Conformations of Tetrahydro-2-(non-1-en-3,5,7-triynyl)pyran-3-acetate (Cunaniol Acetate). Part 1. Crystal and Molecular Structure of Cunaniol Acetate (Violet Modification)

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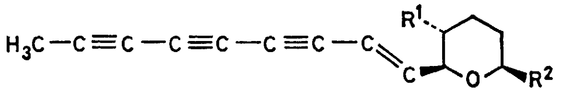
The three-dimensional structure of the title compound, a naturally occurring polyacetylene which is a potent convulsant drug, has been determined by single-crystal *X*-ray diffraction methods. Crystals are orthorhombic, space group $P2_12_12_1$ with $a = 17.512(12)$, $b = 16.378(10)$, $c = 5.128(3)$ Å, $Z = 4$. The structure was solved by direct methods and refined by a least-squares procedure to R 0.049 for 538 observed diffraction maxima. The tetrahydropyran ring is in an undistorted chair conformation with the polyacetylene chain and acetate groups equatorial. The violet colour of the crystals is discussed in terms of the molecular packing which is determined by van der Waals forces.

CUNANIOL ACETATE (I) is isolated from the leaves of *Clibadium sylvestra* (Aubl.) Baill., a shrub found in tropical South America. It is toxic to fish and extremely poisonous to mammals where its action as a convulsant is similar to that of leptazol.[1]



(I) R^1 = OAc (II) R^1 = H
R^2 = H R^2 = OAc

(I) crystallizes from solution as violet needles and as colourless prisms, a phenomenon also observed for (II), a related compound isolated from *Centaurea muricata* L.[2] The crystal and molecular structure of the violet modification of (I) is described.

EXPERIMENTAL

Crystals of the title compound were sealed in glass Lindermann tubes containing mother liquor. They are long violet needles elongated along the *c* axis and have rectangular cross-section.

Crystal Data.—$C_{16}H_{16}O_3$, $M = 256.3$. Orthorhombic, $a = 17.512(12)$, $b = 16.378(10)$, $c = 5.128(3)$ Å, $U = 1\,470.8$ Å^3, $Z = 4$, $D_c = 1.158$ g cm^{-3}. Space group $P2_12_12$ (No. 18, D_2^3) or $P2_12_12_1$ (No. 19, D_2^4) owing to the total absence of reflections of the type $00l$; shown to be the latter by subsequent successful refinement. Mo-K_α radiation, $\lambda = 0.710\,7$ Å, μ(Mo-K_α) = 0.9 cm^{-1}.

Intensity Measurements.—Three-dimensional *X*-ray diffraction intensities from a small single crystal (*ca.* 0.22 × 0.14 × 6.5 mm) were measured on a computer-controlled Stöe four-circle diffractometer[3] by use of graphite monochromatized (002) Mo-K_α radiation and a coupled θ—2θ step scan. Reflections were integrated over a peak width of 1.6° with steps of 0.04° in 2θ and a counting time of 6 s per step. In the range 2θ 5—55°, 538 diffraction maxima out of a possible 1551 in an octant of reciprocal space $(+h, +k, +l)$ had $I \geqslant 3\delta(I)$ and were considered observed. Data were corrected for Lorentz and polarization effects but not for absorption or extinction.

Structure Solution and Refinement.—Normalized structure factors $|E|$ were calculated from the observed structure factors by use of the *K*-curve method, normalizing some of the parity groups of *h*, *k*, *l* separately to obtain the condition $|E^2|_{av} = 1.0$.

An initial set of phases for 195 reflections with $|E| \geqslant 1.5$ was obtained by use of MULTAN,[4] and an *E* map calculated with the phases derived from the most consistent solution revealed the positions of all non-hydrogen atoms in the asymmetric unit. Structure factors calculated using these

TABLE 1

Fractional co-ordinates (×10^4) and thermal motion parameters (×10^3)* derived from least-squares refinement, with estimated standard deviations in parentheses

Atom	*x*	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	−1 655(7)	4 857(7)	−13 042(32)	92(2)	109(3)	128(12)	24(2)	−16(4)	16(5)
C(2)	−1 097(7)	4 702(6)	−11 014(32)	87(2)	60(2)	99(10)	6(2)	−1(5)	25(4)
C(3)	−608(7)	4 544(7)	−9 398(31)	88(2)	56(2)	90(9)	20(2)	6(4)	25(4)
C(4)	−57(7)	4 407(7)	−7 526(28)	86(2)	62(2)	90(10)	10(2)	0(4)	19(4)
C(5)	431(7)	4 315(7)	−5 953(29)	80(2)	66(2)	75(9)	4(2)	−13(4)	7(4)
C(6)	979(7)	4 249(7)	−4 174(29)	77(2)	80(2)	76(8)	21(2)	−6(4)	2(4)
C(7)	1 477(7)	4 178(6)	−2 616(28)	87(2)	56(2)	91(10)	−3(2)	−10(4)	10(4)
C(8)	2 110(7)	4 095(6)	−735(29)	93(2)	62(2)	71(8)	4(2)	−3(4)	3(4)
C(9)	2 741(7)	3 698(6)	−1 417(25)	94(2)	47(2)	74(7)	13(2)	10(4)	−6(3)
C(10)	3 396(7)	3 551(6)	452(24)	71(2)	68(2)	60(6)	3(2)	−12(4)	−15(3)
C(11)	3 434(7)	2 652(6)	1 314(26)	71(2)	62(2)	83(8)	1(2)	−9(4)	−18(3)
C(12)	4 134(7)	2 502(7)	2 956(27)	91(2)	87(2)	81(8)	−3(2)	−19(4)	18(4)
C(13)	4 826(7)	2 753(8)	1 348(34)	74(2)	89(3)	161(12)	20(2)	−14(5)	−7(4)
C(14)	4 752(8)	3 623(8)	573(35)	53(2)	98(3)	178(12)	−9(2)	−16(4)	−19(5)
C(15)	2 202(8)	2 059(8)	2 054(34)	68(2)	74(2)	95(10)	−1(2)	−30(5)	19(4)
C(16)	1 549(7)	2 050(9)	3 831(32)	96(3)	129(4)	117(13)	−48(3)	10(6)	5(6)
O(1)	4 079(5)	3 739(4)	−1 005(16)	67(1)	70(1)	113(5)	−4(1)	28(3)	−4(3)
O(2)	2 762(5)	2 526(4)	2 971(14)	75(1)	76(1)	84(5)	−21(1)	−4(2)	−8(2)
O(3)	2 223(5)	1 716(5)	10(22)	118(2)	112(2)	112(7)	−33(1)	−26(3)	−30(3)

* The Debye–Waller factor is defined as $T = \exp[-2\pi^2\sum_i\sum_j a_i^*a_j^*h_ih_jU_{ij}]$ with U in Å^2.

TABLE 2

Fractional co-ordinates (× 10^3) for hydrogen atoms

Atom	x	y	z
H(11) *	−215	470	−1 250
H(12) *	−166	542	−1 346
H(13) *	−155	441	−1 448
H(8)	202(6)	435(7)	119(27)
H(9)	284(5)	333(6)	−329(22)
H(10)	335(7)	389(6)	197(25)
H(111)	345(6)	238(6)	−54(27)
H(121)	415(6)	191(6)	384(25)
H(122)	418(6)	280(6)	496(21)
H(131)	496(6)	244(5)	−64(25)
H(132)	529(5)	261(7)	213(24)
H(141)	515(5)	386(6)	−90(22)
H(142)	471(6)	404(6)	198(27)
H(161)	172(6)	186(7)	565(27)
H(162)	115(6)	172(6)	399(26)
H(163)	134(7)	244(7)	470(27)

* Not refined. All hydrogen atoms have $U_{\text{iso.}}$ 0.081 Å^2.

atoms as the phasing model gave R 0.305. Three cycles of full-matrix least-squares refinement of non-hydrogen positional parameters, an overall thermal parameter, and an overall scale factor reduced R to 0.131. Further cycles of least-squares refinement, including initially individual isotropic thermal parameters and then individual anisotropic thermal parameters reduced R to 0.086. At this stage in the refinement a difference Fourier synthesis indicated the positions of all hydrogen atoms at heights of 0.37—0.56 e Å^{-3} except for the methyl hydrogens attached to C(1) and C(16) whose heights were 0.23—0.41 and 0.29—0.36 e Å^{-3} respectively [$\sigma(\rho)$ = 0.11 e Å^{-3}]. Furthermore, it was observed that in the difference map other significant peaks existed around these carbon atoms which were considered to be due to disordering of the methyl groups.

The final cycles of refinement of non-hydrogen positional parameters and anisotropic thermal parameters, hydrogen atom positional parameters [except those bonded to C(1) where refinement gave unacceptable bond distances and angles], and an overall scale factor were continued until all parameter shifts were $\leqslant 0.1\sigma$. The function minimised was $\Sigma w(|F_o| - |F_c|)^2$ with $w = 4I/s^2$ where $s = \sigma(I) + 0.05I$. Atomic scattering factors for neutral carbon and oxygen were taken from ref. 5 and for hydrogen from ref. 6. The final R is 0.049 for the 538 data. Final positional and thermal parameters for non-hydrogen atoms are given in Table 1 and hydrogen atom positional parameters in Table 2. Observed and calculated structure factors are listed in Supplementary Publication No. SUP 22569 (3 pp.).*

DISCUSSION

Molecular Structure.—Atom numbering and perspective drawing of the molecule as observed in the crystal are shown in Figure 1.

The polyacetylene chain is linear with none of the relevant bond angles deviating from 180° by more than 3σ (Table 3). All C–C bond distances in this chain are in good agreement with those determined for hexa-2,4-diyne [1.20(2) Å] and octa-2,4,6-triyne [1.20(2) Å].[7] The tetrahydropyran ring is observed in an undistorted chair conformation with the polyacetylene chain and acetate groups equatorial. The orientation of the chain to the ring is such that C(8) is (−)-anticlinal to O(1) about the C(9)–C(10) bond (Table 4). The ester group is planar and is (+)-anticlinal to C(10) about the C(11)–O(2) bond. Distances and angles involving hydrogen atoms are listed in Table 5.

Crystal Packing.—The contents of the unit cell are shown in Figure 2 viewed in the direction of c. The molecular packing is based upon van der Waals interactions with no intermolecular contacts <3.29 Å (Table

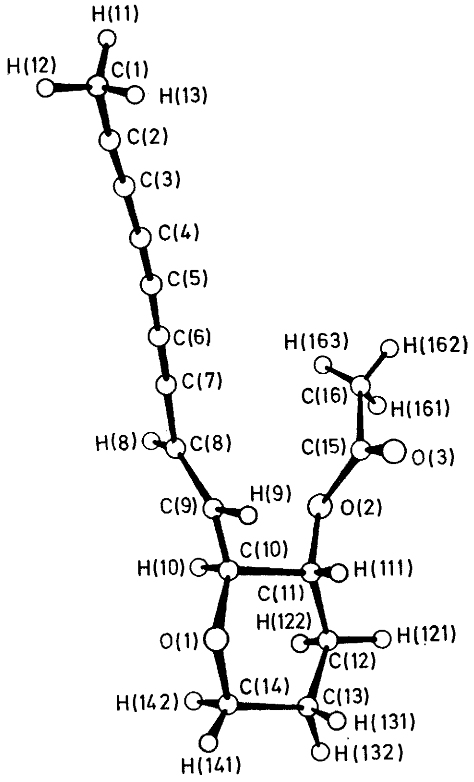


FIGURE 1 Perspective drawing of the molecule showing the atom numbering scheme

TABLE 3

Interatomic distances (Å) and angles (°) for non-hydrogen atoms

(*a*) Distances

C(1)–C(2)	1.45(2)	C(10)–O(1)	1.44(1)
C(2)–C(3)	1.22(2)	C(11)–C(12)	1.51(1)
C(3)–C(4)	1.38(2)	C(11)–O(2)	1.47(1)
C(4)–C(5)	1.18(1)	C(12)–C(13)	1.52(2)
C(5)–C(6)	1.33(2)	C(13)–C(14)	1.49(2)
C(6)–C(7)	1.19(1)	C(14)–O(1)	1.44(1)
C(7)–C(8)	1.48(2)	O(2)–C(15)	1.33(1)
C(8)–C(9)	1.33(1)	C(15)–C(16)	1.46(2)
C(9)–C(10)	1.51(1)	C(15)–O(3)	1.19(1)
C(10)–C(11)	1.54(1)		

(*b*) Angles

C(1)–C(2)–C(3)	177(2)	C(11)–C(10)–O(1)	109(1)
C(2)–C(3)–C(4)	177(1)	C(10)–C(11)–C(12)	111(1)
C(3)–C(4)–C(5)	178(1)	C(10)–C(11)–O(2)	105(1)
C(4)–C(5)–C(6)	177(2)	C(11)–C(12)–C(13)	108(1)
C(5)–C(6)–C(7)	179(2)	C(11)–O(2)–C(15)	118(1)
C(6)–C(7)–C(8)	179(1)	O(2)–C(15)–C(16)	111(2)
C(7)–C(8)–C(9)	120(1)	O(2)–C(15)–O(3)	124(2)
C(8)–C(9)–C(10)	123(1)	C(13)–C(14)–O(1)	110(1)
C(9)–C(10)–C(11)	112(1)	C(14)–O(1)–C(10)	111(1)
C(9)–C(10)–O(1)	105(1)	O(3)–C(15)–C(16)	125(1)

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* See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1978, Index issue.

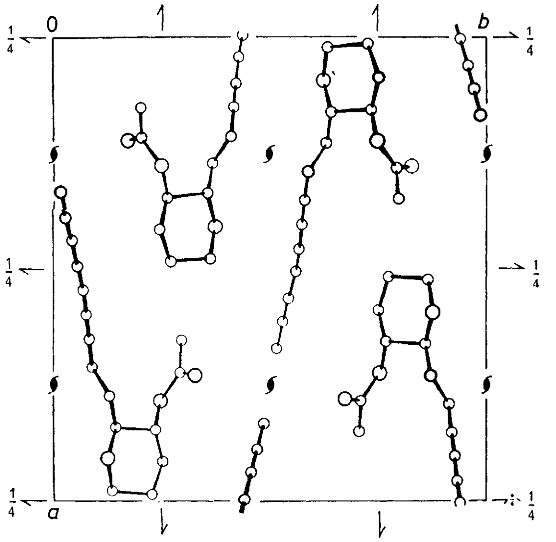

FIGURE 2 Unit-cell contents viewed in the direction of *c*

6). The polyacetylene chains pack in a herring-bone arrangement along the 2_1 symmetry axes parallel to *c* such that the axis of the polyacetylene chain, when extended across the 2_1 axis, is coincident with the terminal carbon atom of the symmetry related chain (see Figure 3) with C(1) $\cdots$ C(1) 3.94 Å, and C(2)–C(1) $\cdots$ C(1) 174(1)°. This arrangement of the polyacetylene chains is similar to that observed in crystals of conjugated diacetylenes[8] which produce highly coloured polymeric compounds when irradiated with u.v. light or heated to temperatures below their melting points. It has been demonstrated that this is due to a solid-state reaction which involves 1,4-addition polymerization of the polyacetylene chain with those of neighbouring molecules in the crystal to produce an infinitely extended conjugated main-chain.[8] It is thought that the violet colour of (I) in the present crystal structure arises from such a process, although because the spacing of the chains in the crystal of 5.128 Å is greater than a suggested[9] value of 3 Å, it is suggested that the polymerization only occurs at dislocations or unobserved regions of disorder in the crystal. The development of colour in (I) by this mechanism is supported by the observations that on prolonged exposure to *X*-rays the crystals deepen in colour and split into bundles of fibrils parallel to *c*, observations consistent with those found in the polymerized diacetylenes.[9]

TABLE 4

Torsion angles (°) for non-hydrogen atoms

C(7)–C(8)–C(9)–C(10)	−177(1)
C(8)–C(9)–C(10)–C(11)	107(1)
C(8)–C(9)–C(10)–O(1)	−135(1)
C(9)–C(10)–C(11)–C(12)	174(1)
C(9)–C(10)–C(11)–O(2)	−69(1)
C(10)–C(11)–O(2)–C(15)	110(1)
C(11)–C(12)–C(13)–C(14)	58(1)
C(12)–C(13)–C(14)–O(1)	−61(2)
C(11)–O(2)–C(15)–C(16)	−175(1)
C(11)–O(2)–C(15)–O(3)	3(2)
C(13)–C(14)–O(1)–C(10)	63(2)

TABLE 5

Interatomic distances (Å) and angles (°) involving hydrogen atoms

(*a*) Distances

H(11)–C(1) *	0.95	H(122)–C(12)	1.14(10)
H(12)–C(1) *	0.95	H(131)–C(13)	1.17(11)
H(13)–C(1) *	1.05	H(132)–C(13)	0.93(9)
H(8)–C(8)	1.08(13)	H(141)–C(14)	1.09(10)
H(8)–C(9)	1.15(11)	H(142)–C(14)	1.00(12)
H(10)–C(10)	0.96(11)	H(161)–C(16)	1.03(13)
H(111)–C(11)	1.05(12)	H(162)–C(16)	0.88(9)
H(121)–C(12)	1.06(12)	H(163)–C(16)	0.86(11)

(*b*) Angles

H(11)–C(1)–C(2) *	111	H(122)–C(12)–C(11)	120(5)
H(12)–C(1)–C(2) *	110	H(131)–C(13)–C(12)	121(6)
H(13)–C(1)–C(2) *	105	H(132)–C(13)–C(12)	116(7)
H(8)–C(8)–C(7)	117(6)	H(141)–C(14)–C(13)	118(6)
H(9)–C(9)–C(8)	127(5)	H(142)–C(14)–C(13)	118(8)
H(10)–C(10)–C(9)	111(7)	H(161)–C(16)–C(15)	110(6)
H(111)–C(11)–C(10)	99(6)	H(162)–C(16)–C(15)	132(5)
H(121)–C(12)–C(11)	114(6)	H(163)–C(16)–C(15)	130(6)

* Not refined.

TABLE 6

Intermolecular contacts <3.5 Å

C(5) $\cdots$ O(1$^{\text{I}}$)	3.30(1)	C(9) $\cdots$ O(2$^{\text{II}}$)	3.46(1)
C(5) $\cdots$ C(14$^{\text{I}}$)	3.49(2)	C(1) $\cdots$ O(3$^{\text{III}}$)	3.40(1)
C(6) $\cdots$ O(1$^{\text{I}}$)	3.43(1)	C(16) $\cdots$ O(3$^{\text{IV}}$)	3.42(1)

Roman numeral superscripts denote the following transformations relative to the origin at x, y, z:

I $0.5 - x, 1 - y, -0.5 + z$ II $x, y, -1 + z$,
III $-x, 0.5 + y, -1.5 - z$ IV $x, y, 1 + z$

Absolute Configuration.—A chemically and physiologically identical compound to (I) has been isolated from *I. terminalis*,[10] a closely related botanical species to *C. sylvestra*. The absolute configuration of this compound has been established[11] as (*S*)-C(10), (*R*)-C(11) and it is probable that (I) also has this configuration. The atomic coordinates in the present structure determination have been chosen to reflect this absolute configuration.

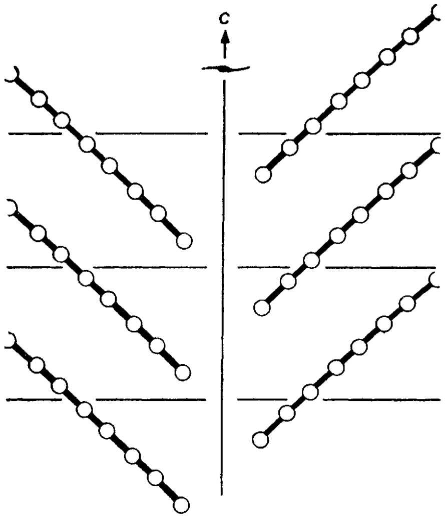

FIGURE 3 The herring-bone arrangement of the polyacetylene chains in the crystal, shown normal to the plane containing the chains. Only the chains have been shown, for clarity, with horizontal lines indicating successive unit cells along *c*

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