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# Structure of 4-Methylumbelliferyl-β-D-glucopyranoside

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**Abstract.** $C_{16}H_{17}O_8.1\cdot5H_2O$, $M_r = 364\cdot33$, monoclinic, $C2$, $a = 14\cdot314\ (3)$, $b = 6\cdot851\ (1)$, $c = 18\cdot178\ (5)$ Å, $\beta = 100\cdot90\ (2)°$, $V = 1750\cdot46$ Å$^3$, $Z = 4$, $D_x = 1\cdot382$ Mg m$^{-3}$, $\lambda$(Mo $K\alpha$) $= 0\cdot71069$ Å, $\mu = 0\cdot933$ mm$^{-1}$, $F(000) = 768$, $T = 294$ K, $R = 0\cdot078$ for all 2160 reflections. The structure is characterized by the close stacking along the $b$ axis of the planar 4-methylumbelliferyl ring system which is nearly perpendicular to **b** and the extensive hydrogen bonding scheme in which all hydroxyl groups are within 2·95 Å of at least two other O atoms.

**Introduction.** The structure of 4-methylumbelliferyl-β-D-glucopyranoside was determined as part of a conformational study of substrates of β-glucosidases. This compound is used as a fluorogenic substrate for the determination of β-glucosidase activity. Clinical applications include the diagnosis of Gaucher disease (Yaqoob & Carroll, 1980). Information regarding the geometry of the sugar–chromophore link and the overall conformation of the molecule is useful for mapping of the active site and for the determination of the enzymatic mechanism.

**Experimental.** The compound was purchased from Sigma (St Louis, Missouri). Needle-shaped crystals were obtained by slow evaporation of an aqueous acetone solution. The crystal used had approximate dimensions of 0·61 × 0·15 × 0·17 mm. Systematic absences ($h + k = 2n$) observed on Weissenberg photographs. The chirality of the molecule excluded all space groups other than $C2$. Nicolet $P3$ diffractometer, Mo $K\alpha$ radiation, Nb filter. Unit-cell dimensions and orientation matrix were determined from 25 reflections with $2\theta$ values in the range 20·0 to 28·5°. 2617 total data with $4 < \theta < 55°$, $-1 < h < 19$, $0 < k < 9$, $-24 < l < 24$, $h + k = 2n$. Intensities of five standard reflections (227, $62\bar{8}$, 621, $24\bar{1}$, $33\bar{4}$) were monitored after every 139th measurement but did not decline significantly. Validity of the orientation matrix was not monitored. Lorentz and polarization corrections were applied but no absorption correction. Of the 2190 unique data, 1605 had $F > 4\sigma(F)$ and were considered observed. $\sigma(F)$ was calculated according to Stout & Jensen (1968): $\sigma^2(F) = (k/4\mathrm{Lp}I)[\sigma^2(I) + (0\cdot01I)^2]$.

$E$ statistics were appropriate for a centrosymmetric space group, indicative of a high degree of pseudosymmetry. Structure determination attempts using *MULTAN* (Germain, Main & Woolfson, 1971) and *SHELX*84 (Sheldrick, 1984) resulted in false solutions. Both programs yielded two-dimensional 'chicken wire' solutions perpendicular to the $b$ axis in which one or more possible solutions for the umbelliferyl portion of the molecule could be identified. However, the peaks in these solutions were offset from the correct positions. The structure was determined using the program *QTAN* (Langs & DeTitta, 1975) after the removal of 18 of the top 200 triples which cosine seminvariant analysis (Hauptman, 1972) indicated to be less likely to be correct and after the starting set was expanded to ten phases to force certain groups of reflections (including *ggg*) to participate in the phasing early on. The correct solution had the lowest NQEST figure-of-merit (DeTitta, Edmonds, Langs & Hauptman, 1975) but not

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the best residual or cosine average. The $E$ map contained only one position for the umbelliferyl group and two correctly placed atoms [C(2′) and C(3′)] not in the same plane perpendicular to **b**. All remaining non-hydrogen atoms including the two water molecules were located in a Fourier map. One of the water molecules O(1*S*) is located on the twofold axis (0·0, $y$, 0·0). The occupancy of this atom ($g = 0{\cdot}5$) and its $x$ and $z$ coordinates were held fixed throughout the refinement. The $y$ coordinate of atom O(1) was held fixed to define the origin. The structure was refined using full-matrix least-squares methods, minimizing $\sum[w(F_o - F_c)^2]$, where $w = 1/\sigma^2(F_o)$. The solvent O atoms were refined with isotropic thermal parameters but the other non-hydrogen atoms were refined with anisotropic thermal parameters. The H atoms that were located in difference maps [all except the one bonded to O(3′) and one of each of the water molecules] were refined in separate cycles after refinement of the non-hydrogen atoms had converged. The extinction factor was not significant. The maximum value of shift/e.s.d. during the last cycle of refinement was 0·12. Final $R$ values are $R = 0{\cdot}057$, $wR = 0{\cdot}047$ for the 1605 observed data and $R_{\text{all}} = 0{\cdot}078$ for all 2160 data; $S = 2{\cdot}383$. The final difference map has maximum and minimum densities of 0·45 (6) and −0·35 e Å$^{-3}$. Inability to model the solvent electron density adequately causes the somewhat high $R$ values. The water molecules could not be refined with anisotropic thermal parameters and the $B_{\text{iso}}$ value of O(2*S*) is very high. The highest peak in the difference map is in the solvent region but could not be modeled. Atomic scattering factors and dispersion corrections were taken from *International Tables for X-ray Crystallography* (1974). Other programs used include the data reduction package *DREAM* (Blessing, 1987), locally modified versions of the Enraf–Nonius (1979) *SDP* refinement package and the plotting program *ORTEP*II (Johnson, 1976).

Table 1. *Atomic coordinates* ($\times 10^4$ *for non-hydrogen atoms*; $\times 10^3$ *for hydrogen atoms*) *and* $B_{eq}$ ($\times 10^2$, *non-hydrogen atoms*) *and* $B_{iso}$ ($\times$ 10, *hydrogen atoms*) *with e.s.d.'s in parentheses*

$B_{\text{eq}}$ is calculated according to Willis & Prior (1975).

| | $x$ | $y$ | $z$ | $B_{\text{iso}}/B_{\text{eq}}$ |
|---|---|---|---|---|
| C(2) | 6538 (3) | 7439 (11) | 11177 (2) | 431 (12) |
| C(3) | 7537 (3) | 7386 (10) | 11465 (2) | 427 (12) |
| C(4) | 8193 (3) | 7352 (10) | 11026 (2) | 355 (10) |
| C(5) | 8463 (3) | 7437 (10) | 9697 (2) | 372 (11) |
| C(6) | 8109 (3) | 7472 (10) | 8939 (2) | 390 (11) |
| C(7) | 7131 (3) | 7419 (9) | 8694 (2) | 319 (10) |
| C(8) | 6515 (2) | 7441 (9) | 9191 (2) | 313 (9) |
| C(9) | 6898 (3) | 7421 (9) | 9949 (2) | 299 (10) |
| C(10) | 7868 (3) | 7438 (9) | 10226 (2) | 306 (9) |
| C(11) | 9232 (3) | 7316 (12) | 11352 (2) | 497 (13) |
| C(1′) | 7242 (3) | 7022 (8) | 7400 (2) | 340 (13) |
| C(2′) | 6549 (3) | 6343 (9) | 6717 (2) | 383 (12) |
| C(3′) | 7094 (3) | 6065 (9) | 6071 (2) | 411 (13) |
| C(4′) | 7641 (3) | 7861 (9) | 5950 (2) | 444 (15) |
| C(5′) | 8265 (3) | 8525 (9) | 6694 (2) | 404 (13) |
| C(6′) | 8763 (4) | 10453 (10) | 6632 (3) | 559 (17) |
| O(1) | 6248 (2) | 7467 | 10420 (1) | 376 (7) |
| O(2) | 5911 (2) | 7509 (9) | 11539 (1) | 636 (11) |
| O(1′) | 6694 (2) | 7466 (8) | 7949 (1) | 411 (8) |
| O(2′) | 6140 (2) | 4538 (7) | 6861 (2) | 506 (10) |
| O(3′) | 6426 (2) | 5566 (7) | 5403 (2) | 548 (10) |
| O(4′) | 8230 (2) | 7473 (9) | 5419 (1) | 575 (10) |
| O(5′) | 7694 (2) | 8779 (7) | 7253 (1) | 410 (9) |
| O(6′) | 9514 (2) | 10770 (9) | 7239 (2) | 647 (12) |
| O(2*S*) | 10115 (4) | 6271 (11) | 6013 (3) | 1268 (17) |
| O(1*S*) | 5000 | 8135 (10) | 5000 | 912 (18) |
| H(C3) | 773 (2) | 740 (6) | 1194 (2) | 41 (7) |
| H(C5) | 916 (2) | 741 (5) | 988 (1) | 38 (7) |
| H(C6) | 852 (2) | 756 (6) | 858 (1) | 35 (7) |
| H(C8) | 581 (2) | 744 (6) | 903 (1) | 43 (7) |
| H(C11*A*) | 935 (3) | 711 (7) | 1183 (2) | 59 (10) |
| H(C11*B*) | 966 (3) | 639 (8) | 1110 (3) | 84 (13) |
| H(C11*C*) | 956 (3) | 833 (6) | 1120 (2) | 47 (9) |
| H(C1′) | 771 (2) | 600 (6) | 760 (2) | 43 (8) |
| H(C2′) | 609 (2) | 722 (6) | 652 (2) | 41 (8) |
| H(O2′) | 562 (3) | 474 (7) | 704 (2) | 68 (11) |
| H(C3′) | 749 (2) | 470 (4) | 614 (1) | 22 (6) |
| H(C4′) | 714 (3) | 898 (6) | 575 (2) | 55 (9) |
| H(O4′) | 846 (4) | 856 (9) | 511 (3) | 117 (17) |
| H(C5′) | 874 (2) | 745 (5) | 684 (1) | 28 (6) |
| H(C6′*A*) | 902 (3) | 1033 (7) | 608 (2) | 77 (12) |
| H(C6′*B*) | 824 (2) | 1136 (5) | 663 (2) | 41 (8) |
| H(O6′) | 933 (3) | 1099 (8) | 766 (3) | 95 (13) |
| H(O2*SA*) | 970 (3) | 539 (9) | 621 (2) | 105 (16) |
| H(O1*SA*) | 555 (3) | 881 (7) | 470 (2) | 72 (11) |

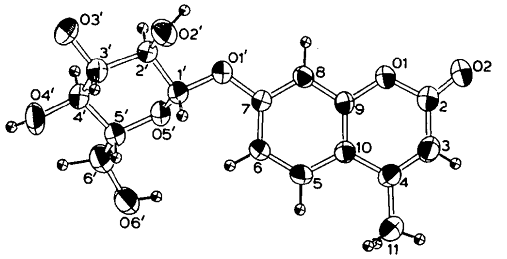

Fig. 1. Molecular conformation of 4-methylumbelliferyl-β-D-glucopyranoside with numbering scheme used.

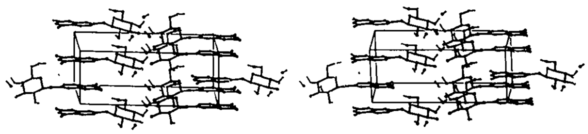

Fig. 2. Stereodiagram showing the crystal packing of 4-methylumbelliferyl-β-D-glucopyranoside, viewed down the $a$ axis. The structure appears as separate layers of hydrophobic and hydrophilic regions each with typical strong intermolecular interactions.

**Discussion.** Atomic coordinates and equivalent isotropic thermal parameters are listed in Table 1.* Fig. 1 shows the molecular conformation and the numbering scheme which is consistent with that used for the study of related compounds (Ueno, Sato & Saito, 1983). The umbelliferyl moiety is essentially planar. The least-squares plane through the 13 atoms has the equation $0{\cdot}018x + 1{\cdot}000y + 0{\cdot}005z = 5{\cdot}36$, with a r.m.s. deviation of 0·02 and a maximum deviation of 0·03 for C(6). However, the long C(2)—C(3) [1·428 (6)] and C(4)—C(10) [1·442 (5) Å] bonds and the short C(3)—C(4)

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* Lists of anisotropic thermal parameters, bond lengths and angles and structure factors have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44674 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

[1·342 (6) Å] bond indicate lack of delocalization. The glycosidic link has torsion angles of C(8)—C(7)—O(1′)—C(1′) = −166·3 (4), C(7)—O(1′)—C(1′)—O(5′) = −85·2 (5), O(1′)—C(1′)—O(5′)—C(5′) = −179·2 (4)°. A search of the conformations of all aromatic β-glucopyranosides in the Cambridge Crystallographic Database (Allen *et al.*, 1979) indicates that this conformation and the one related by an 180° rotation about the C(7)—O(1′) bond are the most commonly observed (14 out of 17 observations). All three exceptions have at least one large *ortho* substituent. The crystal packing, illustrated in Fig. 2, shows two different intermolecular interactions that are completely separated: alternating layers of stacked hydrophobic areas and hydrophilic carbohydrate and solvent regions. The molecules stacked along the *b* axis are related to one another by the transformation 1·5−*x*, 0·5±*y*, 2·0−*z*. The shortest stacking distance is 3·423 (9) Å for C(4)—C(8). The superposition of the molecules along the stacking direction is not perfectly perpendicular. Based on the coordinates of the C(9) and C(10) atoms, the atomic centers are offset by 0·33 and −0·33 Å in the **a** and **c** directions respectively. Table 2 shows the intermolecular hydrogen-bonding distances. Since not all H atoms were located it is not possible to assign a complete image of the bonding pattern. Assignment of donors and acceptors for those bonds for which the H atoms were not located is based on the pattern observed in the structure of 7-β-D-glucopyranoside-8-hydroxycoumarin dihydrate (Ueno, Sato & Saito, 1983) which is similar.

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Table 2. *Hydrogen bonding*

| Donor | Acceptor | | $D\cdots A$ (Å) | $H\cdots A$ (Å) | $D-H\cdots A$ (°) |
|---|---|---|---|---|---|
| O(2′) | O(6′) | $(-0.5+x, -0.5+y, z)$ | 2·679 (5) | 1·83 (4) | 163 (3) |
| O(6′) | O(2) | $(1.5-x, 0.5+y, 2.0-z)$ | 2·691 (5) | 1·88 (5) | 156 (4) |
| O(3′) | O(1*S*) | $(x, y, z)$ | 2·690 (6) | | |
| O(4′) | O(3′) | $(1.5-x, 0.5+y, 1.0-z)$ | 2·691 (7) | 1·68 (6) | 167 (4) |
| O(2*S*) | O(4′) | $(x, y, z)$ | 2·832 (7) | | |
| O(1*S*) | O(2*S*) | $(-0.5+x, 0.5+y, z)$ | 2·815 (9) | 2·23 (5) | 109 (3) |
| O(2*S*) | O(2′) | $(0.5+x, 0.5+y, z)$ | 2·947 (8) | | |

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# Structure of 2,5-Bis(ethylenedithio)-7-(2-methoxy-3-methylphenyl)bicyclo[4.2.0]octane

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**Abstract.** 14-(2-Methoxy-3-methylphenyl)dithiolane-2-spiro-1′-bicyclo[4.2.0]octane-4′-spiro-2″-dithiolane, $C_{20}H_{26}OS_4$, $M_r = 410.69$, monoclinic, $P2_1/c$, $a = 13.850$ (3), $b = 7.453$ (1), $c = 20.161$ (4) Å, $\beta = 104.16$ (2)°, $V = 2017.8$ (6) Å$^3$, $Z = 4$, $D_x = 1.35$ g cm$^{-3}$, Mo $K\alpha$ radiation, $\lambda = 0.71069$ Å, $\mu = 4.21$ cm$^{-1}$, $F(000) = 872.0$, room temperature, $R = 0.062$ and $S = 1.42$ for 3875 independent reflections. The six-membered ring is *cis* fused to the four-membered ring, adopting a flattened chair conformation. The four-membered ring adopts the usual puckered conformation (puckering angle 30·3°) and displays the usual geometrical parameters. The dihedral angle between the best least-squares planes (b.l.s.p.'s) of the six-membered ring and the four-membered ring is 58°. The dihedral angle between the b.l.s.p.'s of the two

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