Sesquiterpenoids. Part XXI.[1] Conformations of the Episantonins: Crystal Structures of 2-Bromo-6-*epi*-α-santonin and 2-Bromo-6-*epi*-β-santonin

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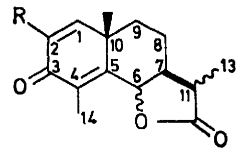
The conformations and absolute stereochemistries of 2-bromo-6-*epi*-α-santonin (7) and 2-bromo-6-*epi*-β-santonin (8) have been determined by *X*-ray diffraction. In each molecule ring A adopts a very flattened boat conformation while ring B, because of *cis*-fusion to the γ-lactone, deviates notably from ideal chair geometry. The puckering of the γ-lactone results in the C(13)-methyl group at C(11) being placed in a quasi-axial orientation in (7) and quasi-equatorial in (8); the differences in torsion angles between the isomers are largest in the region of C(11) and indicate that torsional strain is greater in (7). Crystals of (7) are monoclinic, space group $P2_1$, with $a = 5.997(4)$, $b = 14.230(7)$, $c = 9.081(4)$ Å, $\beta = 111.22(5)°$, and $Z = 2$; crystals of (8) are orthorhombic, space group $P2_12_12_1$, with $a = 12.210(10)$, $b = 10.161(5)$, $c = 11.822(8)$ Å, and $Z = 4$. The structures were solved by the heavy-atom method from diffractometer data, and refined by least-squares calculations to R 6.5 (7; 1 059 reflections) and 7.6% (8; 907 reflections).

THE discovery that the methyl substituent at C(11) in α-santonin is directed towards the α-face of the molecule [2] focused attention on the factors influencing the relative thermodynamic stabilities of α-santonin (1) and β-santonin (2). *X*-Ray studies of 2-bromo-α-santonin (3) [3] and 2-bromo-β-santonin (4)[4] demonstrated that the C(13) · · · C(6) and C(13) · · · C(8) separations are distinctly shorter in the latter molecule than in the former, in accord with the greater stability of the α-isomer.[5]

The order of stability of 6-*epi*-α-santonin (5) and 6-*epi*-β-santonin (6) is the reverse of that in the santonins, the β-isomer being the more stable.[5] We undertook *X*-ray analyses of the 2-bromo-derivatives (7) and (8) in order to elucidate the steric environments of the C(13)-methyl group in these *cis*-fused lactones and the results indicated that van der Waals repulsion arising from steric crowding is not an important aspect of the relative stabilities. Empirical force-field calculations were subsequently used



	R		
(1)	H	6α-O	11α-Me
(2)	H	6α-O	11β-Me
(3)	Br	6α-O	11α-Me
(4)	Br	6α-O	11β-Me
(5)	H	6β-O	11α-Me
(6)	H	6β-O	11β-Me
(7)	Br	6β-O	11α-Me
(8)	Br	6β-O	11β-Me

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[1] Part XX, P. J. Cox, G. A. Sim, and W. Herz, *J.C.S. Perkin II*, 1975, 459.

[2] J. D. M. Asher and G. A. Sim, *Proc. Chem. Soc.*, 1962, 111, 335; D. H. R. Barton, T. Miki, J. T. Pinhey, and R. J. Wells, *ibid.*, 112; M. Nakazaki and H. Arakawa, *ibid.*, 151.

[3] J. D. M. Asher and G. A. Sim, *J. Chem. Soc.*, 1965, 6041.

[4] P. Coggon and G. A. Sim, *J. Chem. Soc.* (*B*), 1969, 237.

[5] W. Cocker, T. B. H. McMurry, M. A. Frisch, T. McAllister, and H. Mackle, *Tetrahedron Letters*, 1964, 2233.

to resolve the question of the factors contributing to the order of stabilities of the α- and β-stereoisomers of santonin and 6-*epi*-santonin and these calculations, which are discussed in detail elsewhere, established that differences in torsional potential energy between the isomers effectively determine the order of stabilities.[6]

EXPERIMENTAL

Crystal Data.—(*a*) 2-Bromo-6-*epi*-α-santonin, (7), $C_{15}H_{17}BrO_3$, $M = 325.2$. Monoclinic, $a = 5.997(4)$, $b = 14.230(7)$, $c = 9.081(4)$ Å, $\beta = 111.22(5)°$, $U = 722$ Å^3, $D_c = 1.50$, $Z = 2$, $D_m = 1.50$ g cm^{-3}, $F(000) = 332$. Space group $P2_1$ (C_2^2). μ(Mo-K_α) $= 30.2$ cm^{-1}.

(*b*) 2-Bromo-6-*epi*-β-santonin, (8), $C_{15}H_{17}BrO_3$, $M = 325.2$, Orthorhombic. $a = 12.210(10)$, $b = 10.161(5)$, $c = 11.822(8)$ Å, $U = 1\,465$ Å^3, $D_c = 1.48, Z = 4, D_m = 1.46$ g cm^{-3} $F(000) = 664$. Space group $P2_12_12_1$ (D_2^4), μ(Mo-K_α) $=$ 29.8 cm^{-1}.

Crystallographic Measurements.—Cell dimensions were initially determined from *X*-ray photographs and subsequently adjusted to comply with setting angles measured with Mo-K_α radiation ($\lambda = 0.7107$ Å) on a Hilger and Watts Y290 four-circle computer-controlled diffractometer. Diffraction intensity data were obtained by the ω—2θ step-scan procedure, with background intensity measurements at each end of the scan range. Two standard reflections were monitored periodically and established that the crystals are stable to irradiation. The α-isomer yielded 1 059 independent reflections with $I > 3\sigma(I)$ in the range θ(Mo-K_α) $\leqslant 23°$, while the β-isomer yielded 907 such reflections. The crystals employed had dimensions $1.0 \times 0.25 \times 0.25$ mm^3 (7) and $0.9 \times 0.3 \times 0.3$ mm^3 (8). Absorption corrections were not applied.

Structure Analysis.—Both crystal structures were solved by straightforward application of the heavy-atom method, despite the pseudosymmetry present in the first Fourier synthesis for (7). Five cycles of least-squares adjustment of positional and anisotropic vibration parameters reduced the residual *R* to 7.5 (7) and 7.9% (8). Inclusion of the hydrogen atoms in fixed positions, which were determined by difference–Fourier syntheses, with subsequently a further two cycles of refinement, in which allowance was made for anomalous dispersion, led to convergence at *R* 6.5 (7) and 7.6% (8). Refinement of co-ordinates and thermal parameters appropriate to the mirror images of (7) and (8) led to values of *R ca.* 2% higher than the previous values, thereby confirming that (7) and (8) incorporate the correct absolute configurations. The weighting schemes employed in the least-squares calculations were $\sqrt{w} = |F_o|/9.13$ when $|F_o| < 9.13$ and $\sqrt{w} = 9.13/|F_o|$ when $|F_o| > 9.13$ for (7); $\sqrt{w} = |F_o|/15.47$ when $|F_o| < 15.47$ and $\sqrt{w}$ $15.47/|F_o|$ when $|F_o| > 15.47$ for (8). Final observed and calculated structure factors and intermolecular contacts < 4 Å are listed in Supplementary Publication No. SUP 21493 (16 pp., 1 microfiche).*

RESULTS AND DISCUSSION

Atomic co-ordinates, thermal parameters, bond lengths, intermolecular distances, valency angles, torsion angles,

TABLE 1

Atomic co-ordinates as fractions of the cell edge, with estimated standard deviations in parentheses

(*a*) For (7)

	x	*y*	*z*
Br	0.2371(2)	0.2500(0)	0.0640(1)
O(1)	0.4370(13)	0.1758(7)	0.4002(10)
O(2)	−0.0110(12)	0.3941(6)	0.7248(8)
O(3)	−0.2002(12)	0.4588(9)	0.8664(8)
C(1)	0.0718(18)	0.3736(8)	0.2417(11)
C(2)	0.2046(18)	0.3004(8)	0.2487(13)
C(3)	0.3315(15)	0.2484(11)	0.3968(11)
C(4)	0.3274(17)	0.2909(8)	0.5431(12)
C(5)	0.1943(13)	0.3684(8)	0.5407(10)
C(6)	0.2076(15)	0.4166(7)	0.6899(10)
C(7)	0.2126(20)	0.5240(8)	0.6916(12)
C(8)	0.0518(23)	0.5666(8)	0.5305(14)
C(9)	0.0938(18)	0.5209(8)	0.3953(12)
C(10)	0.0340(17)	0.4138(7)	0.3855(10)
C(11)	0.1179(22)	0.5443(8)	0.8188(13)
C(12)	−0.0506(18)	0.4641(11)	0.8081(12)
C(13)	0.3146(28)	0.5473(12)	0.9884(18)
C(14)	0.4834(18)	0.2415(11)	0.6922(12)
C(15)	−0.2334(18)	0.3927(10)	0.3564(14)
H(1)	0.0038	0.3839	0.1358
H(6)	0.3314	0.3951	0.7790
H(7)	0.4435	0.5342	0.7375
H(8a)	−0.0382	0.5504	0.4944
H(8b)	0.0604	0.6246	0.5479
H(9a)	0.3028	0.5491	0.4230
H(9b)	0.0194	0.5384	0.2944
H(11)	0.0125	0.5963	0.8288
H(13a)	0.3560	0.5017	1.0044
H(13b)	0.4636	0.5857	1.0047
H(13c)	0.2702	0.5785	1.0744
H(14a)	0.3702	0.3013	0.6952
H(14b)	0.4068	0.2261	0.6917
H(14c)	0.5350	0.2723	0.7433
H(15a)	−0.3836	0.4493	0.2848
H(15b)	−0.2488	0.4035	0.4341
H(15c)	−0.3525	0.3830	0.2543
(*b*) For (8)			
Br	1.1727(2)	0.9837(1)	0.1914(2)
O(1)	1.0391(12)	0.8081(12)	0.0342(11)
O(2)	0.6066(11)	0.9356(9)	0.1499(9)
O(3)	0.4364(10)	1.0014(9)	0.1780(13)
C(1)	0.9553(17)	0.9975(13)	0.2728(14)
C(2)	1.0236(13)	0.9438(12)	0.1966(16)
C(3)	0.9796(15)	0.8543(13)	0.1051(14)
C(4)	0.8633(12)	0.8203(13)	0.1118(12)
C(5)	0.7942(11)	0.8762(10)	0.1847(10)
C(6)	0.6810(11)	0.8318(10)	0.1937(12)
C(7)	0.6315(12)	0.8103(12)	0.3163(13)
C(8)	0.6785(20)	0.9153(16)	0.3976(12)
C(9)	0.7986(20)	0.9312(17)	0.3895(13)
C(10)	0.8356(12)	0.9788(12)	0.2737(10)
C(11)	0.5098(17)	0.8219(13)	0.2952(15)
C(12)	0.5064(13)	0.9276(11)	0.2008(17)
C(13)	0.4309(20)	0.8483(19)	0.3905(16)
C(14)	0.8279(16)	0.7216(12)	0.0212(11)
C(15)	0.7875(15)	1.1161(14)	0.2410(14)
H(1)	0.9875	1.0650	0.3297
H(6)	0.6675	0.7600	0.1500
H(7)	0.6325	0.7233	0.3266
H(8a)	0.6125	0.9900	0.3875
H(8b)	0.6750	0.8967	0.4687
H(9a)	0.8375	0.8566	0.3937
H(9b)	0.7737	0.9883	0.4375
H(11)	0.4750	0.7567	0.2812
H(13a)	0.4175	0.7733	0.3797
H(13b)	0.3700	0.9217	0.4062
H(13c)	0.5175	0.8300	0.4250
H(14a)	0.8725	0.6467	0.0313
H(14b)	0.7875	0.6467	0.0578
H(14c)	0.8575	0.7333	−0.0516
H(15a)	0.7375	1.3333	0.2594
H(15b)	0.8650	1.1367	0.2500
H(15c)	0.8075	1.1300	0.1594

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* For details see Notice to Authors in *J.C.S. Perkin II*, 1974, Index issue.

[6] D. N. J. White and G. A. Sim, *Tetrahedron*, 1973, **29**, 3933.

and deviations of the atoms from various mean planes in the molecules are listed in Tables 1—7. The molecular structures and the arrangement of molecules in the unit cells are shown in Figures 1 and 2.

The various types of bond have lengths in good agreement with those reported for the 2-bromo-α- and -β-santonins: mean C(sp^3)–C(sp^3), C(sp^2)–C(sp^2), C(sp^2)–C(sp^2), and C=C distances are 1.53, 1.51, 1.48, and 1.33 Å.

In comparison with the α- and β-santonin derivatives, the cyclohexadienone ring in the *epi*-santonins departs further from a planar conformation, C(3) and C(10) being displaced by *ca.* 0.1 Å from the C(1), C(2), C(4), C(5) plane.

TABLE 2

Anisotropic * thermal Parameters for the non-hydrogen and isotropic thermal parameters for hydrogen atoms

(*a*) For (7)

	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
Br	0.0588	0.0062	0.0154	−0.0027	0.0379	−0.0039
O(1)	0.0371	0.0059	0.0199	0.0093	0.0329	0.0006
O(2)	0.0222	0.0045	0.0140	−0.0022	0.0206	−0.0010
O(3)	0.0300	0.0090	0.0168	0.0010	0.0358	0.0003
C(1)	0.0245	0.0047	0.0110	−0.0009	0.0201	0.0004
C(2)	0.0137	0.0043	0.0125	−0.0099	0.0079	−0.0004
C(3)	0.0204	0.0037	0.0153	0.0074	0.0166	−0.0047
C(4)	0.0183	0.0034	0.0135	−0.0050	0.0206	0.0000
C(5)	0.0041	0.0041	0.0098	−0.0002	0.0048	0.0025
C(6)	0.0140	0.0032	0.0101	0.0048	0.0122	0.0023
C(7)	0.0308	0.0037	0.0125	0.0030	0.0169	0.0010
C(8)	0.0382	0.0026	0.0170	0.0035	0.0191	0.0041
C(9)	0.0284	0.0034	0.0139	0.0049	0.0165	0.0047
C(10)	0.0192	0.0034	0.0079	0.0036	0.0091	0.0046
C(11)	0.0313	0.0044	0.0132	0.0036	0.0150	0.0003
C(12)	0.0228	0.0067	0.0099	0.0016	0.0087	0.0017
C(13)	0.0438	0.0077	0.0133	−0.0112	0.0089	−0.0040
C(14)	0.0342	0.0047	0.0159	0.0120	0.0163	0.0035
C(15)	0.0116	0.0069	0.0133	0.0001	0.0021	0.0014

	B		*B*
H(1)	3.5	H(13b)	5.3
H(6)	3.1	H(13c)	5.3
H(7)	3.6	H(14a)	4.7
H(8a)	4.3	H(14b)	4.7
H(8b)	4.3	H(14c)	4.7
H(9a)	3.2	H(15a)	3.6
H(9b)	3.2	H(15b)	3.6
H(11)	4.1	H(15c)	3.6
H(13a)	5.3		

(*b*) For (8)

	b_{11}	b_{22}	b_{33}	b_{12}	b_{23}	b_{23}
Br	0.0057	0.0102	0.0143	−0.0021	−0.0003	−0.0056
O(1)	0.0072	0.0163	0.0120	−0.0021	0.0028	−0.0118
O(2)	0.0069	0.0100	0.0074	0.0041	−0.0035	0.0033
O(3)	0.0076	0.0093	0.0155	0.0031	−0.0006	−0.0021
C(1)	0.0127	0.0078	0.0068	−0.0046	−0.0028	−0.0051
C(2)	0.0044	0.0090	0.0099	0.0001	0.0013	−0.0010
C(3)	0.0073	0.0092	0.0064	0.0046	−0.0001	0.0008
C(4)	0.0051	0.0080	0.0062	0.0015	−0.0028	0.0027
C(5)	0.0063	0.0064	0.0015	0.0017	0.0007	−0.0011
C(6)	0.0046	0.0078	0.0064	−0.0005	−0.0007	−0.0035
C(7)	0.0064	0.0089	0.0054	0.0020	0.0022	0.0038
C(8)	0.0087	0.0160	0.0046	0.0009	0.0020	−0.0028
C(9)	0.0132	0.0142	0.0049	0.0095	−0.0102	−0.0073
C(10)	0.0058	0.0083	0.0041	0.0014	0.0002	−0.0060
C(11)	0.0122	0.0085	0.0080	−0.0059	−0.0072	0.0039
C(12)	0.0070	0.0058	0.0127	0.0033	0.0018	−0.0033
C(13)	0.0126	0.0161	0.0099	−0.0049	0.0075	−0.0044
C(14)	0.0098	0.0097	0.0037	−0.0013	0.0029	−0.0053
C(15)	0.0083	0.0081	0.0086	0.0011	0.0053	−0.0030

	B		*B*
H(1)	4.4	H(13b)	6.1
H(6)	3.3	H(13c)	6.1
H(7)	3.3	H(14a)	3.8
H(8a)	4.2	H(14b)	3.8
H(8b)	4.2	H(14c)	3.8
H(9a)	4.4	H(15a)	4.0
H(9b)	4.4	H(15b)	4.0
H(11)	4.7	H(15c)	4.0
H(13a)	6.1		

TABLE 3

Bond lengths (Å) with estimated standard deviations in parentheses

(*a*) For (7)

Br–C(2)	1.90(1)	C(4)–C(6)	1.50(1)
O(1)–C(3)	1.21(2)	C(5)–C(10)	1.53(1)
O(2)–C(6)	1.49(1)	C(6)–C(7)	1.53(2)
O(2)–C(12)	1.32(2)	C(7)–C(8)	1.55(2)
O(3)–C(12)	1.20(1)	C(7)–C(11)	1.49(1)
C(1)–C(2)	1.30(2)	C(8)–C(9)	1.49(2)
C(1)–C(10)	1.52(1)	C(9)–C(10)	1.56(2)
C(2)–C(3)	1.48(2)	C(10)–C(15)	1.56(1)
C(3)–C(4)	1.47(1)	C(11)–C(12)	1.50(2)
C(4)–C(5)	1.36(1)	C(11)–C(13)	1.56(2)
C(4)–C(14)	1.51(2)		

(*b*) For (8)

Br–C(2)	1.87(2)	C(5)–C(6)	1.46(2)
O(1)–C(3)	1.20(2)	C(5)–C(10)	1.57(2)
O(2)–C(6)	1.49(2)	C(6)–C(7)	1.59(2)
O(2)–C(12)	1.37(2)	C(7)–C(8)	1.55(2)
O(3)–C(12)	1.17(2)	C(7)–C(11)	1.51(3)
C(1)–C(2)	1.34(3)	C(8)–C(9)	1.48(3)
C(1)–C(10)	1.47(3)	C(9)–C(10)	1.52(2)
C(2)–C(3)	1.51(2)	C(10)–C(15)	1.56(2)
C(3)–C(4)	1.46(2)	C(11)–C(12)	1.55(1)
C(4)–C(5)	1.33(2)	C(11)–C(13)	1.51(3)
C(4)–C(14)	1.53(2)		

TABLE 4

Some of the shorter intramolecular non-bonded distances involving C(13), with other distances for comparison

	(7)	(8)
C(13) · · · C(6)	3.16	3.84
C(13) · · · C(8)	3.89	3.10
C(13) · · · O(2)	3.30	3.67
C(13) · · · O(3)	3.14	3.00
C(2) · · · C(15)	3.38	3.41
C(4) · · · O(2)	3.38	3.38
C(14) · · · O(2)	3.77	3.79
C(8) · · · C(15)	3.10	3.10

TABLE 5

Valency angles (°)

(*a*) For (7)

C(12)–O(2)–C(6)	108.3(7)	C(6)–C(7)–C(8)	112.2(8)
C(10)–C(1)–C(2)	122.8(8)	C(11)–C(7)–C(6)	101.0(6)
C(1)–C(2)–Br	121.3(5)	C(11)–C(7)–C(8)	112.0(6)
C(3)–C(2)–Br	115.4(5)	C(7)–C(8)–C(9)	111.9(6)
C(1)–C(2)–C(3)	123.3(9)	C(8)–C(9)–C(10)	111.6(8)
C(2)–C(3)–O(1)	122.9(9)	C(1)–C(10)–C(5)	113.1(6)
C(4)–C(3)–O(1)	120.7(8)	C(1)–C(10)–C(9)	108.3(8)
C(2)–C(3)–C(4)	116.4(7)	C(1)–C(10)–C(15)	104.4(5)
C(3)–C(4)–C(5)	121.6(7)	C(9)–C(10)–C(5)	107.8(7)
C(14)–C(4)–C(3)	114.3(8)	C(9)–C(10)–C(15)	113.5(5)
C(14)–C(4)–C(5)	124.1(8)	C(15)–C(10)–C(5)	109.7(5)
C(4)–C(5)–C(6)	121.4(7)	C(7)–C(11)–C(12)	103.8(8)
C(10)–C(5)–C(4)	121.8(7)	C(7)–C(11)–C(13)	113.9(7)
C(10)–C(5)–C(6)	116.7(6)	C(12)–C(11)–C(13)	109.5(9)
C(5)–C(6)–O(2)	109.5(6)	O(3)–C(12)–O(2)	121.6(6)
C(7)–C(6)–O(2)	103.2(8)	C(11)–C(12)–O(2)	110.6(6)
C(5)–C(6)–C(7)	117.5(7)	C(11)–C(12)–O(3)	127.7(11)

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* Of the form $T = \exp[-(b_{11}h^2 + b_{22}k^2 + b_{33}l^2 + b_{12}hk + b_{13}hl + b_{23}kl)]$.

TABLE 5 (*Continued*)

(*b*) For (8)

C(12)–O(2)–C(6)	110.6(9)	C(6)–C(7)–C(8)	109.4(9)
C(10)–C(1)–C(2)	124.6(12)	C(11)–C(7)–C(6)	102.3(11)
C(1)–C(2)–Br	122.6(7)	C(11)–C(7)–C(8)	114.4(13)
C(3)–C(2)–Br	117.0(8)	C(7)–C(8)–C(9)	113.8(14)
C(1)–C(2)–C(3)	120.2(12)	C(8)–C(9)–C(10)	112.8(10)
C(2)–C(3)–O(1)	121.2(12)	C(1)–C(10)–C(5)	113.7(9)
C(4)–C(3)–O(1)	122.1(12)	C(1)–C(10)–C(9)	110.0(10)
C(2)–C(3)–C(4)	116.6(11)	C(1)–C(10)–C(15)	104.8(10)
C(3)–C(4)–C(5)	123.3(8)	C(9)–C(10)–C(5)	107.3(9)
C(14)–C(4)–C(3)	113.0(9)	C(9)–C(10)–C(15)	113.3(11)
C(14)–C(4)–C(5)	123.6(10)	C(15)–C(10)–C(5)	107.9(8)
C(4)–C(5)–C(6)	121.0(9)	C(7)–C(11)–C(12)	101.5(10)
C(10)–C(5)–C(4)	121.0(10)	C(7)–C(11)–C(13)	121.3(13)
C(10)–C(5)–C(6)	117.6(8)	C(12)–C(11)–C(13)	113.5(12)
C(5)–C(6)–O(2)	109.6(8)	O(3)–C(12)–O(2)	121.0(8)
C(7)–C(6)–O(2)	100.6(10)	C(11)–C(12)–O(2)	109.6(10)
C(5)–C(6)–C(7)	118.1(11)	C(11)–C(12)–O(3)	129.1(13)

TABLE 6

Torsion angles (°)

(*a*) For (7)

C(12)–O(2)–C(6)–C(5)	−153	C(4)–C(5)–C(10)–C(1)	−9
C(12)–O(2)–C(6)–C(7)	−27	C(4)–C(5)–C(10)–C(9)	−129
C(6)–O(2)–C(12)–O(3)	−172	C(4)–C(5)–C(10)–C(15)	107
C(6)–O(2)–C(12)–C(11)	7	C(6)–C(5)–C(10)–C(1)	167
C(10)–C(1)–C(2)–Br	178	C(6)–C(5)–C(10)–C(9)	48
C(10)–C(1)–C(2)–C(3)	0	C(6)–C(5)–C(10)–C(15)	−76
C(2)–C(1)–C(10)–C(5)	8	O(2)–C(6)–C(7)–C(8)	−84
C(2)–C(1)–C(10)–C(9)	128	O(2)–C(6)–C(7)–C(11)	35
C(2)–C(1)–C(10)–C(15)	−111	C(5)–C(6)–C(7)–C(8)	37
Br–C(2)–C(3)–O(1)	−4	C(5)–C(6)–C(7)–C(11)	156
Br–C(2)–C(3)–C(4)	174	C(6)–C(7)–C(8)–C(9)	−48
C(1)–C(2)–C(3)–O(1)	173	C(11)–C(7)–C(8)–C(9)	−161
C(1)–C(2)–C(3)–C(4)	−8	C(6)–C(7)–C(11)–C(12)	−31
O(1)–C(3)–C(4)–C(5)	−175	C(6)–C(7)–C(11)–C(13)	88
O(1)–C(3)–C(4)–C(14)	6	C(8)–C(7)–C(11)–C(12)	88
C(2)–C(3)–C(4)–C(5)	7	C(8)–C(7)–C(11)–C(13)	−153
C(2)–C(3)–C(4)–C(14)	−173	C(7)–C(8)–C(9)–C(10)	61
C(3)–C(4)–C(5)–C(6)	−174	C(8)–C(9)–C(10)–C(1)	178
C(3)–C(4)–C(5)–C(10)	2	C(8)–C(9)–C(10)–C(5)	−59
C(14)–C(4)–C(5)–C(6)	5	C(8)–C(9)–C(10)–C(15)	62
C(14)–C(4)–C(5)–C(10)	−178	C(7)–C(11)–C(12)–O(2)	16
C(4)–C(5)–C(6)–O(2)	−105	C(7)–C(11)–C(12)–O(3)	−165
C(4)–C(5)–C(6)–C(7)	138	C(13)–C(11)–C(12)–O(2)	−106
C(10)–C(5)–C(6)–O(2)	78	C(13)–C(11)–C(12)–O(3)	73
C(10)–C(5)–C(6)–C(7)	−39		

(*b*) For (8)

C(12)–O(2)–C(6)–(C5)	−152	C(4)–C(5)–C(10)–C(1)	−4
C(12)–O(2)–C(6)–C(7)	−27	C(4)–C(5)–C(10)–C(9)	−126
C(6)–O(2)–C(12)–O(3)	180	C(4)–C(5)–C(10)–C(15)	112
C(6)–O(2)–C(12)–C(11)	6	C(6)–C(5)–C(10)–C(1)	168
C(10)–C(1)–C(2)–Br	174	C(6)–C(5)–C(10)–C(9)	46
C(10)–C(1)–C(2)–C(3)	−2	C(6)–C(5)–C(10)–C(15)	−76
C(2)–C(1)–C(10)–C(5)	7	O(2)–C(6)–C(7)–C(8)	−83
C(2)–C(1)–C(10)–C(9)	127	O(2)–C(6)–C(7)–C(11)	38
C(2)–C(1)–C(10)–C(15)	−111	C(5)–C(6)–C(7)–C(8)	36
Br–C(2)–C(3)–O(1)	2	C(5)–C(6)–C(7)–C(11)	157
Br–C(2)–C(3)–C(4)	178	C(6)–C(7)–C(8)–C(9)	−47
C(1)–C(2)–C(3)–O(1)	178	C(11)–C(7)–C(8)–C(9)	−161
C(1)–C(2)–C(3)–C(4)	−6	C(6)–C(7)–C(11)–C(12)	−35
O(1)–C(3)–C(4)–C(5)	−176	C(6)–C(7)–C(11)–C(13)	−162
O(1)–C(3)–C(4)–C(14)	0	C(8)–C(7)–C(11)–C(12)	83
C(2)–C(3)–C(4)–C(5)	8	C(8)–C(7)–C(11)–C(13)	−43
C(2)–C(3)–C(4)–C(14)	−176	C(7)–C(8)–C(9)–C(10)	63
C(3)–C(4)–C(5)–C(6)	−175	C(8)–C(9)–C(10)–C(1)	178
C(3)–C(4)–C(5)–C(10)	−3	C(8)–C(9)–C(10)–C(5)	−58
C(14)–C(4)–C(5)–C(6)	9	C(8)–C(9)–C(10)–C(15)	61
C(14)–C(4)–C(5)–C(10)	−179	C(7)–C(11)–C(12)–O(2)	20
C(4)–C(5)–C(6)–O(2)	−111	C(7)–C(11)–C(12)–O(3)	−154
C(4)–C(5)–C(6)–C(7)	135	C(13)–C(11)–C(12)–O(2)	151
C(10)–C(5)–C(6)–O(2)	76	C(13)–C(11)–C(12)–O(3)	−22
C(10)–C(5)–C(6)–C(7)	−38		

The sign convention used is such that the angle is negative if an anticlockwise rotation of atom A is required to eclipse D, whilst viewing down the B–C bond.

TABLE 7

Equations * of mean planes through various sets of atoms and deviations (Å) of atoms from the planes. Atoms not included in the derivation of a plane are italicised

(*a*) For (7)

Plane (i): $-0.8021X - 0.5886Y - 0.1009Z = -3.0505$

C(1) 0.01, C(2) −0.01, C(4) 0.01, C(5) −0.01, *C(3) 0.08, C(10) 0.11, O(1) 0.19*

Plane (ii): $-0.7924X - 0.5896Y - 0.1568Z = -3.1555$

C(1) −0.01, C(2) −0.02, C(3) 0.00, Br 0.01, C(10) 0.01, *O(1) 0.12*

Plane (iii): $-0.8185X - 0.5745Y - 0.0093Z = -2.5748$

C(3) −0.05, C(4) 0.01, C(5) 0.02, C(6) −0.05, C(10) 0.03, C(14) 0.03, *O(1) 0.04*

Plane (iv): $-0.3942X + 0.3946Y - 0.8300Z = -1.9128$

C(11) 0.00, C(12) 0.01, O(2) 0.00, O(3) 0.00, *C(6) −0.19, C(7) 0.39*

Plane (v): $0.09447X + 0.2695Y - 0.1866Z = -0.0222$

C(5) 0.00, C(7) 0.00, C(8) 0.00, C(10) 0.00, *C(6) −0.44, C(9) 0.70*

(*b*) For (8)

Plane (i): $-0.1556X + 0.7618Y - 0.6288Z = 3.8906$

C(1) −0.01, C(2) 0.01, C(4) −0.01, C(5) 0.01, *C(3) 0.08, C(10) 0.07, O(1) 0.14*

Plane (ii): $-0.1554X + 0.7755Y - 0.6119Z = 4.1106$

C(1) −0.04, C(2) −0.04, C(3) 0.00, Br 0.03, C(10) 0.04, *O(1) 0.04*

Plane (iii): $-0.2268X + 0.7340Y - 0.6410Z = 2.8945$

C(3) −0.03, C(4) −0.01, C(5) 0.04, C(6) −0.04, C(10) 0.02, C(14) 0.03, *O(1) −0.01*

Plane (iv): $-0.3206X - 0.6693Y - 0.6702Z = 9.9144$

C(11) −0.01, C(12) 0.03, O(2) −0.01, O(3) −0.01, *C(6) 0.05, C(7) −0.57*

Plane (v): $-0.5690X + 0.7011Y - 0.4298Z = 0.2172$

C(5) 0.00, C(7) 0.00, C(8) 0.00, C(10) 0.00, *C(6) 0.43, C(9) 0.67*

* Where X, Y, and Z are orthogonal co-ordinates, in Å.

This conformational difference cannot readily be attributed to the intermolecular force-fields of the crystals, for it is reproduced by the empirical force-field calculations which were parameterised for isolated molecules (see Table 8). Nevertheless, small conformational changes in a nearly flat cyclohexadienone ring can arise from intermolecular forces; the crystal structure of 9α-fluoro-6α-methylprednisolone contains two independent

TABLE 8

Observed and calculated torsion angles (°) around ring A for the 2-bromo-derivatives of (*a*) α-santonin, (*b*) β-santonin, (*c*) 6-*epi*-α-santonin, and (*d*) 6-*epi*-β-santonin. The sum of the moduli of the angles is shown in each case as a measure of the non-planarity of the ring

	(*a*)		(*b*)		(*c*)		(*d*)	
	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.
C(1)–C(2)	4	0	3	−1	0	−2	−2	−2
C(2)–C(3)	−3	−1	−3	−2	−8	−5	−6	−4
C(3)–C(4)	−2	−1	−1	0	7	3	8	3
C(4)–C(5)	5	3	5	3	2	4	−3	4
C(5)–C(10)	−3	−3	−4	−5	−9	−10	−4	−9
C(10)–C(1)	−1	2	0	4	8	9	7	8
Σ|ω|	18	9	16	14	34	33	30	31

molecules and the sum of the moduli of the ring A torsion angles ($\Sigma|\omega|$) is 23 in one molecule and 11° in the other.[7] These various results suggest that there is only a small potential barrier to conformational distortion of a planar cyclohexadienone by either intra- or inter-molecular forces. It may be pertinent that the electron-diffraction data from acrolein can best be interpreted in terms of a small deviation from planarity, with C=C–C=O torsion angle of 11°, though it is difficult to decide whether this is really significant.[8]

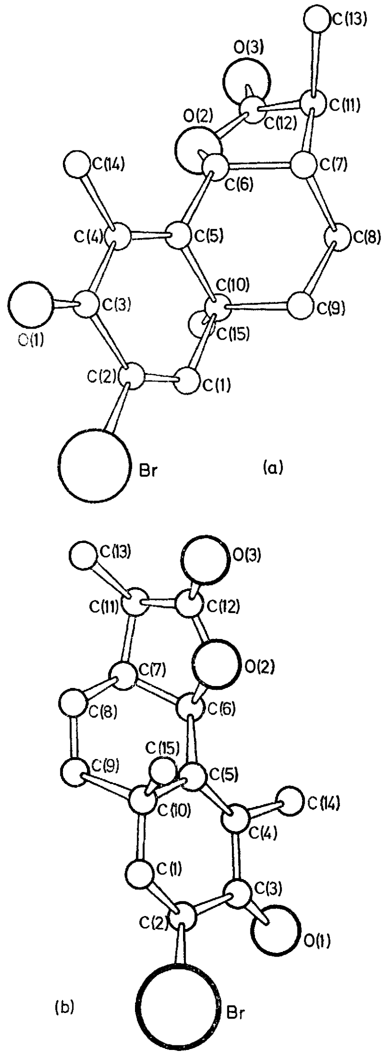

FIGURE 1 The molecules of 2-bromo-6-*epi*-α- (7) and (b) 2-Bromo-6-*epi*-β-santonin (8)

Ring B adopts the chair conformation in both the α- and β-isomers (7) and (8) although, as a consequence of the *cis*-fused γ-lactone, it is somewhat flatter than the cyclohexane ring in the santonins. The mean endocyclic torsion angle for ring B is 58 in 2-bromo-α-and 59° in 2-bromo-β-santonin, similar to values for ring C in steroids,[9] as opposed to 49 and 48° (calculated 50 and 51°) in the *epi*-α-and -β-santonins.

The γ-lactone rings approach envelope forms; C(6) and C(7) are displaced from the C(11), C(12), O(2), O(3) plane by −0.19 and 0.39 Å in the *epi*-α-santonin and by 0.05 and −0.57 Å in the *epi*-β-santonin. It is now well established 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 its C(11)-epimer with a *quasi*-equatorial group, regardless of whether the γ-lactone is *cis*- or *trans*-fused.[10] The 6-*epi*-santonins are no exception and the torsion angles around C(7)–C(11) deviate from the ideal value of 60° by 21°, on average, in the β- and by 28° in the α-isomer, in excellent agreement with results obtained for other sesquiterpenoid γ-lactones.[10] A *quasi*-equatorial substituent at C(11) also leads to a favourable situation around the C(11)–C(12) bond where the minimum energy arrangement corresponds to eclipsing of the carbonyl group by a C(11)–C or C(11)–H bond, carbon being preferred to hydrogen. The

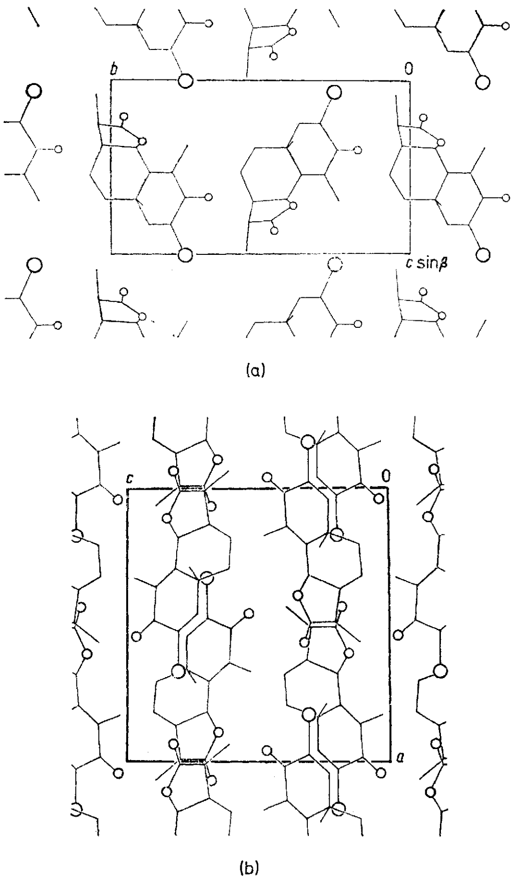

FIGURE 2 (*a*) The crystal packing of (7) viewed in the *a* direction; (b) the crystal packing of (8) viewed in the *b* direction

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C(13)–C(11)–C(12)–O(3) torsion angles are 73 (α-isomer) and —22° (β-isomer), the latter being preferred, and the corresponding values for α- and β-santonin are 33 and —72°, the former being preferred. These results are reproduced by the empirical force-field calculations and are discussed in detail in ref. 6.

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