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SYNTHESIS OF 2,3:4,6-DI-*O*-ISOPROPYLIDENE DERIVATIVES OF ALKYL α- AND β-D-GALACTOPYRANOSIDES, AND ELUCIDATION OF STRUCTURE BY N.M.R. AND X-RAY ANALYSIS

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ABSTRACT

Kinetically controlled reaction of 4.5 equiv. of 2-methoxypropene with some alkyl α- and β-D-galactopyranosides gave the 2,3:4,6-di-*O*-isopropylidene derivatives in high yields (80–85%). With 2 equiv. of 2-methoxypropene, benzyl β-D-galactopyranoside gave the 4,6- and the 3,4-monoacetals in the ratio 30:1 together with ~20% of the 2,3:4,6-diacetal. The structures of methyl 2,3:4,6-di-*O*-isopropylidene-α- and -β-D-galactopyranosides were determined by X-ray analysis. The former crystallised in the orthorhombic system, $P2_12_12_1$, with $a = 5.503$, $b = 16.105$, $c = 16.822$ Å, and $Z = 4$, the latter in the monoclinic system, $P2_1$, with $a = 10.400$, $b = 13.344$, $c = 11.647$ Å, $\beta = 111.50$, and $Z = 4$. The α anomer and the two molecules of the β anomer had the D-galactopyranoside and the 1,3-dioxane rings in twist-chair conformations and the dioxolane ring in a half-chair conformation. N.m.r. spectroscopy suggested the occurrence of similar conformations in solution.

INTRODUCTION

The reaction[1] of α- and β-D-galactopyranosides with 2,2-dimethoxypropane in the presence of catalytic amounts of toluene-*p*-sulfonic acid can give, under selected reaction conditions, high yields of 3,4-*O*-isopropylidene-6-*O*-(1-methoxy-1-methylethyl)-α- and -β-D-galactopyranosides (**1**). In order to elucidate the pathway of formation of **1**, authentic alkyl 2,3:4,6-di-*O*-isopropylidene-α- and -β-D-galactopyranoside derivatives were needed, as these are intermediates and/or by-products of the transacetalation reaction.

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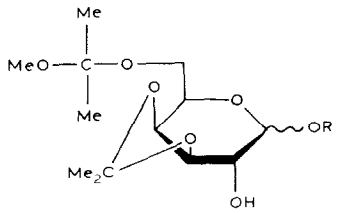

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Owing to the steric strain associated with *trans*-fused dioxolane and tetrahydropyran rings, compounds of this type are usually not formed in appreciable amounts under thermodynamically controlled conditions of acetonation[2]. Transacetalation with 2,2-dimethoxypropane gives high yields of these compounds only in selected reactions[2], *i.e.*, with some thiopyranoses[3]. In the *galacto* series, the sole reported examples of 2,3-*trans*-fused acetals are the methylene derivatives obtained[4] by reaction with dibromomethane and sodium hydroxide. In the earlier stages of the transacetalation of the galactopyranosides **2–4** with acidified 2,2-dimethoxypropane alone or with acetone, variable amounts of the 2,3:4,6 diacetals **6–8** were obtained[1], which were slowly transformed into **1**.

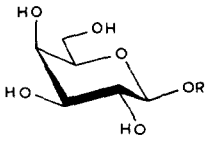
We now report a simple and efficient preparation of the 2,3:4,6-diacetals under kinetically controlled conditions[5] (2-methoxypropene in *N,N*-dimethylformamide and a trace of toluene-*p*-sulfonic acid) used for the preparation of the 2,3:4,6-di-*O*-isopropylidene derivatives of methyl α- and β-D-glucopyranoside. ^{1}H- and ^{13}C-n.m.r. studies and X-ray analysis of **6** and **8** are also reported.

RESULTS AND DISCUSSION

The diacetonation of the β- (**2** and **3**) and α-D-galactopyranosides (**4** and **5**) was carried out by a slight modification of the one-stage procedure described by Gelas and Horton[6], using 4.5 equiv.* of 2-methoxypropene and a catalytic amount of toluene-*p*-sulfonic acid at room temperature with rigorous exclusion of moisture. The reactions were rapid (~15 min) and slightly exothermic, and t.l.c. revealed the almost complete formation of the 2,3:4,6-diacetals with negligible amounts of unidentified by-products.

The high (>80% after chromatography) yields of 2,3:4,6-di-*O*-isopropylidene derivatives can be attributed to a selective reaction of HO-6, leading almost exclusively to the 4,6-monoacetal through the 6-*O*-(1-methoxy-1-methylethyl) derivative **10**. This interpretation agrees well with previous results[5,6] on the reactions of aldoses and aldosides with 2-methoxypropene, but not completely with the result of the reaction of D-galactose that gave[7] 67% of the 4,6- and 14% of the 3,4-*O*-isopropylidene derivative. In order to validate the selective monoacetonation of

*Two equiv. of 2-methoxypropene are needed for each cyclic acetal unit, since one of them is needed for trapping the MeOH liberated in the cyclisation step.



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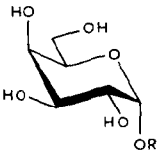
3 R = Bn



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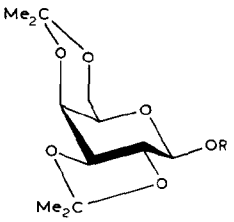
5 R = Allyl



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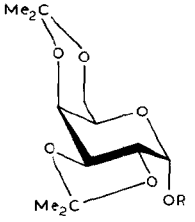
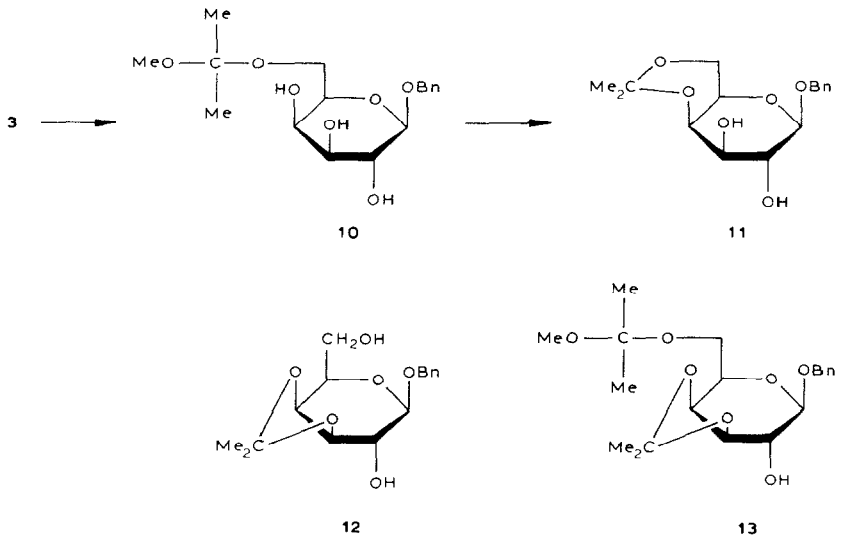


8 R = Me
9 R = Allyl

galactopyranosides, benzyl β-D-galactopyranoside (**3**) in *N,N*-dimethylformamide containing a trace of toluene-*p*-sulfonic acid was treated with 2 equiv. of 2-methoxypropene at room temperature, conditions under which methyl α- and β-D-glucopyranoside gave 90 and 75%, respectively, of the 4,6-*O*-isopropylidene derivatives[6]. H.p.l.c. of the products showed that selectivity of the monoacetalation was high, the ratio of 4,6- (**11**) and 3,4-acetonide (**12**) being 30:1, but ~20% each of the 2,3:4,6-diacetal **7** and unreacted **3** were also present. When the reaction was performed at 0°, the product distribution remained about the same. In contrast to the methyl glucopyranosides[6], monoacetonation with 2-methoxypropene is not a good preparative method for 4,6-*O*-isopropylidene-β-D-galactopyranosides, which are better obtained by transacetalation with 2,2-dimethoxypropane in *N,N*-dimethylformamide[8].

The difference in behaviour of the gluco- and galacto-pyranoside derivatives probably reflects the greater stability of the *trans*-fused tetrahydropyrano[3,2-*d*]-1,3-dioxane system (a *trans*-decalin analogue) in the former compared to that of the *cis* structure in the latter. This could result in a higher rate of reaction in the glucose series, whereas the subsequent acetal ring closure involving HO-2 and HO-3 would probably not be dependent on the configuration at C-4. Other factors can play some role, for instance, there are examples in which the presence of a cyclic acetal causes unpredictable changes in the relative reactivities of the remaining hydroxyl groups. Thus, in the benzylation of methyl 3,4-*O*-isopropylidene-β-D-galactopyranoside, HO-2 was found[9] to be 11 times more reactive than HO-6.

The ^{1}H- and ^{13}C-n.m.r. data for **6–9** substantiated their tricyclic structures. The ^{13}C resonances of the isopropylidene methyl groups clearly indicated the pre-



sence of both 1,3-dioxane and 1,3-dioxolane rings. The data in Table I agreed with Buchanan's conclusions[10], *i.e.*, the 1,3-dioxane system gave a signal for the acetal carbon at δ ~98 and two methyl signals at δ ~29 (equatorial) and ~18 (axial), whereas, in the dioxolane system, the former resonates at δ ~110 and both the latter at δ ~26. These values compared well with those reported for the analogous glucopyranosides[6], and further confirmed the generality of Buchanan's rules[10]. Nevertheless, caution is necessary in assigning the stereochemistry at the junction of the dioxolane system. Indeed, our data indicated the impossibility of defining two separate ranges for *cis*- and *trans*-fused junctions.

The signals of the galactopyranoside carbons, assigned on the basis of well-known additivity rules[11], are collected in Table II; the contributions to the chemical shift caused by the 2,3- and 4,6-acetal groups are similar for both methyl α- and β-galactopyranosides (Table II, values in parentheses).

The ^{1}H-n.m.r. spectra (80 MHz) were completely assigned (Tables III and IV) through double-resonance experiments and/or change of solvent from $CDCl_3$ to C_6D_6 followed by treatment of the spectra as first-order systems, where possible, or with the aid of a computer program. The change of solvent had little effect on the vicinal coupling constants for **6–9**, but the chemical shifts were affected markedly (Table III) as expected. A point of particular interest concerns H-2, the sole galactopyranosidic proton strongly deshielded ($\Delta\delta$ ~0.3 p.p.m.) in C_6D_6 both in the α- and β-series. Only one (unidentified) acetal methyl group signal is affected by the change of solvent, being shifted upfield ($\Delta\delta$ ~0.3 p.p.m.) in C_6D_6. These observations suggest the interaction of **6–9** with one of the solvents used.

The J values for the galactopyranosidic protons (Table IV) are characteristic of a $^4C_1$ conformation and the $J_{5,6}$ values suggest a chair-like conformation also for the 1,3-dioxane ring. The torsion angles between vicinal protons calculated with

TABLE I

^{13}C-N.M.R. CHEMICAL SHIFT DATA (δ, P.P.M.) FOR ISOPROPYLIDENE CARBON ATOMS OF 2,3:4,6-DI-*O*-ISOPROPYLIDENE-D-GALACTOPYRANOSIDES

Compound	*1,3-dioxane ring*		*1,3-dioxolane ring*	
	C-2	*C-24 and C-25*	*C-2*	*C-47 and C-48*
6	98.2	28.8, 18.3	110.7	26.3, 26.1
7	98.3	28.8, 18.9	110.6	26.4, 26.2
8	98.1	29.0, 18.2	109.9	26.3, 26.3
9	98.2	29.0, 18.2	110.0	26.4, 26.4

Altona's modification[12] of the Karplus equation (Table V) supported such a hypothesis, although some deviations from the ideal chair conformations of the six-membered rings are evident, mainly around the bonds engaged in the two ring fusions.

The structures of **6** (Fig. 1) and **8** (Fig. 2) have been determined by X-ray analysis*. The torsional angles in Table VI allow the assignment of a twist-chair conformation to the D-galactopyranoside and the 1,3-dioxane rings, and a half-chair conformation to the dioxolane ring.

The degree to which rings deviate from the ideal symmetry is given in terms of the asymmetry parameters[13] ΔC_S and ΔC_2. For the β-D-galactopyranoside moiety in molecule **A**, these values give, as the most relevant symmetry, a mirror plane through C-2,C-5 (ΔC_S 5.0°) and in molecule **B**, a mirror plane through C-1,C-4 (ΔC_S 1.9°). The α-D-galactopyranoside ring exhibits a mirror plane through C-2,C-5

TABLE II

^{13}C-N.M.R. CHEMICAL SHIFT DATA (δ, P.P.M.) FOR GALACTOPYRANOSIDIC CARBON ATOMS OF 2,3:4,6-DI-*O*-ISOPROPYLIDENE-D-GALACTOPYRANOSIDES[a]

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
6	102.8	72.4	77.8	65.0[b]	67.0[b]	62.5
	(−1.7)	(+0.7)	(+4.0)	(−4.7)	(−9.0)	(+0.5)
7	100.8	72.5	77.9	66.0[b]	67.2[b]	62.6
8	98.9	71.0	72.5	67.1	62.7	62.5
	(−1.2)	(+1.8)	(+2.0)	(−3.1)	(−8.9)	(+0.3)
9	97.2	71.0	72.5	67.2	62.8	62.8

[a]Values in parentheses are obtained as differences between the chemical shifts of the carbon atoms of the diacetal derivative and those of the corresponding[11b] unsubstituted galactopyranoside. [b]Assignments can be reversed.

*The vibrational parameters β_{ij} of the heavy atoms, the co-ordinates and B_{iso} values of the H atoms, Tables of bond lengths and valence angles, and a list of F_o and F_c structure factors are deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/391 *Carbohydr. Res.*, 177 (1988) 29–41.

TABLE III

^{1}H-N.M.R. CHEMICAL SHIFT DATA (δ, P.P.M.) FOR 2,3:4,6-DI-*O*-ISOPROPYLIDENE-D-GALACTOPYRANOSIDES

Compound	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	*Acetal methyls*
6 ($CDCl_3$)	4.53	3.98	3.53	4.43	3.33	4.00	4.16	1.48, 1.47, 1.46, 1.46
(C_6D_6)	4.35	4.31	3.24	3.93	2.58	3.82	3.58	1.42, 1.42, 1.41, 1.13
7 ($CDCl_3$)	4.68	4.05	3.50	4.42	3.31	4.02	4.12	1.56, 1.48, 1.48, 1.46
(C_6D_6)	4.59	4.39	3.25	3.94	2.59	3.85	3.61	1.42, 1.42, 1.42, 1.16
8 ($CDCl_3$)	5.18	4.16	4.05	4.50	3.43	3.94	4.20	1.51, 1.47, 1.47, 1.47
(C_6D_6)	5.04	4.45	4.12	4.07	2.89	3.78	3.57	1.49, 1.47, 1.47, 1.16
9 ($CDCl_3$)	5.30	4.13	4.12	4.51	3.58	3.89	4.17	1.65, 1.48, 1.48, 1.48
(C_6D_6)	5.23	4.43	4.14	4.10	2.98	3.78	3.58	1.46, 1.46, 1.46, 1.17

(ΔC_S 3.9°). It follows that the dioxolane ring in each of the molecules of the β anomer shows a two-fold axis passing through C-2–C-3 and C-23 [ΔC_2 4.1° (**A**) and 5.7° (**B**)]. A similar situation exists in **8**, but with a larger deviation from the ideal symmetry (ΔC_2 7.5°). The 1,3-dioxane ring in molecule **A** of the β anomer exhibits a mirror plane through C-5,C-46 (ΔC_S 2.2°) and in molecule **B** a mirror plane through C-6,O-4 (ΔC_S 1.4°). In the α anomer, the 1,3-dioxane moiety exhibits a mirror plane through C-5,C-46 (ΔC_S 4.0°).

Each of the molecular structures of **6** and **8** show, for the first time in the D-galactopyranoside series, a 2,3-acetal possessing a *trans*-fused dioxolane system (this structure has been reported in 2,3:4,6-di-*O*-isopropylidene-5-thio-α-D-gluco-pyranose[3a]). The 4,6-acetal shows, as expected, a *cis*-fused 1,3-dioxanic system.

The *trans*-fused dioxolane ring forces the exocyclic angle O-2–C-2–C-3–O-3 to be <60° and induces an opposite effect on the endocyclic angle C-1–C-2–C-3–C-4 and makes it the largest endocyclic angle. The *cis*-fused dioxane ring induces a closing effect on both the exocyclic O-4–C-4–C-5–C-6 and endocyclic C-3–C-4–C-5–O-5 torsion angles, and the latter has the smallest endocyclic value.

The values of the torsion angles (Table V) for the D-galactopyranoside ring have been derived from the $^3J_{H,H}$ values using the equation proposed by Altona[12]. With the exception of the torsion angle H-2–C-2–C-3–H-3, which defines the *trans*-fused junction, the others compare well with those found in the crystal and suggest

TABLE IV

^{1}H-N.M.R. COUPLING CONSTANTS (Hz) FOR 2,3:4,6-DI-*O*-ISOPROPYLIDENE-D-GALACTOPYRANOSIDES[a]

Compound	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	*Other*
6	7.7	9.5	2.6	1.4	1.8	2.3	12.9	
7	7.8	9.4	2.8	1.5	1.8	2.5	12.7	
8	3.0	9.8	3.2	~2.0	1.6	2.2	12.6	$J_{1,4}$ 0.6
9	2.9	9.8	2.8	~1.0	1.7	2.3	12.8	$J_{1,4}$ 0.5

[a]In $CDCl_3$; the *J* values in C_6D_6 are similar, the differences being of the same order as the experimental error (<0.1 Hz).

TABLE V

TORSION ANGLES (°) BETWEEN GALACTOPYRANOSIDIC VICINAL PROTONS OF COMPOUNDS **6** AND **8**

	6			**8**	
	^{1}H-N.m.r.	*X-Ray*		*^{1}H-N.m.r.*	*X-Ray*
		Molec. **A**	*Molec.* **B**		
H-1–C-1–C-2–H-2	173	173	172	59	60
H-2–C-2–C-3–H-3	150	167	166	153	162
H-3–C-3–C-4–H-4	58	60	51	53	51
H-4–C-4–C-5–H-5	−53	−52	−59	−48	−50
H-5–C-5–C-6–H-6*a*	46	45	47	47	46
H-5–C-5–C-6–H-6*e*	−74	−74	−72	−78	−73

that **6** and **8** adopt similar conformations in both the solid state and in solution.

Both **6** and **8** have bowl-like shapes, with most hydrogen atoms and methyl groups protruding from the convex face. The only exceptions are H-2 and C-24 which lie in the cavity, surrounded by oxygen lone-pairs. This geometrical feature may explain the above-mentioned "solvent effect" in the ^{1}H chemical shift.

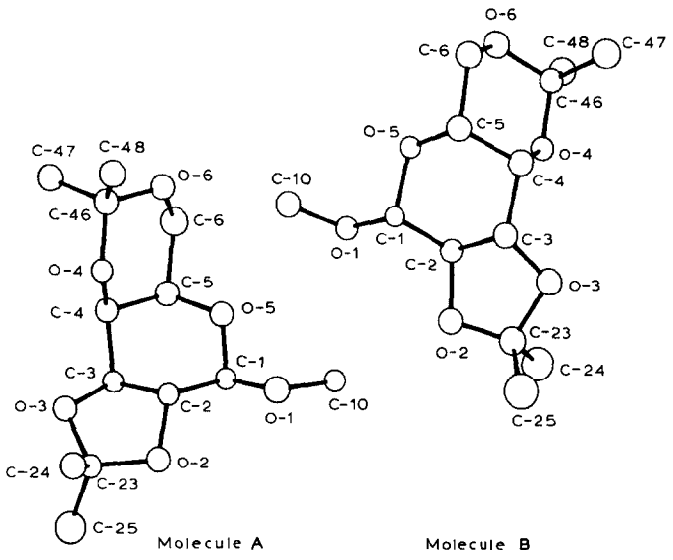


Fig. 1. Molecular conformation and mutual orientation of the two independent molecules of **6**

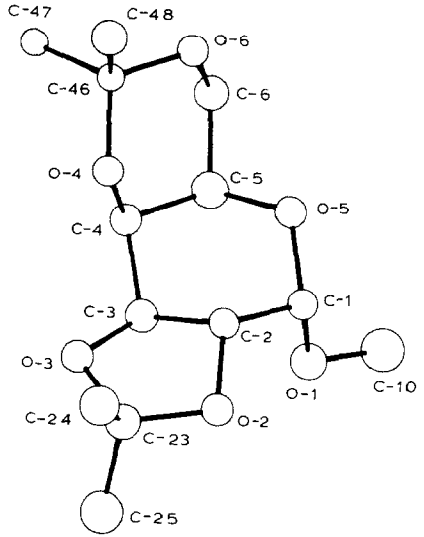


Fig. 2. Molecular conformation of **8**.

TABLE VI

TORSION ANGLES (°) FOR COMPOUNDS **6** AND **8**[a]

	6		**8**
	Molec. **A**	*Molec.* **B**	
D-*Galactopyranoside*			
C-1–C-2–C-3–C-4	−69(1)	−65(1)	−67.3(9)
C-2–C-3–C-4–C-5	62(1)	55(1)	56.5(9)
C-3–C-4–C-5–O-5	−52(1)	−54(1)	−49(1)
C-4–C-5–O-5–C-1	59(1)	62(1)	53(1)
C-5–O-5–C-1–C-2	−63(1)	−63(1)	−57.0(9)
O-5–C-1–C-2–C-3	64(1)	64(1)	62(1)
1,3-Dioxolane			
C-2–O-2–C-23–O-3	13(1)	19(2)	17.0(9)
O-2–C-23–O-3–C-3	18(1)	12(2)	9.1(9)
C-23–O-3–C-3–C-2	−40(1)	−36(1)	−30.4(8)
O-3–C-3–C-2–O-2	47(1)	47(1)	40.9(7)
C-3–C-2–O-2–C-23	−37(1)	−40(1)	−35.4(8)
1,3-Dioxane			
C-4–O-4–C-46–O-6	−58(1)	−56(1)	−54.6(9)
O-4–C-46–O-6–C-6	55(2)	52(1)	57.5(8)
C-46–O-6–C-6–C-5	−52(1)	−51(1)	−56.2(9)
O-6–C-6–C-5–C-4	48(1)	49(1)	48(1)
C-6–C-5–C-4–O-4	−49(1)	−51(1)	−46(1)
C-5–C-4–O-4–C-46	54(1)	57(1)	50.2(9)

[a]Values in parentheses are e.s.d.

TABLE VII

CRYSTAL DATA FOR COMPOUNDS **6** AND **8**

	6	**8**
Molecular formula	$C_{13}H_{22}O_6$	$C_{13}H_{22}O_6$
Molecular weight	274.31	274.31
Crystal system	Monoclinic	Orthorhombic
Space group	$P2_1$	$P2_12_12_1$
Cell dimensions		
a (Å)	10.400(11)	5.503(2)
b	13.344(4)	16.105(3)
c	11.647(7)	16.822(5)
β (°)	111.50(6)	
Cell volume (Å^3)	1503.9(1.8)	1490.9(7)
Z	4	4
F(000) (e$^-$)	592	592
μ(Cu-*K*α) (cm^{-1})	8.09	8.16
D (kg.m^{-3})	1.210	1.223
Crystal dimensions (mm)	0.4 × 0.2 × 0.1	0.3 × 0.2 × 0.2

EXPERIMENTAL

General. — Melting points (Kofler apparatus) are uncorrected. ^{1}H- (79.6 MHz) and ^{13}C-n.m.r. (20.0 MHz) were recorded with a Varian CFT-20 spectrometer in the stated solvents (internal Me_4Si). Optical rotations were determined at 20 ±2° with a Perkin–Elmer 241 polarimeter. Microanalyses were performed on a Carlo Erba Elemental Analyzer Model 1106. Analytical h.p.l.c. was performed on a Pye-Unicam 4002 instrument, using a Lichrosorb 10 RP-18 column (25 cm, Chrompack), monitoring at 200 nm, and elution at 1 mL/min with CH_3CN–H_2O 3:7 (1 min), 3-min gradient to 65:35, 10 min, 2-min gradient to 3:7; the relative retention times of **3, 11, 12, 13,** and **7** were 1.00:1.83:1.97:3.38:3.80. Analytical t.l.c. was carried out on Silica Gel 60 F_{264} (Merck) with detection by charring with 10% ethanolic phosphomolybdic acid. Column chromatography was performed on Kieselgel 60 (Merck, 70–230 mesh).

Commercial 2-methoxypropene was utilised immediately after distillation under argon. Benzyl β-D-galactopyranoside[14] (**3**) and allyl α-D-galactopyranoside[15] (**4**) were obtained by literature methods. Reference samples of **11–13** were obtained according to published procedures[1,14,16]

Diacetonation procedure. — 2-Methoxypropene (1.1 mL, 11.5 mmol) was added dropwise at room temperature under argon to a stirred solution of the predried (5–8 h at 50°/0.1 mmHg) D-galactopyranoside (**2–5**, 2.5 mmol) in anhydrous *N,N*-dimethylformamide (15 mL) containing toluene-*p*-sulfonic acid (40 mg). After 15 min, t.l.c. showed that the starting material had disappeared and there was a single faster-moving product with negligible by-products. After stirring for an additional 1 h, each mixture was treated with NEt_3 (0.5 mL) and concentrated *in vacuo*,

TABLE VIII

ATOMIC CO-ORDINATES AND ISOTROPIC THERMAL PARAMETERS FOR COMPOUNDS **6** AND **8**[a]

Atom	**6**								**8**			
	Molecule **A**				*Molecule* **B**							
	x	y	z	B(*eq*)[b]	x	y	z	B(*eq*)[b]	x	y	z	B(*eq*)[b]
C-1	0.476(1)	0.5671(9)	0.042(1)	4.8(4)	0.053(1)	0.282(1)	−0.059(1)	5.7(4)	0.282(2)	0.0307(5)	0.2289(5)	4.0(3)
C-2	0.534(1)	0.5949(9)	0.180(1)	5.0(4)	−0.040(1)	0.3253(9)	−0.181(1)	5.1(4)	0.372(2)	−0.0327(5)	0.2859(4)	3.6(2)
C-3	0.688(1)	0.5883(8)	0.219(1)	4.8(4)	−0.188(1)	0.291(1)	−0.210(1)	5.7(4)	0.597(2)	−0.0732(5)	0.2551(5)	3.0(2)
C-4	0.732(1)	0.482(1)	0.220(1)	5.1(4)	−0.198(1)	0.1779(9)	−0.228(1)	4.8(4)	0.538(2)	−0.1247(5)	0.1819(4)	4.1(2)
C-5	0.663(1)	0.446(1)	0.085(1)	5.1(4)	−0.090(1)	0.1339(9)	−0.108(1)	5.0(4)	0.418(2)	−0.0653(5)	0.1223(5)	4.4(2)
C-6	0.676(1)	0.337(1)	0.077(1)	5.6(4)	−0.077(1)	0.022(1)	−0.130(1)	5.6(4)	0.296(2)	−0.1136(5)	0.0594(4)	4.3(2)
O-1	0.3287(9)	0.5690(7)	0.0055(8)	5.5(3)	0.1893(9)	0.3115(8)	−0.0368(8)	6.7(3)	0.457(2)	0.0906(4)	0.2151(3)	5.9(2)
O-2	0.5174(9)	0.6976(6)	0.2091(7)	5.4(3)	−0.061(1)	0.4322(6)	−0.1802(7)	6.2(3)	0.444(1)	−0.0044(4)	0.3631(3)	4.9(2)
O-3	0.7293(9)	0.6369(7)	0.3391(8)	5.7(3)	−0.262(1)	0.3545(7)	−0.3090(8)	6.2(3)	0.685(1)	−0.1159(4)	0.3238(3)	4.7(2)
O-4	0.6875(8)	0.4218(6)	0.3002(6)	4.7(2)	−0.1664(9)	0.1526(7)	−0.3322(7)	5.5(3)	0.387(1)	−0.1905(3)	0.2061(3)	3.7(1)
O-5	0.5149(9)	0.4674(6)	0.0396(7)	5.5(3)	0.0464(8)	0.1750(6)	−0.0805(7)	5.2(2)	0.223(1)	−0.0160(3)	0.1577(3)	4.3(2)
O-6	0.638(1)	0.2821(7)	0.1687(8)	5.9(3)	−0.0576(9)	0.0022(7)	−0.2446(8)	5.8(3)	0.148(1)	−0.1782(3)	0.0910(3)	4.3(1)
C-10	0.259(1)	0.546(1)	−0.123(1)	5.9(4)	0.285(2)	0.285(1)	0.082(1)	7.4(5)	0.390(3)	0.1550(6)	0.1629(6)	6.9(4)
C-23	0.635(1)	0.7199(9)	0.323(1)	4.8(4)	−0.189(2)	0.450(1)	−0.280(1)	7.2(5)	0.610(2)	−0.0679(5)	0.3917(5)	4.7(2)
C-24	0.591(2)	0.721(1)	0.433(1)	6.0(5)	−0.168(2)	0.484(1)	−0.395(1)	8.7(7)	0.487(3)	−0.1266(6)	0.4472(7)	7.6(4)
C-25	0.702(2)	0.817(1)	0.303(2)	7.8(6)	−0.274(2)	0.523(1)	−0.239(2)	8.6(7)	0.818(2)	−0.0235(7)	0.4283(6)	6.5(3)
C-46	0.708(2)	0.318(1)	0.290(1)	5.9(4)	−0.156(1)	0.050(1)	−0.351(1)	5.4(4)	0.276(2)	−0.2341(5)	0.1416(4)	3.3(2)
C-47	0.855(2)	0.286(1)	0.341(2)	8.5(6)	−0.296(2)	−0.006(1)	−0.385(2)	7.0(6)	0.452(2)	−0.2857(5)	0.0954(5)	4.2(2)
C-48	0.628(2)	0.270(1)	0.363(1)	6.6(5)	−0.100(2)	0.034(1)	−0.450(1)	7.6(5)	0.083(2)	−0.2891(6)	0.1793(6)	5.4(3)

[a]Values in parentheses are e.s.d. [b]$B(\mathrm{eq}) = (4/3)^{*}\mathrm{SUM}(ij)[a(i)a(j)b(ij)]$.

and toluene (3 × 30 mL) was evaporated from the residue. Each crude product was added to a column of SiO_2 (100 g) and rapidly eluted with hexane–ethyl acetate (3:2) containing 0.1% of NEt_3, to give homogeneous (t.l.c., ^{1}H-n.m.r.) samples of the 2,3:4,6-di-*O*-isopropylidene derivatives **6–9** in yields of 80, 83, 84, and 82%, respectively. Analytical samples were obtained by crystallisation from hexane and/or sublimation.

The following compounds were prepared thus, for which the ^{1}H-n.m.r. data are recorded in Tables III and IV, and the ^{13}C-n.m.r. data in Tables I and II except those cited below.

Methyl 2,3:4,6-di-*O*-isopropylidene-β-D-galactopyranoside (**6**) had m.p. 105–107°, $[\alpha]_D$ −27° (*c* 1, chloroform); R_F 0.23 (hexane–ethyl acetate, 3:2). N.m.r. data ($CDCl_3$): ^{1}H, δ 3.67 (s, 3 H, OMe); ^{13}C, δ 56.3 (OMe).

Anal. Calc. for $C_{13}H_{22}O_6$: C, 56.9; H, 8.1. Found: C, 57.0; H, 8.0.

Benzyl 2,3:4,6-di-*O*-isopropylidene-β-D-galactopyranoside (**7**) had m.p. 128–130°, $[\alpha]_D$ −52° (*c* 1, chloroform); R_F 0.35. N.m.r. data ($CDCl_3$): ^{1}H, δ 7.25–7.39 (m, 5 H, Ph), 4.94 and 4.59 (2 d, 2 H, *J* 12.1 Hz, OCH_2Ph); ^{13}C, δ 69.7 (OCH_2Ph), 127.4, 127.7, 128.0 (tertiary aromatics), 136.4 (quaternary aromatic).

Anal. Calc. for $C_{19}H_{26}O_6$: C, 64.7; H, 6.9. Found: C, 65.1; H, 7.4.

Methyl 2,3:4,6-di-*O*-isopropylidene-α-D-galactopyranoside (**8**) had m.p. 72–73°, $[\alpha]_D$ +157° (*c* 1, chloroform); R_F 0.35. N.m.r. data ($CDCl_3$): ^{1}H, δ 3.46 (s, 3 H, OMe); ^{13}C, δ 55.4 (OMe).

Anal. Calc. for $C_{13}H_{22}O_6$: C, 56.9; H, 8.1. Found: C, 57.4; H, 8.2.

Allyl 2,3:4,6-di-*O*-isopropylidene-α-D-galactopyranoside (**9**) had m.p. 63–64°, $[\alpha]_D$ +143° (*c* 0.9, chloroform); R_F 0.49. N.m.r. data ($CDCl_3$): ^{1}H, δ 4.12 (m, 2 H, $OCH_2CH=CH_2$), 5.85 (m, 1 H, $OCH_2CH=CH_2$), 5.08 and 4.92 (m, 2 H, $OCH_2CH=CH_2$), *J* 17.3, 10.1, and 2.4 Hz; ^{13}C, δ 68.6 ($OCH_2CH=CH_2$), 116.9 ($OCH_2CH=CH_2$), 133.6 ($OCH_2CH=CH_2$).

Anal. Calc. for $C_{15}H_{24}O_6$: C, 60.0; H, 8.0. Found: C, 59.9; H, 7.8.

Monoacetonation of benzyl β-D-galactopyranoside (**3**). — To a stirred solution of **3** (57.3 mg, 0.21 mmol) in dry *N,N*-dimethylformamide (2 mL), containing toluene-*p*-sulfonic acid (2 mg), was added dropwise under argon a freshly prepared solution (2 mL, 0.42 mmol) of 2-methoxypropene (1 mL) in *N,N*-dimethylformamide (50 mL). The reaction was monitored by taking small amounts, adding one drop of NEt_3 and applying h.p.l.c. A constant composition was reached after 30 min and was 3:11:12:7 = 20:58:2:20.

X-Ray analysis. — Suitable single crystals of **6** and **8** were grown at 5° by slow concentration of solutions in hexane. The crystals were stable in air and at room temperature only for 2–3 days, due to the slow evaporation of the trapped hexane and therefore were sealed in Lindeman glass capillaries. The space group and approximate unit-cell parameters were determined from oscillation and Weissenberg photographs. The intensity data were measured at room temperature with a Syntex P 2_1 automatic diffractometer equipped with graphite monochromator, using Cu-$K\alpha$ radiation in the ϑ–2ϑ scan mode. Accurate unit-cell parameters were

determined by least-squares fit of the setting angles of 15 selected reflections. The crystal data are given in Table VII.

Three standard reflections measured every 100 revealed that the crystals of **6** and **8** underwent appreciable decay and X-ray damage during the data collections: 50% and 25% decrease of the intensities, respectively. Intensity data were corrected for the average change in the intensities of the reference reflections. Lorentz and polarisation corrections were applied, but no absorption corrections were made.

Data collection parameters for **6** were as follows: $\Delta\vartheta = 2.0° + 1.41 \tan\vartheta$, $(\sin\vartheta/\lambda)_{max} = 0.56$ Å^{-1}; scan speed, 1.50–29.3°/min according to the intensity. The intensity data were merged to give 2244 unique reflections, merging $R = 0.08$, of which 1776 $F_o \geq 1.0\sigma(F_o)$ were used in the subsequent calculations. For **8**, the experimental conditions were: $\Delta\vartheta = 1.6° + 1.41 \tan\vartheta$, $(\sin\vartheta/\lambda)_{max} = 0.56$ Å^{-1}; scan speed, 1.75–29.3°/min according to the intensity. The intensity data were merged to give 1317 unique reflections, merging $R = 0.04$, of which 979 $F_o \geq 1.0\sigma(F_o)$ were used in the subsequent calculations.

Structure determinations and refinements. — The structures were solved by direct methods using the Semi-Invariant-Representation package (S.I.R.)[17].

The *E*-syntheses, calculated with the phase sets having the best figure of merits, unambigously revealed 34, out of 38, of the heavy atoms belonging to the two independent molecules of **6** present in the crystal, and all the heavy atoms of the molecule belonging to **8**. The remaining atoms of the two independent molecules of **6** were obtained for standard Fourier procedures. The structures were then refined isotropically and anisotropically minimising the function $\Sigma w(|F_o| - |F_c|)^2$ where $w = (a + |F_o| + b|F_o|^2)^{-1}$. The parameters a and b were given values of $2F_{omin}$ and $2/F_{omax}$, respectively, in order to obtain $[\Sigma w(|F_o| - |F_c|^2)]$ nearly constant in the range of F_o and $(\sin\vartheta/\lambda)$.

The hydrogen atoms could not be located from difference Fourier syntheses because of the poor quality of the data. These were included in the later refinements in the geometrically calculated positions. The methyl groups were set up in the staggered conformation. In **6**, the hydrogen atoms were fixed positionally and isotropically with the B_{iso} values equal to those of the carrier atoms. In **8**, the hydrogen atoms were allowed to ride with the B_{iso} equal to those of the carrier atoms.

The refinements converged to $R = 0.102$, $R_w = 0.147$, and $R = 0.084$, $R_w = 0.132$ for **6** and **8**, respectively. At the convergence, the maximum shift-to-error ratios for the refined parameters were 0.45 and 0.12, respectively. Table VIII lists the positional parameters of the heavy atoms and B_{eq} values for **6** and **8**.

The atomic scattering factors were taken from the International Tables for X-Ray Crystallography[18].

The calculations were performed on a Data General Eclipse MV 8000 II, using the S.I.R.–C.A.O.S. crystallographic software[19].

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