Sesquiterpenoids. Part XIII.[1] Constitution and Absolute Stereochemistry of Elephantol: *X*-Ray Analysis of Elephantol *p*-Bromobenzoate

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The constitution and absolute stereochemistry of elephantol, $C_{15}H_{16}O_6$, a novel germacrane sesquiterpenoid dilactone, have been defined by crystal-structure analysis of elephantol *p*-bromobenzoate. The ten-membered carbocyclic ring adopts a conformation which is characterized by a short C(1) · · · C(5) transannular separation of 2·98 Å and by both C(14)- and C(15)-substituents being on the β-face of the molecule. The *trans*-ethylenic group in the ten-membered ring is distinctly distorted from planarity, the C(2)–C(1)–C(10)–C(9) torsion angle being 163°. Elephantol *p*-bromobenzoate crystallizes in the orthorhombic space group $P2_12_12_1$, with $Z = 4$ in a cell of dimensions: $a = 10{\cdot}64$, $b = 30{\cdot}34$, $c = 6{\cdot}41$ Å. The atomic co-ordinates were determined from photographic data by Fourier and least-squares methods, the final *R* being 11·9% over 1690 independent reflections. The absolute configuration of the sesquiterpene was established by the anomalous-dispersion method.

DURING a search for tumour inhibitors from plant sources, Kupchan *et al.*[2] found that alcoholic extracts of dried *Elephantopus elatus* Bertol. (Compositae) exhibited significant inhibitory activity *in vitro* against cells derived from human carcinoma of the nasopharynx (KB). Fractionation of the extracts produced two novel cytotoxic sesquiterpene esters (elephantin, $C_{20}H_{22}O_7$, and elephantopin, $C_{19}H_{20}O_7$), alkaline hydrolysis of which yielded a sesquiterpene alcohol, elephantol, of composition $C_{15}H_{16}O_6$.[2]

We undertook an *X*-ray crystal-structure analysis of elephantol *p*-bromobenzoate in order to define the structure of the sesquiterpene. The heavy-atom approach was adopted and the atoms were located in electron-density distributions calculated with weighted Fourier coefficients.[3] The atomic co-ordinates were adjusted by least-squares calculations, and at the conclusion of the analysis *R* was 11·9% over 1690 independent *X*-ray reflections. The absolute configuration of the molecule was determined by Bijvoet's

TABLE 1

Atomic co-ordinates (fractional), standard deviations (Å), and thermal parameters (Å²)

	x	*y*	*z*	σ(*X*)	σ(*Y*)	σ(*Z*)	*B*
C(1)	−0·1456	0·4548	0·3133	0·016	0·015	0·019	4·6
C(2)	−0·2464	0·4228	0·2473	0·016	0·016	0·019	4·9
C(3)	−0·1940	0·3771	0·1908	0·018	0·017	0·021	5·7
C(4)	−0·0919	0·3609	0·3396	0·015	0·014	0·017	4·2
C(5)	0·0371	0·3803	0·3161	0·015	0·014	0·018	4·2
C(6)	0·1337	0·3822	0·4890	0·012	0·012	0·015	3·1
C(7)	0·1483	0·4293	0·5644	0·012	0·012	0·015	3·1
C(8)	0·0426	0·4415	0·7246	0·013	0·013	0·016	3·4
C(9)	−0·0435	0·4800	0·6564	0·015	0·015	0·017	4·2
C(10)	−0·1413	0·4613	0·5180	0·013	0·013	0·015	3·5
C(11)	0·2663	0·4365	0·6890	0·013	0·012	0·015	3·2
C(12)	0·2277	0·4506	0·9017	0·014	0·013	0·018	4·1
C(13)	0·3865	0·4355	0·6387	0·017	0·016	0·019	5·0
C(14)	−0·2516	0·4405	0·5870	0·015	0·014	0·019	4·4
C(15)	−0·1386	0·3389	0·5492	0·021	0·020	0·024	6·6
O(16)	−0·3151	0·4178	0·4464	0·010	0·010	0·012	4·4
O(17)	−0·2891	0·4374	0·7787	0·012	0·011	0·013	5·4
O(18)	0·1034	0·4546	0·9167	0·009	0·009	0·012	4·1
O(19)	0·2952	0·4571	1·0592	0·012	0·011	0·014	5·9
O(20)	0·0088	0·3365	0·2386	0·014	0·012	0·015	6·5
O(21)	0·2485	0·3689	0·3878	0·008	0·008	0·010	3·4
C(22)	0·3094	0·3345	0·4649	0·012	0·012	0·015	3·2
O(23)	0·2810	0·3174	0·6282	0·011	0·011	0·013	5·4
C(24)	0·4123	0·3190	0·3323	0·011	0·011	0·013	2·5
C(25)	0·4859	0·2834	0·3969	0·014	0·014	0·019	4·2
C(26)	0·5761	0·2666	0·2731	0·014	0·015	0·018	4·4
C(27)	0·5956	0·2847	0·0797	0·014	0·014	0·018	4·2
C(28)	0·5242	0·3193	0·0083	0·015	0·015	0·017	4·3
C(29)	0·4317	0·3373	0·1297	0·013	0·013	0·016	3·6
Br	0·7222	0·2610	−0·0962	0·002	0·002	0·003	*

* For the bromine atom an anisotropic temperature factor was employed of the form: $T = \exp[-b_{11}h^2 + b_{22}k^2 + b_{33}l^2 + b_{12}hk + b_{13}hl + b_{23}kl)]$ with parameters:

b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
0·0160	0·0022	0·0491	0·0051	0·0247	−0·0025

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

[2] S. M. Kupchan, Y. Aynehchi, J. M. Cassady, A. T. McPhail, G. A. Sim, H. K. Schnoes, and A. L. Burlingame, *J. Amer. Chem. Soc.*, 1966, **88**, 3674.

[3] G. A. Sim, *Acta Cryst.*, 1959, **12**, 813; 'Computing Methods and the Phase Problem in *X*-ray Crystal Analysis,' eds. R. Pepinsky, J. M. Robertson, and J. C. Speakman, Pergamon Press, Oxford, 1961, p. 227.

anomalous-dispersion method.[4] The atomic co-ordinates are listed in Table 1, the interatomic distances

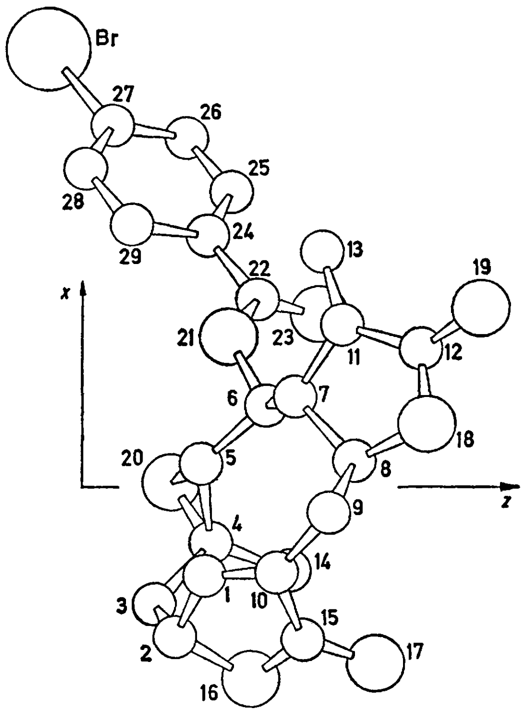
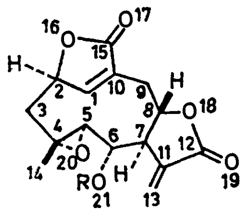
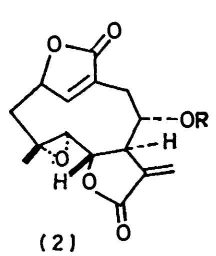


FIGURE 1 The atomic arrangement in the molecule

and valency angles in Table 2, and the torsion angles about the bonds in Table 3. The atomic arrangement is explained in Figure 1.

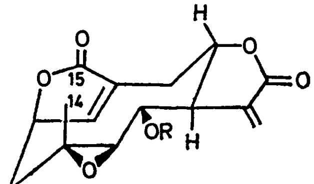


(1)

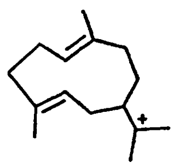


(2)

a; R = CO·CH:CMe$_2$
b; R = CO·C(Me):CH$_2$



(3)



(4)

Our results establish that elephantol *p*-bromobenzoate has the constitution and absolute stereochemistry shown in (1; R = CO·C$_6$H$_4$·Br). The chemical studies re-

[4] J. M. Bijvoet, A. F. Peerdeman, and A. J. van Bommel, *Nature*, 1951, **168**, 271.

TABLE 2

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

(*a*) Bond lengths

C(1)–C(2)	1·51(0·023)	C(10)–C(15)	1·40(0·020)
C(1)–C(10)	1·33(0·024)	C(11)–C(12)	1·49(0·023)
C(2)–C(3)	1·54(0·024)	C(11)–C(13)	1·32(0·022)
C(2)–O(16)	1·48(0·022)	C(12)–O(18)	1·33(0·017)
C(3)–C(4)	1·53(0·025)	C(12)–O(19)	1·25(0·021)
C(4)–C(5)	1·50(0·021)	C(14)–O(16)	1·32(0·020)
C(4)–C(14)	1·58(0·028)	C(14)–O(17)	1·30(0·023)
C(4)–O(20)	1·45(0·021)	O(21)–C(22)	1·32(0·015)
C(5)–C(6)	1·51(0·022)	C(22)–O(23)	1·21(0·019)
C(5)–O(20)	1·45(0·019)	C(22)–C(24)	1·46(0·018)
C(6)–C(7)	1·52(0·017)	C(24)–C(25)	1·40(0·018)
C(6)–O(21)	1·44(0·015)	C(24)–C(29)	1·43(0·020)
C(7)–C(8)	1·57(0·020)	C(25)–C(26)	1·35(0·022)
C(7)–C(11)	1·50(0·019)	C(26)–C(27)	1·37(0·025)
C(8)–C(9)	1·55(0·020)	C(27)–C(28)	1·37(0·021)
C(8)–O(18)	1·45(0·019)	C(27)–Br	1·90(0·016)
C(9)–C(10)	1·48(0·021)	C(28)–C(29)	1·37(0·021)

(*b*) Intramolecular non-bonded distances

C(1) ··· C(5)	2·98	C(14) ··· C(15)	3·32
C(5) ··· C(10)	3·36	C(14) ··· O(16)	3·11
C(13) ··· C(22)	3·36		

(*c*) Valency angles

C(2)–C(1)–C(10)	113(1·5)	C(7)–C(11)–C(12)	107(1·1)
C(1)–C(2)–C(3)	113(1·3)	C(7)–C(11)–C(13)	133(1·5)
C(1)–C(2)–O(16)	100(1·4)	C(12)–C(11)–C(13)	120(1·4)
C(3)–C(2)–O(16)	107(1·3)	C(11)–C(12)–O(18)	112(1·3)
C(2)–C(3)–C(4)	114(1·5)	C(11)–C(12)–O(19)	129(1·3)
C(3)–C(4)–C(5)	117(1·4)	O(18)–C(12)–O(19)	120(1·5)
C(3)–C(4)–C(14)	116(1·4)	C(10)–C(15)–O(16)	117(1·5)
C(3)–C(4)–O(20)	114(1·4)	C(10)–C(15)–O(17)	126(1·5)
C(14)–C(4)–C(5)	123(1·5)	O(16)–C(15)–O(17)	117(1·3)
C(14)–C(4)–O(20)	113(1·3)	C(15)–O(16)–C(2)	106(1·2)
C(5)–C(4)–O(20)	59(1·0)	C(8)–O(18)–C(12)	111(1·2)
C(4)–C(5)–C(6)	124(1·4)	C(4)–O(20)–C(5)	62(1·0)
C(4)–C(5)–O(20)	59(1·0)	C(6)–O(21)–C(22)	118(1·0)
C(6)–C(5)–O(20)	115(1·2)	O(21)–C(22)–O(23)	123(1·2)
C(5)–C(6)–C(7)	110(1·1)	O(21)–C(22)–C(24)	114(1·2)
C(5)–C(6)–O(21)	104(1·2)	O(23)–C(22)–C(24)	124(1·2)
C(7)–C(6)–O(21)	109(0·9)	C(22)–C(24)–C(25)	120(1·2)
C(6)–C(7)–C(8)	111(1·0)	C(22)–C(24)–C(29)	121(1·1)
C(6)–C(7)–C(11)	113(1·0)	C(25)–C(24)–C(29)	119(1·2)
C(8)–C(7)–C(11)	103(1·1)	C(24)–C(25)–C(26)	121(1·6)
C(7)–C(8)–C(9)	115(1·2)	C(25)–C(26)–C(27)	119(1·4)
C(7)–C(8)–O(18)	108(1·0)	C(26)–C(27)–C(28)	122(1·5)
C(9)–C(8)–O(18)	107(1·1)	C(26)–C(27)–Br	120(1·1)
C(8)–C(9)–C(10)	107(1·2)	C(28)–C(27)–Br	119(1·3)
C(9)–C(10)–C(1)	132(1·4)	C(27)–C(28)–C(29)	121(1·5)
C(9)–C(10)–C(15)	125(1·4)	C(24)–C(29)–C(28)	118(1·2)
C(1)–C(10)–C(15)	102(1·4)		

(*d*) Intermolecular separations (<3·8 Å)

O(17) ··· C(2$^{\mathrm{I}}$)	3·07	Br ··· C(14$^{\mathrm{VII}}$)	3·60
O(19) ··· C(9$^{\mathrm{II}}$)	3·32	O(18) ··· C(13$^{\mathrm{II}}$)	3·63
C(1) ··· O(17$^{\mathrm{III}}$)	3·35	O(23) ··· C(29$^{\mathrm{I}}$)	3·64
O(17) ··· C(3$^{\mathrm{I}}$)	3·37	C(1) ··· C(15$^{\mathrm{III}}$)	3·66
O(19) ··· C(11$^{\mathrm{II}}$)	3·40	Br ··· C(25$^{\mathrm{V}}$)	3·66
C(26) ··· O(23$^{\mathrm{VI}}$)	3·41	C(27) ··· C(3$^{\mathrm{IV}}$)	3·66
O(19) ··· O(21$^{\mathrm{I}}$)	3·44	O(18) ··· C(1$^{\mathrm{I}}$)	3·67
C(13) ··· O(16$^{\mathrm{IV}}$)	3·45	C(28) ··· C(3$^{\mathrm{IV}}$)	3·67
O(18) ··· C(5$^{\mathrm{I}}$)	3·48	O(19) ··· C(8$^{\mathrm{II}}$)	3·68
O(19) ··· C(7$^{\mathrm{II}}$)	3·50	O(19) ··· C(7$^{\mathrm{I}}$)	3·69
Br ··· C(24$^{\mathrm{V}}$)	3·50	O(19) ··· O(18$^{\mathrm{II}}$)	3·68
C(10) ··· O(17$^{\mathrm{III}}$)	3·51	Br ··· C(29$^{\mathrm{V}}$)	3·73
O(23) ··· C(28$^{\mathrm{I}}$)	3·55	C(2) ··· C(9$^{\mathrm{III}}$)	3·75
C(13) ··· O(17$^{\mathrm{IV}}$)	3·57	O(17) ··· C(1$^{\mathrm{I}}$)	3·79
O(19) ··· C(12$^{\mathrm{II}}$)	3·57		

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

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

vealed that a lactone rearrangement[5] from C(6) to C(8) had taken place during the alkaline hydrolysis of elephantin and elephantopin, and it was deduced that these esters have structures (2a) and (2b), respectively.

TABLE 3

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.* 2°

C(10)–C(1)–C(2)–C(3)	−104	C(3)–C(2)–O(16)–C(15)	113
C(10)–C(1)–C(2)–O(16)	10	C(3)–C(4)–O(20)–C(5)	109
C(1)–C(2)–C(3)–C(4)	42	C(14)–C(4)–O(20)–C(5)	−115
O(16)–C(2)–C(3)–C(4)	−67	C(6)–C(5)–O(20)–C(4)	116
C(2)–C(3)–C(4)–C(5)	−77	C(5)–C(6)–O(21)–C(22)	−123
C(2)–C(3)–C(4)–C(14)	82	C(7)–C(6)–O(21)–C(22)	120
C(2)–C(3)–C(4)–O(20)	−143	C(6)–C(7)–C(11)–C(12)	−118
C(3)–C(4)–C(5)–C(6)	156	C(6)–C(7)–C(11)–C(13)	67
C(3)–C(4)–C(5)–O(20)	−103	C(8)–C(7)–C(11)–C(12)	1
C(14)–C(4)–C(5)–C(6)	−2	C(8)–C(7)–C(11)–C(13)	−173
C(14)–C(4)–C(5)–O(20)	99	C(7)–C(8)–O(18)–C(12)	−3
O(20)–C(4)–C(5)–C(6)	−101	C(9)–C(8)–O(18)–C(12)	−126
C(4)–C(5)–C(6)–C(7)	−108	C(9)–C(10)–C(15)–O(16)	−166
O(20)–C(5)–C(6)–C(7)	−176	C(9)–C(10)–C(15)–O(17)	5
C(4)–C(5)–C(6)–O(21)	136	C(1)–C(10)–C(15)–O(16)	7
O(20)–C(5)–C(6)–O(21)	68	C(1)–C(10)–C(15)–O(17)	179
C(5)–C(6)–C(7)–C(8)	82	C(7)–C(11)–C(12)–O(18)	−3
C(5)–C(6)–C(7)–C(11)	−163	C(13)–C(11)–C(12)–O(18)	173
O(21)–C(6)–C(7)–C(8)	−165	C(7)–C(11)–C(12)–O(19)	175
O(21)–C(6)–C(7)–C(11)	−51	C(13)–C(11)–C(12)–O(19)	−10
C(6)–C(7)–C(8)–C(9)	−119	C(11)–C(12)–O(18)–C(8)	3
C(6)–C(7)–C(8)–O(18)	122	O(19)–C(12)–O(18)–C(8)	−174
C(11)–C(7)–C(8)–C(9)	120	C(6)–O(21)–C(22)–O(23)	−9
C(11)–C(7)–C(8)–O(18)	1	C(6)–O(21)–C(22)–C(24)	170
C(7)–C(8)–C(9)–C(10)	83	C(10)–C(15)–O(16)–C(2)	−1
O(18)–C(8)–C(9)–C(10)	−157	O(17)–C(15)–O(16)–C(2)	−174
C(8)–C(9)–C(10)–C(1)	−89	O(21)–C(22)–C(24)–C(25)	179
C(8)–C(9)–C(10)–C(15)	82	O(21)–C(22)–C(24)–C(29)	−7
C(9)–C(10)–C(1)–C(2)	163	O(23)–C(22)–C(24)–C(25)	−2
C(15)–C(10)–C(1)–C(2)	−10	O(23)–C(22)–C(24)–C(29)	172
C(1)–C(2)–O(16)–C(15)	−5		

It has recently been shown that germacranolides containing lactonizable α-oxygen groups at C(6) and C(8) generally relactonize to C(8).[6]

The conformation of the molecule in the crystal approximates to that shown in (3), which may be described as an extended chair conformation. This type of conformation has been observed in *X*-ray studies of the silver nitrate adducts of germacratriene[7] and costunolide,[8] and measurements of the intramolecular Overhauser effects indicate that the germacrane sesquiterpenoids dihydrotamaulipin-A acetate[9] and furanodienone[10] adopt this type of conformation in solution. Derivatives of pregeijerene[11] and shiromodiol[12] have a related conformation (the 'boat–chair' type) which also is characterized by the *syn* relationship of C(14) and C(15). The cyclization of *trans*-farnesyl pyrophosphate to the cation (4) has been postulated[13] as a common step in the biogenesis of the germacrane, eudesmane, and guaiane classes of sesquiterpenes, and most of the eudesmane sesquiterpenes have stereochemistries which are derived from a conformation of the cation (4) in which the C(14)- and C(15)-methyl groups are *syn*.

The C(1) ··· C(5) transannular separation in (3) is distinctly short (2·98 Å), and this is also the case in pregeijerene–silver nitrate (2·91 Å)[11] and shiromodiol acetate *p*-bromobenzoate (3·05 Å).[12] The u.v. spectra of several unsaturated germacrane sesquiterpenes have been interpreted in terms of transannular interactions between double bonds,[14] consistent with short C(1) ··· C(5) and C(10) ··· C(5) separations.

Trans-double bonds in medium-ring olefins are subject to some strain,[15] and in accord with this the C(2)–C(1)–C(10)–C(9) torsion angle of 163° is notably different from the ideal unstrained value of 180°. The analogous C(2)–C(1)–C(10)–C(9) torsion angles in pregeijerene–silver nitrate and shiromodiol acetate *p*-bromobenzoate are 165 and 167°. The C(5)–C(6) double bond in the pregeijerene complex and the double bonds in the silver nitrate complexes of *trans*-cyclodecene[16] and *trans*-cyclo-octene[17] exhibit still larger distortions, the torsion angles about the bonds being 150, 138, and 136°, respectively. The torsion angle C(3)–C(4)–C(5)–C(6) in the epoxide system of the elephantol derivative is 156° and the corresponding angle in shiromodiol acetate *p*-bromobenzoate is −151°, results which, interestingly, are close to that of 150° for the torsion angle about the distorted C(5)–C(6) ethylenic bond in pregeijerene.

The conjugated exocyclic ethylenic and carbonyl double bonds of the γ-lactone which is fused to the ten-membered ring at C(7) and C(8) depart a little from coplanarity, the C(13)–C(11)–C(12)–O(19) torsion angle being −10°. Other γ-lactones with adjacent exocylic methylene and oxygen functions display a similar feature, *cf.* torsion angles of −9° in bromomexicanin (calculated from the co-ordinates listed in ref. 18) and −10° in vernolepin *p*-bromobenzenesulphonate.[19] Both γ-lactone rings in (1) are distinctly flatter than are γ-lactones fused to six- or seven-membered rings; thus, the sum of the absolute values of the five torsion angles in the C(7), C(8)-lactone is 11° and in the C(2), C(1), C(10)-lactone is 33°, in contrast with, *e.g.*, 86 in bromo-

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gaillardin,[1] 104 in 2-bromo-(—)-β-desmotroposantonin,[20] and 118° in bromogeigerin acetate.[21]

The C–C–R valency angles of the epoxide group (R = substituent carbon atom) have a mean value of 121°, which is somewhat larger than the mean of the O–C–R valency angles, 114°. The difference is apparent in the analogous angles in other epoxides, *e.g.* 119 and 114 in withaferin A acetate *p*-bromobenzoate,[22] 121 and 115 in shiromodiol acetate *p*-bromobenzoate,[12]

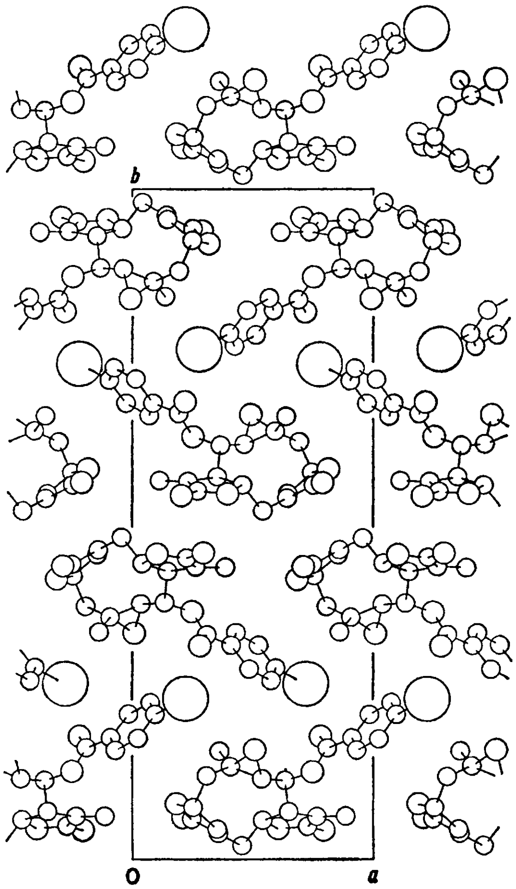

FIGURE 2 The crystal structure viewed in projection along the *c* axis

122 and 114 in 6β-bromo-7β,7*a*β-epoxy-4α,6α-dihydroxy-7α-methoxycarbonyl-3β,4β-dimethyl-3*a*β,7*a*β-octahydrobenzo[*c*]furan-1-one,[23] and 118 and 116° in tetracyanoethylene oxide.[24]

* Final observed and calculated structure factors are listed in Supplementary Publication No. SUP 20408 (33 p., 1 microfiche). For details see Notice to Authors No. 7 in *J. Chem. Soc.* (*A*), 1970, Issue No. 20.

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The packing of the molecules in the crystal is shown in Figure 2. The intermolecular separations (Table 2) are normal.

EXPERIMENTAL

Crystal Data.—$C_{22}H_{19}O_7Br$, $M = 475{\cdot}3$, Orthorhombic, $a = 10{\cdot}64$, $b = 30{\cdot}34$, $c = 6{\cdot}41$ Å, $U = 2069$ Å^3, $Z = 4$, $D_c = 1{\cdot}53$, $F(000) = 968$. Space group $P2_12_12_1$ (D_2^4). Cu-K_α radiation, $\lambda = 1{\cdot}5418$ Å; μ(Cu-K_α) = 33·6 cm^{-1}.

Crystallographic Measurements.—The *X*-ray intensities were estimated visually from multiple-film equi-inclination Weissenberg photographs of the *hk*0—5 layers, taken with Cu-K_α radiation. The films were indexed as prescribed by Bijvoet and Peerdeman.[25] The intensity measurements yielded a total of 1690 independent structure amplitudes.

Structure Analysis.—The atomic co-ordinates and vibration parameters were adjusted by a series of full-matrix least-squares calculations with a modified version of the Gantzel, Sparks, and Trueblood UCLA programme. The weighting scheme adopted was $\sqrt{w} = 1$ for $|F_o| \leqslant 20$, $\sqrt{w} = 20/|F_o|$ for $|F_o| > 20$. Isotropic thermal parameters were employed initially, and three rounds of calculations reduced R to 19·7%. An anisotropic temperature factor was then assigned to the bromine atom but isotropic parameters retained for the other atoms; three rounds of calculations converged at R 12·1%.

At this stage the absolute configuration of the molecule was examined by Bijvoet's method.[4] Values of $\Delta f'$ and $\Delta f''$ for bromine were taken from ref. 26 and two sets of structure factors were calculated with co-ordinates appropriate to the alternative absolute configurations. On examining the various layers of reflections, the differences between the alternative values of R were consistently in the same sense and they indicated that the absolute configuration of elephantol is as shown in (1); the overall value of R for the 1690 observed reflections was 12·0% for the absolute configuration shown in (1) and 12·3% for the mirror image of (1). Hamilton has shown that a relatively small change in R, such as obtained here, provides a reliable demonstration of absolute configuration.[27] The absolute stereochemistry established by these calculations is in accord with biogenetic considerations.

Two additional cycles of least-squares calculations were carried out with allowance for anomalous dispersion, and the refinement was then terminated. The final value of R is 11·9%.*

Most of the extensive calculations were performed on the IBM 7094 computer of the University of Illinois. We thank Professor S. Morris Kupchan for a specimen of elephantol *p*-bromobenzoate, the U.S. National Science Foundation, Eli Lilly and Company, and the Hoffmann–La Roche Foundation for financial support.

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