Synthesis and Conformation of a Derivative of 2,9,15,16-Tetraoxatricyclo-[9.3.1.1^{4,8}]hexadecane

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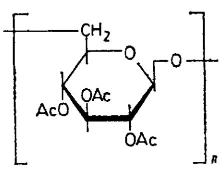
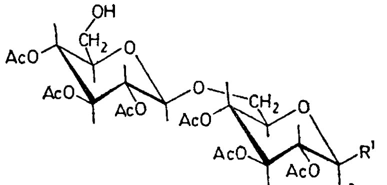
Summary Internal cyclisation of a derivative (**3**) of gentiobiose affords the highly rigid tricyclic compound (**4**) which has the tetraoxatricyclo[9.3.1.1^{4,8}]hexadecane skeleton; the conformation of (**4**), determined by n.m.r. spectroscopy, is compared with the results of an empirical calculation on the unsubstituted model (**5**).

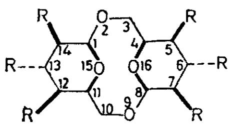
In connection with syntheses of cyclic or linear[1] oligomers of β-(1 → 6)-glucans of the general type (**1**), the bromide (**3**) was prepared by the action of $TiBr_4$ on the dimer (**2**) by a method derived for other compounds.[2] Autocondensation of (**3**) under the glycosylation conditions described by Helferich[3] in acetonitrile or 1,2-dichloroethane leads to a mixture of the expected oligomers; the unexpected derivative (**4**), which corresponds to an intramolecular reaction, is also formed in a relative yield of *ca.* 10% and is easily separated by column chromatography on SiO_2, with C_6H_6–Et_2O (6·5 : 3·5) as eluant, m.p. 165 °C (from $CHCl_3$–Et_2O). It gives satisfactory analyses and molecular weight by vapour-phase osmometry (found 630, calc. 576·5).



(1)



(2); R^1 = OAc; R^2 = H
(3); R^1 = H; R^2 = Br



(4); R = OAc
(5); R = H

To our knowledge, this is the first report of a synthesis of a derivative of 2,9,15,16-tetraoxatricyclo[9.3.1.$1^{4,8}$]hexadecane. By modifying the configurations of the different carbon atoms of the starting carbohydrate, a wide variety of stereoisomers with the same skeleton should be obtainable. Compound (**4**) is optically active (C-4 and C-11, *S*; C-1 and C-8, *R*) and forms a strongly rigid system; the six-membered rings are in a twisted conformation rather than a chair or a boat form (Figure).

The ^{1}H and ^{13}C n.m.r. spectra show that the two symmetrical parts of the molecule of (**4**) are magnetically equivalent; ^{13}C spectrum ($CDCl_3$; Me_4Si ref.) δ 99·94, 74·93, 73·16, 72·86, 71·09, and 66·6 (skeleton C atoms); 20·80 (OAc); and 170·7, 169·7, and 168·7 p.p.m (CO). The ^{1}H n.m.r. spectrum is first order at 250 MHz; δ ($CDCl_3$) 6·00 (5- and 12-H), 5·12 (6- and 13-H), 4·98 (7- and 14-H), 4·76 (1-and 8-H), 4·03 and 3·67 (3- and 10-H_2), 3·87 (4- and 11-H), and 2·12 and 2·04 (2 : 1 ratio, 6 × OAc). Coupling constants (Table) were calculated from second-order analysis of the 100 MHz ^{1}H spectra. These results imply a symmetrical structure for compound (**4**), and as one β-glycosidic bond is present in the starting material, only a β-glycosidic bond can be formed. This was supported by the mass spectrum, which did not show a molecular ion, but a peak was found at *m/e* 487 [$M^+ - (AcOH + CH_2O)$], similar to those observed with 1 → 6 anhydro sugars.[4]

TABLE

Protons[a]		Calc. Φ for (**5**)	Found *J*/Hz for (**4**)
endo-3–4 ..	..	−65	1·5
exo-3–4 ..	..	50	1·5
4–*endo*-5 ..	..	176	10
endo-5–*exo*-6	..	−145	9
exo-6–*endo*-7	..	89	3
endo-7–8 ..	..	61	1·7

[a] *exo*- and *endo*- refer to the bicyclo[9.3.1]nonane system.

A conformational study using the program ENERMOL[5] was carried out on the model (**5**), in which the OAc groups had been replaced by H. This program uses a 'simplex' method, assessing the minimum energy of a molecule with respect to the geometrical parameters, and allowing the use of symmetry constraints. Electrostatic point charge and dipole interactions were not taken into account.

Calculations made with, and then without, a symmetry constraint due to a C_2 axis show that the two rings are nearly related by C_2 symmetry; the minimum energy conformation obtained and a projection of one of the six-membered rings are shown in the Figure.

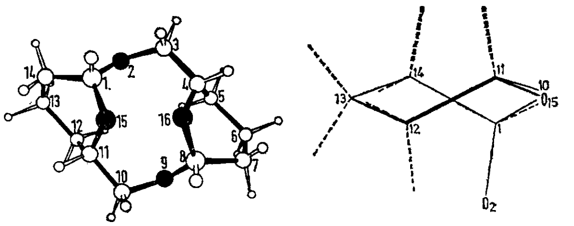


FIGURE (a) Minimum energy conformation of (**5**) calculated using the ENERMOL[5] program. Filled circles represent oxygen. (b) Projection of one of the six-membered rings.

The largest angular deformations are those at oxygen: θ(1–15–11) = θ(8–16–4) = 116·3° (0·54 kcal mol^{-1}); θ(1–2–3) = θ(8–9–10) = 115·9° (0·45 kcal mol^{-1}). The principal energy contribution arises from the dihedral deformations: 4 kcal mol^{-1} for each six-membered ring existing in a twist form. The energy of interaction between non-bonded atoms (calculated by Hill's law[6]) arises principally from three pairs of atoms: O(15)–O(16) (2·35 Å); H(1)–H(3-*exo*) =H(8)–H(10-*exo*) (2·30 Å).

The Table shows that the experimental *J* values for compound (**4**) correlate reasonably well with the calculated Φ values for (**5**), the larger *J* values corresponding to the larger Φ values. However, the theoretical results were calculated using a simple model.

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