in the presence of $(Ph_3P)_4Pd$ [8].

The lactonization of methyl-α-D-galactopyranosideuronic acid on heating with Ac_2O (70°C, 30 min) proceeds with the formation of methyl-2,4-di-O-acetyl-α-D-galactopyranosideurono-6,3-lactone (II) together with other reaction products having a lower chromatographic mobility. By subsequently adding pyridine to the reaction mixture, the number of products in the mixture can be reduced to (II) only, and therefore the selected variant of lactonization (heating with Ac_2O and subsequent acetylation in the presence of pyridine) was also applied to other D-hexopyranosideuronic acids.

The lactonization of methyl-α-D-galactopyranosideuronic acid [9] leads to lactone (II) in a 72% yield. The closure of the lactone ring immobilizing the $^1C_4$ conformation is indicated by the PMR spectral data. Instead of SSCC ($J_{1,2}$ = 2.5-3.5, $J_{2,3}$ = 9, $J_{4,5}$ = 1.5 Hz)

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characteristic of α-D-galactopyranoside-uronates (the $^4C_1$ conformation) [10], the SSCC ($J_{1,2}$ = 1.5, $J_{2,3}$ = 1.5, $J_{4,5}$ = 2.9 Hz) are observed in the spectrum of (II).

The lactonization of methyl-α-D-mannopyranosideuronic acid (obtained by the oxidation of methyl-α-D-mannopyranoside [11-13]) leads to a reaction product (yield 75%) which is homogeneous according to the data of TLC and high performance liquid chromatography (HPLC) on silica gel. However, the analysis of the reaction product by the GLC method shows that it consists of two components (III) and (IV), with the content of (III) (having a shorter retention time) being 42 ± 3%. Using the method of a selective ^1H_i-{^1H_i} homonuclear resonance, it was found that a mixture of methyl-2,4-di-O-acetyl-α-D-mannopyranoside-urono-6,3-lactone (III) (44%) and methyl-3,4-di-O-acetyl-α-D-manopyranoside-urono-6,2-lactone (IV) (56%) is formed. Thus, specifically, only for the $^1C_4$ conformation of methyl-α-D-mannopyranosides [the 6,3-lactone (III)], can we expect a large value of SSCC $J_{1,2}$ = 7.2 Hz, observed in the spectrum of a mixture of (III) and (IV). Judging from the PMR spectral data, the isomeric 6,2-lactone (IV) exists in a distorted boat conformation (all the SSCC of the vicinal protons have a value of an order of magnitude of 2-3 Hz). The presence of far-range interactions of protons in the PMR spectra of the 6,3-lactones (I) and (III) and of the 6,2-lactone (IV) should be noted.

The structure of lactones (I)-(IV) is confirmed also by the results of their opening under alcoholysis conditions, cited below. The alcoholysis of acetates of hexopyranoside-uronic acid lactones depends on the ratio of the relative rates of several processes. These are the primary processes of lactone ring opening and partial deacetylation, and secondary processes involving the migration of the acetyl groups. The relative rate of these reactions is determined by the nature of the lactone and of the alcohol and the presence of a catalyst, the concentration of the latter and the temperature of the reaction (cf. [14]). Taking the alcoholysis of lactone (II) with a galacto configuration as an example, we have revealed that with increase in the temperature, not only the rate of opening of the lactone ring increases, but also the yield of deacetylation products and products resulting from migration of the acetyl groups increases sharply, and therefore all the experiments on the alcoholysis of lactones were carried out at ~20°C. In each case, the reaction time was selected according to the rate of transformation of the initial lactone and the amount of the monohydroxylic compounds formed (evaluation by means of TLC) (see scheme).

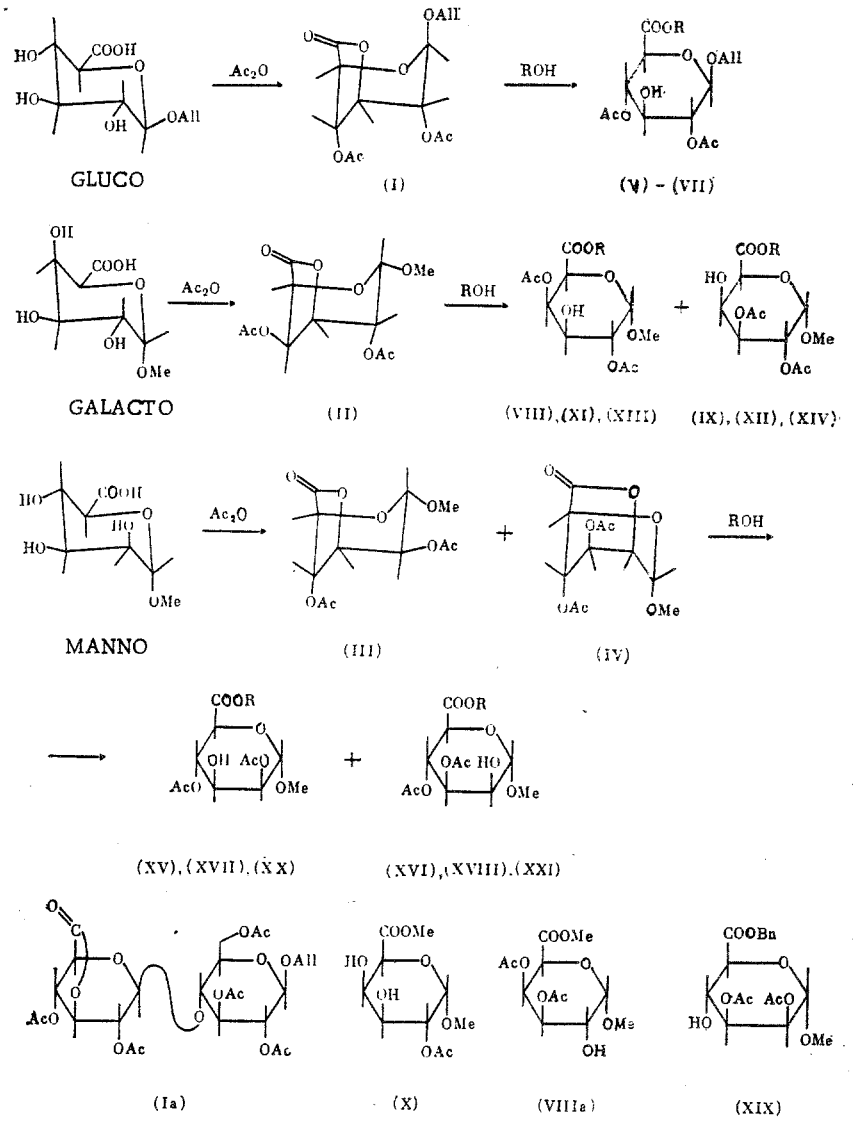
Methanolysis of acetates of D-hexopyranoside-uronolactones proceeds in the absence of a basic catalyst. The methanolysis of the gluco-6,3-lactone (I) proceeds practically selectively, and after four days, 81% of methyl (allyl-2,4-di-O-acetyl-β-D-glucopyranoside)uronate (V) is formed, which is identical with the sample previously obtained in [6]. In the absence of a base, the methanolysis of mannolactones (III) and (IV) proceeds at different rates. According to the GLC data, after 2.5 h, in a reaction mixture containing a considerable amount of lactone (IV), there remains <1% of lactone (III). After 6 days, some (IV) still remains in the reaction mixture, and as a result of methanolysis methyl (methyl-2,4- and methyl-3,4-di-O-acetyl-α-D-mannopyranoside)uronates (XV) and (XVI) are formed (yield 42 and 31%). These, in contrast to the starting lactones can easily be separated by chromatography on silica gel. The structure of compounds (XV) and (XVI) follows from the data of the PMR spectra. In particular, the SSCC of vicinal protons have values characteristic of methyl-α-D-mannopyranosideuronates (the $^4C_1$ conformation) (cf. [15]). The position of the free hydroxyl group is confirmed by the position of the signal of the corresponding ring proton [H^3 for (XV) and H^2 for (XVI)] in a strong field.

The methanolysis of lactone (II) proceeds even more slowly and two weeks are required for the reaction to be completed. The process is accompanied by the formation of a considerable amount of deacetylation products and products resulting from the migration of the acetyl groups (Table 1), which were identified (TLC) by comparison with authentic samples described below.

The rate of methanolysis of acetates of D-hexopyranosideuronolactones increases noticeably in the presence of a base (AcONa). Thus, the methanolysis of a mixture of mannolactones (III) and (IV) in the presence of AcONa (concentration 5 mg/ml) is completed even after 2.5 h, while in the methanolysis of lactone (I) [6] in the presence of AcONa (concentration 1.2 mg/ml), 52% of methyl uronate (V) is isolated by crystallization from the reaction mixture after 1.5 h.

During the methanolysis of lactone (II) in the presence of AcONa under standard conditions (variant B, see the Experimental section), the initial lactone disappears after 20 h.

Scheme



R = Me(V), (VIII), (IX), (XV), (XVI); R = $PhCH_2$(VI), (XI), (XII), (XVII), (XVIII); R = All(VII), (XIII), (XIV), (XX), (XXI).

A product of the lactone ring opening (VIII) is formed in 25% yield, but the main reaction product is a dihydroxylic compound (X) (yield 54%). In addition, minor products due to migration of acetyl groups (VIIIa) and (IX) were isolated from the reaction mixture. When the concentration of the base was decreased, the methanolysis slowed down sharply, but no substantial change in the ratio between the reaction products was thus observed. When the concentration of AcONa was increased or when the temperature was increased, the methanolysis proceeded more rapidly, but the amount of the deacetylation products and products resulting from migration of the acetyl groups thus also increased. Similar observations were also made in the study of the methanolysis of acetates of aldonic acid lactones [14]. The structure of the methanolysis products of galactolactone (II) follows from the PMR spectral data, the main characteristic of which are the SSCC of vicinal protons with values close to those described for methyl (methyl-α-D-galactopyranoside)uronates (cf. [10]).

Since the alcoholysis of lactones by benzyl and allyl alcohols proceeds more slowly than their methanolysis, further experiments on the alcoholysis were carried out in the presence of a base under standard conditions (variant B, see the Experimental section). As with methanolysis, the alcoholysis of gluco-6,3-lactone (I) by benzyl and allyl alcohols proceeds fairly selectively. In the case of $PhCH_2OH$, the initial lactone already disappears (TLC) after 2 h, and benzyl (allyl-2,4-di-O-acetyl-β-D-glucopyranoside)uronate (VI) is iso-

TABLE 1. Alcoholysis of Acetates of D-Hexopyranosideuronic Acid Lactones

Initial lactone (configuration)	Alcohol	Method (variant)	Time of reaction	Recovery of lactone, %	Reaction products, yield, %			
					with free OH group			partial deacetylation products
					2-OH	3-OH	4-OH	
(I)(gluco)	CH_3OH	A	4 days	16	–	81 (V)	Traces	Traces
		B**	1.5h	Traces	–	52 (V)	–	Traces
	$PhCH_2OH$	B	2h	Not determined	–	52 (VI)	–	Traces
	$CH_2=CHCH_2OH$	B	1 day	27	–	41 (VII)	–	Traces
(II)(galacto)	CH_3OH	A	2 weeks	Traces	+	++++	++	++
		B	20 h	–	Traces (VIIIa)	25 (VIII)	Traces (IX)	54 (X)
	$PhCH_2OH$	B	2 days	4	–	38 (XI)	25 (XII)	Traces
	$CH_2=CHCH_2OH$	B***	3 days	8	–	27 (XIII)	4 (XIV)	Considerable amount
(III) and (IV) (manno)	CH_3OH	A	6 days	(III) absent 4 (IV)	31 (XVI)	42 (XV)	–	Traces
		B	2.5 h	–	+++	+++	–	+
	$PhCH_2OH$	B	28 h	–	32 (XVIII)	57 (XVII)	5 (XIX)	3
	$CH_2=CHCH_2OH$	B***	8 h	4 (IV)	43 (XXI)	45 (XX)	–	Traces

*Amount + reflects a relative amount of the reaction product (visual evaluation of spots during TLC).
**Concentration of AcONa 1.2 mg/ml; data from [6].
***The alcoholysis products were separated by HPLC on silica gel in system E.

lated from the reaction mixture in 52% yield. In the case of $CH_2=CHCH_2OH$, the alcoholysis of (I) proceeds much more slowly, and after 24 h ~50% of the initial lactone has opened. Allyl (allyl-2,4-di-O-acetyl-β-D-glucopyranoside) uronate (VII) was isolated in a 41% yield.

In the alcoholysis of lactone (II), the opening of the lactone ring is generally accompanied by migration of the acetyl groups. Thus, in the reaction with $PhCH_2OH$, lactone (II) disappears after 2 days, and the product of lactone ring opening (XI) (yield 38%) and that resulting from the migration (XII) (25%) were isolated. The alcoholysis of lactone (II) by allyl alcohol proceeds less smoothly. After 3 days, 8% of the initial lactone remains in the reaction mixture, but the yield of allyl (methyl-2,4-di-O-acetyl-α-D-galactopyranoside) uronate (XIII) is low (27%). A minor amount of the migration product (XIV) and an appreciable amount of components with low chromatographic mobility (the TLC data) are also formed.

The alcoholysis by benzyl and allyl alcohols of a mixture of mannolactones (III) and (IV) proceeds more slowly than methanolysis, and leads to similar results; a mixture of isomeric partially acetylated uronates (XVII), (XVIII) and (XX), (XXI) is formed, with isomers with a free OH group at the 3-position predominating [(XVII) and (XX), respectively]. During alcoholysis with $PhCH_2OH$, a migration product of the acetyl group (XIX) was isolated as a minor component.

The structures of the isolated partially acetylated benzyl and allyl (methyl-D-hexopyranoside)uronates are confirmed by the data of PMR spectra. The SSCC values of the vicinal protons are similar to the SSCC values in the spectra of the structurally similar above-described methyl uronates, while the position of the O-acetyl groups follows from the character of the shift of the ring proton signals in the spectra.

Thus, by using the lactonization of D-hexopyranosideuronic acids and the subsequent alcoholysis of the acetates of the D-hexopyranoside-uronolactones formed, we can obtain in two stages partially acetylated alkyl (alkyl-D-hexopyranoside) uronates, which are potentially suitable as monohydroxylated glycosylating components for the synthesis of oligosaccharides, including the residues of hexuronic acids.

TABLE 2. Optical Rotation and PMR Spectral Data (in $CDCl_3$) of Alcoholysis Products of D-Hexopyranosideuronate Acetates

Compound	$[\alpha]_D$, degree ($CHCl_3$, T, °C)	Chemical shifts of proton signals (δ, ppm) and SSCC (J, Hz)						Chemical shifts of proton signals (δ, ppm) and SSCC (J, Hz)							
		H^1	H^2	H^3	H^4	H^5	CH_3CO	OCH_3	OH	$COOCH_3$	CH_2Ph	Ph	$CH_2CH=CH_2$	$CH_2CH=CH_2$	$CH_2CH=CH_2$
(V) *	−70 (c 1,03, 20)	4,56 d $J_{1,2}$=7,5	4,93 dd $J_{2,3}$=9,0	3,75–3,82 m	5,14 dd $J_{4,5}$=9,5	3,98 d	2,10 s 2,15 s	–	2,97 d $J_{3,OH}$=6,5	3,75 s	–	–	4,05–4,15 m 4,33–4,42 m	5,77–5,93 m	5,16–5,34 m
(VI)	−30 (c 2,0, 25)	4,56 d $J_{1,2}$=7,25	4,93 dd $J_{2,3}$=9,0	3,76 dd $J_{3,4}$=9,0	5,17 dd $J_{4,5}$=9,0	4,02d	1,89 s 2,14s	–	2,85 br. s	–	5,14 d 5.23 d $J_{A,B}$=11,7	7,38 m	4,10 ddt 4,35 ddt	5,83 dddd	5,20 tdd
(VII) **	−35 (c 1,4, 25)	4,55 d $J_{1,2}$=7,25	4,92 dd $J_{2,3}$=9,25	3,78 m $J_{3,4}$=9,63	5,15 dd $J_{4,5}$=9,63	3,99 d	2,08 s 2,13 s	–	2,90 br. s,	–	–	–	4,10 (1H) ddt 4,36 (1H) ddt 4,63 (2H, (ester) ddt	5,88 (2H) dddd	5,30 (4H) tdd
(VIII)	+94 (c 1,0, 24)	5,07 d $J_{1,2}$=3,5	5,04 dd $J_{2,3}$=10,0	4,24 m	5,03 dd $J_{4,3}$=3,75	4,52 d $J_{5,4}$=1,6	2,12 s 2,14 s	3,42 s	2,48 br. s	3,75 s	–	–	–	–	–
(VIIIa)	+183 (c 0,35, 23)	5,02 d $J_{1,2}$=3,5	4,00 ddd $J_{2,3}$=10,0 $J_{2,OH}$=10,0	5,18 dd $J_{3,4}$=3,5 $J_{3,2}$=10,0	5,69 dd $J_{4,5}$=1,5	4,56 d	2,06 s 2,10 s	3,50	–	3,75 s	–	–	–	–	–
(IX)	+155 (c 1,0, 24)	5,08 d $J_{1,2}$=2,9	5,25 dd $J_{2,3}$=10,4	5,31 dd $J_{3,4}$=2,4	4,50 br. s (2H)		2,08 s 2,10 s	3,43 s	2,67 br. s	3,82 s	–	–	–	–	–
(X)	+121 (c 0,6, 23)	5,05 d $J_{1,2}$=3,5	5,09 dd $J_{2,3}$=9,2	4,08 ddd $J_{3,OH}$=2,0	4,38 br. dd $J_{4,3}$=2,2	4,47 d $J_{5,4}$=1,6	2,16 s	3,44 s	2,83 br. s (2H)	3,85 s	–	–	–	–	–
(XI)	+101 (c 2,0, 25)	5,07 d $J_{1,2}$=3,5	5,03 dd $J_{2,3}$=9,6	4,22 dd $J_{3,4}$=3,5	5,05 dd $J_{4,5}$=1,5	4,54 d	1,94 s 2,12 s	3,40 s	2,70 br. s	–	5,12 d 5,18 d $J_{A,B}$=11,5	7,38 m	–	–	–
(XII)	+130 (c 2,0, 25)	5,11 d $J_{1,2}$=3,0	5,29 dd $J_{2,3}$=10,5	5,35 dd $J_{3,4}$=2,75	4,51 br. s	4,55 d $J_{5,4}$=1,75	2,08 s 2,10 s	3,45 s	2,45 br. s	–	5,28 br. s (2H)	7,38 m	–	–	–
(XIII)	+139 (c 2,0, 25)	5,09 d $J_{1,2}$=2,75	5,06 dd $J_{2,3}$=8,9	4,27 br. dd $J_{3,4}$=2,5	5,69 dd $J_{4,5}$=1,5	4,56 d	2,13 s 2,16 s	3,45 s	2,66 br. s	–	–	–	4,63 ddt 4,67 ddt	5,92 dddd	5,32 tdd
(XIV) ***	+130 (c 0,5, 26)	5,10 d $J_{1,2}$=2,5	5,28–5,33 m (2H)		4,54 br. s (2H)		2,10 s 2,12 s	3,45 s	2,78 br. s $J_{4,OH}$=5,4	–	–	–	4,72 ddt (2H)	5,92 dddd	5,32 tdd

TABLE 2 (continued)

(XV)	+29 (c 1,2, 23)	4,87 d $J_{1,2}$=2,12	5,06 dd $J_{2,3}$=3,88	4,11 m	5,22 dd $J_{4,3}$=9,75	4,21 d $J_{5,4}$=9,25	2,09 s 2,16 s	3,42 s	2,50 m	3,76 s	–	–	–	–	–
(XVI)	+175 (c 0,26, 23)	4,89 d $J_{1,2}$=3,25	4,05 m	5,30 dd $J_{3,2}$=3,37 $J_{3,4}$=8,95	5,45 dd	4,33 d $J_{5,4}$=8,75	2,04 s 2,09 s	3,49 s	2,29 m	3,78 s	–	–	–	–	–
(XVII)	+10 (c 1,8, 29,5)	4,88 d $J_{1,2}$=2,25	5,06 dd $J_{2,3}$=3,5	4,09 br. dd	5,23 dd $J_{4,3}$=9,5	4,26 d $J_{5,4}$=9,4	1,85 s 2,17 s	3,42 s	2,48 br. s	–	5,12 d 5,21 d $J_{A,B}$=11,5	7,38 m	–	–	–
(XVIII)	+64 (c 1,0, 29,5)	4,89 d $J_{1,2}$=3,0	4,02 m	5,28 dd $J_{3,2}$=3,13 $J_{3,4}$=8,93	5,37 dd	4,38 d $J_{5,4}$=8,6	1,85 s 2,06 s	3,48 s	2,34 m	–	5,14 d 5,22 d $J_{A,B}$=11,5	7,38	–	–	–
(XIX) ****	+92 (c 0,4, 27	4,52 d $J_{1,2}$=1,75	5,50dd $J_{2,3}$=3,5	5,56 dd $J_{3,4}$=9,75	4,50 dd	4,23 d $J_{5,4}$=9,5	1,71 s 1,80s	2,98 s	2,65 br. s	–	4,92 d 5,00 d $J_{A,B}$=12,0	7,17 m	–	–	–
(XX)	+66 (c 0,5, 27)	4,89 d $J_{1,2}$=2,25	5,07 dd $J_{2,3}$=3,5	4,12 m	5,26 dd $J_{4,3}$=9,75	4,25 d $J_{5,4}$=9,38	2,11 s 2,19 s	3,45 s	2,32 m	–	–	–	4,65 ddt (2H)	5,92 dddd	5,35 tdd
(XXI)	+78 (c 0,49, 24)	4,89 d $J_{1,2}$=2,63	4,04 dd	5,28 dd $J_{3,2}$=3,25 $J_{3,4}$=8,75	5,45 dd	4,33 d $J_{5,4}$=8,4	2,03 s 2,08 s	3,48 s	–	–	–	–	4,59 ddt 4,69 ddt	5,92 dddd	5,32 tdd

*Data taken from [6].

**Mp 99-101°C (alcohol). Found, %: C 54.35; H 6.25. $C_{16}H_{22}O_9$. Calculated, %: C 53.63; H 6.19.

***Mp 117-119°C (alcohol). Found, %: C 50.33; H 6.05. $C_{14}H_{20}O_9$. Calculated, %: C 50.60; H 6.07.

****The PMR spectrum was run in C_6D_6.

EXPERIMENTAL

The TLC was carried out on Kieselgel 60F-254 plates ("Merck") using the following systems of solvents: EA–AcOH–HCOOH–water 18:4:1:3 (A); ether–benzene 1:1 (B); EA–heptane 3:2 (C), 1:2 (D), 1:3 (E), 2:3 (F), followed by the detection of the compounds by 25% H_2SO_4 with heating. The preparative separation was carried out on columns with silica gel L 40/100 μm (Chemapol). The preparative HPLC was carried out on a 25 × 2.5 cm column with a Silasorb 600 (10 μm) sorbent (Chemapol), using a "Gilson" pump, model 303 and a "Knauer" differential refractometer. The GLC was carried out on a Pye Unicam-104 apparatus, using a 150 × 0.2 cm glass column with 3% OV-1 on a CQ diatomite (100-200 mesh) at 160°C and at a flow rate of the carrier gas (nitrogen) of 30 ml/min. The PMR and ^{13}C NMR spectra were obtained on a "Bruker WM-250" spectrometer with a working frequency of 250 MHz (protons) and 62.89 MHz (carbon-13), relative to TMS. The melting points were determined on a Koffler microblock, and the optical rotation on a "Perkin–Elmer 141" polarimeter. Allyl alcohol was distilled over CaO and was stored over a 4 Å molecular sieves, while $PhCH_2OH$ was distilled in vacuo over CaO in an Ar current and was stored under Ar.

General Method of Lactonization of D-hexopyranosideuronic Acids. A mixture of glucopyranoside of uronic acid (1 mmole) and Ac_2O (4 ml) was heated at 70°C. After 2 h pyridine (4 ml) was added and the mixture was allowed to stand overnight at ~20°C. The reaction mixture was repeatedly distilled with toluene, n-butanol, and n-heptane, and the lactone (yield 60-80%) was isolated from the residue by chromatography on silica gel (a 25 × 1.2 cm column) in an ether in benzene gradient (0 → 20%).

Methyl-2,4-di-O-acetyl-α-D-galactopyranosideurono-6,3-lactone (II) was obtained from methyl-α-D-galactopyranosideuronic acid [9] by a general method, syrup (yield 72%), homogeneous according to the TLC data, R_f 0.83 (C), 0.68 (A), $[\alpha]_D^{20}$ +28° (c 1.2; $CHCl_3$). PMR spectrum ($CDCl_3$, δ, ppm, J, Hz): 2.12 s, 2.17 s (6H, 2AcO), 3.54 s (3H, OCH_3), 4.29 dd (1H, H^2. $J_{1,2}$ = 1.47), 4.87 d (1H, H^5, $J_{4,5}$ = 2.9), 4.88 dd (1H, H^3, $J_{2,3}$ = 1.47, $J_{3,4}$ = 4.75), 5.42 dd (1H, H^4), 5.47 d (1H, H^1). ^{13}C NMR spectrum ($CDCl_3$, δ, ppm): 170.2 (C^6), 169.3 and 169.2 ($2\underline{C}OCH_3$), 97.54 (C^1), 78.8, 71.2 (2C), 68.1 ($C^{2,3,4,5}$), 57.9 ($O\underline{C}H_3$), 20.5 ($2OCO\underline{C}H_3$).

Methyl-2,4-di-O-acetyl-α-D-mannopyranosideurono-6,3-lactone (III) and Methyl-3,4-di-O-acetyl-α-D-mannopyranosideurono-6,2-lactone (IV). Application of the general method of lactonization to methyl-α-D-mannopyranoside-uronic acid [13] leads to a chromatographically homogeneous mixture of (III) and (IV) (yield 75%), $[\alpha]_D^{28.5}$ +21° (c 2.0; $CHCl_3$), R_f 0.83 (C), 0.29 (D), 0.74 (B). According to the PMR spectral data, the mixture contains 44% of (III) and according to GLC – 42 ± 3% of (III). PMR spectrum (C_6D_6, 60°C, δ, ppm, J, Hz); signals of (III): 1.55 s, 1.67 s (6H, 2AcO), 3.18 s (3H, OCH_3), 4.32 dd (1H, H^5, $J_{3,5}$ = 1.12, $J_{4,5}$ = 2.9), 4.56 dd (1H, H^4, $J_{3,4}$ = 5.75), 4.68 ddd (1H, H^3, $J_{2,3}$ = 1.5), 4.78 d (1H, H^1, $J_{1,2}$ = 7.2), 5.30 dd (1H, H^2); signals of (IV): 1.63 s, 1.65 s (6H, 2AcO), 3.10 s (3H, OCH_3) 4.43-4.48 m (2H, H^2 and H^4), 4.55 d (1H, H^5, $J_{4,5}$ = 3), 5.00 ddd (1H, H^3, $J_{2,3}$ = 2.12, $J_{3,4}$ = 1.0, $J_{1,3}$ = 2.06), 5.50 dd (1H, H^1, $J_{1,2}$ = 2.25).

General Method of Alcoholysis of Acetates of D-hexopyranosideuronic Acid Lactones. Variant A. A solution of the lactone (1 mmole) in absolute MeOH (concentration of the lactone 20 mg/ml) was held at 18-25°C. The course of the reaction was monitored by TLC (system C). The mixture was evaporated, and the residue was distilled with benzene (2 × 5 ml). The alcoholysis products were isolated from the residue by chromatography on silica gel (a 25 × 1.2 cm column) with elution gradient of ether in benzene (0 → 60%).

Variant B. A solution of the lactone (1 mmole) in alcohol (concentration of the lactone 20 mg/ml), containing AcONa (5 mg/ml) was held at 18-25°C. The course of the reaction was monitored by TLC (systems C and E). The reaction mixture was treated by a KU-2 cation exchanger (in the H^+ form), preliminarily washed with ethanol, was then filtered, and the resin was washed with ethanol (2 × 50 ml). The combined filtrate was evaporated (in the case of $PhCH_2OH$, it was removed by azeotropic distillation with water). The alcoholysis products were isolated by chromatography (a 25 × 1.2 cm column), with an elution gradient of EA in heptane (0 → 60%), or ether in benzene (0 → 60%).

The characteristics of the compounds obtained during the alcoholysis are given in Table 2.

CONCLUSIONS

1. Acetylated lactones of D-hexopyranosideuronic acids with D-galacto and D-manno configurations were synthesized.

2. A selective alcoholysis of acetates of D-hexopyranosideuronolactones was carried out using various alcohols (methyl, benzyl, and allyl alcohols) leading to partially acetylated alkyl-D-hexopyranosideuronates was carried out.

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