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The Crystal and Molecular Structure of Isosteganol

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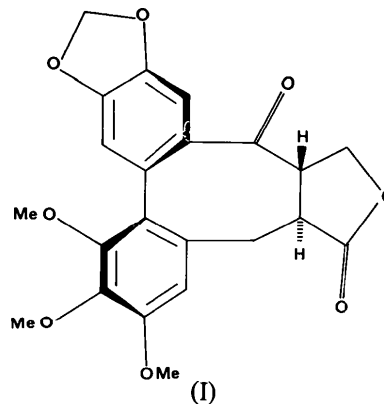
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As part of the synthetic study of a group of antileukæmic lignans the structure of isosteganol, $C_{22}H_{22}O_8$, a reduction product of an isomer of steganone, was determined. The crystals are triclinic, space group $P\bar{1}$, $a = 7.146$ (1), $b = 9.407$ (1), $c = 14.326$ (2) Å, $\alpha = 79.25$ (1), $\beta = 86.57$ (1), $\gamma = 83.76$ (1)°, $Z = 2$. The structure was solved by direct methods and refined to $R = 0.062$ for the 2583 unique reflexions measured on a diffractometer. The conformation of isosteganol is compared with that of episteganol [Bryan, Gilmore & Restivo (1976), personal communication]. The major difference between the two stereoisomers lies in the conformation of the cyclooctadiene ring which approximates to a distorted crown in isosteganol and a strained tub in episteganol. Apart from the cyclooctadiene ring there is close agreement in the bond length/bond angle values in the two structures.

Introduction

A recent synthetic study of a group of antileukæmic lignans from *Steganotaenia araliacea* Hochst has achieved a total synthesis of the key steganone (I). The approach used resulted in the production of a stereoisomer termed isosteganone, which was found to undergo a smooth thermal rearrangement to give steganone itself. The mild nature of this rearrangement suggested that it might be due to the presence of the



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biphenyl system (atropisomerism) and to clarify the situation unambiguously an X-ray analysis of the highly crystalline reduction product, isosteganol, was undertaken.

Experimental

The crystals were obtained as colourless prisms from chloroform–methanol.

Crystal data

$C_{22}H_{22}O_8$, $M_r = 414$, triclinic, $a = 7.146$ (1), $b = 9.407$ (1), $c = 14.326$ (2) Å, $\alpha = 79.25$ (1), $\beta = 86.57$ (1), $\gamma = 83.76$ (1)°, $U = 940$ Å³, $D_c = 1.46$ ($Z = 2$), $F(000) = 436$, space group $P\bar{1}$, $\mu(Cu K\alpha) = 8.4$ cm⁻¹, $\lambda(Cu K\alpha) = 1.5418$ Å, crystal size: $0.8 \times 0.6 \times 0.3$ mm.

Unit-cell parameters were determined by least-squares refinement on 15 automatically centred reflexions.

Intensities were measured on a Syntex $P2_1$ automatic four-circle diffractometer. 2583 unique reflexions were collected using a $2\theta/\omega$ scan with monochromated Cu $K\alpha$ radiation. The scan range for each reflexion was 2° plus an allowance for the expected α_1/α_2 splitting. The scan rate varied between 1° and 29° min⁻¹ depending on the reflexion intensity. The background was measured at each end of the scan range for half the total scan time. Data were collected to $2\theta_{max} = 115^\circ$. A monitored standard reflexion showed no significant variation during data collection. No absorption corrections were applied.

Structure determination and refinement

The structure was solved by direct methods using the computer program *MULTAN* (Main, Woolfson, Lessinger, Germain & Declercq, 1974), and refined by the program *SHELX 76* (Sheldrick, 1976). All H atoms were located except for one bonded to O(3), which did not appear in any difference Fourier synthesis (ρ_{max} for the final difference map was 0.25 e Å⁻³). Positional and anisotropic temperature factor parameters were refined for the heavy atoms, but the H atoms were constrained to lie at fixed distances from the C atoms to which they were bonded (benzene type C–H: 1.08 Å; methyl C–H: 1.10 Å; other C–H: 1.07 Å). One isotropic temperature factor was refined for the methyl H atoms and a second for the remaining H atoms. The final $R' = \Sigma w^{1/2} \Delta / \Sigma w^{1/2} |F_o|$ was 0.082 with a corresponding R of 0.062 for all 2583 unique reflexions; the weighting scheme was $w = |\sigma^2(F) + 0.001F^2|^{-1}$. Final atomic

coordinates are listed in Table 1.* The H atoms are numbered such that H(mn) is the n th H atom on C(m).

* Lists of structure factors, thermal parameters, bond lengths and angles, and non-bonded distances have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33110 (22 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 1. Atom coordinates ($\times 10^4$)

	<i>x</i>	<i>y</i>	<i>z</i>
C(1)	3555 (3)	4255 (3)	9156 (2)
H(011)	4271 (37)	3248 (17)	9517 (18)
C(2)	2508 (3)	5250 (3)	9594 (2)
C(3)	1555 (3)	6462 (3)	9090 (2)
C(4)	1612 (3)	6733 (3)	8116 (2)
H(041)	797 (36)	7693 (20)	7754 (18)
C(5)	2812 (3)	6206 (3)	6554 (2)
H(051)	1703 (29)	7034 (23)	6339 (20)
C(6)	4593 (3)	6955 (3)	6219 (2)
H(061)	4747 (40)	7659 (26)	6706 (17)
C(7)	6377 (3)	5941 (3)	6107 (2)
H(071)	5995 (40)	5171 (25)	5713 (19)
C(8)	7300 (3)	5119 (3)	7019 (2)
H(081)	6914 (41)	5691 (29)	7594 (15)
H(082)	8803 (8)	4976 (32)	6920 (21)
C(9)	7855 (4)	2485 (3)	7001 (2)
H(091)	9211 (21)	2741 (31)	6676 (19)
C(10)	7350 (4)	1083 (3)	7171 (2)
C(11)	5609 (4)	791 (3)	7635 (2)
C(12)	4411 (4)	1922 (3)	7907 (2)
C(13)	4528 (4)	7884 (3)	5226 (2)
H(131)	3917 (38)	8983 (12)	5201 (21)
H(132)	3923 (39)	7344 (29)	4737 (17)
C(14)	7579 (4)	6919 (3)	5433 (2)
C(15)	6664 (3)	3620 (3)	7276 (2)
C(16)	4918 (3)	3355 (2)	7737 (2)
C(17)	3688 (3)	4499 (3)	8145 (2)
C(18)	2708 (3)	5737 (3)	7637 (2)
C(19)	1207 (4)	6617 (3)	10621 (2)
H(191)	-51 (23)	6606 (32)	11065 (17)
H(192)	2161 (32)	7268 (27)	10855 (20)
C(20)	10082 (7)	225 (4)	6330 (3)
H(201)	10310 (74)	-745 (35)	5996 (36)
H(202)	11145 (54)	614 (58)	6721 (34)
H(203)	9702 (75)	1130 (38)	5745 (24)
C(21)	6052 (5)	-1640 (3)	8455 (3)
H(211)	5484 (71)	-2665 (31)	8407 (36)
H(212)	6258 (76)	-1228 (58)	9108 (22)
H(213)	7446 (33)	-1955 (61)	8144 (37)
C(22)	2217 (7)	545 (4)	8977 (4)
H(221)	905 (39)	520 (57)	9422 (34)
H(222)	3623 (36)	281 (57)	9277 (36)
H(223)	2118 (75)	-240 (47)	8504 (32)
O(1)	2152 (3)	5207 (2)	10559 (1)
O(2)	552 (3)	7261 (2)	9701 (1)
O(3)	2687 (3)	5037 (2)	6057 (1)
O(4)	6501 (3)	8024 (2)	4937 (1)
O(5)	9265 (3)	6772 (2)	5291 (1)
O(6)	8396 (4)	-82 (2)	6910 (2)
O(7)	5046 (3)	-594 (2)	7767 (1)
O(8)	2631 (3)	1741 (2)	8297 (2)

Results and discussion

The X-ray analysis of episteganol, derived from the reduction of naturally occurring steganone was reported by Bryan, Gilmore & Restivo (1976) and we adopt their numbering scheme for the isomeric isosteganol (Fig. 1). The only significant difference in bond lengths between iso- and episteganol is between the bonds O(9)–C(22) (1.389 Å in iso and 1.453 in epi) due probably to the high temperature factor of C(22) in isosteganol. The bond angles and torsion angles in the benzene, lactone and methylenedioxy rings are in good agreement between the two structures.

The major difference between the two structures lies in the conformation of the cyclooctadiene ring. Torsion angles within this ring are shown in Fig. 2. In episteganol the ring is described as a strained tub (Bryan, Gilmore & Restivo, 1976); in isosteganol the ring approximates to a distorted crown. Conformational studies of 1,3-cyclooctadiene (Anet & Yavari, 1975), using ^{13}C NMR techniques, have shown that its most stable conformations are the twist-boat-chair

(TBC) and the twist-boat (TB) and that these forms are most likely to be interconverted through the axial-symmetrical-boat (B) conformation. The conformation of episteganol is closest to the B form and that of isosteganol to the TBC form, which has a large torsion angle across the 2–3 [C(16)–C(17)] bond and an angle of similar magnitude but opposite sign across the diametrically opposed 6–7 [C(6)–C(7)] bond. A conformation very similar to our findings for isosteganol has recently been briefly reported for 9-bromo-isosteganacin (Kende, Liebeskind, Kubiak & Eisenberg, 1976) which is a brominated derivative of an isosteganol ester. In all the compounds the cyclooctadiene conformations are distorted by the effects of the fused substituted benzene rings, resulting in a torsion angle about the C(16)–C(17) bond of approximately 70° . Because of the strain in the eight-membered ring, the torsion angles across the C(15)–C(16) and C(17)–C(18) bonds within the larger ring are distorted from their ideal value of zero; the distortion is slightly greater in episteganol (13 and 9°) than isosteganol (10 and 4°).

The difference between isosteganol and episteganol can most clearly be seen in the opposite sign of the torsion angle about the C(16)–C(17) bond. In both structures the magnitude of this angle is approximately 70° , as it is in gomisin D (Ikeya, Taguchi & Itaka, 1976), a compound which has a similar ring system except for the absence of the fused lactone. In isosteganol the dihedral angle between the benzene ring planes is 67° (*cf.* biphenyl 42° , Hargreaves & Rizvi, 1962). The lactone ring is *trans*-fused almost identically in the two steganol structures and the torsion angles about the remaining four bonds in the ring adjust to comply with the constraints imposed by the geometry of the C(6)–C(7), C(15)–C(16), C(16)–C(17) and C(17)–C(18) bonds.

The major difference between isosteganol and episteganol seems to be the enhanced bond-angle strain in the cyclooctadiene ring of the former. This is most severe at C(17) (endocyclic bond angle 125.2° ; compared with 119.9° in episteganol) and C(18) (126.6 ; 120.2°): this strain is to some extent offset by the lessening of strain at C(15) (122.5 ; 124.0°), C(16) (122.2 ; 125.3°) and C(18) (110.0 ; 115.7°). The only significant differences outside the cyclooctadiene ring are at C(12), where the angle C(11)–C(12)–C(16) is 118.7° in episteganol and 115.8° in isosteganol; in the endocyclic valence angles at C(1) and C(4), which are closer to the normal value in benzene rings in isosteganol than in episteganol; and in the angle C(6)–C(5)–O(3) (110.1 ; 105.3°). In episteganol there is a short (2.85 Å) $1 \cdots 4$ contact between C(7) and C(18); in isosteganol the shortest contact of this type is 3.61 Å between C(8) and C(17). The C–H contacts across the ring are also more favourable in isosteganol where the shortest contact is 2.69 Å between H(081)

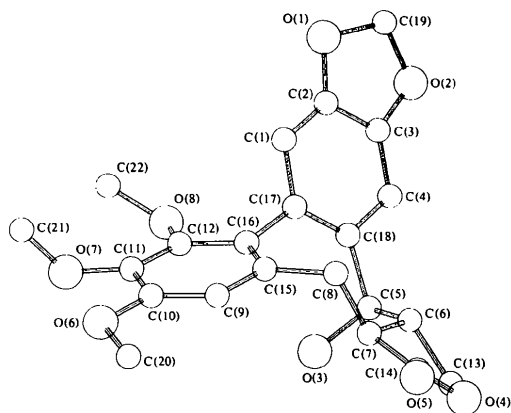


Fig. 1. A view of isosteganol showing the *trans* lactone function, the cyclooctadiene ring conformation and the numbering scheme.

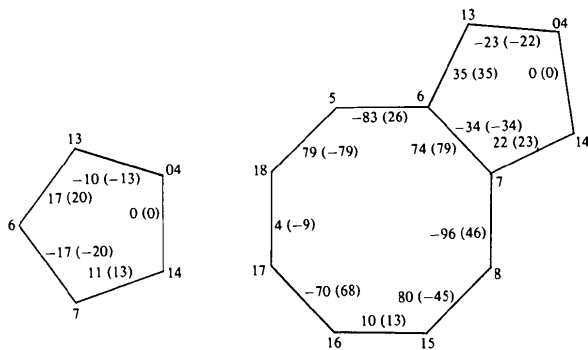


Fig. 2. Torsion angles ($^\circ$) for isosteganol. The figures in parentheses are those quoted by Bryan, Gilmore & Restivo (1976) for episteganol with the signs reversed to make the absolute configurations of both molecules at the ring junctions identical.

and C(17). In episteganol the H atom on C(7) is 2.43 Å from C(17) and 2.34 Å from C(18). There are, however, short contacts between H atoms attached to the ring and exocyclic H atoms.

The shortest H...H contacts are about 2.2 Å and the shortest C...C contacts are about 3.4 Å. It is possible that there is a very weak intermolecular hydrogen bond between O(3) and O(5), which are 2.94 Å apart, although this is not indicated by the bond lengths C(5)–O(3) (1.431 Å) and C(14)–O(6) (1.207 Å).

We thank the MRC for financial support and the SRC for the provision of the diffractometer. Fig. 1 was drawn using the program *PLUTO* written by Dr W. D. S. Motherwell. We are grateful to Dr R. F. Bryan for sending us details of his work prior to publication.

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The Crystal and Molecular Structure of Adeninium Sulphate, C₅H₅N₅·H₂SO₄

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The crystal and molecular structure of the title compound was determined from 1645 observed three-dimensional data measured by a single-crystal automated X-ray diffractometer. The unit cell is orthorhombic with $a = 11.664$ (1), $b = 13.685$ (2), $c = 11.023$ (2) Å, $V = 1759.4$ (5) Å³ and contains eight formula units. The space group is *Pbca*. The crystal structure was solved by the heavy-atom method and refined by the least-squares method in a block-diagonal approximation. The final *R* factor is 0.055. The adenine base is diprotonated on N(1) and N(7). The crystal-packing arrangement consists of seven negatively charged sulphate groups surrounding each positively charged base. There is no hydrogen bonding between the bases.

Introduction

The crystal structure of adeninium sulphate was determined as a part of a complex programme of study of the energy and information transfer in nucleic acids, carried out in cooperation with the Institute of Physics of the Charles University in Praha. Single crystals of the title compound serve as a good physical model for the explanation of the emission characteristics of polynucleotides.

Structures containing the adenine base have been reviewed in papers by Voet & Rich (1970) and Ringertz (1972). Data on adenine bases diprotonated on N(1) and N(7) are presented in papers by Kistenmacher & Shigematsu (1974) and Iwasaki (1974) for

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the same compound, and in a paper by Bryan & Tomita (1962). Protonation on O(1) and N(7) was observed by Prusiner & Sundaralingam (1972) in the N¹-oxide of adeninium sulphate. Preliminary crystal data on adeninium sulphate have been published by Moravcová (1975).

Experimental

Crystals of C₅H₅N₅·H₂SO₄, used in the structure determination, were prepared by Zachová (1973) at the Institute of Physics, Charles University, Praha. The molecular formula was confirmed by elemental chemical analysis. The crystals thus obtained were colourless.