Constitutional Isomerism in Bicyclic Diacetals and the Conformational Behaviour of *cis*-Fused 1,3,6,8-Tetraoxabicyclo[5,3,0]decanes

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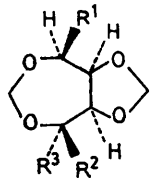
Summary The equilibrium proportions of the constitutional isomers (**1**)—(**4**) and the conformational behaviour of the *cis*-fused 1,3,6,8-tetraoxabicyclo[5,3,0]decanes (**1a**)—(**4a**) provide no evidence for the *gauche* arrange ment of the vicinal oxygen substituents being a stabilising feature *in these systems*.

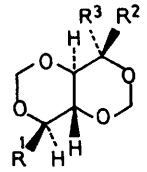
IN the acid-catalysed condensations of tetritols with aldehydes and ketones, *cis*-fused 1,3,6,8-tetraoxabicyclo[5,3,0]-decane ('7/5' isomer) and *trans*-fused 1,3,6,8-tetraoxabicyclo[4,4,0]decane ('6/6' isomer) ring systems, in addition to a 4,4'-bis-1,3-dioxolan ('5-5' isomer) derivative, may result when carbon atoms previously associated with hydroxy-groups in the *erythro* configuration form the ring junctions.

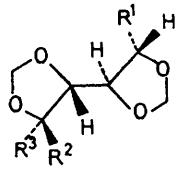
Acid-catalysed methylenation (paraformaldehyde–conc.

H_2SO_4) of tetritols with *erythro*, *ribo*, *arabino*, and *galacto* configurations under conditions of equilibrium control has yielded the following compounds (*cf.* Table): (i) erythritol affords (**1a**) and (**1b**); (ii) methyl D-ribonate affords (**2a**) and (**2b**); (iii) methyl-D-arabinonate affords (**3a**), (**3b**), and



(1a) $R^1 = R^2 = R^3 = H$
(2a) $R^1 = R^2 = H^3$; $R = CO_2Me$
(3a) $R^1 = R^3 = H$; $R^2 = CO_2Me$
(4a) $R^1 = R^2 = CO_2Me$; $R^3 = H$





(1b) $R^1 = R^2 = R^3 = H$
(2b) $R^1 = R^2 = H$; $R^3 = CO_2Me$
(3b) $R^1 = R^3 = H$; $R^2 = CO_2Me$
(3c) $R^1 = R^3 = H$; $R^2 = CO_2Me$
(4c) $R^1 = R^2 = CO_2Me$; $R^3 = H$

(**3c**); and (iv) dimethyl galactarate affords (**4a**) and (**4c**). The constitutions of all these compounds follow directly from their ^1H n.m.r. spectra using (a) the topic relationships[3] of the $-OCH_2O-$ groups as defined by molecular symmetry and (b) the criterion[4] that $-OCH_2O-$ protons give rise to AB systems with $J_{AB} < 1{\cdot}0$ Hz (1,3-dioxolan ring) and $J_{AB} = 6{\cdot}0$—$7{\cdot}5$ Hz (1,3-dioxan or 1,3-dioxepan rings).

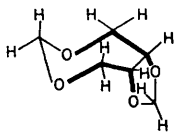
TABLE

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

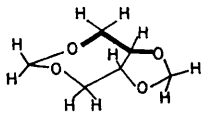
Configurational series	Isomer ratio[a] '7/5' (**a**)	'6/6' (**b**)	'5-5' (**c**)
erythro (**1**)	9[b]	91[c]	0
ribo (**2**)	8[d]	92[e]	0
arabino (**3**)	54[f]	24[g]	22[d]
galacto (**4**)	32[h]	0	68[i]

[a] By g.l.c. for (**1**) and based on yields after silica gel chromatography for (**2**)—(**4**). [b] M.p. 88—89°, [c] M.p. 100° (lit.,[1] m.p. 97—98°). [d] Oil. [e] M.p. 116—117°. [f] M.p. 100—103° (lit.,[2] m.p. 99—100°). [g] M.p. 200—203° (lit.,[2] m.p. 200—201°). [h] M.p. 162—163°. [i] M.p. 104—105°.

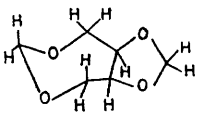
Inspection of molecular models of 1,4:2,3-di-*O*-methylene-erythritol (**1a**) reveals that there are three conformations in which the 1,3-dioxepan rings can adopt the relatively stable twist-chair conformations.[5] If attention is focused on the torsional angles involving the oxygen atoms in the $-O-\overset{|}{C}-\overset{|}{C}-O-$ units between the 5- and 7-membered rings, then these conformations may be identified (Figure) as the *gauche–gauche* (**5**), *gauche-anti* (**6**), and *anti–anti* (**7**). Vicinal coupling constant data computed from ^1H n.m.r. spectra recorded in $CDCl_3$ and CS_2 indicate major contributions to a conformational equilibrium from conformations [*i.e.* (**6**) and (**7**)] with oxygen atoms in the *anti*-relationship in $-O-\overset{|}{C}-\overset{|}{C}-O-$ fragments. The preponderance of *anti* $-O-\overset{|}{C}-\overset{|}{C}-O-$ fragments is greater in CS_2 than in $CDCl_3$.



gauche–gauche
(**5**)



gauche–anti
(**6**)



anti–anti
(**7**)

Another significant observation is the very similar ratios found (Table) in the case of the bicyclic diacetals with the *erythro* and *ribo* configurations. While the '6/6' isomer (**2b**) has an equatorial CO_2Me group associated with its *trans*-decalin-like conformation, the '7/5' isomer (**2a**) *must* contain at least one *anti* $-O-\overset{|}{C}-\overset{|}{C}-O-$ fragment in order to accommodate the CO_2Me group equatorially. This is borne out by the vicinal coupling constant data computed from the ^1H n.m.r. spectrum of (**2a**). Thus, *anti* $-O-\overset{|}{C}-\overset{|}{C}-O-$ fragments do not appear to constitute a net destabilising influence in '7/5' isomers (**a**) (*cf.* ref. 6). Such a conclusion is also consistent with the results of studies[7] on the positions of the configurational equilibrium between *cis*- and *trans*-2-isopropyl-5-methoxy-1,3-dioxan† in 17 different solvents which indicate a small preference for the *anti*-arrangement of vicinal oxygen substituents.

When the '6/6' isomers (**b**) have to carry one (*arabino*) or two (*galacto*) axial CO_2Me groups in *trans*-decalin-like conformations then their contribution to the isomeric equilibrium decreases dramatically and '5-5' isomers (**c**) are formed in addition to '7/5' isomers (**a**). Conformational constraints imposed upon dimethyl 2,5:3,4-di-*O*-methylene galactarate (**4a**) by the CO_2Me groups dictate that it *must* assume a *gauche–gauche* conformation, a fact confirmed by ^1H n.m.r. spectroscopy. In this situation, the '5-5' isomer (**4c**) is found (Table) to be more stable than the '7/5' isomer (**4a**).

We are led to the conclusion that there is no evidence for the *gauche* arrangement of the vicinal oxygen substituents being a stabilising feature *in any of the compounds discussed in this communication.*

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† This is probably the most suitable model system available at present with which to compare the conformational behaviour of the '7/5' isomers (**a**).

[1] M. Schulz and B. Tollens, *Annalen*, 1896, **289**, 20.
[2] E. J. Bourne and L. F. Wiggins, *J. Chem. Soc.*, 1944, 517.
[3] H. Hirschmann and K. R. Hanson, *European J. Biochem.*, 1971, **22**, 301.
[4] R. Cahill, R. C. Cookson, and T. A. Crabb, *Tetrahedron*, 1969, **25**, 4681.
[5] J. F. Stoddart and W. A. Szarek, *J. Chem. Soc.* (*B*), 1971, 437.
[6] L. Phillips and V. Wray, *J.C.S. Chem. Comm.*, 1973, 90.
[7] E. L. Eliel and O. Hofer, *J. Amer. Chem. Soc.*, 1973, **94**, 8041.