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THE CHEMICAL-TRANSFORMATION PRODUCTS OF 1,6-DIBROMO-1,6-DIDEOXYGALACTITOL AND 1,2:5,6-DIANHYDROGALACTITOL IN AQUEOUS SOLUTION

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ABSTRACT

After hydrolysis of 1,6-dibromo-1,6-dideoxygalactitol (**1**) and 1,2:5,6-dianhydrogalactitol (**2**), 11 compounds were isolated, three of them as tritylated derivatives. Their structures were established on the basis of chemical evidence and, for four compounds, by X-ray diffraction. The main product of the hydrolysis of **1** was 3,6-anhydro-1-bromo-1-deoxy-DL-galactitol; the end-products of the hydrolysis of **2** were 1,5-anhydro-DL-galactitol, 2,5-anhydro-DL-altritol, and galactitol.

INTRODUCTION

1,6-Dibromo-1,6-dideoxygalactitol (**1**, Mitolactol) and 1,2:5,6-dianhydrogalactitol (**2**) are bifunctional alkylating agents having significant cytostatic activity[1,2]. Metabolism studies[3–6] of **1** and **2** indicate that, in addition to alkylation[9], the main reaction is that with water. We now report on the hydrolysis of **1** and **2** in neutral and weak alkaline solution.

RESULTS AND DISCUSSION

1,6-Dibromo-1,6-dideoxygalactitol (**1**) was transformed into 3,6-anhydro-1-bromo-1-deoxy-DL-galactitol (**3**) in water (at pH 6.5) and methanol. At reflux temperature, **1** completely decomposed in 20 min; at room temperature, ~5% decomposition occurred in 24 h. 1-Bromo-1-deoxy-DL-galactitol (**4**), which was a side-product of the synthesis of **1**, could not be detected in the reaction mixture.

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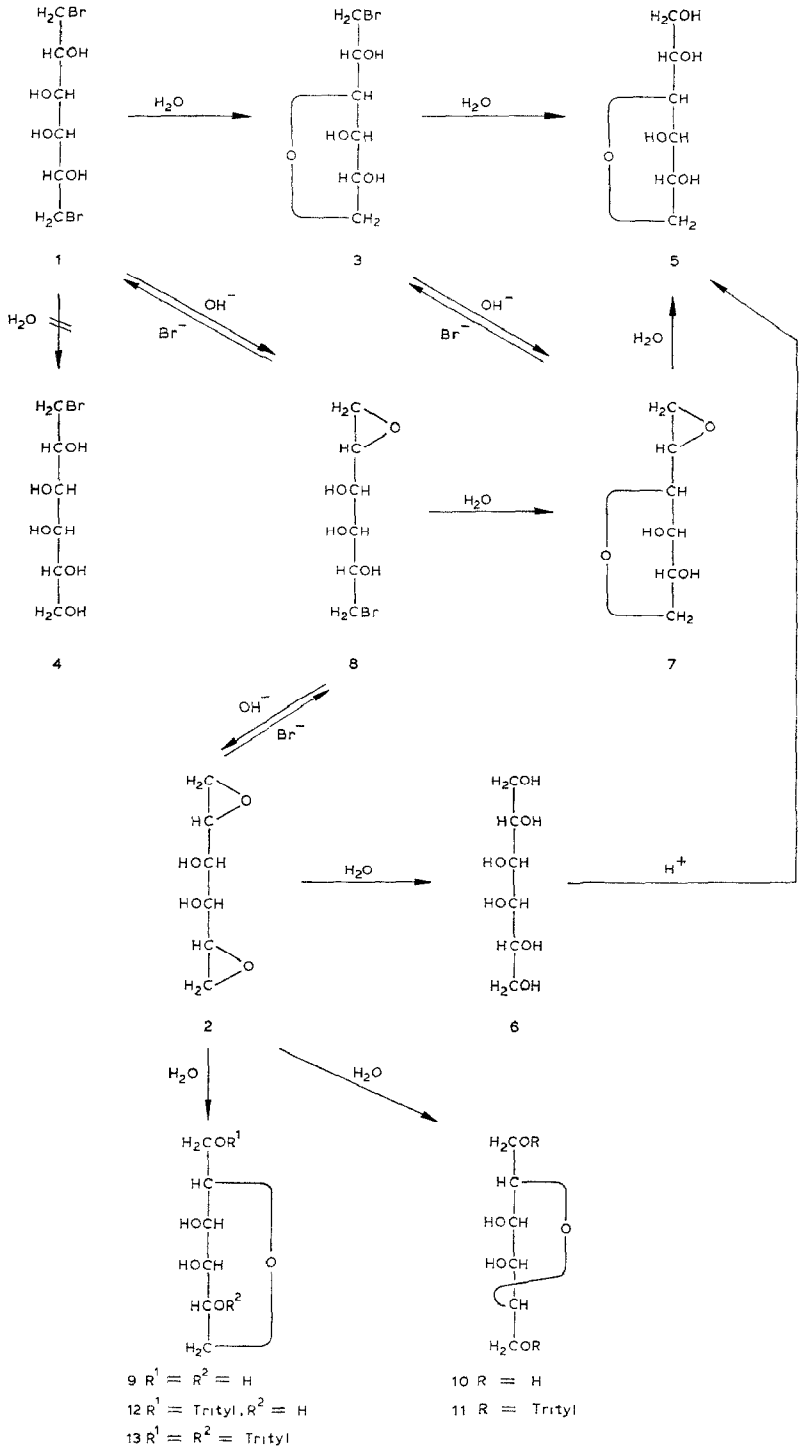
1
3
5
4
8
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2
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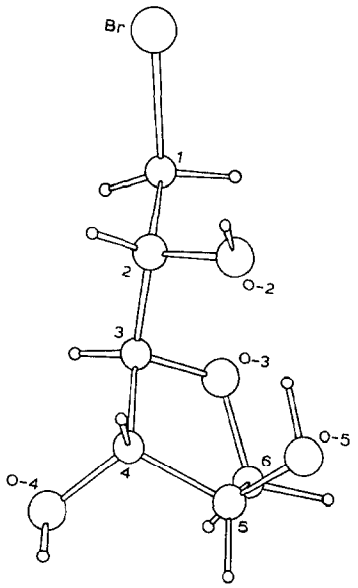
9 R¹ = R² = H
12 R¹ = Trityl, R² = H
13 R¹ = R² = Trityl
10 R = H
11 R = Trityl



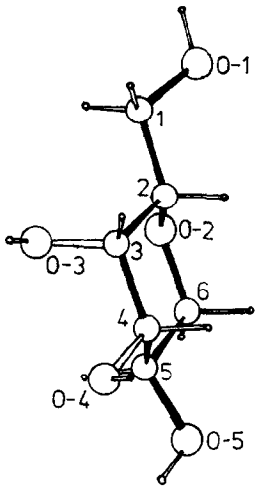


Fig. 1. Molecular diagram of compound **3**; the five-membered ring has a $^{6}T_{5}$ conformation, C-2 is isoclinical, O-4 is equatorial, and O-5 is axial.

Fig. 2. Molecular diagram of compound **9**; the six-membered ring adopts an almost ideal $^{O-2}C_{4}$ conformation, with C-1, O-4, and O-5 equatorial, and O-3 axial.

Hydrolysis of **3** gave 1,4-anhydro-DL-galactitol (**5**), which could also be obtained by acid-catalysed dehydration[7] of galactitol (**6**). The structure of **3** was established by X-ray analysis (Fig. 1).

Treatment of **3** with weak alkali (pH 7.5–8) gave 1,2:3,6-dianhydro-DL-galactitol (**7**) from which **3** was obtained by reaction with hydrogen bromide. Hydrolysis of **7** gave **5**.

Hydrolysis of **1** with weak alkali (pH 7.5–8) gave 1,2-anhydro-6-bromo-6-deoxy-DL-galactitol[3] (**8**). Further transformation of **8** in an alkaline medium afforded **2** and **7**. The absence of **4** and galactitol (**6**) as hydrolysis products indicated that the breaking of the C–Br bond was accompanied by an intramolecular elimination of hydrogen bromide.

In boiling, neutral, aqueous solution, the hydrolysis of 1,2:5,6-dianhydro-galactitol (**2**) was complete after 8 h. No alkylating agent then remained (t.l.c.). None of the hydrolysis products was equivalent to **5**, and fractional crystallisation of the product mixture gave galactitol (**6**) and 2,6-anhydro-DL-galactitol (1,5-anhydro-DL-galactitol; **9**). The structure of **9** was established by X-ray analysis (Fig. 2). Tritylation of the remaining products followed by column chromatography gave two detrityl derivatives (**11** and **13**) and one monotrityl derivative (**12**). The structure of **12** was indicated when detritylation gave **9**. X-Ray analyses indicated **11** to be 2,5-anhydro-1,6-di-*O*-trityl-DL-altritol (Fig. 3), and **13** to be 2,6-anhydro-1,5-di-*O*-trityl-DL-galactitol (Fig. 4). Detritylation of **13** gave **9**.

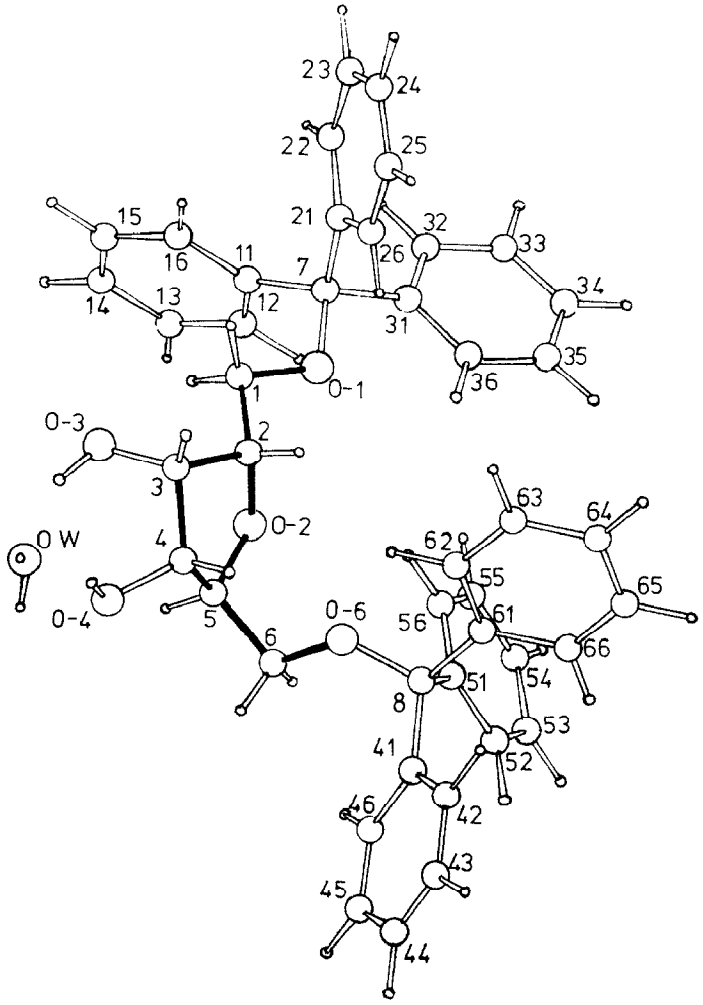


Fig. 3. Molecular diagram of compound **11**; the five-membered ring assumes the ^3E conformation, with C-1 and O-4 equatorial, O-3 axial, and C-6 isoclinical.

Compounds **6**, **9**, and **10** were probably formed *via* monoepoxides, and t.l.c. showed that two other alkylating products were formed, but they could not be isolated.

For the compounds (**3**, **9**, **11**, **13**) studied by X-ray diffraction, the bond lengths are summarised in Table I, bond angles in Table II, torsion angles for the sugar moiety in Table III, and selected torsion angles for the trityl groups in Table IV. The presence of the trityl group in **11** and **13** causes significant distortions, *i.e.*, the C-7-C_{Ph} and C-8-C_{Ph} bonds (average value 1.538 Å), and the C-1–O-1–C-7 as well as the C-5(6)–O-5(6)–C-8 angles are enlarged. The positions of the trityl groups relative to the sugar moiety are determined by planar zigzag chains formed by C-2–C-1–O-1–C-7–C-31 (C-21 in **13**), C-5–C-6–O-6–C-8–C-61 (in **11**), and C-6–C-5–

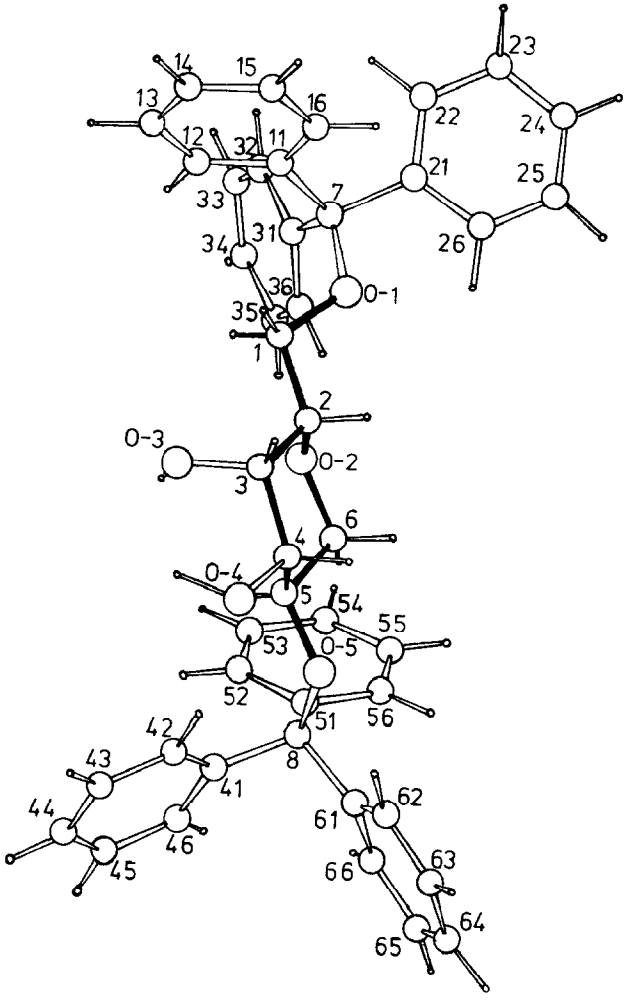
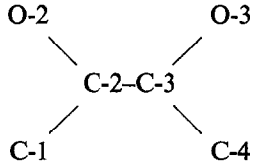


Fig. 4. Molecular diagram of compound **13**; the shape of the pyranoid ring and the orientation of the substituents resemble those for **9** (Fig. 2).

O-5–C-8–C-61 (in **13**). Variable temperature, ^{1}H-n.m.r. studies showed[14] that the rotation of the trityl group attached to a secondary hydroxyl group in **13** is hindered at 25°.

Of the 10 common torsion angles, four have the same signs and magnitudes (within 20°), indicating that the conformation of the



segment is approximately the same in all cases. A comparison of the torsion angles

TABLE I

BOND LENGTHS[a] (Å)

Bond	**3**	**9**	**11**	**13**
O-1–C-1		1.414(3)	1.431(2)	1.429(3)
O-1–C-7			1.444(2)	1.446(4)
O-2–C-2	1.417(8)	1.437(2)	1.438(2)	1.426(4)
O-2–C-5			1.439(2)	
O-2–C-6		1.429(3)		1.429(4)
O-3–C-3	1.455(7)	1.430(3)	1.418(2)	1.427(3)
O-3–C-6	1.418(8)			
O-4–C-4	1.440(7)	1.423(3)	1.420(2)	1.433(2)
O-5–C-5	1.419(8)	1.425(3)		1.439(4)
O-5–C-8				1.459(4)
O-6–C-6			1.433(2)	
O-6–C-8			1.445(2)	
C-1–C-2	1.515(9)	1.506(3)	1.502(3)	1.512(5)
C-1–Br	2.021(6)			
C-2–C-3	1.505(9)	1.523(3)	1.525(3)	1.521(3)
C-3–C-4	1.557(8)	1.523(3)	1.524(3)	1.534(5)
C-4–C-5	1.520(9)	1.518(3)	1.538(3)	1.526(4)
C-5–C-6	1.540(9)	1.523(3)	1.506(3)	1.528(3)
C-7–C-11			1.544(3)	1.529(3)
C-7–C-21			1.551(3)	1.533(3)
C-7–C-31			1.534(3)	1.543(4)
C-8–C-41			1.540(3)	1.530(3)
C-8–C-51			1.539(3)	1.531(3)
C-8–C-61			1.545(3)	1.537(4)
C_{Ph}–C_{Ph}(av)			1.387	1.383
C_{Ph}–C_{Ph}(min)			1.365	1.366
C_{Ph}–C_{Ph}(max)			1.403	1.397

[a]E.s.d. in parenthesis.

of **9** and **13** shows the similarity in the shape of the sugar moiety, although some significant differences in the magnitude of the torsion angles can be seen probably caused by the bulky trityl groups in **13**.

The geometry of the pyranoid ring is an almost ideal $^{O-2}C_4$ chair[13] in **9** and **13**, as shown by the Cremer–Pople puckering[11] parameters (e.s.d. in parentheses[12]) [**9**: Q = 0.575(3) Å, ϑ = 4.3(3)°, φ = 259(4)°; **13**: Q = 0.581(4), ϑ = 5.4(4)°, φ = 53(4)°] and the ring-torsion angles. This conformation enables three of the four substituents to be in equatorial positions.

The furanoid ring in **3** has the $^6T_5$ conformation [puckering parameters, Q = 0.408(10) Å, φ = 237.3(1)°] with O-5 axial, O-4 equatorial, and C-2 isoclinal, which allows intramolecular hydrogen-bonding between O-2 and O-5 (Table V). In **11**, the furanoid ring has the ^3E conformation [Q = 0.373(3) Å, φ = 286.8(5)], with C-1 and O-4 equatorial, O-3 axial, and C-6 isoclinal.

TABLE II

BOND ANGLES[a] (DEGREES)

Bonds	**3**	**9**	**11**	**13**
C-1–O-1–C-7			116.4	117.7
C-2–O-2–C-5			110.2	
C-2–O-2–C-6		111.9		112.2
C-3–O-3–C-6	109.4			
C-5–O-5–C-8				119.6
C-6–O-6–C-8			119.3	
O-1–C-1–C-2		109.1	107.6	105.6
C-2–C-1–Br	110.4			
O-2–C-2–C-1	111.8	108.3	109.4	106.7
O-2–C-2–C-3	108.9	109.9	105.2	109.9
C-1–C-2–C-3	109.4	112.6	114.2	114.3
O-3–C-3–C-2	109.3	109.9	109.5	112.8
O-3–C-3–C-4	104.1	110.4	112.5	109.9
C-2–C-3–C-4	115.4	109.0	100.8	110.8
O-4–C-4–C-3	107.6	111.7	114.8	108.2
O-4–C-4–C-5	111.6	109.9	109.0	113.2
C-3–C-4–C-5	104.9	110.2	103.7	111.6
O-5/2–C-5–C-4	111.9	111.0	105.4	106.9
O-2–C-5–C-6			110.4	
O-5–C-5–C-6	111.4	104.7		110.8
C-4–C-5–C-6	99.4	109.0	114.6	106.9
O-2–C-6–C-5		113.4		110.5
O-3–C-6–C-5	104.1			
O-6–C-6–C-5			107.7	
O-1–C-7–C-11			108.2	107.9
O-1–C-7–C-21			110.5	104.2
O-1–C-7–C-31			105.0	110.2
O-5–C-8–C-41				111.5
O-6–C-8–C-41			109.1	
O-5–C-8–C-51				109.0
O-6–C-8–C-51			110.5	
O-5–C-8–C-61				104.2
O-6–C-8–C-61			104.3	

[a]Maximum e.s.d.: **3**, 0.9°; **9**, 0.3°; **11**, 0.3°; **13**, 0.4°.

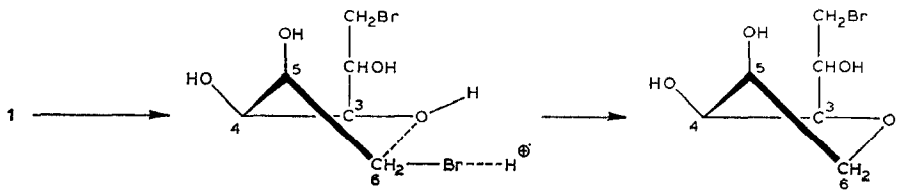
The transition state (**14**) associated with the conversion **1**→**3** (Scheme 1) is probably similar to that proposed[7] for the acid-catalysed dehydration of hexitols[7], according to which HO-5 should be axial. A different reaction mechanism (Scheme 2) is proposed for the transformation of **2** into 2,6- and 2,5-anhydro derivatives, the latter involving inversion of configuration at C-5.

TABLE III

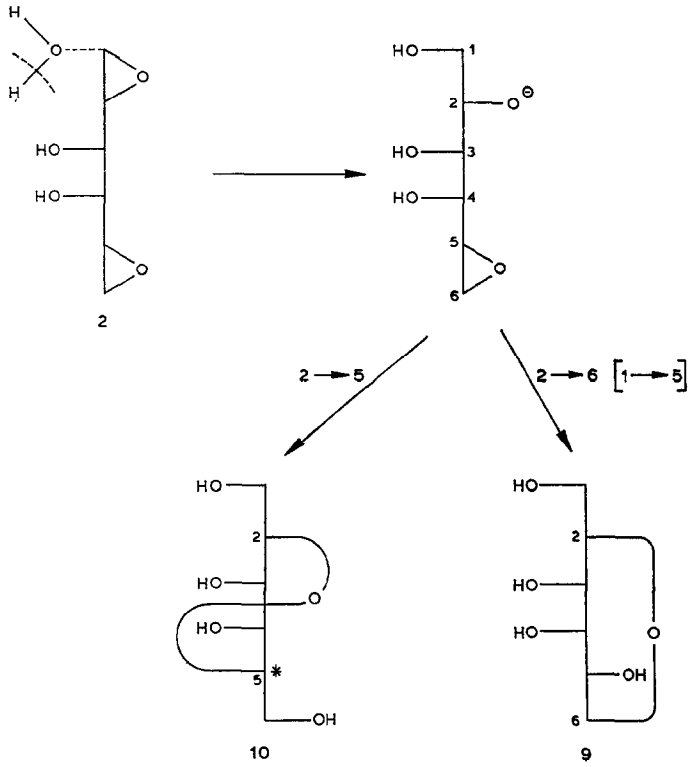
TORSIONAL ANGLES (DEGREES) FOR THE SUGAR MOIETY[a]

Bonds	3	9	11	13
C-5–O-2–C-2–C-1			−146.6	
C-5–O-2–C-2–C-3			−23.4	
C-6–O-2–C-2–C-1		176.4		174.6
C-6–O-2–C-2–C-3		−60.3		−61.0
C-2–O-2–C-5–C-4			0.2	
C-2–O-2–C-5–C-6			−124.2	
C-2–O-2–C-6–C-5		58.1		65.7
C-6–O-3–C-3–C-2	136.6			
C-6–O-3–C-3–C-4	12.8			
C-3–O-3–C-6–C-5	−35.3			
O-1–C-1–C-2–O-2		−71.7	−67.8	−81.0
O-1–C-1–C-2–C-3		166.6	174.5	157.3
Br–C-1–C-2–O-2	−70.5			
Br–C-1–C-2–C-3	168.8			
O-2–C-2–C-3–O-3	−62.5	−61.3	−82.3	−70.3
O-2–C-2–C-3–C-4	54.3	59.8	36.5	53.4
C-1–C-2–C-3–O-3	59.9	59.5	37.7	49.6
C-1–C-2–C-3–C-4	176.8	180.7	156.4	173.3
O-3–C-3–C-4–O-4	−104.0	−59.0	−37.9	−52.0
O-3–C-3–C-4–C-5	14.9	63.5	80.8	73.2
C-2–C-3–C-4–O-4	136.2	−179.8	−154.4	−177.3
C-2–C-3–C-4–C-5	−104.9	−57.4	−35.7	−52.1
O-4–C-4–C-5–O-2			145.7	
O-4–C-4–C-5–O-5	−160.0	−68.3		−65.0
O-4–C-4–C-5–C-6	82.3	176.8	−92.6	176.3
C-3–C-4–C-5–O-2			23.0	
C-3–C-4–C-5–O-5	83.8	168.2		172.6
C-3–C-4–C-5–C-6	−33.9	53.4	144.7	53.9
O-2–C-5–C-6–O-6			63.2	
O-5–C-5–C-6–O-2		−172.6		−176.1
O-5–C-5–C-6–O-3	−75.8			
C-4–C-5–C-6–O-3/2	42.3	−53.8		−59.9
C-4–C-5–C-6–O-6			−55.7	

[a]Maximum e.s.d.: **3**, 1.0°; **9**, 0.3°; **11**, 0.3°; **13**, 0.4°.



Scheme 1. Proposed mechanism for the transformation of **1** into **3** through the transition state **14**, based on the paper of Barker[7].



Scheme 2. Proposed mechanism for the transformation of **2** into **9** and **10**. *Inversion.

TABLE IV

TORSIONAL ANGLES (DEGREES) FOR THE TRITYL GROUPS[a]

Bonds	**11**	**13**	*Bonds*	**11**	**13**
C-7–O-1–C-1–C-2	−171.0	161.8	C-6–O-6–C-8–C-51	56.5	
C-1–O-1–C-7–C-11	−54.0	49.8	C-6–O-6–C-8–C-61	171.2	
C-1–O-1–C-7–C-21	71.9	170.4	O-1–C-7–C-11–C-21	−78.4	−94.7
C-1–O-1–C-7–C-31	−175.5	−76.4	O-1–C-7–C-21–C-26	21.7	19.5
C-8–O-5–C-5–C-4		154.8	O-1–C-7–C-31–C-36	−21.6	−17.4
C-8–O-5–C-5–C-6		−89.0	O-5–C-8–C-41–C-42		−13.7
C-5–O-5–C-8–C-41		−73.7	O-5–C-8–C-51–C-56		74.6
C-5–O-5–C-8–C-51		50.6	O-5–C-8–C-61–C-62		28.9
C-5–O-5–C-8–C-61		172.2	O-6–C-8–C-41–C-46	74.0	
C-8–O-6–C-6–C-5	−156.8		O-6–C-8–C-51–C-56	40.3	
C-6–O-6–C-8–C-41	−68.9		O-6–C-8–C-61–C-62	6.2	

[a]Maximum e.s.d.: **11**, 0.4°; **13**, 0.5°.

TABLE V

HYDROGEN BONDS IN THE CRYSTAL STRUCTURE OF **3**, **9**, **11**, AND **13**

X-H···Y[transformation]	*X···Y (Å)*	*H···Y (Å)*	*X-H···Y (degrees)*
Compound **3**			
O-2–H-O2···O-4[x, y, $-1+z$]	2.803(6)	2.02	156
O-4–H-O4···O-5[$1-x$, $1-y$, $1/2+z$]	2.718(6)	1.85	170
O-5–H-O5···O-2[x, y, z]	2.764(6)	1.79	168
Compound **9**			
O-1–H-O1···O-2[$1-x$, $1/2+y$, $-z$]	2.914(3)	1.99	167
O-3–H-O3···O-5[x, $-1+y$, z]	2.694(3)	1.86	163
O-4–H-O4···O-3[x, $1/2-y$, $-1/2-z$]	2.761(3)	1.89	168
O-5–H-O5···O-4[$1/2-x$, $1/2+y$, z]	2.698(3)	1.87	155
Compound **11**			
O-3–H-O3···O-4[$1-x$, y, $3/2-z$]	2.854(3)	2.04	147
O-4–H-O4···O-W[x, y, z]	2.760(3)	1.93	165
O-W–H-W1···O-2[x, $1+y$, z]	2.914(3)	1.97	173
O-W–H-W2···O-W[$1-x$, y, $3/2-z$]	2.915(3)	1.96	165
Compound **13**			
O-3–H-O3···O-4[$3/2-x$, $-1/2+y$, $3/2-z$]	2.804(4)	1.85	161

EXPERIMENTAL

General. — Melting points are uncorrected. T.l.c. was effected on Kieselgel G with *A*, benzene–methanol–1-pentanol–water–2-propanol (62:62:30:23:20); *B*, ethyl acetate; *C*, hexane–ethyl acetate (4:1); *D*, hexane–ethyl acetate (1:1); and detection with *A*, *p*-nitrobenzylpyridine + triethylamine[11]; *B*, periodate–benzidine; and *C*, u.v. light. Column chromatography was performed on Kieselgel 60 (0.063–0.125 mm).

All evaporations were performed in a rotary evaporator under diminished pressure at $\leqslant 40°$. Crystal and refinement parameters for **3**, **9**, **11**, and **13** are summarised in Table VI; atomic scattering factors were taken from International Tables[17].

3,6-Anhydro-1-bromo-1-deoxy-DL-*galactitol* (**3**). — A solution of **1** (20 g) in water (100 mL) was boiled for 10 min. No **1** then remained (t.l.c.). The solution was concentrated to 40 mL and extracted with ethyl acetate (2 × 500 mL), and the combined extracts were dried, concentrated to 50 mL, and stored overnight at 0°, to give **3** (9.1 g, 61.6%), m.p. 100–103°, R_F 0.77 (solvent *A*, reagent *A*).

When a solution of **1** (2 g) in methanol (100 mL) was boiled for 3 h and then worked-up as described above, pure **3** (0.8 g, 54.2%) was obtained after recrystallisation from ethyl acetate.

X-Ray analysis of **3**. — Suitable crystals were grown from water. Intensity measurements were carried out on an ENRAF-NONIUS CAD4, four-circle diffractometer up to $\vartheta = 25°$.

The space group $Pna2_1$ was determined on the basis of systematic extinctions

TABLE VI

CRYSTAL AND REFINEMENT PARAMETERS FOR COMPOUNDS **3**, **9**, **11**, AND **13**

	3	**9**	**11**	**13**
Crystal parameters				
Formula	$C_6H_{11}BrO_4$	$C_6H_{12}O_5$	$C_{44}H_{42}O_5 \cdot H_2O$	$C_{44}H_{42}O_5$
Cell dimensions	a = 7.061(3) Å	a = 23.247(2) Å	a = 31.17(1) Å	a = 36.31(2) Å
	b = 18.049(3)	b = 6.491(6)	b = 8.651(3)	b = 8.709(1)
	c = 6.555(1)	c = 9.708(1)	c = 26.36(1)	c = 24.26(1)
				β = 112.4(1)°
	V = 835.4 Å^3	V = 1464.9 Å^3	V = 7109 Å^3	V = 7093 Å^3
Space group	$Pna2_1$	Pbca	Pbcn	C2/c
Molecules per u.c.	4	8	8	8
Density calc.	1.805 g.cm^{-3}	1.488 g.cm^{-3}	1.248 g.cm^{-3}	1.238 g.cm^{-3}
Lin. abs. coff.	51.8 cm^{-1}	10.8 cm^{-1}	6.7 cm^{-1}	6.6 cm^{-1}
Radiation	MoKα	CuKα	CuKα	CuKα
Refinement parameters				
Number of reflections	1994	1291	6811	6745
Non-zero reflections included in the ref.	1349	1186	4428	4348
R index	0.056	0.058	0.043	0.044
Weighted R index	0.050	0.070	0.049	0.052
Weighting scheme	$1/[\sigma(F) + 0.01F^2]$	$1.4/(\sigma^2F + 0.004F^2)$	$1.72(\sigma^2F + 0.001F^2)$	$1/[\sigma(F) + 0.01F^2]$

TABLE VII

FRACTIONAL ATOMIC CO-ORDINATES[a] FOR **3**

Atom	x	y	z	*Atom*	x	y	z
C-1	−246(8)	3193(4)	2689(9)	H-11	−118	311	396
C-2	947(9)	3863(4)	3222(9)	H-12	72	278	233
C-3	1614(8)	3799(3)	5395(8)	H-2	14	428	307
C-4	2955(8)	4429(4)	6134(8)	H-3	50	374	636
C-5	4915(9)	4081(3)	6179(9)	H-4	296	487	503
C-6	4372(9)	3286(4)	6804(10)	H-5	585	433	714
Br	−1585(1)	3351(0)	0000(0)	H-61	557	292	653
O-2	2546(6)	3929(3)	1928(7)	H-62	404	325	825
O-3	2740(6)	3129(2)	5620(6)	H-O5	470	397	334
O-4	2345(7)	4647(3)	8143(6)	H-O4	305	503	841
O-5	5795(5)	4096(3)	4234(6)	H-O2	236	424	101

[a]Values are $\times 10^4$ for non-hydrogen atoms, and $\times 10^3$ for hydrogen atoms. Estimated standard deviations given in parentheses refer to the least-significant digit.

0k1 k + 1 = 2n + 1, and h01 h = 2n + 1. Pnam could be excluded because of the non-symmetrical character of the molecule, and density measurements. The position of the bromine atom was determined from the Patterson map and refined isotropically and anisotropically (R = 0.24). The Fourier map obtained on the basis of the bromine atom was naturally centrosymmetric and caused difficulties in the location of the other ten non-hydrogen atoms. Isotropic refinement for non-hydrogen atoms resulted in R = 0.086; further anisotropic refinement gave R = 0.046 for 756 reflections, $I \geqq 10\sigma(I)$. CH hydrogens were generated, and OH hydrogens could be located. After two more anisotropic cycles of refinement with reflections $I \geqq 3\sigma(I)$, R = 0.046 was obtained. The polarity of the crystal structure was also checked; the R value with $xy\bar{z}$ co-ordinates was 0.06. All calculations were carried out on a PDP 11/34 minicomputer using the SDP program package[20] with local modifications. The co-ordinates are given in Table VII.

1-Bromo-1-deoxy-DL-*galactitol* (**4**). — Crude **1** (50 g), prepared by the bromination[16] of galactitol (**6**), was stirred with methanol (500 mL) for 30 min. The solution was filtered and concentrated, and the residue (2 g) was stirred with water (20 mL) for 30 min. The aqueous solution was filtered and concentrated, and the residue, which contained **4** and some **1**, was crystallised from 96% ethanol and 1,1-dichloroethane–*N*,*N*-dimethylformamide, to give **4** (0.4 g), m.p. 132–134°, R_F 0.65 (solvent *A*, reagent *A* or *B*).

Anal. Calc. for $C_6H_{13}BrO_5$: 29.38; H, 5.30; Br, 32.65. Found: C, 29.59; H, 5.09; Br, 33.07.

1,4-Anhydro-DL-*galactitol* (**5**). — (*a*) A mixture of galactitol (50 g), conc. H_2SO_4 (0.55 g), and water (7 mL) was distilled at 135–140°/10–15 mmHg during 30 min. The resulting, dark syrup was diluted with water (500 mL), and the solution was treated with charcoal, neutralised with aqueous 40% NaOH, and concentrated. The syrupy residue was mixed with methanol (200 mL), the non-soluble part (10 g of galactitol) was removed, and the filtrate was concentrated. The residue was subjected to column chromatography (solvent *A*). Fractions containing the component with R_F 0.57 were combined and concentrated, and the residue (20 g) was crystallised from ethyl acetate and recrystallised from methanol, to give **5** (10.7 g, 23%), m.p. 60–65°, R_F 0.57 (solvent *A*, reagent *B*).

Anal. Calc. for $C_6H_{12}O_5$: C, 43.90; H, 7.31. Found: C, 43.85; H, 7.3.

(*b*) An aqueous solution (10 mL) of **3** (0.5 g) was boiled for 3 h when the pH changed from neutral to 1. T.l.c. (solvent *A*, reagent *A* or *B*) revealed **5** after 30 min; after 4 h, **3** was completely transformed into **5**.

1,2:3,6-Dianhydro-DL-*galactitol* (**7**). — A solution of **3** (10 g) in water (50 mL) was stirred with VARION AD (HO^-) resin (100 mL) for 10 min at ambient temperature. The resin was collected and washed with water, and the combined filtrate and washings were concentrated. The syrupy residue was subjected to column chromatography (ethyl acetate). Fractions containing the component of R_F 0.685 (solvent *A*, reagent *A*) were concentrated, to afford **7** as a colorless oil (4.5 g, 70%) that crystallised at 0°; m.p. 5–7°.

Anal. Calc. for $C_6H_{10}O_4$: C, 49.2; H, 6.85. Found: C, 49.01; H, 6.97.

A solution of **7** (0.6 g) in water (1 mL) was added dropwise to conc. HBr (2 mL) with stirring and cooling in ice–water. The solution was cooled and stirred for 30 min, and then extracted with ethyl acetate (2 × 75 mL). The combined extracts were concentrated and the residue was recrystallised from ethyl acetate, to give **3** (0.5 g, 54%).

1,5-Anhydro-DL-*galactitol* (**9**). — A solution of **2** (50 g) in ion-free water (1 L) was boiled until the decomposition of **2** was complete (6 h), and then concentrated. Methanol (30 mL) was added to the residue and, after cooling, galactitol (6.8 g, 11%) was precipitated. The mother liquor was concentrated and the residue was recrystallised several times from ethanol, to afford **9** (17.5 g, 31%), m.p. 120°, R_F 0.45 (solvent *A*, reagent *A*).

Anal. Calc. for $C_6H_{12}O_5$: C, 43.9; H, 7.3. Found: C, 43.93; H, 7.6.

X-Ray analysis of **9**. — Accurate cell-parameters were obtained from Guinier–Hägg photographs using KCl as internal standard. Intensities up to $2\vartheta = 130°$ were collected on a four-circle, PW 1100 Philips diffractometer; reflections with $I \geq 3\sigma(I)$ were included in the refinement. The intensities were corrected for polarisation and Lorentz effect.

The initial structural model was obtained by the automatic, direct-method routine of program SHELX[18] using 224 reflections with $E \geq 1.2$. Atomic parameters were refined by the full-matrix least-squares procedure, using anisotropic thermal parameters for the non-hydrogen atoms. The hydroxyl H atoms were taken from the difference map and the remainder were positioned using geometric criteria. Hydrogen atoms were constrained to the atom to which they were linked, and only the common

TABLE VIII

FRACTIONAL ATOMIC CO-ORDINATES[a] FOR **9**

Atom	x	y	z	*Atom*	x	y	z
O-1	5124(1)	2325(3)	1806(2)	H-O1	534	132	228
O-2	4069(1)	4681(2)	1727(1)	H-O3	322	38	33
O-3	3353(1)	1402(2)	792(1)	H-O4	305	345	−240
O-4	2936(1)	3647(2)	−1545(1)	H-O5	272	765	−66
O-5	3073(1)	7732(2)	−316(2)	H-11	465	31	64
C-1	4586(1)	1551(3)	1364(2)	H-12	435	98	224
C-2	4253(1)	3259(3)	681(2)	H-2	453	401	−6
C-3	3734(1)	2470(3)	−117(2)	H-3	387	141	−91
C-4	3428(1)	4289(3)	−785(2)	H-4	373	499	−150
C-5	3253(1)	5848(3)	302(2)	H-5	291	516	90
C-6	3779(1)	6422(3)	1154(2)	H-61	364	741	199
				H-62	408	725	50

[a]Values are $\times 10^4$ for non-hydrogen atoms, and $\times 10^3$ for hydrogen atoms. Estimated standard deviations given in parentheses refer to the least-significant digit.

TABLE IX

FRACTIONAL ATOMIC CO-ORDINATES[a] FOR **11**

Atom	x	y	z	*Atom*	x	y	z
O-1	6230(0)	6112(2)	6975(1)	C-64	7649(1)	8436(4)	8844(1)
O-2	5744(1)	7644(2)	7737(1)	C-65	7503(1)	7489(4)	9228(1)
O-3	5472(0)	10032(2)	6992(1)	C-66	7066(1)	7292(3)	9310(1)
O-4	5351(0)	11422(2)	7937(1)	O-W	5449(1)	14463(2)	7642(1)
O-6	6083(0)	8586(2)	8682(1)	H-O3	527	1073	710
C-1	6011(1)	7537(2)	6885(1)	H-O4	543	1232	784
C-2	6009(1)	8428(2)	7374(1)	H-11	617	818	661
C-3	5823(1)	10051(2)	7331(1)	H-12	571	730	676
C-4	5688(1)	10341(2)	7878(1)	H-2	629	853	752
C-5	5536(1)	8747(2)	8062(1)	H-3	605	1078	722
C-6	5633(1)	8405(3)	8610(1)	H-4	594	1065	809
C-7	6324(1)	5183(2)	6534(1)	H-5	522	863	800
C-8	6289(1)	7800(2)	9099(1)	H-61	553	730	870
C-11	5904(1)	4912(2)	6242(1)	H-62	546	915	881
C-12	5615(1)	3808(3)	6412(1)	H-12	571	304	672
C-14	5087(1)	4666(3)	5813(3)	H-14	477	457	565
C-15	5372(1)	5758(3)	5638(1)	H-15	528	652	533
C-16	5779(1)	5886(3)	5853(1)	H-16	600	675	572
C-21	6683(1)	5941(2)	6215(1)	H-22	654	464	555
C-22	6757(1)	5478(3)	5720(1)	H-23	715	572	506
C-23	7098(1)	6076(3)	5445(1)	H-24	763	762	545
C-24	7370(1)	7149(3)	5667(1)	H-25	751	844	633
C-25	7302(1)	7606(3)	6156(1)	H-26	691	735	682
C-26	6962(1)	6993(2)	6434(1)	H-32	641	240	607
C-31	6522(1)	3694(2)	6745(1)	H-33	681	9	636
C-32	6556(1)	2388(2)	6439(1)	H-34	713	5	721
C-33	6775(1)	1090(3)	6605(1)	H-35	707	233	776
C-34	6959(1)	1069(3)	7081(1)	H-36	668	465	747
C-35	6922(1)	2340(3)	7389(1)	H-42	672	977	974
C-36	6705(1)	3651(3)	7224(1)	H-43	647	1096	1054
C-41	6142(1)	8531(2)	9602(1)	H-44	575	1041	1086
C-42	6402(1)	9534(3)	9879(1)	H-45	527	869	1037
C-43	6257(1)	10193(3)	10327(1)	H-46	552	748	958
C-44	5856(1)	9884(3)	10507(1)	H-52	614	567	987
C-45	5589(1)	8927(3)	10235(1)	H-53	607	283	978
C-46	5731(1)	8240(3)	9789(1)	H-54	609	160	895
C-51	6207(1)	6049(2)	9069(1)	H-55	618	322	818
C-52	6154(1)	5131(3)	9497(1)	H-56	626	604	826
C-53	6114(1)	3537(3)	9450(1)	H-62	669	959	838
C-54	6123(1)	2841(3)	8982(1)	H-63	747	993	824
C-55	6172(1)	3753(3)	8555(1)	H-64	799	859	878
C-56	6219(1)	5336(2)	8596(1)	H-65	773	689	947
C-61	6770(1)	8050(2)	9004(1)	H-66	695	655	961
C-62	6919(1)	8994(3)	8619(1)	H-W1	557	1547	767
C-63	7356(1)	9188(4)	8541(1)	H-W2	514	1446	761
C-13	5209(1)	3684(3)	6197(1)	H-13	499	282	633

[a]Values are multiplied by 10^4 for non-hydrogen atoms, and by 10^3 for hydrogen atoms. Estimated standard deviations given in parentheses refer to the least-significant digit.

temperature factor for them was subjected to refinement. The final atomic coordinates are given in Table VIII.

*2,5-Anhydro-1,6-di-*O*-trityl-*DL*-altritol* (**11**). — The material in the mother liquor of **9** was dissolved in pyridine (25 mL) and stirred with trityl chloride (15 g) at ambient temperature for 6 days. The mixture was filtered into water (150 mL) and extracted with dichloromethane (3 × 75 mL), and the combined extracts were concentrated. The residue (20 g) was subjected to column chromatography (ethyl acetate). Fractions containing the component with R_F 0.9–1.0 (solvent *B*, reagent *C*) were combined and concentrated. The syrupy residue (13.2 g) crystallised from ethyl acetate (5 vol.)–hexane, to give **11** (9.2 g, 14%, based on **2**), m.p. 155–156°, R_F 0.08 (solvent *C*, reagent *C*).

Anal. Calc. for $C_{44}H_{40}O_5$: C, 81.5; H, 6.18. Found: C, 81.42; H, 6.2.

X-Ray analysis of **11**. — Reflections up to $2\vartheta = 130°$ were collected on a Philips four-circle diffractometer; intensities with $I > 3\sigma(I)$ were included in the refinement.

The structure was solved by using the program MULTAN[19] with 350 reflections having $E > 1.96$. The E-map with the best figure of merit showed all non-hydrogen atoms, except the solvent oxygen which was found in the subsequent Fourier map. The structure model was refined by using anisotropic thermal parameters and the blocked full-matrix technique[18] for the C and O atoms. Hydrogen positions for the water and OH groups were deduced from difference Fourier synthesis, and the remainder were generated. The isotropic thermal parameter of the corresponding parent atoms was assigned to the hydrogen atoms and kept fixed while their positional parameters were varied in the last steps of refinement. Final atomic parameters are listed in Table IX.

*2,6-Anhydro-1,5-di-*O*-trityl-*DL*-galactitol* (**13**). — The mother liquor of **11** was concentrated and the residue was subjected to column chromatography (solvent *D*). The fractions containing the component with R_F 0.17 (solvent *C*, reagent *C*) were combined and concentrated, and the residue was recrystallised from hexane–ethyl acetate (1:1), to give **13** (2.7 g, 4.2% based on **2**), m.p. 197–198°.

Anal. Calc. for $C_{44}H_{40}O_5$: C, 81.5; H, 6.18. Found: C, 81.11; H, 6.08.

X-Ray analysis of **13**. — Reflections up to $2\vartheta = 145°$ were collected on an ENRAF-NONIUS CAD4, four-circle, automatic diffractometer; those with $I > 3\sigma(I)$ were used in the refinement. An E-map calculated from a phase combination of program MULTAN[19] for 400 E-values having $E > 1.9$ revealed all but three atoms of the molecule. These were routinely obtained from Fourier calculation. The structural model was refined by applying anisotropic parameters to the non-hydrogen atoms, and OH hydrogens were taken from the difference map; CH hydrogens were generated and added to the last cycles of the refinement, but their positions were not refined. Final atomic parameters are listed in Table X.

*2,6-Anhydro-1-*O*-trityl-*DL*-galactitol* (**12**). — Fractions containing the compo-

TABLE X

FRACTIONAL ATOMIC CO-ORDINATES[a] FOR **13**

Atom	x	y	z	*Atom*	x	y	z
O-1	6196(1)	8034(2)	5477(1)	C-31	6022(1)	5432(3)	5077(1)
O-2	7051(1)	7611(2)	6106(1)	C-32	5766(1)	4191(3)	4876(1)
O-3	7015(1)	7861(2)	7310(1)	C-33	5900(1)	2821(3)	4727(1)
O-4	7593(1)	10075(2)	7671(1)	C-34	6289(1)	2678(3)	4774(1)
O-5	8028(1)	9427(2)	6914(1)	C-35	6546(1)	3905(3)	4979(1)
C-1	6403(1)	7819(3)	6104(1)	C-36	6414(1)	5276(3)	5129(1)
C-2	6798(1)	8631(3)	6260(1)	C-8	8386(1)	8544(3)	6993(1)
C-3	6996(1)	9092(3)	6912(1)	C-41	8565(1)	7829(3)	7615(1)
C-4	7415(1)	9731(3)	7047(1)	C-42	8449(1)	8277(3)	8073(1)
C-5	7664(1)	8637(3)	6839(1)	C-43	8631(1)	7653(3)	8640(1)
C-6	7424(1)	8301(3)	6181(1)	C-44	8934(1)	6598(3)	8760(1)
C-7	5866(1)	7019(3)	5170(1)	C-45	9055(1)	6167(3)	8314(1)
C-11	5593(1)	6997(3)	5519(1)	C-46	8875(1)	6774(3)	7747(1)
C-12	5624(1)	5882(3)	5942(1)	C-51	8286(1)	7335(3)	6499(1)
C-13	5415(1)	6011(4)	6314(1)	C-52	8197(1)	5827(3)	6589(1)
C-14	5170(1)	7267(4)	6263(1)	C-53	8056(1)	4805(3)	6111(1)
C-15	5136(1)	8384(3)	5845(1)	C-54	7999(1)	5272(4)	5546(1)
C-16	5347(1)	8256(3)	5480(1)	C-55	8086(1)	6760(4)	5449(1)
C-21	5670(1)	7725(3)	4547(1)	C-56	8232(1)	7787(3)	5920(1)
C-22	5289(1)	7283(3)	4168(1)	C-61	8687(1)	9755(3)	6967(1)
C-23	5126(1)	7850(4)	3586(1)	C-62	8665(1)	11246(3)	7147(1)
C-24	5338(1)	8864(4)	3388(1)	C-63	8958(1)	12303(3)	7178(1)
C-25	5712(1)	9306(4)	3760(1)	C-64	9272(1)	11890(4)	7024(1)
C-26	5877(1)	8738(3)	4335(1)	C-65	9293(1)	10415(4)	6844(1)
				C-66	9003(1)	9356(3)	6813(1)
H-52	823	546	701	H-12	580	494	599
H-53	800	370	619	H-13	544	521	663
H-54	790	451	520	H-14	501	738	653
H-55	805	708	503	H-15	495	932	581
H-56	829	891	584	H-16	532	908	517
H-62	843	1156	725	H-22	513	653	432
H-63	894	1341	733	H-23	485	753	331
H-64	948	1269	703	H-24	522	929	297
H-65	953	1008	672	H-25	587	1005	362
H-66	902	827	666	H-26	616	905	460
H-111	645	669	621	H-32	548	430	483
H-112	625	826	634	H-33	571	191	459
H-2	674	962	603	H-34	638	168	465
H-3	682	991	699	H-35	684	380	503
H-4	740	1070	681	H-36	660	618	528
H-5	772	763	707	H-42	823	907	799
H-61	758	761	601	H-43	854	797	897
H-62	738	931	595	H-44	907	616	917
H-O3	715	695	723	H-45	929	541	840
H-O4	750	918	793	H-46	896	639	742

[a]Values are multiplied by 10^4 for non-hydrogen atoms, and by 10^3 for hydrogen atoms. Estimated standard deviations given in parentheses refer to the least-significant digit.

nent with R_F 0.415 (solvent *B*, reagent *C*) were concentrated, to give **12** (4.4 g, 10.8%, based on **2**), m.p. 147–150°.

Anal. Calc. for $C_{25}H_{26}O_5$: C, 74.0; H, 6.4. Found: C, 73.48; H, 6.2.

Detritylation reactions. — (*a*) A solution of **11** (1 g) in glacial acetic acid (4 mL) and water (1 mL) was boiled for 30 min, filtered, and concentrated. The resulting syrup was subjected to column chromatography (solvent *A*), to give 2,5-anhydro-DL-altritol (**10**; 0.17 g, 64%), R_F 0.48 (solvent *A*, reagent *B*).

(*b*) Treatment of **12** (1 g) as described in (*a*), followed by column chromatography (solvent *A*) and recrystallisation from ethanol, gave **9** (0.21 g, 52%).

(*c*) Treatment of **13** (1 g) as described in (*b*) gave **9** (0.12 g, 48%).

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