à envisager un désordre de position de cette liaison. Pour essayer de vérifier cette hypothèse nous avons affiné les positions des atomes, le facteur de températures isotropes et leurs taux d'occupations respectifs (0,7 et 0,3). Les distances C(3)–C(4) C(3′)–C(4′) augmentent un peu (1,36 Å) mais la détermination des hydrogènes devient aléatoire, leur position se confondant avec celles des carbones. Enfin, le groupement amine est fortement agité. Le facteur de température équivalent des atomes de ce groupement est le double de celui des atomes du groupement phényle. Les distances et les angles de liaisons N–H(N)···Cl [N–H(N) = 0,97 (3), H(N)···Cl = 2,20 (3) Å, ∠N–H(N)···Cl = 165°] et O(3)–H(O3)···Cl [O(3)–H(O3) = 0,88 (3), H(O3)···Cl = 2,36 (3) Å, ∠O(3)–H(O3)···Cl = 176°] indiquent clairement l'établissement des liaisons hydrogène entre le chlore et les deux atomes H(N) et H(O3). Ceci explique le repliement de la chaîne piperidinoéthyle ainsi que la faible valeur due facteur de Debye–Waller de l'azote par rapport aux autres atomes du groupement.

La détermination de la structure cristalline de PDG et des comparaisons entre la conformation de la molécule et la géométrie moléculaire de la morphine peuvent éclairer l'interprétation de son mode d'action.

La structure de PDG présente un groupement aromatique (Ph, Fig. 2) et un groupement aminé (N) dont les positions relatives (distance N–centre de Ph = 7,83 Å; distance N–plan de Ph = 0,78 Å) sont en accord avec une liaison aux sites sur lesquels se fixe la morphine (Roques, Gacel, Fournié-Zaluski, Senault & Lecomte, 1979). Néanmoins, les différences structurales au niveau du site hydrophile (H) expliquent en partie la perte pour PDG de certains effets secondaires.

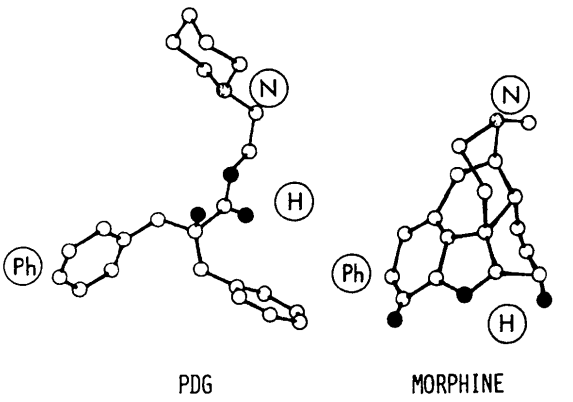

Fig. 2. Accessibilité aux sites opiacés de PDG et de la morphine.

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Structure of the Novel α-Glucosidase Inhibitor 4-*O*-α-D-Glucopyranosyl-*N*-methylmoranoline

BY YOHJI EZURE, YOSHIAKI YOSHIKUNI, NOBUTOSHI OJIMA AND MAKOTO SUGIYAMA

Research Laboratories, Nippon Shinyaku Co. Ltd, Nishioji-Hachijo, Kyoto 601, *Japan*

AND KEN HIROTSU AND TAIICHI HIGUCHI

Department of Chemistry, Faculty of Science, Osaka City University, Sugimoto, Sumiyoshi-ku, Osaka 558, *Japan*

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Abstract. $C_{13}H_{25}NO_9.2H_2O$, $M_r = 375{\cdot}371$, orthorhombic, $P2_12_12_1$, $a = 17{\cdot}952$ (1), $b = 11{\cdot}147$ (1), $c = 8{\cdot}411$ (1) Å, $V = 1683{\cdot}2$ (2) Å^3, $Z = 4$, $D_x = 1{\cdot}481$ Mg m^{-3}, λ(Mo $K\alpha$) = 0·7107 Å, $\mu = 0{\cdot}139$ mm^{-1}, $F(000) = 808$, $T = 293$ K, final $R = 0{\cdot}026$ for 1506 observed reflections. The conformation about the α-1,4-linkage of the title compound is similar to those of maltose and its related compounds and is

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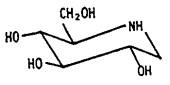
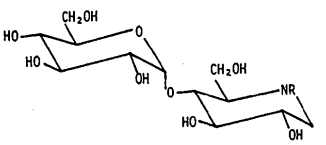
stabilized by one OH···O intramolecular hydrogen bond. The molecules pack together with a three-dimensional network of hydrogen bonds.

Introduction. Moranoline (I), a strong α-glucosidase inhibitor, was isolated from culture filtrates of a *Streptomyces* species (Murao & Miyata, 1980; Ezure, Maruo, Miyazaki & Kawamata, 1985). In a previous paper (Ezure, 1985) dealing with the enzymatic synthesis of 4-*O*-α-D-glucopyranosylmoranoline (II), a novel α-glucosidase inhibitor, it was shown that the α-1,4-linkage between glucose and moranoline was not easily hydrolyzed by glucoamylase. The X-ray crystallographic study of 4-*O*-α-D-glucopyranosyl-*N*-methylmoranoline (III), which is also a strong α-glucosidase inhibitor, was undertaken to determine its molecular conformation.



(I)



(II) $R = H$
(III) $R = CH_3$

Experimental. (II) was refluxed in 35% formaldehyde for 35 h at 383 K to the corresponding formyl derivative, which was successively converted into (III) by treating with sodium borohydride in methanol for 24 h at room temperature (43·4% yield). (III) did not show a sharp melting point, incomplete melting beginning at 384 and ending at 395 K. $[\alpha]_D^{24}$ +101·0° (*c*, 1·1%, H_2O). Anal. Found: C, 41·88; H, 7·74; N, 3·74%. Calc. for $C_{13}H_{25}NO_9.2H_2O$: C, 41·60; H, 7·79; N, 3·73%.

Colourless crystal 0·35 × 0·41 × 0·67 mm from aqueous solution. Rigaku AFC-6A four-circle diffractometer, graphite-monochromated Mo $K\alpha$ radiation, lattice parameters from a least-squares fit of 20 reflections with $20 < 2\theta < 24°$. Intensities of 1712 reflections measured, of which 1506 treated as observed in the refinement with $I > 3\sigma(I)$, $2\theta_{max} = 50°$ ($0 \le h \le 22$, $0 \le k \le 14$, $0 \le l \le 11$), $\omega/2\theta$ scan mode, scan speed 2° min^{-1}, scan width $(1·0 + 0·3 \tan\theta)°$, background measured for 8 s on each side of the peaks, three standard reflections monitored every 150 reflections, no significant variation in intensity, no absorption correction. Structure solved by direct methods with use of *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), all H atoms located in a difference synthesis (Sakurai, 1973) and refined isotropically. Full-matrix least-squares refinement carried out on F (Busing, Martin & Levy, 1965), function minimized $\sum w(|F_o| - |F_c|)^2$, $w = 1·0/[\sigma(F_o^2) + 0·02F_o^2]$, $R = 0·029$, $wR = 0·033$, $S = 1·9$ for 342 refined parameters. $(\Delta/\sigma)_{max} = 0·16$ for non-H and 0·25 for H atoms, $\Delta\rho_{max} = 0·13$ and $\Delta\rho_{min} = -0·20$ e Å^{-3}. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974). Diagrams drawn with *ORTEP*II (Johnson, 1976).

Table 1. *Fractional coordinates* (×10⁴) *and* U_{eq} *values* (Å² ×10⁴) *for non-hydrogen atoms*

$U_{eq} = \frac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	*y*	*z*	U_{eq}
C(1)	2387 (1)	1290 (2)	8762 (3)	212 (6)
C(2)	1948 (1)	984 (2)	7262 (3)	223 (6)
C(3)	1175 (1)	1521 (2)	7367 (3)	223 (6)
C(4)	789 (1)	1164 (2)	8912 (3)	215 (6)
C(5)	1290 (1)	1375 (2)	10353 (3)	212 (6)
C(6)	991 (1)	903 (2)	11898 (3)	292 (7)
C(1′)	3847 (1)	5380 (2)	9731 (3)	321 (7)
C(2′)	3879 (1)	4851 (2)	8080 (3)	307 (7)
C(3′)	3222 (1)	4029 (2)	7841 (3)	251 (6)
C(4′)	3149 (1)	3114 (2)	9156 (2)	202 (6)
C(5′)	3143 (1)	3714 (2)	10804 (3)	228 (6)
C(6′)	3060 (1)	2792 (2)	12118 (3)	308 (7)
C(7′)	3904 (1)	4994 (2)	12539 (3)	336 (7)
N	3832 (1)	4438 (2)	10957 (2)	248 (5)
O(1)	2443 (1)	2547 (1)	8868 (2)	204 (4)
O(2)	2330 (1)	1445 (1)	5896 (2)	304 (5)
O(3)	750 (1)	1139 (1)	6025 (2)	323 (5)
O(4)	134 (1)	1869 (1)	9094 (2)	303 (5)
O(5)	2011 (1)	816 (1)	10104 (2)	222 (4)
O(6)	835 (1)	−343 (1)	11763 (2)	400 (6)
O(2′)	3848 (1)	5800 (2)	6950 (2)	467 (6)
O(3′)	3276 (1)	3460 (2)	6331 (2)	367 (5)
O(6′)	3649 (1)	1941 (1)	12117 (2)	412 (6)
O(*W*1)	−206 (1)	4094 (2)	10384 (2)	354 (5)
O(*W*2)	4508 (1)	2398 (2)	4943 (2)	434 (6)

Table 2. *Bond lengths* (Å), *angles* (°) *and selected dihedral angles* (°) *with e.s.d.'s in parentheses*

C(1)–C(2)	1·526 (3)	C(1′)–C(2′)	1·510 (4)
C(1)–O(1)	1·408 (2)	C(1′)–N	1·472 (3)
C(1)–O(5)	1·417 (3)	C(2′)–C(3′)	1·507 (3)
C(2)–C(3)	1·514 (3)	C(2′)–O(2′)	1·423 (3)
C(2)–O(2)	1·433 (3)	C(3′)–C(4′)	1·511 (3)
C(3)–C(4)	1·525 (3)	C(3′)–O(3′)	1·423 (3)
C(3)–O(3)	1·428 (3)	C(4′)–C(5′)	1·539 (3)
C(4)–C(5)	1·528 (3)	C(4′)–O(1)	1·437 (2)
C(4)–O(4)	1·423 (2)	C(5′)–C(6′)	1·517 (3)
C(5)–C(6)	1·502 (3)	C(5′)–N	1·483 (3)
C(5)–O(5)	1·451 (2)	C(6′)–O(6′)	1·421 (3)
C(6)–O(5)	1·422 (3)	C(7′)–N	1·473 (3)

C(2)–C(1)–O(1)	108·1 (2)	C(1′)–C(2′)–O(2′)	108·8 (2)
C(2)–C(1)–O(5)	109·2 (2)	C(3′)–C(2′)–O(2′)	109·4 (2)
O(1)–C(1)–O(5)	110·7 (2)	C(2′)–C(3′)–C(4′)	112·4 (2)
C(1)–C(2)–C(3)	109·7 (2)	C(2′)–C(3′)–O(3′)	109·7 (2)
C(1)–C(2)–O(2)	109·6 (2)	C(4′)–C(3′)–O(3′)	111·0 (2)
C(3)–C(2)–O(2)	110·2 (2)	C(3′)–C(4′)–C(5′)	111·5 (2)
C(2)–C(3)–C(4)	111·3 (2)	C(3′)–C(4′)–O(1)	104·5 (2)
C(2)–C(3)–O(3)	109·0 (2)	C(5′)–C(4′)–O(1)	109·7 (2)
C(4)–C(3)–O(3)	110·7 (2)	C(4′)–C(5′)–C(6′)	111·3 (2)
C(3)–C(4)–C(5)	111·6 (2)	C(4′)–C(5′)–N	108·0 (2)
C(3)–C(4)–O(4)	108·8 (2)	C(6′)–C(5′)–N	112·8 (2)
C(5)–C(4)–O(4)	108·5 (2)	C(5′)–C(6′)–O(6′)	112·3 (2)
C(4)–C(5)–C(6)	114·9 (2)	C(1′)–N–C(5′)	110·1 (2)
C(4)–C(5)–O(5)	110·2 (2)	C(1′)–N–C(7′)	109·3 (2)
C(6)–C(5)–O(5)	107·1 (2)	C(5′)–N–C(7′)	112·4 (2)
C(5)–C(6)–O(6)	110·1 (2)	C(1)–O(1)–C(4′)	120·7 (1)
C(2′)–C(1′)–N	111·5 (2)	C(1)–O(5)–C(5)	112·3 (2)
C(1′)–C(2′)–C(3′)	109·3 (2)		

ψ_1 O(5)–C(1)–O(1)–C(4′)	109·5 (2)	ψ_1' C(1)–O(1)–C(4′)–C(3′)	127·3 (2)
ψ_2 C(2)–C(1)–O(1)–C(4′)	−130·9 (2)	ψ_2' C(1)–O(1)–C(4′)–C(5′)	−113·1 (2)

Discussion. Final atomic coordinates are shown in Table 1, bond distances, bond angles and selected dihedral angles in Table 2.* Fig. 1 is a perspective drawing of (III) with the atom-numbering scheme. The two inner bonds of the C(5)–O(5)–C(1)–O(1)–C(4′) sequence are significantly shorter than the two outer bonds. This bond-length variation was also found in β-maltose monohydrate (Quigley, Sarko & Marchessault, 1970; Gress & Jeffrey, 1977), α-maltose (Takusagawa & Jacobson, 1978) and methyl β-maltopyranoside (Chu & Jeffrey, 1967), and agrees with theoretical calculations on model compounds by Jeffrey, Pople & Radom (1974). The other bond lengths and angles agree well with the accepted values for given bond types. The torsional angles O(5)–C(1)–O(1)–C(4′) (ψ_1) and C(1)–O(1)–C(4′)–C(3′) (ψ_1') of (III) are 109·5 and 127·3°, respectively. The torsional angles ψ_1 and ψ_1' in β-maltose, methyl β-maltopyranoside and α-maltose are 123·1, 109·9 and 116·1° (ψ_1), and 132·4, 129·2 and 122·2° (ψ_1'), respectively. These values indicate that the overall geometry of (III) is similar to those of maltose and its related compounds. The geometry about the α-1,4-linkage is such that H(C1), C(1), O(1) C(4′) and H(C4′) are planar within 0·02 Å and the H(C1)···H(C4′) non-bonding distance is 2·14 (3) Å. This conformation is due to the constraint for the formation of an intramolecular hydrogen bond [O(2)···O(3′), 2·839 (2) Å]. The O(2)···O(3′) intramolecular hydrogen bonds are observed in all known crystal structures with the maltose linkages (Saenger, 1980). The arrangement of the molecules in the structure is shown in Fig. 2. The molecules are linked by the complex system of hydrogen-bond sequences. The hydrogen-bond system is

$$\begin{array}{lllll} & & O(3^{ii}) & \rightarrow O(W1^{iii}) \leftarrow & O(2'^{i}) \\ & & \uparrow & & \\ O(6'^{iv}) & \rightarrow O(W2^{i}) & \rightarrow O(3'^{i}) & \rightarrow O(2^{i}) & \rightarrow O(5^{v}) \\ & & \uparrow & & \\ & & O(6^{v}) & \leftarrow O(W1^{vi}) \rightarrow & O(4^{vi}) \rightarrow N^{i} \end{array}$$

where → indicates the donor direction and symmetry codes are: (i) x, y, z; (ii) $\frac{1}{2}+x, \frac{1}{2}-y, 1-z$; (iii) $\frac{1}{2}-x, 1-y, -\frac{1}{2}+z$; (iv) $x, y, -1+z$; (v) $\frac{1}{2}-x, -y, -\frac{1}{2}+z$; (vi) $\frac{1}{2}+x, \frac{1}{2}-y, 2-z$. Each hydroxyl group except O(2′) and O(6′) participates in two hydrogen bonds as both a donor and an acceptor. O(2′)–H and O(6′)–H serve as donors only. The ring oxygen O(5) and the N atom take part in hydrogen bonds as acceptors. Both water molecules are involved in four hydrogen bonds.

We thank Nippon Shinyaku Co. Ltd for granting permission for this publication.

* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and bond distances and angles involving H atoms have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43999 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

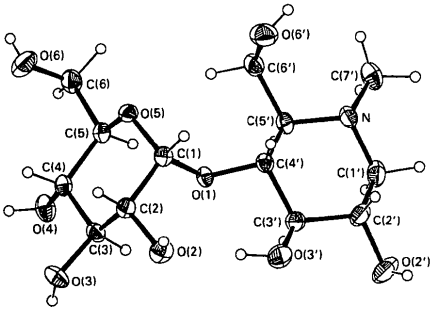


Fig. 1. View of molecule (III) with the atom-numbering scheme.

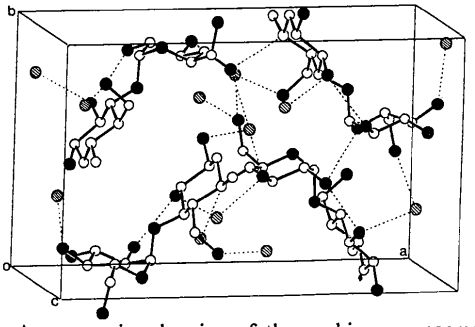


Fig. 2. A perspective drawing of the packing arrangement. The dotted lines indicate the intermolecular hydrogen bonds. Oxygen atoms of molecule (III) and water oxygen atoms are shown by full and hatched circles, respectively.

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