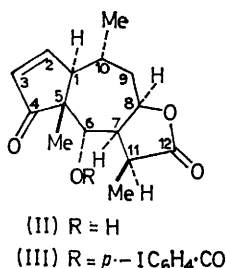
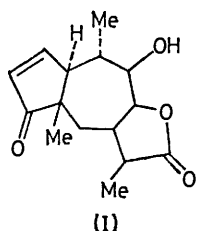


## Structure and Absolute Configuration of Plenolin: X-Ray Analysis of Plenolin *p*-Iodobenzoate

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The structure and absolute configuration of the cytotoxic pseudoguaianolide sesquiterpene lactone, plenolin (II), have been determined by X-ray analysis of the *p*-iodobenzoate derivative (III). Crystals of (III) are orthorhombic, space group  $P2_12_12$ , with  $a = 9.29(1)$ ,  $b = 26.85(1)$ ,  $c = 8.45(1)$  Å,  $Z = 4$ . The structure was solved by the heavy-atom method and the atomic parameters refined by full-matrix least-squares calculations to  $R = 0.041$  over 1165 independent reflections from diffractometer measurements. The absolute configuration was established by the anomalous dispersion effect. The cycloheptane ring adopts a twist chair conformation, the  $\gamma$ -lactone ring is in an envelope conformation, and the cyclopentenone ring approximates a half-chair form.

PLENOLIN,  $C_{15}H_{20}O_4$ , initially isolated as a minor constituent (0.0003%) of *Baileya pleniradiata* Harv. and Grey was assigned structure (I) on the basis of very limited studies.<sup>1</sup> More recently, Lee *et al.* obtained plenolin in greater yield from Florida *Helenium autumnale* L. Reinvestigations showed that the original assign-



ment was incorrect and that the structure should be modified to (II), *i.e.* 11,13-dihydrohelenalin, with undefined stereochemistry at C(11). We here report the results of an X-ray analysis of the *p*-iodobenzoate derivative (III) performed to establish the stereochemistry at C(11) and to provide details of the molecular conformation.<sup>2</sup>

### EXPERIMENTAL

**Crystal Data.**— $C_{22}H_{23}O_5I$ ,  $M = 494.4$ . Orthorhombic,  $a = 9.29(1)$ ,  $b = 26.85(1)$ ,  $c = 8.45(1)$  Å,  $U = 2107$  Å<sup>3</sup>,  $D_m$  (floatation) = 1.55,  $Z = 4$ ,  $D_c = 1.559$ ,  $F(000) = 992$ . Mo- $K_\alpha$  radiation,  $\lambda = 0.7107$  Å;  $\mu$ (Mo- $K_\alpha$ ) = 15.7 cm<sup>-1</sup>. Space group  $P2_12_12$  ( $D_2^3$ ) from systematic absences:  $h00$  when  $h \neq 2n$ ,  $0k0$  when  $k \neq 2n$ .

**Crystallographic Measurements.**—A crystal of dimensions *ca.* 0.40 × 0.20 × 0.14 mm was oriented with the *a* axis parallel to the  $\phi$  axis of an Enraf-Nonius CAD 3 diffractometer (Zr-filtered Mo- $K_\alpha$  radiation; 3° take-off angle). Preliminary cell parameters having been obtained from

precession photographs, more accurate values were determined by centring 37 high-angle reflections on the diffractometer. One octant of intensity data up to 2 $\theta$  50° was measured by use of the  $\theta$ —2 $\theta$  scanning technique as described previously.<sup>3</sup> Instrument and crystal stability were monitored throughout the course of data collection by periodically re-measuring the intensities for two standard reflections and these showed no significant variation. From 2198 measurements, 1165 reflections with  $I > 2\sigma(I)$  were corrected for Lorentz and polarization effects and used in the structure analysis; no allowance was made for absorption.

**Structure Analysis.**—The structure was solved by the heavy-atom approach. Initial co-ordinates for the iodine atom were obtained from the three-dimensional Patterson map and positions for the carbon and oxygen atoms were revealed clearly in an iodine phased ( $R = 0.33$ ) three-dimensional  $F_o$  Fourier synthesis. After several cycles of full-matrix least-squares adjustment of positional and isotropic thermal parameters, anomalous scattering corrections for the iodine atom were introduced into the structure-factor calculations to establish the absolute configuration. For co-ordinates corresponding to the absolute stereochemistry represented by (III),  $R$  was 0.139 whereas for the enantiomer it was 0.144. The highly significant difference<sup>4</sup> indicates that (III) correctly represents the absolute stereochemistry.

Refinement was continued by allowing for anisotropic temperature factors and several cycles reduced  $R$  to 0.054. Following confirmation that there was significant positive electron-density in a difference Fourier map at sites calculated for hydrogen atoms (assuming C-H 1.05 Å) these atoms were included with fixed positions and  $B = 4.0$  Å<sup>2</sup> in subsequent least-squares iterations. Refinement converged at  $R = 0.041$ . Observed and calculated structure factors are listed in Supplementary Publication No. SUP 21231 (9 pp., 1 microfiche).†

Atomic scattering factors used in the structure-factor calculations were those for iodine, carbon, and oxygen from ref. 5 with that of iodine corrected for anomalous scattering<sup>6</sup> of Mo- $K_\alpha$  radiation; the scattering factor of ref. 7 was used for hydrogen. In the least-squares iterations the weighting scheme used initially  $\sqrt{w} = 1$  for  $|F_o| \leq 26.0$

† See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1974, Index issue.

<sup>1</sup> T. G. Waddell and T. A. Geissman, *Phytochemistry*, 1969, **8**, 2371.

<sup>2</sup> K. H. Lee, T. Ibuka, A. T. McPhail, K. D. Onan, T. A. Geissman, and T. G. Waddell, *Tetrahedron Letters*, 1974, 1149.

<sup>3</sup> D. L. McFadden and A. T. McPhail, *J.C.S. Dalton*, 1974, 363.

<sup>4</sup> W. C. Hamilton, *Acta Cryst.*, 1965, **18**, 502.

<sup>5</sup> D. T. Cromer and J. T. Waber, *Acta Cryst.*, 1965, **18**, 104.

<sup>6</sup> 'International Tables for X-Ray Crystallography,' vol. III, Kynoch Press, Birmingham, 1962.

<sup>7</sup> R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 1965, **42**, 3175.

TABLE 1

Fractional atomic co-ordinates ( $\times 10^4$ ) and temperature factor parameters,\* with estimated standard deviations in parentheses

Atom	$x$	$y$	$z$	$10^4 b_{11}$	$10^5 b_{22}$	$10^4 b_{33}$	$10^4 b_{12}$	$10^4 b_{13}$	$10^4 b_{23}$
C(1)	1525(14)	3191(3)	2836(13)	191(19)	71(14)	125(21)	-7(9)	-28(35)	1(9)
C(2)	2885(15)	2936(4)	2246(16)	193(20)	124(17)	183(25)	-12(11)	84(40)	-31(11)
C(3)	4062(15)	3102(5)	2948(17)	200(20)	170(19)	191(25)	21(12)	148(41)	-15(12)
C(4)	3704(14)	3439(4)	4249(16)	151(19)	113(16)	175(23)	6(10)	18(39)	-1(11)
C(5)	2037(12)	3411(4)	4480(16)	99(14)	80(14)	205(23)	10(8)	-18(33)	-6(11)
C(6)	1388(13)	3897(4)	4908(14)	143(17)	103(15)	127(19)	-5(9)	-21(35)	5(10)
C(7)	-264(13)	3941(3)	5133(14)	124(14)	99(14)	214(21)	-8(9)	98(39)	23(10)
C(8)	-1364(15)	3560(4)	4493(16)	163(20)	152(19)	185(24)	-3(11)	-30(14)	45(11)
C(9)	-1155(15)	3256(5)	3007(18)	179(20)	204(22)	203(28)	-36(11)	-63(47)	11(15)
C(10)	94(14)	2895(4)	2889(14)	177(19)	115(14)	187(23)	-9(10)	-38(47)	-2(10)
C(11)	-784(14)	3960(4)	6859(19)	154(16)	145(19)	257(27)	24(10)	96(44)	9(15)
C(12)	-1306(14)	3444(4)	7187(18)	165(18)	146(17)	238(30)	24(10)	87(41)	30(12)
C(13)	194(16)	4153(5)	8169(17)	226(19)	232(22)	287(23)	-23(14)	274(47)	-42(14)
C(14)	1882(14)	3029(4)	5859(16)	157(19)	152(18)	145(21)	22(11)	21(39)	21(11)
C(15)	-40(19)	2572(5)	1402(16)	279(28)	166(19)	245(28)	-23(14)	-198(59)	-10(13)
O(16)	4478(10)	3704(3)	4982(11)	153(13)	234(16)	238(18)	-17(8)	-4(30)	-25(10)
O(17)	-1635(9)	3211(3)	5784(12)	137(12)	168(13)	237(17)	-9(7)	51(27)	24(9)
O(18)	-1479(12)	3236(3)	8401(13)	252(17)	204(16)	242(19)	2(9)	73(40)	37(10)
O(19)	1779(8)	4237(2)	3607(9)	166(11)	83(10)	169(15)	-6(6)	25(23)	-4(6)
C(20)	2136(16)	4701(4)	4004(16)	188(20)	125(17)	199(24)	-2(11)	83(42)	-29(12)
O(21)	2029(12)	4862(2)	5340(11)	249(17)	109(14)	224(17)	-9(7)	117(32)	-16(7)
C(22)	2310(14)	4872(4)	1045(17)	119(17)	108(20)	284(28)	-15(9)	-97(40)	2(11)
C(23)	2898(14)	5136(4)	-200(16)	131(18)	146(21)	203(24)	-18(9)	10(4)	43(11)
C(24)	3811(13)	5531(4)	167(16)	134(17)	153(21)	247(26)	4(10)	41(41)	71(11)
C(25)	4122(12)	5667(4)	1685(17)	114(14)	118(18)	243(24)	-7(9)	10(42)	14(13)
C(26)	3543(13)	5407(4)	2914(16)	133(16)	106(15)	212(27)	15(9)	10(40)	-6(11)
C(27)	2656(12)	4998(5)	2632(14)	117(17)	93(12)	222(20)	-9(9)	44(35)	21(14)
I	4786(1)	5897.5(3)	-1756(1)	139(1)	215(1)	274(2)	-9(1)	19(3)	64(1)

\* In the form:  $B \sin^2\theta/\lambda^2 = b_{11}h^2 + b_{22}k^2 + b_{33}l^2 + b_{12}hk + b_{13}hl + b_{23}kl$ .

and  $\sqrt{w} = 26.0/|F_o|$  for  $|F_o| > 26.0$ , was later adjusted to  $\sqrt{w} = (6.38 - 0.203 |F_o| + 0.00348 |F_o|^2)^{1/2}$  to give no systematic dependence of  $\langle w\Delta^2 \rangle$  when analysed in

angles in Table 3, torsion angles <sup>8</sup> in Table 4, and displacements of selected atoms from various mean planes in Table 5.

TABLE 2

Calculated fractional co-ordinates ( $\times 10^3$ ) for hydrogen atoms, labelled according to the carbon atom to which they are bonded

Atom	$x$	$y$	$z$
H(1)	133	348	206
H(2)	314	269	133
H(3)	500	293	252
H(6)	187	402	600
H(7)	-51	429	456
H(8)	-231	378	425
H(9 $\alpha$ )	-103	351	206
H(9 $\beta$ )	-209	305	284
H(10)	11	267	390
H(11)	-168	422	688
H(13 $\alpha$ )	-14	417	935
H(13 $\beta$ )	55	451	793
H(13 $\gamma$ )	107	390	811
H(14 $\alpha$ )	234	268	558
H(14 $\beta$ )	78	301	606
H(14 $\gamma$ )	222	317	696
H(15 $\alpha$ )	-99	237	146
H(15 $\beta$ )	84	232	134
H(15 $\gamma$ )	-1	281	45
H(22)	161	458	71
H(23)	264	506	-140
H(25)	480	597	192
H(26)	382	551	411

ranges of  $|F_o|$ . Final atomic co-ordinates and temperature factors are in Tables 1 and 2, interatomic distances and

<sup>8</sup> W. Klyne and V. Prelog, *Experientia*, 1960, **16**, 521.

<sup>9</sup> J. B. Hendrickson, *J. Amer. Chem. Soc.*, 1967, **89**, 7036.

## RESULTS AND DISCUSSION

This X-ray analysis confirms that plenolin is 11,13-dihydrohelenalin and defines the configuration of the C(11)-methyl group as  $\beta$ . Figure 1 shows the molecular conformation of plenolin *p*-iodobenzoate in the crystal.

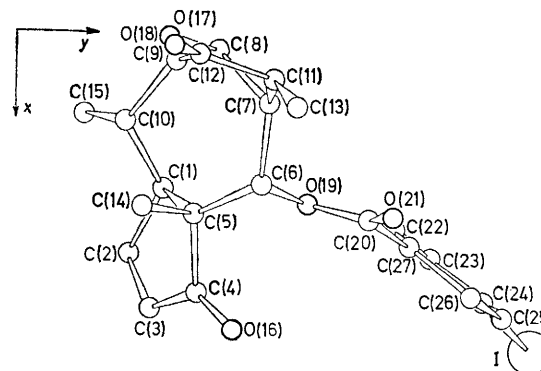


FIGURE 1 Molecular conformation and atom numbering scheme

Comparison of the cycloheptane ring torsion angles in (III) with those calculated for twist-chair ( $C_2$ ) and chair ( $C_s$ ) conformations <sup>9</sup> are presented in Table 6. Analysis of the deviations of the observed angles from ideal symmetry-related values indicates that in (III) the ring

adopts a conformation which lies closer to a twist-chair form with the approximate  $C_2$  axis passing through C(7). The presence of a *cis*-fused  $\gamma$ -lactone ring in

crystals of bromohelenalin<sup>10</sup> (IV) where this ring also adopts a conformation closer to a twist chair than a

TABLE 3

Interatomic distances (Å) and angles (deg.), with estimated standard deviations in parentheses

## (a) Bond lengths

C(1)–C(2)	1.521(18)	C(10)–C(15)	1.531(17)
C(1)–C(5)	1.582(17)	C(11)–C(12)	1.494(17)
C(1)–C(10)	1.550(18)	C(11)–C(13)	1.523(20)
C(2)–C(3)	1.321(20)	C(12)–O(17)	1.374(17)
C(3)–C(4)	1.462(19)	C(12)–O(18)	1.179(18)
C(4)–C(5)	1.563(17)	O(19)–C(20)	1.334(13)
C(4)–O(16)	1.186(16)	C(20)–O(21)	1.213(16)
C(5)–C(6)	1.484(15)	C(20)–C(27)	1.486(18)
C(5)–C(14)	1.558(17)	C(22)–C(23)	1.379(18)
C(6)–C(7)	1.551(17)	C(22)–C(27)	1.419(19)
C(6)–O(19)	1.473(13)	C(23)–C(24)	1.395(16)
C(7)–C(8)	1.545(17)	C(24)–C(25)	1.364(20)
C(7)–C(11)	1.536(20)	C(24)–I	2.103(13)
C(8)–C(9)	1.508(20)	C(25)–C(26)	1.363(18)
C(8)–O(17)	1.458(16)	C(26)–C(27)	1.393(16)
C(9)–C(10)	1.516(18)		

## (b) Valency angles

C(2)–C(1)–C(5)	101.8(10)	C(1)–C(10)–C(9)	109.3(9)
C(2)–C(1)–C(10)	119.5(9)	C(1)–C(10)–C(15)	109.7(10)
C(5)–C(1)–C(10)	115.1(9)	C(9)–C(10)–C(15)	110.7(11)
C(1)–C(2)–C(3)	112.9(11)	C(7)–C(11)–C(12)	104.4(10)
C(2)–C(3)–C(4)	110.9(12)	C(7)–C(11)–C(13)	120.8(11)
C(3)–C(4)–C(5)	106.8(10)	C(12)–C(11)–C(13)	112.0(12)
C(3)–C(4)–O(16)	128.7(12)	C(11)–C(12)–O(17)	109.5(12)
C(5)–C(4)–O(16)	124.4(11)	C(11)–C(12)–O(18)	130.2(13)
C(1)–C(5)–C(6)	101.9(10)	O(17)–C(12)–O(18)	120.3(11)
C(1)–C(5)–C(14)	112.5(8)	C(8)–O(17)–C(12)	108.4(9)
C(4)–C(5)–C(6)	113.0(9)	C(6)–O(19)–C(20)	116.9(9)
C(4)–C(5)–C(14)	102.6(9)	O(19)–C(20)–O(21)	123.2(11)
C(6)–C(5)–C(14)	111.1(10)	O(19)–C(20)–C(27)	112.7(11)
C(5)–C(6)–C(7)	119.9(9)	O(21)–C(20)–C(27)	124.2(11)
C(5)–C(6)–O(19)	105.2(9)	C(23)–C(22)–C(27)	120.6(11)
C(7)–C(6)–O(19)	106.8(8)	C(22)–C(23)–C(24)	117.5(12)
C(6)–C(7)–C(8)	124.2(9)	C(23)–C(24)–C(25)	122.7(12)
C(6)–C(7)–C(11)	115.5(10)	C(23)–C(24)–I	116.5(10)
C(8)–C(7)–C(11)	98.4(9)	C(25)–C(24)–I	120.7(9)
C(7)–C(8)–C(9)	124.3(11)	C(24)–C(25)–C(26)	119.7(11)
C(7)–C(8)–O(17)	106.1(10)	C(25)–C(26)–C(27)	120.5(12)
C(9)–C(8)–O(17)	107.4(9)	C(20)–C(27)–C(22)	122.4(11)
C(8)–C(9)–C(10)	119.9(12)	C(20)–C(27)–C(26)	118.7(11)
		C(22)–C(27)–C(26)	118.9(11)

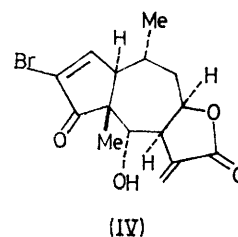
(c) Intermolecular separations  $\leq 3.7$  Å

O(16) ... IV	3.03	C(11) ... O(21 <sup>II</sup> )	3.60
O(18) ... C(15 <sup>III</sup> )	3.37	C(24) ... C(24 <sup>I</sup> )	3.61
O(16) ... C(26 <sup>I</sup> )	3.48	C(7) ... O(21 <sup>III</sup> )	3.61
C(26) ... C(26 <sup>I</sup> )	3.48	C(22) ... C(25 <sup>I</sup> )	3.66
O(16) ... C(25 <sup>I</sup> )	3.51	C(13) ... C(22 <sup>III</sup> )	3.67
C(23) ... C(24 <sup>I</sup> )	3.56	C(8) ... C(26 <sup>III</sup> )	3.69
C(25) ... C(27 <sup>I</sup> )	3.58	C(26) ... C(27 <sup>I</sup> )	3.70

Roman numeral superscripts refer to the following transformations of co-ordinates of Table 1:

$$\begin{array}{ll} \text{I } 1-x, 1-y, z & \text{III } x, y, 1+z \\ \text{II } -x, 1-y, z & \text{IV } 1-x, 1-y, 1+z \end{array}$$

addition to a  $\beta$ -oriented C(5)-methyl group produces severe steric compression on the  $\beta$ -face of the molecule and consequently the distortions from ideal symmetry reflect the adjustment necessary to reduce these interactions. It is of interest to compare the cycloheptane conformation found here with that which occurs in



chair form but analysis of the torsion angles shows that in this case C(10) is the approximate  $C_2$  axis carbon.

TABLE 4

## Torsion angles (deg.)

C(5)–C(1)–C(2)–C(3)	–20	C(6)–C(7)–C(8)–O(17)	94
C(10)–C(1)–C(2)–C(3)	–148	C(11)–C(7)–C(8)–C(9)	–159
C(2)–C(1)–C(5)–C(6)	23	C(11)–C(7)–C(8)–O(17)	–34
C(2)–C(1)–C(5)–C(14)	145	C(6)–C(7)–C(11)–C(12)	–101
C(2)–C(1)–C(5)–C(4)	–87	C(6)–C(7)–C(11)–C(13)	26
C(10)–C(1)–C(5)–C(4)	153	C(8)–C(7)–C(11)–C(12)	33
C(10)–C(1)–C(5)–C(6)	–84	C(8)–C(7)–C(11)–C(13)	160
C(10)–C(1)–C(5)–C(14)	44	C(7)–C(8)–C(9)–C(10)	62
C(2)–C(1)–C(10)–C(9)	–162	O(17)–C(8)–C(9)–C(10)	–63
C(2)–C(1)–C(10)–C(15)	–41	C(7)–C(8)–O(17)–C(12)	23
C(5)–C(1)–C(10)–C(9)	76	C(9)–C(8)–O(17)–C(12)	158
C(5)–C(1)–C(10)–C(15)	–162	C(8)–C(9)–C(10)–C(1)	–68
C(1)–C(2)–C(3)–C(4)	7	C(8)–C(9)–C(10)–C(15)	171
C(2)–C(3)–C(4)–C(5)	9	C(7)–C(11)–C(12)–O(17)	–22
C(2)–C(3)–C(4)–O(16)	–169	C(7)–C(11)–C(12)–O(18)	159
C(3)–C(4)–C(5)–C(1)	–20	C(13)–C(11)–C(12)–O(17)	–155
C(3)–C(4)–C(5)–C(6)	–143	C(13)–C(11)–C(12)–O(18)	27
C(3)–C(4)–C(5)–C(14)	97	C(11)–C(12)–O(17)–C(8)	–1
O(16)–C(4)–C(5)–C(1)	158	O(18)–C(12)–O(17)–C(8)	178
O(16)–C(4)–C(5)–C(6)	34	C(6)–O(19)–C(20)–C(21)	–7
O(16)–C(4)–C(5)–C(14)	–85	C(6)–O(19)–C(20)–C(27)	174
C(1)–C(5)–C(6)–C(7)	62	O(19)–C(20)–C(27)–C(22)	22
C(1)–C(5)–C(6)–O(19)	–58	O(19)–C(20)–C(27)–C(26)	–157
C(4)–C(5)–C(6)–C(7)	178	O(21)–C(20)–C(27)–C(22)	–157
C(4)–C(5)–C(6)–O(19)	58	O(21)–C(20)–C(27)–C(26)	24
C(14)–C(5)–C(6)–C(7)	–67	C(27)–C(22)–C(23)–C(24)	–1
C(14)–C(5)–C(6)–O(19)	173	C(23)–C(22)–C(27)–C(20)	–175
C(5)–C(6)–C(7)–C(8)	–18	C(22)–C(23)–C(24)–C(25)	–1
C(5)–C(6)–C(7)–C(11)	103	C(22)–C(23)–C(24)–I	176
O(19)–C(6)–C(7)–C(8)	101	C(23)–C(24)–C(25)–C(26)	1
O(19)–C(6)–C(7)–C(11)	–138	I–C(24)–C(25)–C(26)	–176
C(5)–C(6)–O(19)–C(20)	–141	C(24)–C(25)–C(26)–C(27)	1
C(7)–C(6)–O(19)–C(20)	91	C(25)–C(26)–C(27)–C(20)	175
C(6)–C(7)–C(8)–C(9)	–31	C(25)–C(26)–C(27)–C(22)	–3

TABLE 5

Displacements (Å) of atoms from mean planes through various groups of atoms; atoms not included in the derivation of the plane are italicised

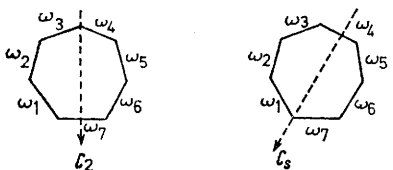
Plane (a): C(1) 0.18, C(2) 0.00, C(3) 0.00, C(4) 0.00, C(5) –0.22, O(16) 0.18
Plane (b): C(7) 0.56, C(8) –0.01, C(11) 0.00, C(12) 0.01, C(13) 0.61, O(17) 0.01, O(18) –0.01
Plane (c): C(6) –0.04, O(19) 0.05, C(20) 0.01, O(21) 0.01, C(27) –0.03
Plane (d): C(20) 0.11, C(22) –0.01, C(23) 0.00, C(24) 0.01, C(25) 0.00, C(26) –0.01, C(27) 0.02, I 0.14

<sup>10</sup> Mazhar-Ul-Haque and C. N. Caughlan, *J. Chem. Soc. (B)*, 1969, 956.

The *cis,trans*-fusion of five-membered rings to a cycloheptane ring without introduction of considerable torsional strain is restricted to certain positions for each

TABLE 6

Comparison of the torsion angles (deg.) in (III) and (IV) with calculated values<sup>a</sup>

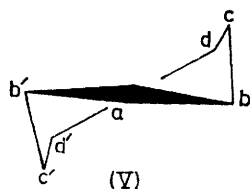


	Twist-chair ( $C_2$ )	Chair ( $C_s$ )	(III)	(IV)
$\omega_1$	-72	-64	-68	61
$\omega_2$	88	84	62	-98
$\omega_3$	-39	-66	-31	53
$\omega_4$	-39	0	-18	32
$\omega_5$	88	66	62	-81
$\omega_6$	-72	-84	-84	59
$\omega_7$	54	64	76	-36
$\Sigma_2^b$	0	104	29	40
$\Sigma_s^c$	122	0	77	124
$\Sigma_2/(\Sigma_2 + \Sigma_s)$	0	1	0.27	0.24
Approx. $C_2$ axis			C(7)	(C10)

<sup>a</sup> J. B. Hendrickson, *J. Amer. Chem. Soc.*, 1967, **89**, 7036.

<sup>b</sup>  $\Sigma_2 = (|\omega_1 - \omega_6| + |\omega_2 - \omega_5| + |\omega_3 - \omega_4|)$ . <sup>c</sup>  $\Sigma_s = (|\omega_1 + \omega_7| + |\omega_2 + \omega_6| + |\omega_3 + \omega_5| + |\omega_4|)$ .

of the possible chair, twist-chair, boat, or twist-boat conformations.<sup>11</sup> In particular, for the most stable twist-chair form (V) *cis*-fusion occurs preferentially at a-b or d-d' type bonds whereas for *trans*-fusion b-c or



c-d type bonds are favoured. Although the twist-chair conformation found in (IV) corresponds to a more strained combination of *cis,trans*-ring-fusions than are found in (III), this is compensated by removal of the severe unfavourable C(5)-methyl- $\gamma$ -lactone transannular interactions. The difference in steric overcrowding is reflected in the smaller mean valency angle (116°) in (IV) compared with that (118°) in (III).

If it is assumed that neither the introduction of the bromine atom at C(3) nor the reduction of the 11,13-double bond has produced a significant change in the

relative stabilities of the two cycloheptane forms found in (III) and (IV) from the corresponding helenalin values, then the occurrence of these two strained conformations in different crystalline environments suggests that they are probably sufficiently close in energy that relatively facile interconversion may occur in solution. Experimental observations on the formation of plenolin from helenalin and the lack of an observable circular dichroism<sup>12</sup> of the  $n \rightarrow \pi^*$  transition of the  $\alpha$ -methylene- $\gamma$ -lactone chromophore in helenalin may be rationalised in the light of such a suggestion. Catalytic hydrogenation of helenalin to yield plenolin as the major product would be expected to occur if the cycloheptane ring adopts a conformation similar to that found in (III) for then the approach of the  $\beta$  face to the catalyst surface would be completely hindered. The sign of the Cotton effect<sup>13</sup> for the  $n \rightarrow \pi^*$  transition of the  $\alpha$ -methylene- $\gamma$ -lactone chromophore has been related to the chirality of the C=C-C=O chromophore. A recent survey of results from X-ray diffraction studies has shown that the C=C-C=O and  $\gamma$ -lactone C-C-C=O torsion angles have paired signs regardless of the nature of the ring junction.<sup>14</sup> In addition, for a *cis*-ring-fusion the cycloheptane endocyclic torsion angle at the ring fusion will also have the same sign as the C=C-C=O torsion angle. Consequently, knowledge of the value of the cycloheptane torsion angle allows prediction of the sign of the Cotton effect. Thus, the conformation found in (III) with  $\omega_{7,8}$  negative corresponds to a negative chirality while that in (IV) with  $\omega_{7,8}$  positive corresponds to a positive chirality. If both conformers of helenalin are present to an appreciable extent in solution, then they would be expected to give rise to Cotton effects of opposite sign, thereby resulting in no net observable effect.

In the *cis*-fused  $\gamma$ -lactone ring the mean internal valency angle is 105° and the ring adopts the usual envelope conformation with C(7) 0.54 Å out of the mean plane through atoms C(8), C(11), C(12), O(2), and O(3). Corresponding values for other  $\gamma$ -lactones which also approximate envelope forms are 106°, 0.60 Å in deacetyl-dihydrogaillardin,<sup>15</sup> and 106°, 0.63 Å in bromogeigerin acetate.<sup>16</sup>

The cyclopentenone ring approximates to a half-chair form with C(1) and C(5) displaced 0.18 and 0.22 Å to opposite sides of the plane through atoms C(2)—(4). This contrasts with the more normal envelope form adopted by the corresponding ring of (IV) where C(5) is 0.27 Å from the C(1)—(4) plane. These conformational differences are a further consequence of the greater steric overcrowding present in the cycloheptane ring conformation found in (III). Note, however, that this conformational difference does not alter the sign of the torsion angles [-169° (III), and -175° (IV)] which would both yield the same (negative) Cotton effect for the  $n \rightarrow \pi^*$  transition in accord with those

<sup>11</sup> J. B. Hendrickson, *Tetrahedron*, 1963, **19**, 1387.

<sup>12</sup> W. Stöcklin, T. G. Waddell, and T. A. Geissman, *Tetrahedron*, 1970, **26**, 2397.

<sup>13</sup> A. F. Beecham, *Tetrahedron*, 1972, **28**, 5543.

<sup>14</sup> A. T. McPhail and G. A. Sim, *Tetrahedron*, 1973, **29**, 1751.

<sup>15</sup> T. A. Dullforce, G. A. Sim, and D. N. J. White, *J. Chem. Soc. (B)*, 1971, 1399.

<sup>16</sup> J. A. Hamilton, A. T. McPhail, and G. A. Sim, *J. Chem. Soc.*, 1962, 708.

found<sup>12</sup> for plenolin and helenalin. These results provide the basis for the earlier observations of Herz *et al.*<sup>17</sup> who noted that cyclopentenone rings *trans*-fused to cycloheptane rings in a number of pseudoguaianolide

The arrangement of molecules in the crystal as viewed in projection along the *c* axis is shown in Figure 2, and the shorter intermolecular separations are listed in Table 3. The smallest distance O(16) ··· I (3.03 Å)

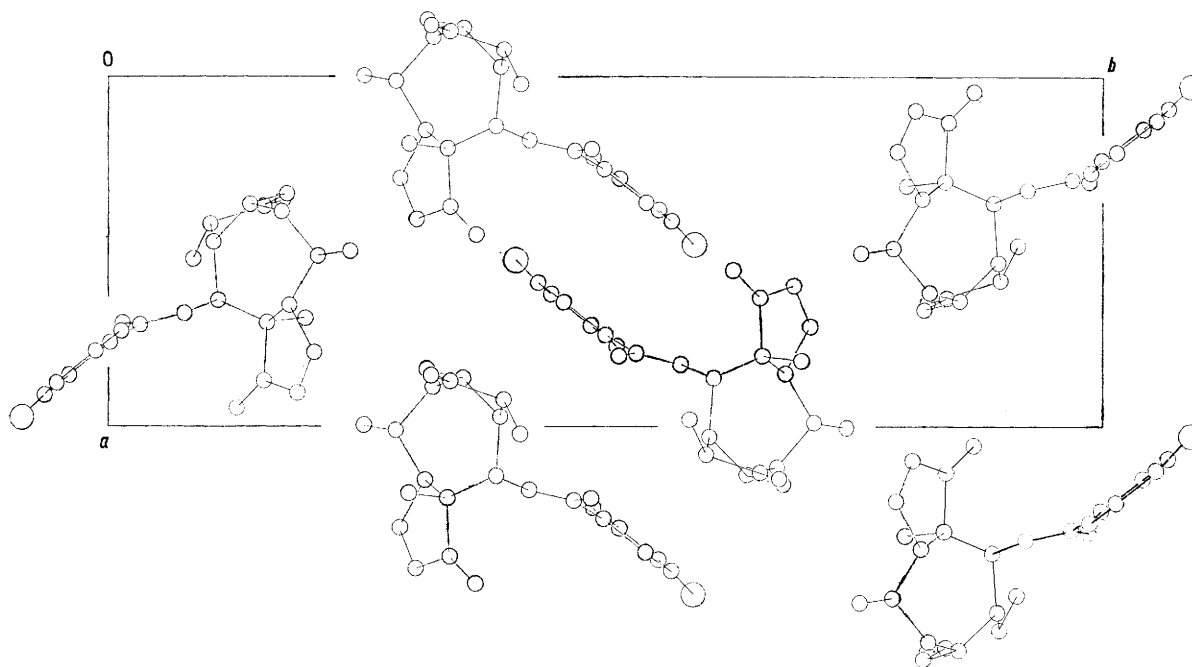


FIGURE 2 The crystal structure, viewed in projection along the *c* axis

sesquiterpenes gave rise to Cotton effects of the same sign leading to the conclusion that the chromophore had the same chirality in each compound regardless of the cycloheptane conformation.

The *p*-iodobenzoate group is distinctly non-planar with the iodine atom and C(20) displaced significantly to the same side of the phenyl ring plane (Table 5). In addition to this pronounced bowing, the dihedral angle between the approximately planar ester C-CO-O-C group and the phenyl ring plane is 25°. These distortions from coplanarity appear to be due to the intermolecular I ··· O(carbonyl) interaction discussed later. From the values found for the C(5)-C(6)-O(19)-C(20) and C(7)-C(6)-O(19)-C(20) torsion angles (-141 and 91°), the H(6)-C(6)-O(19)-C(20) torsion angle must lie close to -25°. The latter is in accord with those found at several other secondary ester groups,<sup>15,18</sup> and indicates that the C=O bond adopts the usual conformation where it is approximately *syn*-planar<sup>19</sup> with the C-H bond.

The mean values of chemically equivalent bonds are in good agreement with accepted values:<sup>20</sup> C(*sp*<sup>3</sup>)-C(*sp*<sup>3</sup>) 1.535, C(*sp*<sup>3</sup>)-C(*sp*<sup>2</sup>) 1.526, C(*sp*<sup>2</sup>)-C(*sp*<sup>2</sup>) 1.474, C(*sp*<sup>2</sup>)=C(*sp*<sup>2</sup>) 1.321, C(ar)-C(ar) 1.386, C(*sp*<sup>3</sup>)-O 1.466, C(*sp*<sup>2</sup>)-O 1.354, C=O 1.193, and C(ar)-I 2.103 Å.

<sup>17</sup> W. Herz, M. V. Lakshmikantham, and R. N. Mirrington, *Tetrahedron*, 1966, **22**, 1709.

<sup>18</sup> C. Chothia and P. Pauling, *Nature*, 1970, **226**, 541.

occurs between molecules related by the crystallographic two-fold axis and it is significantly smaller than the sum of the van der Waals radii<sup>21</sup> (3.55 Å). Such

TABLE 7

Some examples of *n*-donor-acceptor interactions; distances (Å), angles (deg.)

Donor	Acceptor	O ··· I	C-I ··· O
Ester CO	<i>p</i> -Iodobenzenesulphonyl <sup>a</sup>	3.02	174
Ester CO	<i>p</i> -Iodobenzenesulphonyl <sup>b</sup>	3.06	176
Amide CO	Iodoacetate <sup>c</sup>	3.10	171
Methoxy O	<i>p</i> -Iodobenzoate <sup>d</sup>	3.01	175
Ethanol O	<i>p</i> -Iodobenzamide <sup>e</sup>	3.16	162
Enone CO	<i>p</i> -Iodobenzoate <sup>f</sup>	3.03	164

<sup>a</sup> A. T. McPhail and G. A. Sim, *J. Chem. Soc. (C)*, 1966, 1394.

<sup>b</sup> M. Brufani, S. Cerrini, W. Fedeli, and A. Vaciago, *J. Chem. Soc. (B)*, 1971, 2021. <sup>c</sup> A. T. McPhail and G. A. Sim, *J. Chem. Soc. (B)*, 1968, 923. <sup>d</sup> A. T. McPhail, G. A. Sim, J. D. M. Asher, J. M. Robertson, and J. V. Silverton, *J. Chem. Soc. (B)*, 1966, 18. <sup>e</sup> A. T. McPhail, G. A. Sim, A. J. Frey, and H. Ott, *J. Chem. Soc. (B)*, 1966, 377. <sup>f</sup> Present work.

contacts are of fairly frequent occurrence; some similar distances involving iodine and oxygen atoms in a variety of chemical environments are listed in Table 7. In all

<sup>19</sup> A. McL. Mathieson, *Tetrahedron Letters*, 1965, 4137.

<sup>20</sup> *Chem. Soc. Special Publ.*, No. 11, 1958; No. 18, 1965.

<sup>21</sup> L. Pauling, 'The Nature of the Chemical Bond,' 3rd edn., Cornell University Press, Ithaca, New York, 1960, p. 260.

these, the C-I...O angle lies close to linear and the interaction appears to be of an *n*-donor-acceptor type.<sup>22</sup>

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performed on an IBM 370 165 computer located at the Triangle Universities Computation Centre, Research Triangle Park, North Carolina.

[4/2027 Received, 1st October, 1974]

<sup>22</sup> R. Foster, 'Organic Charge-Transfer Complexes,' Academic Press, New York, 1969.

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