Sesquiterpenoids. Part XIV.[1] *X*-Ray Study of 13β-*p*-Bromophenylthio-11α,13-dihydropulchellin-C Diacetate (2α,3β-Diacetoxy-13β-*p*-bromophenylthio-11α,13-dihydroisolantolactone): Stereochemistry of Addition of Thiols to Sesquiterpenoid α-Methylene γ-Lactones †

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The molecular structure of the *p*-bromobenzenethiol adduct of the sesquiterpenoid pulchellin-C diacetate (2α,3β-diacetoxyisolantolactone) has been determined by *X*-ray diffraction. In the formation of the adduct addition of the hydrogen atom to C(11) of the α-methylene γ-lactone took place *cis* to the hydrogen atom at C(8), causing the bulky $RSCH_2$-group at C(11) to adopt a *quasi*-equatorial orientation on the envelope-like lactone ring. The cyclohexane ring A approximates closely to an ideal chair form with torsion angles in the range 56—62, mean 60°, but ring B, because of *cis*-fusion to the γ-lactone, is considerably distorted from ideal chair form and has torsion angles in the range 41—64, mean 51°. The adduct crystallizes in the orthorhombic space group $P2_12_12_1$, with $Z = 4$, and $a = 11{\cdot}076(3)$, $b = 7{\cdot}194(2)$, $c = 31{\cdot}189(6)$ Å. The structure was solved, from *X*-ray data measured on an automatic diffractometer, by Patterson and Fourier methods, and refined by least-squares techniques to R 6·0% for 1980 reflections. The absolute configuration of the sesquiterpenoid was established by the anomalous-dispersion effect.

YOSHIOKA *et al.* have recently reviewed the n.m.r. spectra of α,β′-unsaturated sesquiterpene γ-lactones, and observed that in a number of the compounds the signal of the proton H_a in the fragment (1) appears at a lower field than normal.[2] Examination of molecular models indicated that in these molecules the adjacent hydroxy-oxygen atom is only *ca.* 2·0—2·5 Å from H_a, and the paramagnetic shift was attributed to the van der Waals proximity effect [3,4] of the hydroxy-group on H_a. Furthermore, acetylation of the hydroxy-group causes the H_a signal to undergo a diamagnetic shift, presumably because delocalization of electron density away from the oxygen atom diminishes the interaction with H_a. The fragment (1) is a feature of pulchellin-C (2α,3β-dihydroxyisolantolactone) (2), and the proton H(14a) exhibits a diamagnetic shift when the compound is acetylated.[5]

Kupchan has suggested that the tumour-inhibitory activity of sesquiterpenoids containing the α-methylene γ-lactone function is connected with the nucleophilic addition of biologically important sulphydryl groups, and has supported this hypothesis by demonstrating that several of these sesquiterpenoids are potent inhibitors of the sulphydryl enzyme phosphofructokinase.[6] *p*-Bromobenzenethiol adducts of α-methylene γ-lactones provide simple models of the type of adduct he discussed, and since the stereochemistry of the addition of *p*-bromobenzenethiol to the sesquiterpenoid *trans*-lactone photoisabelin is already known [7] we considered it timely to elucidate the stereochemistry of addition to a *cis*-lactone.

X-Ray diffraction data for the *p*-bromobenzenethiol adduct of pulchellin-C diacetate were obtained by use of an automatic four-circle diffractometer. The atomic co-ordinates were deduced by Fourier and least-squares methods, and the absolute configuration defined by the anomalous-dispersion effect,[8] the analysis terminating at R 6·0% over 1980 independent reflections. Atomic co-ordinates and vibration parameters are listed in Tables 1 and 2, interatomic distances in Table 3, valency angles in Table 4, torsion angles about the bonds in Table 5, and displacements of the atoms from various planes in Table 6. The arrangement of atoms in the molecule is shown in Figure 1 and the packing of the molecules in the crystal in Figure 2.

Our results establish that the *p*-bromobenzenethiol adduct has the absolute stereochemistry shown in (3), and thus confirm the stereochemistry assigned to pulchellin-C.[5] Moreover, we find that the stereoselective formation of the adduct involves addition of a proton to C(11) from the α-face of the molecule, whereas in the case of photoisabelin, which has a *trans*-fused lactone, addition of the proton took place from the opposite direction to give an adduct with stereochemistry (4); in each case, however, the proton added at C(11) is *cis* to that at C(8). Since the torsion angle C(11)–C(12)–O(1)–C(8) is −3° the lactone ring in (3) has a conformation which approximates closely to the envelope type with C(7) constituting the out-of-plane atom, and the hydrogen atom at C(8) is thereby placed in a *quasi*-axial orientation. The stereochemistry found for the adduct (3) is therefore that in which the bulky $RSCH_2$-group at C(11) is in a *quasi*-equatorial orientation *trans* to the hydrogen atom at C(8), and so evades an unfavourable interaction with that *quasi*-axial hydrogen atom. C(11),C(13)-Saturated sesquiterpenoid γ-lactones generally have conformations which approximate closely to the envelope type,[9] and the

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† No reprints available.

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[7] H. Yoshioka, T. J. Mabry, and A. Higo, *J. Amer. Chem. Soc.*, 1970, **92**, 923.

[8] J. M. Bijvoet, A. F. Peerdeman, and A. J. van Bommel, *Nature*, 1951, **169**, 271.

[9] D. N. J. White, D.Phil. Thesis, University of Sussex, 1970.

α-orientation of the $RSCH_2$-group at C(11) in the photoisabelin adduct (4) [7] therefore likewise makes that group *quasi*-equatorial and keeps it away from the *quasi*-axial β-oriented hydrogen atom at C(8). A related observation is that the more stable C(11)-epimer of the C(6),C(7)-fused γ-lactone santonin has the methyl substituent at C(11) *trans* to the quasi-axial hydrogen on C(6).[10]

TABLE 1

Atomic co-ordinates (fractional × 10^4) with standard deviations in parentheses

	x	y	z
C(1)	1382(8)	4479(13)	6091(3)
C(2)	595(8)	3781(14)	6462(3)
C(3)	−534(8)	2848(14)	6286(2)
C(4)	−152(8)	1192(15)	6010(2)
C(5)	585(7)	1860(12)	5634(2)
C(6)	847(8)	341(13)	5303(3)
C(7)	1394(8)	1229(14)	4892(2)
C(8)	2463(8)	2498(16)	4996(3)
C(9)	2356(9)	3765(15)	5384(3)
C(10)	1759(8)	2833(12)	5790(3)
C(11)	2030(9)	−225(14)	4606(3)
C(12)	3275(10)	−336(16)	4807(3)
C(13)	1455(10)	−2152(15)	4548(3)
C(14)	−423(9)	−541(13)	6100(3)
C(15)	2641(9)	1487(15)	6026(3)
C(16)	617(9)	−1732(15)	3701(3)
C(17)	−289(10)	−1479(20)	3394(3)
C(18)	3(9)	−1245(20)	2970(3)
C(19)	1199(9)	−1243(15)	2853(3)
C(20)	2113(8)	−1472(15)	3149(3)
C(21)	1804(9)	−1743(15)	3583(3)
C(22)	−2467(9)	−1950(15)	6533(3)
C(23)	−3188(10)	1371(16)	6929(3)
C(24)	916(9)	6068(18)	7014(3)
C(25)	384(10)	7725(17)	7243(3)
O(1)	3493(6)	1213(11)	5041(2)
O(2)	4027(7)	−1532(13)	4772(2)
O(3)	−1286(5)	2273(10)	6640(2)
O(4)	−2848(6)	2100(11)	6178(2)
O(5)	168(6)	5418(9)	6705(2)
O(6)	1894(7)	5410(14)	7076(3)
S	92(3)	−2131(5)	4232(1)
Br	1622(1)	−909(2)	2262(0·4)
H(1a)	880	5490	5910
H(1b)	2180	5130	6220
H(2)	1100	2930	6670
H(3)	−1050	3780	6100
H(5)	80	2840	5450
H(6a)	50	−420	5230
H(6b)	1460	−670	5430
H(7)	650	1930	4750
H(8)	2550	3520	4750
H(9a)	3260	4120	5480
H(9b)	1840	4930	5300
H(11)	2010	240	4280
H(13a)	1300	−2680	4860
H(13b)	2140	−3010	4400
H(14a)	−940	−1010	6360
H(14b)	−160	−1680	5910
H(17)	−1220	−1450	3490
H(18)	−670	−1030	2730
H(20)	3040	−1440	3030
H(21)	2490	−1990	3820

TABLE 2

Anisotropic vibration parameters, $b_{ij} \times 10^4$

	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
C(1)	61(8)	164(21)	9(1)	−52(24)	9(5)	−15(8)
C(2)	60(8)	151(21)	8(1)	11(24)	3(5)	−33(8)
C(3)	62(8)	152(21)	5(1)	−19(24)	10(4)	−5(7)
C(4)	54(8)	184(23)	5(1)	47(26)	−3(4)	−2(7)
C(5)	44(7)	129(19)	6(1)	−4(21)	0(4)	0(7)
C(6)	53(8)	159(21)	6(1)	−75(22)	5(4)	−12(7)
C(7)	53(8)	170(21)	5(1)	11(24)	6(4)	3(7)
C(8)	61(8)	180(21)	8(1)	−9(25)	16(5)	0(8)
C(9)	70(9)	207(26)	8(1)	−82(28)	14(5)	−13(9)
C(10)	60(8)	138(19)	7(1)	−9(24)	5(5)	−9(7)
C(11)	86(10)	173(23)	5(1)	3(27)	2(5)	−1(7)
C(12)	83(10)	262(29)	7(1)	25(34)	15(6)	−9(9)
C(13)	110(12)	191(24)	7(1)	8(34)	0(6)	−14(8)
C(14)	86(10)	120(21)	9(1)	−32(25)	5(5)	7(8)
C(15)	74(9)	216(28)	9(1)	95(28)	−10(5)	−19(9)
C(16)	69(9)	205(25)	8(1)	−21(26)	3(5)	−21(9)
C(17)	73(10)	380(41)	12(1)	−23(36)	0(6)	−27(12)
C(18)	71(9)	330(36)	10(1)	15(37)	−10(6)	5(12)
C(19)	81(9)	168(24)	9(1)	−48(27)	2(5)	−8(8)
C(20)	50(8)	204(27)	10(1)	57(25)	0(5)	−28(9)
C(21)	60(9)	232(26)	9(1)	69(27)	−6(5)	−19(9)
C(22)	63(9)	150(23)	11(1)	−41(26)	13(6)	−10(9)
C(23)	88(11)	239(28)	10(1)	−13(31)	38(6)	5(9)
C(24)	78(10)	215(28)	9(1)	−54(32)	1(5)	−27(10)
C(25)	114(12)	234(29)	12(1)	−4(33)	−8(7)	−49(12)
O(1)	61(6)	265(18)	9(1)	23(22)	11(4)	−19(7)
O(2)	100(8)	355(26)	14(1)	172(26)	−9(5)	−46(9)
O(3)	66(6)	180(15)	6(1)	−32(17)	5(3)	−6(5)
O(4)	62(6)	278(20)	10(1)	−63(20)	−4(4)	36(7)
O(5)	60(6)	181(16)	9(1)	2(17)	1(3)	−27(6)
O(6)	94(8)	414(30)	16(1)	81(28)	−31(5)	−82(10)
S	87(3)	337(9)	10(0·3)	−50(10)	12(2)	−34(3)
Br	129(1)	350(4)	10(0·1)	−30(5)	−4(1)	5(1)

* The b_{ij} are components of expression $T = \exp[-(b_{11}h^2 + b_{22}k^2 + b_{33}l^2 + 2b_{12}hk + 2b_{13}hl + 2b_{23}kl)]$.

TABLE 3

Interatomic distances (Å)

(*a*) Bond lengths

C(1)–C(2)	1·535(12)	C(13)–S	1·803(11)
C(2)–C(3)	1·522(13)	C(14)–C(4)	1·313(14)
C(3)–C(4)	1·529(13)	C(16)–S	1·777(9)
C(4)–C(5)	1·507(12)	C(16)–C(17)	1·400(14)
C(5)–C(6)	1·532(12)	C(16)–C(21)	1·365(14)
C(5)–C(10)	1·554(12)	C(17)–C(18)	1·371(15)
C(6)–C(7)	1·554(11)	C(18)–C(19)	1·375(14)
C(7)–C(8)	1·530(13)	C(19)–C(20)	1·382(13)
C(7)–C(11)	1·544(13)	C(19)–Br	1·916(9)
C(8)–C(9)	1·520(14)	C(20)–C(21)	1·409(13)
C(8)–O(1)	1·476(12)	O(3)–C(3)	1·443(10)
C(9)–C(10)	1·578(12)	O(3)–C(22)	1·369(12)
C(10)–C(1)	1·567(13)	O(4)–C(22)	1·191(12)
C(10)–C(15)	1·561(13)	O(5)–C(2)	1·477(11)
C(11)–C(12)	1·516(15)	O(5)–C(24)	1·356(12)
C(11)–C(13)	1·537(15)	O(6)–C(24)	1·197(14)
C(12)–O(2)	1·202(14)	C(22)–C(23)	1·527(14)
C(12)–O(1)	1·355(13)	C(24)–C(25)	1·509(17)

(*b*) Intermolecular distances (<3·7 Å)

C(11) $\cdots$ O(4$^{\mathrm{I}}$)	3·32	C(20) $\cdots$ C(23$^{\mathrm{II}}$)	3·55
O(2) $\cdots$ C(6$^{\mathrm{II}}$)	3·41	C(21) $\cdots$ C(22$^{\mathrm{I}}$)	3·56
O(1) $\cdots$ C(5$^{\mathrm{I}}$)	3·42	C(20) $\cdots$ O(3$^{\mathrm{I}}$)	3·56
C(20) $\cdots$ C(22$^{\mathrm{I}}$)	3·43	O(2) $\cdots$ C(13$^{\mathrm{II}}$)	3·56
C(21) $\cdots$ O(4$^{\mathrm{I}}$)	3·44	C(19) $\cdots$ C(23$^{\mathrm{I}}$)	3·63
O(2) $\cdots$ S$^{\mathrm{II}}$	3·46	C(25) $\cdots$ O(3$^{\mathrm{III}}$)	3·64
O(2) $\cdots$ C(14$^{\mathrm{II}}$)	3·49	C(25) $\cdots$ C(24$^{\mathrm{III}}$)	3·64
O(6) $\cdots$ C(23$^{\mathrm{III}}$)	3·49	C(7) $\cdots$ O(4$^{\mathrm{I}}$)	3·64
C(20) $\cdots$ O(5$^{\mathrm{I}}$)	3·50	O(6) $\cdots$ Br$^{\mathrm{V}}$	3·68
O(6) $\cdots$ C(18$^{\mathrm{I}}$)	3·50	C(20) $\cdots$ C(23$^{\mathrm{I}}$)	3·69
O(5) $\cdots$ C(14$^{\mathrm{IV}}$)	3·53	C(8) $\cdots$ O(4$^{\mathrm{I}}$)	3·69
O(6) $\cdots$ C(17$^{\mathrm{I}}$)	3·53	C(21) $\cdots$ C(23$^{\mathrm{II}}$)	3·69

The superscripts refer to the following transformations of the co-ordinates:

I $\frac{1}{2} + x, \frac{1}{2} - y, 1 - z$
II $\frac{1}{2} + x, -\frac{1}{2} - y, 1 - z$
III $-x, \frac{1}{2} + y, \frac{3}{2} - z$
IV $x, 1 + y, z$
V $\frac{1}{2} - x, -y, \frac{1}{2} + z$

The torsion angles (Figure 3) for the C(7)–C(11) bond in the pulchellin-C adduct deviate from the ideal value of 60° by an average of 23°. The corresponding mean deviations for the more stable C(11)-epimers

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[10] P. Coggon and G. A. Sim, *J. Chem. Soc.* (*B*), 1969, 237; W. Cocker, personal communication.

of 2-bromo-6-*epi*-santonin and 2-bromodesmotroposantonin (*cis*-fused lactones) and 2-bromosantonin (*trans*-fused lactone) are 21, 22, and 21°, whereas for the less stable C(11)-epimers they are 28, 28, and 27°.[9] It follows that a sesquiterpenoid γ-lactone in which the exocyclic group at C(11) is in a *quasi*-axial orientation is subject to greater torsional strain than is its C(11) epimer with a *quasi*-equatorial group.

TABLE 4

Valency angles (deg.)

C(2)–C(1)–C(10)	110·9(5)	C(7)–C(11)–C(12)	102·3(6)
C(1)–C(2)–C(3)	109·7(6)	C(7)–C(11)–C(13)	119·4(6)
C(1)–C(2)–O(5)	107·9(5)	C(12)–C(11)–C(13)	112·2(7)
C(3)–C(2)–O(5)	105·9(6)	C(11)–C(12)–O(1)	110·0(8)
C(2)–C(3)–C(4)	108·6(7)	C(11)–C(12)–O(2)	129·1(7)
C(2)–C(3)–O(3)	108·9(5)	O(1)–C(12)–O(2)	120·9(6)
C(4)–C(3)–O(3)	111·5(7)	C(11)–C(13)–S	113·9(6)
C(3)–C(4)–C(5)	109·8(7)	S–C(16)–C(17)	115·1(5)
C(3)–C(4)–C(14)	123·9(5)	S–C(16)–C(21)	124·5(4)
C(5)–C(4)–C(14)	126·3(6)	C(17)–C(16)–C(21)	120·4(7)
C(4)–C(5)–C(6)	113·6(5)	C(16)–C(17)–C(18)	120·4(8)
C(4)–C(5)–C(10)	110·7(6)	C(17)–C(18)–C(19)	119·0(7)
C(6)–C(5)–C(10)	112·0(6)	C(18)–C(19)–C(20)	121·8(7)
C(5)–C(6)–C(7)	109·7(6)	C(18)–C(19)–Br	119·5(5)
C(6)–C(7)–C(8)	111·9(6)	C(20)–C(19)–Br	118·7(5)
C(6)–C(7)–C(11)	112·0(6)	C(19)–C(20)–C(21)	118·8(6)
C(8)–C(7)–C(11)	100·0(6)	C(20)–C(21)–C(16)	119·5(7)
C(7)–C(8)–C(9)	112·2(7)	C(23)–C(22)–O(3)	110·5(7)
C(7)–C(8)–O(1)	104·2(6)	C(23)–C(22)–O(4)	126·2(8)
C(9)–C(8)–O(1)	111·0(6)	O(3)–C(22)–O(4)	123·3(5)
C(8)–C(9)–C(10)	114·7(6)	C(25)–C(24)–O(5)	111·7(7)
C(5)–C(10)–C(9)	107·0(6)	C(25)–C(24)–O(6)	126·1(9)
C(5)–C(10)–C(1)	107·7(5)	O(5)–C(24)–O(6)	122·1(6)
C(1)–C(10)–C(9)	105·7(7)	C(8)–O(1)–C(12)	109·0(7)
C(5)–C(10)–C(15)	113·0(6)	C(3)–O(3)–C(22)	114·5(6)
C(1)–C(10)–C(15)	110·7(6)	C(2)–O(5)–C(24)	116·3(6)
C(9)–C(10)–C(15)	112·3(6)	C(13)–S–C(16)	103·6(5)

TABLE 5

Torsion angles (deg.). The angle *A*–*B*–*C*–*D* is defined as positive if, when viewed along the B–C bond, atom *A* must be rotated clockwise to eclipse atom *D*. The standard deviations of the angles are *ca*. 1°

C(10)–C(1)–C(2)–C(3)	−59	C(8)–C(9)–C(10)–C(1)	−163
C(10)–C(1)–C(2)–O(5)	−174	C(8)–C(9)–C(10)–C(5)	−49
C(1)–C(2)–C(3)–C(4)	61	C(8)–C(9)–C(10)–C(15)	76
C(1)–C(2)–C(3)–O(3)	−178	C(9)–C(10)–C(1)–C(2)	170
O(5)–C(2)–C(3)–C(4)	177	C(5)–C(10)–C(1)–C(2)	56
O(5)–C(2)–C(3)–O(3)	−61	C(15)–C(10)–C(1)–C(2)	−68
C(2)–C(3)–C(4)–C(5)	−62	C(7)–C(11)–C(12)–O(1)	−21
C(2)–C(3)–C(4)–C(14)	117	C(7)–C(11)–C(12)–O(2)	161
O(3)–C(3)–C(4)–C(5)	178	C(13)–C(11)–C(12)–O(1)	−150
O(3)–C(3)–C(4)–C(14)	−3	C(13)–C(11)–C(12)–O(2)	32
C(3)–C(4)–C(5)–C(6)	−171	C(7)–C(11)–C(13)–S	70
C(3)–C(4)–C(5)–C(10)	62	C(12)–C(11)–C(13)–S	−170
C(14)–C(4)–C(5)–C(6)	10	C(11)–C(12)–O(1)–C(8)	−3
C(14)–C(4)–C(5)–C(10)	−117	C(11)–C(13)–S–C(16)	73
C(4)–C(5)–C(6)–C(7)	169	C(17)–C(16)–S–C(13)	−174
C(10)–C(5)–C(6)–C(7)	−64	C(21)–C(16)–S–C(13)	9
C(4)–C(5)–C(10)–C(1)	−58	S–C(16)–C(17)–C(18)	−177
C(4)–C(5)–C(10)–C(9)	−171	S–C(16)–C(21)–C(20)	178
C(4)–C(5)–C(10)–C(15)	65	C(16)–C(17)–C(18)–C(19)	−1
C(6)–C(5)–C(10)–C(1)	175	C(17)–C(18)–C(19)–C(20)	0
C(6)–C(5)–C(10)–C(9)	61	C(17)–C(18)–C(19)–Br	180
C(6)–C(5)–C(10)–C(15)	−63	C(18)–C(19)–C(20)–C(21)	1
C(5)–C(6)–C(7)–C(8)	51	Br–C(19)–C(20)–C(21)	−179
C(5)–C(6)–C(7)–C(11)	163	C(19)–C(20)–C(21)–C(16)	−1
C(6)–C(7)–C(8)–C(9)	−42	O(2)–C(12)–O(1)–C(8)	175
C(6)–C(7)–C(8)–O(1)	82	C(21)–C(16)–C(17)–C(18)	0
C(11)–C(7)–C(8)–C(9)	−160	C(17)–C(16)–C(21)–C(20)	1
C(11)–C(7)–C(8)–O(1)	−37	C(1)–C(2)–O(5)–C(24)	−86
C(6)–C(7)–C(11)–C(12)	−84	C(3)–C(2)–O(5)–C(24)	156
C(6)–C(7)–C(11)–C(13)	40	C(2)–O(5)–C(24)–C(25)	−179
C(8)–C(7)–C(11)–C(12)	34	C(2)–O(5)–C(24)–O(6)	3
C(8)–C(7)–C(11)–C(13)	159	C(2)–C(3)–O(3)–C(22)	161
C(7)–C(8)–C(9)–C(10)	41	C(4)–C(3)–O(3)–C(22)	−79
O(1)–C(8)–C(9)–C(10)	−79	C(3)–O(3)–C(22)–C(23)	−179
C(7)–C(8)–O(1)–C(12)	26	C(3)–O(3)–C(22)–O(4)	1
C(9)–C(8)–O(1)–C(12)	154		

TABLE 6

Displacements (Å) of the atoms from various planes

Plane (*a*): O(1), O(2), C(11), C(12)

[O(1) −0·00, O(2) −0·00, C(11) −0·00, C(12) 0·01, C(7) 0·51, C(8) −0·10, C(13) 0·73]

Plane (*b*): C(5), C(7), C(8), C(10)

[C(5) −0·07, C(7) 0·07, C(8) −0·07, C(10) 0·07, C(6) 0·69, C(9) −0·55]

Plane (*c*): C(2), C(3), C(5), C(10)

[C(2) 0·01, C(3) −0·01, C(5) 0·01, C(10) −0·01, C(1) −0·70, C(4) 0·73]

Plane (*d*): Br, S, C(16)—(21)

[Br −0·02, S −0·04, C(16) 0·02, C(17) 0·02, C(18) 0·00, C(19) −0·00, C(20) 0·01, C(21) 0·01, C(13) 015]

Plane (*e*): O(3), O(4), C(22), C(23)

O(3) −0·00, O(4) −0·00, C(22) 0·00, C(23) −0·00, C(3) 0·02]

Plane (*f*): O(5), O(6), C(24), C(25)

O(5) −0·01, O(6) −0·01, C(24) 0·02, C(25) −0·00, C(2) 0·02]

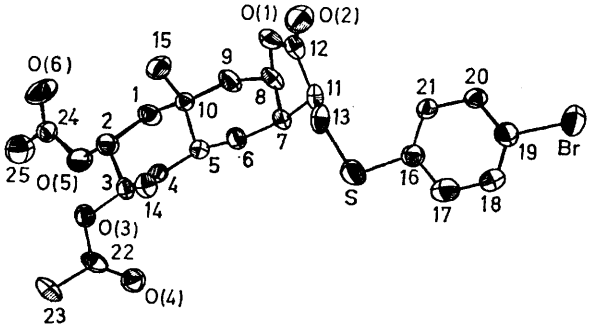
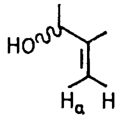
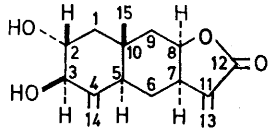


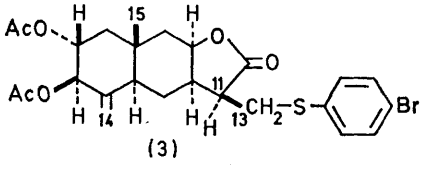
FIGURE 1 The molecular structure of the pulchellin-C diacetate *p*-bromophenylthiol adduct



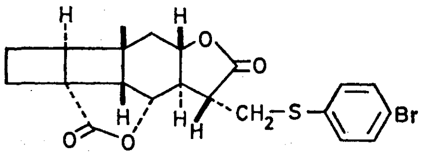
(1)



(2)



(3)



(4)

The conformation associated with thiol addition can be described by the torsion angles C(12)–C(11)–C(13)–S, −170°, and C(11)–C(13)–S–C(16), 73°. Atom C(13) is not far from the plane of the *p*-bromophenylthiol ring, the torsion angle C(13)–S–C(16)–C(21) being only 9°.

Ring A of the sesquiterpenoid derivative deviates slightly from the ideal chair form of a cyclohexane ring, with internal torsion angles in the range 56—62, mean 60°, and valency angles in the range 108—111, mean 110°. Since torsion angles in a sesquiterpenoid *γ*-lactone ring are always substantially smaller than 60°, the ring-B torsion angle at the *cis*-junction C(7)–C(8) is also necessarily smaller than 60° (actually −42°), and ring B is notably flattened from ideal chair geometry with torsion angles in the range 41—64, mean 51°.

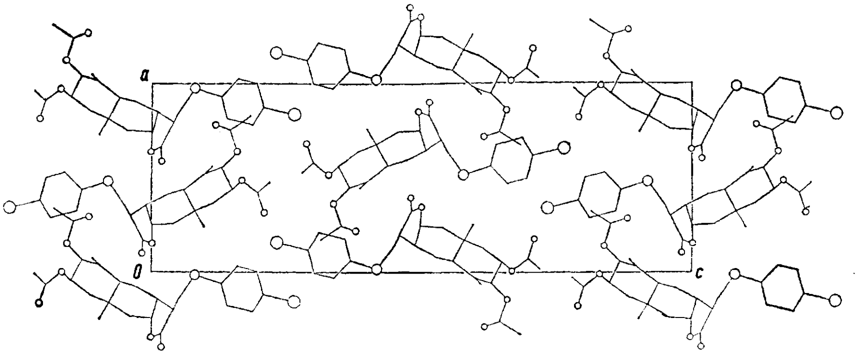


FIGURE 2 The crystal structure, viewed in projection along the *b* axis

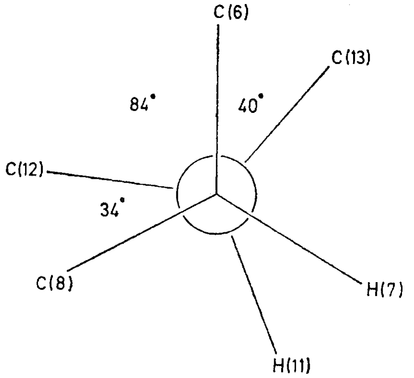


FIGURE 3 Newman projection along the C(7)–C(11) bond

Though the hydrogen atoms of the exocyclic methylene group on ring A were not directly located, the *X*-ray results are in accord with the n.m.r. measurements in indicating that atom H(14a) must be in the vicinity of atom O(3). The torsion angle O(3)–C(3)–C(4)–C(14) is only −4°, and the O(3) · · · H(14a) distance is therefore estimated to be 2·54 Å if the H–C–H angle and C–H distances are normal (110° and 1·08 Å, respectively) and the methylene hydrogen atoms lie in the plane defined by atoms C(3), C(4), C(5), and C(14). Since our estimate of the O · · · H approach is not notably smaller than the sum of van der Waals radii (2·6 Å), it is unlikely that repulsion between O(3) and H(14a) is sufficiently great to favour a significant increase in the H · · · O separation at the expense of a large angular distortion of the ethylenic group or an appreciable displacement of H(14a) from the ethylenic plane. We conclude that the O(3) · · · H(14a) separation is *ca.* 2·5—2·6 Å.

The C(sp^3)–C(sp^3) bond lengths are 1·520—1·578, mean 1·545 Å, and C(sp^3)–C(sp^3) 1·507—1·529, mean 1·518 Å. The benzene bond lengths are 1·365—1·409, mean 1·384 Å. The mean C(sp^3)–O distance (1·465 Å) is *ca.* 0·1 Å longer than the mean C(sp^2)–O distance (1·360 Å) a distinction which is customary in lactones and esters.[11] The C(sp^3)–S, 1·803 Å, and C(sp^2)–S, 1·777 Å, bonds, on the other hand, differ by only 0·026 Å, an amount which can be accounted for by the difference between radii of 0·77 and 0·74 Å assigned to sp^3- and sp^2-carbon atoms.

EXPERIMENTAL

Crystal Data.—$C_{25}H_{29}O_6SBr$, $M = 537·5$. Orthorhombic, $a = 11·076(3)$, $b = 7·194(2)$, $c = 31·189(6)$ Å, $U = 2485$ Å^3, $D_m = 1·43$, $Z = 4$, $D_c = 1·44$, $F(000) = 1112$. Mo-K_α radiation, $\lambda = 0·7107$ Å, μ(Mo-K_α) = 18·8 cm^{-1}. Space group $P2_12_12_1$ (D_2^4).

Crystallographic Measurements.—Final values of the cell dimensions and their standard deviations were obtained by a least-squares treatment of the θ,ϕ,χ-setting angles of twelve reflections measured on a Hilger and Watts computer-controlled diffractometer with zirconium-filtered Mo-K_α radiation. The intensities of 3106 independent reflections with $\theta \leqslant 27°$ were measured by the 2θ—ω step-scan method with background counts at each end of the scan range; of these reflections 1986 had $I > 3\sigma(I)$. The crystal employed had dimensions 0·35 × 0·35 × 0·55 mm^3, and no correction was applied for absorption.

Structure Analysis.—Preliminary estimates of the coordinates of the atoms were obtained by Patterson and electron-density calculations. The atomic parameters were subsequently adjusted by a series of least-squares calculations with a modified version of the Gantzel, Sparks, and Trueblood full-matrix programme. Two cycles of refinement based on all 3106 reflections and isotropic vibration parameters gave R 0·180 and R' $[(\Sigma w\Delta^2/\Sigma w|F_o|^2)^{\frac{1}{2}}]$

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[11] A. McL. Mathieson and J. C. Taylor, *Tetrahedron Letters*, 1961, 590; K. K. Cheung, K. H. Overton, and G. A. Sim, *Chem. Comm.*, 1965, 634.

0·155. Anisotropic thermal parameters were then introduced, and two rounds of calculations gave R 0·113 and R' 0·106. A subsequent cycle of refinement incorporating only the 1986 data with $I > 3\sigma(I)$ reduced R to 0·079 and R' to 0·090. At this point, corrections for anomalous dispersion were introduced for bromine and sulphur ($\Delta f'$ and $\Delta f''$ taken from ref. 12) and structure factors were calculated for the two possible sets of co-ordinates, x,y,z and $\bar{x},\bar{y},\bar{z}$. The co-ordinates appropriate to the absolute stereochemistry shown in (3) gave R 0·075, whilst those appropriate to the mirror image of (3) gave R 0·091. The absolute stereochemistry established by these calculations is in accord with that deduced by chemical correlations.[5] Hydrogen positions were calculated and a difference-Fourier map showed satisfactory peaks for sixteen of these atoms, namely, those listed in Table 1 apart from H(1a), H(1b), H(14a), and H(14b). The hydrogen atoms were included in structure-factor calculations with isotropic thermal parameters equivalent to the anisotropic parameters of the atoms to which they are bound, but their parameters were held constant in the least-squares adjustment. Three additional rounds of calculations were carried out with allowance for anomalous dispersion, and R was reduced to 0·066 (R' 0·075). Six reflections appeared to be affected by extinction and were omitted from a final two cycles of refinement, when convergence was reached at R 0·060 and R' 0·064. Unit weights were used throughout the refinement, and were judged to be satisfactory by an analysis of $w\Delta^2$ as a function of $|F_o|$.*

Calculations were performed on a KDF 9 computer at the University of Glasgow and a Univac 1108 at N.E.L. East Kilbride. We thank Dr. H. Yoshioka and Professor T. J. Mabry for the pulchellin-C derivative and for helpful correspondence, and the S.R.C. for the funds which enabled us to purchase the diffractometer.

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* Final observed and calculated structure factors are listed in Supplementary Publication No. SUP 20605 (5 pp., 1 microfiche). For details see Notice to Authors No. 7 in *J. Chem. Soc.* (*A*), 1970, Issue No. 20 (items less than 10 pp. are sent as full size copies).

[12] 'International Tables for *X*-Ray Crystallography,' vol. III, Kynoch Press, Birmingham, 1962.