Carbohydrate Research, 144 (1985) 137–147
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Note

Methods for the preparation of alkyl 1,2-orthoacetates of D-glucopyranose and D-galactopyranose in high yield*

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(Received August 6th, 1984; accepted for publication in revised form, April 23rd, 1985)

Monosaccharide 1,2-alkyl orthoesters are of considerable importance as precursors in the synthesis of glycosides and oligosaccharides[1–4]. For the preparation of orthoesters, Kochetkov and Bochkov[2] have pointed out that acylglycosyl halides can be treated with an alcohol in the presence of silver oxide and carbonate. However, use of such acid acceptors result in the formation of water, which must be removed rapidly by dessicants to prevent the formation of by-products. 2,4,6-Trimethyl- and 2,6-dimethyl-pyridine which, unlike quinoline and pyridine, do not react rapidly with glycosyl halides to form quaternary glycosylammonium salts because of steric hindrance of the nitrogenous component are preferable acid acceptors not giving rise to water. Variations on the latter approach have been the use of 2,4,6-trimethylpyridine-containing tetraalkylammonium bromide[5], silver triflate[6], or silver nitrate[7]. Orthoesters have also been prepared in high yield from appropriate reactants in dichloromethane containing *N,N*-dimethylformamide dialkyl acetal and silver triflate[8].

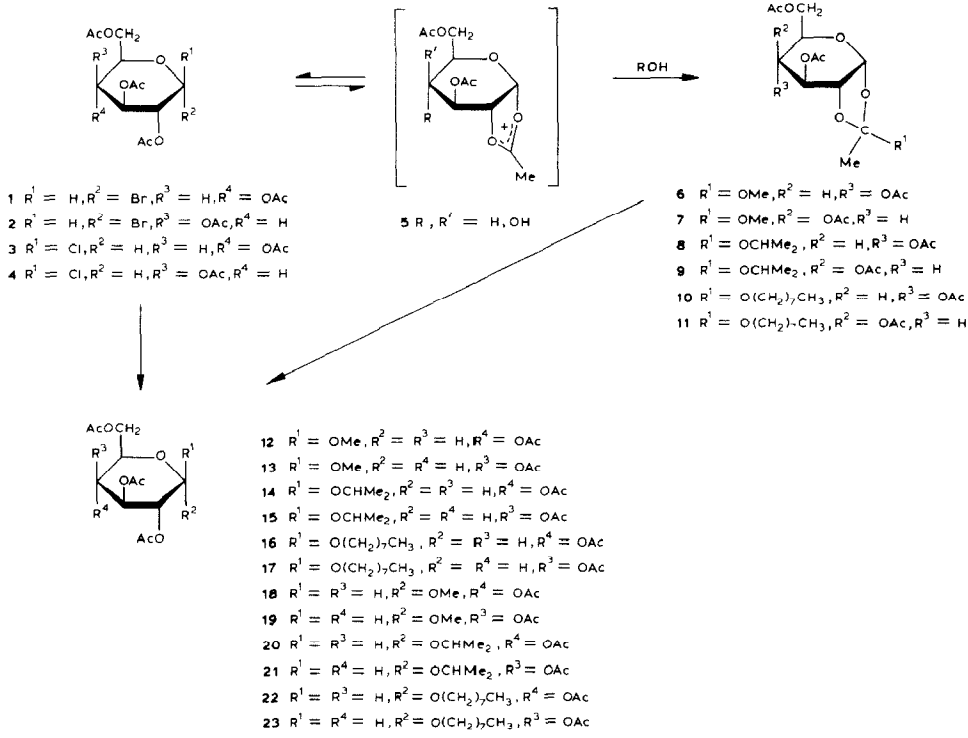
The present investigation concerns a search for reactions that result in the formation of the simple alkyl 1,2-orthoesters of D-glucopyranose and D-galactopyranose in high yield, without formation of glycosides. One method, that of Zurabyan *et al.*[7], seemed particularly promising since orthoesters of partially protected sugar derivatives were prepared by 1,2-*cis* acylglycosyl halides without apparent formation of glycosides. The reaction was carried out in acetonitrile in the presence of 2,4,6-trimethylpyridine and silver nitrate. In the following experiments, similar conditions were used in the treatment of 1,2-*cis* and 1,2-*trans* halides with such simple alcohols as methanol, 2-propanol, and 1-octanol. In addition to silver nitrate, other silver salts were tested and the products analyzed, in terms of forma-

*Portions of this work were presented by D. Tsui at the 185th Meeting of the American Chemical Society, Seattle, WA, March 20–25, 1983.

0008-6215/85/$ 03.30

tion of 1,2-orthoacetate, α- and β-glycosides, and other products, by a combination of ^{13}C- and ^{1}H-n.m.r. spectroscopy.

The synthesis of sugar 1,2-orthoacetates was studied by use of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl (**1**) and -D-galactopyranosyl bromide (**2**), 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl[9] (**3**) and -D-galactopyranosyl chloride[10] (**4**) as precursors, and suitable alcohols. Methanol and 2-propanol were selected as short-chain primary and secondary alcohols, and 1-octanol was chosen since it is chemically similar to 8-methoxycarbonyloctanol, which is frequently used as a spacer molecule in synthetic antigens[11].



In preliminary experiments where silver carbonate was used as an acid acceptor with dichloromethane as solvent, water was formed in the course of the reaction and a large amount of molecular sieve 4A was needed for its removal. In the case of the reaction of 1,2-*trans*-acylglycosyl halides (**3** and **4**) with alcohols, it proceeded, as expected, much in favor of the formation of 1,2-orthoacetate over alkyl glycosides, but there was also formation of by-products in yields from 28–57% (Table I). Thus, it appears that under these conditions, the molecular sieve does not behave efficiently. Surprisingly, 1,2-orthoacetate was formed in 21–34% yield from 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**1**) under the same conditions, in contrast to the experiment with the α-D-galactopyranosyl derivative **2** which gave rise to little 1,2-orthoacetate.

TABLE I

REACTION OF 2,3,4,6-TETRA-*O*-ACETYL-D-GLYCOPYRANOSYL HALIDES **1–4** WITH ALKYL ALCOHOLS IN THE PRESENCE OF 2,6-DIMETHYL-, OR 2,4,6-TRIMETHYL-PYRIDINE, OR SILVER CARBONATE

Halide	*Catalyst–solvent*	*Alcohol*	*Yield (%)*			
			Orthoacetate	*Glycoside*[b]	*Other*	*Unchanged halide*
1	Ag_2CO_3–CH_2Cl_2[a]	Me	32	28	40	
		2-Pro	21	71	8	
		1-Oct	34	65	1	
2	Ag_2CO_3–CH_2Cl_2[a]	Me	5	70	25	
		2-Pro	3	90	7	
		1-Oct	0	92	8	
3	Ag_2CO_3–CH_2Cl_2[a]	Me	63	3	34	
		2-Pro	58	0	42	
		1-Oct	70	2	28	
4	Ag_2CO_3–CH_2Cl_2[a]	Me	62	6	32	
		2-Pro	41	2	57	
		1-Oct	53	10	37	
1	$Me_2C_5H_3N$[c]	Me	33	51		16
		2-Pro	42	27	8	23
2	$Me_2C_5H_3N$[c]	Me	24	76		
		2-Pro	53	8	39	
3	$Me_2C_5H_3N$[c]	Me	78	0	22	
		2-Pro	62	0	38	
4	$Me_2C_5H_3N$[c]	Me	52	0	48	
		2-Pro	53	0	47	
1	$Me_3C_5H_2N$–MeCN[d]	Me	27	5		68
		2-Pro	10		4	86
		1-Oct	48		4	48
2	$Me_3C_5H_2N$–MeCN[d]	Me	76	14		10
		2-Pro	53	2	29	16
		1-Oct	80		13	7
1	$Me_2C_5H_3N$–MeCN[d]	1-Oct	38		4	58
2	$Me_2C_5H_3N$–MeCN[d]	1-Oct	79		13	8

[a]In the presence of molecular sieve 4A. [b]2,3,4,6-Tetra-*O*-acetyl-β-D-glycopyranoside. [c]At room temperature for 3 days with a large excess of alcohol. [d]At room temperature for 2 days with a limited excess of alcohol.

Under the conditions originally employed by Kochetkov *et al.*[1], in which an excess of alcohol was used in the presence of 2,6-dimethylpyridine*, the 1,2-*cis*-acylglycosyl bromides **1** and **2** gave 1,2-orthoacetates in yields of 24–53% with considerable formation of glycoside. Much unreacted **1** was present after 3 days at room temperature where methanol or 2-propanol was the acceptor.

For comparative studies of the methods of synthesis of 1,2-orthoacetates, acetonitrile was selected as a solvent since it dissolves acylglycosyl halides and certain silver salts. In order to discriminate between 2,6-dimethyl- and 2,4,6-tri-

*In these reactions 1,2-*trans*-acylglycosyl halides were used.

methyl-pyridine as acid acceptor, each was used in the reaction of the 1,2-*cis*-acylglycosyl bromide **1** and **2** with 1-octanol. After 2 days at room temperature, marginally higher yields were noted in the presence of 2,4,6-trimethylpyridine (Table I).

In the study of the role of the concentration of alcohol, the best results were obtained in the case of 1,2-*cis*-acylglycosyl bromides **1** and **2** with a limited excess of alcohol in the presence of 2,4,6-trimethylpyridine in acetonitrile as solvent after 2 days at room temperature, and only low proportions of alkyl β-D-glycopyranosides were formed (Table I). However, much unchanged starting material was present and the reaction rate was too slow for practicality.

Several silver salts were tested in reaction mixtures containing 1,2-*cis*-acylglycosyl bromides **1** and **2**. No starting material remained and, in many cases, the yields were high (Table II). In contrast with the results of Zurabayan *et al.*[7], who used silver nitrate under comparable conditions with partly substituted carbohydrates as aglycon, a small proportion of glycoside was observed and the yield of 1,2-orthoacetates was 80–92%. An equally high yield was obtained in the presence of silver *p*-toluenesulfonate (Table II). Two methods were used for the preparation of 1,2-orthoacetates in larger scale. Treatment of bromide **1** with 2-propanol in the presence of silver *p*-toluenesulfonate gave, in 92% yield, the 1,2-orthoacetate **8** which was isolated by crystallization. In the presence of silver nitrate and 1-octanol, bromide **2** gave the 1,2-orthoacetate **11** which was purified by silica gel column chromatography.

Silver salts other than silver *p*-toluenesulfonate and silver nitrate* were less efficient in converting the 1,2-*cis*-acylglycosyl bromides **1** and **2** into orthoacetates. Silver nitrite gave substantial yields of 1,2-orthoacetate but many by-products also. Silver triflate and tetrafluoroborate gave alkyl β-D-glycopyranosides almost exclusively. On the other hand, silver carbonate promoted very little reaction of the *cis*-1,2 bromides, thus being similar to 2,4,6-trimethylpyridine when used alone with an alcohol in acetonitrile for 4 h. The latter result corresponds to that of Lemieux and Morgan[5] who observed that no reaction occurred when **1** was treated with a mixture of 2,4,6-trimethylpyridine and alcohol over 5 days.

The most promising approach for the preparation of 1,2-orthoacetates was the reaction of the readily prepared 1,2-*trans* chlorides **3** and **4** with an alcohol in the presence of silver salts, such as silver *p*-toluenesulfonate, nitrate, carbonate, sulfate, or acetate in acetonitrile containing 2,4,6-trimethylpyridine (Table III); in many cases, nearly quantitative yields of 1,2-orthoacetates and no alkyl β-D-glycoside formation were observed.

In the absence of silver salts, fewer by-products were formed in the reactions of 1,2-*trans* chloride using a limited excess of alcohol in acetonitrile in the presence of 2,4,6-trimethylpyridine (Table III) than with a large excess of alcohol without

*The possible formation of a trace of alkyl α-D-glycoside in reactions involving octanol and this salt was observed.

TABLE II

YIELDS (%) OF ORTHOESTER (A), GLYCOSIDE (B)[a], OTHER (C), AND UNCHANGED HALIDE (D) IN THE REACTION[b] OF TETRA-*O*-ACETYL-α-D-GLYCOPYRANOSYL BROMIDES **1** AND **2**, ALKYL ALCOHOLS[c], AND 2,4,6-TRIMETHYLPYRIDINE[d] IN ACETONITRILE IN THE PRESENCE OR ABSENCE OF SILVER SALTS[d]

Bromide	*Silver salt*	*Alcohol*											
		Methanol				*2-Propanol*				*1-Octanol*			
		A	*B*[d]	*C*	*D*	*A*	*B*	*C*	*D*	*A*	*B*	*C*	*D*
1	CF_3SO_3Ag		74(2)	24		16	32(3)	49		44	22(1)	33	
	AgOAc		30	70				100				100	
	$AgNO_2$	45	7	48		55		45		25		75	
	$AgBF_4$		98(2)				85(3)	12		21	52(2)	25	
	$CH_3C_6H_4SO_3Ag$	84	16			92	1	7		77	2	21	
	$AgNO_3$	87	3	10		80		20		87	3	10	
	$AgCO_3$[e]		6	1	93				100				100
	None				100				100				100
2	CF_3SO_3Ag		90(1)	9			54(2)	44			50	50	
	AgOAc		33	67			15	85			16	84	
	$AgNO_2$	39	20	41		48	6	46		48	2	50	
	$AgBF_4$		99(1)				90(3)	7			95	5	
	$CH_3C_6H_4SO_3Ag$	60	40			71	10	19		95	5		
	$AgNO_3$	81	18	1		80		20		92		8	
	Ag_2CO_3[e]				100		4		96				100
	None			3	97				100				100

[a]2,3,4,6-Tetra-*O*-acetyl-β-D-glycopyranoside and α-D anomer (in parentheses). [b]Reaction for 4 h at room temperature. [c]Limited excess of alcohol. [d]Two equimolar amount of reagents. [e]In the presence of molecular sieve 4A.

acetonitrile in the presence of 2,6-dimethylpyridine under the conditions previously employed[1] (Table I). In the former cases, the yield of 1,2-orthoacetate from **3** and **4** was high because of the concerted, favored formation of acetoxonium ion **5**, followed by its attack by the alcohol in the presence of 2,4,6-trimethylpyridine in acetonitrile. It was found that the *trans* chlorides **3** and **4** did not react completely within 4 h. Thus, the presence of silver salts, by removal of the chloride ion, accelerated this process. The total absence of alkyl glycoside in the product represents an advantage over the reaction using 1,2-*cis*-acylglycosyl bromides. These can react with alcohols to form β-D-glycosides prior to the formation of ion **5** which is necessary for 1,2-orthoacetate formation. The advantage in using such silver salts as silver nitrate in the reaction in the presence of 2,4,6-trimethylpyridine, is that the base is removed as insoluble 2,4,6-trimethylpyridinium nitrate. The isolated product can often be used for further reactions without purification.

Lower yields were observed when silver carbonate was used as acid acceptor and when methanol was the reactant. The formation of by-products was due to reaction with water, which was not removed efficiently by molecular sieve 4A in the presence of methanol. It was observed that little or no 1,2-orthoacetate was formed when silver triflate or silver tetrafluoroborate was used as catalyst with the 1,2-*trans* series, and silver nitrite gave a low yield of 1,2-orthoacetate also. The same proportion of products other than glycoside and 1,2-orthoacetate was observed when 1,2-*trans*-acylglucopyranosyl bromide **1** or 1,2-orthoacetate **8** was treated with 2-propanol in the presence of silver tetrafluoroborate and 2,4,6-trimethylpyridine in acetonitrile under similar conditions. These results indicate that the 1,2-orthoacetate was initially formed, and then it reacted with an excess of catalyst to give by-products.

The composition of orthoacetates and glycosides was analyzed by n.m.r. spectroscopy[5,12–16]. For fully acylated products arising from reaction with methanol, the ^{1}H-n.m.r. spectrum showed methyl signals of glycosides and 1,2-orthoacetates that were resolved and could be used for quantitative determination. For the products of the reactions with 2-propanol and 1-octanol, this approach could not be used because of overlapping resonances. In the ^{13}C-n.m.r. spectra, however, the C-1 signals of 1,2-orthoacetate, glycoside, and by-products were well resolved, and the C-1 signals of 1,2-orthoacetates and glycosides, which occur in the same spectral region, could be assigned; in cases where the yield of 1,2 orthoacetate was high, the typical quaternary carbon resonance at δ 121.5 was matched with a large C-1 region. The relative yields of *exo* and *endo* isomers of orthoacetates could be determined by reference to ^{1}H-n.m.r. signals. For D-glucose derivatives, two H-1 doublets centered at ~δ 5.72 and 5.59 and two orthoester CH_3 singlets at δ 1.72 and 1.58, respectively, were observed. In the D-galactose series, the signals were at ~δ 5.80 and 5.68 (H-1), and δ 1.68 and 1.58 (CCH_3).

The ^{13}C-n.m.r. signals of 3,4,6-tri-*O*-acetyl-α-D-glucopyranose 1,2-(alkyl orthoacetates) were assigned by use of known chemical shifts of ^{1}H-n.m.r. signals and applying the ^{1}H-n.m.r. single-frequency, off-resonance decoupling technique.

TABLE III

YIELDS (%) OF ORTHOESTER (A), GLYCOSIDE (B)[a], OTHER (C), AND UNCHANGED HALIDE (D) IN THE REACTION[b] OF TETRA -*O*-ACETYL-β-D-GLYCOPYRANOSYL CHLORIDES **3** AND **4**, ALKYL ALCOHOLS[c], AND 2,4,6-TRIMETHYLPYRIDINE[d] IN ACETONITRILE IN THE PRESENCE OR ABSENCE OF SILVER SALTS[d]

Chloride	*Silver salt*	*Alcohol*											
		Methanol				*2-Propanol*				*1-Octanol*			
		A	*B*	*C*	*D*	*A*	*B*	*C*	*D*	*A*	*B*	*C*	*D*
3	CF_3SO_3Ag		30	70				100				100	
	AgOAc	88		12		80		20		73		27	
	$AgNO_2$	61		39		42		58		47		53	
	$AgBF_4$			100				100				100	
	$CH_3C_6H_4SO_3Ag$	88		12		80		20		82		18	
	$AgNO_3$	94		6		75		25		85		15	
	Ag_2CO_3[e]	72		14	14	85		10	5	91		9	
	Ag_2SO_4	88		12		60		40		88		12	
	No salt	84		15	1	63		20	17	80		20	
4	CF_3SO_3Ag		3	97		25		75				100	
	AgOAc	95		5		82		18		96		4	
	$AgNO_2$	75		25		47		53		67		33	
	$AgBF_4$	52	1	47				100		67		33	
	$CH_3C_6H_4SO_3Ag$	100				86		14		94		6	
	$AgNO_3$	93		7		84		16		93		7	
	Ag_2CO_3[e]	72		4	24	67		15	18	99		1	
	Ag_2SO_4	98		2		72		28		88		12	
	None	86		3	11	44		18	38	50		5	45

[a]Tetra-*O*-acetyl-β-D-glycopyranoside and α-D anomer (in parentheses). [b]Reaction for 4 h at room temperature. [c]Limited excess of alcohol. [d]Two equimolar amount of reagents. [e]In the presence of molecular sieve 4A.

TABLE IV

^{13}C-CHEMICAL SHIFTS [a] (δ) OF 3,4,6-TRI-*O*-ACETYL-α-D-GLYCOPYRANOSE 1,2-(ALKYL ORTHOACETATES) AND ALKYL 2,3,4,6-TETRA-*O*-ACETYL-α- AND -β-D GLYCOPYRANOSIDES

Compound	*Alkyl aglycon*	*D-Glucose or D-galactose residue*						*Acetyl, aglycon, and 1,2-orthoacetate group*												
		C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C=O*				*=C=*	*-OCH=*	*CH_3-(CH_2)$_n$*[b]						
6	Me(*exo*)	96 9	73 2	70 2	68 3	67 1	63 1	170 6	169 6	169 1		121 3	50 9	20 7	20 1					
	(*endo*)	97 8										122 1								
7	Me(*exo*)	97 5	74 1	71 4	66 1	69 2	61 4	170 3	169 9	169 6		121 6	50 1	23 2	20 5	20 4				
	(*endo*)	98 1	73 6	71 6	66 3	69 1	61 5					122 0	50 9							
8	2-Pro(*exo*)	96 9	73 1	70 3	68 4	67 0	63 1	170 6	169 5	169 1		121 4	66 5	23 7	21 5	20 7				
	(*endo*)	95 3																		
9	2-Pro(*exo*)	97 4	73 6	71 4	66 0	69 0	61 5	170 4	170 0	169 7		121 34	66 3	24 2	23 8	20 7	20 5			
	(*endo*)	95 9	73 3	71 8		69 4	61 0													
10	1-Oct(*exo*)	97 0	73 3	70 4	68 4	67 1	63 2	170 6	169 6	169 1		121 4	63 7	29 7	29 3	29 2	26 1	22 6	20 6	20 7	14 0
	(*endo*)	97 8										122 1									
11	1-Oct(*exo*)	97 5	73 7	71 3	66 0	69 0	61 4	170 3	169 9	169 7		121 2	63 0	31 8	29 5	29 3	29 2	26 1	23 6	22 6	20 6
	(*endo*)	97 9	73 3	71 7	66 3	69 0	61 5					121 6	63 8								
12	Me (β)	101 6	71 4	73 0	68 6	71 9	62 0	170 6	170 2	169 3			56 85	20 6	20 5						
18	(α)	96 7	70 7	70 1	68 5	67 0	61 8	170 4	169 9	169 4			55 31	20 6	20 5						
13	Me (β)	102 0	70 7	68 9	67 2	71 0	61 3	170 2	170 1	170 0	169 3		56 75	20 6	20 5	20 4					
19	(α)	97 0	68 0	67 4	66 0	68 0	61 6	170 2	170 0	169 70			55 30	20 8	20 6						
14	2-Pro (β)	99 7	71 7	73 0	68 8	71 7	62 3	170 4	170 0	169 2	169 0		73 0	23 2	22 0	20 7	20 6				
20	(α)	94 3	71 7	70 3	68 9	67 2	62 1	170 5	170 1	170 0	169 6		71 5	23 1	21 6	20 7	20 6	20 5			
15	2-Pro (β)	100 1	70 5	69 0	67 0	70 9	61 2	170 1	170 0	169 9	169 0		73.0	23 1	21 6	20 7	20 6	20 5			
21	(α)	94 8	68 3	67 7	66 2	68 3	61 8	172 3	170 1	170 0	169 8		71 3	23 0	21 6	20 8	20 5	20 5			
16	1-Oct (β)	100 9	71 5	73 0	68 7	71 83	62 1	170 5	170 2	169 3	169 1		70 1	31 8	29 4	29 2	25 8	22 6	20 6	20 5	14 0
22	(α)	95 7	71 0	70 4	68 8	67 21	62 0	170 5	190 1	170 0	169 5		68 8	31 8	29 4	29 2	26 0	22 6	20 6	20 5	14 0
17	1-Oct (β)	101 3	70 6	69 0	67 2	71 0	61 3	170 2	170 0	169 9	169 1		70 1	31 7	29 4	29 2	25 7	22 6	20 6	20 5	14 0
23	(α)	96 2	68 3	67 8	66 2	68 3	61 8						68 8	31 8	29 3	29 2	25 7	22 6	20 7	20 6	14 0

[a] For a solution in (^{2}H) chloroform at 30°. [b] n = 0–8

Although the H-2 and -5 signals of 3,4,6-tri-*O*-acetyl-α-D-galactopyranose 1,2-(alkyl orthoacetates) **7**, **9** and **11** fully overlapped for solutions in (^{2}H)chloroform, a resolution was observed for solutions in ($^2H_6$)benzene. In turn, the ^{13}C-n.m.r. chemical shifts of C-2 and -5 were observed for solutions in ($^2H_6$)benzene (δ 74.5 and 69.6, respectively, for the *exo* isomer of **9**). The complete assignments of ^{13}C-n.m.r. signals of 3,4,6-tri-*O*-acetyl-α-D-glycopyranose 1,2-(alkyl orthoacetates) for solution in (^{2}H)chloroform (Table IV) were compared with those of compound **9** in ($^2H_6$)benzene and compounds **8** and **9** in (^{2}H)chloroform by assuming a similar sequence in the same sugar residue. The ^{13}C chemical shifts δ of compounds **12**, **18**, **19**, and **20** have been reported[14–16]. The sequence of the ^{13}C-n.m.r. chemical shifts of the alkyl 2,3,4,6-tetra-*O*-acetyl-α- and -β-D-glycopyranosides was based on literature data for the same and analogous compounds.

The structures of the acylated 1,2-(alkyl orthoacetates) were ascertained by comparison of the ^{13}C-n.m.r. spectra with those of their corresponding alkyl 2,3,4,6-tetra-*O*-acetyl-α-D-glycopyranoside (Table I). A significant difference between the two series was observed for the resonances of C-2 of the D-glucose and D-galactose derivatives, and an additional difference for the resonance of C-3 only for the D-galactose series. Thus, there was a downfield shift of the C-2 signals of the fully acylated α-D-galactopyranose and α-D-glucopyranose 1,2-(alkyl orthoacetate) by ~6.1 and 2.8 p.p.m., respectively, and of the C-3 signals of the 1,2-orthoacetate of α-D-galactopyranose by ~3.0 p.p.m., relative to the corresponding signals of the spectra of α-D-glycopyranoside peracetates. In addition, a similar shift of each of the C-1, -2, and -3 signals for all the 1,2-orthoacetates presently studied was observed at about δ 97.1, 73.4, and 71.4, respectively. A slight downfield shift of the C-1 signal was also observed for the *endo* isomer of 1,2-orthoacetates of primary alcohols, but for the 1,2-orthoacetate of 2-propanol (a secondary alcohol), a slight upfield shift was observed.

EXPERIMENTAL

General. — Acetonitrile was purified according to a procedure in the literature[7]. Optical rotations were measured at ~20–25° with a Perkin–Elmer 141 automatic polarimeter. N.m.r. spectra were recorded with a Varian XL-100 spectrometer for solutions in (^{2}H)chloroform and tetramethylsilane as internal standard. Column chromatography was carried out on silica gel (70–230 mesh), supplied by Sigma Chemical Co. T.l.c. was performed on precoated sheets (100-nm-thick; Eastman Kodak Co., Rochester, N.Y.), in solvent system (*A*) {1:1 (v/v) hexane–ethyl acetate} and the spots made visible by spraying with 50% H_2SO_4 and heating the sheet for a few min at 110°.

The same procedure was used for the preparation of β-D-glycosides **13–17** as for the preparation of 1,2-orthoacetates **6–11**, except that silver tetrafluoraborate and 2,4,6-trimethylpyridine were the catalysts and bromides **1** or **2** the starting halides (Table II). α-D-Glycosides **18–23** were prepared by anomerization of the

corresponding β-D anomer in the presence of boron trifluoride etherate in benzene[17].

*3,4,6-Tri-*O*-acetyl-α-*D*-glucopyranose 1,2-(methyl orthoacetate)* (**6**). — This compound was obtained by condensation of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl chloride[9] (**3**) with methanol in the presence of 2,6-dimethylpyridine as already described[1]. A mixture of chloride (0.5 g), methanol (5 mL), and 2,6-dimethylpyridine (0.5 mL) was kept at room temperature for 2 days and the solvent evaporated. Diethyl ether (30 mL) was added, and the precipitate was filtered off and washed with diethyl ether (30 mL). The combined filtrates were washed with water and dried (Na_2SO_4). Xylene was added and evaporated *in vacuo* at 45°, and the azeotropic removal of 2,6-dimethylpyridine was repeated several times. Chromatography on silica gel (20 g; elution with 1:2, v/v, ethyl acetate–hexane) gave **6** (89:11 *exo/endo*), $[\alpha]_D^{22}$ +54° (*c* 3.5, chloroform); t.l.c. R_F 0.69 (solvent *A*); lit. $[\alpha]_D$ +34° (ref. 1) and +65° (ref. 9) (chloroform).

*3,4,6-Tri-*O*-acetyl-α-*D*-glycopyranose 1,2-(alkyl orthoacetates)* **7, 8, 9, 10,** *and* **11.** — These alkyl orthoacetates were also prepared in an analogous fashion to the preparation of a complex alcohol orthoacetate[7] *via* the corresponding 2,3,4,6-tetra-*O*-acetyl-α-D-glycopyranosyl bromide in the presence of $AgNO_3$ and 2,4,6-trimethylpyridine as acid acceptor, except that a 2,3,4,6-tetra-*O*-acetyl-α-D-glycopyranosyl chloride[9,10] (**3** and **4**) was used in place of the bromide. Each chloride (0.22 g) was added to a solution of alkyl alcohol (0.5 mL), $AgNO_3$ (0.207 g), and 2,4,6-trimethylpyridine (0.164 mL) in acetonitrile, (5 mL) and the mixture stirred for 4 h at room temperature. $AgNO_3$ (another 0.1 g) was added and the mixture stirred for further 1 h. The precipitate was filtered off and washed with dichloromethane (20 mL). The combined filtrates were washed with water, dried (Na_2SO_4), and evaporated to a syrup. The crude mixture was chromatographed on a silica gel column (20 g). Hexane containing 33, 25, and 20% of ethyl acetate eluted methyl, 2-propyl, and 1-octyl orthoacetate, respectively. The following products were isolated:

*3,4,6-Tri-*O*-acetyl-α-*D*-galactopyranose 1,2-(methyl orthoacetate)* (**7**). (77:23 *exo/endo*), $[\alpha]_D^{22}$ +94.3° (*c* 2.3, chloroform); t.l.c. R_F 0.69 (solvent *A*); lit.[18] $[\alpha]_D^{20}$ +79.5° (chloroform).

*3,4,6-Tri-*O*-acetyl-α-*D*-glucopyranose 1,2-(2-propyl orthoacetate)* (**8**). (47:3 *exo/endo*); *exo*-isomer, m.p. 116–117° (ether–hexane); $[\alpha]_D^{22}$ +29° (*c* 3.0, chloroform); t.l.c. R_F 0.74 (solvent *A*); lit.[5] m.p. 120–121°, $[\alpha]_D$ +30° (chloroform).

*3,4,6-Tri-*O*-acetyl-α-*D*-galactopyranose 1,2-(2-propyl orthoacetate)* (**9**). (43:7 *exo/endo*), $[\alpha]_D^{22}$ +89.5° (*c* 3.9, chloroform); t.l.c. R_F 0.74 (solvent *A*); lit.[18] $[\alpha]_D^{20}$ +67.1° (chloroform).

*3,4,6-Tri-*O*-acetyl-α-*D*-glucopyranose 1,2-(1-octyl orthoacetate)* (**10**). (43:7 *exo/endo*), $[\alpha]_D^{22}$ +22.8° (*c* 2.9, chloroform); t.l.c. R_F 0.78 (solvent *A*).

Anal. Calc. for $C_{22}H_{36}O_{10}$: C, 57.37; H, 7.88. Found: C, 57.17; H, 7.79.

*3,4,6-Tri-*O*-acetyl-α-*D*-galactopyranose 1,2-(1-octyl orthoacetate)* (**11**). (41:9 *exo/endo*), $[\alpha]_D^{22}$ +73.2° (*c* 3.6, chloroform); t.l.c. R_F 0.78 (solvent *A*).

Anal. Calc. for $C_{22}H_{36}O_{10}$: C, 57.37; H, 7.88. Found: C, 57.38; H, 7.83.

Condensation of 2,3,4,6-tetra-O-acetyl-α-D-glycopyranosyl bromides **1** *and* **2**, *and β-D-glycopyranosyl chlorides* **3** *and* **4** *with alkyl alcohols.* — (*a*) *In the presence of* Ag_2CO_3 *and molecular sieve 4A.* A mixture of 1,2-*cis*- or -*trans*-acylglycosyl halide (0.84 g; 2 mmol), alkyl alcohol (0.84 mL), and molecular sieve 4A (10 g) in dichloromethane (10 mL) was shaken for 30 min. Ag_2CO_3 (2.75 g; 10 mmol) was added and the mixture shaken for 7 h at room temperature. The solids were filtered off and washed with dichloromethane (80 mL). The combined filtrates were evaporated to a syrup which was examined by n.m.r. spectroscopy (Table I).

(*b*) *In the presence of 2,6-dimethylpyridine.* The condensations were carried out as described for the preparation of fully acylated α-D-glucopyranose 1,2-(methyl orthoacetate) (**6**), but for a longer reaction period of 3 days. The results are summarized in Table I.

(*c*) *In the presence of silver salts and 2,4,6-trimethylpyridine.* The procedure was the same as the preparation of the fully acylated α-D-glycopyranose 1,2-(alkyl orthoacetates) (**7–11**), but without purification. After stirring for 4 h, the solvent was evaporated and ether (60 mL) added. The ether extract was filtered and the filtrate evaporated to give a sample for n.m.r. analysis (Tables I and IV).

(*d*) *In the presence of 2,4,6-trimethylpyridine alone.* The procedure used was the same as procedure (*c*), except that the reactions were carried out for 4 h (Tables II and III) and 2 days (Table I), respectively.

ACKNOWLEDGMENT

The recording of n.m.r. spectra by Mr. M. Mazurek was much appreciated.

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