**844.** *The Crystal Structure of 22,23-Dibromo-12-methyl-18-norergosta-8,11,13-trien-3β-yl Acetate, a Novel Benzenoid Steroid.*

By T. N. Margulis, C. F. Hammer, and Robert Stevenson.

The structure (IV) proposed for a benzenoid product obtained from ergosterol has been confirmed by crystal-structure analysis, using the heavy-atom method and least-squares refinement of the three-dimensional X-ray diffraction data. The unit cell dimensions are $a = 24 \cdot 33$, $b = 5 \cdot 86$, $c = 21 \cdot 25$ Å, $\beta = 106 \cdot 6°$, space group $C2$, $Z = 4$.

THE natural occurrence of benzenoid steroids, such as the œstrogenic hormones, has stimulated interest in the development of selective aromatization procedures, utilising as precursors abundantly available steroids, possessing the customary angular methyl groups; a comprehensive review of available methods has recently appeared.[1] Ergosterol (I) has thus been converted into a benzenoid steroid by a three-step sequence.[2,3] Catalytic hydrogenation of ergosteryl acetate [4] gave 5,6-dihydroergosteryl acetate (II) from which 7,11,22,23-tetrabromoergost-8-en-3β-yl acetate (III) was isolated on treatment with
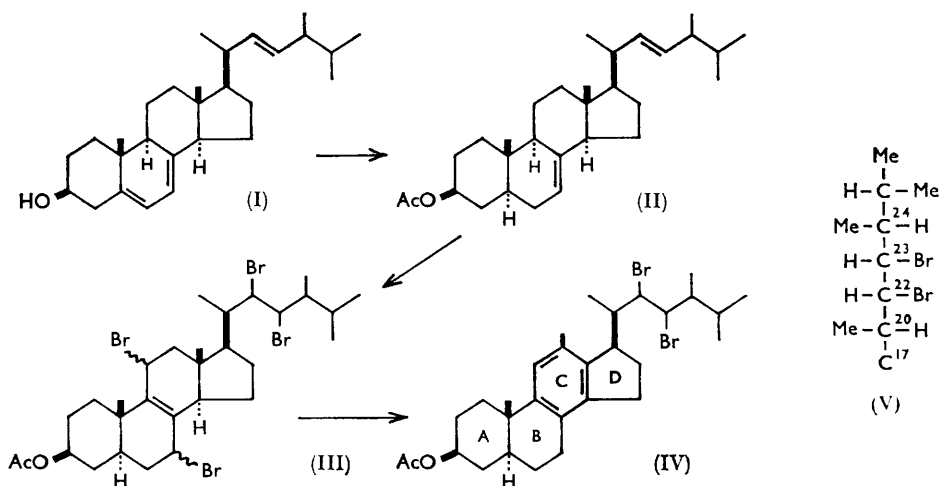
bromine. When a benzene solution of (III) is passed over chromatographic alumina, partial dehydrobromination occurs, and a benzenoid product, $C_{30}H_{44}Br_2O_2$, can be isolated in more than 90% yield; it crystallizes from acetone–methanol as needles (M 596·5), m. p. 136—137·5°, $[\alpha]_D$ —4° (c 1·6 in chloroform). The structure, 22,23-dibromo-12-methyl-18-norergosta-8,11,13-trien-3β-yl acetate (IV) has been proposed for this product,[2,3] a novel feature being the benzenoid system in ring C. A crystal-structure analysis confirms this structure and, in particular, establishes (i) that no ring-D juxtaposition occurred, (ii) that the 17β-configuration of the side-chain was retained during the molecular rearrangement of (III), and (iii) the configurations of the bromine atoms at C-22 and C-23. Little physical or chemical evidence with direct bearing on these three aspects was available.

STRUCTURE DETERMINATION

The cell dimensions of the dibromo-benzenoid acetate were obtained from rotation and Weissenberg photographs, using Cu-K_α radiation ($\lambda = 1 \cdot 5418$ Å). Monoclinic, $a = 24 \cdot 33 \pm$

[1] Shapiro, " Steroid Reactions," ed. Djerassi, Holden-Day, San Francisco, 1963, p. 371.
[2] Hammer, Savage, Thomson, and Stevenson, *Tetrahedron Letters*, 1963, 1261.
[3] Hammer, Savage, Thomson, and Stevenson, *Tetrahedron*, 1964, **20**, 929.
[4] Anderson, Stevenson, and Spring, *J.*, 1952, 2901.

TABLE 1.

Observed and calculated structure factors.

Column 1

h	l	$|F_{obs}|$	A_{calc}	B_{calc}
		k·0		
0	3	145	163	0
0	5	42	-41	0
0	6	26	17	0
0	8	90	-77	0
0	10	111	87	0
0	11	112	109	0
0	12	126	109	0
0	13	54	65	0
0	15	69	-39	0
0	16	36	33	0
0	17	113	-91	0
2	1	117	136	0
2	2	29	34	0
2	3	36	-27	0
2	4	143	-139	0
2	5	147	-151	0
2	6	97	-98	0
2	7	71	-67	0
2	8	77	-60	0
2	11	58	48	0
2	12	116	101	0
2	13	89	91	0
2	14	59	63	0
2	15	50	38	0
2	-2	87	-90	0
2	-3	136	-141	0
2	-4	118	-141	0
2	-5	197	-221	0
2	-6	206	-214	0
2	-7	136	-145	0
2	-8	119	-105	0
2	-9	77	-61	0
2	-15	84	-72	0
2	-16	80	-70	0
2	-17	91	-90	0
4	0	226	-257	0
4	1	81	90	0
4	2	48	65	0
4	3	111	109	0
4	4	118	40	0
4	5	71	-73	0
4	6	31	-25	0
4	7	175	-172	0
4	8	102	-103	0
4	9	88	-74	0
4	10	79	-62	0
4	11	61	-55	0
4	12	45	-54	0
4	-2	100	-87	0
4	-3	111	-103	0
4	-4	60	-63	0
4	-6	61	51	0
4	-7	71	61	0
4	-8	144	123	0
4	-9	174	169	0
4	-10	177	178	0
4	-11	94	86	0
4	-12	93	83	0
4	-13	53	46	0
6	1	203	212	0
6	2	104	108	0
6	3	161	165	0
6	4	172	206	0
6	5	69	80	0
6	6	54	54	0
6	7	97	80	0
6	13	71	67	0
6	14	64	60	0
6	15	53	47	0
6	-1	120	-115	0
6	-3	35	-43	0
6	-4	63	-74	0
6	-5	33	32	0
6	-6	49	37	0
6	-8	62	65	0
6	-9	97	97	0
6	-13	115	-103	0
6	-14	129	-122	0
6	-16	61	-41	0
8	0	88	-76	0
8	1	131	-120	0
8	2	77	-74	0
8	5	36	22	0
8	6	87	-86	0
8	8	67	-71	0
8	9	94	-83	0
8	10	81	-80	0
8	11	69	-72	0
8	-1	125	-121	0
8	-2	238	-237	0
8	-4	164	-174	0
8	-5	69	-58	0
8	-6	44	33	0
8	-7	51	66	0
8	-12	81	-77	0
8	-13	70	-69	0
8	-14	56	-62	0
10	2	87	84	0
10	3	85	79	0
10	4	102	98	0
10	5	98	116	0
10	6	111	112	0
10	-4	153	146	0
10	-5	108	104	0
10	-6	124	124	0
10	-7	175	170	0
10	-8	142	136	0
10	-9	101	103	0
10	-10	49	38	0

Column 2

h	l	$|F_{obs}|$	A_{calc}	B_{calc}
12	0	123	-129	0
12	1	103	-112	0
12	5	44	45	0
12	6	72	62	0
12	7	58	53	0
12	8	49	59	0
12	-1	144	-143	0
12	-2	45	-41	0
12	-3	64	-71	0
12	-4	79	66	0
12	-5	72	-64	0
12	-8	63	-56	0
12	-9	71	-80	0
12	-10	120	-115	0
12	-11	108	-107	0
12	-12	104	-97	0
12	-13	82	-68	0
14	0	82	-82	0
14	1	100	-101	0
14	2	94	-108	0
14	3	72	-67	0
14	5	48	-21	0
14	-1	66	-75	0
14	-3	80	77	0
14	-5	80	90	0
14	-6	72	72	0
14	-14	50	49	0
14	-15	63	51	0
14	-16	65	76	0
14	-17	76	78	0
14	-18	86	71	0
14	-19	76	47	0
16	0	81	89	0
16	-1	90	114	0
16	-2	56	74	0
16	-3	104	104	0
16	-4	64	65	0
16	-5	72	72	0
16	-6	46	45	0
18	2	90	-110	0
18	4	65	-70	0
18	-5	49	-36	0
18	-6	60	-42	0
18	-7	70	-75	0
18	-8	79	-90	0
18	-9	72	-76	0
18	-10	63	-64	0
		k·l		
1	0	93	30	76
1	1	238	-99	189
1	2	110	-28	-103
1	3	79	61	-49
1	4	133	124	1
1	5	189	149	-45
1	6	221	196	28
1	7	178	159	-32
1	8	172	134	-3
1	9	160	129	-51
1	10	45	42	-23
1	-1	104	-98	-25
1	-3	65	18	60
1	-4	31	20	-23
1	-5	35	73	-3
1	-6	102	72	64
1	-7	35	44	0
1	-8	46	-47	2
1	-9	101	-84	-10
1	-10	125	-111	15
1	-12	87	-80	20
1	-13	65	-52	7
1	-15	59	-48	14
3	0	257	-249	9
3	1	188	-183	-17
3	2	234	-213	28
3	3	297	-272	61
3	4	182	-161	46
3	5	53	-52	4
3	6	36	9	30
3	8	66	46	27
3	9	55	-26	50
3	10	59	-57	19
3	12	38	-60	-2
3	13	69	-77	7
3	14	94	-63	25
3	-1	233	-2	-202
3	-2	134	-90	102
3	-3	23	-44	8
3	-4	138	112	-50
3	-5	112	66	27
3	-6	55	-39	17
3	-7	60	-48	27
3	-8	80	-79	12
3	-9	249	-197	0
3	-10	106	-68	52
3	-11	57	-54	-9
3	-14	55	49	-16
3	-15	41	60	-19
3	-16	42	53	-11
3	-17	62	79	-30
5	0	67	-4	-70
5	1	92	31	-83
5	3	32	-27	20
5	6	63	45	-45
5	7	128	118	-45
5	8	120	105	-62
5	9	83	79	3
5	10	36	36	7
5	-1	121	111	-42

Column 3

h	l	$|F_{obs}|$	A_{calc}	B_{calc}
5	-2	195	131	-114
5	-3	247	252	-20
5	-4	267	263	-12
5	-5	244	229	-27
5	-6	114	79	-61
5	-7	44	39	-40
5	-8	61	22	-60
5	-9	79	0	50
5	-15	57	82	16
5	-16	117	63	26
7	0	57	-47	10
7	1	54	-25	47
7	2	69	-76	8
7	3	95	-93	-15
7	4	108	-95	13
7	5	41	-34	-18
7	6	44	-43	-17
7	7	46	49	-4
7	8	49	40	-4
7	9	75	66	-25
7	10	66	69	-25
7	11	40	39	-4
7	-1	79	5	82
7	-2	68	15	64
7	-4	64	-41	45
7	-5	85	-71	15
7	-6	116	-108	3
7	-7	135	-140	15
7	-8	121	-128	10
7	-9	67	-64	27
7	-10	123	-104	-26
7	-11	58	-44	25
7	-12	55	-32	18
9	0	74	64	38
9	1	76	12	57
9	3	67	-53	-31
9	4	125	-131	4
9	5	106	-111	23
9	6	68	-81	13
9	7	51	-63	-12
9	-1	90	80	47
9	-2	134	116	68
9	-3	106	95	-44
9	-10	66	65	-12
9	-11	70	71	-29
9	-12	82	81	-5
9	-13	124	119	-16
9	-14	89	82	3
9	-15	41	39	-3
11	0	100	106	-14
11	1	86	68	-31
11	2	72	82	7
11	3	58	58	6
11	4	49	37	-38
11	-1	125	131	-23
11	-2	136	128	-73
11	-3	42	6	59
11	-4	52	43	-33
11	-5	68	-65	-10
11	-6	44	-60	-23
11	-13	56	31	19
13	5	56	-62	-8
13	6	57	-68	4
13	7	73	-79	0
13	8	75	-68	10
13	-2	92	-91	-16
13	-3	109	-115	33
13	-4	116	-123	25
13	-5	126	-136	-17
13	-6	103	-93	33
13	-7	85	-98	18
15	0	66	64	-12
15	1	67	81	-14
15	2	80	103	-24
15	3	53	23	14
15	-7	53	54	-17
15	-8	77	89	-3
15	-9	68	90	5
15	-10	89	99	-5
15	-11	71	71	-9
15	-12	59	72	-20
		k·2		
0	0	202	165	-70
0	1	169	164	-28
0	2	139	145	-57
0	3	63	65	-22
0	4	52	24	-40
0	5	41	-25	-38
0	6	37	13	13
0	8	74	-32	61
0	9	93	-74	-54
0	10	89	78	7
0	11	87	92	-23
0	12	82	71	-2
0	13	43	42	-7
2	1	45	21	45
2	2	22	4	26
2	3	36	-5	29
2	4	75	-61	37
2	5	101	-97	57
2	6	45	-36	10
2	7	69	-65	22
2	11	57	55	7
2	12	74	62	-31
2	13	77	52	-28
2	14	57	55	13
2	-1	27	-10	34
2	-2	101	-49	87
2	-3	181	-173	-43

Column 4

h	l	$|F_{obs}|$	A_{calc}	B_{calc}
2	-4	84	-84	-9
2	-5	145	-128	-84
2	-6	176	-188	36
2	-7	142	-151	-13
2	-8	61	-57	49
2	-9	52	-37	3
4	0	108	85	-33
4	1	84	63	3
4	2	124	93	13
4	3	60	46	19
4	5	29	-8	10
4	6	69	-50	18
4	7	91	-92	22
4	8	87	-92	-28
4	9	114	-99	46
4	10	98	-91	-7
4	11	52	-50	14
4	-1	53	60	-30
4	-2	79	-74	-9
4	-3	78	-12	-91
4	-4	75	-47	56
4	-5	34	-40	-27
4	-6	73	11	-70
4	-7	81	88	-23
4	-8	140	108	-85
4	-9	66	67	-14
4	-10	87	99	-23
4	-11	46	64	-16
4	-12	69	54	-35
4	-13	51	43	-6
6	0	68	29	-41
6	1	116	122	-4
6	2	156	142	0
6	3	137	132	-34
6	4	105	101	-30
6	5	97	107	-23
6	-1	48	8	-30
6	-2	123	-90	-76
6	-3	30	-34	12
6	-4	92	-92	-10
6	-5	38	-40	-24
6	-6	72	62	-10
6	-7	71	62	9
6	-9	83	75	32
8	0	132	-126	45
8	1	124	-86	78
8	2	85	-48	73
8	-1	196	-204	49
8	-2	154	-146	57
8	-3	129	-113	58
8	-4	65	-57	18
8	-5	60	-54	29
8	-6	44	-11	-19
8	-8	41	43	38
8	-9	50	51	14
10	0	33	2	-37
10	1	59	-1	-61
10	2	82	84	-19
10	4	93	93	-7
10	5	93	80	-27
10	6	71	71	-17
10	7	60	54	0
10	-1	52	-45	25
10	-2	56	36	9
10	-4	46	58	-26
10	-5	105	96	-24
10	-6	113	106	-23
10	-7	96	106	-33
10	-8	73	78	-23
10	-9	59	58	-40
12	0	53	62	-2
12	1	66	-59	-34
12	2	62	-35	-21
12	-1	38	-38	2
12	-9	57	-56	1
12	-10	72	-92	22
12	-11	96	-109	-11
12	-12	76	-93	27
14	0	59	-59	-7
14	1	73	-68	25
14	2	53	-53	10
14	3	50	-77	-4
14	-1	41	-15	-19
		k·3		
1	1	62	-55	-14
1	2	34	-19	-27
1	3	39	7	-49
1	4	58	53	-32
1	5	84	84	-32
1	6	70	75	13
1	7	103	100	-70
1	8	58	55	-4
1	9	52	21	-46
1	10	52	45	16
1	-1	44	-46	-12
1	-2	17	-15	-12
1	-3	34	29	14
1	-4	63	71	-5
1	-5	36	26	21
1	-6	56	33	45
1	-7	54	-1	-57
1	-8	40	-3	22
1	-9	53	-18	6
1	-10	70	-46	55
1	-11	71	-56	5
1	-12	60	-46	27
1	-13	54	-45	-2
3	0	94	-89	40
3	1	100	-105	40

Column 5

h	l	$|F_{obs}|$	A_{calc}	B_{calc}
3	2	97	-126	38
3	3	91	-88	35
3	4	75	-76	31
3	5	55	-23	67
3	6	42	17	42
3	7	72	34	95
3	10	45	-40	-25
3	11	76	-61	24
3	12	54	-40	35
3	13	51	-38	4
3	-1	56	-60	23
3	-2	21	-23	13
3	-3	21	8	9
3	-4	77	41	65
3	-6	61	45	-28
3	-7	37	0	32
3	-8	46	-38	-11
3	-9	54	-36	10
3	-10	66	-55	-17
3	-11	44	-20	15
5	1	32	25	-31
5	3	60	-30	-3
5	4	54	32	-42
5	6	61	48	-34
5	7	69	59	-22
5	8	72	66	-39
5	9	56	51	-21
5	10	48	31	-38
5	-1	91	76	-52
5	-2	99	99	-60
5	-3	121	120	-56
5	-4	87	92	-38
5	-5	112	89	-92
5	-6	84	81	-25
5	-8	47	-14	-55
5	-9	34	0	-21
5	-10	46	-22	-29
5	-13	58	31	12
5	-14	55	44	1
7	0	41	-4	39
7	1	44	-44	9
7	2	57	-39	28
7	3	60	-46	40
7	4	74	-64	-19
7	5	58	-35	-24
7	6	52	-28	-23
7	7	44	0	-29
7	8	57	51	-28
7	9	53	49	0
7	10	50	46	4
7	11	51	61	-11
7	-1	31	27	25
7	-2	34	31	14
7	-3	57	23	54
7	-4	43	-40	6
7	-5	56	-14	68
7	-6	94	-85	39
7	-7	108	-93	25
7	-8	86	-70	37
7	-9	118	-103	51
7	-10	87	-75	41
7	-11	62	-30	41
7	-12	47	-17	32
9	0	63	56	0
9	1	42	12	14
9	2	46	-40	6
9	3	54	-53	27
9	4	67	-57	29
9	5	70	-86	11
9	6	66	-72	19
9	-1	48	36	22
9	-2	46	36	-2
9	-4	35	26	-5
9	-6	56	-52	-23
9	-7	60	-49	-30
9	-8	39	-38	-32
9	-10	42	36	-4
9	-11	84	66	-14
9	-12	73	61	-31
9	-13	73	61	-17
9	-14	61	39	-35
9	-15	57	46	-17
11	0	73	66	-26
11	1	71	67	-22
11	2	58	46	-34
11	-1	67	56	-25
11	-2	71	74	1
11	-3	41	35	8
11	-4	41	12	-11
11	-5	66	-34	-30
11	-6	41	-22	-26
11	-7	41	-22	-24
13	-1	43	13	20
13	-2	45	-23	44
13	-3	68	-72	28
13	-4	66	-64	17
13	-5	72	-74	21
13	-6	58	-36	36
13	-7	55	-12	39
13	-8	50	-20	-33
15	0	50	38	-19
15	-8	49	17	
15	-9	60	56	-14
15	-10	69	42	-38
		k·4		
0	0	89	64	-46
0	1	76	74	-27
8	0	70	-52	40

0·05, $b = 5·86 \pm 0·02$, $c = 21·25 \pm 0·04$ Å, $\beta = 106·6° \pm 0·5°$, $Z = 4$, $D_c = 1·36$. Systematic absences of reflexions on the Weissenberg photographs indicate $C2$ or Cm as the probable space group; $C2$ was chosen since the substance is optically active, and this choice is confirmed by the successful structure determination.

Three-dimensional equi-inclination Weissenberg data were collected using three different single crystals; one for layers $h0l$—$h2l$, another for layer $h3l$, and a third for layers $hk0$—$hk1$. The multiple-film technique was used throughout. The relative intensities of 544 independent reflexions were measured by visual comparison with a calibrated film strip. The intensities were converted into structure factors, and placed on the same relative scale by comparing reflexions occurring on more than one film. No absorption corrections were made.

Since the space group is polar along [010], one bromine atom was placed arbitrarily at $y = 1·0$. The x- and z-co-ordinates of the two bromine atoms were obtained from the (010) projection of the Patterson function. The y-co-ordinate of the second bromine atom was determined by estimation of the bromine–bromine interatomic distance. Structure factors calculated on the basis of these two atoms gave a value for the unreliability index, $R = \Sigma|(|F_0| - |F_c|)|/\Sigma|F_0|$, of 0·29 for the observed reflexions. A three-dimensional, bromine-phased, electron-density map revealed more then half of the light atoms. Repeated structure-factor and electron-density calculations gave chemically reasonable trial positions for all atoms.

The trial structure was refined by 22 cycles of full-matrix least-squares calculations,[*] using the 544 observed reflexions, to a value of $R = 0·11$. In the last few cycles the Hughes [5] weighting scheme was used, and isotropic temperature factors were allowed to vary for each atom. Hydrogen atoms were not included in the calculations. Atomic scattering factors for neutral atoms were those of the International Tables.[6] An electron-density map with phases calculated from the twentieth least-squares cycle showed strong ripples in the region of the bromine atoms owing to series termination errors, but revealed all atoms clearly. A difference map calculated at this point showed no abnormal features. Structure factors are listed in Table 1.

RESULTS

The atomic co-ordinates from the final least-squares cycle are listed in Table 2. The estimated standard deviations of the interatomic distances between light atoms are

TABLE 2.

Atomic co-ordinates.[*]

	x	y	z		x	y	z		x	y	z
Br(1)	0·4560	1·000	0·0853	C(11)	0·423	0·68	0·369	C(22)	0·389	0·79	0·076
Br(2)	0·3088	0·463	0·0161	C(12)	0·435	0·78	0·312	C(23)	0·385	0·62	0·022
C(1)	0·417	0·55	0·497	C(13)	0·385	0·81	0·255	C(24)	0·373	0·75	0·956
C(2)	0·415	0·40	0·557	C(14)	0·335	0·72	0·266	C(25)	0·378	0·55	0·902
C(3)	0·354	0·39	0·561	C(15)	0·287	0·82	0·200	C(26)	0·430	0·40	0·929
C(4)	0·319	0·24	0·497	C(16)	0·312	0·98	0·173	C(27)	0·373	0·70	0·833
C(5)	0·315	0·41	0·439	C(17)	0·379	0·90	0·187	C(28)	0·327	0·92	0·933
C(6)	0·276	0·36	0·367	C(18)	0·491	0·90	0·313	C(29)	0·368	0·34	0·678
C(7)	0·272	0·55	0·312	C(19)	0·400	0·18	0·429	C(30)	0·381	0·11	0·730
C(8)	0·331	0·61	0·320	C(20)	0·389	0·72	0·144	O(1)	0·357	0·22	0·613
C(9)	0·376	0·56	0·376	C(21)	0·442	0·57	0·172	O(2)	0·389	0·50	0·692
C(10)	0·379	0·43	0·436								

* Origin as in " International Tables for X-Ray Crystallography," Kynoch Press, Birmingham, vol. I, 1952.

about 0·1 Å, implying that the limit of error for a bond length is about 0·2 Å, obviating the listing of detailed bond lengths. The carbon–bromine bond lengths are 2·02 and 2·04 Å ($\sigma = 0·07$ Å). The carbon–carbon single bond lengths are between 1·36 and 1·69 Å

* Least-squares calculations were carried out using the computer programme of Gantzel, Sparks. and Trueblood, of the University of California, Los Angeles.

[5] Hughes, *J. Amer. Chem. Soc.*, 1941, **63**, 1737.

[6] " International Tables for X-Ray Crystallography," Kynoch Press, Birmingham, Vol. III, 1962.

Fig. 1. The crystal structure projected down the *b*-axis. One unit cell is shown.
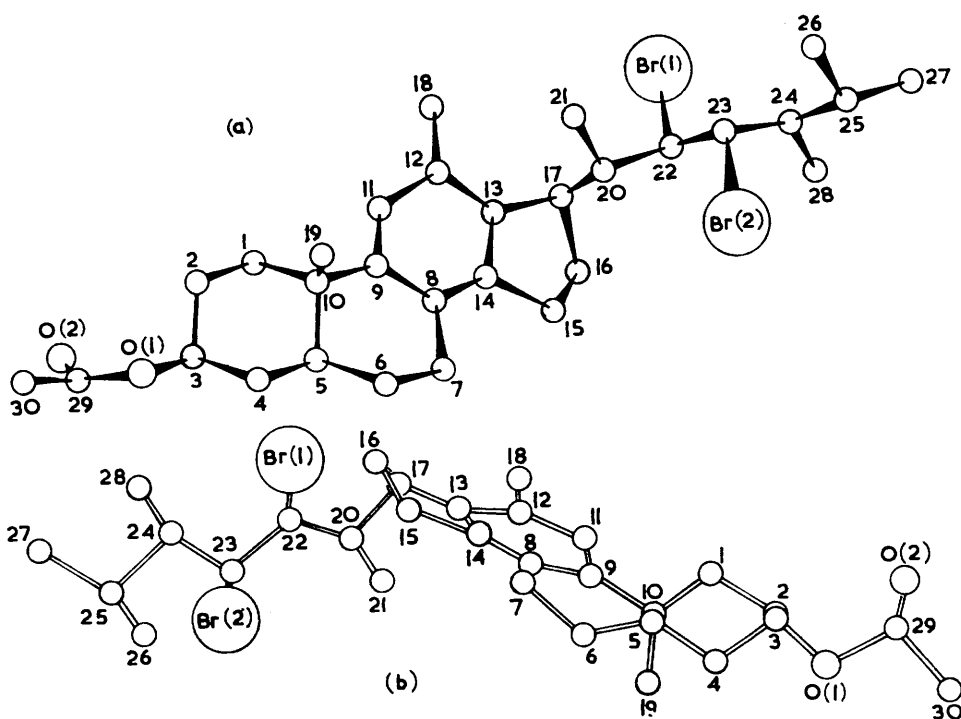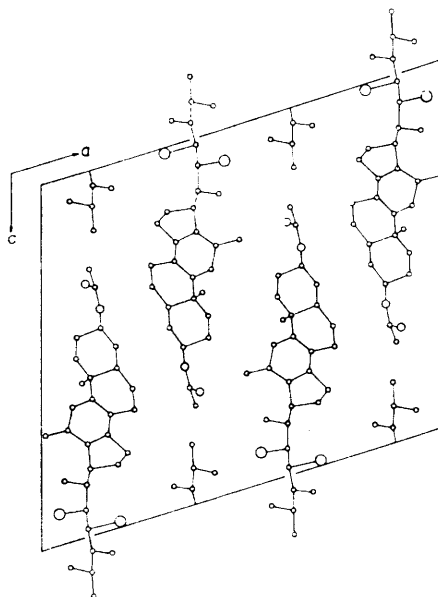

Fig. 2. (a) One molecule in conventional steroid arrangement with correct absolute configuration. (b) One molecule projected down the *a*-axis.

Atoms not marked with an element symbol are carbon.

and average 1·55 Å. The bonds in the benzenoid ring range from 1·35 to 1·48 Å and average 1·41 Å. There are no intermolecular contacts less than 3·3 Å. The isotropic temperature factors are in the range 0—14 Å² with an average value of 4 Å². Since the standard deviations of the temperature factors exceed 2 Å², these parameters have little physical significance.

The crystal structure of the benzenoid product is shown, projected down the *b*-axis, in Fig. 1. Fig. 2 (a), derived by projecting one molecule along the *b*-axis in the direction opposite to that in Fig. 1, and by reflecting in (010), shows the molecule in the conventional steroid arrangement with correct absolute configuration, and fully confirms the structure (IV). The extent of molecular rearrangement from (III) to (IV) is clearly limited to migration of the 18-methyl group to position 12, and the 17β-configuration of the side-chain has been maintained. The chair conformation of ring A, indicated from nuclear magnetic resonance data,[3] is clearly shown [Fig. 2 (b)] in the *a*-axis projection of the molecule, as are the half-chair conformation of ring B and the planar ring C. The side-chain stereochemistry is of interest, being essentially planar, and with the bromine and methyl chain branches adopting completely staggered conformations. When the side-chain is arranged in a Fischer projection (V), both bromine atoms can be assigned α-configurations on the nomenclature convention proposed by Plattner and Fieser.[7]

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[7] Discussed in Fieser and Fieser, " Steroids," Reinhold, New York, 1959, pp. 336—340.