The observation of both the *cisoid* and *transoid* conformers of T_4 in the same crystal lattice suggests that they are both stable low-energy conformers. Further studies are required to establish the relevance of these conformations to binding.

In conclusion, this crystallographic determination of thyroxine has provided structural evidence which shows: (1) a 4'-phenoxide geometry, (2) possible hydrogen-bonding geometry to binding sites of a receptor protein, and (3) structural confirmation of theoretical structure–activity models. Since the outer ring of thyroxine, as a phenoxide ion, is of major importance in binding to serum proteins, these structural observations may shed light on the mechanisms of thyroxine binding and help to explain binding-affinity differences among the thyroactive compounds.

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The Structure of 1,2-*O*-Ethylene-β-D-glucopyranose at 120 K

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Abstract

$C_8H_{14}O_6$, tetragonal, $I4$, $a = b = 15.545$ (6), $c = 7.703$ (2) Å, $V = 1861.4$ Å^3 at 120 K, $Z = 8$, $D_{calc} = 1.46$ Mg m^{-3}. The 182 structural parameters were refined *versus* the 1219 (84%) most significant unique reflections ($d > 0.71$ Å) collected at 120 K, to a linear R of 0.033. Owing to the 1,2-*O*-ethylene substitution the conformational preference ascribed to the *exo*- anomeric effect is cancelled. The molecule can thus be considered as a 'pseudo-disaccharide' with the glycosidic-link conformation *trans–trans* as described by the conventional torsion angles θ and φ. Both rings of the molecule adopt chair conformations. The pyranose ring is slightly distorted owing to an intermolecular hydrogen bond. Bond distances and angles around the anomeric carbon resemble those found in glycosides with the conventional *gauche–gauche* and

gauche–trans conformations, *viz* C(1)—O(1) and C(1)—O(5) = 1·405 (2) and 1·413 (2) Å, respectively, and O(5)—C(1)—O(1) = 105·2 (1)°.

Introduction

In the conformational analyses of carbohydrates two terms, the anomeric and *exo*-anomeric effects (see *e.g.* Lemieux, Koto & Voisin, 1979; Wolfe, Whangbo & Mitchell, 1979), have been introduced to describe interactions between the atoms in the molecular fragment —C(5)—O(5)—C(1)—O(1)—C(7)— (*cf.* Fig. 1). The preferred chair conformation of the pyranose ring and thus the relative position of O(1), as specified by the torsion angle *θ* over the O(5)—C(1) bond, is to a large extent determined by the anomeric effect. The preferred orientation of the aglycone of a glycoside and thus the relative position of C(7), as specified by the torsion angle *φ* over the C(1)—O(1) bond, is ascribed to the *exo*-anomeric effect.

According to their *θ* and *φ* values, glycopyranosides can generally be divided into two distinct classes, the *gauche–gauche* type for α-glycopyranosides and the *trans–gauche* type for *β*-glycopyranosides (Pérez & Marchessault, 1978). Accordingly, the *exo*-anomeric effect can in general be referred to as the '*gauche* effect', as regards the preferred conformation specified by *φ*, for both α- and *β*-glycopyranosides.

The interactions between the atoms in the molecular fragment discussed have also been shown to affect the bond distances and bond angles. Thus, the two C(1)—O bond lengths are generally significantly shorter than normal C—O bonds (Berman, Chu & Jeffrey, 1967), while the O—C(1)—O angle is about 112° for the *gauche–gauche* and about 107° for the *trans–gauche* conformations (Sundaralingam, 1968).

The present structural investigation of 1,2-*O*-ethylene-*β*-D-glucopyranose was undertaken in order to provide structural data for a carbohydrate with an alternative conformation, *trans–trans*, fixed by the molecular structure. In this molecule, the conformational preference (the *gauche* effect) due to the

exo-anomeric effect is cancelled, which might yield other structural effects. Generally, the molecule can be considered as a 'pseudo-disaccharide' with the glycosidic-link conformation *trans–trans–gauche*, as described by the torsion angles *θ*, *φ* and *χ*, where *χ* is the endocyclic torsion angle over the O(1)—C(7) bond.

Experimental

A crystalline specimen (m.p. 483–484 K), synthetized according to Helferich & Werner (1942), was obtained by slow evaporation of an ethanolic solution. Investigation by single-crystal X-ray photographic and diffractometer techniques indicated *I*4 as the most probable noncentrosymmetric space group. A crystal with the dimensions 0·16 × 0·20 × 0·30 mm was selected for data collection on a computer-controlled diffractometer (CAD-4), using graphite-monochromatized Mo *Kα* radiation and a scintillation detector with pulse-height discrimination. Unit-cell parameters, $a = 15\cdot595$ (6) and $c = 7\cdot754$ (2) Å, were determined at room temperature (294 K) from 13 observed *θ* values ($8\cdot5 < \theta < 12\cdot6°$) with relatively high intensities. If it is assumed that the molecules occupy the general eightfold position of the space group, the unit-cell volume of 1885·8 Å³ implies a volume of 16·8 Å³ per non-hydrogen atom, which by experience is a reasonable value for structures with extensive intermolecular hydrogen bonding. By means of a conventional cryogenic device (*cf.* van Bolhuis, 1971) utilizing a flow of cold nitrogen gas, the single crystal was cooled to 120 K. Remeasurement of the unit-cell parameters at this temperature yielded the values $a = 15\cdot545$ (6) and $c = 7\cdot703$ (2) Å. The intensities of all 1448 unique reflections with $d > 0\cdot71$ Å were collected using the ω–2θ scan technique and a scan interval of $(0\cdot6 + 0\cdot35 \tan\theta)°$. The intensity data were corrected for background, Lorentz and polarization effects and also for the relatively negligible absorption ($\mu = 0\cdot12$ mm⁻¹) effects.

Structure determination

The solution of the crystal structure by means of direct methods created some problems. The preliminary *E* maps were contaminated by several spurious peaks, while there were no reasonable peaks corresponding to positions for the non-hydrogen atoms furthest away from the plane through the molecule. Eventually, a chemically reasonable model consistent with several of the peaks in an *E* map, based on a molecular fragment of ten atoms, refined satisfactorily with full-matrix least-squares techniques. The 182 parameters describing anisotropically vibrating non-hydrogen atoms and isotropic H atoms (located from difference electron
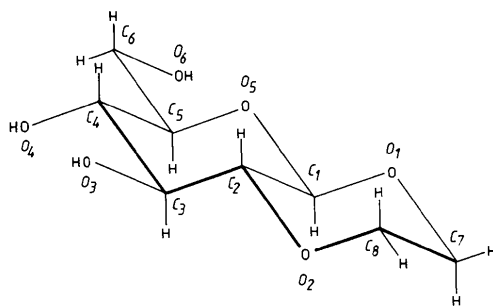

Fig. 1. Schematic structural formula of 1,2-*O*-ethylene-*β*-D-glucopyranose, with atomic labels used in the present study.

density maps) were refined *versus* the 1219 most significant structure values $[|F_o| \geq 6\sigma(F_o)]$ by minimizing $\sum w\||F_o| - |F_c|\|^2$. The individual weights were estimated as $w = 1/[\sigma^2(I_o) + (kI_o)^2/4I_o]$, where $\sigma(I_o)$ values are the e.s.d.'s of the observed intensities from counting statistics and where the constant k was

Table 1. *Fractional coordinates* $(\times 10^4)$ *and equivalent isotropic temperature factors* (*cf. Hamilton*, 1959) *for the nonhydrogen atoms*

E.s.d.'s are in parentheses.

	x	y	z	U_{eq} (Å$^2 \times 10^4$)
O(1)	2666 (1)	2146 (1)	3379 (4)	148 (4)
O(2)	842 (1)	2215 (1)	3560 (4)	173 (4)
O(3)	158 (1)	3834 (1)	4625 (4)	181 (5)
O(4)	1106 (1)	5291 (1)	3130 (4)	176 (5)
O(5)	2745 (1)	3584 (1)	3451 (3)	129 (4)
O(6)	3776 (1)	5087 (1)	2580 (4)	202 (5)
C(1)	2203 (1)	2895 (1)	2965 (4)	125 (5)
C(2)	1366 (1)	2933 (1)	4006 (4)	124 (5)
C(3)	897 (1)	3753 (1)	3550	134 (5)
C(4)	1495 (1)	4529 (1)	3794 (4)	130 (5)
C(5)	2381(1)	4398 (1)	2954 (4)	121 (5)
C(6)	3000 (1)	5092 (1)	3553 (4)	169 (6)
C(7)	2141 (1)	1403 (1)	2996 (5)	184 (6)
C(8)	1301 (1)	1437 (1)	3979 (4)	200 (6)

Table 2. *Fractional coordinates* $(\times 10^3)$ *and isotropic temperature factors for the hydrogen atoms*

E.s.d.'s are in parentheses.

	x	y	z	U (Å$^2 \times 10^3$)
H(1)	208 (2)	292 (2)	173 (4)	10 (6)
H(2)	154 (2)	292 (2)	518 (4)	11 (6)
H(3)	75 (2)	372 (2)	227 (4)	21 (7)
H(4)	159 (2)	462 (2)	510 (4)	12 (6)
H(5)	236 (2)	443 (2)	172 (3)	8 (5)
H(6a)	311 (2)	501 (2)	486 (4)	24 (7)
H(6b)	272 (2)	565 (2)	339 (4)	15 (6)
H(7a)	203 (2)	137 (2)	172 (4)	12 (6)
H(7b)	249 (2)	92 (2)	337 (4)	18 (6)
H(8a)	147 (2)	148 (2)	521 (4)	14 (6)
H(8b)	90 (2)	98 (2)	361 (4)	22 (7)
H(O3)	−25 (2)	415 (2)	421 (5)	34 (9)
H(O4)	110 (2)	526 (2)	205 (5)	42 (10)
H(O6)	400 (2)	464 (2)	267 (4)	22 (7)

Table 3. *Bond distances* (Å) *involving non-hydrogen atoms, with e.s.d.'s in parentheses*

C(1)–C(2)	1·530 (3)	C(7)–C(8)	1·510 (3)
C(2)–C(3)	1·510 (3)	C(8)–O(2)	1·441 (2)
C(3)–C(4)	1·534 (3)	O(2)–C(2)	1·425 (2)
C(4)–C(5)	1·535 (3)	C(3)–O(3)	1·422 (2)
C(5)–O(5)	1·438 (2)	C(4)–O(4)	1·425 (2)
O(5)–C(1)	1·413 (2)	C(5)–C(6)	1·517 (3)
C(1)–O(1)	1·405 (2)	C(6)–O(6)	1·420 (2)
O(1)–C(7)	1·445 (2)		

Table 4. *Bond angles* (°) *involving non-hydrogen atoms, with e.s.d.'s in parentheses*

O(5)–C(1)–C(2)	109·8 (2)	O(4)–C(4)–C(5)	109·9 (2)
O(1)–C(1)–C(2)	110·4 (2)	C(4)–C(5)–O(5)	110·9 (1)
O(1)–C(1)–O(5)	105·2 (1)	C(4)–C(5)–C(6)	110·3 (2)
C(1)–C(2)–C(3)	108·7 (2)	C(6)–C(5)–O(5)	107·2 (1)
C(1)–C(2)–O(2)	109·3 (2)	C(5)–O(5)–C(1)	111·2 (1)
O(2)–C(2)–C(3)	109·2 (1)	C(5)–C(6)–O(6)	112·0 (2)
C(2)–C(3)–C(4)	110·0 (1)	C(1)–O(1)–C(7)	109·1 (1)
C(2)–C(3)–O(3)	109·2 (2)	O(1)–C(7)–C(8)	111·0 (2)
O(3)–C(3)–C(4)	110·4 (2)	C(7)–C(8)–O(2)	110·2 (2)
C(3)–C(4)–C(5)	112·8 (1)	C(8)–O(2)–C(2)	108·7 (1)
C(3)–C(4)–O(4)	110·6 (2)		

estimated from measurements of 140 symmetry-equivalent reflections to be 0·04. The origin along the polar axis c was specified by fixing the z value of C(3) during the refinements. The final linear R was 0·033 and $R_w = 0·031$, where $R_w = [\sum w\||F_o| - |F_c|\|^2/ \sum w|F_o|^2]^{1/2}$. The atomic scattering factors were those of *International Tables for X-ray Crystallography* (1974). For the longer crystallographic calculations a local version of the program system *SHELX* 78 (Sheldrick, 1978) was used, and for shorter ones the interactive system *XTAPL* (R. Norrestam) was used.

The atomic coordinates, intramolecular bond distances and bond angles are listed in Tables 1, 2, 3 and 4.* The atomic labels used are indicated in Fig. 1.

Discussion

The molecular packing in the crystal structure and the intermolecular hydrogen bonds are shown in Fig. 2. The crystal structure can be considered as composed of molecular layers along [001], separated by $c/2$ (3·85 Å). For clarity, only one such layer is shown in Fig. 2. Four molecules are linked together around the fourfold axis through $\frac{1}{2},\frac{1}{2},0$ by hydrogen bonds between the hydroxy groups at C(6), *e.g.* O(6)–H···O(6; $1 - y, x, z$) with O···O = 2·697 Å and OHO = 157°. These 'tetramers' are held together within the layers by hydrogen bonds of the type O(3)–H···O(4; $-x, 1 - y, z$) (O···O = 2·654 Å and OHO = 180°), around the twofold axes. One hydrogen bond per molecule, O(4)–H···O(3; $\frac{1}{2} - y, \frac{1}{2} + x, -\frac{1}{2} + z$), is formed between the layers (O···O 2·709 Å and OHO = 177°). This hydrogen-bond scheme and the layer-type structure are reflected in the anisotropic decrease of the unit-cell parameters when the crystals are cooled from 294 to 120 K. Thus, the a axis decreases by 0·3%, while c decreases more rapidly by 0·7%. None of the

three endocyclic oxygens O(1), O(2) and O(5) participates in any hydrogen bonds.

As is evident from Fig. 3, the two rings of the molecules adopt the chair conformation ($^4C_1$ and $^2C_7$, respectively). An evaluation of the puckering parameters Q_p, θ_p and φ_p (mod 60°) (Cremer & Pople, 1975) yields the values 0·573 (2) Å, 9·5 (2)° and 0 (1)° for the pyranose ring and 0·587 (2) Å, 2·6 (2)° and −3 (1)° for the dioxane ring. A calculation of the puckering parameters for an average glucopyranose ring from the coordinates given by Sheldrick & Akrigg
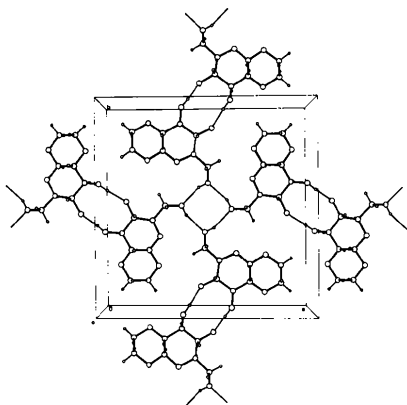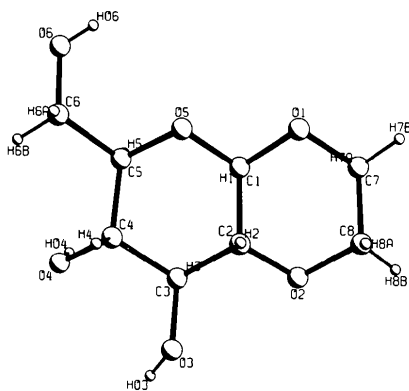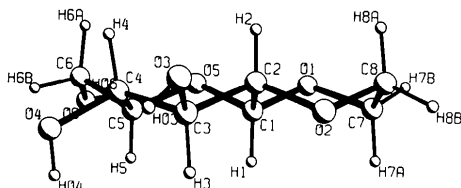

Fig. 2. Packing diagram of the crystal structure viewed along the c axis. For clarity only one layer of molecules has been plotted. Intermolecular hydrogen bonds are indicated by thin lines.

(a)

(b)

Fig. 3. Conformation of the 1,2-O-ethylene-β-D-glucopyranose molecule viewed (a) perpendicular and (b) parallel to a plane through the molecule.

(1980) yields the values 0·57 (2) Å, 2 (2)° and −4 (60)°, respectively. From the θ_p and φ_p values it might be concluded that the pyranose ring in the ethyleneglucose molecule is distorted more towards a half-boat conformation than the average glucopyranose ring, while the dioxane ring has a rather regular chair conformation. From Fig. 3(b) it is evident that this distortion is mainly due to a displacement of C(4) from its ideal position. This is also shown by the numerical values of the torsion angles (Table 5) involving C(4), which are about 7° smaller than those of an average pyranose ring. Thus, C(4) is located 0·192 (4) Å from a least-squares plane through the atoms −C(3)−C(2)−O(2)−C(8)−, which all deviate less than 0·005 (4) Å from this plane. As discussed above, the crystal structure is composed of layers of hydrogen-bonded molecules. The only interlayer hydrogen bond is formed between the hydroxyl groups at C(3) and C(4). This hydrogen bond is perpendicular to the layers, and to the average molecular plane, and apparently imposes some strain on the molecule. Since C(4) has a more flexible position within the molecule than C(3), it is likely that the ring distortion in the vicinity of C(4) is due to the existence of this interlayer hydrogen bond. Such distortions of pyranose rings due to hydrogen bonding are fairly common. Thus, different hydrogen-bond schemes are probably one of the major reasons for the relatively high e.s.d.'s (cf. Table 6) obtained when calculating average ring conformations. This limits the relevance of such average structures.

Table 5. Endocyclic torsion angles (°)

The average values were calculated from the average coordinates (121 rings) given by Sheldrick & Akrigg (1980).

	Present study	Average		Present study
C(1)–C(2)	63·4 (2)	57 (2)	C(2)–C(1)	61·9 (2)
C(2)–C(3)	−53·4 (2)	−54 (2)	C(1)–O(1)	59·0 (2)
C(3)–C(4)	48·0 (2)	55 (2)	O(1)–C(7)	−57·4 (2)
C(4)–C(5)	−49·5 (2)	−56 (3)	C(7)–C(8)	57·6 (2)
C(5)–O(5)	58·7 (2)	62 (3)	C(8)–O(2)	−59·1 (2)
O(5)–C(1)	−66·4 (2)	−62 (2)	O(2)–C(2)	60·4 (2)

Table 6. Geometry for the four-atom sequence
C(5)–O(5)–C(1)–O(1)

The average values are taken from Pérez & Marchessault (1978).

	Present study (trans–trans)	Average gauche–gauche	Average trans–gauche
C(5)–O(5)	1·438 (2) Å	1·438 Å	1·439 Å
O(5)–C(1)	1·413 (2)	1·417	1·428
C(1)–O(1)	1·405 (2)	1·409	1·387
C(5)–O(5)–C(1)	111·2 (1)°	113·9°	111·8°
O(5)–C(1)–O(1)	105·2 (1)	111·7	107·3

The torsion angles θ, φ and ψ, frequently used to describe the conformations of glycosidic linkages as discussed above, are 174·8 (2), 177·4 (2) and −57·4 (2)°, respectively. The close agreement with the ideal values for a *trans–trans–gauche* conformation is obviously due to the restrictions of the molecular flexibility imposed by the attached dioxane ring.

The average endocyclic C—C bond length in the pyranose ring is 1·527 (12) Å, which agrees well with that, 1·526 (3) Å, calculated from the data on averaged glucopyranose rings. The average endocyclic bond angles are 110·4 (14)° for the pyranose ring and 109·8 (9)° for the dioxane ring. The largest angular deviation, 2·3°, from these averages occurs for C(3)—C(4)—C(5) and is possibly also the result of the molecular distortion caused by the interlayer hydrogen bonding.

After classifying carbohydrate molecules into two distinct types according to their θ and φ values, *viz* the *gauche–gauche* ($52 \leq \theta \leq 67°$ and $75 \leq \varphi \leq 121°$) and *trans–gauche* ($171 \leq \theta \leq 193°$ and $-71 \leq \varphi \leq 105°$) types, Pérez & Marchessault (1978) have calculated the average geometries of the molecular fragment —C(5)—O(5)—C(1)—O(1)—. The present study concerns a molecule of a third class, the *trans–trans* type ($\theta = 174·8°$ and $\varphi = 177·4°$). Thus, the *exo*-anomeric effect, which stabilizes φ values corresponding to a *gauche* conformation, has been eliminated in the present structure by formation of the dioxane ring. As

shown in Table 6, the bond angles and bond distances are somewhat different from those of the other two types. Thus, the bond-angle distribution in 1,2-*O*-ethylene-β-D-glucopyranose resembles that of the *trans–gauche* type, while the bond-distance distribution is more similar to the *gauche–gauche* type.

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Structure Determination of the Mannotrehalose Derivative 6-*O*-Acetyl-2-azido-3,4-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl 2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranoside

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Abstract

The crystal structure of the title compound, $C_{36}H_{43}N_3O_{15}$, $M_r = 757·8$, is orthorhombic, $P2_12_12_1$, with $a = 18·414$ (6), $b = 17·025$ (5), $c = 12·918$ (4) Å, $Z = 4$, $V_c = 4050$ (3) Å^3, $D_x = 1·235$ Mg m^{-3}, μ(Cu $K\alpha$) = 0·833 mm^{-1}. The structure was solved by direct methods, and the data were refined to an R value of 0·065 for 3802 reflections. In the C(5)—O(5)—C(1)—O(1)—C(1')—O(5')—C(5') bond sequence, which is specific for carbohydrates of trehalose type, the C(1)—O bonds tend to be 0·2 Å shorter than the