Isomerism in Bicyclic Diacetals. Part II.[1] Bicyclic Methylene Diacetals in the *galacto*, *arabino*, and *ribo* Series

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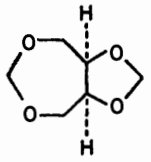
Studies of the acid-catalysed methylenation of tetritols with the *galacto*, *arabino*, and *ribo* configurations have led to the following observations: (i) dimethyl galactarate affords dimethyl 2,3:4,5- and 2,5:3,4-di-*O*-methylene-galactarate, (ii) methyl-D-arabinonate affords methyl 2,3:4,5-, 2,4:3,5-, and 2,5:3,4-di-*O*-methylene-D-arabinonate, and (iii) methyl D-ribonate affords methyl 2,4:3,5- and 2,5:3,4-di-*O*-methylene-D-ribonate. Vicinal coupling constant data obtained by ^{1}H n.m.r. spectroscopy show that dimethyl 2,5:3,4-di-*O*-methylenegalactarate and methyl 2,5:3,4-di-*O*-arabinonate exist predominantly in *gauche,gauche* conformations in solution whereas the *gauche,anti* conformation is highly populated in solutions of methyl 2,5:3,4-di-*O*-methylene-D-ribonate. The relative stabilities of the constitutional isomers are discussed in terms of electronic effects associated with *gauche* oxygen–oxygen interactions in O–C–C–O fragments as well as in terms of steric effects. There is no strong evidence to support the view that such *gauche* oxygen–oxygen interactions are an important stabilising feature in *cis*-fused 3,5,8,10-tetraoxabicyclo[5.3.0]decanes.

THE synthesis and characterisation [1] of 1,4:2,3-di-*O*-methylene-erythritol (1) as the first reported *cis*-fused



(1)

3,5,8,10-tetraoxabicyclo[5.3.0]decane derivative suggested that other alditols which could potentially exhibit spectroscopic characterisation of the bicyclic methylene diacetals in the three configurational series will be considered separately.

(A) *The* galacto *Series.*—Although three constitutionally isomeric diacetals could be obtained in principle from the acid-catalysed methylenation of dimethyl galactarate (Figure 1) only two were isolated, both as crystalline compounds (m.p.s 106—107 and 162—163°). An unambiguous assignment of constitution to these isomers can be made [1] on the basis of the nature of the ^{1}H n.m.r. signals for the dioxymethylene protons. The isomer with m.p. 106—107° was characterised as dimethyl

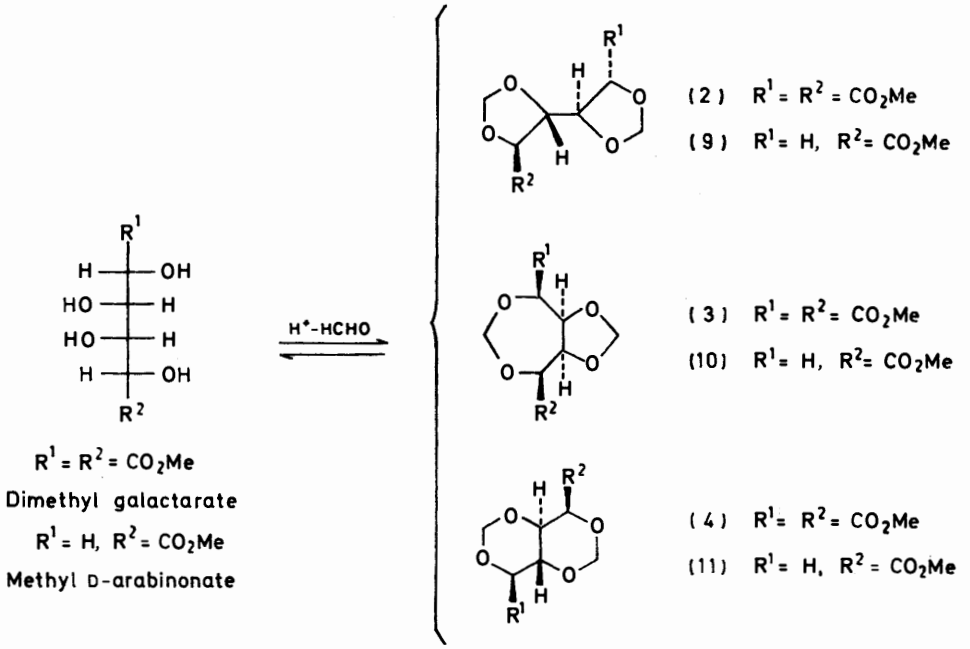


FIGURE 1 Acid-catalysed methylenation of dimethyl galactarate and methyl D-arabinonate

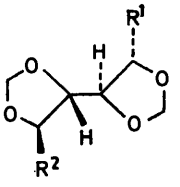
category (ii) reactivity [1] should be investigated. This paper describes the results obtained on acid-catalysed methylenation of dimethyl galactarate, methyl D-arabinonate, and methyl D-ribonate. The synthesis and

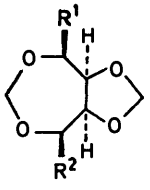
[1] I. J. Burden and J. F. Stoddart, *J.C.S. Perkin I*, preceding paper.

2,3:4,5-di-*O*-methylenegalactarate (2) on the basis of the *two isochronous* AB systems with $J_{AB} < 1{\cdot}0$ Hz for the *enantiotopic* dioxymethylene groups in the five-membered rings. The isomer with m.p. 162—163° was characterised as dimethyl 2,5:3,4-di-*O*-methylenegalactarate (3) since it exhibits *two anisochronous* AB systems with

$J_{AB} < 1{\cdot}0$ Hz (five-membered ring) and J_{AB} 7·5 Hz (seven-membered ring) for the *constitutionally heterotopic* dioxymethylene groups. No dimethyl 2,4:3,5-di-*O*-methylenegalactarate (4) was detected under reaction conditions of thermodynamic control.

Reduction of the diacetals (2) and (3) with lithium aluminium hydride afforded 2,3:4,5- (5) and 2,5:3,4-di-*O*-methylenegalactitol (6), which were characterised as their dimethyl ethers (7) and (8). The nature of the ^{1}H n.m.r.





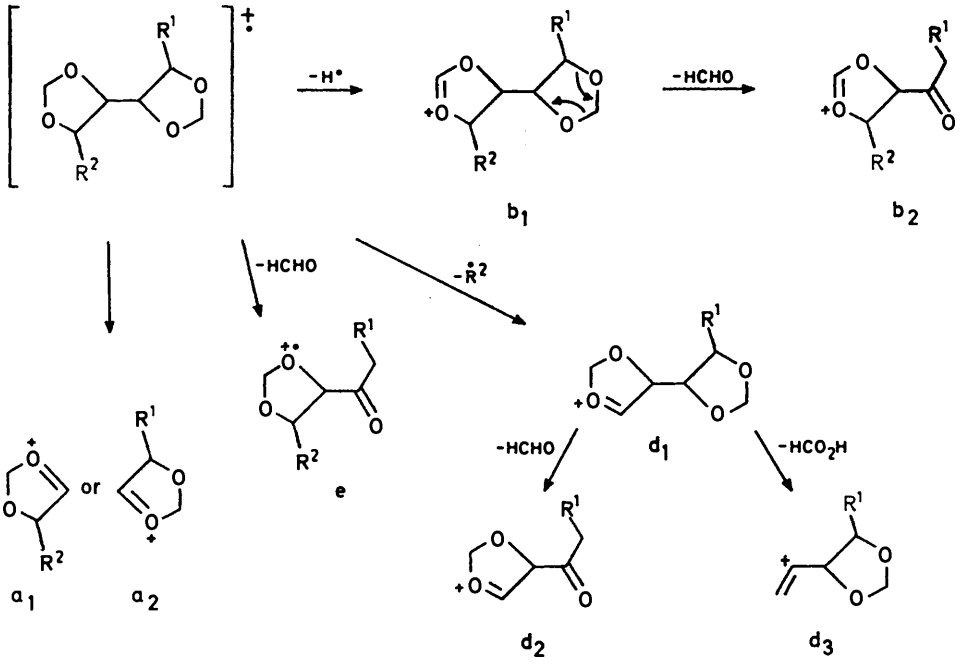
(5) $R^1 = R^2 = CH_2OH$ (6) $R^1 = R^2 = CH_2OH$

(7) $R^1 = R^2 = CH_2OMe$ (8) $R^1 = R^2 = CH_2OMe$

(12) $R^1 = H$, $R^2 = CH_2OH$

signals for their dioxymethylene groups is also consistent with their constitutional assignments.

of methyl D-arabinonate afforded all three possible constitutionally isomeric diacetals. One isomer was isolated as an oil with b.p. 150—160° at 2 mmHg and $[\alpha]_D$ +3·7°. The other two isomers were isolated as crystalline compounds, (i) with m.p. 100—103° and $[\alpha]_D$ −73·5°, and (ii) with m.p. 200—203° and $[\alpha]_D$ −33·8°. The isolation of two crystalline compounds, (i) with m.p. 99—100° and $[\alpha]_D$ −75·2°, and (ii) with m.p. 200—201° and $[\alpha]_D$ −31·1° from the acid-catalysed reaction of paraformaldehyde with methyl D-arabinonate has been reported [2] previously without constitutional assignments. The liquid isomer was characterised as methyl 2,3:4,5-di-*O*-methylene-D-arabinonate (9) on the basis of its ^{1}H n.m.r. spectrum which exhibits *two anisochronous* AB systems *each* with $J_{AB} < 1{\cdot}0$ Hz arising from the *constitutionally heterotopic* dioxymethylene groups in the five-membered rings. The isomer with m.p. 100—103° was characterised as methyl 2,5:3,4-di-*O*-methylene-D-arabinonate (10), since its *constitutionally heterotopic* dioxymethylene groups give rise to *two anisochronous* AB systems, one with $J_{AB} < 1{\cdot}0$ Hz (five-membered ring) and the other with J_{AB} 6·7 Hz (seven-membered ring). In the case of the isomer with m.p. 200—203°, *two anisochronous* AB systems each with J_{AB} 6·3 Hz (six-membered rings) were



SCHEME 1 Mass spectral fragmentation patterns for 4,4′-bis-1,3-dioxolans

An analysis of the mass spectral fragmentation patterns of the 2,3:4,5-diacetals [(2), (5), and (7)] and of the 2,5:3,4-diacetals [(3), (6), and (8)] permits [1] confirmation of the constitutional assignments made on the basis of ^{1}H n.m.r. spectroscopy. The fragmentation patterns summarised in Table 1 are accounted for in Schemes 1 and 2 for the 2,3:4,5-diacetals [(2), (5), and (7)] and the 2,5:3,4-diacetals [(3), (6), and (8)], respectively.

(B) *The* arabino *Series.*—Acid-catalysed methylenation observed for the *constitutionally heterotopic* dioxymethylene groups indicating that the isomer is methyl 2,4:3,5-di-*O*-methylene-D-arabinonate (11).

Reduction of the diacetals (10) and (11) with lithium aluminium hydride afforded 2,5:3,4- (12) and 2,4:3,5-di-*O*-methylene-D-arabinitol (13), respectively. The nature of the ^{1}H n.m.r. signals for their dioxymethylene groups is also consistent with their constitutional assignments.

[2] E. J. Bourne and L. F. Wiggins, *J. Chem. Soc.*, 1944, 517.

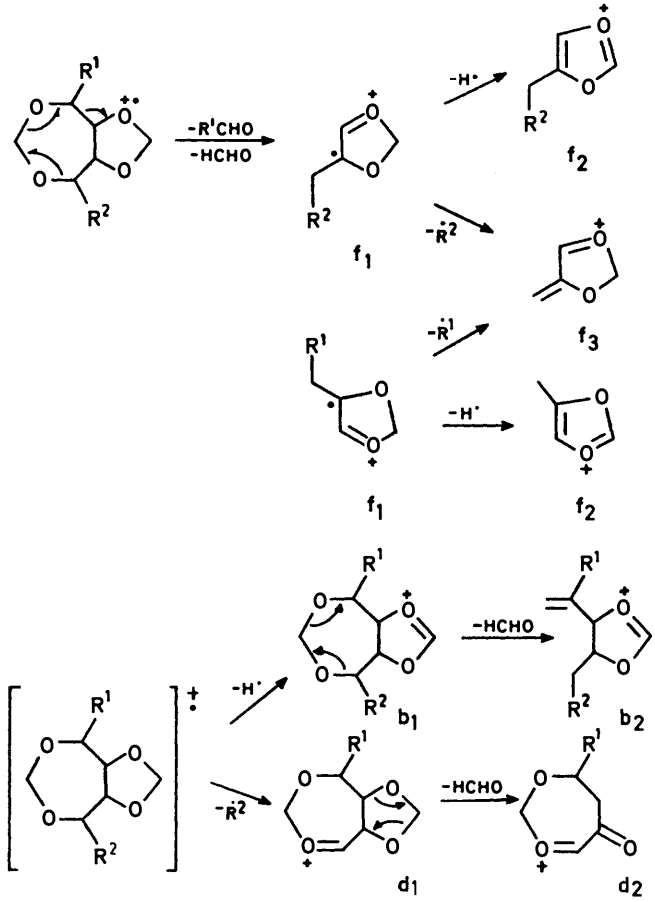
The mass spectral fragmentation patterns summarised in Table 1 for the 2,3:4,5-diacetal (9), the 2,5:3,4-diacetals [(10) and (12)], and the 2,4:3,5-diacetals [(11) and (13)] are accounted for in Schemes 1—3, respectively.

TABLE 1

Mass spectral fragmentation patterns (*m/e* values) for the 4,4′-bis-1,3-dioxolans, the *cis*-fused 3,4,8,10-tetraoxabicyclo[5.3.0]decanes, and the *trans*-fused 2,4,7,9-tetraoxabicyclo[4.4.0]decanes

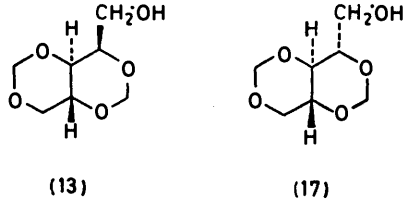
Compound	$M^{+\cdot}$	a_1	a_2	b_1	b_2	d_1	d_2	d_3	e	f_1	f_2	f_3	f_1'	f_2'	h_1	h_2
(2)	262	131	131	261		203	173									
(3)	262			261	231	203	173			144	143	85				
(5)		103	103	205		175	145									
(6)				205	175	175	145			116	115	85				
(7)		117	117	233		189	159									
(8)				233	203	189	159			130	129	85				
(9)	204	131	73	203	173	145	115	89	174							
(10)	204			203	173	145	115			144		85	86	85		
(11)	204			203		145	115		174	144	143	85			73	131
(12)	176			175	145	145	115			116	115	85	86	85		
(13)	176			175	145	145	115		146	116	115	85			73	103
(15)	204			203	173	145	115		174	116	115	85			73	131
(16)	204			203	173	145	115			144		85	86	85		
(17)	176				145	145	115			116	115	85	86	85		

(C) *The* ribo *Series*.—Of the three possible constitutionally isomeric bicyclic diacetals of methyl D-ribonate



SCHEME 2 Mass spectral fragmentation patterns for *cis*-fused 3,5,8,10-tetraoxabicyclo[5.3.0]decanes

shown in Figure 2, two were isolated from the acid-catalysed methylenation, one as a crystalline compound with m.p. 116—117°, and the other as an oil, b.p. 175—185° at 2 mmHg. The crystalline isomer was characterised as methyl 2,4:3,5-di-*O*-methylene-D-ribonate (15) on the basis of its ^{1}H n.m.r. spectrum, which exhibits *two anisochronous* AB systems each with J_{AB} 6·2 Hz (six-membered rings) for the *constitutionally heterotopic* dioxymethylene groups. The non-crystalline isomer was characterised as methyl 2,5:3,4-di-*O*-methylene-D-ribonate (16), since its two *constitutionally heterotopic* dioxymethylene groups give rise to *two anisochronous* AB systems, one with J_{AB} <1·0 Hz (five-membered ring) and the other with J_{AB} 6·7 Hz (seven-membered ring).



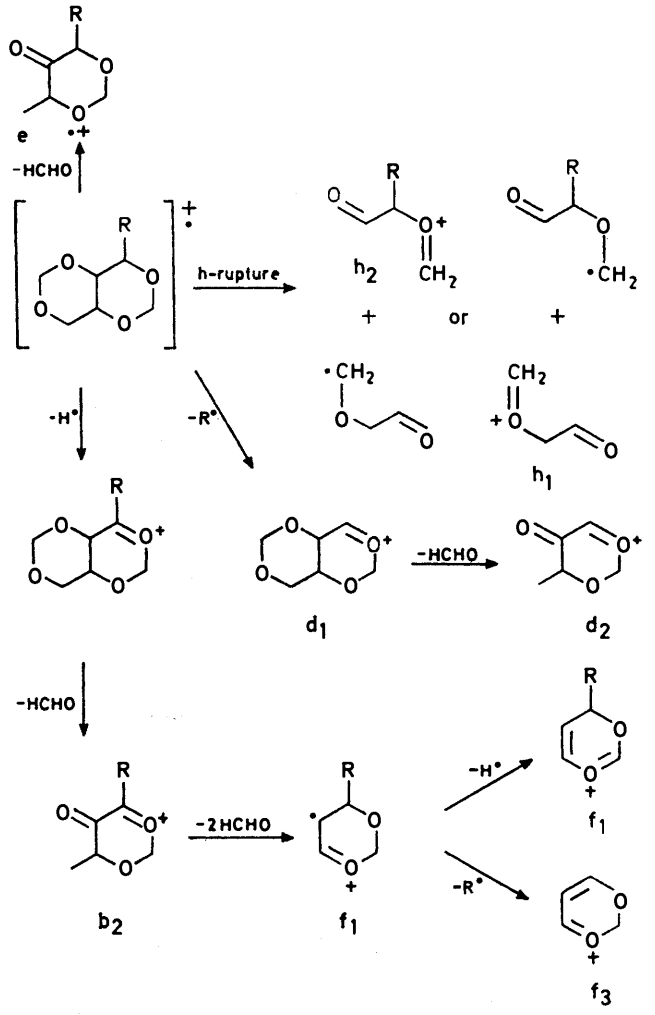
Although the corresponding ribitol derivatives were not prepared by reduction of the diacetals (15) and (16), ribitol itself was subjected to acid-catalysed methylenation and 1,3:2,4-di-*O*-methylene-DL-ribitol[3] (17) was isolated as the sole product. The mass spectrum of this compound was almost identical with that of 2,4:3,5-di-*O*-methylene-D-arabinitol (13).

The mass spectral fragmentation patterns summarised in Table 1 for the 2,4:3,5-diacetals [(15) and (17)] and the 2,5:3,4-diacetal (16) are accounted for in Schemes 2 and 3, respectively.

Conformational Behaviour of the cis-*Fused* 3,5,8,10-*Tetraoxabicyclo*[5.3.0]*decanes*. Molecular models of dimethyl 2,5:3,4-di-*O*-methylenegalactarate (3) and 1,6-di-*O*-methyl-2,5:3,4-di-*O*-methylenegalactitol (8) indicate that the substituents on C-2 and -5 can only assume equatorial orientations in the *gauche,gauche* conformation (18). In the *gauche,anti* conformation (19) one of the two substituents must be axial whereas in the *anti,anti* conformation (20) the two axial substituents enter into severe non-bonded interactions with each other. Thus, one

[3] R. M. Hann and C. S. Hudson, *J. Amer. Chem. Soc.*, 1944, **66**, 1906.

predicts that the *gauche,gauche* conformation (18) should be preferred for the diacetals (3) and (8). Since the 1,3-dioxepan ring will most likely adopt a relatively stable



SCHEME 3 Mass spectral fragmentation patterns for *trans*-fused 2,4,7,9-tetraoxabicyclo[4.4.0]decanes

twist-chair conformation,[4] the conformational behaviour of (3) and (8) is probably best described (Figure 3) by a rapid equilibrium between enantiomeric *gauche,gauche* conformations in which the average torsion angle involving the vicinal protons on C-2 and -3 (and on C-4 and -5) is *ca.* 90°. The fact that $J_{2,3}$ ($\equiv J_{4,5}$) is close to 0 in the ^{1}H n.m.r. spectra of (3) and (8) strongly suggests that both compounds exist predominantly in the *gauche,gauche* conformation [(18) and Figure 3] in solution.

In methyl 2,5:3,4-di-*O*-methylene-D-arabinonate (10), the methoxycarbonyl substituent on C-2 can occupy an equatorial position in either the *gauche,gauche* (21) or the *gauche,anti* (22) conformation. On the basis of the vicinal coupling constant data (Table 2) obtained by computation (LAOCOON II) from the ^{1}H n.m.r. spectrum of (10)

[4] T. B. Grindley, J. F. Stoddart, and W. A. Szarek, *J. Chem. Soc.* (*B*), 1969, 172, 623; J. F. Stoddart and W. A. Szarek, *ibid.*, 1971, 437.

in deuteriochloroform, the *gauche,gauche* conformation (21) appears to be favoured although a small contribution

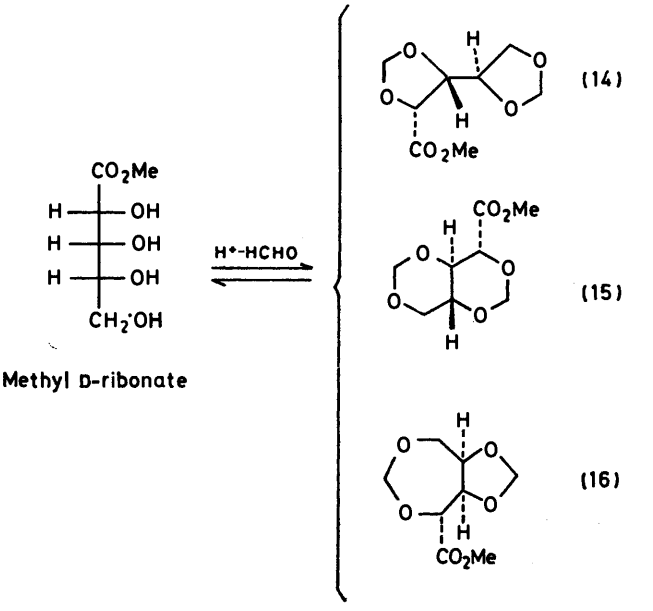


FIGURE 2 Acid-catalysed methylenation of methyl D-ribonate

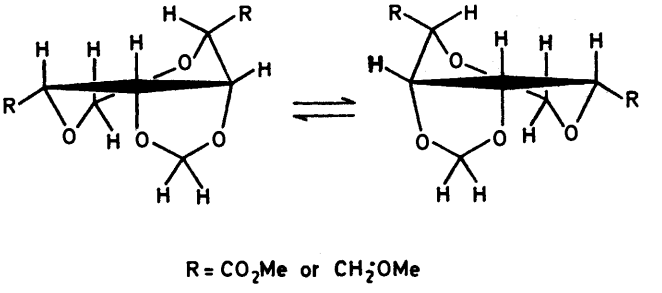
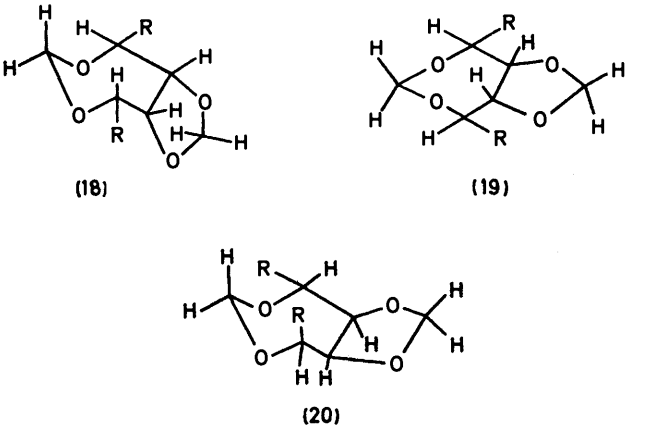


FIGURE 3 Conformational inversion in the *gauche,gauche* conformation (18) of dimethyl 2,5:3,4-di-*O*-methylenegalactarate (3) and 1,6-di-*O*-methyl-2,5:3,4-di-*O*-methylenegalactitol (8)

to a conformational equilibrium from the *gauche,anti* conformation (22)—or, for that matter, from other conformations—cannot be discounted.



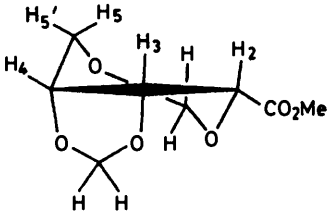
In methyl 2,5:3,4-di-*O*-methylene-D-ribonate (16) a *gauche,gauche* conformation would demand an axial methoxycarbonyl substituent whereas the *gauche,anti*

TABLE 2

Vicinal coupling constants and the corresponding approximate torsion angles deduced from the Karplus relationship [5] for methyl 2,5:3,4-di-*O*-methylene-D-arabinonate (10)

Protons	*J*/Hz	Torsion angle (°)
2,3	1·3	60—70
3,4	7·5	15—25
4,5	0·0	80—100
4,5′	5·5	30—40

(23) and *anti,anti* (24) conformations allow it to assume an equatorial orientation. The ^{1}H n.m.r. spectrum of (16) exhibited too many coincident peaks to permit



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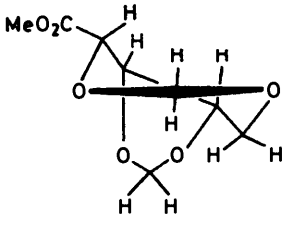

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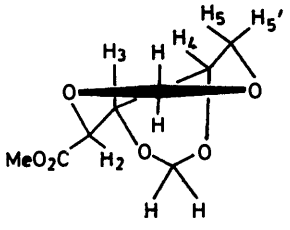

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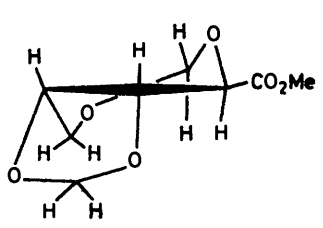


(24)

detailed analysis. However, a spectrum with considerable first-order characteristics was obtained on addition of 1·03 mol. equiv. of Eu(fod)$_3$ without any apparent changes in vicinal coupling constants having occurred during the progressive stepwise addition of the shift reagent. Analysis of the vicinal coupling constants (Table 3) with the aid of a computer program (LAOCOON II)

TABLE 3

Vicinal coupling constants and corresponding approximate torsion angles deduced from the Karplus relationship [5] for methyl 2,5:3,4-di-*O*-methylene-D-ribonate (16)

Protons	*J*/Hz	Torsion angle (°)
2,3	7·0	140—160
3,4	1·0	60—65
4,5	2·5	50—60
4,5′	2·5	50—60

indicates that the *gauche,anti* conformation (23) of methyl 2,5:3,4-di-*O*-methylene-D-ribonate (16) is probably highly populated.

* It is convenient to refer to *cis*-fused 3,5,8,10-tetraoxabicyclo[5.3.0]decanes, *trans*-fused 2,4,7,9-tetraoxabicyclo[4.4.0]-decanes, and 4,4-bis-1,3-dioxolans as ' 7/5,' ' 6/6,' and ' 5-5 ' isomers, respectively.

*Relative Thermodynamic Stabilities of ' 7/5,' ' 6/6,' and ' 5-5 ' Isomers.**—Although it did not prove practicable to analyse the reaction mixtures obtained on acid-catalysed methylenation of dimethyl galactarate, methyl D-arabinonate, and methyl D-ribonate by g.l.c., isomer ratios based on yields (see Experimental section) were considered to reflect, at least approximately, the situation which pertains under conditions of thermodynamic control. In Table 4, isomer ratios obtained in the

TABLE 4

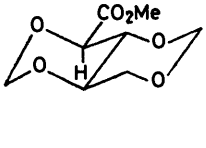
Ratios of the ' 7/5,' ' 6/6,' and ' 5-5 ' isomers obtained on acid-catalysed methylenation of dimethyl galactarate, methyl D-arabinonate, methyl D-ribonate, and erythritol

	Isomer ratios		
Configuration	' 7/5 '	' 6/6 '	' 5-5 '
galacto [a]	32	0	68
arabino [a]	54	24	22
ribo [a]	8	92	0
erythro [b]	9	91	0

[a] Based on yields (see Experimental section). [b] By g.l.c. (see Part I [1]).

galacto, arabino, and *ribo* series are compared with that already obtained [1] for the *erythro* configuration.

The first significant observation is that the relative thermodynamic stabilities of the ' 7/5 ' and ' 6/6 ' isomers are almost identical in the *erythro* and *ribo* series. While the ' 6/6 ' isomer (15) has an equatorial methoxycarbonyl group associated with its *trans*-decalin-like conformation (24), the ' 7/5 ' isomer (16) *must* contain at least one *anti* –O–C–C–O– fragment in order to accommodate the methoxycarbonyl group equatorially. This is borne out by the vicinal coupling constant data (Table 3) computed from the ^{1}H n.m.r. spectrum of (16) which indicates



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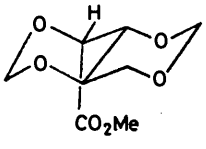

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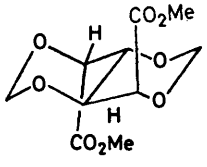

(26)

that the *gauche,anti* conformation is highly populated. Thus, *anti* –O–C–C–O– fragments do not appear to constitute a net destabilising influence in the ' 7/5 ' isomers (1) and (16).

If methyl 2,5:3,4-di-*O*-methylene-D-arabinonate (10) adopts † a *trans*-decalin-like conformation (25), then the methoxycarbonyl must occupy the axial position. This feature clearly destabilises the ' 6/6 ' isomer with respect

† The vincinal coupling constants obtained from comparison of the ^{1}H n.m.r. spectrum of (10) with computed (LAOCOON II) spectra have values $\leqslant$2·5 Hz (see Experimental section). It is difficult to reconcile these low values with a *trans*-decalin-like conformation, or, for that matter, with any conformation. A convincing explanation for this observation is not apparent.

[5] J. F. Stoddart, ' Stereochemistry of Carbohydrates,' Wiley, New York, 1971, p. 137.

to the ' 7/5 ' and ' 5-5 ' isomers and this is reflected in the isomer ratios (Table 4). In dimethyl 2,4:3,5-di-*O*-methylene-galactarate (4) a *trans*-decalin-like conformation (26) would have to carry two axial methoxycarbonyl groups. Not surprisingly, this compound was not obtained from the acid-catalysed methylenation of dimethyl galactarate. However, both the ' 7/5 ' and ' 5-5 ' isomers were isolated (Table 4) and characterised. Although the ' 7/5 ' isomers in the *arabino* and *galacto* series both adopt *gauche,gauche* conformations [(18) and (21)], the absence of any strong stabilising *gauche* oxygen–oxygen interaction is indicated by the competitive formation of ' 5-5 ' isomers.

Thus, the conclusion drawn [1] in Part I can be echoed. There is no evidence that vicinal oxygen substituents are a stabilising feature in any of the compounds discussed in this paper.

EXPERIMENTAL

General methods are described in Part I.[1]

Dimethyl 2,3:4,5- (2) *and* 2,5:3,4- (3) *Di*-O-*methylene-galactarate*.—Concentrated sulphuric acid (6 ml) was added to a mixture of dimethyl galactarate (10·0 g) and paraformaldehyde (10·0 g) and the mixture was set aside for 3 days at room temperature. Methanol (180 ml) was added and the mixture was refluxed for 2 h. After cooling, the solution was neutralised with barium carbonate. Methanol was removed under reduced pressure and the white residue was extracted with chloroform. Removal of the chloroform gave the crude product (6·0 g). T.l.c. indicated the presence of three main components, R_F 0·86, 0·40, and 0·24 in ethyl acetate–light petroleum (b.p. 60—80°) (1 : 1 v/v). A portion (3·0 g) of this product was chromatographed on a silica gel column (75 × 2·5 cm) with ethyl acetate–light petroleum (b.p. 60—80°) (1 : 1 v/v) as eluant to give three fractions.

Fraction 1, on recrystallisation from ethyl acetate–light petroleum (b.p. 60—80°), yielded needles of the 2,3:4,5-*diacetal* (2) (1·05 g), m.p. 106—107° (Found: C, 45·95; H, 5·5%; $M^{+\cdot}$, 262. $C_{10}H_{14}O_8$ requires C, 45·8; H, 5·4%; *M*, 262), $\nu_{max.}$ 1735 cm^{-1} (CO_2Me), τ (220 MHz; $CDCl_3$) 4·76 and 4·94 (4H, AB systems, J_{AB} < 1·0 Hz, 2,3:4,5-O·CH_2·O), 5·39 and 5·73 (4H, AA'BB' system, $J_{AA'}$ 5·5, $J_{BB'}$ 0, J_{AB} = $J_{A'B'}$ = 4·0 Hz, H-2, -3, -4, and -5), and 6·22 (6H, s, 2 × CO_2Me).

Fraction 2 (40 mg) had m.p. 97—101°. The mass and ^{1}H n.m.r. spectra showed that it was not a diacetal. It was not investigated further.

Fraction 3, on recrystallisation from ethyl acetate–light petroleum (b.p. 60—80°), yielded needles of the 2,5:3,4-*diacetal* (3) (500 mg), m.p. 162—163° (Found: C, 45·6; H, 5·12%; $M^{+\cdot}$, 262), $\nu_{max.}$ (Nujol) 1750 cm^{-1} (CO_2Me), τ (100 MHz; $CDCl_3$) 4·56 and 5·52 (2H, AB system, J_{AB} 7·5 Hz, 2·5-O·CH_2·O), 4·73 and 5·20 (2H, AB system, J_{AB} < 1·0 Hz, 3,4-O·CH_2·O), 5·69br (2H, s, H-2 and -5), 5·20br (2H, s, H-3 and -4), and 6·16 (6H, s, 2 × CO_2Me).

2,3:4,5-*Di*-O-*methylenegalactitol* (5).—Dimethyl 2,3:4,5-di-*O*-methylenegalactarate (2) (560 mg) was added to a suspension of lithium aluminium hydride (600 mg) in dry tetrahydrofuran (50 ml) and the mixture was refluxed for 6 h. Excess of lithium aluminium hydride was destroyed by careful addition of water to the cooled mixture. The inorganic material was filtered off and the tetrahydrofuran was removed under reduced pressure to give the crude product, which was dissolved in chloroform, dried (Na_2SO_4), and left to crystallise. Recrystallisation from chloroform yielded pure 2,3:4,5-*di*-O-*methylenegalactitol* (5) (303 mg, 69%), m.p. 100—102° [Found: C, 47·0; H, 7·3%; ($M^{+\cdot}$ − H), 205. $C_8H_{14}O_6$ requires C, 46·6; H, 6·85%; *M*, 206], $\nu_{max.}$ (Nujol) 3520 cm^{-1} (OH), τ (100 MHz; CD_3SOCD_3–D_2O) 5·07 and 5·10 (4H, AB systems, J_{AB} < 1·0 Hz, O·CH_2·O), and 5·97—6·70 (8H, AA'BB'XX'YY' system, which has not been analysed).

2,5:3,4-*Di*-O-*methylenegalactitol* (6).—Dimethyl 2,5:3,4-di-*O*-methylenegalactarate (3) (450 mg) was refluxed for 6 h with lithium aluminium hydride (500 mg) in tetrahydrofuran (40 ml). The crude product was isolated as described for the 2,3:4,5-diacetal (5). Recrystallisation from chloroform gave 2,5:3,4-*di*-O-*methylenegalactitol* (6) (150 mg, 42%), m.p. 160—162° [Found: C, 44·9; H, 7·1%; ($M^{+\cdot}$ − H), 205], $\nu_{max.}$ 3520 (OH), τ (100 MHz; CD_3SOCD_3) 5·02 and 5·56 (2H, AB system, J_{AB} 7·3 Hz, 2,5-O·CH_2·O), 5·01 and 5·26 (2H, AB system, J_{AB} < 1·0 Hz, 3,4-O·CH_2·O), 5·78 (2H, s, H-3 and -4), 6·29 and 6·47 (6H, AB_2 system, J_{AB} 6·7 Hz, H-2 and -5, and 2 × CH_2·OH), and 6·06br (2H, s, 2 × OH).

1,6-*Di*-O-*methyl*-2,3:4,5-*di*-O-*methylenegalactitol* (7).—2,3:4,5-Di-*O*-methylenegalactitol (5) (175 mg) was dissolved in dimethylformamide (3 ml) and methylated with methyl iodide (3 ml) and silver oxide (350 mg) at room temperature for 48 h. Silica gel chromatography gave the *dimethyl ether* (7) as a crystalline (from methanol) compound (58 mg, 29%), m.p. 58—60° [Found: C, 51·4; H, 7·5%; ($M^{+\cdot}$ − H), 233. $C_{10}H_{18}O_6$ requires C, 51·3; H, 7·75%; *M*, 234], τ (100 MHz; $CDCl_3$) 4·99br (4H, s, O·CH_2·O), 5·76—5·96 (2H, m, H-2 and -5), 6·07—6·26 (2H, m, H-3 and -4), 6·30—6·56 (4H, m, 2 × CH_2OMe), and 6·59 (6H, s, 2 × OMe).

1,6-*Di*-O-*methyl*-2,5:3,4-*di*-O-*methylenegalactitol* (8).—2,5:3,4-Di-*O*-methylenegalactitol (140 mg) was methylated as described for the 2,3:4,5-diacetal (7) to give the *dimethyl ether* (8) as a crystalline [from light petroleum (b.p. 60—80°)] compound (33 mg, 24%), m.p. 69—71° [Found: C, 51·2; H, 7·6%; ($M^{+\cdot}$ − H), 233], τ (100 MHz; $CDCl_3$) 4·78 and 5·50 (2H, AB system, J_{AB} 7·5 Hz, 2,5-O·CH_2·O), 4·80 and 5·12 (2H, AB system, J_{AB} < 1·0 Hz, 3,4-O·CH_2·O), 5·76 (2H, s, H-3 and -4), 6·21 and 6·36 (6H, AB_2 system, J_{AB} 6·2 Hz, H-2 and -5, and 2 CH_2·OMe), and 6·60 (6H, s, 2 × OMe).

Methyl 2,3:4,5- (9), 2,5:3,4- (10), *and* 2,4:3,5- (11) *Di*-O-*methylene*-D-*arabinonate*.—Methyl D-arabinonate (5·0 g) was mixed into a paste with paraformaldehyde (5·0 g) and concentrated sulphuric acid (3·0 ml). The mixture was set aside at room temperature for 3 days before being refluxed with methanol (100 ml) for 1 h. On cooling, the solution was neutralised with barium carbonate and the methanol was distilled off under reduced pressure to give a residue which was extracted with chloroform. Removal of the chloroform gave a yellow syrup (4·0 g) and t.l.c. indicated the presence of three components, R_F 0·54, 0·33, and 0·12 in chloroform. A portion (2·75 g) of this product was chromatographed on a silica gel column (75 × 2·5 cm) with ethyl acetate–light petroleum (b.p. 60—80°) (1 : 3 v/v) as eluant, to give three fractions.

Fraction 1, on vacuum distillation, yielded *methyl* 2,3:4,5-*di*-O-*methylene*-D-*arabinonate* (9) as an oil (210 mg), b.p. 150—160° at 2 mmHg, $[\alpha]_D$ +3·7° (*c* 1·52 in $CHCl_3$) (Found: C, 48·4; H, 6·25%; $M^{+\cdot}$, 204·0630. $C_8H_{12}O_6$ requires C, 47·1; H, 5·9%; *M*, 204·0633), τ (100 MHz; $CDCl_3$) 4·81, 4·91, 4·96, and 5·15 (4H, 2 AB systems, both

with J_{AB} <1·0 Hz, 2,3- and 4,5-O·CH_2·O), 5·44 (1H, d, H-2), 5·80—6·10 (4H, m, H-3, -4, -5, and -5′), and 6·21 (3H, s, CO_2Me).

Fraction 2, on recrystallisation from ethyl acetate–light petroleum (b.p. 60—80°), gave *methyl* 2,5:3,4-*di*-O-*methylene*-D-*arabinonate* (10) (527 mg), m.p. 100—103° (lit.,[2] 99—100°), $[\alpha]_D$ −73·5° (*c* 1·56 in $CHCl)_3$ [lit.,[2] −75·2° (in $CHCl_3$)] (Found: C, 47·2; H, 5·85%; $M^{+\cdot}$, 204), τ (220 MHz; $CDCl_3$) 4·74 and 5·07 (2H, AB system, J_{AB} <1·0 Hz, 3,4-O·CH_2·O), 4·81 and 5·48 (2H, AB system, J_{AB} 6·7 Hz, 2,5-O·CH_2·O), 5·38 (1H, q, $J_{2,3}$ 1·3, $J_{3,4}$ 7·5 Hz, H-3), 5·62 (1H, d, $J_{2,3}$ 1·3 Hz, H-2), 5·70 (1H, m, $J_{3,4}$ 7·5, $J_{4,5'}$ 5·5, $J_{4,5}$ 0 Hz, H-4), 5·74 (1H, $J_{4,5'}$ 5·5, $J_{5,5'}$ 11·0 Hz, H-5′), 6·29 (1H, m, $J_{4,5}$ 0, $J_{5,5'}$ 11·0 Hz, H-5), and 6·15 (3H, s, CO_2Me).

Fraction 3, on recrystallisation from ethyl acetate–light petroleum (b.p. 60—80°), gave *methyl* 2,4:3,5-*di*-O-*methylene*-D-*arabinonate* (11) (233 mg), m.p. 200—202° (lit.,[2] 200—201°), $[\alpha]_D$ −33·8° (*c* 1·58 in $CHCl_3$) [lit.,[2] −31·1° (in $CHCl_3$)] (Found: C, 46·9; H, 5·8%; $M^{+\cdot}$ 204), τ (220 MHz; $CDCl_3$) 4·67, 4·83, 5·18, and 5·25 (4H, 2 AB systems, both with J_{AB} 6·3 Hz, signals for A protons broadened by long-range coupling to H-2 and -5*eq*, 2,4- and 3,5-O·CH_2·O), 5·65 (1H, d, $J_{2,3}$ 2·2 Hz, H-2), 5·80 (1H, dt, $J_{4,5eq}$ 2·5, $J_{5ax,5eq}$ 12·6 Hz, H-5*eq*), 5·95 (1H, t, $J_{3,4}$ 2·5, $J_{4,5eq}$ 2·5, $J_{4,5ax}$ 2·5 Hz, H-4), 6·15 (1H, dd, $J_{4,5ax}$ 2·5, $J_{5ax,5eq}$ 12·6 Hz, H-5*ax*), 6·16 (3H, s, CO_2Me), and 6·35 (1H, t, $J_{2,3}$ 2·2, $J_{3,4}$ 2·5 Hz, H-3).

2,5:3,4-*Di*-O-*methylene*-D-*arabinitol* (12).—Methyl 2,5:3,4-di-*O*-methylene-D-arabinonate (10) (150 mg) was added to a suspension of lithium aluminium hydride (300 mg) in dry tetrahydrofuran (15 ml) and the mixture was refluxed overnight. Excess of lithium aluminium hydride was destroyed by careful addition of water (2 ml) to the cooled mixture. The clear tetrahydrofuran layer was decanted from the inorganic material, which was extracted successively with ether (3 × 15 ml) and chloroform (15 ml). The combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure to give a white solid residue, which, on recrystallisation from ethyl acetate–light petroleum (b.p. 60—80°), yielded 2,5:3,4-*di*-O-*methylene*-D-*arabinitol* (12) (66 mg, 51%), m.p. 131—134°, $[\alpha]_D$ −34·1° (*c* 0·92 in $CHCl_3$) (Found: C, 47·3; H, 6·8%; $M^{+\cdot}$, 176. $C_7H_{12}O_5$ requires C, 47·7; H, 6·85%; *M*, 176), τ (100 MHz; $CDCl_3$) 4·77 and 5·14 (2H, AB system, J_{AB} <1·0 Hz, 3,4-O·CH_2·O), 4·92 and 5·48 (2H, AB system, J_{AB} 6·5 Hz, 2,5-O·CH_2·O), 5·60—6·60 (7H, complex spin system, H-2, -3, -4, -5, and -5′, and CH_2OH), and 7·75 (1H, s, OH).

2,4:3,5-*Di*-O-*methylene*-D-*arabinitol* (13).—This was prepared from methyl 2,4:3,5-di-*O*-methylene-D-arabinonate (11) (106 mg) by a procedure similar to that described for the 2,5:3,4-diacetal (12). Recrystallisation of the crude product from ethyl acetate gave needles of 2,4:3,5-*di*-O-*methylene*-D-*arabinitol* (13) (50 mg, 55%), m.p. 204° with sublimation, $[\alpha]_D$ −20·3° (*c* 1·4 in Me_2SO) (Found: C, 47·6; H, 7·05%; $M^{+\cdot}$, 176), τ (100 MHz; CD_3SOCD_3) 4·97, 5·04, 5·26, and 5·32 (4H, 2 AB systems both with J_{AB} 6·0 Hz, 2,4- and 3,5-O·CH_2·O) and 5·94—6·82 (8H, complex spin system, H-2, -3, -4, -5*eq*, and -5*ax*, CH_2·OH, and OH).

Methyl 2,4:3,5- (15) *and* 2,5:3,4- (16) *Di*-O-*methylene*-D-*ribonate*.—Methyl D-ribonate (5·0 g) was mixed into a paste with paraformaldehyde (5·0 g) and concentrated sulphuric acid (3 ml). The mixture was set aside for 3 days at room temperature and the crude product was isolated as described previously in the *galacto* and *arabino* series. T.l.c. indicated the presence of four components, R_F 0·69, 0·58, 0·45, and 0·25 in ethyl acetate–light petroleum (b.p. 60—80°) (3 : 7 v/v). Chromatography on a silica gel column (75 × 2·5 cm) with ethyl acetate–light petroleum (b.p. 60—80°) (3 : 7 v/v) as eluant gave four fractions.

Fraction 1, on recrystallisation from light petroleum (b.p. 60—80°), yielded *methyl* 2,4:3,5-*di*-O-*methylene*-D-*ribonate* (15) (260 mg), m.p. 116—117°, $[\alpha]_D$ −14·7° (*c* 1·66 in $CHCl_3$) (Found: C, 47·1; H, 6·0%; $M^{+\cdot}$, 204. $C_8H_{12}O_6$ requires C, 47·1; H, 5·9%; *M*, 204), τ (100 MHz; $CDCl_3$) 4·91 and 5·20 (2H, AB system, J_{AB} 6·0 Hz, 2,4-O·CH_2·O), 4·99 and 5·31 (2H, AB system, J_{AB} 6·4 Hz, 3,5-O·CH_2·O), 5·70—6·00 (2H, m, H-2 and -5*eq*), 6·19 (3H, s, CO_2Me), and 6·29—6·49 (3H, m, H-3, -4, and -5*ax*), τ [100 MHz; Eu(fod)$_3$ (33·1 mg) and compound (15) (14·0 mg) in $CDCl_3$ (0·4 ml)] −1·54 (1H, d, $J_{2,3}$ 10·0 Hz, H-2), 0·43 and 1·33 (2H, AB system, J_{AB} 6·0 Hz, 2,4-O·CH_2·O), 0·87br (1H, t, $J_{2,3}$ 10·0, $J_{3,4}$ 9·0 Hz, H-3), 2·86 and 3·40 (2H, AB system, J_{AB} 6·4 Hz, 3,5-O·CH_2·O), 3·19 (1H, sextet, $J_{3,4}$ 10·0, $J_{4,5ax}$ 9·0, $J_{4,5eq}$ 5·0 Hz, H-4), 4·32 (3H, s, CO_2Me), 4·43 (1H, q, $J_{4,5eq}$ 5·0 Hz, $J_{5ax,5eq}$ 13·0 Hz, H-5*eq*), and 5·10 (1H, t, $J_{4,5ax}$ 9·0, $J_{5eq,5ax}$ 13·0 Hz, H-5*ax*).

Fraction 2 was a pale yellow liquid. Its mass and ^1H n.m.r. spectra indicated that it was not a diacetal; it was not investigated further.

Fraction 3, on vacuum distillation, yielded *methyl* 2,5:3,4-*di*-O-*methylene*-D-*ribonate* (16) as an oil (21 mg), b.p. 175—185° at 2 mmHg, $[\alpha]_D$ −59·5° (*c* 1·15 in $CHCl_3$) (Found: $M^{+\cdot}$, 204·0634. $C_8H_{12}O_6$ requires *M*, 204·0628), τ (100 MHz; $CDCl_3$) 4·93 and 5·00 (2H, AB system, J_{AB} < 1·0 Hz, 3,4-O·CH_2·O), 5·16 and 5·37 (2H, AB system, J_{AB} 5·6 Hz, 2,5-O·CH_2·O), 5·24br (1H, t, H-4), 5·34—5·48 (2H, m, H-2 and -3), 6·08—6·33 (2H, m, H-5 and -5′), and 6·67 (3H, s, CO_2Me), τ [100 MHz; Eu(fod)$_3$ (43·9 mg) and compound (16) (8·4 mg) in $CDCl_3$ (0·4 ml)] −2·44 and 1·30 (2H, AB system, J_{AB} 5·6 Hz, 2,5-O·CH_2·O), −0·12br (2H, s, 3,4-O·CH_2·O), 2·29br (1H, t, $J_{3,4}$ 1·0, $J_{4,5} = J_{4,5'}$ = 2·5 Hz, H-4), 3·23br (1H, d, $J_{2,3}$ 7·0 Hz, H-2), 3·27br (1H, d, $J_{2,3}$ 7·0, $J_{3,4}$ 1·0 Hz, H-3), 3·91 (1H, dd, $J_{4,5'}$ 2·5, $J_{5,5'}$ 11·0 Hz, H-5′), and 4·12 (1H, dd, $J_{4,5}$ 2·5, $J_{5,5'}$ 11·0 Hz, H-5).

Fraction 4 was a pale yellow liquid. Spectroscopic examination indicated it was not a diacetal; it was not investigated further.

1,3:2,4-*Di*-O-*methylene*-DL-*ribitol* (17).—Ribitol (3·0 g) was mixed into a paste with paraformaldehyde (3·0 g) and concentrated sulphuric acid (3 ml). The mixture was set aside for 4 days at room temperature before the acid was neutralised with sodium hydrogen carbonate. The mixture was extracted several times with chloroform and the combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure. The residue was shown by t.l.c. to contain three main components, R_F 0·68, 0·43, and 0·27 in ethyl acetate–light petroleum (b.p. 60—80°) (1 : 1 v/v). The crude product was chromatographed on a silica gel column (75 × 2·5 cm) with ethyl acetate–light petroleum (b.p. 60—80°) (1 : 3 v/v) as eluant to give three fractions.

Fractions 1 and 2 were both crystalline products and were recrystallised from ethyl acetate–light petroleum (b.p. 60—80°); m.p.s 74—78 and 40—42°, respectively. Their mass and ^1H n.m.r. spectra confirmed that they were not diacetals and so they were not investigated further.

Fraction 3, on recrystallisation from ethyl acetate–light petroleum (b.p. 60—80°), gave 1,3:2,4-di-*O*-methylene-DL-ribitol (17) (82 mg), m.p. 150° (lit.,[3] 149—151°) (Found: $M^{+\cdot}$, 176·0681. Calc. for $C_7H_{12}O_5$: *M*, 176·0685), τ (100 MHz; CD_3SOCD_3–$CDCl_3$) 5·03, 5·06, 5·23, and 5·36 (4H, 2 AB systems both with J_{AB} 6·2 Hz, 1,3- and 2,4-O·CH_2·O),

5·86—6·04 and 6·24—6·70 (7H, in the ratio 1 : 6, m, H-1*eq*, -1*ax*, -2, -3, -4, -5, and -5′), and 6·74 (1H, s, OH).

ADDENDUM

Since the completion of the research described here and in Part I, the following ^{13}C n.m.r. spectra have been obtained for representative samples of the three different systems (JEOL-PS-100 spectrometer with deuteriochloroform lock and tetramethylsilane as internal standard): (i) dimethyl 2,3:4,5-di-*O*-methylenegalactarate (2), δ ($CDCl_3$) 170·6 (CO), 96·8 (O·CH_2·O), 78·9 (C-2 and -5), 75·1 (C-3 and -4), and 52·6 (CO_2Me); (ii) dimethyl 2,5:3,4-di-*O*-methylenegalactarate (3), δ ($CDCl_4$) 168·4 (CO), 98·2 and 96·6 (2 × O·CH_2·O), 80·8 (C-2 and -5), 78·0 (C-3 and -4), and 52·9 (CO_2Me); (iii) 1,3:2,4-di-*O*-methylene-erythritol, δ ($CDCl_4$) 94·1 (O·CH_2·O), 74·1 (C-2 and -3), and 68·4 (C-1 and -4). While these results are consistent with the constitutional assignments already made on the basis of ^1H n.m.r. spectroscopy, ^{13}C n.m.r. spectroscopy appears to be less diagnostic of constitution. The chemical shift differences amongst dioxymethylene carbon atoms in five-, six-, and seven-membered rings are small. They are unlikely to be as reliable as geminal coupling constant data available from ^1H n.m.r. spectra.

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