Tetrahedron, 1967, Vol. 23, pp. 693 to 707. Pergamon Press Ltd. Printed in Northern Ireland

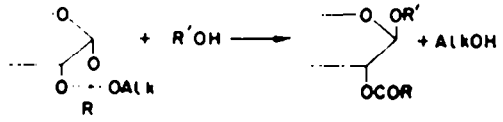
A NEW METHOD OF GLYCOSYLATION

N. K. KOCHETKOV, A. J. KHORLIN, A. F. BOCHKOV
Institute for Chemistry of Natural Products, USSR Academy of Sciences, Moscow

(*Received* 30 *September* 1965; *in revised form* 22 *February* 1966)

Abstract—A novel method of glycosylation using 1,2-O-alkyl orthoesters of sugars as glycosylating agents and a new convenient synthesis of these orthoesters is described.

THE synthesis of various complex glycosides require methods which are highly stereospecific, convenient and reliable in addition to their being applicable to different types of sugars and aglycones. The only general method of glycosylation—the Koenigs-Knorr reaction[1–5] and its modifications—does not resolve all the synthetic problems of modern sugar chemistry and further does not guarantee satisfactory and reproducible yields of glycosides. The weakness of Helferich modification is the absence of sufficient stereospecificity of the reaction.* In this paper, a new method of O-glycosylation is described in which 1,2-O-alkyl orthoesters lead stereospecifically to 1,2-*trans*-glycosides.[10]



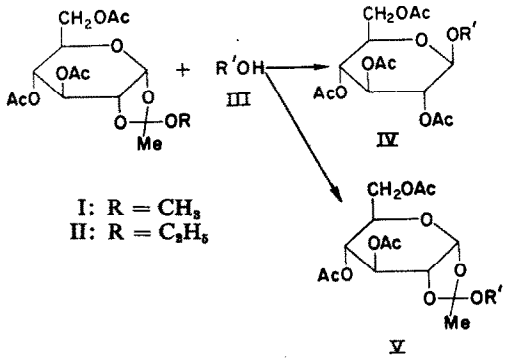
1. *Condensation of acetylated* D-*glucopyranose* 1,2-O-*alkyl orthoacetates with cholesterol*

The reaction of acetylated D-glucose-1,2-O-alkyl orthoacetates (I or II) with cholesterol (III) provides a basis for a new method of glycosylation. It has been shown that the condensation of I (or II) with III can proceed in one of two directions [glycosylation (1) or reesterification (2)][11] depending on the reaction conditions

As may be seen from Table 1, the formation of the acetylated glycoside (IV) or the new orthoester (V) is determined by the nature of the solvent and the type and amount

* cf. Refs. 6, 7 and 8, 9.

[1] W. Koenigs and E. Knorr, *Ber. Dtsch. Chem. Ges.* **34**, 957 (1901).
[2] W. L. Evans, D. D. Reynolds and E. A. Talley, *Adv. Carb. Chem.* **6**, 27 (1951).
[3] R. U. Lemieux, *Adv. Carb. Chem.* **9**, 1 (1954).
[4] L. J. Haynes and F. H. Newth, *Adv. Carb. Chem.* **10**, 207 (1955).
[5] J. Conchie, G. A. Levvy and C. A. Marsh, *Adv. Carb. Chem.* **12**, 157 (1957).
[6] H. N. Flowers and R. W. Jeanloz, *J. Org. Chem.* **28**, 1377 (1963).
[7] H. N. Flowers and R. W. Jeanloz, *J. Org. Chem.* **28**, 2983 (1963).
[8] B. Helferich and J. Zirner, *Chem. Ber.* **95**, 2604 (1962).
[9] J. Lemann and D. Beck, *Liebigs Ann.* **630**, 56 (1960).
[10] N. K. Kochetkov, A. J. Khorlin and A. F. Bochkov, *Tetrahedron Letters* 289 (1964).
[11] A. J. Khorlin, A. F. Bochkov and N. K. Kochetkov, *Khim. prirodnich soedineniy* 6 (1966).



(1)

(2)

I: R = CH_3
II: R = C_2H_5

R′ = cholesteryl

of catalyst used. In solvents of weak polarity all the catalysts investigated give rise to reesterification (2). *p*-Toluenesulfonic acid (TsOH) as catalyst in all solvents investigated gives similar results but with catalysts such as $HgBr_2$ or $CuBr_2$ in polar solvents ($MeNO_2$, MeCN) both reactions (1) and (2) take place. In these cases, each solvent–catalyst system is characterized by a definite amount of catalyst per mole of orthoester and if less catalyst is used only reesterification occurs. If the amount of catalyst is higher than this critical value, glycosylation (2) predominates. The smallest amount of catalyst was required when nitromethane as solvent and $HgBr_2$ with 0·00025 moles of TsOH as catalyst were used. In this case the amounts of $HgBr_2$ corresponding to the change in the reaction pathway was 0·001–0·008 mole per mole of orthoester.

The data thus obtained, resulted in the preparation of the tetra-acetate of cholesteryl β-D-glucopyranoside (IV) in 45% yield and a standard procedure of glycosylation was developed. This involves the condensation of sugar orthoesters with alcohols in boiling nitromethane in the presence of $HgBr_2$ (0·02–0·07 mole per mole of alcohol). The procedure was successfully applied to the synthesis of various compounds containing glycosidic bonds.

2. *Synthesis of sugar orthoesters*

The syntheses of sugar orthoesters starting from the corresponding 1,2-*trans*-acylhalogenoses have been described in the literature.[12–17] But since these halogenoses are generally unstable and sometimes unobtainable, the method of synthesis of orthoesters described by Helferich[18] and later applied by Schulz and Steinmaus,[19] starting from more stable 1,2-*cis*-acylhalogenoses, have been modified. The time of reaction has been shortened and the isolation of orthoesters improved. Furthermore, a new method of orthoester synthesis based on the condensation of 1,2-*cis*-acylhalogenoses with alcohols in boiling ethyl acetate in the presence of $PbCO_3$ and $CaSO_4$

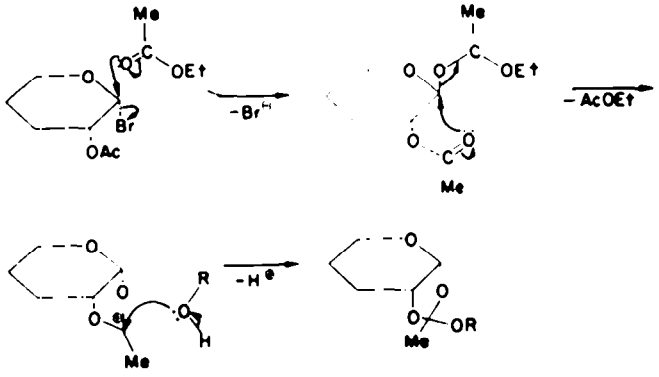
[12] E. Fisher, M. Borgmann and A. Rabe, *Ber. Dtsch. Chem. Ges.* **53**, 2362 (1920).
[13] H. G. Fletcher Jr. and R. K. Ness, *J. Amer. Chem. Soc.* **77**, 5337 (1955).
[14] W. N. Haworth, E. H. Hirst and M. Stacey, *J. Chem. Soc.* 2864 (1931).
[15] R. N. Ness and H. G. Fletcher Jr., *J. Amer. Chem. Soc.* **76**, 1663 (1954).
[16] R. U. Lemieux and C. Brice, *Canad. J. Chem.* **33**, 109 (1955).
[17] R. U. Lemieux and J. D. T. Cipera, *Canad. J. Chem.* **34**, 906 (1956).
[18] B. Helferich and K. Weiss, *Chem. Ber.* **89**, 314 (1956).
[19] M. Shulz and H. Steinmaus, *Zeitschrift für Naturforschung* **196**, 263 (1964).

TABLE 1. CONDENSATION OF CHOLESTEROL (III) WITH ACETYLATED 1,2-O-ALKYLORTHOACETYL-α-D-GLUCOPYRANOSES (I OR II).

No of experiment	Orthoester, mmoles	Cholesterol, mmoles	Solvent, ml	Time of the reaction hr	Catalyst, mmoles per mmole of orthoester	Unchanged cholesterol obtained, %%	Reaction products, yield %%	Mode of purification of products	Mode of identification of products
1	2	3	4	5	6	7	8	9	10
9	I, 0·43	0·43	DCE, 4	4	TsOH, 0·0005	—	V	—	*c*
10	I, 0·33	0·31	DCE, 3·5	2·5	$HgBr_2$, 0·001	—	V, 18	*a*	*c, d*
11	II, 1·50	1·00	DCE, 10	2	$HgBr_2$, 0·33	—	V, 59	*b*	*c, d, e*
12	I, 0·36	0·28	$MeNO_2$, 3	2	TsOH, 0·0004	—	V	—	*c*
13	I, 0·36	0·36	$MeNO_2$, 4	2	$HgBr_2$, 0·001	57	V	—	*c*
14	I, 1·50	1·50	$MeNO_2$, 16	4	$HgBr_2$, 0·001 + TsOH, 0·0005	40	IV, 15 + V, 26	*a*	*c, d, e*
15	I, 1·00	1·00	$MeNO_2$, 8	2	$HgBr_2$ 0·008 + TsOH, 0·00025	41	IV, 45	*b*	*c, d, e*
16	II, 1·00	1·00	$MeNO_2$, 8	2	$HgBr_2$, 0·008 + TsOH, 0·00025	37	IV, 45	*b*	*c, d, e*
17	II, 2·00	2·00	$MeNO_2$, 15	1·5	$Hg(OAc)_2$, 0·1	91	V	—	*c*
18	II, 1·55	1·55	$MeNO_2$, 15	1·5	$Cu(OAc)_2$, 0·1	—	V, 30	*b*	*c*
19	II, 1·50	1·00	$MeNO_2$, 15	1·5	$HgCl_2$, 0·013	28	IV + V	—	*c*
20	II, 1·00	1·00	$MeNO_2$, 10	2	$HgCl_2$, 0·2	31	IV, 42	*b*	*c*
21	II, 1·50	1·00	$MeNO_2$, 15	1	$CuBr_2$, 0·013	20·5	IV, 22 + V	*b*	*c, d*
22	II, 1·00	1·00	$MeNO_2$, 10	2	$TiCl_4$, 0·02	44	V	—	*c*
23	II, 1·00	1·00	MeCN, 12	2	$HgBr_2$, 0·008 + TsOH, 0·00025	50	V	*b*	*c, d*
24	II, 1·00	1·00	MeCN, 12	2	$HgBr_2$, 0·1 + TsOH, 0·0025	—	IV, 12·5 + V	*b*	*c, d*
25	II, 1·30	1·00	MeCN, 15	1	$CuBr_2$, 0·0385	60	V > IV	—	*c*
26	II, 2·00	1·30	EtOAc, 15	1	$HgBr_2$, 0·1	—	V	—	*c*
					Rearrangement of orthoesters				
27	II, 1·00	—	$MeNO_2$, 10	3	$HgBr_2$, 0·05	—	Ethyl β-D-glucopyranoside tetraacetate, 33	*a, f*	*c, d, e*
28	V, 0·30	—	$MeNO_2$, 2	3	$HgBr_2$, 0·05	—	IV	—	*c*

[a] Chromatography on alumina with following crystallization from MeOH
[b] Crystallization from MeOH.
[c] Chromatographical identification (System A) with authentic specimen.
[d] M.p. corresponds to literature data.
[e] $[\alpha]_D$ corresponds to literature data.
[f] Crystallization from Et_2O–pet. ether.

(dryerite)[20] has been developed. The method affords high yields of a series of acetylated sugar-1,2-alkyl orthoacetates and acetylated 1,2-O-cholesteryl orthoacetyl-D-glucopyranose (V). The formation of orthoesters by the condensation of 1,2-*cis*-acylhalogenoses with alcohols probably depends on the double inversion of configuration at the glycosidic centre which involves participation of ethyl acetate:



Many acylhalogenoses exist as mixtures of anomers and when used as such for orthoester synthesis, one of the anomers gives rise to the 1,2-orthoester and the other to the isomeric glycoside. When the 2,3,4-tri-O-benzoyl-L-arabinopyranosyl bromides or 2,3,5-tri-O-benzoyl-L-arabinofuranosyl bromides were condensed with methanol under conditions required for a conversion of the predominating anomer of each mixture to the orthoester, the corresponding orthoesters contaminated with some isomeric glycosides were obtained. The successful use of these orthoesters (without separation from the corresponding methylglycosides) in the synthesis of disaccharides (see below) shows, that the presence of the glycosides does not interfere in the condensation of orthoesters with alcohols. Thus, whereas the mixtures of anomeric acylhalogenoses cannot be applied as such for the stereospecific Koenigs-Knorr synthesis of glycosides, conversion to orthoesters renders them effective and stereospecific (see below) glycosylating agents.

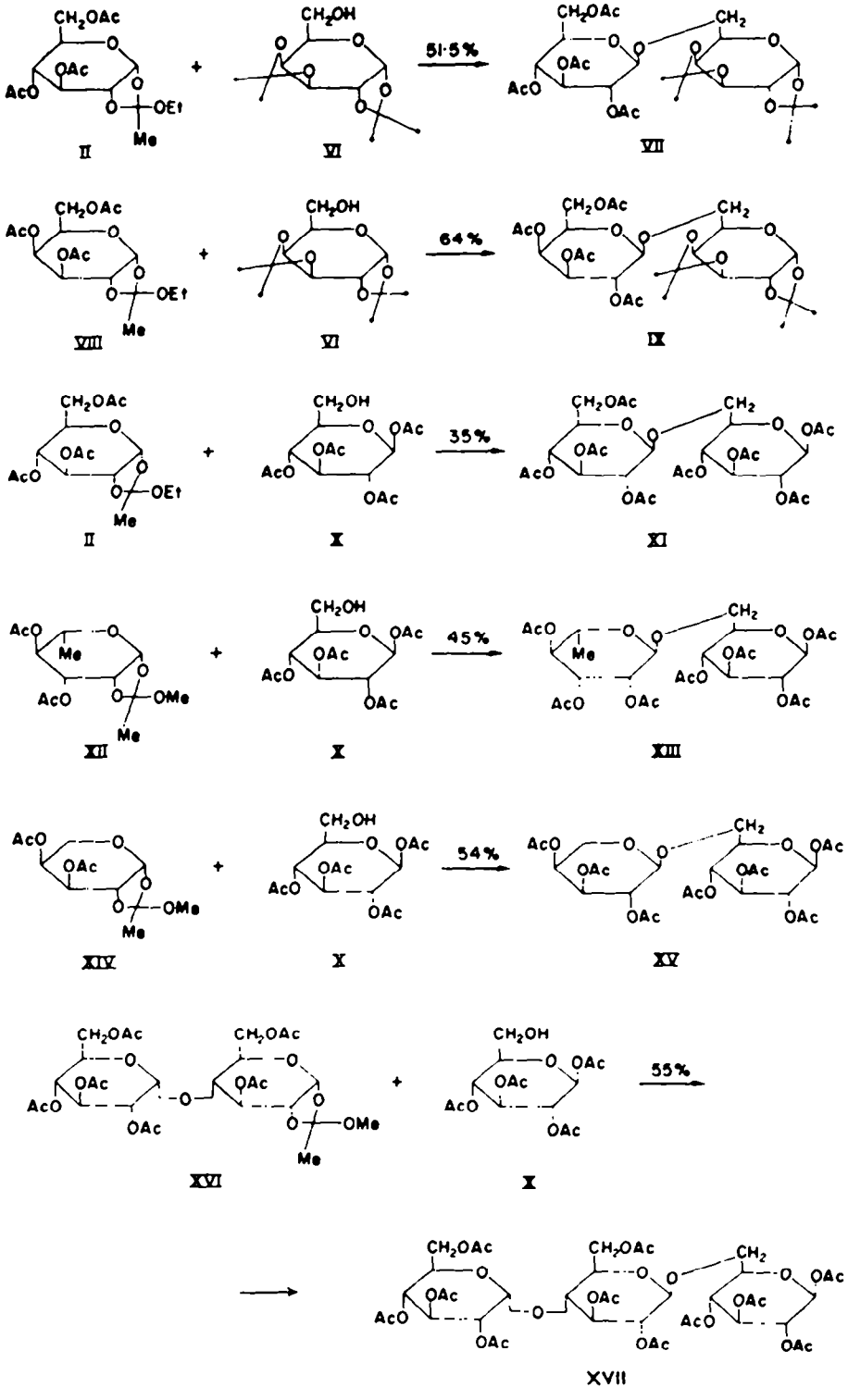
Since the usual aldoses are capable of forming orthoester functions, the sugar orthoesters are important new glycosylating agents and are generally more available than 1,2-*cis*-acylhalogenoses which are used in the stereospecific synthesis of glycosides by the Koenigs-Knorr reaction.

3. *Scope and synthetic application of the glycosylation reaction*

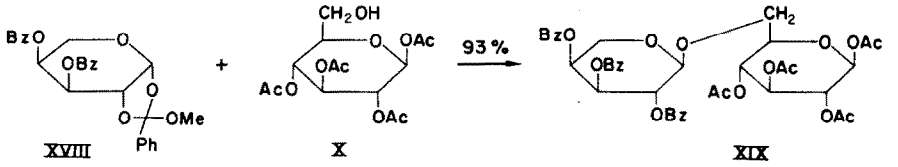
The influence of orthoester structure. In order to compare the reactivity of sugar orthoesters of different types, a series of oligosaccharides with 1 → 6 glycosidic bonds were synthesized[21] using the standard conditions of glycosylation. The oligosaccharide derivatives (VII, IX, XI, XIII, XV, XVII)—the only products of glycosylation isolated from the reaction mixtures by crystallization or chromatography—were identical with those described in the literature.

The orthoesters of hexoses, 6-deoxyhexoses, pentoses and disaccharides are

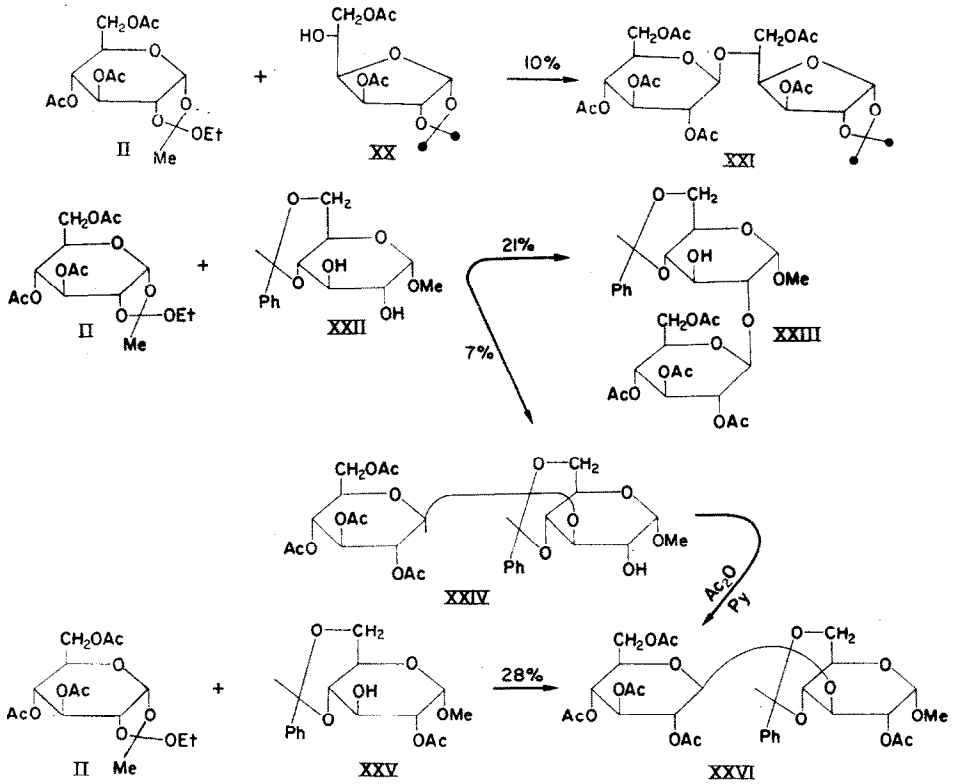
[20] A. J. Khorlin, A. F. Bochkov and N. K. Kochetkov, *Izv. Akad. Nauk SSSR, ser. Khim.* 2214 (1964).
[21] N. K. Kochetkov, A. J. Khorlin and A. F. Bochkov, *Dokl. Akad. Nauk SSSR* **162**, 104 (1965).


II
VI
51·5%
VII
VIII
64%
IX
35%
X
XI
XII
45%
XIII
XIV
54%
XV
XVI
55%
XVII

glycosylating reagents of about equal reactivity and yield the corresponding oligosaccharides in high yields. The synthesis of the trisaccharide derivative (XVII) from the disaccharide orthoester (XVI), demonstrates the possibility of elongating a carbohydrate chain by two monosaccharide units simultaneously and the synthesis of higher oligosaccharides and glycosides with long carbohydrate chains.[22] The synthesis of XIX (93%) and XV (54%) in the yields indicated from 3,4-di-O-benzoyl-1,2-O-methylorthobenzoyl-β-L-arabinopyranose (XVIII) and the corresponding orthoacetate (XIV), respectively shows that saccharide orthobenzoates are more active glycosylating agents than the orthoacetates.



The reactivity of different hydroxyl groups. A series of β-D-glucopyranosyl-D-glucoses[21,23] were synthesized by condensation of 3,4,6-tri-O-acetyl-1,2-O-ethyl orthoacetyl-α-D-glucopyranose (II) with various partially protected glucoses containing free OH-groups at $C_{(2)}$ (XXII), $C_{(3)}$ (XXII and XXV) and $C_{(5)}$ (XX) in order to establish the comparative reactivity of the hydroxyl groups of different types.



[22] N. K. Kochetkov and A. J. Khorlin, *Dokl. Akad. Nauk SSSR* **150,** 1289 (1963).

[23] A. J. Khorlin, A. F. Bochkov and N. K. Kochetkov, *Izv. Akad. Nauk SSSR, ser. Khim* 168 (1966).

The disaccharide derivatives resulting from the condensations were isolated from the reaction mixture and purified by chromatography and crystallization. Compounds XXI and XXIII were identified by comparison with known compounds and the structure of unknown laminaribiose derivatives (XXIV and XXVI) was proved by removal of protecting groups followed by periodate oxidation. The recently described syntheses of laminaribiose[24] and its derivative[25] are invalidated by complications and low yields. The new approach to the synthesis of XXV should make the derivatives of laminaribiose and, probably, other 3-O-glycosyl-glucoses more available.

The lowest yield was obtained on the glycosylation of XX. This result is in a good agreement with poor reactivity of this compound in the Koenigs-Knorr reaction.[25] The glycosylation of methyl 4,6-O-benzylidene-α-D-glucopyranoside (XXII) containing two free hydroxyl groups yielding disaccharides XXIII and XXIV provided a direct comparison of the reactivity of hydroxyls at $C_{(2)}$ and $C_{(3)}$. The comparison of the yields in this series shows that activity of sugar hydroxyls decreases as follows: $C_{(6)} > C_{(2e)} \geqslant C_{(3e)} > C_{(5)}$.

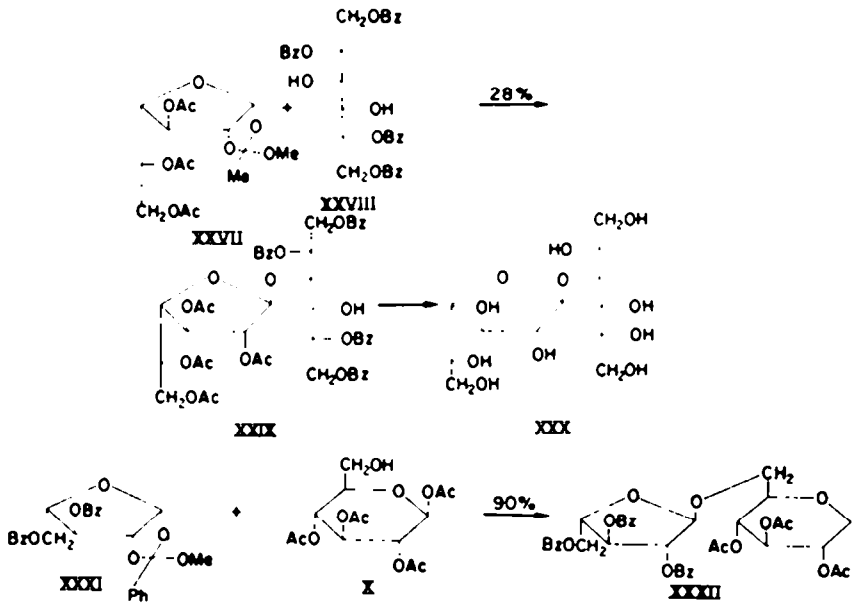
The above data show clearly the possibility of preparative syntheses of different 1,2,-*trans*-glycopyranosides with complex aglycones via sugar orthoesters.

Synthesis of furanosides. Although furanoside bonds are widely distributed in natural carbohydrates, the synthesis of glycosides and oligosaccharides with this type of bonding is difficult. Moreover, the partial hydrolysis of polysaccharides, yielding new oligosaccharides, cannot, as a rule, lead to these compounds. On the other hand, as there is an essential steric difference in the structure of pyranose and furanose orthoesters, the former belonging to the *cis*-hydrindane type and the latter to the *cis*-pentalane type, the application of the new method to the synthesis of furanosides was both of preparative and theoretical interest.

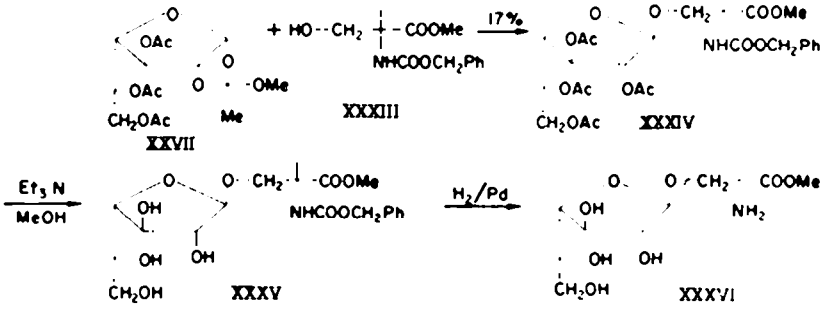
The condensation of 3,5,6-tri-O-acetyl-1,2-O-methyl orthoacetyl-α-D-galactofuranose (XXVII), obtained from the corresponding 1,2-*trans*-chloride,[26] with 1,2,5,6-tetra-O-benzoyl-D-mannitol (XXVIII) under normal conditions of glycosylation gave 1,2,5,6-tetra-O-benzoyl-3-O-(2,3,5,6-tetra-O-acetyl-β-D-galactofuranosyl)-D-mannitol (XXIX) as the only glycosylation product.[28]. The saponification of XXIX led to 3-O-(β-D-galactofuranosyl)-D-mannitol (XXX), identical with the natural compound isolated by Lindberg *et al.* from *Peltigera horizontalis*[27] and thus confirming its structure.

In order to determine the comparative activity of pyranose and furanose orthoesters the condensation of 3,5-di-O-benzoyl-1,2-O-methyl orthobenzoyl-β-L-arabinofuranose (XXXI) with 1,2,3,4-tetra-O-acetyl-β-D-glucopyranose (X) was carried out under conditions similar to those used in the synthesis of vicianose derivatives (XV and XIX). The reaction gave rise to the corresponding derivative of 6-O-(α-L-arabinofuranosyl)-D-glucose (XXXII); its structure was established by conversion into the disaccharide recently described. A comparison of the yields of XXXII (90%) and XIX (93%) indicates that the size of the sugar ring (pyranose or furanose) has practically no influence on the glycosylating activity of the orthoesters.

[24] P. Bächli and E. C. V. Percival, *J. Chem. Soc.* 1243 (1952).
[25] K. Freudenberg and K. v. Oertzen, *Liebigs Ann.* **574**, 37 (1951).
[26] M. L. Wolfrom, P. McWain, R. Pagnucco and A. Thompson, *J. Org. Chem.* **29**, 454 (1964).
[27] B. Lindberg, B. -G. Silvander and C. A. Wachtmeister, *Acta Chem. Scand.* **18**, 213 (1964).
[28] N. K. Kochetkov, A. J. Khorlin and A. F. Bochkov, *Dokl. Akad. Nauk SSSR* **161**, 1342 (1965).



In connection with the investigation of the bonds between carbohydrate and peptide components of glycopeptides and their stability,[29-31] O-(β-D-galactofuranosyl)-L-serine methyl ester (XXXVI) was synthesized according to the scheme:[32]



The synthesis of this compound as well as galactofuranosyl-mannitol (XXX) could not be carried out by any other known method as the corresponding 1,2-*cis*-acyl-halogenoses are not known.

4. *The possible mechanism of the reaction*

In all cases of glycoside synthesis via orthoesters, it was proved by careful analysis of reaction mixtures (TLC), that 1,2-*trans*-glycosides are the only product of the

[29] M. G. Vafina, V. A. Derevitskaya and N. K. Kochetkov, *Izv. Akad. Nauk SSSR, Ser. Khim.* 1814 (1965).

[30] N. K. Kochetkov, V. A. Derevitskaya, L. M. Lichoscherstov, N. V. Molodtsov and S. G. Kara-Murza, *Tetrahedron* **18**, 273 (1962).

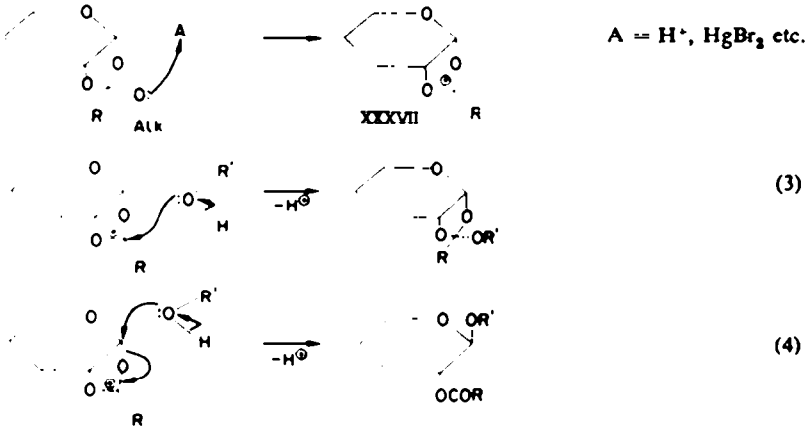
[31] N. K. Kochetkov, V. A. Derevitskaya and N. V. Molodtsov, *Izv. Akad. Nauk SSSR, Ser. Khim.* in press.

[32] N. K. Kochetkov, V. A. Derevitskaya, A. J. Khorlin, M. G. Vafina and A. F. Bochkov, *Izv. Akad. Nauk SSSR, Ser. Khim.* 1698 (1965).

condensation of orthoesters with alcohols. Occasionally, traces of unidentified by-products were observed. The protecting groups used (acetates, benzoates, alkylidenes, methylglycosides, benzyloxycarbonyl) are, therefore, stable under the reaction conditions.

The first considerations concerning the mechanism of this new reaction of glycosylation, based on the general concept of nucleophilic substitution at the glycosidic centre,[3] although in agreement with experimental data, require special investigation.

The first step of glycosylation should be the formation of a carbonium cation (XXXVII) which then undergoes a nucleophilic attack either on the electrophilic orthoester carbon [giving rise to the new orthoester, (3)] or on the glycosidic centre [resulting in the glycoside formation (4)].



The direction of the reaction is determined probably by a complex anion such as $[HgBr_3]^-$ which can arise by dissociation of $HgBr_2$ in polar solvents. This anion forms a close ion pair with the cation (XXXVII) thus shielding of the electrophilic orthoester carbon and directing the reaction to glycosylation. In media of low polarity or when catalysts such as TsOH or $Hg(OAc)_2$ are used or when the complex anion is present in low concentrations or its formation inhibited, then the electrophilic orthoester carbon of XXXVII is subject to nucleophilic attack and transglycosylation occurs.

The rearrangement of the orthoester into methylglycoside described by Helferich[18] probably proceeds via preliminary splitting of methanol and its subsequent glycosylation by a cation of type XXXVII, the reaction mechanism being essentially analogous to that mentioned above. Under conditions resembling glycosylation, the rearrangement of orthoesters into isomeric glycosides was observed (Table 1). The formation of this type of compound from the starting orthoesters limits the yields of glycosides obtained by this method. In fact, in all cases methyl or ethylglycosides isomeric with starting orthoesters were detected as contamination products of glycosylation. The improved glycosylating activity of orthobenzoates is due to stabilization of the cation (XXXVII) by conjugation with an aromatic nucleus.

EXPERIMENTAL

The $CHCl_3$ and CCl_4 used were freed from traces of acid by two-fold distillation over $CaCO_3$; $MeNO_2$ was distilled over urea at 100–200 mm Hg and twice over P_2O_5. AcOEt was washed with

$NaHCO_3$aq, then with sat. $CaCl_2$aq, dried over $CaCl_2$ and redistilled twice over P_2O_5. MeCN was redistilled twice over P_2O_5. 1,2-dichloroethane (DCE) was distilled over $CaCO_3$ and $CaCl_2$. The commercial alumina was neutralized by 50-fold boiling with distilled water and developed to the activity III after Brockman.

Preparative chromatography on alumina. The column charge was about 0·5–1·0 g of mixture per 1 cm^3, the height of adsorbent being 12–20 cm; the stepwise elution procedure was adopted, solvents $CCl_4 \rightarrow CHCl_3$ or $C_6H_6 \rightarrow CHCl_3$ being used.

Preparative chromatography on silica gel. The column charge was about 0·4–0·6 g of mixture per 1 cm^3, the height of adsorbent being 20–30 cm; the stepwise elution procedure was adopted.

TLC on alumina was performed using (A) $CHCl_3$–MeCOEt (98·5:1·5);* (B) $CHCl_3$; (C) $CHCl_3$–Me_2CO (95:5) and (D) $CHCl_3$–Me_2CO (90:10). TLC on silica gel was carried out using (E) $CHCl_3$–MeOH (90:10). The solvent systems (F) n-BuOH–C_5H_5N–H_2O (6:4:3) and (G) EtOAc–C_5H_5N–H_2O (10:4:3) were used for paper chromatography. Paper electrophoresis was performed in (H) pyrydine–acetate buffer, pH 4·5, 900 v.

Evaporation was carried out under reduced press. at 40–50°. The yields listed refer to chromatographically homogenous products. M.ps were determined on the Kofler hot-stage apparatus.

Synthesis of sugar orthoesters. All the sugar orthoesters are completely hydrolysed by 0·01N H_2SO_4 in 90% Me_2COaq at 20° for 10–30 min, except the cases mentioned. The hydrolysis was controlled by TLC (disappearance of an orthoester spot and simultaneous appearance of a spot R_f 0·0 attributed to hydrolysis products).

1. 3,4,6-*tri*-O-*acetyl*-1,2-O-*ethylorthoacetyl*-α-D-*glucopyranose* (II)

(a) To a mixture of 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide (XXXVIII) (10·0 g, 24·3 mmoles) in AcOEt (100 ml), $PbCO_3$ (20 g) and drierite (15 g) heated under reflux, abs EtOH (2·9 ml, 50 mmoles) was added in two portions during 4 hr. After cooling, Ag_2O (5 g) and 95% Me_2COaq (50 ml) were added and the mixture stirred for several hr until a negative reaction with $AgNO_3$ was obtained and then filtered and evaporated. The crystallization of the residue from EtOHaq yielded II (5·65 g, 62%), m.p. 94–96°, $[\alpha]_D$ −32° (*c* 0·76; $CHCl_3$). Lit.[17]: m.p. 97–97·5°, $[\alpha]_D$ +31° ($CHCl_3$).

(b) Compound XXXVIII (8·22 g, 20 mmoles) was dissolved in a mixture of $MeNO_2$ (20 ml), 2,6-lutidine (4·65 ml, 40 mmoles) and abs EtOH (5·8 ml, 100 mmoles). After standing at 37° for 45 hr, 2N $AgNO_3$ (15 ml, 30 mmoles), water (25 ml) and Me_2CO (50 ml) were added. The solution was filtered, diluted with $CHCl_3$ (100 ml) and hexane (250 ml) and the organic layer separated and washed twice with water. Evaporation yielded chromatographically pure II (7·3 g), which crystallized from EtOH and Et_2O-hexane, yielding 4·3 g (57%), m.p. 92–94°, $[\alpha]_D$ +36° (*c* 0·8, $CHCl_3$) System A.

2. 3,4,6-*Tri*-O-*acetyl*-1,2-O-*methylorthoacetyl*-α-D-*glucopyranose* (I)

This was prepared by the method described in 1(a) from 20 g of XXXVIII and purified by means of chromatography on alumina, yielding a syrup (66%), $[\alpha]_D$ +34° (*c* 1·86, $CHCl_3$), n_D^{20} 1·4554. Lit.[16]: $[\alpha]_D$ +65° in $CHCl_3$. (Found: C, 49·86; H, 6·14. Calc. for $C_{15}H_{22}O_{10}$: C, 49·72, H, 6·12%.) System A.

3. 3,4,6-*Tri*-O-*acetyl*-1,2-O-*ethylorthoacetyl*-α-D-*galactopyranose* (VIII)

(a) This was prepared by the procedure described under 2 from 20 g 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide (XXXIX) yielding a syrup (58%); $[\alpha]_D$ −78° (*c* 1·09, $CHCl_3$), n_D^{20} 1·4590. (Found: C, 50·88; H, 6·42. $C_{16}H_{24}O_{10}$ requires: C, 51·05; H, 6·42%.)

(b) Compound VIII was prepared as in 1(b), yield 4·64 g (62%), $[\alpha]_D$ +78° (*c* 1·0, $CHCl_3$), n_D^{20} 1·4596, System A.

4. 3,4,6-*Tri*-O-*acetyl*-1,2-O-*cholesterylorthoacetyl*-α-D-*glucopyranose* (V)

This was prepared as described in 1(a) from cholesterol (1·00 g, 2·6 mmoles) and XXXVIII (1·06 g, 2·6 mmoles). The unchanged cholesterol was removed by crystallization from $MeNO_2$; V was obtained from the mother liquor by chromatography on alumina with subsequent crystallization from MeOH, yield 0·23 g (12·4%), m.p. 98–100°(dec), $[\alpha]_D$ +2° (*c* 1·3, $CHCl_3$). (Found: C, 68·97; H, 8·88. $C_{41}H_{64}O_{10}$ requires: C, 68·86; H, 9·00%.) System A.

* The system noted at the end of each experiment was used for investigation of reaction mixtures, also for fraction's analysis, identification and control of homogeneity of the compounds obtained.

5. 3,4-*Di*-O-*acetyl*-1,2-O-*methylorthoacetyl*-β-L-*arabinopyranose* (XIV)

This was prepared as described in 1(b) from 2,3,4-tri-O-acetyl-β-L-arabinopyranosyl bromide[83] (5·40 g, 16 mmoles). Traces of lutidine were removed by chromatography on alumina, yield 1·96 g (42%) of a syrup, $[\alpha]_D$ +52° (*c* 1·22, $CHCl_3$), n_D^{20} 1·4569. (Found: C, 50·17; H, 6·05. $C_{15}H_{16}O_8$ requires: C, 49·65; H, 6·25%.) System A.

6. 3,4-*Di*-O-*benzoyl*-1,2-O-*methylorthobenzoyl*-β-L-*arabinopyranose* (XVIII)

A mixture of anomeric 2,3,4-tri-O-benzoyl-L-arabinopyranosyl bromides were prepared as the β-D-isomer,[84] $[\alpha]_D$ −318° ($CHCl_3$) (pure β-D-isomer has $[\alpha]_D$ −353·3°).[84] The mixture of bromides (2·10 g, 4·00 mmoles) were dissolved in $MeNO_2$ (4 ml), 2,6-lutidine (0·95 ml, 8·0 mmoles) and MeOH (0·32 ml, 8·0 mmoles). After standing at 37° for 48 hr, 2N $AgNO_3$ (3 ml) and Me_2CO (10 ml) were added and the mixture filtered. The filtrate was diluted with $CHCl_3$ (10 ml) and pet. ether (50 ml) and the organic layer separated, washed with water (5 × 20 ml) and evaporated, yielding crude XVIII (XVIIIa) 0·88 g (46%). About ⅓ of the substance was hydrolysed under the conditions of analytical hydrolysis described above, System B.

7. 3,5-*Di*-O-*benzoyl*-1,2-O-*methylorthobenzoyl*-β-L-*arabinofuranose* (XXXI)

A mixture of anomeric 2,3,5-tri-O-benzoyl-L-arabinofuranosyl bromides,[84] obtained from 10 g methyl 2,3,5-tri-O-benzoyl-α-L-arabinofuranoside was dissolved in 2,6-lutidine (10 ml) and abs MeOH (40 ml). After 17 hr at 20°, ether (30 ml), pet. ether (70 ml) and water (60 ml) were added. The aqueous layer was separated and extracted with ether–pet. ether (3:7; 2 × 100 ml). The combined organic layer were washed with water, 2N $AgNO_3$ (20 ml), again with water (4 times) and evaporated. After removal of the lutidine by chromatography on alumina, chromatographically pure syrup (XXXIa; 5·65 g, 56%) was obtained. About ⅓ of this is hydrolysed under the conditions of analytical hydrolysis described above, System B.

8. 3,5,6-*Tri*-O-*acetyl*-1,2-O-*methylorthoacetyl*-α-D-*galactofuranose* (XXVII)

This was prepared as described in 7 from 2,3,5,6-tetra-O-acetyl-β-D-galactofuranosyl chloride[80,84] (4·0 g, 10·9 mmoles). A pet. ether–ether mixture (2:1) was used for extraction and the traces of lutidine removed by drying for a long time *in vacuo* yielding 1·95 g (49%) of a syrup, $[\alpha]_D$ +24° (*c* 0·33, $CHCl_3$), n_D^{20} 1·4599. (Found: C, 50·13; H, 5·94. $C_{16}H_{22}O_{10}$ requires: C, 49·72; H, 6·12%.) System A.

Reaction of cholesterol with acetylated 1,2-O-*alkyl-orthoacetyl*-α-D-*glucopyranoses*

General procedure. A solution of cholesterol (III) and orthoester (I or II) was distilled at atm. press. with addition of fresh solvent so as to keep the volume constant. After collecting 2–5 ml of distillate, a catalyst (usually a dilute solution in DCE) was added and the procedure continued for a definite time. The reaction mixture was then cooled, a few drops of pyridine added and the solution evaporated (at this stage in some experiments unchanged cholesterol was removed by crystallization from $MeNO_2$) and the residue analysed by TLC.[87] Reaction products were separated by crystallization from MeOH or by means of chromatography on alumina and subsequent crystallization from MeOH. The details of experiments are presented in Table 1, System A.

Syntheses of oligosaccharides and other glycosides

The general procedure was analogous to the reaction of cholesterol with glucose orthoacetates described above. $MeNO_2$ was used as solvent and $HgBr_2$ as catalyst. The reaction mixtures were analysed by means of TLC in a corresponding solvent system. In all cases (except when mentioned) a chromatogram analogous to that in Fig. 1 was obtained and showed the absence of any by-products of condensation of orthoesters with aglyconic components.

[83] M. Hehrke and F. X. Aichner, *Ber. Dtsch. Chem. Ges.* **60**, 918 (1927).
[84] H. G. Fletcher Jr. and C. S. Hudson, *J. Amer. Chem. Soc.* **72**, 4173 (1950).
[85] R. L. Wistler and M. L. Wolfrom, *Methods in Carbohydrate Chemistry* Vol. 2; p. 228. New York–London (1963).
[86] M. L. Wolfrom and W. Groebke, *J. Org. Chem.* **28**, 2986 (1963).
[87] A. J. Khorlin and A. F. Bochkov, *Izv. Akad. Nauk SSSR, Otdel. Khim. Nauk* 1120 (1962).

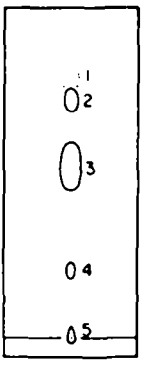


FIG. 1. The typical chromatogram of reaction mixture.

1—unchanged orthoester
2—methyl or ethyl glycoside
3—condensation product
4—unchanged alcoholic component
5—products of degradation of orthoester

In all the cases investigated the fair separation of the spots 2, 3 and 4 was obtained. The pairs of spots 1–2 and 4–5 were separated rather sharply except very few experiments.

29. 1,2:3,4-*Di*-O-*isopropylidene*-6-O-(2,3,4,6-*tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-α-D-*galactopyranose* (VII)

A mixture of II (1·01 g, 2·71 mmoles), VI (0·47 g, 1·81 mmoles), $MeNO_2$ (15 ml) and $HgBr_2$ (0·1 mmoles) was allowed to react for 1·5 hr. The product (VII) was purified by chromatography on alumina, yield 0·55 g (51·5%). After crystallization from Et_2O–hexane, VII had m.p. 140–142°, $[\alpha]_D$ −54·5° (*c* 0·46, $CHCl_3$). Lit.[38]: m.p. 141°, $[\alpha]_D$ −52·6° in $Cl_2CHCHCl_2$. (Found: C, 52·83; H, 6·51. Calc. for $C_{26}H_{38}O_{16}$: C, 52·89; H, 6·48%.) System A.

30. 1,2:3,4-*Di*-O-*isopropylidene*-6-O-(2,3,4,6-*tetra*-O-*acetyl*-β-D-*galactopyranosyl*)-α-D-*galactopyranose* (IX)

A mixture of VIII (1·36 g, 3·63 mmoles), VI (0·70 g, 2·68 mmoles), $MeNO_2$ (20 ml) and $HgBr_2$ (0·085 mmoles) was allowed to react for 1·5 hr. The product (IX) was purified by chromatography on alumina, yield 1·05 g (64%) as a syrup, $[\alpha]_D$ −47° (*c* 0·61, $CHCl_3$). Lit.[39]: m.p. 101–102°, $[\alpha]_D$ −44·7° ($Cl_2CHCHCl_2$), System A.

6-O-(β-D-*Galactopyranosyl*)-D-*galactose* (XL)

Compound IX obtained in the foregoing experiment was saponified (0·02N MeONa, 20°, 12 hr) and hydrolysed (0·1N H_2SO_4, 80°, 1·5 hr) and XL purified by partition chromatography on Sephadex G-25, yield 0·39 g (43%, calc. for VI). Reprecipitation with Me_2CO from MeOH gave XL, $[\alpha]_D$ +39° (*c* 0·53; equil., H_2O), R_g 0·26. Lit.[39]: $[\alpha]_D$ +34·1° (equil., H_2O). (Found: C, 41·88; H, 6·52. Calc. for $C_{12}H_{22}O_{11}$: C, 42·13; H, 6·48%.) System F.

31. 1,2,3,4-*Tetra*-O-*acetyl*-6-O-(2,3,4,6-*tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-β-D-*glucopyranose* (XI)

A mixture of II (0·57 g, 1·50 mmoles), X (0·35 g, 1·00 mmole), $MeNO_2$ (10 ml) and $HgBr_2$ (0·03 mmole) was allowed to react for 1·5 hr. After two crystallizations from Et_2O–hexane, the product (XI; 0·24 g, 35%) had m.p. 191–193·5°, $[\alpha]_D$ −4° (*c* 4·2, $CHCl_3$). Lit.[40]: m.p. 196°, $[\alpha]_D$ −5·35° ($CHCl_3$). (Found: C, 49·59; H, 5·75. Calc. for $C_{26}H_{38}O_{19}$: C, 49·55; H, 5·64%.) System A.

[38] K. Freudenberg, A. Noe and E. Knopf, *Ber. Dtsch. Chem. Ges.* **60**, 938 (1927).
[39] K. Freudenberg, A. Wolf, E. Knopf and S. H. Zaheer, *Ber. Dtsch. Chem. Ges.* **61**, 1743 (1928).
[40] D. D. Reynolds and W. H. Evans, *J. Amer. Chem. Soc.* **60**, 2559 (1938).

32. 1,2,3,4-*Tetra*-O-*acetyl*-6-O-(2,3,4-*tri*-O-*acetyl*-α-L-*rhamnopyranosyl*)-β-D-*glucopyranose* (XIII)

A mixture of XII[11] (0·32 g, 1·00 mmole), X (0·35 g, 1·00 mmole), $MeNO_2$ (10 ml) and $HgBr_2$ (0·03 mmole) was allowed to react for 3 hr. Chromatography on silica gel ($CCl_4 \rightarrow CHCl_3$) followed by crystallization from EtOH yielded XIII (0·26 g, 45%), m.p. 169–171°, $[\alpha]_D$ −30·8° (*c* 2·0, $CHCl_3$). Lit.[41]: m.p. 168–169°, $[\alpha]_D$ −29·66° ($CHCl_3$). (Found: C, 50·64; H, 5·95. Calc. for $C_{28}H_{36}O_{17}$: C, 50·33; H, 5·85%.) System A.

33. 1,2,3,4-*Tetra*-O-*acetyl*-6-O-(2,3,4-*tri*-O-*acetyl*-α-L-*arabinopyranosyl*)-β-D-*glucopyranose* (XV)

A mixture of XIV (0·45 g, 1·50 mmoles), X (0·35 g, 1·00 mmole), $MeNO_2$ (10 ml) and $HgBr_2$ (0·05 mmoles) was allowed to react for 2·5 hr. The resulting mixture was benzoylated with BzCl (0·5 ml) in pyridine (5 ml) at 20° for 30 min and XV isolated by chromatography on silica gel (benzene–pet. ether 1:1 → benzene → benzene–ether 95:5), yield 0·33 g (54·5%). After crystallization from ether–pet. ether and MeOH (−78°) XV had m.p. 88–90°/158·5–160·5°, $[\alpha]_D$ +15° (*c* 2·03, $CHCl_3$). Lit.[42,43]: m.p. 158–160°, $[\alpha]_D$ +9·4° ($CHCl_3$). (Found: C, 49·65; H, 5·68. Calc. for $C_{28}H_{34}O_{17}$: C, 49·50; H, 5·65%.) System A.

34. 1,2,3,4-*Tetra*-O-*acetyl*-6-O-(2,3,6,2′,3′,4′,6′ *hepta*-O-*acetyl*-β-*maltosyl*)-β-D-*glucopyranose* (XVII)

Compound XVI[44] (0·97 g, 1·50 mmoles), X (0·35 g, 1·00 mmole), $MeNO_2$ (5 ml) and $HgBr_2$ (0·03 mmole); reacted for 2·5 hr. Crystallization from $CHCl_3$–EtOH, yielded XVII (0·53 g, 55%) which after crystallization from EtOH had m.p. 241°, $[\alpha]_D$ +42° (*c* 1·0, $CHCl_3$). Lit.[45]: m.p. 242·7°, $[\alpha]_D$ +42·5° ($CHCl_3$). (Found: C, 49·52; H, 5·66. Calc. for $C_{40}H_{54}O_{27}$: C, 49·07; H, 5·63%.) System D.

35. 1,2,3,4-*Tetra*-O-*acetyl*-6-O-(2,3,4-*tri*-O-*benzoyl*-α-L-*arabinopyranosyl*)-β-D-*glucopyranose* (XIX)

Compound XVIIIa (see 6; 0·98 g, 2·06 mmoles), X (0·35 g, 1·00 mmole), $MeNO_2$ (10 ml) and $HgBr_2$ (0·05 mmole); reacted for 2·5 hr. Chromatography on silica gel as in 33 gave XIX contaminated with products of degradation of XVIII (R_f 0·0), which was benzoylated as in 33 and then chromatographed under similar conditions to yield pure XIX (0·74 g, 93%). Crystallization by rapid dilution of a benzene solution of XIX with a large volume of pet. ether yielded finely crystalline XIX, m.p. 93–95°, $[\alpha]_D$ +121° (*c* 2·22, $CHCl_3$). (Found: C, 61·09; H, 4·98. $C_{66}H_{48}O_{17}$ requires: C, 60·60; H, 5·09%.) System A.

6-O-(α-L-*Arabinopyranosyl*)-D-*glucose* (*vicianose*) (XLI). Compound XIX (0·52 g) was saponified with 0·1N MeONa (10 ml) at 20°, for 4 hr. After two crystallizations from glacial AcOH, the disaccharide had no definite m.p. (~100–190°), $[\alpha]_D$ +50° (*c* 0·3; equil., H_2O), R_Q 0·50. Lit.[46]: m.p. 210°, $[\alpha]_D$ +39·7° (equil., H_2O). (Found: C, 41·18; H, 6·36. Calc. for $C_{11}H_{20}O_{10} \cdot \frac{1}{2}H_2O$: C, 41·11; H, 6·59%.) System G.

36. 1,2-O-*Isopropylidene*-3,6-*di*-O-*acetyl*-5-O-(2,3,4,6-*tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-α-D-*glucofuranose* (XXI)

Compound II (0·70 g, 1·86 mmoles), XX[24] (0·40 g, 1·31 mmoles), $MeNO_2$ (5 ml) and $HgBr_2$ (0·093 mmole); reacted for 2·5 hr. Chromatography on alumina followed by crystallization from MeOH and Et_2O yielded XXI (0·08 g, 10%), m.p. 170°, $[\alpha]_D$ −26·3° (*c* 0·42, $CHCl_3$). Lit.[26]: m.p. 173°, $[\alpha]_D$ −28° ($CHCl_3$). (Found: C, 51·34; H, 6·11. Calc. for $C_{27}H_{36}O_{17}$: C, 51·10; H, 6·04%.) System A.

37. *Methyl* 2-O-(2,3,4,6-*tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-4,6-O-*benzylidene*-α-D-*glucopyranoside* (XXIII)

Compound II (2·00 g, 5·32 mmoles), XXII (1·19 g, 4·22 mmoles), $MeNO_2$ (25 ml) and $HgBr_2$ (0·134 mmole); reacted for 3·5 hr. Crystallization from ethylcellosolve yielded XXIII (0·54 g, 21%). After recrystallization, XXIII had m.p. 221–224°, $[\alpha]_D$ +45° (*c* 1·3, $CHCl_3$). There was no depression

[41] G. Zemplen and A. Gerecs, *Ber. Dtsch. Chem. Ges.* **67**, 2049 (1934).
[42] B. Helferich and H. Rauch, *Liebigs Ann.* **455**, 168 (1927).
[43] C. M. McCloskey and G. H. Coleman, *J. Amer. Chem. Soc.* **65**, 1778 (1943).
[44] W. Koritnic and J. A. Mills, *J. Chem. Soc.* 636 (1959).
[45] S. H. Nichols, W. L. Evans and H. D. McDowell, *J. Amer. Chem. Soc.* **62**, 1754 (1940).

of m.p. on admixture with an authentic sample; both substances being identical chromatographically. Lit.[46]: m.p. 232°, $[\alpha]_D$ +47° ($CHCl_3$);[47] m.p. 227–228°, $[\alpha]_D$ +42·4° ($CHCl_3$).

In the mother liquor a considerable amount of XXIII (R_f 0·41) and a substance with R_f 0·18 (XXIV) were observed, System D.

38. *Methyl* 2-O-*acetyl*-3-O-(2,3,4,6-*tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-4,6-O-*benzylidene*-α-D-*glucopyranoside* (XXVI)

(a) Amorphous XXIV (R_f 0·18, system D) present in the foregoing mother liquor (37) was isolated by chromatography on alumina, yield XXIV, 0·18 g (7%). This was acetylated with Ac_2O (0·7 ml) in pyridine (1·0 ml) at 20° for 48 hr and the reaction mixture evaporated with benzene. Crystallization of the residue from benzene–pet. ether yielded XXVI (0·11 g), which after recrystallization had m.p. 164·5–166·5°, $[\alpha]_D$ +22° (*c* 1·36, $CHCl_3$). (Found: C, 55·04; H, 6·18. $C_{36}H_{44}O_{16}$ requires: C, 55·04; H, 5·85%.) System C.

(b) Compound II (0·85 g, 2·26 mmoles), XXV[48] (0·50 g, 1·51 mmoles), $MeNO_2$ (10 ml) and $HgBr_2$ (0·045 mmole); reacted for 3 hr. Chromatography on alumina followed by crystallization from benzene–pet. ether yielded XXVI (0·28 g, 28%). After recrystallization, XXVI had m.p. 168–170°, $[\alpha]_D$ +22·5° (*c* 1·34, $CHCl_3$). A mixture of XXVI with the compound obtained in 38(a) showed no depression of m.p.; the both substances are identical chromatographically, System C.

Methyl 2,4,6,2′,3′,4′,6′-*hepta*-O-*acetyl*-α-*laminaribioside* (XLII). A solution of XXVI (0·28 g, 0·43 mmole) in 60% AcOHaq (10 ml) was heated at 80° for 15 min and then evaporated. The residue obtained was acetylated with Ac_2O (3 ml) in pyridine (5 ml). After 48 hr at 20°, the mixture was poured onto ice, extracted with $CHCl_3$ and the extract, after usual treatment evaporated. Crystallization of the dry residue from Et_2O–pet. ether yielded XLII (0·22 g, 79%), which after recrystallization had m.p. 189–192°, $[\alpha]_D$ +39° (*c* 2·18, $CHCl_3$). (Found: C, 50·08; H, 6·06. $C_{37}H_{44}O_{18}$ requires: C, 49·84; H, 5·89%.) System C.

Methyl α-*laminaribioside* (XLIII). Compound XLII (0·17 g, 0·265 mmole) was saponified with 0·1N MeONa (10 ml, 20°, 3 hr). Neutralization with a cation-exchanger followed evaporation and crystallization of the residue from EtOH–Me_2CO–Et_2O yielded XLIII, m.p. 177–179°, $[\alpha]_D$ +85° (*c* 1·37, H_2O), System G.

Periodate oxidation of XLIII. Compound XLIII (10 mg, 0·027 mmole) was treated with $NaIO_4$ (0·5 mmole) in acetate buffer (0·75 ml, pH 4·6) at 20° for 20 hr in the dark. After demineralization, half of the solution was evaporated, the residue treated with 0·1N H_2SO_4 (100°, 1 hr), then neutralized with $BaCO_3$, treated with $NaBH_4$ (20 mg) in 1 ml of 80% MeOHaq (20°, 24 hr) and demineralized. Methyl α-D-glucopyranoside, glycerol and ethylene glycol were identified in the solution obtained by paper chromatography. The second half of the solution obtained after oxidation of XLIII was evaporated, the residue hydrolysed with 2N H_2SO_4 (100°, 2 hr) and neutralized with $BaCO_3$. Glucose was identified in the hydrolysate by paper chromatography, System G.

39. 1,2,5,6-*Tetra*-O-*benzoyl*-3-O-(2,3,5,6-*tetra*-O-*acetyl*-β-D-*galactofuranosyl*)-D-*mannitol* (XXIX)

Compound XXVII (1·81 g, 5·00 mmoles), XXVIII[49] (2·00 g, 4·00 mmoles), $MeNO_2$ (20 ml) and $HgBr_2$ (0·2 mmole); reacted for 3·5 hr (with heating under reflux during the last 1·5 hr). Crystallization from $CHCl_3$ (10 ml)–Et_2O (90 ml)–pet. ether (40 ml) yielded XXIX (1·05 g, 28·3%), m.p. 159–162°, $[\alpha]_D$ −36° (*c* 2·0, $CHCl_3$). (Found: C, 62·26; H, 5·27. $C_{46}H_{48}O_{19}$ requires: C, 62·07; H, 5·21%.) System C.

3-O-(β-D-*Galactofuranosyl*)-D-*mannitol* (XXX). Compound XXIX (0·27 g) in $CHCl_3$ (10 ml) was treated with 10% Et_3N in abs MeOH at 37° for 5hr. The residue obtained after evaporation was then treated with 10% Et_3N in abs MeOH (20 ml) at 37° for 13 hr, the solution evaporated and the carefully dried residue crystallized from EtOH–Me_2CO–Et_2O, yielding XXX (0·10 g, 100%). After recrystallization, XXX had m.p. 158·5–159°, $[\alpha]_D$ 60° (*c* 1·86, H_2O). A mixture of XXX with the natural compound showed no depression of m.p. and both substances were identical by chromatographic behaviour and IR spectra. Lit.[37]: m.p. 161–163°, $[\alpha]_D$ −64° (H_2O). (Found: C, 41·66; H, 7·15. Calc. for $C_{12}H_{24}O_{11}$: C, 41·85; H, 7·03%.) System F.

[46] K. Freudenberg, H. Toepffer and C. C. Anderson, *Ber. Dtsch. Chem. Ges.* **61**, 1750 (1928).
[47] B. Coxon and H. G. Fletcher Jr., *J. Org. Chem.* **26**, 2892 (1961).
[48] R. W. Jeanloz and D. A. Jeanloz, *J. Amer. Chem. Soc.* **79**, 2579 (1957).
[49] E. Fischer, *Ber. Dtsch. Chem. Ges.* **48**, 266 (1915).

40. 1,2,3,4-*Tetra*-O-*acetyl*-6-O-(2,3,5-*tri*-O-*benzoyl*-α-L-*arabinofuranosyl*)-β-D-*glucopyranose* (XXXII)

A crude sample of XXXIa (see 7; 0·95 g, 2·00 mmoles), X (0·35 g, 1·00 mmole), $MeNO_2$ (10 ml) and $HgBr_2$ (0·05 mmole); reacted for 2·5 hr. Isolation according to the procedure described in 35 yielded XXXII (0·71 g, 90%), which was dissolved in toluene (8 ml) and rapidly precipitated with pet. ether (100 ml). A finely crystalline XXXII was obtained (0·58 g) m.p. 72–75°, $[\alpha]_D$ +23° (*c* 1·87, $CHCl_3$). (Found: C, 60·87, H, 4·90. $C_{40}H_{40}O_{17}$ requires: C, 60·60; H, 5·09%.) System A.

6-O-(α-L-*Arabinofuranosyl*)-D-*glucose* (XLIV). Compound XXXII (0·40 g) was saponified with 0·1N MeONa (10 ml) at 20° for 3 hr. Precipitation of the reaction product with Et_2O from EtOH yielded amorphous XLIV (0·16 g, 100%) which after crystallization from MeOH–EtOAc yielded finely crystalline XLIV, m.p. 153–155°, $[\alpha]_D$ −37° (*c* 1·4; equil., H_2O), R_G 1·16. Lit.[50]: m.p. 163–165°, $[\alpha]_D$ −40° (equil., H_2O), R_G 1·20. (Found: C, 42·41; H, 6·58. Calc. for $C_{11}H_{20}O_{10}$: C, 42·30; H, 6·46%.) System G.

41. O-(2,3,5,6-*Tetra*-O-*acetyl*-β-D-*galactofuranosyl*)-N-*benzyloxycarbonyl*-L-*serine methyl ester* (XXXIV)

Compound XXVII (2·30 g, 6·35 mmoles), XXXIII (2·00 g, 7·9 mmoles), $MeNO_2$ (20 ml) and $HgBr_2$ (0·4 mmole); reacted for 3·5 hr. The product was dissolved in $CHCl_3$ (10 ml) and Et_2O (30 ml) and pet. ether (100 ml) added with gentle heating. The mixture was set aside for several hr. The oil which separated (the mother liquor contained practically no XXXIV) was subjected to chromatography on alumina and yielded XXXIV (0·64 g, 17·3%) as a syrup, $[\alpha]_D$ −17·4° (*c* 1·12, $CHCl_3$). (Found: C, 53·49, H, 5·88, N, 2·62. $C_{26}H_{33}O_{14}N$ requires: C, 53·50, H, 5·69, N, 2·41%.) System A.

O-(β-D-*Galactofuranosyl*)-N-*benzyloxycarbonyl*-L-*serine methyl ester* (XXXV). Compound XXXIV (0·57 g) was saponified with 10% Et_3N in abs MeOH (5 ml) at 20° for 10 hr. Evaporation with MeOH until complete removal of Et_3N was followed by chromatography of the residue on silica gel yielding XXXV (0·31 g, 76%), as a syrup, $[\alpha]_D$ −37° (*c* 1·80, MeOH), System E.

O-(β-D-*Galactofuranosyl*)-L-*serine methyl ester* (XXXVI) (oxalate). Compound XXXV (235 mg) was hydrogenated in 70% MeOHaq (12 ml) in the presence of 5% Pd–$BaSO_4$ (100 mg) and $(COOH)_2$ (37·5 mg). After the completion of the reaction the catalyst was removed and the solution evaporated. The residue obtained was twice precipitated with Me_2CO from a minimal volume of MeOH. The amorphous oxalate of XXXVI was separated by centrifugation and washed with Et_2O, yield 130 mg (70%), $[\alpha]_D$ −57° (*c* 1·0, H_2O). (Found: C, 40·91; H, 6·33, N, 4·28. $C_{22}H_{40}O_{20}N_2$ requires: C, 40·45; H, 6·63; N, 4·29%.) System H.

Acknowledgement—The authors thank D.Sci. V. A. Derevitskaja and Miss M. G. Vafina for collaboration in the synthesis of O-(β-D-galactofuranosyl)-L-serine methyl ester and Mrs. L. B. Diomushkina for taking part in the synthesis of undecaacetate of 6-O-(β-maltosyl)-β-D-glucopyranose. The authors thank Prof. B. Lindberg (Stockholm) for a gift of natural 3-O-(β-D-galactofuranosyl)-D-mannitol.

[50] P. A. Gorin, *Canad. J. Chem.* **40**, 275 (1962).