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Harringtonolide: A Complex Tropone

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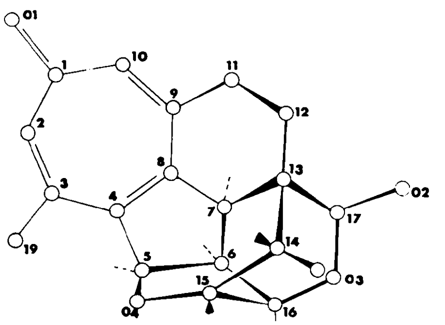
Abstract. $C_{19}H_{18}O_4$, $P2_12_12_1$, a = 8·38 (2), b = 22·34 (4), c = 7·68 (2) Å, Z = 4, d_c = 1·43 Mg m^{-3} (~0·7 × 0·4 × 0·3 mm). The molecule, which is a potent plant-growth inhibitor, was shown to be a complex tropone–furanolactone which includes a cage system composed of three six-membered rings each having a boat conformation.

Introduction. During a screening program to search for new naturally occurring plant-growth regulators, an extract of *Cephalotaxus harringtonia* (plum yew) was found to effectively control the growth of several species of test plants (Buta, Flippen & Lusby, 1978). The structural formula of this compound (harringtonolide) was too complex to be derived from spectral data alone and, therefore, the following X-ray analysis was performed.



Crystals of harringtonolide were provided by J. George Buta of USDA, Beltsville, Maryland, USA. 1399 independent reflections were collected on an automatic diffractometer with the θ–2θ scan technique, Cu $K\alpha$ radiation, λ = 1·54178 Å, Ni filter, $2\theta_{max}$ = 126·5°. Cell dimensions were determined from a least-squares fit of 12 independently measured reflections.

A partial structure was obtained by application of the symbolic addition procedure for non-centrosymmetric crystals (Karle & Karle, 1966). The fragment was then developed into the full structure by successive cycles of tangent-formula refinement and expansion (Karle, 1968). The results are displayed in Fig. 1. The full-matrix least-squares program *ORXFLS*3 (Busing *et al.*, 1975) was used to refine the structure. Atomic scattering factors used were those listed in *International Tables for X-ray Crystallography* (1962). All 18 hydrogens were located in a difference map and their coordinates were included in the final cycles of refinement as constant parameters. A correction for isotropic extinction was also included in the refinement. The function minimized by least squares was $\sum w(|F_o| - |F_c|)^2$, where the weights (w) were derived from estimated standard deviations of observed intensity (Gilardi, 1973). All reflections were included in the refinement and the final R factors were R = 0·078 and R_w = 0·086 and the standard deviation for an observation of unit weight was 2·7. Bond lengths and angles are illustrated in Fig. 2. Table 1 lists the final positional parameters for the molecule.†

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† Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34156 (8 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

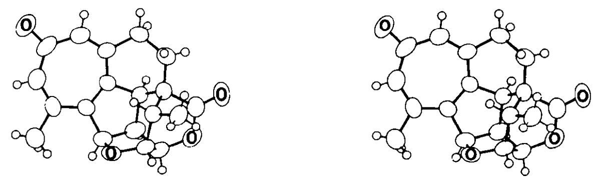

Fig. 1. Results of the structure analysis. The illustration, drawn using program *ORTEP* (Johnson, 1965), shows the atoms at their final refined positions with final anisotropic thermal parameters.

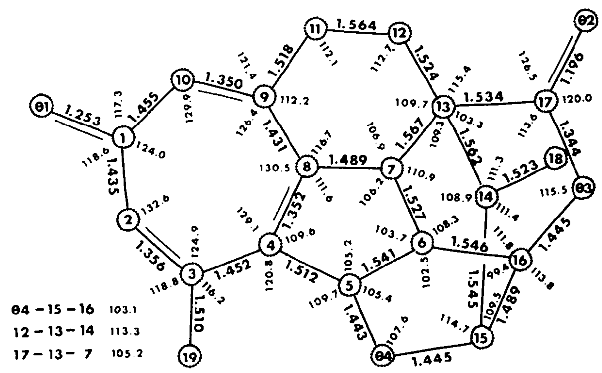

Fig. 2. Bond lengths (Å) and angles (°). Standard deviations are of the order of 0·007 Å for bond lengths and 0·4° for bond angles.

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Table 1. *Refined coordinates for non-hydrogen atoms with standard deviations (based solely on least-squares results) in parentheses*

	x	*y*	*z*
O(1)	1·2973 (6)	−0·0921 (1)	0·2990 (8)
O(2)	1·1083 (5)	0·2882 (1)	0·2914 (6)
O(3)	0·8696 (4)	0·2491 (1)	0·3272 (5)
O(4)	0·7384 (3)	0·1007 (1)	0·2038 (4)
C(1)	1·2099 (7)	−0·0468 (2)	0·3100 (8)
C(2)	1·0400 (7)	−0·0548 (2)	0·3108 (9)
C(3)	0·9168 (6)	−0·0163 (1)	0·3338 (7)
C(4)	0·9334 (5)	0·0469 (1)	0·3745 (6)
C(5)	0·7891 (5)	0·0875 (2)	0·3792 (8)
C(6)	0·8504 (6)	0·1473 (2)	0·4535 (7)
C(7)	1·0306 (5)	0·1440 (2)	0·4259 (6)
C(8)	1·0677 (5)	0·0799 (1)	0·3913 (6)
C(9)	1·2297 (5)	0·0660 (2)	0·3484 (8)
C(10)	1·2881 (6)	0·0114 (2)	0·3082 (9)
C(11)	1·3344 (6)	0·1214 (2)	0·3425 (10)
C(12)	1·2597 (6)	0·1721 (2)	0·2282 (10)
C(13)	1·0814 (6)	0·1800 (1)	0·2598 (6)
C(14)	0·9763 (5)	0·1600 (2)	0·1021 (6)
C(15)	0·7996 (5)	0·1592 (2)	0·1591 (7)
C(16)	0·7813 (6)	0·1935 (2)	0·3241 (8)
C(17)	1·0265 (7)	0·2444 (2)	0·2936 (7)
C(18)	1·0018 (8)	0·2006 (2)	−0·0548 (8)
C(19)	0·7483 (8)	−0·0399 (2)	0·3216 (10)

Difference-map coordinates for hydrogen atoms

	x	*y*	*z*
H(2)	1·001	−0·091	0·271
H(5)	0·689	0·076	0·440
H(6)	0·819	0·161	0·552
H(7)	1·097	0·156	0·539
H(10)	0·398	1·010	0·262
H(11*A*)	1·373	0·138	0·452
H(11*B*)	1·448	0·113	0·283
H(12*A*)	1·291	0·207	0·252
H(12*B*)	1·281	0·163	0·114
H(14)	1·021	0·120	0·068
H(15)	0·739	0·172	0·055
H(16)	0·681	0·205	0·344
H(18*A*)	0·958	0·237	−0·036
H(18*B*)	0·949	0·186	−0·146
H(18*C*)	1·109	0·203	−0·116
H(19*A*)	0·692	−0·026	0·436
H(19*B*)	0·683	−0·015	0·252
H(19*C*)	0·750	−0·075	0·325

Table 2. *Selected torsion angles* (°)

E.s.d.'s are of the order of 0·8°.

7-membered tropone ring		5-membered rings	
C(10)–C(1)–C(2)–C(3)	−10·5	C(8)–C(4)–C(5)–C(6)	−15·9
C(1)–C(2)–C(3)–C(4)	−3·4	C(4)–C(5)–C(6)–C(7)	19·2
C(2)–C(3)–C(4)–C(8)	2·6	C(5)–C(6)–C(7)–C(8)	−16·3
C(3)–C(4)–C(8)–C(9)	11·1	C(6)–C(7)–C(8)–C(4)	7·2
C(4)–C(8)–C(9)–C(10)	−12·6	C(7)–C(8)–C(4)–C(5)	5·5
C(8)–C(9)–C(10)–C(1)	−5·1		
C(9)–C(10)–C(1)–C(2)	17·8	C(5)–O(4)–C(15)–C(16)	−38·4
		O(4)–C(15)–C(16)–C(6)	46·5
		C(15)–C(16)–C(6)–C(5)	−37·6
		C(16)–C(6)–C(5)–O(4)	16·0
		C(6)–C(5)–O(4)–C(5)	13·1
6-membered rings			
C(11)–C(9)–C(8)–C(7)	−1·3	C(13)–C(7)–C(6)–C(16)	−8·9
C(9)–C(8)–C(7)–C(13)	57·1	C(7)–C(6)–C(16)–O(3)	−48·9
C(8)–C(7)–C(13)–C(12)	−60·6	C(6)–C(16)–O(3)–C(17)	57·1
C(7)–C(13)–C(12)–C(11)	11·7	C(16)–O(3)–C(17)–C(13)	−0·5
C(13)–C(12)–C(11)–C(9)	43·2	O(3)–C(17)–C(13)–C(7)	−56·6
C(12)–C(11)–C(9)–C(8)	−50·2	C(17)–C(13)–C(7)–C(6)	59·4
C(13)–C(7)–C(6)–C(16)	−8·9	C(13)–C(14)–C(15)–C(16)	16·0
C(7)–C(6)–C(16)–C(15)	71·6	C(14)–C(15)–C(16)–O(3)	43·0
C(6)–C(16)–C(15)–C(14)	−76·0	C(15)–C(16)–O(3)–C(17)	−54·6
C(16)–C(15)–C(14)–C(13)	16·0	C(16)–O(3)–C(17)–C(13)	−0·5
C(15)–C(14)–C(13)–C(7)	47·0	O(3)–C(17)–C(13)–C(14)	58·0
C(14)–C(13)–C(7)–C(6)	−51·0	C(17)–C(13)–C(14)–C(15)	−64·2

Discussion. The molecule is composed of an unusual and complex ring system. There are basically two groups of rings at approximately right angles to one another. One ring system is almost planar and consists of the conjugated seven-membered tropone ring and four atoms from each of the two rings fused to it. The other system is globular and contains the remaining five rings. The molecule exhibits great strain as is evident from the bond lengths and angles. In order to maintain its essentially planar configuration, all the angles in the tropone ring have been forced to deviate significantly from the ideal values. The greatest deviation is shown by the C(1)–C(2)–C(3) angle with a value of 132·6°.

In the remainder of the molecule, the strain is spread over both the distances and angles. The C–C bonds are either compressed or stretched from the ideal value of 1·54 Å and most of the tetrahedral carbon angles deviate markedly from the expected value (109·5°), especially C(6)–C(16)–C(15) at 99·4°. Three of the four six-membered rings are in the boat form while the fourth six-membered ring, fused to the tropone ring, is in a half-boat conformation with C(7) and C(13) out of the plane of the other four atoms. The five-membered ring fused to the tropone ring is virtually planar while the other five-membered ring is a distorted envelope with C(16) out of the plane of the other four atoms. Pertinent torsion angles are given in Table 2. The molecules are held together solely by van der Waals forces. The closest intermolecular approaches are O(4)···C(19) at 3·24 Å and O(2)···C(6) at 3·17 Å.

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