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SYNTHESIS AND CRYSTAL STRUCTURE OF 3-DEOXY-3-FLUORO-1,2:5,6-DI-O-ISOPROPYLIDENE-α-D-GLUCOFURANOSE

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SUMMARY

3-Deoxy-3-fluoro-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose 4 has been synthesized and obtained crystalline. X-Ray structure analysis of the crystals has been performed. The space group was determined to be C2, a = 20.883 (12). b = 5.599 (1), c = 24.866 (13) Å, β = 111.03 (3)° Two independent molecules are present in the asymmetric unit: on the basis of puckering parameters they show different conformations, which can be ascribed to crystal-packing requirements.

INTRODUCTION

In functional studies of the human brain, glucose derivatives, labelled with short-lived positron emitters, find a broad application [1]. For instance, (^{18}F)-3-deoxy-3-fluoro-D-glucose ('(^{18}F)3-FDG') can be used as an indicator for local unidirectional transport studies through the blood-brain-barrier. The related equilibrium constants for this compound are very similar to those obtained for D-glucose [2,3]. Contrary to 2-FDG, 3-FDG is not metabolized, hence it is not trapped inside the brain cell. Local defects of the blood-

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brain-barrier as well as cerebral diseases caused by this physiological background, can be successfully studied using this radiopharmaceutical and positron emission tomography [4,5].

3-FDG is synthesized by nucleophilic substitution of the triflyl group in 1,2:5,6-di-O-isopropylidene-3-trifluoromethanesulfonyloxy-α-D-allofuranose 3 with fluoride ions to 3-deoxy-3-fluoro-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose 4 [6] followed by acid hydrolysis to 3-deoxy-3-fluoro-D-glucose (Fig. 1). Compound 4 however, was previously always obtained in the form of a noncrystallizable oil [7,8], which gives normally non-reproducible yield in (^{18}F)3-FDG. Thus, the aim of this investigation was (a): to synthesize the compound 4 in crystallizable form and, (b): for evidence, to detect the crystal structure of this compound.

RESULTS AND DISCUSSION

For the definitive identification of the (^{18}F)3-FDG an inactive synthesis was carried out (Fig. 1) according to prior publications [6-10].

The starting material was 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose 1 whi was converted to the epimer 1,2:5,6-di-O-isopropylidene-α-D-allofuranose 2 by oxidation of the C(3)-hydroxyl group with acetic anhydride in DMSO, followed by reduction of the resulting ketone with sodium borohydride [11].

To obtain very pure final products,however,it was necessary to change the literature procedures in two points:

a) the oxidation of the starting material was carried out in two short steps, instead of only a long one, to avoid the insertion of one O-atome in the furanose ring [12],
b) the reduction to the product 2 was carried out with a large excess of sodium borohydride.

With these improvements the title compound 4 3-deoxy-3-fluoro-1,2:5,6-di-O isopropylidene-α-D-glucofuranose was obtained in the form of colorless needles, purified for elemental analysis by recrystallisation from petroleum ether (65-80°) to m.p. 106-107°.

The results of the elemental analysis and the theoretical molecular formula $C_{12}H_{19}FO_5$ are compared in the experimental part.

Within the normal error limits, the correctness of the formula is confirmed.

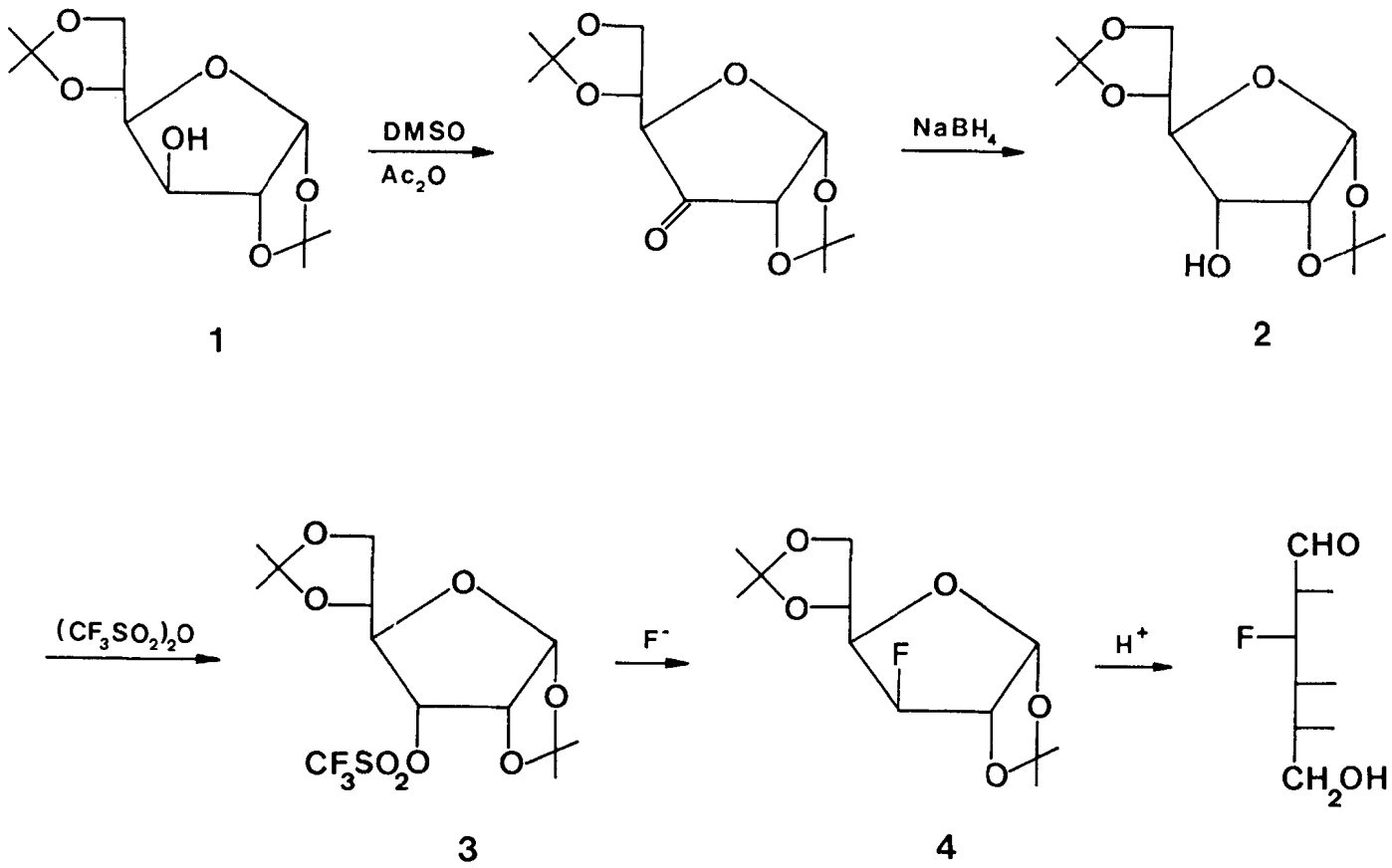

Fig. 1. Synthesis of 3-deoxy-3-fluoro-D-glucose

X-Ray analysis of the title compound 4 showed two independent molecules to be present in an asymmetric unit. Their geometries are shown in Fig. 2a and 2b. The small differences between the two independent molecules in the asymmetric unit (Fig. 3) can be ascribed to packing requirements to achieve the lowest energy for the crystal.

The corresponding bond lengths and angles in the two molecules are similar: small but significant differences between the furanose and the isopropylidene rings can be observed mainly in the torsion angles along the junction C(4)-C(5) (Table 5). Some differences in the conformation of the rings themselves were observed: the puckering parameters [13] and the asymmetric parameters [14] are reported in Table 6.

In particular, it can be noticed that in molecule 1 (Fig. 2a) both the furanose and the fused isopropylidene rings are midway between the twist and the envelope (ϕ_2 = n.18 with n even) conformations, while in molecule 2 (Fig. 2b) they are in the twist conformation (ϕ_2 = n.18 with n odd).

The free isopropylidene rings are in a slightly distorted twist conformation (molecule 1) and envelope conformation (molecule 2).

Bond lengths and angles of the fused and the free isopropylidene rings and of the furanose ring are close to those reported for the related compounds spiro-3,4'-R-(3,3-dideoxy-1,2:5,6-di-O-isopropylidene-α-D-ribo-hexafurano-se)-3'-S(and 3'-R)-acetamido-2'-pyrrolidones [15].

Only the O(1)-C(5) bond (1.382 and 1.361 Å for the two molecules, respectively) is significantly shorter than that reported previously (1.405-1.418 Å) [15]. The carbon fluorine bond (1.450-1.427 Å respectively) is considerably longer than quoted (1.392-1.410 Å) for a fluorine atom bonded to a pyranose ring [16,17].

No hydrogen bond is possible in compound 4: only weak intermolecular interactions of the type O....H-C are present, among which the shortest are O(1B)...C(4B), 3.43 Å; O(1)...C(4), 3.49 Å; O(6)...C(13), 3.49 Å; O(12B)...C(17B), 3.49 Å; O(10B)...C(15B), 3.55 Å; O(12)...C(17), 3.58 Å; O(3)...C(16), 3.60 Å.

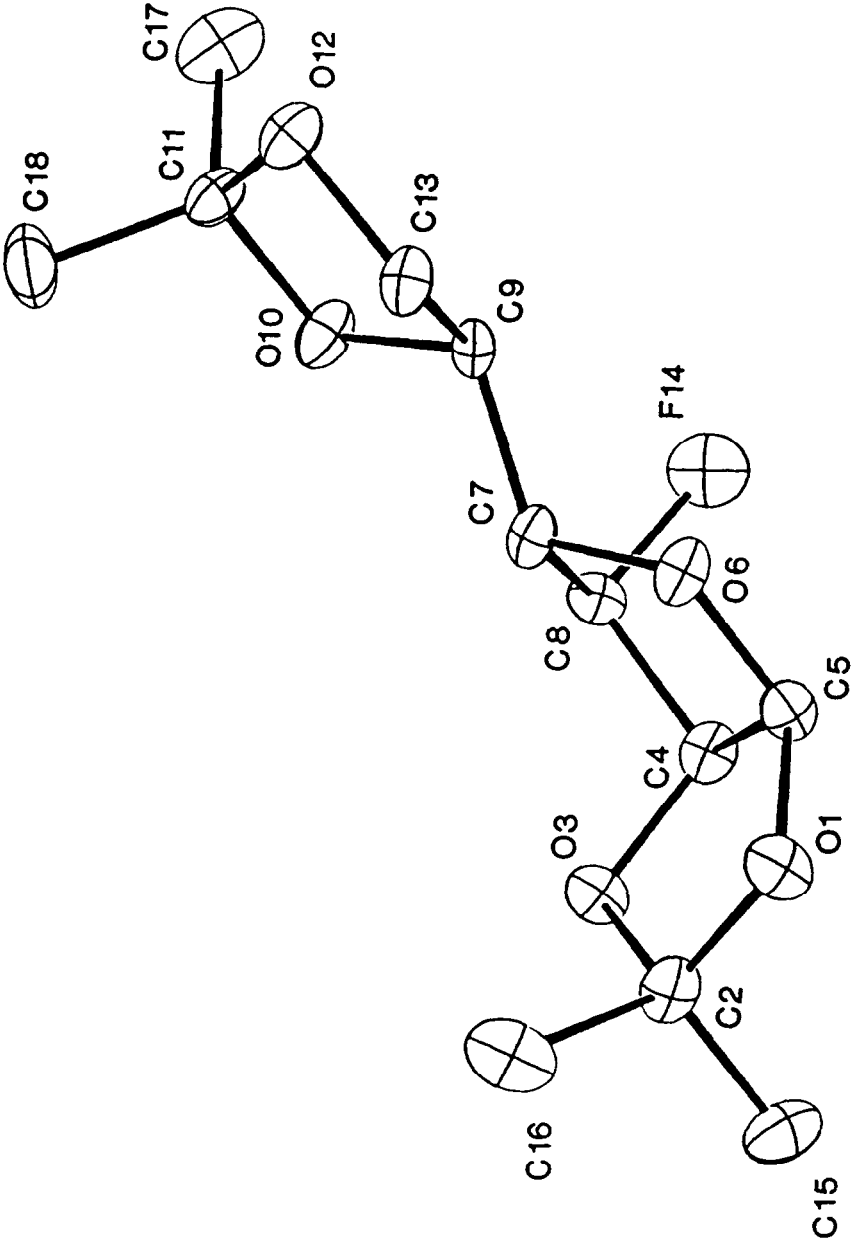

Fig. 2a. (see overleaf for legend)

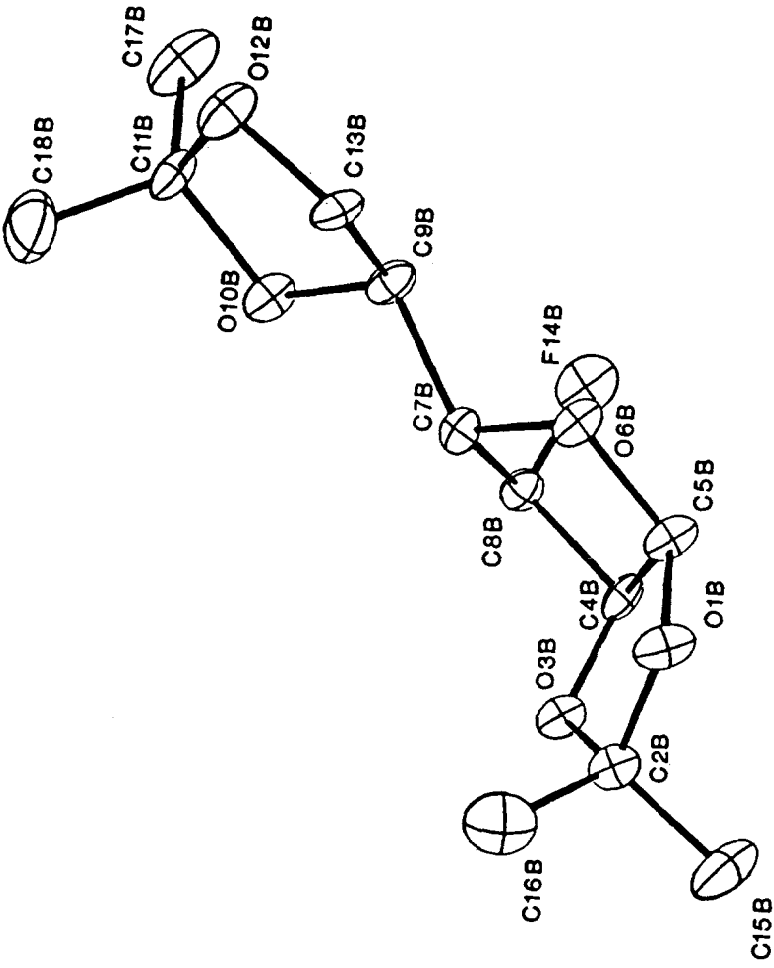

Fig. 2 a and b. ORTEP perspective view and atomic numbering for the two independent molecules in the asymmetric unit.

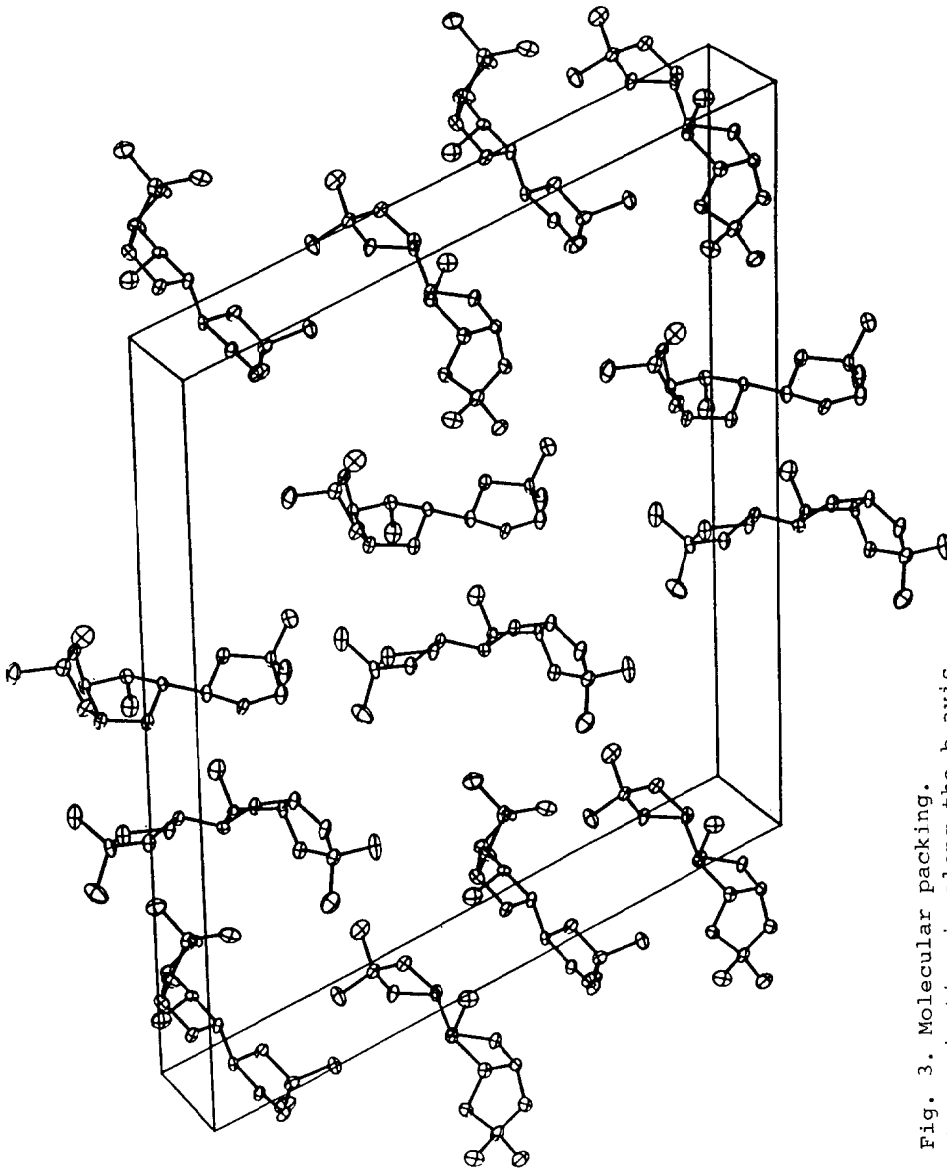

Fig. 3. Molecular packing.
The projection is along the b axis.

EXPERIMENTAL

Synthesis

1,2:5,6-Di-O-isopropylidene-α-D-allofuranose 2

6 g of 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (Fluka) were oxidized with a mixture of 20 ml of acetic anhydride and 60 ml dry dimethylsulfoxide in a 250 ml round bottomed flask at 70° (water bath). After 1 hour the solution was distilled in vacuo. The residue was treated again with a fresh mixture of 10 ml of acetic anhydride and 50 ml of dry dimethylsulfoxide, 1 hour at 70°. The solution was distilled in vacuo, and the remaining yellow oil was washed two times with petroleum ether (60-80°), then dried overnight in vacuo at room temperature.
This oil was now dissolved in 100 ml of 70 % ethanol and 5 g of sodium borohydride were added under careful stirring. The temperature was kept below 20° (water bath). After the addition of sodium borohydride was completed, stirring was continued for 5 hours at room temperature. The reaction mixture was shaken with 200 ml of water and extracted with ethyl acetate (3 x 100 ml). After removal of the solvent on a rotary evaporator, a white crystalline residue remained, purified by repeated crystallization from ligroin to constant melting point: 4,4 g, m.p. 70-71°, yield 88 %.

1,2:5,6-Di-O-isopropylidene-3-trifluoromethanesulfonyloxy-α-D-allofuranose 3

2.6 g 1,2:5,6-di-O-isopropylidene-α-D-allofuranose 2 were dissolved in 30 ml methylene chloride and 5 ml pyridine and cooled to -20° in an ice/acetone bath. A solution of 2 ml of trifluoromethanesulfonic anhydride in 10 ml methylene chloride was added dropwise. After addition was complete, the solution was allow to stir for 2 hours at -20° and then poured into 100 ml of water. It was extracted with methylene chloride (3 x 100 ml) and dried over sodium sulfate. After removal of the solvent in vacuo the residual yellow oil was dissolved in toluene and evaporated in vacuo. This procedure was repeated till no more pyridine was detectable in the residue. n-Hexane extraction of the residue followed by in vacuo solvent removal gave the triflate ester 3: 3.6 g, m.p. 45-46° from petroleum ether (40-60°), yield 90 %.

3-Deoxy-3-fluoro-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose 4

4,5 g 1,2:5,6-di-O-isopropylidene-3-trifluoromethanesulfonyloxy-α-D-allofuranose and 2 g dry cesium fluoride were dissolved in 150 ml dimethylformamide. The solution was refluxed for 30 min., then the solvent was removed in vacuo. The dark brown residue was refluxed 15 minutes with 100 ml petroleum ether (65-100°), then filtered. After cooling, the product 4 crystallized in white needles: 1.4 g, m.p. 106-107°, yield 43 %.

Elemental analysis for $C_{12}H_{19}FO_5$: Calcd. C 55.0, H 7.2, F 7.2 %; Found C 55.0, H 7.3, F 7.1 %.

X-Ray analysis

X-Ray single-crystal analysis and data collection were performed on a Philips PW 1100 4-circle diffractometer. The crystal data of 3-deoxy-3-fluoro-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose 4 are shown in Table 1. Accurate lattice parameters were measured from 25 rows in the θ range 2-25° by using a locally modified version of the Philips LAT routine. Data collection was performed in the θ range 2-22° (Mo-K_α radiation, λ = 0.7107 Å). Two equivalent monoclinic reflections were measured and then merged after correction for absorption [18] and for Lp factors.

Atomic coordinates were determined by direct methods [19], except for nine non-hydrogen atoms which were subsequently located on a Fourier map. The isotropic full-matrix least-squares refinement was carried out with the 1864 independent reflections by using a locally modified version of the computer program ORFLS [20] and by giving each reflection a weight based on counting statistics ($w = 1/\sigma(F_0)$).

The position of all the H atoms were calculated geometrically [21] and included into the structure factor calculations but not into the subsequent anisotropic least-squares refinement. The final discrepancy index was 3.43 %

The atomic scattering factors for neutral atoms were taken from International Tables for X-Ray crystallography [22]. The program PARST [23] was used to calculate molecular parameters. Figures were drawn with ORTEP II [24].

Atomic coordinates and equivalent isotropic temperature factors, as well as bond distances, bond angles and torsion angles for non-hydrogen atoms are reported in Tables 2 to 6.

TABLE 1

Crystal data of 3-Deoxy-3-fluoro-1,2-5,6-di-O-isopropylidene-α-glucofuranose 4

Chemical formula	$C_{12}H_{19}FO_5$
Crystal size	1 x 0.33 x 0.05 mm
Cell dimensions	a = 20.883(12), b = 5.599(1) Å c = 24.866(13) Å β = 111.03(3)°
Cell volume	2713.9 Å^3
Space group	C2 Z = 8
θ_{max} (λ = 0.7107 Å)	22°
Scan mode	ω
Range of h k l	from 0,-22,0 to 11,22,26
Number of check reflections	3
Measured at intervals	4 h
Intensity variation (%)	2.8
μ	1.009 cm^{-1}
Reflections measured	3303
Unique reflections	1864
Merging R (%)	6.0
Final R_w (%)	3.4
$(\Delta/\sigma)_{max}$ in the final LS cycle	0.25

TABLE 2

Atomic fractional coordinates and equivalent isotropic temperature factors (A^2) for non-hydrogen atoms. E.s.d. in parentheses

Atom	x/a	y/b	z/c	B_{eq}
O(1)	-0.0268 (2)	0.5679 (0)	-0.1846 (2)	4.1 (2)
C(2)	0.0139 (3)	0.4739 (15)	-0.2152 (3)	4.0 (3)
O(3)	0.0447 (2)	0.2576 (11)	-0.1858 (2)	3.6 (2)
C(4)	0.0025 (3)	0.1765 (14)	-0.1554 (2)	3.4 (3)
C(5)	-0.0287 (3)	0.4080 (14)	-0.1428 (3)	3.6 (3)
O(6)	0.0134 (2)	0.4768 (10)	-0.0863 (2)	3.3 (2)
C(7)	0.0725 (3)	0.3276 (14)	-0.0632 (2)	3.1 (2)
C(8)	0.0493 (3)	0.0935 (14)	-0.0956 (2)	3.2 (3)
C(9)	0.0965 (3)	0.3148 (14)	0.0012 (2)	3.2 (2)
O(10)	0.1576 (2)	0.1833 (10)	0.0199 (2)	4.2 (2)
C(11)	0.1995 (3)	0.2689 (17)	0.0755 (2)	3.9 (3)
O(12)	0.1648 (2)	0.4741 (10)	0.0868 (2)	3.9 (2)
C(13)	0.1183 (3)	0.5522 (15)	0.0320 (3)	3.6 (2)
F(14)	0.0069 (2)	-0.0321 (10)	-0.0698 (1)	6.1 (2)
C(15)	-0.0312 (3)	0.4111 (16)	-0.2766 (3)	6.0 (3)
C(16)	0.0719 (3)	0.6394 (14)	-0.2119 (3)	5.7 (3)
C(17)	0.2035 (4)	0.0909 (15)	0.1213 (3)	6.2 (3)
C(18)	0.2683 (3)	0.3390 (19)	0.0746 (3)	6.6 (3)
O(1B)	0.8094 (2)	0.1426 (11)	0.3418 (2)	4.4 (2)
C(2B)	0.7854 (3)	0.0291 (15)	0.2865 (3)	4.2 (3)
O(3B)	0.8220 (2)	-0.1911 (11)	0.2950 (2)	3.7 (2)
C(4B)	0.8420 (3)	-0.2554 (14)	0.3537 (3)	3.3 (3)
C(5B)	0.8445 (3)	-0.0128 (14)	0.3842 (2)	3.7 (3)
O(6B)	0.9152 (2)	0.0494 (10)	0.4098 (2)	3.4 (2)
C(7B)	0.9553 (3)	-0.1057 (14)	0.3863 (2)	3.0 (2)
C(8B)	0.9161 (3)	-0.3417 (14)	0.3763 (2)	3.4 (2)
C(9B)	1.0286 (3)	-0.1146 (13)	0.4296 (2)	3.6 (3)
O(10B)	1.0682 (2)	-0.2373 (11)	0.4030 (2)	3.9 (2)
C(11B)	1.1388 (3)	-0.1549 (15)	0.4312 (3)	4.1 (3)
O(12B)	1.1347 (2)	0.0555 (10)	0.4618 (2)	4.7 (2)
C(13B)	1.0650 (3)	0.1268 (14)	0.4447 (2)	3.6 (2)
F(14B)	0.9302 (2)	-0.4637 (10)	0.4297 (2)	6.1 (2)
C(15B)	0.7101 (3)	-0.0105 (18)	0.2664 (3)	7.8 (3)
C(16B)	0.8066 (4)	0.1742 (16)	0.2453 (3)	7.3 (4)
C(17B)	1.1777 (3)	-0.3376 (15)	0.4764 (3)	6.6 (3)
C(18B)	1.1680 (3)	-0.1043 (19)	0.3864 (3)	8.5 (4)

TABLE 3

Bond distances (Å) for non-hydrogen atoms.
E.s.d. in parentheses

O(1)-C(2)	1.429 (9)	O(1B)-C(2B)	1.431 (8)
O(1)-C(5)	1.383 (8)	O(1B)-C(5B)	1.361 (8)
C(2)-O(3)	1.440 (9)	C(2B)-O(3B)	1.426 (10)
C(2)-C(15)	1.520 (8)	C(2B)-C(15B)	1.487 (8)
C(2)-C(16)	1.503 (10)	C(2B)-C(16B)	1.495 (11)
O(3)-C(4)	1.426 (8)	O(3B)-C(4B)	1.411 (7)
C(4)-C(5)	1.532 (10)	C(4B)-C(5B)	1.548 (11)
C(4)-C(8)	1.529 (7)	C(4B)-C(8B)	1.523 (8)
C(5)-O(6)	1.419 (7)	C(5B)-O(6B)	1.426 (7)
O(6)-C(7)	1.428 (7)	O(6B)-C(7B)	1.465 (9)
C(7)-C(8)	1.524 (10)	C(7B)-C(8B)	1.527 (10)
C(7)-C(9)	1.499 (8)	C(7B)-C(9B)	1.524 (7)
C(8)-F(14)	1.450 (8)	C(8B)-F(14B)	1.427 (8)
C(9)-O(10)	1.400 (7)	C(9B)-O(10B)	1.409 (8)
C(9)-C(13)	1.520 (11)	C(9B)-C(13B)	1.529 (10)
O(10)-C(11)	1.428 (7)	O(10B)-C(11B)	1.462 (7)
C(11)-O(12)	1.440 (10)	C(11B)-O(12B)	1.422 (10)
C(11)-C(17)	1.493 (11)	C(11B)-C(17B)	1.522 (10)
C(11)-C(18)	1.496 (10)	C(11B)-C(18B)	1.475 (11)
O(12)-C(13)	1.430 (7)	O(12B)-C(13B)	1.419 (7)

REFERENCES

1 M.E. Phelps, J.C. Mazziotta and S.C. Huang, J. Cereb. Blood Flow Metab. 2 (1982) 113.

2 J.E.G. Barnett, G.D. Holman and K.A. Munday, Biochem. J. 131 (1973) 211

3 J.E.G. Barnett, Carbon Fluorine Compounds, Ciba Foundation Symposium (1972).

4 G.J. Riley and N.F. Taylor, Biochem. J. 135 (1973) 773.

5 K. Vyska, M. Profant, F. Schwier, E.J. Knust, H.J. Machulla, H.M. Mehdorn, W.H. Knapp, G. Spohr, R. von Seggern, I. Kimmling, V. Becker and L.E. Feinendegen in Tumor Cell Physiology and Positron-Emission Tomography, W.H. Knapp and K. Vyska eds., Springer, Berlin, Heidelberg, New York, Tokyo (1984) 37.

6 R.W. Binkley, M.G. Ambrose and D.G. Hehemann, J. Org. Chem. 45 (1980), 4387.

7 T.J. Tewson and M.J. Welch, J. Org. Chem. 43 (1978) 1090.

8 A.B. Foster, R. Hems and J.M. Weber, Carbohydr. Res. 5 (1967) 292.

9 M. Argentini, J. Müller and P. Bläuenstein, unpublished results (1984).

TABLE 4

Bond angles (°) for non-hydrogen atoms. E.s.d. in parentheses

C(2)-O(1)-C(5)	110.1	(4)	C(2B)-O(1B)-C(5B)	111.5	(6)
O(1)-C(2)-C(16)	111.4	(6)	O(1B)-C(2B)-C(16B)	109.3	(6)
O(1)-C(2)-C(15)	110.3	(6)	O(1B)-C(2B)-C(15B)	110.7	(6)
O(1)-C(2)-O(3)	106.4	(5)	O(1B)-C(2B)-O(3B)	104.9	(5)
C(15)-C(2)-C(16)	113.2	(6)	C(15B)-C(2B)-C(16B)	112.8	(7)
O(3)-C(2)-C(16)	106.7	(7)	O(3B)-C(2B)-C(16B)	107.2	(7)
O(3)-C(2)-C(15)	108.5	(6)	O(3B)-C(2B)-C(15B)	111.5	(7)
C(2)-O(3)-C(4)	106.8	(6)	C(2B)-O(3B)-C(4B)	108.5	(6)
O(3)-C(4)-C(8)	108.1	(6)	O(3B)-C(4B)-C(8B)	110.3	(6)
O(3)-C(4)-C(5)	103.1	(6)	O(3B)-C(4B)-C(5B)	103.2	(6)
C(5)-C(4)-C(8)	103.3	(6)	C(5B)-C(4B)-C(8B)	104.3	(6)
O(1)-C(5)-C(4)	105.4	(5)	O(1B)-C(5B)-C(4B)	105.5	(5)
C(4)-C(5)-O(6)	105.9	(6)	C(4B)-C(5B)-O(6B)	106.2	(6)
O(1)-C(5)-O(6)	113.2	(6)	O(1B)-C(5B)-O(6B)	111.9	(6)
C(5)-O(6)-C(7)	112.2	(5)	C(5B)-O(6B)-C(7B)	109.1	(5)
O(6)-C(7)-C(9)	111.5	(6)	O(6B)-C(7B)-C(9B)	108.1	(5)
O(6)-C(7)-C(8)	103.1	(6)	O(6B)-C(7B)-C(8B)	103.2	(6)
C(8)-C(7)-C(9)	116.4	(6)	C(8B)-C(7B)-C(9B)	115.5	(6)
C(4)-C(8)-C(7)	102.9	(6)	C(4B)-C(8B)-C(7B)	101.5	(6)
C(7)-C(8)-F(14)	108.2	(6)	C(7B)-C(8B)-F(14B)	110.1	(6)
C(4)-C(8)-F(14)	107.3	(6)	C(4B)-C(8B)-F(14B)	109.8	(6)
C(7)-C(9)-C(13)	114.9	(6)	C(7B)-C(9B)-C(13B)	115.4	(6)
C(7)-C(9)-O(10)	107.2	(6)	C(7B)-C(9B)-O(10B)	107.1	(5)
O(10)-C(9)-C(13)	102.7	(6)	O(10B)-C(9B)-C(13B)	102.9	(6)
C(9)-O(10)-C(11)	108.3	(6)	C(9B)-O(10B)-C(11B)	106.4	(5)
O(10)-C(11)-C(18)	109.4	(6)	O(10B)-C(11B)-C(18B)	108.5	(6)
O(10)-C(11)-C(17)	111.2	(6)	O(10B)-C(11B)-C(17B)	108.7	(7)
O(10)-C(11)-O(12)	106.3	(5)	O(10B)-C(11B)-O(12B)	105.9	(7)
C(17)-C(11)-C(18)	113.3	(7)	C(17B)-C(11B)-C(18B)	115.6	(7)
O(12)-C(11)-C(18)	110.3	(7)	O(12B)-C(11B)-C(18B)	111.4	(7)
O(12)-C(11)-C(17)	106.1	(6)	O(12B)-C(11B)-C(17B)	106.3	(6)
C(11)-O(12)-C(13)	105.9	(5)	C(11B)-O(12B)-C(13B)	109.0	(6)
C(9)-C(13)-O(12)	101.0	(6)	C(9B)-C(13B)-O(12B)	101.0	(6)

TABLE 5

Torsion angles (°). E.s.d. in parentheses

C(2)-O(1)-C(5)-O(6)	104.5	(7)	C(2B)-O(1B)-C(5B)-O(6B)	113.9	(7)
C(2)-O(1)-C(5)-C(4)	-10.8	(8)	C(2B)-O(1B)-C(5B)-C(4B)	-1.2	(8)
C(5)-O(1)-C(2)-C(16)	-122.7	(7)	C(5B)-O(1B)-C(2B)-C(16B)	-128.7	(7)
C(5)-O(1)-C(2)-C(15)	110.7	(7)	C(5B)-O(1B)-C(2B)-C(15B)	106.5	(8)
C(5)-O(1)-C(2)-O(3)	-6.9	(8)	C(5B)-O(1B)-C(2B)-O(3B)	-13.9	(8)
O(1)-C(2)-O(3)-C(4)	23.0	(8)	O(1B)-C(2B)-O(3B)-C(4B)	24.8	(8)
C(15)-C(2)-O(3)-C(4)	-95.7	(7)	C(15B)-C(2B)-O(3B)-C(4B)	-95.1	(8)
C(16)-C(2)-O(3)-C(4)	142.0	(6)	C(16B)-C(2B)-O(3B)-C(4B)	140.9	(7)
C(2)-O(3)-C(4)-C(5)	-28.6	(7)	C(2B)-O(3B)-C(4B)-C(5B)	-25.0	(8)
C(2)-O(3)-C(4)-C(8)	-137.6	(6)	C(2B)-O(3B)-C(4B)-C(8B)	-135.9	(6)
O(3)-C(4)-C(5)-O(1)	24.3	(7)	O(3B)-C(4B)-C(5B)-O(1B)	16.0	(8)
O(3)-C(4)-C(8)-F(14)	-168.6	(6)	O(3B)-C(4B)-C(8B)-F(14B)	-164.8	(6)
O(3)-C(4)-C(8)-C(7)	77.4	(7)	O(3B)-C(4B)-C(8B)-C(7B)	78.7	(7)
O(3)-C(4)-C(5)-O(6)	-95.9	(7)	O(3B)-C(4B)-C(5B)-O(6B)	-103.0	(7)
C(8)-C(4)-C(5)-O(1)	136.9	(6)	C(8B)-C(4B)-C(5B)-O(1B)	131.3	(6)
C(5)-C(4)-C(8)-F(14)	82.5	(7)	C(5B)-C(4B)-C(8B)-F(14B)	85.0	(7)
C(5)-C(4)-C(8)-C(7)	-31.5	(7)	C(5B)-C(4B)-C(8B)-C(7B)	-31.5	(7)
C(8)-C(4)-C(5)-O(6)	16.7	(7)	C(8B)-C(4B)-C(5B)-O(6B)	12.4	(8)
C(4)-C(5)-O(6)-C(7)	6.0	(8)	C(4B)-C(5B)-O(6B)-C(7B)	13.2	(8)
O(1)-C(5)-O(6)-C(7)	-109.0	(7)	O(1B)-C(5B)-O(6B)-C(7B)	-101.4	(7)
C(5)-O(6)-C(7)-C(8)	-26.1	(8)	C(5B)-O(6B)-C(7B)-C(8B)	-33.5	(7)
C(5)-O(6)-C(7)-C(9)	-151.7	(6)	C(5B)-O(6B)-C(7B)-C(9B)	-156.3	(6)
O(6)-C(7)-C(8)-C(4)	35.0	(7)	O(6B)-C(7B)-C(8B)-C(4B)	39.5	(7)
O(6)-C(7)-C(9)-O(10)	-174.8	(6)	O(6B)-C(7B)-C(9B)-O(10B)	-172.2	(6)
O(6)-C(7)-C(9)-C(13)	-61.4	(8)	O(6B)-C(7B)-C(9B)-C(13B)	-58.4	(8)
O(6)-C(7)-C(8)-F(14)	-78.3	(7)	O(6B)-C(7B)-C(8B)-F(14B)	-76.8	(7)
C(9)-C(7)-C(8)-C(4)	157.4	(6)	C(9B)-C(7B)-C(8B)-C(4B)	157.2	(6)
C(8)-C(7)-C(9)-O(10)	67.3	(8)	C(8B)-C(7B)-C(9B)-O(10B)	72.8	(8)
C(8)-C(7)-C(9)-C(13)	-179.2	(6)	C(8B)-C(7B)-C(9B)-C(13B)	-173.3	(6)
C(9)-C(7)-C(8)-F(14)	44.0	(8)	C(9B)-C(7B)-C(8B)-F(14B)	41.0	(9)
C(7)-C(9)-C(13)-O(12)	-154.9	(6)	C(7B)-C(9B)-C(13B)-O(12B)	-154.6	(6)
C(7)-C(9)-O(10)-C(11)	149.3	(6)	C(7B)-C(9B)-O(10B)-C(11B)	154.9	(6)
O(10)-C(9)-C(13)-O(12)	-38.9	(7)	O(10B)-C(9B)-C(13B)-O(12B)	-38.4	(7)
C(13)-C(9)-O(10)-C(11)	27.8	(8)	C(13B)-C(9B)-O(10B)-C(11B)	32.8	(7)
C(9)-O(10)-C(11)-O(12)	-6.3	(8)	C(9B)-O(10B)-C(11B)-O(12B)	-15.1	(8)
C(9)-O(10)-C(11)-C(17)	108.8	(7)	C(9B)-O(10B)-C(11B)-C(17B)	98.7	(7)
C(9)-O(10)-C(11)-C(18)	-125.3	(7)	C(9B)-O(10B)-C(11B)-C(18B)	-134.8	(7)
O(10)-C(11)-O(12)-C(13)	-19.7	(8)	O(10B)-C(11B)-O(12B)-C(13B)	-10.7	(8)
C(17)-C(11)-O(12)-C(13)	-138.2	(7)	C(17B)-C(11B)-O(12B)-C(13B)	-126.3	(7)
C(18)-C(11)-O(12)-C(13)	98.8	(7)	C(18B)-C(11B)-O(12B)-C(13B)	107.0	(7)
C(11)-O(12)-C(13)-C(9)	35.5	(7)	C(11B)-O(12B)-C(13B)-C(9B)	29.8	(7)

TABLE 6

Puckering parameters and asymmetric parameters for the isopropylidene and furanose rings. q2 and $\phi 2$ are the puckering coordinates defined by Cremer and Pople (13); ΔC_s and ΔC_2 are the asymmetric parameters following Nardelli (14)

Atoms defining the rings	Molecule 1		Molecule 2	
O(1) C(2) O(3) C(4) C(5)	q2	0.267		0.234 Å
	$\phi 2$	94.3		76.3
O(1)	ΔC_s 0.218	ΔC_2 0.011	ΔC_s 0.187	ΔC_2 0.035
C(2)	0.185	0.084	0.123	0.108
O(3)	0.082	0.148	0.013	0.140
C(4)	0.052	0.155	0.102	0.119
C(5)	0.167	0.103	0.179	0.052
C(4) C(5) O(6) C(7) C(8)	q2	0.345		0.383 Å
	$\phi 2$	137.0		127.1
C(4)	ΔC_s 0.171	ΔC_2 0.145	ΔC_s 0.245	ΔC_2 0.132
C(5)	0.270	0.035	0.305	0.003
O(6)	0.248	0.086	0.248	0.129
C(7)	0.130	0.177	0.097	0.211
C(8)	0.037	0.199	0.092	0.213
C(9) O(10) C(11) O(12) C(13)	q2	0.327		0.383 Å
	$\phi 2$	151.8		165.7
C(9)	ΔC_s 0.145	ΔC_2 0.197	ΔC_s 0.074	ΔC_2 0.210
O(10)	0.276	0.129	0.229	0.138
C(11)	0.302	0.039	0.297	0.014
O(12)	0.212	0.161	0.251	0.116
C(13)	0.042	0.222	0.110	0.202

10 T.J. Tewson, M.J. Welch and M.E. Raichle, J. Nucl. Med 19 (1978) 1339.

11 W. Sowa and G.H.S. Thomas, Can. J. Chem. 44 (1966) 836.

12 R.F. Nutt, B. Arison, F.W. Holly and E. Walton, J. Am. Chem. Soc. 87 (1965) 3273.

13 D. Cremer and J.A. Pople, J. Am. Chem. Soc. 97 (1975) 1354.

14 M. Nardelli, Acta Cryst. C39 (1983) 1141.

15 S.J. Rettig and J. Trotter, Can. J. Chem. 55 (1977) 1454.

16 W. Choong, D.C. Craig, N.C. Stephenson and J.D. Stevens, Cryst. Struct. Comm. 4 (1975) 111.

17 W. Choong, N.C. Stephenson and J.D. Stevens, Cryst. Struct. Comm. 4 (1975) 491.

18 A.C.T. North, D.S. Philips and F.S. Matthews, Acta Cryst. A24 (1968) 351.

19 P. Main, S.J. Fiske, S.E. Hull, L. Lessinger, G. Germain, J.P. Declercq and M.M. Woolfson, 'MULTAN 80: A system of computer programs for the automatic solution of crystal structures from X-Ray diffraction data', Universities of York, Great Britain, and Louvain, Belgium (1978).

20 W.R. Busing, K.O. Martin and H.A. Levy, ORFLS, Report ORNL-TM 305, (1962) Oak Ridge National Laboratory, Tennessee, USA.

21 P. Roberts and G.M. Sheldrick, 'XANADU: Program for crystallographic calculations', University of Cambridge, Great Britain (1975).

22 International tables for X-Ray crystallography, Vol. IV, Kynoch Press, Birmingham, Great Britain (1974).

23 M. Nardelli, 'PARST: A system of computer routines for calculating molecular parameters from results of crystal structure analysis.' University of Parma, Italy (1982).

24 C.K. Johnson, ORTEP II, Report ORNL 5138 (1976), Oak Ridge National Laboratory, Tennessee, USA.