ORTHOESTERS OF SUGARS

COMMUNICATION 13. SYNTHESIS OF 1,2-ORTHOESTERS OF 4,6-O-BENZYLIDENE-α-D-GALACTOPYRANOSE*

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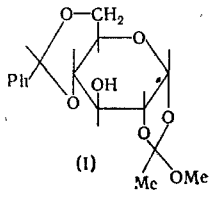
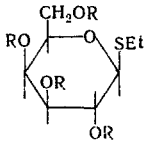
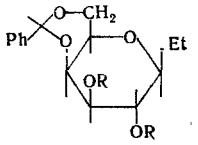
According to [2, 3], 1,2-methylorthoacetyl-4,6-O-benzylidene-α-D-glucopyranose (I) is easily cyclized to the trimeric macrocyclic orthoester, the polymerization of which under the conditions of the orthoester method of glycosylation leads to the regular β-1 → 3-D-glucan. To study the possibility of synthesizing the β-1 → 3-D-galactan we undertook the below described synthesis of the 1,2-orthoesters of 4,6-O-benzylidene-α-D-galactopyranose using a sequence of reactions similar to those that lead to orthoester (I).



(I)



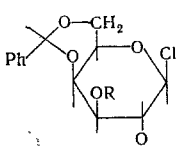
R = H (II); Ac (III)



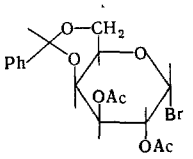
R = H (IV); Ac (V); Bz (VI)

The starting thiogalactoside (II) was obtained by the modified method given in [4] and was characterized as the known tetraacetate (III). Its condensation with benzaldehyde in the presence of $ZnCl_2$ at elevated temperature leads to 4,6-O-benzylidene-β-ethylthio-D-galactopyranoside (IV), from which were obtained diacetate (V) and dibenzoate (VI).

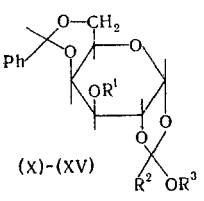
To synthesize the desired orthoesters (X), (XII), and (XIV) from thiogalactosides (V) and (VI) we obtained the corresponding galactopyranosyl halides (VII)–(IX). Here the chlorination under the conditions that were used previously for the gluco epimer [3] led to the 1,2-trans chlorides (VII) and (VIII). Without isolation, these chlorides were used to synthesize orthoesters (X) and (XIV) under conditions similar to those used to synthesize orthoester (I) from the corresponding trans chloride [3]. The bromination of thiogalactoside (V) in CCl_4 leads to the 1,2-cis bromide (IX), which, also without isolation, was used to synthesize orthoester (XII) by the Helferich method [5] as modified in [6]. Then after deacetylation the free orthoesters (X), (XII), and (XIV) were isolated from the mixtures. The acetates of orthoesters (XI) and (XIII) were obtained by acetylation with Ac_2O in pyridine.



R = Ac (VII) Bz (VIII)



(IX)



(X)-(XV)

* See [1] for Communication 12.

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TABLE 1. NMR Spectral Data for Thiogalactosides (III), (V), and (VI)

Compound	Solvent	Chemical shifts of protons*										Spin–spin coupling constants, Hz					
		H^1	H^2	H^3	H^4	H^5	H^6	$H^{6'}$	$OCOCH_3$	CH_3CH_2S	Ph, O, C, O, H	1,2	2,3	3,4	4,5	5,6	5,6'	6,6'
										CH_3 / CH_2								
(III)	C_6H_6	4,30	5,50	5,12	5,46	3,58	4,08	4,08	1,62—1,80	1,08 / 2,60	—	10,0	10,0	3,0	1,0	6,5	6,5	—
(V)	C_6D_6	4,21	5,78	4,95	4,00	2,59	3,93	3,30	1,68—1,82	1,11 / 2,73	5,46	10,0	10,0	3,5	0,8	1,5	1,5	12
(VI)	C_6D_6	4,52	6,27	5,47	4,27	2,92	4,03	3,43	—	1,12 / 2,82	5,22	10,0	10,0	3,5	0,8	1,5	2,1	12

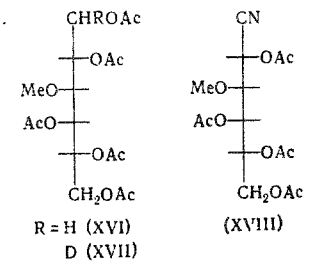
*Here and subsequently the chemical shifts are given in δ, ppm from TMS. The signals from the protons of the pyranose ring were assigned employing double resonance (H^2 irradiation).

The NMR spectra of thiogalactosides (III), (V), and (VI) (Table 1) confirm their structure (presence of benzylidene groupings for (V) and (VI), acetate groups for (III) and (V), and the C_2H_5 group for (III), (V), and (VI)). The spin–spin splitting constants of the ring protons of these compounds testify to the C^1-conformation of their pyranose ring.

The NMR spectra of orthoesters (X)–(XV) (Table 2) confirm the presence of the benzylidene group in them, and of the acetate groups for orthoesters (XI) and (XIII). The spectra of orthoesters (X)–(XIII) contain the characteristic signals of the $C-CH_3$ groups of the orthoester moiety, in which connection in each case these signals appear as a pair of singlets that belong to the endo-$C-CH_3$ and exo-$C-CH_3$ isomers (cf. [7]); a similar pairing of the signals is observed for the OCH_3 groups of orthoesters (X) and (XI). In the case of derivatives (X) and (XII) the pure endo-$C-CH_3$ isomers (respectively (Xa) and (XIIa)) were isolated from the obtained mixtures of epimers by recrystallization. Orthoesters (X)–(XIV) had $J_{1,2} \sim 4.5$ Hz, which is characteristic for the 1,2-orthoesters of the pyranose forms of sugars with an axial orientation of the oxygen at C^1 and an equatorial orientation at C^2 (cf. [7]). The IR spectral data for compounds (III)–(VI) and (X)–(XIV) also confirm the presence of characteristic groupings (OH, $>C=O$, monosubstituted aromatic ring) in these compounds. Finally, the presence of the orthoester grouping in compounds (X)–(XIV) was also confirmed by the hydrolytic test for the orthoesters of sugars [6].

The position of the free hydroxyl in the orthoesters, and consequently the position of the benzylidene and orthoester groupings, was established by methylation on the example of orthoester (X). When orthoester (X) was treated with dimethyl sulfate and alkali, under conditions similar to those used previously for the methylation of the orthoesters of sugars [8], we obtained its methyl ether (XV), the structure of which was also confirmed by the data of the NMR spectrum and the hydrolytic test.

Then via acid hydrolysis we cleaved the orthoester function and benzylidene protective group of orthoester (XV), followed by reduction with $NaBH_4$, using $NaBD_4$ in a parallel experiment, and finally acetylation. The thus obtained two 3-O-methyl-D-dulcitol pentaacetate samples (XVI) and (XVII) gave a mass spectrum that is characteristic for the acetates of 3-O-methylhexitols [9], in which connection in the second case (XVII) the peak of the characteristic fragment, containing C^1 (m/e 189), was shifted by one mass unit (m/e 190).



The absence of the isomer with a free hydroxyl group at C^6 as contaminant in orthoester (X) was proved by the absence of the 6-O-methyl derivatives as contaminants both in the dulcitol acetate (XVI) and in the 3-O-methylgalactonitrile acetate (XVIII), which were obtained from the crude orthoester (XV).

Next we undertook the synthesis of the β-1 → 3-galactan from orthoesters (X), (XII), and (XIV) by two routes: polymerization and polycondensation. For the polymerization we first had to synthesize the

TABLE 2. NMR Spectral Data for Orthoesters (X)–(XV)

Compound	Solvent	Chemical shifts							Ratio of exo: endo CCH_3
		CCH_3		OCH_3		$H^1(J_{1,2})$	Ph, O, H, C, O	$OCOCH_3$	
		exo	endo	exo	endo				
(X)	$CDCl_3$	1,55	1,65	3,30	3,37	6,10(4,5)	5,55	—	1 : 5
(XI)	C_6H_6	1,53	1,83	3,11	3,45	5,19(4,5)	5,32	1,92	1 : 3
(XII)	$CDCl_3$	1,53	1,63	—	—	5,97(4,5)	5,46	—	1 : 5
(XIII)	$CHCl_3$	1,58	1,70	—	—	6,12(4,5)	5,47	2,13	1 : 3
(XIV)	C_6H_6	—	—	3,04	3,34	6,14(4,2)	5,14	—	1 : 1,5*
(XV)	$CDCl_3$	1,49	1,62	3,20	3,30	5,88(3,5)	5,48	—	1 : 2,6

*Established from the ratio of the OMe signals.

galacto epimer of the corresponding macrocyclic glucose orthoester [3]. However, it proved that orthoester (X) under the conditions for the synthesis of this macrocyclic orthoester (refluxing in dichloroethane with p-toluenesulfonic acid and distilling off the cleaved methanol), in contrast to orthoester (I), forms a mixture of compounds that have a low chromatographic mobility and are stable under the conditions of the hydrolytic test for orthoesters. This caused us to run further experiments using a high-vacuum technique, which made it possible to exclude the entrance of atmospheric moisture into the reaction mixture and thus eliminate the complications arising from the possible hydrolysis of the orthoester during reaction. Molecular sieves 4A [1] were used to remove the methanol. The reaction was run in dichloroethane and chlorobenzene at 90-120°. Judging by the chromatographic behavior, the reaction products represented a mixture of oligosaccharides. Their study via NMR spectroscopy revealed that in all cases the spectra contained the signals of acetyl groups (the integral ratio to the signal of the benzyl proton = 3 : 1) and did not contain the signals of the orthoester $C-CH_3$ groups. As a result, the galactopyranose moieties in the reaction product are attached by glycoside rather than by orthoester linkages. The small OCH_3 signal (ratio of intensity to acetate signal = 1 : 2.6) made it possible to conclude that the reducible end of the oligosaccharide is the methylgalactoside moiety, and to estimate the average degree of polymerization as equal to 2-3.

As a result, orthoester (X) does not transesterify under conditions where this reaction is characteristic for many other sugar orthoesters, and unexpectedly proves to be capable of glycosylation under conditions where this reaction fails to occur for other sugar orthoesters (cf. [6, 7]). In view of this the question of whether the galacto epimer of the macrocyclic glucopyranose orthoester [3] can be formed and used to synthesize the galactan still remains unanswered.

Next we attempted to synthesize the β-1 → 3-D-galactan from orthoester (X) and its analogs by polycondensation under the usual conditions for the glycosylation of orthoesters. The preliminary data obtained here indicate that the polycondensation of orthoesters (X) and (XII), either in nitromethane in the presence of $HgBr_2$, or in chlorobenzene in the presence of 2,6-lutidinium perchlorate, gives only a small amount of the polysaccharide (2-5% yield). A study of the reaction products after removing the protective groups revealed that the formed polysaccharides are not regular, while the specific rotation (+60- +80°) indicates the presence of a certain amount of α-linkages; the methylation data suggest that, together with the 1 → 3 linkages, ~20% of 1 → 6 linkages is present. The periodate oxidation data also testify to the nonregularity of the polycondensation product. Apparently, this result is associated with a migration of the benzylidene protection during polycondensation. The attempted polycondensation of orthoester (XIV) in nitromethane in the presence of $HgBr_2$, using the high-vacuum technique, led only to low-molecular substances that were not investigated in greater detail.

EXPERIMENTAL METHOD

The solvents and adsorbents were prepared as described in [3, 6]. The TLC on Al_2O_3 was run in the systems: 98 : 2 $CHCl_3$–MeCOEt (A) and 5 : 1 $CHCl_3$–acetone (B). The NMR spectra were taken on a Varian DA-60-IL spectrometer, the IR spectra were taken on a UR-20 spectrometer, while the GLC was run on an LKhM-8MD, Model 5, instrument using a flame-ionization detector, a 1-m column, 3% PNPGS deposited on Chromatone, and nitrogen as the carrier gas. The mass spectra were taken on a Varian CH-6 MAT instrument. All of the obtained orthoesters were chromatographically homogeneous in systems A or B, and are cleaved completely under the conditions of the hydrolytic test [6]. The solutions were evaporated in vacuo. The melting points were determined on a Kofler stand.

β-Ethylthio-D-galactopyranoside (II). To 400 ml of absolute MeOH was quickly added 175 g (0.43 mole) of 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide and then, employing cold water cooling, a solution of 0.45 mole of potassium mercaptide in absolute MeOH (from 23 ml of ethyl mercaptan, 17.5 g of K, and 60 ml of absolute MeOH) was added immediately. With periodic shaking, the mixture was kept at 5-10°C for 2 h, the KBr precipitate was filtered, washed with absolute MeOH, and the filtrate was kept at 20° for 2 h, occasionally checking the alkalinity of the solution (if neutral the reaction was made alkaline with methylate solution). The mixture was evaporated to dryness and the residue was dried in vacuo. The obtained crude thiogalactoside (absence of carbonyl absorption in the IR spectrum) (85 g) was used in the next step. A sample of the sirupy (II) was dissolved in alcohol and allowed to stand for several weeks. The obtained crystals were recrystallized from a 3:1 alcohol–benzene mixture, mp 120-121°, $[\alpha]_D$ −22.5° (C 1.0, water); cf. [4]. The acetylation of (II) with a mixture of Ac_2O and CH_3COONa gave tetraacetate (III), mp 73° (from alcohol), $[\alpha]_D$ −8° (C 4.4, $CHCl_3$); cf. [4].

4,6-O-Benzylidene-β-ethylthio-D-galactopyranoside (IV). To 85 g of crude (II) were added 60 g of ground anhydrous $ZnCl_2$ and 160 ml of benzaldehyde. The mixture was heated rapidly up to 60-80° and shaken vigorously until a homogeneous solution was formed (20-40 min), after which it was let stand at ~20° for 1 h. The mixture was extracted several times with petroleum ether to remove the benzaldehyde, poured into 800 ml of cold water, and shaken vigorously for several minutes. Immediately after a bulky crystalline precipitate appeared it was separated by centrifuging, washed with 500 ml of water, and dried in vacuo. The obtained crude product (IV) (41 g, 35%), mp 134-141°, was used as such in the next step. A sample of (IV) was recrystallized from 150 ml of benzene and 220 ml of hexane (5°). We obtained (IV) as fine needles, mp 154-156°, $[\alpha]_D$ −55° (C 3.0, $CHCl_3$). Found: C 57.32; H 6.58; S 10.37%. $C_{15}H_{20}O_5S$. Calculated: C 57.68; H 6.46; S 10.25%.

2,3-Di-O-acetyl-4,6-O-benzylidene-β-ethylthio-D-galactopyranoside (V). A solution of 14.1 g of (IV) in 40 ml of pyridine was acetylated with 25 ml of Ac_2O. After 12 h the mixture was worked up in the usual manner and the product recrystallized from alcohol to give 14.0 g (78%) of (V) with mp 111°, which was used as such in the next step. A sample was recrystallized 3 times from alcohol to give a chromatographically homogeneous specimen, mp 118-119°, $[\alpha]_D$ −25.2° (C 3, $CHCl_3$). Found: C 57.77; H 6.09; S 9.07%. $C_{19}H_{24}O_7S$. Calculated: C 57.57; H 6.10; S 8.88%.

2,3-Di-O-benzoyl-4,6-O-benzylidene-β-ethylthio-D-galactopyranoside (VI). A solution of 18.0 g of thioglycoside (IV) in 60 ml of pyridine was benzoylated with 40 ml of C_6H_5COCl (20°, 24 h). After the usual workup and recrystallization from alcohol we obtained 23.0 g (95%) of dibenzoate (VI), mp 148-150°, $[\alpha]_D$ + 99.5°, (C 4.0, $CHCl_3$). Found: C 66.91; H 5.31; S 6.10%. $C_{29}H_{28}O_7S$. Calculated: C 66.91; H 5.42; S 6.16%.

1,2-Methylorthoacetyl-4,6-O-benzylidene-α-D-galactopyranose (X). To a solution of 10.0 g (25 mmoles) of diacetate (V) in 100 ml of CCl_4 was added a solution of 2.5 g (35 mmoles) of Cl_2 in 30 ml of $CHCl_3$, after which the mixture was kept in the dark for 30 min and then evaporated below 35°. The residue was dried in vacuo, a solution of 15 ml of 2,6-lutidine in 15 ml of absolute MeOH was added, and the mixture was let stand overnight. Then the mixture was poured into 150 ml of water, 18 ml of 2 M aqueous $AgNO_3$ solution was added, the precipitate was separated and washed with benzene, the aqueous layer of the filtrate was extracted with benzene (5 × 30 ml), and the combined benzene solutions were washed with water (5 × 50 ml) and evaporated. The residue was dried in vacuo, covered with 80 ml of absolute MeOH, and 0.1 ml of 1 N MeONa solution was added. After 2 h the mixture was diluted with 250 ml of water, extracted with $CHCl_3$ (3 × 50 ml), and the extract was washed with water (2 × 20 ml) and evaporated. The residue (3.5 g) was chromatographed on Al_2O_3 (S = 3.5 cm^2, h = 20 cm, with gradient elution from CCl_4 to $CHCl_3$, and then to a 97:3 $CHCl_3$–acetone mixture) to give 2.00 g (24%) of sirupy orthoester (X), $[\alpha]_D$ + 27.3° (C 4.0, $CHCl_3$). The NMR spectrum is given in Table 2. The compound crystallizes on standing. Found: C 59.45; H 6.38%. $C_{16}H_{20}O_7$. Calculated: C 59.25; H 6.25%. The recrystallization of 2.0 g of orthoester (X) from 40 ml of absolute benzene and 120 ml of petroleum ether (5°) gave 1.3 g of orthoester (Xa), mp 125-127°, $[\alpha]_D$ + 35.8° (C 2.7, $CHCl_3$).

1,2-Ethylorthoacetyl-4,6-O-benzylidene-α-D-galactopyranose (XII). To a suspension of 10.0 g (25 mmoles) of diacetate (V) in 60 ml of CCl_4, cooled to 0°, was added 3.2 ml (62 mmoles) of bromine and the mixture, with periodic shaking, was let stand in the dark at 0-5° for 1 h. The obtained homogeneous solution was evaporated below 35°, the residue was repeatedly evaporated with 30 ml of CCl_4, and the pale yellow crystalline residue (NMR spectrum in CCl_4: 6.71 H^1, $J_{1,2}$ = 4 Hz; α-bromide) was dissolved in a mixture of 2.5 ml (43 mmoles) of absolute alcohol, 10 ml (86 mmoles) of 2,6-lutidine, and 20 ml of $MeNO_2$ and let stand at ~20° for 4 days. Then 80 ml of benzene, 12.5 ml of 2 M aqueous $AgNO_3$ solution, and 150

ml of water were added. The mixture was filtered, the precipitate was washed with benzene, and the benzene layer of the combined filtrate was separated, washed with water (5 × 20 ml), and evaporated. The precipitate was evaporated in vacuo and then deacetylated and chromatographed as described in the preceding experiment. In this way we obtained 1.2 g (14.5%) of orthoester (XII), which, based on the TLC (system B) was homogeneous, $[\alpha]_D$ + 30.5° (C 2.0, $CHCl_3$). The NMR spectrum is given in Table 2. Recrystallization of the obtained orthoester from 25 ml of absolute benzene and 75 ml of petroleum ether gave 0.35 g of the pure endo-CCH_3 isomer (XIIa), mp 113-115°, $[\alpha]_D$ + 34.5° (C 3.0, $CHCl_3$). Found: C 59.95; H 6.67%. $C_{17}H_{22}O_7$. Calculated: C 60.34; H 6.55%.

1,2-Methylorthobenzoyl-4,6-O-benzylidene-α-D-galactopyranose (XIV). To a suspension of 10.0 g (19 mmoles) of dibenzoate (VI) in 100 ml of CCl_4 was added a solution of 1.65 g (23 mmoles) of Cl_2 in 20 ml of absolute $CHCl_3$, and then the mixture was worked up as described in the synthesis of orthoester (X). After chromatographing on Al_2O_3 and recrystallization from a 1:3 benzene–petroleum ether mixture the yield of orthoester (XIV) was 0.90 g (12%), mp 150-152°, $[\alpha]_D$ + 61.4° (C 4.0, $CHCl_3$). Found: C 65.10; H 5.74%. $C_{21}H_{22}O_7$. Calculated: C 65.25; H 5.74%.

1,2-Methylorthoacetyl-3-O-acetyl-4,6-O-benzylidene-α-D-galactopyranose (XI). A solution of 0.20 g of orthoester (X) in 5 ml of pyridine was acetylated with 2 ml of Ac_2O (20°, 12 h), the reaction solution was poured into 50 ml of water, extracted with $CHCl_3$, and the extract was washed in succession with water and aqueous $NaHCO_3$ solution, and evaporated to dryness. We obtained orthoester (XI) in 92% yield, $[\alpha]_D$ + 114.4° (C 3.0, $CHCl_3$). Found: C 59.50; H 6.25%. $C_{18}H_{22}O_8$. Calculated: C 59.01; H 6.05%.

1,2-Ethylorthoacetyl-3-O-acetyl-4,6-O-benzylidene-α-D-galactopyranose (XIII). Obtained in the same manner as the preceding from orthoester (XII), $[\alpha]_D$ + 103.3° (C 4.0, $CHCl_3$). Found: C 59.80; H 6.59%. $C_{19}H_{24}O_8$. Calculated: C 59.99; H 6.36%.

1,2-Methylorthoacetyl-3-O-methyl-4,6-O-benzylidene-α-D-galactopyranose (XV). To 0.90 g (2.80 mmoles) of orthoester (X) in 14 ml of absolute THF were added 2.80 g (70 mmoles) of NaOH and 1.3 ml (16 mmoles) of dimethyl sulfate. The mixture was stirred at 30° for 1 h and then at ~20° for 3 h, after which 10 ml of benzene and 4 ml of triethylamine were added, and then 3 ml of water in drops. The mixture was kept at 60° for 30 min, cooled, 15 ml of water was added, and the whole was extracted with benzene (3 × 30 ml). The extract was evaporated, and the residue, which contained substances with R_f 0.65 (main compound) and 0.0 (TLC in system A), was separated by chromatographing on Al_2O_3 (S = 0.5 cm^2, h = 15 cm, with gradient elution from CCl_4 to $CHCl_3$). We obtained 0.62 g (65%) of crystalline orthoester (XV), mp 108-112°. After recrystallization from a 1:5 toluene–petroleum ether mixture, mp 122-126°, $[\alpha]_D$ + 27.2° (C 1.0, $CHCl_3$). Found: C 59.71; H 6.52%. $C_{17}H_{22}O_7$. Calculated: C 60.34; H 6.55%.

Analysis of Methylated Orthoester (XV). A solution of 0.24 g of orthoester (XV) (before recrystallization) in a mixture of 40 ml of acetone and 4 ml of 0.1 N H_2SO_4 solution was kept at 20° for 30 min, after which 0.25 ml of pyridine was added, and the mixture was poured into 20 ml of water and extracted with $CHCl_3$ (5 × 20 ml). The extract was evaporated to dryness to give a crystalline residue (mp 184-188°). The latter (0.12 g) was dissolved in 3 ml of AcOH, 1.8 ml of water was added, the whole was heated at 85-90° for 25 min, evaporated to dryness with heptane, and the residue was dissolved in 6 ml of water and separated into two equal portions. The first portion was reduced with $NaBH_4$ and acetylated in the usual manner to give 3-O-methyldulcitol pentaacetate (XVI). Treatment of the second portion in the same manner but using $NaBD_4$ gave 1-deutero-3-O-methyl-D-dulcitol pentaacetate (XVII). The mass spectra of the obtained derivatives contain, among other characteristic peaks, peaks with the following m/e values: acetate (XVI) 189 and 261; acetate (XVII) 190 and 261. Based on the GLC data (210°), both of the acetates are practically homogeneous. A sample of the crude methylation product of orthoester (X) was subjected to acid treatment, as described above, and then separated into two equal portions. Treatment of one portion as described in [10] gave nitrile (XVIII), which, based on the GLC data (190°), was homogeneous and was not contaminated with the 6-O-methyl isomer. The second portion was treated as described above to give 3-O-methyldulcitol pentaacetate, which, based on the GLC data (210°), was also free of the 6-O-methyl isomer.

Reactions of Orthoester (X), Catalyzed by p-Toluenesulfonic Acid. a) A solution of 0.38 g (1.15 mmoles) of orthoester (X) in 14 ml of dichloroethane was refluxed in the presence of 1.7 mg (0.01 mmole) of p-toluenesulfonic acid for 2 h, with removal of the solvent by distillation (see [3]). The reaction product gives a number of spots with different mobilities (R_f ranging from 0.0 to 0.7 in the system: 3:1 $CHCl_3$ –acetone). After the hydrolytic test for orthoesters the mobility of the products remains constant.

Acetylation of the mixture in the usual manner gave a mixture of substances with R_f ranging from 0 to 0.90, which also remain unchanged under the conditions of the hydrolytic test for orthoesters.

b) The reaction was run in a ⅄-shaped ampul. In one leg was placed 0.0023 mmole of TsOH, 0.05 mmole of orthoester (X) was placed in the other leg, while molecular sieves 4A were placed in the vertical portion. The contents were carefully dried in a high vacuum, then 1 ml of the solvent, distilled in a vacuum system over CaH_2, was distilled into the ampul under vacuum, the ampul was sealed in vacuo (see [11] for the experimental technique), and the contents of the lower branches of the ampul were mixed and heated in a bath, while the upper portion was cooled by a water jacket, which served as a reflux condenser. The reaction was run for 2.5 h in chlorobenzene at 90, 100, 110, and 120°, and also in dichloroethane at 60 and 90°. The ampuls were opened, a drop of pyridine was added, and the mixture was evaporated and studied as in the case of a). Based on the TLC and their behavior in the hydrolytic test, all of the reaction mixtures behave the same and correspond to the mixture obtained in the case of a). Orthoester (I) under the same conditions is converted to the macrocyclic trimeric orthoester in 65-70% yield [1]. The NMR spectra of the reaction products of orthoester (X) (in $CDCl_3$) lacked signals in the 1.5-1.8 ppm region (CCH_3), and contained complex signals at 2.0-2.2 (OAc) and at 3.4-3.6 ppm (OMe), the ratio of whose intensities was on the average 2.6; they also contained a singlet signal at 5.5 ppm (benzyl proton) and a complex signal at 7.2-7.7 ppm (C_6H_5), the ratio of whose intensities was on the average 1:6.

Polycondensation of orthoesters (X), (XII), and (XIV). a) The polycondensation of 1.8 g (5.5 mmoles) of orthoester (XII) in the presence of 6 mg (0.028 mmole) of lutidinium perchlorate in 35 ml of chlorobenzene (refluxing for 3 h with removal of the solvent by distillation) was run as described in [12]. After treatment with 25 ml of 70% AcOH solution (85°, 20 min), distilling off the solvent, and deacetylation by the Zemplen method, the product was reduced with $NaBH_4$ and the borate was removed. Precipitation with alcohol from aqueous solution gave 27.5 mg of polysaccharide with $[\alpha]_D$ + 44.8° (C 2, water).

b) The polycondensation of 2.2 g (6.6 mmoles) of orthoester (X) in the presence of 120 mg (0.33 mmole) of $HgBr_2$ in 10 ml of nitromethane (refluxing for 5 h with removal of the solvent by distillation) was run as described in [6]. After removal of the protective groups, as described above, a sample of the product was methylated by the Hakomori method, followed by methanolysis (2 N HCl in MeOH, 5 h, 100°), hydrolysis (1 N HCl solution, 3.5 h, 100°), reduction with $NaBH_4$, and acetylation. Employing GLC (170°) and authentic specimens, the full acetates of the 2,3,4,6-tetra-O-methyl-, 2,4,6-tri-O-methyl-, 2,3,6-tri-O-methyl-, and 2,3,4-tri-O-methyldulcitols were identified in the mixture.

c) The polycondensation of 0.45 g (1.17 mmoles) of orthoester (XIV) was run in the presence of 4.2 mg (0.017 mmole) of $HgBr_2$ and with molecular sieves 4A using the high vacuum technique; cf. [1, 11]. After removal of the protective groups as described above, and employing gel chromatography on Biogel P-4, we failed to detect any high-molecular product.

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CONCLUSIONS

1. A number of 1,2-orthoesters of 4,6-O-benzylidene-α-D-galactopyranose were synthesized.

2. These orthoesters form a mixture of glycosylation products under the conditions of acid-catalyzed transesterification, and a nonregular polysaccharide in low yield under the conditions of the orthoester method of glycosylation.

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