A geometrical analysis of the nortricyclene moiety gives the following results. Nortricyclene has non-crystallographic $3m$ symmetry for both molecules. The planes defined by C(9)–C(8)–C(13), C(9)–C(14)–C(12) and C(9)–C(10)–C(11) form an average interplanar angle of 120 ± 1°, and form with the threefold axis, defined by C(9) and the cyclopropane centre, an average angle of 0·2 ± 0·2° (0·2° being the r.m.s.d.). Planes C(11)–C(12)–C(13) and C(10)–C(14)–C(8) are parallel and are normal to the threefold axis, with a deviation of 0·5 ± 0·2°. All these values indicate no significant deviation from $3m$ symmetry, which is not distorted by the substitution at C(8). Table 4 shows the nortricyclene geometry compared with previously reported results.

The Cl^- ions are hydrogen bonded to the positively charged N atoms at distances of 3·080 (4) and 3·116 (4) Å for molecules A and B, respectively. There are no contacts between non-H atoms less than 3·4 Å.

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The Structure of the Sesquiterpene Aplysistatin

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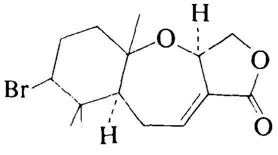
Abstract

A crystal structure analysis of the sesquiterpene aplysistatin has established the absolute configuration of the molecule. The molecular structure consists of a 6–7–5 set of fused rings, all with equatorial ring junctions. The seven-membered ring has a heterocyclic O atom in the bridging position and the five-membered ring is formed by a cyclic ester. The structure was solved by heavy-atom analysis of data from a crystal with $a = 9{\cdot}982\ (9)$, $b = 7{\cdot}182\ (2)$, $c = 20{\cdot}586\ (9)$ Å, $Z = 4$ and $\rho_c = 1{\cdot}482$, $\rho_o = 1{\cdot}469$ Mg m^{-3} in the space group $P2_12_12_1$. An automated diffractometer was used to collect the 1967 reflections available within the range $2\theta \leq 55°$ for monochromated Mo $K\alpha$ radiation. Anisotropic least-squares refinement converged to a conventional residual $R = 0{\cdot}0945$ ($R_w = 0{\cdot}0649$) for 1701 unique non-zero reflections and the best enantiomer.

Introduction

During the course of an evaluation of a chloroform extraction of a South Pacific Ocean sea hare (sp. *Aplysia angasi*) for antineoplastic activity, the sesquiterpene aplysistatin (I) had been isolated and an



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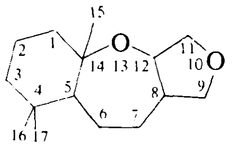

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X-ray crystal structure analysis which unequivocally established its structure was briefly reported (Pettit, Herald, Allen, Von Dreele, Vanell, Kao & Blake, 1977). We now report the details of the structure analysis and molecular bonding parameters for this natural product.

Experimental

Data collection

Crystals of aplysistatin, $C_{15}H_{21}BrO_3$, were obtained from acetone–hexane solution. Precession photographs revealed *mmm* Laue symmetry and the extinctions $h00$: $h = 2n + 1$; $0k0$: $k = 2n + 1$; and $00l$: $l = 2n + 1$ uniquely consistent with the space group $P2_12_12_1$. A refinement of the setting angles for 15 reflections ($6{\cdot}0 \leq 2\theta \leq 19{\cdot}9°$) obtained on a Syntex $P\bar{1}$ autodiffractometer gave the lattice parameters $a = 9{\cdot}982$ (9), $b = 7{\cdot}182$ (2), $c = 20{\cdot}586$ (9) Å, which for $Z = 4$ gives $\rho_c = 1{\cdot}482$ Mg m^{-3} ($\rho_o = 1{\cdot}469$ Mg m^{-3}; flotation in CCl_4/hexane).

The diffraction intensities for 2107 reflections ($2\theta \leq 55°$) were measured with graphite-monochromated Mo $K\alpha$ radiation from a crystal of approximate dimensions 0·3 × 0·3 × 0·3 mm bounded by the faces (102), $(\bar{1}02)$, $(10\bar{2})$, $(\bar{1}0\bar{2})$, (010), $(0\bar{1}0)$, $(00\bar{1})$ and $(00\bar{1})$. For each reflection the scan speed (between 1 and 12° min^{-1}) was determined from the intensity found in a rapid sampling scan and covered the range ±1° about the $K\alpha_1$–$K\alpha_2$ doublet with background counts for 0·125 of the scan time taken at each end of the scan. The intensities of three reflections periodically monitored showed a mean fluctuation of 1% during the data collection. There were 1701 non-zero reflections used in all subsequent calculations with each assigned a weight $w = 1/\sigma_F^2$; $\sigma_F = 0{\cdot}025|F_o| + (C + k^2B)^{1/2}R/(2|F_o|\mathrm{Lp})$, where C is the total count in a scan taken at the rate R and k (=4) is the ratio of scanning time to the time for the total background count B. Corrections were applied for Lorentz and polarization effects for monochromated radiation (Azaroff, 1955), analytical absorption corrections (de Meulenaer & Tompa, 1965) were applied for an absorption coefficient of $\mu = 2{\cdot}677$ mm^{-1}, and extinction effects were considered to be negligible.

The structure was solved by standard heavy-atom techniques.* A three-dimensional Patterson synthesis provided the position of the Br atom. A Fourier synthesis phased with this position revealed the positions of 16 additional atoms. The structure was completed from inspection of successive difference syntheses and the atoms were identified by refinement of the thermal parameters and inspection of the interatomic distances. The model with anisotropic thermal motion for Br and isotropic thermal motion for all other atoms was refined by full-matrix least squares to give $R = 0{\cdot}1320$ and $R_w = [\sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2]^{1/2} = 0{\cdot}1200$. Scattering factors for Br^0, C^0, O^0 and anomalous-dispersion terms for Br (*International Tables for X-ray Crystallography*, 1974) were used in the calculation of structure factors. H atoms were placed at their idealized positions with an assigned thermal parameter of $U = 0{\cdot}05$ Å^2 and the above refinement was repeated to give $R = 0{\cdot}1137$ and $R_w = 0{\cdot}0834$ using the scattering factor for H^0. A refinement of the model with anisotropic thermal parameters for all nonhydrogen atoms by large-block least squares (172 parameters in two blocks) converged with $R = 0{\cdot}0945$ and $R_w = 0{\cdot}0649$ with a shift over error less than 0·20 for all parameters.* A similar refinement of the enantiomorphic model gave the residuals $R = 0{\cdot}1018$ and $R_w = 0{\cdot}0719$, thus establishing the absolute configuration of aplysistatin.

Results

Final atomic coordinates for aplysistatin are presented in Table 1. Bond distances and angles within the

Table 1. *Fractional coordinates* (× 10^4) *and equivalent temperature factors* (× 10^3) *for aplysistatin*

The estimated standard deviations are listed in parentheses.

	x	y	z	U_{eq} (Å^2)*
Br	2892·4 (9)	7710·3 (15)	10462·5 (4)	65
C(1)	3748 (7)	8596 (10)	8467 (4)	40
C(2)	3848 (8)	8622 (11)	9216 (4)	44
C(3)	2768 (7)	7432 (10)	9514 (3)	40
C(4)	2806 (7)	5375 (10)	9308 (3)	39
C(5)	2718 (7)	5420 (9)	8532 (3)	32
C(6)	2570 (7)	3511 (10)	8214 (4)	41
C(7)	1655 (7)	3561 (11)	7632 (4)	37
C(8)	1474 (7)	5043 (10)	7262 (4)	40
C(9)	601 (8)	5125 (14)	6690 (4)	52
O(9)	−288 (5)	4117 (10)	6536 (3)	68
O(10)	936 (5)	6619 (9)	6329 (3)	58
C(11)	2114 (8)	7483 (12)	6603 (4)	58
C(12)	2182 (8)	6823 (11)	7292 (3)	47
O(13)	3531 (4)	6724 (7)	7504 (2)	40
C(14)	3797 (7)	6649 (10)	8196 (3)	36
C(15)	5226 (7)	5890 (11)	8218 (4)	45
C(16)	4031 (8)	4342 (11)	9565 (4)	50
C(17)	1536 (8)	4397 (13)	9566 (4)	55

* Calculated from $U_{eq} = (U_1U_2U_3)^{1/3}$, where U_i are the principal radii of the thermal ellipsoid.

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* From this point all calculations were performed with the *CRYSTALS* system of computer programs (Rollett & Carruthers, 1974), adapted for the Univac 1110 computer.

* Lists of structure factors, anisotropic thermal parameters and H atom coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35475 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Bond distances* (Å) *and angles* (°) *for aplysistatin*

The estimated standard deviations are listed in parentheses.

C(1)–C(2)	1·546 (10)	C(14)–C(1)–C(2)	112·3 (6)
C(1)–C(14)	1·506 (10)		
C(2)–C(3)	1·506 (10)	C(1)–C(2)–C(3)	110·6 (6)
C(3)–C(4)	1·537 (9)	C(2)–C(3)–C(4)	114·6 (6)
C(3)–Br	1·968 (6)	C(2)–C(3)–Br	107·5 (5)
		C(4)–C(3)–Br	111·7 (4)
C(4)–C(5)	1·599 (9)	C(3)–C(4)–C(5)	104·7 (5)
C(4)–C(16)	1·525 (10)	C(3)–C(4)–C(16)	113·0 (6)
C(4)–C(17)	1·543 (10)	C(3)–C(4)–C(17)	108·8 (6)
		C(5)–C(4)–C(16)	113·6 (6)
		C(5)–C(4)–C(17)	108·0 (6)
		C(16)–C(4)–C(17)	108·5 (6)
C(5)–C(6)	1·527 (10)	C(4)–C(5)–C(6)	114·5 (6)
C(5)–C(14)	1·555 (9)	C(4)–C(5)–C(14)	114·7 (5)
		C(6)–C(5)–C(14)	112·7 (6)
C(6)–C(7)	1·507 (10)	C(5)–C(6)–C(7)	112·2 (6)
C(7)–C(8)	1·321 (10)	C(6)–C(7)–C(8)	124·1 (7)
C(8)–C(9)	1·466 (10)	C(7)–C(8)–C(9)	125·2 (7)
C(8)–C(12)	1·462 (10)	C(7)–C(8)–C(12)	127·9 (7)
		C(9)–C(8)–C(12)	106·6 (7)
C(9)–O(9)	1·188 (9)	C(8)–C(9)–O(9)	129·3 (8)
C(9)–O(10)	1·348 (10)	C(8)–C(9)–O(10)	109·1 (7)
		O(9)–C(9)–O(10)	121·5 (8)
O(10)–C(11)	1·444 (9)	C(9)–O(10)–C(11)	109·2 (6)
C(11)–C(12)	1·497 (10)	O(10)–C(11)–C(12)	105·7 (6)
C(12)–O(13)	1·418 (8)	C(8)–C(12)–C(11)	102·4 (6)
		C(8)–C(12)–O(13)	115·3 (6)
		C(11)–C(12)–O(13)	110·5 (6)
O(13)–C(14)	1·450 (7)	C(12)–O(13)–C(14)	118·6 (5)
C(14)–C(15)	1·528 (9)	C(1)–C(14)–C(5)	109·9 (6)
		C(1)–C(14)–O(13)	108·9 (6)
		C(1)–C(14)–C(15)	110·5 (6)
		C(5)–C(14)–O(13)	109·4 (5)
		C(5)–C(14)–C(15)	115·6 (6)
		O(13)–C(14)–C(15)	102·3 (5)

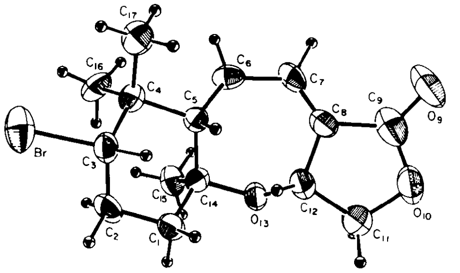

Fig. 1. A perspective representation of the structure of aplysistatin.

molecule are given in Table 2 and a list of torsion angles fully characterizing the molecular conformation is given in Table 3. The perspective view in Fig. 1 displays the correct absolute configuration of aplysistatin and each nonhydrogen atom is represented by an ellipsoid indicating the apparent anisotropic thermal motion determined in this analysis. The four chiral centers are C(3)-*S*, C(5)-*S*, C(12)-*R* and C(14)-*S*, as shown in Fig. 1. The unit-cell contents and molecular packing are shown in the stereoscopic Fig. 2.

Discussion

The molecular structure of aplysistatin as shown in Fig. 1 consists of a 6–7–5 set of fused rings and the 15-C-atom sesquiterpene skeleton has been designed as aplysistane (II) (Pettit, Herald, Allen, Von Dreele, Vanell, Kao & Blake, 1977). The six-membered ring is attached equatorially to the seven-membered ring and

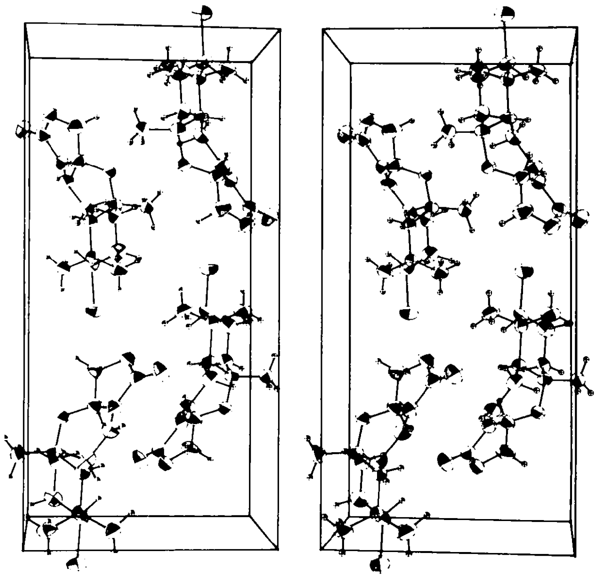

Fig. 2. A stereodiagram of the unit cell and four molecules of aplysistatin. The *a* axis is horizontal, the *c* axis is vertical and the *b* axis into the paper.

Table 3. *Torsion angles* (°) *for aplysistatin*

A right-hand rotation down the atom sequence is given a positive torsion angle. The eclipsed conformation is defined as a zero torsion angle.

C(1)–C(2)–C(3)–C(4)	59·5 (8)	C(4)–C(5)–C(6)–C(7)	142·7 (6)	C(7)–C(8)–C(12)–O(13)	31·1 (11)
C(1)–C(14)–C(5)–C(4)	−54·9 (8)	C(4)–C(5)–C(14)–O(13)	−174·4 (5)	C(8)–C(9)–O(10)–C(11)	5·6 (9)
C(1)–C(14)–C(5)–C(6)	171·6 (6)	C(5)–C(6)–C(7)–C(8)	28·3 (10)	C(8)–C(12)–C(11)–O(10)	26·1 (8)
C(1)–C(14)–O(13)–C(12)	−81·8 (7)	C(5)–C(14)–O(13)–C(12)	38·2 (8)	C(8)–C(12)–O(13)–C(14)	−82·2 (8)
C(2)–C(1)–C(14)–C(5)	53·2 (8)	C(6)–C(5)–C(14)–O(13)	52·2 (7)	C(9)–C(8)–C(12)–C(11)	−22·9 (8)
C(2)–C(1)–C(14)–O(13)	173·0 (5)	C(6)–C(7)–C(8)–C(9)	179·4 (7)	C(9)–C(8)–C(12)–O(13)	−143·0 (6)
C(2)–C(3)–C(4)–C(5)	−56·6 (7)	C(6)–C(7)–C(8)–C(12)	6·3 (13)	C(9)–O(10)–C(11)–C(12)	−20·3 (8)
C(3)–C(2)–C(1)–C(14)	−55·8 (8)	C(7)–C(6)–C(5)–C(14)	−83·7 (7)	O(10)–C(9)–C(8)–C(12)	11·6 (9)
C(3)–C(4)–C(5)–C(6)	−173·0 (6)	C(7)–C(8)–C(9)–O(10)	−162·7 (14)	O(10)–C(11)–C(12)–O(13)	149·6 (6)
C(3)–C(4)–C(5)–C(14)	54·3 (7)	C(7)–C(8)–C(12)–C(11)	151·2 (8)	C(11)–C(12)–O(13)–C(14)	162·2 (6)

is in the chair conformation. The conformation of the seven-membered ring is restricted to a twist-boat by the double bond at C(7)—C(8). The nearly flat (r.m.s. displacement 0·112 Å) five-membered ring is also attached to the seven-membered ring; O(13) in the seven-membered ring is in the bridging position between the two outer rings.

The bonding pattern within the six-membered ring is normal with an average C—C single-bond length of 1·542 (35) Å. The longest of these, C(4)—C(5), 1·599 (9) Å, can be ascribed to the high degree of substitution on these two C atoms. The C(2)—Br bond length, 1·968 (6) Å, is slightly longer than expected for a C—Br single bond, 1·938 Å (*Tables of Interatomic Distances and Configuration in Molecules and Ions*, 1965). The bond angles within the ring, except C(3)C(4)C(5), are slightly larger than the normal tetrahedral angle, as expected for a six-membered ring. The bonding within the seven-membered ring is also normal; C(7)C(8) is a normal double bond and the other bonds are all C—C or C—O single bonds. The bond angles are all larger than the ideal tetrahedral or trigonal angles, which is typical for this size ring. In the five-membered ring the effect of ring strain is evident in the bond distances and angles. The bond angle, C(8)C(9)O(10), at the carbonyl is much less, 109·1 (15)°, than expected for an sp^2 C and has probably resulted in the short carbonyl bond, 1·188 (9) Å, and long ester C—O bond, 1·348 (10) Å, found at this point. The other bonds within the ring are more nearly normal and the angles are all smaller than the ideal angles, as is typical for a five-membered ring.

All intermolecular contacts are at or greater than the sum of the van der Waals radii. Two contacts, C(1)···C(6), 3·757 Å and C(11)···C(15), 3·630 Å, between adjacent molecules seem to be less than the sum of the methyl-group radii, but inspection of the H···H contacts between these groups shows no abnormally short contacts. Evidently, the protons on these groups must intermesh. The only other contact of interest is between the Br atom and the C(9)—O(9) carbonyl on an adjacent molecule. The contact distances, 3·511 Å for Br···O(9) and 3·577 Å for Br···C(9), are at the sum of the van der Waals radii for these atoms.

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The Structure of the Cyclic Trimer of Poly(ethylene terephthalate)*

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Abstract

$C_{30}H_{24}O_{12}$, $M_r = 576·5$, is monoclinic, space group Cc, with $a = 17·101$ (4), $b = 19·695$ (5), $c = 8·360$ (2) Å, $\beta = 96·47$ (2)°, $V = 2798$ (1) Å^3, $D_m = 1·375$ (2), $D_c = 1·365$ Mg m^{-3}, $Z = 4$, μ(Cu $K\alpha$) = 0·77 mm^{-1}, $F(000) = 1200$. The structure was solved by direct methods and refined by block-diagonal least-squares calculations to the final $R = 0·034$. The absolute configuration was not determined. The double bonds of the ester groups cross one another and form parallel rows. Two carbonyl groups (all are in the *cis* position) show large deviations from the benzene plane, thus explaining irregularities found in the IR spectra.

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* 3,8,11,16,19,24-Hexaoxotribenzo[*fgh*,*pqr*,*za*$_1$*b*$_1$]-[1,4,11,14,21,24]hexaoxacyclotriacontane.

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