Sesquiterpenoids. Part XX.[1] X-Ray Crystallographic Determination of the Molecular Structure of Berlandin, a Guaianolide Epoxide. Comments on the Circular Dichroism of Sesquiterpenoid α-Methylene γ-Lactones with αβ-Unsaturated Ester Side Chains †

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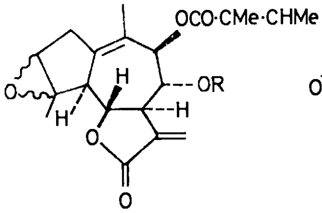
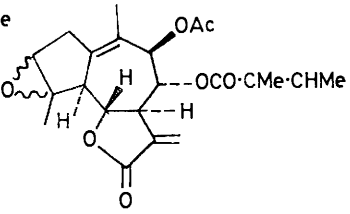
X-ray analysis of the crystal structure of berlandin (3), a guaianolide epoxide, has resolved stereochemical and structural ambiguities remaining from the earlier chemical and spectroscopic investigation of the sesquiterpenoid; in particular, the acetyl function has been shown to be at C(9) and the C(3), C(4)-epoxide has α-orientation. The c.d. spectra of berlandin and subacaulin have positive Cotton effects, in apparent contradiction of the empirical rule relating the sign of the Cotton effect of the $n \rightarrow \pi^*$ transition of the C:C·C:O chromophore of an α-methylene γ-lactone to ring-junction stereochemistry. The cycloheptene ring adopts a chair conformation which is slightly skewed, the torsion angle about the double bond C(1)=C(10) being 6°. The cyclopentane ring has an envelope (C_s) conformation with C(1) the out-of-plane atom and torsion angles in the range $|\omega|$ 1—19°. The α-methylene γ-lactone is *trans*-fused to the cycloheptene at C(6) and C(7) and has a half-chair (C_2) conformation. Crystals are orthorhombic, $a = 6{\cdot}306(3)$, $b = 37{\cdot}040(11)$, $c = 8{\cdot}959(3)$ Å, space group $P2_12_12_1$, $Z = 4$. The structure was solved by direct methods and refined by least squares to R 7·9% over 2226 diffractometer reflections.

BERLANDIN and subacaulin are two closely related guaianolides which were isolated from *Berlandiera subacaulis* (Nutt.) Nutt. Chemical and spectroscopic studies established that subacaulin has the constitution and partial stereochemistry (1a) while berlandin is either (2) or differs from acetylsubacaulin (1b) in the configuration of the epoxide ring.[2] We undertook an X-ray analysis of berlandin to settle the outstanding structural questions and to obtain details of the conformations of the cycloheptene and lactone rings.



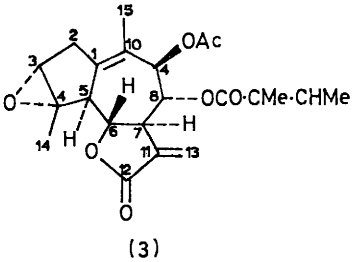
(1a) R = H
(1b) R = Ac



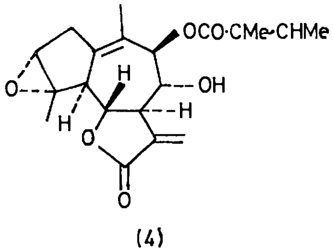
(2)

Intensity measurements were made by means of a four-circle diffractometer with Mo-K_α radiation and the crystal structure was elucidated by non-centrosymmetric direct phasing procedures; subsequent least-squares adjustment of the atomic parameters converged to R 7·9% over 2226 reflections. The atomic co-ordinates are given in Table 1, thermal parameters in Table 2, and bond lengths, valency angles, torsion angles, and intermolecular separations in Tables 3—6. The molecular structure of the guaianolide is shown in Figure 1 and the arrangement of molecules in the crystal in Figure 2.

The results of our X-ray study establish that berlandin has the constitution and relative stereochemistry shown in (3) from which it follows that subacaulin is represented by (4). The absolute configuration shown in these formulae is based on the assumption that the C(7) side chain has the customary β-orientation of guaianolides of established absolute stereochemistry; if this configurational assignment proves to be incorrect then the signs of the torsion angles in Table 5 will require to be reversed.



(3)



(4)

The cycloheptene ring has the double bond in the C(1),C(10)-position and the conformation of the ring approximates to a C_s-chair form (5). The torsion angles of the ring are in good agreement with theoretical

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† No reprints available.

[1] Part XIX, P. J. Cox and G. A. Sim, preceding paper.

[2] W. Herz, S. V. Bhat, and A. Srinivasan, *J. Org. Chem.*, 1972, **37**, 2532.

values derived for the C_s-chair conformer of cycloheptene from force-field calculations,[3] the mean deviation between experimental and theoretical angles being 7°.

Several force-field calculations have been reported for cycloheptene,[3-6] and the later ones [3-5] agree that the symmetric C_s-chair form is the most stable conformer, whereas earlier calculations [6] had favoured a C_s-boat form (6). Ermer [3] and Allinger [4] agree that a C_2-twist form (7) is only slightly less stable, by *ca.* 0·5 kcal mol^{-1}, than the chair form and that the boat, or a distorted version of it,[3] is appreciably less stable than the chair form, by *ca.* 2·6 (ref. 3) or 3·4 kcal mol^{-1} (ref. 4). Spectroscopic studies of cycloheptene and some simple deriva-

TABLE 1

Fractional atomic co-ordinates, with standard deviations in parentheses

Atom	*x*	*y*	*z*
O(1)	−0·1943(10)	0·0682(1)	1·2652(7)
O(2)	0·1091(7)	0·0408(1)	0·8386(5)
O(3)	0·2134(10)	0·0177(1)	0·6182(5)
O(4)	0·4768(8)	0·1493(1)	0·7862(5)
O(5)	0·8292(8)	0·1485(1)	0·8255(6)
O(6)	0·4473(9)	0·1782(1)	1·0524(5)
O(7)	0·1679(11)	0·2051(1)	1·1586(8)
C(1)	0·1864(11)	0·0952(1)	1·1881(7)
C(2)	0·1851(15)	0·0693(2)	1·3193(8)
C(3)	−0·0024(13)	0·0464(2)	1·2926(9)
C(4)	−0·0895(10)	0·0517(2)	1·1385(9)
C(5)	0·0513(10)	0·0804(1)	1·0638(7)
C(6)	0·2038(11)	0·0660(1)	0·9481(7)
C(7)	0·2959(9)	0·0951(1)	0·8428(6)
C(8)	0·4355(10)	0·1242(1)	0·9094(6)
C(9)	0·3291(10)	0·1453(1)	1·0319(7)
C(10)	0·3205(11)	0·1232(2)	1·1763(6)
C(11)	0·3852(11)	0·0716(1)	0·7208(7)
C(12)	0·2345(12)	0·0402(2)	0·7134(8)
C(13)	0·5581(14)	0·0733(2)	0·6406(8)
C(14)	−0·2162(14)	0·0245(2)	1·0527(10)
C(15)	0·4766(16)	0·1335(2)	1·2941(8)
C(16)	0·3478(14)	0·2056(2)	1·1177(9)
C(17)	0·4938(17)	0·2371(2)	1·1409(10)
C(18)	0·6790(13)	0·1602(2)	0·7595(7)
C(19)	0·6746(15)	0·1883(2)	0·6345(8)
C(20)	0·8212(20)	0·1859(3)	0·5296(10)
C(21)	0·5015(17)	0·2170(2)	0·6426(12)
C(22)	0·9855(18)	0·1586(3)	0·5136(11)
H(2A)	0·1691(100)	0·0836(14)	1·4079(62)
H(2B)	0·3250(92)	0·0538(13)	1·3188(56)
H(3)	−0·0210(88)	0·0213(12)	1·3523(56)
H(5)	−0·0650(107)	0·0973(15)	1·0389(66)
H(6)	0·3119(95)	0·0507(13)	1·0096(54)
H(7)	0·1723(87)	0·1107(12)	0·7893(55)
H(8)	0·5736(101)	0·1131(14)	0·9593(63)
H(9)	0·1698(90)	0·1542(12)	1·0036(52)
H(13A)	0·6297(98)	0·0558(14)	0·5842(60)
H(13B)	0·6745(90)	0·0952(13)	0·6373(56)
H(14A)	−0·3345(105)	0·0392(14)	0·9521(63)
H(14B)	−0·1110(90)	0·0013(13)	0·9702(56)
H(14C)	−0·3421(129)	0·0127(17)	1·1103(79)
H(15A)	0·5690(132)	0·1550(19)	1·3012(81)
H(15B)	0·3985(132)	0·1497(19)	1·3717(83)
H(15C)	0·4960(125)	0·1189(19)	1·3580(80)
H(17A)	0·4028(133)	0·2616(19)	1·1593(85)
H(17B)	0·5991(140)	0·2333(21)	1·1481(91)
H(17C)	0·5228(154)	0·2435(22)	1·0177(103)
H(20)	0·8095(129)	0·2020(18)	0·4249(82)
H(21A)	0·3606(138)	0·2086(19)	0·6802(94)
H(21B)	0·5348(152)	0·2335(21)	0·6984(99)
H(21C)	0·4301(146)	0·2214(20)	0·5584(97)

TABLE 2

Thermal parameters

(*a*) Anisotropic thermal parameters * for the oxygen and carbon atoms (× 10^4)

Atom	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
O(1)	410(19)	11(0)	268(11)	5(5)	367(26)	2(4)
O(2)	247(12)	8(0)	145(6)	−16(3)	−17(16)	2(2)
O(3)	513(22)	9(0)	160(7)	−24(5)	−60(24)	−14(3)
O(4)	298(14)	7(0)	126(6)	−11(4)	−35(16)	14(2)
O(5)	228(13)	15(1)	206(9)	−6(5)	−17(20)	38(4)
O(6)	401(17)	7(0)	166(7)	−18(4)	69(21)	−9(3)
O(7)	542(24)	9(0)	304(13)	21(6)	222(34)	−19(4)
C(1)	262(18)	6(0)	130(8)	16(5)	57(23)	4(3)
C(2)	495(31)	8(1)	126(9)	6(7)	90(32)	4(4)
C(3)	333(23)	8(1)	186(12)	12(6)	195(30)	15(4)
C(4)	196(16)	8(0)	229(13)	14(5)	131(27)	13(5)
C(5)	220(17)	6(0)	163(9)	12(5)	29(23)	16(4)
C(6)	287(19)	6(0)	120(8)	−12(5)	−13(24)	6(3)
C(7)	197(15)	6(0)	120(8)	−3(4)	−27(20)	7(3)
C(8)	218(16)	6(0)	112(7)	−6(4)	−25(20)	7(3)
C(9)	226(16)	6(0)	135(8)	−7(5)	−22(21)	0(3)
C(10)	305(19)	7(0)	100(7)	15(5)	3(22)	−1(3)
C(11)	304(20)	7(0)	108(8)	−3(5)	−70(23)	3(3)
C(12)	334(23)	7(0)	147(10)	−6(6)	−102(27)	8(4)
C(13)	460(29)	9(1)	169(11)	−6(7)	194(34)	−13(4)
C(14)	367(28)	9(1)	265(15)	−43(7)	27(38)	20(5)
C(15)	570(36)	8(0)	167(11)	1(8)	−232(38)	−1(4)
C(16)	374(25)	7(0)	177(12)	0(6)	8(32)	2(4)
C(17)	608(39)	9(1)	275(16)	−37(9)	5(49)	−23(5)
C(18)	382(24)	7(0)	117(9)	−31(6)	38(27)	4(3)
C(19)	498(31)	10(1)	139(10)	−80(8)	−35(34)	2(4)
C(20)	633(43)	15(1)	168(13)	−113(11)	−19(45)	4(6)
C(21)	720(42)	7(1)	348(22)	−33(9)	−456(57)	45(6)
C(22)	508(40)	19(1)	237(17)	−1(12)	226(47)	−20(8)

(*b*) Isotropic thermal parameters (B/Å^2) † for the hydrogen atoms

H(2A)	2·31	H(14C)	5·03
H(2B)	1·43	H(15A)	4·84
H(3)	1·40	H(15B)	8·11
H(5)	3·30	H(15C)	7·62
H(6)	1·38	H(17A)	5·99
H(7)	1·22	H(17B)	6·51
H(8)	2·51	H(17C)	7·35
H(9)	1·06	H(20)	5·36
H(13A)	2·18	H(21A)	5·74
H(13B)	1·41	H(21B)	7·43
H(14A)	2·42	H(21C)	6·30
H(14B)	1·34		

* In the form: $T = \exp[-(b_{11}h^2 + b_{22}k^2 + b_{33}l^2 + b_{12}hk + b_{13}hl + b_{23}kl)]$. † Mean σ 1·8 Å^2.

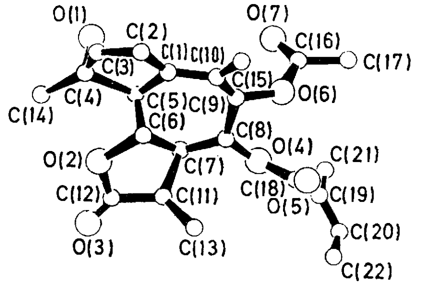

FIGURE 1 Atomic arrangement in the molecule of (3)

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[3] O. Ermer and S. Lifson, *J. Amer. Chem. Soc.*, 1973, **95**, 4121.

[4] N. L. Allinger and J. T. Sprague, *J. Amer. Chem. Soc.*, 1972, **94**, 5734.

[5] G. Favini, G. Buemi, and M. Raimondi, *J. Mol. Struct.*, 1968, **2**, 137.

[6] R. Pauncz and D. Ginsburg, *Tetrahedron*, 1960, **9**, 40.

tives have generally found a predominance of the chair form.[7]

Torsion angles for the cycloheptene rings of three sesqui- and three di-terpenoid derivatives are listed in Table 7 along with the values derived by force-field calculations for C_s-chair, C_2-twist, C_s-boat, and distorted

TABLE 3

Intramolecular bonded distances (Å), with standard deviations in parentheses

O(1)–C(3)	1·476(10)	C(18)–C(19)	1·528(10)
O(1)–C(4)	1·450(10)	C(19)–C(20)	1·321(14)
O(2)–C(6)	1·480(7)	C(19)–C(21)	1·526(13)
O(2)–C(12)	1·372(8)	C(20)–C(22)	1·454(16)
O(3)–C(12)	1·201(8)	C(2)–H(2A)	0·96(6)
O(4)–C(8)	1·468(7)	C(2)–H(2B)	1·05(6)
O(4)–C(18)	1·358(9)	C(3)–H(3)	1·08(5)
O(5)–C(18)	1·198(9)	C(5)–H(5)	0·99(6)
O(6)–C(9)	1·440(7)	C(6)–H(6)	1·04(5)
O(6)–C(16)	1·330(9)	C(7)–H(7)	1·08(5)
O(7)–C(16)	1·192(11)	C(8)–H(8)	1·06(6)
C(1)–C(2)	1·517(9)	C(9)–H(9)	1·09(6)
C(1)–C(5)	1·505(9)	C(13)–H(13A)	0·94(6)
C(1)–C(10)	1·342(9)	C(13)–H(13B)	1·10(5)
C(2)–C(3)	1·473(12)	C(14)–H(14A)	1·29(6)
C(3)–C(4)	1·499(11)	C(14)–H(14B)	1·31(5)
C(4)–C(5)	1·538(9)	C(14)–H(14C)	1·04(8)
C(4)–C(14)	1·497(11)	C(15)–H(15A)	0·99(8)
C(5)–C(6)	1·512(9)	C(15)–H(15B)	1·04(7)
C(6)–C(7)	1·547(8)	C(15)–H(15C)	0·80(7)
C(7)–C(8)	1·513(8)	C(17)–H(17A)	1·08(8)
C(7)–C(11)	1·508(8)	C(17)–H(17B)	0·68(9)
C(8)–C(9)	1·506(8)	C(17)–H(17C)	1·14(9)
C(9)–C(10)	1·533(8)	C(20)–H(20)	1·12(7)
C(10)–C(15)	1·494(11)	C(21)–H(21A)	1·00(9)
C(11)–C(12)	1·503(9)	C(21)–H(21B)	0·82(8)
C(11)–C(13)	1·308(11)	C(21)–H(21C)	0·89(9)
C(16)–C(17)	1·502(12)		

TABLE 4

Valency angles (deg.), with standard deviations in parentheses

C(4)–O(1)–C(3)	61·6(5)	C(3)–C(2)–C(1)	104·0(5)
C(2)–C(3)–O(1)	111·8(5)	C(10)–C(1)–C(5)	125·4(4)
C(4)–C(3)–O(1)	58·3(5)	C(4)–C(5)–C(1)	104·8(4)
C(3)–C(4)–O(1)	60·0(4)	C(6)–C(5)–C(1)	106·0(4)
C(5)–C(4)–O(1)	108·2(4)	C(9)–C(10)–C(1)	120·1(5)
C(14)–C(4)–O(1)	116·3(5)	C(15)–C(10)–C(1)	123·9(5)
C(12)–O(2)–C(6)	108·6(4)	C(4)–C(3)–C(2)	111·6(5)
C(5)–C(6)–O(2)	114·9(4)	C(5)–C(4)–C(3)	106·2(4)
C(7)–C(6)–O(2)	100·8(4)	C(14)–C(4)–C(3)	125·5(5)
O(3)–C(12)–O(2)	121·8(3)	C(14)–C(4)–C(5)	123·3(5)
C(11)–C(12)–O(2)	108·4(4)	C(6)–C(5)–C(4)	114·9(4)
C(11)–C(12)–O(3)	129·7(5)	C(7)–C(6)–C(5)	114·2(4)
C(18)–O(4)–C(8)	119·2(4)	C(8)–C(7)–C(6)	118·3(4)
C(7)–C(8)–O(4)	105·0(3)	C(11)–C(7)–C(6)	100·2(4)
C(9)–C(8)–O(4)	107·2(3)	C(11)–C(7)–C(8)	118·7(4)
O(5)–C(18)–O(4)	123·2(3)	C(9)–C(8)–C(7)	113·4(4)
C(19)–C(18)–O(4)	108·3(4)	C(12)–C(11)–C(7)	104·1(4)
C(19)–C(18)–O(5)	128·5(5)	C(13)–C(11)–C(7)	133·0(4)
C(16)–O(6)–C(9)	117·3(5)	C(10)–C(9)–C(8)	110·7(4)
C(8)–C(9)–O(6)	107·6(4)	C(15)–C(10)–C(9)	115·9(5)
C(10)–C(9)–O(6)	111·3(4)	C(13)–C(11)–C(12)	122·8(4)
O(7)–C(16)–O(6)	124·9(4)	C(20)–C(19)–C(18)	117·6(6)
C(17)–C(16)–O(6)	111·5(6)	C(21)–C(19)–C(18)	116·9(6)
C(17)–C(16)–O(7)	123·6(6)	C(21)–C(19)–C(20)	125·5(6)
C(5)–C(1)–C(2)	109·9(4)	C(22)–C(20)–C(19)	127·9(7)
C(10)–C(1)–C(2)	123·6(4)		

TABLE 5

Torsion angles * (deg.)

C(4)–O(1)–C(3)–C(2)	103
C(3)–O(1)–C(4)–C(5)	−99
C(3)–O(1)–C(4)–C(14)	118
C(12)–O(2)–C(6)–C(5)	158
C(12)–O(2)–C(6)–C(7)	35
C(6)–O(2)–C(12)–O(3)	167
C(6)–O(2)–C(12)–C(11)	−14
C(18)–O(4)–C(8)–C(7)	−132
C(18)–O(4)–C(8)–C(9)	107
C(8)–O(4)–C(18)–O(5)	5
C(8)–O(4)–C(18)–C(19)	−176
C(16)–O(6)–C(9)–C(8)	159
C(16)–O(6)–C(9)–C(10)	−80
C(9)–O(6)–C(16)–O(7)	−1
C(9)–O(6)–C(16)–C(17)	176
C(5)–C(1)–C(2)–C(3)	−19
C(10)–C(1)–C(2)–C(3)	173
C(2)–C(1)–C(5)–C(4)	18
C(2)–C(1)–C(5)–C(6)	−104
C(10)–C(1)–C(5)–C(4)	−174
C(10)–C(1)–C(5)–C(6)	64
C(2)–C(1)–C(10)–C(9)	173
C(2)–C(1)–C(10)–C(15)	−3
C(5)–C(1)–C(10)–C(9)	6
C(5)–C(1)–C(10)–C(15)	−170
C(1)–C(2)–C(3)–O(1)	−52
C(1)–C(2)–C(3)–C(4)	12
O(1)–C(3)–C(4)–C(5)	102
O(1)–C(3)–C(4)–C(14)	−102
C(2)–C(3)–C(4)–O(1)	−103
C(2)–C(3)–C(4)–C(5)	−1
C(2)–C(3)–C(4)–C(14)	155
O(1)–C(4)–C(5)–C(1)	53
O(1)–C(4)–C(5)–C(6)	169
C(3)–C(4)–C(5)–C(1)	−10
C(3)–C(4)–C(5)–C(6)	106
C(14)–C(4)–C(5)–C(1)	−166
C(14)–C(4)–C(5)–C(6)	−51
C(1)–C(5)–C(6)–O(2)	163
C(1)–C(5)–C(6)–C(7)	−82
C(4)–C(5)–C(6)–O(2)	47
C(4)–C(5)–C(6)–C(7)	163
O(2)–C(6)–C(7)–C(8)	−172
O(2)–C(6)–C(7)–C(11)	−41
C(5)–C(6)–C(7)–C(8)	64
C(5)–C(6)–C(7)–C(11)	−165
C(6)–C(7)–C(8)–O(4)	−174
C(6)–C(7)–C(8)–C(9)	−57
C(11)–C(7)–C(8)–O(4)	64
C(11)–C(7)–C(8)–C(9)	−179
C(6)–C(7)–C(11)–C(12)	34
C(6)–C(7)–C(11)–C(13)	−141
C(8)–C(7)–C(11)–C(12)	164
C(8)–C(7)–C(11)–C(13)	−11
O(4)–C(8)–C(9)–O(6)	−47
O(4)–C(8)–C(9)–C(10)	−169
C(7)–C(8)–C(9)–O(6)	−162
C(7)–C(8)–C(9)–C(10)	76
O(6)–C(9)–C(10)–C(1)	168
O(6)–C(9)–C(10)–C(15)	−16
C(8)–C(9)–C(10)–C(1)	−73
C(8)–C(9)–C(10)–C(15)	104
C(7)–C(11)–C(12)–O(2)	−14
C(7)–C(11)–C(12)–O(3)	165
C(13)–C(11)–C(12)–O(2)	162
C(13)–C(11)–C(12)–O(3)	−19
O(4)–C(18)–C(19)–C(20)	−137
O(4)–C(18)–C(19)–C(21)	43
O(5)–C(18)–C(19)–C(20)	42
O(5)–C(18)–C(19)–C(21)	−137
C(18)–C(19)–C(20)–C(22)	3
C(21)–C(19)–C(20)–C(22)	−178

* The sign convention of the torsion angles is such that the sign is negative if an anticlockwise rotation is required of atom (1) to eclipse atom (4) whilst looking down the (2)–(3) bond. Mean σ 0·8°.

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[7] N. Neto, C. di Laure, and S. Califano, *Spectrochim. Acta*, 1970, **A26**, 1489; M. St.-Jacques and C. Vaziri, *Canad. J. Chem.*, 1971, **49**, 1256; R. Knorr, C. Ganter, and J. D. Roberts, *Angew. Chem. Internat. Edn.*, 1967, **6**, 556; S. Kabuss, H. Friebolin, and H. Schmid, *Tetrahedron Letters*, 1965, 469.

TABLE 6

Intermolecular contacts $<3{\cdot}85$ Å

O(3) ··· C(2^{I})	3·295	O(7) ··· C(22^{III})	3·796
O(3) ··· C(3^{I})	3·390	C(15) ··· C(22^{III})	3·784
C(11) ··· C(2^{I})	3·813	O(2) ··· O(3^{IV})	3·494
C(12) ··· C(2^{I})	3·704	C(2) ··· O(3^{IV})	3·745
C(13) ··· O(2^{I})	3·720	C(3) ··· O(3^{IV})	3·376
C(20) ··· C(15^{I})	3·597	C(3) ··· C(12^{IV})	3·695
O(1) ··· C(10^{II})	3·760	C(4) ··· O(3^{IV})	3·501
O(1) ··· C(15^{II})	3·197	C(6) ··· O(3^{IV})	3·491
C(5) ··· O(5^{II})	3·588	C(14) ··· O(3^{IV})	3·583
C(7) ··· O(5^{II})	3·548	C(14) ··· C(13^{IV})	3·839
C(9) ··· O(5^{II})	3·656	O(3) ··· C(14^{V})	3·552
O(1) ··· C(13^{III})	3·713		

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

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

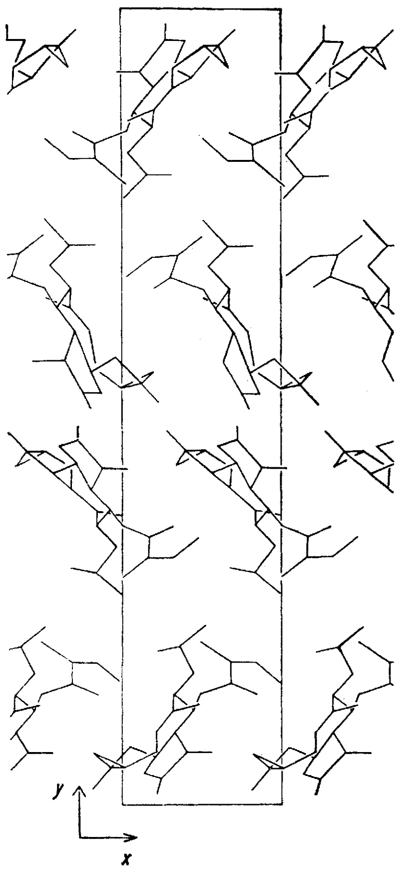
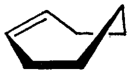


FIGURE 2 Crystal structure of (3), viewed in projection along the *c* axis


(5)


(6)


(7)

boat forms of cycloheptene. The experimental results show that the rings in the sesquiterpenoids berlandin, bromogaillardin,[8] and deacetyldihydrogaillardin *p*-bromobenzoate [8] are best described as chair forms, those in the diterpenoids phorbol [9] and neophorbol [9] as distorted boat forms, and that in portulal *p*-bromophenylsulphonylhydrazone [10] as a twist form. This is a striking diversity of conformational forms in a small sample of natural products.

TABLE 7

Comparison of the torsion angles (deg.) in terpenoid cycloheptene rings with theoretical values for the C_s-chair, C_2-twist, C_s-boat, and distorted-boat conformations of cycloheptene

	I	II	III	IV	V	VI	VII	VIII	IX	X
ω_1	−57	−93	−66	40	48	67	−68	43	67	30
ω_2	76	69	76	43	45	−78	75	−78	25	49
ω_3	−73	−30	−61	−68	−81	19	−59	28	−72	−63
ω_4	6	−1	4	9	−1	4	0	8	0	5
ω_5	64	29	60	11	62	40	59	28	72	10
ω_6	−82	−52	−85	40	−15	−68	−75	−78	−25	47
ω_7	64	74	69	−92	−68	12	68	43	−67	−87

I, Berlandin (3) (present work); II, bromogaillardin (ref. 8); III, deacetyldihydrogaillardin *p*-bromobenzoate (ref. 8); IV, phorbol (calc. from the co-ords. listed in ref. 9); V, neophorbol (calc. from the co-ords. listed in ref. 9); VI, portulal *p*-bromophenylsulphonylhydrazone (calc. from the co-ords. listed in ref. 10); VII, C_s-chair conformer (5) (ref. 3); VIII, C_2-twist conformer (7) (ref. 3); IX, C_s-boat conformer (6) (ref. 5); X, distorted boat conformer (ref. 3).

The five-membered carbocycle and the α-methylene γ-lactone are fused to the cycloheptene ring of berlandin at the C(1),C(5)- and C(6),C(7)-positions, respectively, and the geometry around these ring junctions is characterized by the torsion angles C(4)–C(5)–C(6)–O(2) (47°) and C(1)–C(5)–C(6)–C(7) (−82°); the same ring-junction system in the cycloheptane guaianolide euparotin bromoacetate [11] exhibits torsion angles of 63 and −63°. The cyclopentane adopts a flattened envelope conformation in which atom C(1) is out-of-plane by 0·28 Å and the largest torsion angle is 18°. The αβ′-unsaturated γ-lactone adopts a half-chair conformation with C(6) and C(7) displaced by 0·33 and 0·35 Å, respectively, to opposite sides of the plane through atoms O(2), C(11), and C(12).

The c.d. curve of berlandin exhibits a positive Cotton effect with a maximum at 246 nm, while that of subacaulin is similar with a maximum at 249 nm. However, Stöcklin *et al.*'s correlation between the sign of the Cotton effect of the $n \rightarrow \pi^*$ transition of an α-methylene γ-lactone and the position and stereochemistry of the lactone ring junction [12] predicts that berlandin and subacaulin should have a negative Cotton effect. Because the maximum occurs at somewhat shorter wavelength than in α-methylene γ-lactones which contain no α,β-unsaturated ester side chain, the observed c.d. curve may well be the summation of two

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[8] T. A. Dullforce, G. A. Sim, and D. N. J. White, *J. Chem. Soc.* (*B*), 1971, 1399.

[9] V. F. Brandl, M. Röhrl, K. Zechmeister, and W. Hoppe, *Acta Cryst.*, 1971, **B27**, 1718.

[10] S. Yamazaki, S. Tamura, F. Marumo, and Y. Saito, *Acta Cryst.*, 1971, **B27**, 2097.

[11] A. T. McPhail and G. A. Sim, *Tetrahedron*, 1973, **29**, 1751.

[12] W. Stöcklin, T. G. Waddell, and T. A. Geissman, *Tetrahedron*, 1970, **26**, 2397.

superimposed Cotton effects: one due to the inherently dissymmetric unsaturated lactone chromophore, and the second to the inherently symmetric, but asymmetrically perturbed, unsaturated ester chromophore. One or both of these could be positive, but if the lactone c.d. were negative (to harmonize with the empirical rule) its amplitude would have to be quite small since the c.d. curve as a whole never becomes negative.

Beecham[13] has suggested that the Cotton effect of the α-methylene γ-lactone depends on the chirality of the C:C·C:O chromophore. A survey of *X*-ray results for several sesquiterpenoids of established absolute configuration indicates that a C(6),C(7)-*trans*-ring-junction gives rise to left-handed chirality (ω negative) and a C(7),C(8)-*trans*-ring-junction to right-handed chirality (ω positive); if the absolute configuration shown in (3) is accepted for berlandin, then the C:C·C:O group in the α-methylene γ-lactone has left-handed chirality (ω −19°) in accord with other C(6),C(7)-*trans*-lactones. The *cis*-fused lactones, on the other hand, appear to be more flexible and do not provide a consistent relation between ring-junction position and C:C·C:O chirality;[11] indeed, measurements for several *cis*-fused lactones indicate that the sign of the Cotton effect for such compounds is not directly determined by the chromophore torsion angle in the crystal.

An analysis of the n.m.r. spectrum of berlandin yielded a number of coupling constants[2] and these can now be correlated with the torsion angles derived from the *X*-ray study: $J_{6,7}$, $J_{7,8}$, and $J_{8,9}$ are all 10·0 Hz and $J_{5,6}$ is 10·7 Hz, while the appropriate torsion angles H–C(6)–C(7)–H, H–C(7)–C(8)–H, H–C(8)–C(9)–H, and H–C(5)–C(6)–H are −176, 175, −169, and 176°.

Yoshioka *et al.* have observed that the n.m.r. signal of the exocyclic methylene proton adjacent to the C(8)-oxygen function in sesquiterpenoids which contain C(6),C(7)-fused α,β′-unsaturated lactone and α-oriented C(8)-hydroxy-groups generally undergoes a diamagnetic shift when the hydroxy-group is acetylated; the effect depends on the proximity of the C(8)-oxygen and H(13a)-hydrogen atoms and from inspection of models an O · · · H separation of 2·0—2·5 Å was suggested.[14] The O(3) · · · H(13a) distance is rather greater in berlandin (3·00 Å) and hence presumably in subacaulin, which exhibits the diamagnetic shift on acetylation.

EXPERIMENTAL

Crystal Data.—Berlandin, $C_{22}H_{26}O_7$, $M = 402·5$. Orthorhombic, $a = 6·306(3)$, $b = 37·040(11)$, $c = 8·959(3)$ Å, $U = 2093$ Å^3, $D_m = 1·27$, $Z = 4$, $D_c = 1·28$, $F(000) = 856$. Space group $P2_12_12_1$ (D_2^4). Mo-K_α radiation, $\lambda = 0·7107$ Å, μ(Mo-K_α) = 1·02 cm^{-1}.

Crystallographic Measurements.—Cell dimensions were determined by least-squares treatment of the angular settings of 12 reflections measured on a Hilger and Watts computer-controlled four-circle diffractometer at θ(Mo-K_α) *ca.* 16°. For intensity measurements the octant *hkl* was surveyed out to $\theta \leqslant 27°$ by means of 2θ—ω scans which consisted of sixty steps of 0·02° s^{-1} in 2θ; background counts were taken at each end of the scan range for 15 s. In all, the intensities of 2649 independent reflections were obtained of which 2226 with $I > 2\sigma(I)$ were employed in the crystal-structure determination. No correction was applied for absorption.

Structure Analysis.—The crystal structure was elucidated by direct phase-determining methods using the '*X*-Ray '70' series of programmes. The $|E|$ values were derived from intensities, on the basis of an overall isotropic temperature factor B 4·6 Å^2, and Σ2 relationships generated for the 302 reflections with $|E| \geqslant 1·5$. The initial set of phases consisted of three to define the origin and one the enantiomorph together with two phases to which values of $\pm\pi/4$, $\pm 3\pi/4$ were given. This procedure yielded sixteen starting sets of six phases for input to the 'Tangen' programme, which then generated phase sets characterized by R_K 0·20 and 0·27—0·35. An E map calculated from the phases with the lowest value of R_K yielded positions for 25 of the 29 carbon and oxygen atoms. An initial structure-factor calculation gave R 35·5% and after one cycle of least-squares adjustment a Fourier difference map revealed the remaining carbon atom positions.

Subsequent least-squares calculations with isotropic thermal parameters lowered R to 17·6% and when allowance was made for anisotropic thermal motion R fell to 10·2%. A difference electron-density distribution then revealed the hydrogen atom positions, apart from those on the methyl carbon atom C(22) of the ester side chain, and further least-squares refinement, with anisotropic thermal parameters for the carbon and oxygen atoms and isotropic thermal parameters for the hydrogen atoms, converged to R 7·9%. A unit weighting scheme ($w = 1$) was retained throughout these calculations. A final $(F_o - F_c)$ synthesis did not reveal the C(22)-methyl hydrogen atoms. Observed and calculated structure amplitudes and details of the initial phases are included in Supplementary Publication No. SUP 21200 (15 pp., 1 microfiche).*

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

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