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X-ray Crystallographic Analysis of *cis*-2-(2-Hydroxyethyl)-*trans*-2-methyl-*cis*-3-(6-methoxy-2-naphthyl)cyclopentanol, a Biologically Active Steroid Analogue

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$C_{19}H_{24}O_3$ crystallizes in the monoclinic space group $P2_1/c$, with $a = 17.010$ (10), $b = 7.264$ (5), $c = 13.368$ (7) Å, $\beta = 93.52$ (4)°, $Z = 4$. The structure was refined to $R = 0.077$ for 2006 counter intensities. The hydroxyl groups are associated in an intramolecular hydrogen bond, with $O(2) \cdots O(3)$ 2.60 Å. There is also an intermolecular hydrogen bond with $O(2) \cdots O(3^v)$ ($1 - x, \frac{1}{2} + y, \frac{3}{2} - z$) 2.67 Å. The O(methoxy-naphthyl) $\cdots O(3)$ intramolecular separation, analogous to the distance between the O atoms at positions 3 and 17 in natural oestrogens, is 11.35 Å.

This compound is the only one of four stereoisomeric methoxynaphthylcyclopentanols (Brain, Cassidy, Constantine, Hanson & Tidy, 1971) to possess significant oestrogenic activity.

Experimental

Crystal data

$C_{19}H_{24}O_3$, $M_r = 300.4$. Monoclinic, $a = 17.010$ (10), $b = 7.264$ (5), $c = 13.368$ (7) Å, $\beta = 93.52$ (4)°, $U = 1657$ Å³, $D_m = 1.19$, $Z = 4$, $D_c = 1.20$ g cm⁻³, $F(000) = 648$, space group $P2_1/c$, Mo $K\alpha$ radiation, $\lambda = 0.7107$ Å, $\mu(\text{Mo } K\alpha) = 0.87$ cm⁻¹.

Crystallographic measurements

Approximate values for the cell dimensions, obtained from X-ray photographs, were adjusted by least squares from the angular settings of 12 reflections measured on a Hilger & Watts Y290 four-circle diffractometer at $\theta(\text{Mo } K\alpha)$ ca 16°. For the intensity measurements, the octants hkl and $h\bar{k}l$ were surveyed in the range $\theta \leq 27^\circ$; 60 θ - ω steps of 1 s were employed for each reflection with 15 s background counts at each end of the scan range. The intensities of 3563 independent reflections were obtained, of which 2011 had $I > 3\sigma(I)$. No absorption correction was applied.

Structure analysis

Based on an overall isotropic thermal parameter $B = 4.5$ Å², $|E|$ values were derived and Σ_2 relationships generated for 251 reflections with $|E| > 1.8$. Three phases were fixed to define the origin (Karle & Karle,

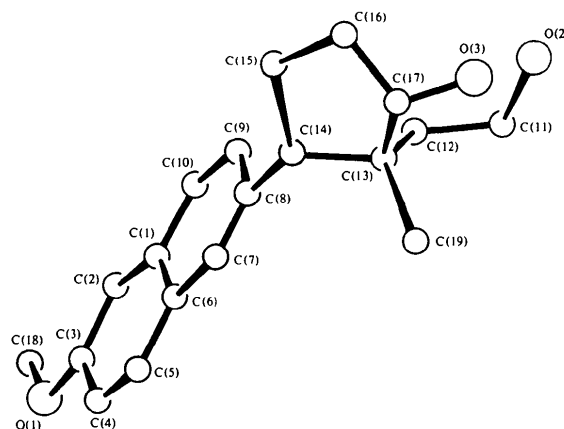


Fig. 1. The atomic arrangement in the molecule.

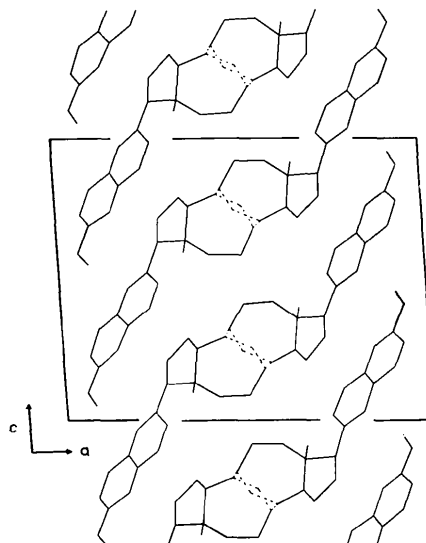


Fig. 2. The crystal structure viewed in projection along b .

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Table 1. Fractional atomic coordinates with *e.s.d.*'s

	<i>x</i>	<i>y</i>	<i>z</i>		<i>x</i>	<i>y</i>	<i>z</i>
O(1)	0.05934 (19)	0.52858 (58)	0.59867 (27)	H(O2)	0.515	0.285	1.255
O(2)	0.54451 (19)	0.29800 (50)	1.18061 (28)	H(O3)	0.4425 (21)	0.0559 (53)	1.3011 (27)
O(3)	0.44145 (21)	0.16143 (49)	1.29473 (26)	H(1)	0.0861 (29)	0.1294 (75)	0.8465 (37)
C(1)	0.09714 (28)	0.25513 (80)	0.81949 (44)	H(2)	0.0374 (28)	0.2546 (72)	0.6759 (36)
C(2)	0.06782 (29)	0.31572 (87)	0.72754 (43)	H(4)	0.1679 (23)	0.7098 (58)	0.7223 (30)
C(3)	0.09330 (26)	0.48535 (80)	0.69102 (38)	H(6)	0.2557 (25)	0.7520 (63)	0.8651 (32)
C(4)	0.14886 (26)	0.58717 (71)	0.74391 (36)	H(7)	0.3069 (23)	0.6222 (57)	1.0256 (30)
C(5)	0.18065 (24)	0.52427 (68)	0.83865 (36)	H(9)	0.1674 (20)	0.1795 (52)	0.9979 (26)
C(6)	0.24019 (27)	0.62088 (68)	0.89418 (36)	H(11A)	0.5069 (25)	0.1057 (63)	1.0787 (31)
C(7)	0.26976 (27)	0.55693 (66)	0.98613 (37)	H(11B)	0.5267 (25)	0.2919 (69)	1.0162 (34)
C(8)	0.24320 (25)	0.38934 (68)	1.02636 (35)	H(12A)	0.3986 (20)	0.3292 (52)	0.9991 (26)
C(9)	0.18703 (26)	0.29281 (70)	0.97229 (37)	H(12B)	0.4154 (23)	0.4761 (59)	1.1107 (30)
C(10)	0.15559 (25)	0.35311 (70)	0.87727 (37)	H(14)	0.2319 (23)	0.2305 (58)	1.1453 (30)
C(11)	0.50163 (29)	0.25876 (73)	1.08721 (40)	H(15A)	0.2959 (26)	0.5942 (62)	1.1877 (32)
C(12)	0.41661 (25)	0.32934 (68)	1.08362 (34)	H(15B)	0.2326 (26)	0.5051 (67)	1.2460 (34)
C(13)	0.35460 (24)	0.21575 (59)	1.13723 (31)	H(16A)	0.3903 (28)	0.4899 (72)	1.2935 (36)
C(14)	0.27335 (26)	0.32369 (67)	1.12876 (33)	H(16B)	0.3225 (22)	0.4022 (57)	1.3646 (29)
C(15)	0.28160 (31)	0.47165 (76)	1.21087 (39)	H(17)	0.3286 (23)	0.1072 (57)	1.2822 (29)
C(16)	0.34271 (35)	0.40108 (79)	1.28983 (37)	H(18A)	0.1396 (33)	0.6816 (85)	0.5396 (41)
C(17)	0.36520 (28)	0.21277 (67)	1.25365 (33)	H(18B)	0.3286 (32)	0.1074 (81)	1.2822 (41)
C(18)	0.08122 (37)	0.69780 (107)	0.55609 (47)	H(18C)	0.0711 (28)	0.8182 (72)	0.5930 (36)
C(19)	0.34694 (29)	0.02348 (67)	1.09496 (37)	H(19A)	0.3415 (23)	0.0352 (58)	1.0145 (30)
				H(19B)	0.3930 (25)	-0.0677 (63)	1.1021 (32)
				H(19C)	0.3048 (28)	-0.0453 (68)	1.1255 (35)

Table 2. Intramolecular bonded distances with *e.s.d.*'s (Å)

O(1)—C(3)	1.368 (6)	C(13)—C(17)	1.556 (6)
O(1)—C(18)	1.415 (8)	C(13)—C(19)	1.509 (6)
O(2)—C(11)	1.437 (6)	C(14)—C(15)	1.537 (7)
O(3)—C(17)	1.432 (6)	C(15)—C(16)	1.527 (8)
C(1)—C(2)	1.371 (8)	C(16)—C(17)	1.509 (7)
C(1)—C(10)	1.417 (7)	O(2)—H(O2)	1.15
C(2)—C(3)	1.404 (8)	O(3)—H(O2)	1.66
C(3)—C(4)	1.366 (7)	O(3)—H(O3)	0.77 (4)
C(4)—C(5)	1.423 (7)	C(1)—H(1)	1.01 (5)
C(5)—C(6)	1.409 (7)	C(2)—H(2)	0.95 (5)
C(5)—C(10)	1.422 (7)	C(4)—H(4)	1.00 (4)
C(6)—C(7)	1.381 (7)	C(6)—H(6)	1.07 (5)
C(7)—C(8)	1.415 (7)	C(7)—H(7)	0.93 (4)
C(8)—C(9)	1.361 (7)	C(11)—H(11A)	1.12 (5)
C(8)—C(14)	1.511 (6)	C(11)—H(11B)	1.09 (5)
C(9)—C(10)	1.418 (7)	C(12)—H(12A)	1.15 (4)
C(11)—C(12)	1.539 (7)	C(12)—H(12B)	1.13 (4)
C(12)—C(13)	1.553 (6)	C(14)—H(14)	1.01 (4)
C(13)—C(14)	1.593 (6)	C(15)—H(15A)	0.98 (5)
C(15)—H(15B)	1.01 (5)	C(18)—H(18C)	1.01 (5)
C(16)—H(16A)	1.04 (5)	C(19)—H(19A)	1.08 (4)
C(16)—H(16B)	1.08 (4)	C(19)—H(19B)	1.03 (5)
C(18)—H(18A)	1.04 (6)	C(19)—H(19C)	0.99 (5)
C(18)—H(18B)	1.17 (6)		
O(2)···O(3)	2.597 (5)		

1966)* and were used to generate the phases of 195 of the 251 reflections. A resultant *E* map yielded positions for 16 of the C and O atoms, and the remaining atoms were located in a difference synthesis after two cycles of refinement.

* See deposition footnote.

Table 3. Valency angles (°) with *e.s.d.*'s

C(18)—O(1)—C(3)	117.0 (4)	C(5)—C(4)—C(3)	120.2 (4)
C(2)—C(3)—O(1)	113.1 (4)	C(10)—C(5)—C(4)	119.8 (3)
C(13)—C(17)—O(3)	115.8 (3)	C(7)—C(6)—C(5)	121.0 (3)
C(5)—C(10)—C(1)	117.3 (4)	C(9)—C(10)—C(5)	119.3 (3)
C(6)—C(5)—C(4)	122.2 (3)	C(8)—C(7)—C(6)	121.3 (3)
C(10)—C(5)—C(6)	117.9 (3)	C(14)—C(8)—C(7)	121.1 (3)
C(9)—C(8)—C(7)	118.3 (3)	C(14)—C(8)—C(9)	120.5 (3)
C(13)—C(14)—C(8)	117.9 (3)	C(10)—C(9)—C(8)	122.2 (3)
C(17)—C(13)—C(12)	115.4 (3)	C(15)—C(14)—C(8)	115.9 (4)
C(19)—C(13)—C(14)	111.9 (3)	C(13)—C(12)—C(11)	118.6 (3)
C(16)—C(17)—C(13)	107.0 (4)	C(14)—C(13)—C(12)	108.8 (3)
C(17)—C(16)—C(15)	105.1 (4)	C(19)—C(13)—C(12)	111.4 (3)
C(4)—C(3)—O(1)	125.9 (3)	C(17)—C(13)—C(14)	97.2 (3)
C(12)—C(11)—O(2)	113.0 (3)	C(15)—C(14)—C(13)	104.6 (3)
C(16)—C(17)—O(3)	110.9 (3)	C(19)—C(13)—C(17)	111.3 (3)
C(10)—C(1)—C(2)	122.3 (4)	C(16)—C(15)—C(14)	106.7 (3)
C(3)—C(2)—C(1)	119.3 (4)	O(3)—H(O2)—O(2)	135
C(9)—C(10)—C(1)	123.3 (4)	O(3)—H(O3)—O(2)*	175
C(4)—C(3)—C(2)	121.0 (4)		

* O(2) coordinates transposed by the symmetry operation $1 - x, -\frac{1}{2} + y, \frac{1}{2} - z$.

The crystal structure was elucidated by direct phasing with a modified version of the *PHASE* program from the XRAY 63 package. Full-matrix least-squares refinement with isotropic thermal parameters lowered *R* to 16.8%, after which a cycle of calculations with anisotropic parameters gave *R* = 14.8%. A difference map was then calculated, and the H atoms located, though those of the hydroxyl and methyl groups were less well defined than the others. Initially, the H atoms were included in the analysis with

Table 4. *Torsion angles* ($^{\circ}$)

The sign convention used for the torsion angles is such that the sign is negative if an anticlockwise rotation is required of atom (1) to eclipse atom (4) whilst looking down the (2)–(3) bond. The average e.s.d. of the torsion angles is 0.6° .

C(18)–O(1)–C(3)–C(2)	180	C(6)–C(5)–C(10)–C(9)	4	C(12)–C(13)–C(14)–C(15)	–80
C(18)–O(1)–C(3)–C(4)	–3	C(5)–C(6)–C(7)–C(8)	2	C(17)–C(13)–C(14)–C(8)	170
C(10)–C(1)–C(2)–C(3)	–3	C(6)–C(7)–C(8)–C(9)	0	C(17)–C(13)–C(14)–C(15)	40
C(2)–C(1)–C(10)–C(5)	3	C(7)–C(8)–C(9)–C(10)	1	C(19)–C(13)–C(14)–C(8)	–73
C(2)–C(1)–C(10)–C(9)	–180	C(14)–C(8)–C(9)–C(10)	178	C(19)–C(13)–C(14)–C(15)	156
C(1)–C(2)–C(3)–O(1)	–180	C(7)–C(8)–C(14)–C(13)	–83	C(12)–C(13)–C(17)–O(3)	–52
C(1)–C(2)–C(3)–C(4)	2	C(7)–C(8)–C(14)–C(15)	42	C(12)–C(13)–C(17)–C(16)	72
O(1)–C(3)–C(4)–C(5)	–179	C(9)–C(8)–C(14)–C(13)	100	C(14)–C(13)–C(17)–O(3)	–167
C(2)–C(3)–C(4)–C(5)	–1	C(9)–C(8)–C(14)–C(15)	–135	C(14)–C(13)–C(17)–C(16)	–43
C(3)–C(4)–C(5)–C(6)	178	C(8)–C(9)–C(10)–C(1)	–180	C(19)–C(13)–C(17)–O(3)	76
C(3)–C(4)–C(5)–C(10)	1	C(8)–C(9)–C(10)–C(5)	–3	C(19)–C(13)–C(17)–C(16)	–160
C(4)–C(5)–C(6)–C(7)	180	O(2)–C(11)–C(12)–C(13)	–79	C(8)–C(14)–C(15)–C(16)	–156
C(10)–C(5)–C(6)–C(7)	–4	C(11)–C(12)–C(13)–C(14)	176	C(13)–C(14)–C(15)–C(16)	–25
C(4)–C(5)–C(10)–C(1)	–2	C(11)–C(12)–C(13)–C(17)	68	C(14)–C(15)–C(16)–C(17)	–2
C(4)–C(5)–C(10)–C(9)	–179	C(11)–C(12)–C(13)–C(19)	–60	C(15)–C(16)–C(17)–O(3)	157
C(6)–C(5)–C(10)–C(1)	–178	C(12)–C(13)–C(14)–C(8)	50	C(15)–C(16)–C(17)–C(13)	29

Table 5. *Displacements* (\AA) *of atoms from various planes*

- (i) O(2) 0.05, C(11) –0.06, C(13) 0.06, C(17) –0.05, O(3)* –0.66, C(12)* 0.70
- (ii) C(14) 0.01, C(15) –0.01, C(16) 0.01, C(17) –0.01, C(13)* 0.69
- (iii) C(1) 0.00, C(2) 0.03, C(3) –0.01, C(4) –0.01, C(5) –0.02, C(6) 0.02, C(7) 0.01, C(8) 0.00, C(9) –0.01, C(10) 0.01

* Atom not included in the derivation of the plane.

fixed parameters and least-squares calculations reduced R to 7.9%. The H atoms, apart from H(O2) which was identified with a small peak in the difference map, were then included in the refinement with isotropic thermal parameters and the calculations converged at $R = 7.7\%$. Since $\langle w\Delta^2 \rangle$ was approximately constant over various ranges of $|F_o|$ and $\sin \theta$, unit weights were retained throughout the analysis.

The atomic arrangement is illustrated in Fig. 1; Fig. 2 shows the packing of the molecules in the crystal. The atomic coordinates are listed in Table 1, and the bond lengths, valency angles, torsion angles and displacements of the atoms from various planes in Tables 2–5.*

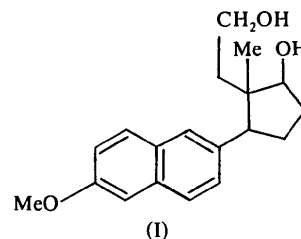
Discussion

The hydroxyl groups of the molecule are paired by a hydrogen bond O(2)H...O(3), 2.597 (5) \AA . The

* Lists of structure factors, intermolecular separations, thermal parameters, and origin-determining reflections and E statistics have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33418 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

O(2)...O(3) separation could be regarded as completing a six-membered ring of the chair type, in which C(12) and O(3) are displaced by 0.70 and 0.66 \AA , respectively, to opposite sides of the mean plane through O(2), C(11), C(13) and C(17).

The O(methoxynaphthyl)...O(3) separation in the molecule is 11.35 \AA , and this may be compared with the separation of *ca* 11 \AA between the O atoms at positions 3 and 17 in natural oestrogens (Weeks, Pokrywieski & Duax, 1973). The O(methoxynaphthyl)...O(2) separation is similar, 11.14 \AA , and it is tempting to suggest that these results may be pertinent to the oestrogenic activity of this stereoisomer of (I).



The cyclopentane ring adopts an envelope conformation with C(13) out-of-plane by 0.69 \AA . The valency angles in the ring range from 97.2 to 107.0 $^{\circ}$, the smallest being at the fully substituted C(13).

The C(sp^3)–C(sp^3) lengths lie in the range 1.509–1.593, mean 1.540 \AA . The longest, C(13)–C(14) 1.593 and C(13)–C(17) 1.556 \AA , have one H atom only, whereas the bonds with three or four H atoms have lengths of 1.509–1.539 \AA . A similar trend has been noted in other molecules (Hall & Maslen, 1965; Muir & Sim, 1968).

The bond lengths in the naphthalene nucleus agree well with those in naphthalene itself (Cruickshank, 1957) and in perylene (Kerr, 1966).

The crystal structure features an intermolecular O(2)···HO(3^v) hydrogen bond, 2.669 (7) Å. The O···H—O angle is 175°, whereas that in the intramolecular hydrogen bond is 135°. Though the positions of the H atoms have not been defined with great accuracy, the latter angle appears to deviate significantly from 180°.

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Crystal Structure and Conformation of 5-Aminouridine

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C₉H₁₃N₃O₆ is orthorhombic, space group *P*2₁2₁2₁, with *a* = 16.565 (8), *b* = 12.341 (6), *c* = 5.268 (5) Å, *Z* = 4. The structure, which was refined to *R* = 0.076, reveals the influence of a π -electron-donating 5-substituent, not only on the base geometry but also on the N(1)—C(1') and C(1')—O(1') lengths, which is discussed in comparison with other 5-substituted uridines. The orientation of the base at the glycosidic bond is *anti* (χ = 61.0°); the ribosyl moiety shows a C(2')-*endo* conformation and a *gauche-gauche* arrangement of C(4')—C(5'). These conformational features are stabilized by the characteristic intramolecular interaction C(6)—H···O(5'). The bases are stacked along *c* with a short base-base distance of 3.30 Å. Two base stacks are nearly perpendicular to each other and are connected by interbase hydrogen bonds N(5)—H···O(4) leading to a helical arrangement.

5-Aminouridine (a⁵Urd) has a wide range of biological effects and inhibits the growth of tumours and viruses. It is incorporated into the DNA of Ehrlich ascites cells (Werkheiser, Winzler & Visser, 1955). The homopoly-nucleotide poly(a⁵U), comparable to polyuridylylate, stimulates the binding of Phe-tRNA to bacterial ribosomes and promotes polyphenylalanine synthesis in the same system. Trinucleoside diphosphates, however, like U-U-a⁵U containing the 5-aminouridine in the 3'-terminal position (the wobble position) do not stimulate the binding of their cognate tRNA in a Nirenberg-Leder assay system (Hillen & Gassen, 1975). This may be taken as evidence that no aminouridine-guanosine

base pair is formed in the triplet coded binding of a tRNA. Furthermore, oligonucleotides terminating in 5-aminouridine have been used as affinity labels with iodoacetyl chloride as bridging agent to identify the proteins of the aminoacyl site on ribosomes (Luehrmann & Gassen, 1976).

In our attempt to clarify the function of 5-substitution on the structure of nucleosides and oligonucleotides, we now report the structure of 5-aminouridine. The comparison with 5-nitrouridine (–*M*), whose structure has been reported (Egert, Lindner, Hillen & Gassen, 1977*a*), demonstrates the (+*M*) effect of a π -electron-donating substituent.