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The Crystal and Molecular Structure of a Derivative of the Triterpene Spergulagenin A
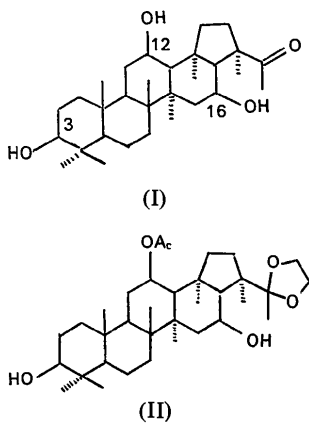
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12-*O*-Acetylspergulagenin A ethylene ketal, $C_{34}H_{56}O_6$, m.p. 265°C, orthorhombic, $P2_12_12_1$, $Z=4$, $a=9\cdot903$ (1), $b=15\cdot127$ (1), $c=21\cdot184$ (1) Å, $M=560\cdot8$, $D_m=1\cdot16$ (1) g cm^{-3}, $D_x=1\cdot174$ g cm^{-3}, 23°C, $\mu=6\cdot3$ cm^{-1}. Intensity data were collected with an automatic X-ray diffractometer. The structure was solved by direct methods including calculation of structure invariants and refined by least-squares methods to a final conventional R of 0·037. Spergulagenin A possesses a new migrated hopane skeleton with a methyl ketone moiety in the E ring as a side chain.

Introduction

Spergulagenin A (I), $C_{30}H_{50}O_4$, is a new triterpene which was isolated as one of the root sapogenols from *Mollugo spergula L*. Chemical and spectroscopic studies suggested that (I) had a migrated hopane or a lupane skeleton. In order to determine the chemical structure, an X-ray analysis of 12-*O*-acetylspergulagenin ethylene ketal (II) was undertaken. A preliminary report of this work has already been published (Kitagawa, Suzuki, Yosioka, Akiyama & Silverton, 1974).

(I)

(II)

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Experimental

Crystals were obtained by the conversion of spergulagenin A (I) to an ethylene ketal followed by partial acetylation. The product (II) was separated by chromatography and crystallized from ethanol as colorless prisms. Crystals used were ground to spheres (No. 1; $r=0\cdot2$ mm, No. 2; $r=0\cdot3$ mm). Cell dimensions were obtained by least-squares refinement using 15 Bragg angles measured at $\pm\theta$. (Cu $K\alpha$ X-radiation $\lambda=1\cdot5418$ Å) 3505 independent data (304 unobserved: 3σ) were measured (maximum $\sin\theta/\lambda$: 0·617 Å^{-1}) on an Enraf–Nonius CAD-4 diffractometer using techniques described by Silverton, Milne, Eaton, Nyi & Temme (1974). Three standard reflections, measured at intervals of every 45 reflections, showed some irradiation damage to be taking place and, after the intensities of the standards had dropped by 4%, the data crystal was replaced. The second crystal, used for about one third of the data, showed a drop of 2% in the intensities of the standards. The first data set was divided into two nearly equal parts and three scale factors, initially evaluated from the standards, were used as parameters in the refinement but final relative refined scale factors did not differ significantly from their original values. Lorentz and polarization corrections were applied but no corrections for absorption were made (no significant intensity changes were observed in azimuthal scans of several reflections.) The distribution of E values

Table 1. *Atomic parameters for the heavier atoms* ($\times 10^4$)

The temperature factor used had the form exp $[-2\pi^2(\sum_i\sum_j U_{ij}a_i^* a_j^* h_i h_j)]$.

|	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	2395 (2)	4976 (2)	3284 (1)	375 (8)	433 (11)	317 (10)	54 (8)	−42 (8)	−113 (9)
C(2)	1245 (2)	5398 (2)	2909 (1)	416 (9)	600 (14)	347 (11)	86 (10)	−105 (9)	−171 (10)
C(3)	105 (2)	5696 (2)	3339 (1)	342 (9)	522 (13)	431 (11)	64 (9)	−94 (9)	−126 (10)
C(4)	564 (2)	6360 (1)	3849 (1)	335 (8)	396 (11)	330 (10)	48 (8)	−27 (8)	−45 (9)
C(5)	1801 (2)	5935 (1)	4201 (1)	299 (8)	335 (10)	288 (9)	25 (7)	1 (7)	−54 (8)
C(6)	2315 (2)	6487 (1)	4758 (1)	345 (8)	378 (10)	314 (10)	71 (8)	−23 (8)	−87 (9)
C(7)	3203 (2)	5926 (1)	5189 (1)	331 (8)	383 (10)	275 (9)	61 (8)	12 (7)	−57 (9)
C(8)	4426 (2)	5506 (1)	4849 (1)	271 (7)	315 (9)	262 (9)	0 (7)	12 (7)	−31 (8)
C(9)	3962 (2)	5063 (1)	4221 (1)	274 (7)	324 (9)	283 (9)	8 (7)	−2 (6)	−49 (8)
C(10)	3001 (2)	5611 (1)	3780 (1)	294 (7)	376 (10)	262 (9)	3 (7)	−5 (7)	−43 (8)
C(11)	5190 (2)	4674 (1)	3872 (1)	357 (8)	468 (12)	269 (9)	73 (8)	3 (7)	−84 (9)
C(12)	6066 (2)	4063 (1)	4275 (1)	276 (7)	333 (10)	330 (9)	1 (7)	32 (7)	−71 (8)
C(13)	6418 (2)	4441 (1)	4926 (1)	259 (7)	299 (9)	284 (9)	9 (7)	16 (7)	−34 (8)
C(14)	5087 (2)	4744 (1)	5369 (1)	261 (7)	309 (9)	277 (9)	−8 (7)	27 (7)	−10 (8)
C(15)	5404 (2)	5098 (1)	5940 (1)	310 (8)	418 (11)	254 (9)	57 (8)	23 (7)	−31 (8)
C(16)	6379 (2)	4542 (1)	6334 (1)	338 (8)	390 (10)	255 (9)	44 (8)	49 (7)	10 (8)
C(17)	7664 (2)	4425 (1)	5948 (1)	296 (7)	336 (9)	275 (9)	41 (7)	12 (7)	5 (8)
C(18)	7379 (2)	3872 (1)	5339 (1)	315 (8)	321 (10)	319 (9)	43 (7)	7 (7)	−30 (8)
C(19)	8838 (2)	3794 (1)	5086 (1)	335 (8)	424 (11)	342 (10)	99 (8)	8 (7)	−63 (9)
C(20)	9678 (2)	3583 (2)	5671 (1)	382 (9)	515 (13)	393 (11)	144 (9)	−27 (8)	−71 (10)
C(21)	8997 (2)	4059 (1)	6246 (1)	346 (8)	402 (11)	313 (10)	96 (8)	0 (7)	28 (9)
C(22)	9927 (2)	4818 (2)	6466 (1)	358 (8)	510 (12)	261 (9)	46 (9)	18 (7)	20 (9)
C(23)	9381 (2)	6453 (2)	4320 (1)	345 (9)	574 (14)	451 (12)	89 (9)	11 (9)	−68 (11)
C(24)	841 (2)	7277 (2)	3567 (1)	554 (12)	438 (12)	461 (12)	93 (10)	−57 (10)	19 (11)
C(25)	3758 (2)	6364 (1)	3440 (1)	415 (9)	446 (11)	330 (10)	−11 (9)	11 (8)	33 (9)
C(26)	5452 (2)	6262 (1)	4732 (1)	345 (8)	337 (10)	357 (10)	−47 (7)	−30 (8)	−16 (9)
C(27)	4084 (2)	3968 (1)	5359 (1)	328 (8)	366 (11)	424 (11)	−27 (8)	38 (8)	35 (9)
C(28)	6864 (2)	2925 (1)	5459 (1)	498 (10)	311 (11)	537 (13)	23 (9)	−30 (10)	11 (10)
C(29)	8752 (2)	3422 (2)	6797 (1)	496 (11)	522 (13)	441 (12)	127 (11)	20 (10)	140 (11)
C(30)	1292 (2)	4510 (2)	6717 (1)	392 (10)	749 (17)	412 (12)	78 (11)	−87 (9)	−37 (12)
C(31)	34 (4)	6294 (2)	6191 (1)	1400 (30)	497 (16)	616 (17)	−125 (20)	287 (20)	−37 (14)
C(32)	9643 (3)	6229 (2)	6866 (1)	863 (18)	524 (16)	636 (17)	−77 (14)	163 (15)	−121 (14)
C(33)	7428 (2)	3321 (2)	3501 (1)	501 (11)	403 (12)	414 (11)	−15 (10)	74 (10)	−136 (10)
C(34)	8818 (3)	3286 (2)	3207 (1)	543 (12)	658 (16)	552 (15)	59 (12)	173 (12)	−187 (13)
O(3)	9043 (2)	6093 (1)	2981 (1)	509 (8)	893 (14)	580 (10)	275 (9)	−259 (8)	−274 (10)
O(12)	7350 (1)	3951 (1)	3935 (1)	298 (6)	408 (8)	354 (7)	14 (6)	41 (5)	−113 (7)
O(16)	6576 (1)	5000 (1)	6924 (1)	372 (6)	640 (10)	227 (6)	95 (7)	21 (5)	−22 (7)
O(31)	140 (1)	5427 (1)	5956 (1)	430 (7)	508 (9)	315 (7)	−23 (7)	39 (6)	28 (7)
O(32)	9255 (1)	5326 (1)	6941 (1)	466 (7)	506 (9)	341 (8)	−15 (7)	73 (6)	−61 (7)
O(33)	6502 (2)	2860 (2)	3346 (1)	837 (13)	879 (15)	950 (16)	−402 (13)	387 (13)	−570 (14)
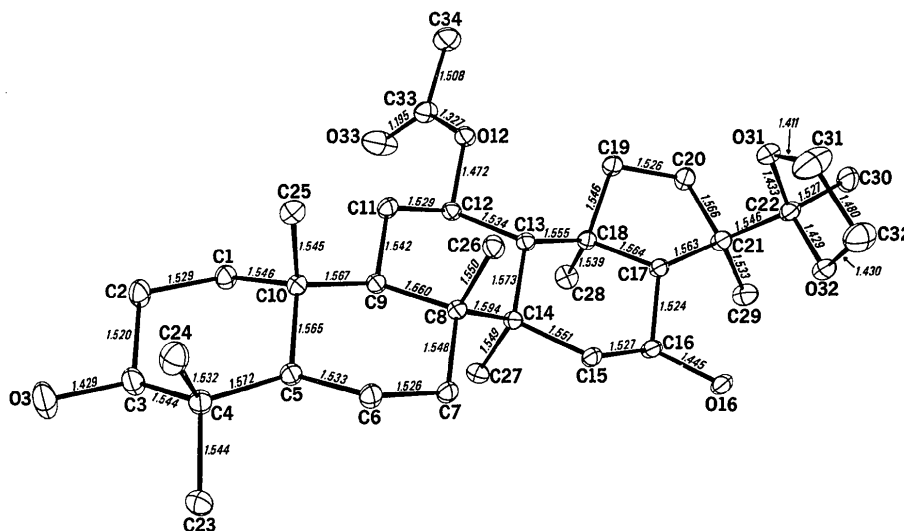
Fig. 1. *ORTEP* (Johnson, 1965) drawing of spergulagenin A ketal in its crystal orientation. 50% probability ellipsoids are shown.

[evaluated using the X-RAY 72 system of Stewart, Kruger, Ammon, Dickinson & Hall (1972) which was used for all calculations unless otherwise stated] is in good agreement with that for an acentric crystal.

The structure was solved via MDKS calculation of structure invariants (Hauptman, 1972). Approximately 2000 two- and three-dimensional triplet structure invariants were evaluated by the MDKS formula using the APHASE segment of the X-RAY 72 system. After some unsuccessful attempts to use the tangent formula starting with restricted phases determined via APHASE, 64 three-dimensional phases in addition to 48 two-dimensional phases were determined and tangent formula expansion and refinement were then carried out using a local program (Silverton & Lloyd, 1975) to give 187 additional phases. The E map of the solution with the highest figure of merit showed the triterpenoid skeleton, although not the side chains. The rest of the molecule was found routinely by a series of least-squares refinements and difference maps. All hydrogen atoms were eventually located. With anisotropic thermal parameters for the carbon and oxygen atoms and isotropic thermal parameters for the hydrogen atoms, the structure was refined by full-matrix least-squares methods, partitioned because of the number of parameters, to convergence at a conventional R value (observed reflections only) of 0·037. The final weighted R value was 0·055 and the function minimized was $\sum w[|F_o| - |F_c|]^2$ with w as in Peterson & Levy (1957). The scattering factors for C(valence) and O used in the refinement were taken from International Tables for X-ray Crystallography (1962). The scattering factor curve calculated by Stewart, Davidson & Simpson (1965) was used for the hydrogen atoms. The final positional coordinates and thermal parameters and their standard deviations are listed in Tables 1 and 2.*

Discussion

The present X-ray analysis establishes the structure of spergulagenin A as in (I) in accordance with the results of the chemical and spectroscopic investigation.

Table 2. *Atomic parameters for hydrogen atoms* ($\times 10^3$)

|	x	y	z	U		x	y	z	U
1A	208 (3)	444 (2)	351 (1)	70 (7)	1E	312 (3)	476 (2)	297 (1)	66 (7)
2A	159 (2)	597 (2)	262 (1)	59 (6)	2E	92 (3)	495 (2)	262 (1)	74 (8)
3A	977 (2)	512 (2)	359 (1)	67 (7)	5A	140 (2)	535 (1)	439 (1)	50 (6)
6A	283 (2)	707 (1)	460 (1)	43 (5)	6E	151 (2)	675 (2)	499 (1)	62 (7)
7A	267 (2)	548 (1)	539 (1)	45 (5)	7E	356 (2)	629 (2)	556 (1)	54 (6)
9A	338 (2)	457 (1)	432 (1)	42 (5)	11A	576 (2)	518 (2)	370 (1)	61 (7)
11E	489 (2)	435 (2)	351 (1)	54 (6)	12A	564 (2)	350 (1)	431 (1)	43 (5)
13A	690 (2)	498 (1)	485 (1)	38 (5)	15A	586 (2)	572 (2)	596 (1)	64 (7)
15E	459 (2)	509 (1)	618 (1)	41 (5)	16A	600 (3)	393 (2)	643 (1)	63 (7)
17A	789 (2)	501 (1)	579 (1)	36 (5)	19A	918 (2)	436 (1)	489 (1)	54 (6)
19E	891 (2)	338 (2)	477 (1)	71 (7)	20A	977 (2)	292 (2)	575 (1)	75 (7)
20E	66 (3)	375 (2)	562 (1)	75 (8)	23A	930 (3)	594 (2)	457 (1)	79 (8)
23B	858 (3)	657 (2)	409 (1)	71 (7)	23C	954 (3)	690 (2)	463 (1)	80 (8)
24A	6 (3)	760 (2)	346 (1)	93 (9)	24B	128 (3)	767 (2)	389 (1)	83 (8)
24C	144 (3)	734 (2)	320 (1)	91 (9)	25A	461 (3)	615 (2)	329 (1)	87 (9)
25B	321 (3)	658 (2)	308 (1)	68 (7)	25C	383 (3)	686 (2)	369 (1)	67 (7)
26A	610 (3)	616 (2)	439 (1)	66 (7)	26B	601 (3)	641 (2)	505 (1)	84 (8)
26C	494 (3)	683 (2)	461 (1)	80 (8)	27A	407 (3)	353 (2)	509 (1)	95 (9)
27B	424 (3)	364 (2)	574 (1)	66 (7)	27C	314 (3)	415 (2)	537 (1)	73 (8)
28A	677 (3)	263 (2)	500 (1)	104 (10)	28B	748 (3)	258 (2)	564 (1)	79 (8)
28C	603 (3)	292 (2)	570 (1)	85 (9)	29A	803 (3)	303 (2)	670 (1)	87 (9)
29B	960 (3)	316 (2)	691 (1)	85 (9)	29C	847 (3)	369 (2)	716 (1)	83 (8)
30A	181 (3)	414 (2)	641 (1)	94 (9)	30B	179 (3)	509 (2)	682 (1)	88 (9)
30C	108 (3)	417 (2)	712 (1)	89 (9)	31A	66 (4)	663 (3)	609 (2)	114 (13)
31B	909 (5)	668 (3)	596 (2)	181 (19)	32A	891 (4)	661 (2)	698 (2)	112 (12)
32B	38 (5)	655 (4)	718 (2)	202 (20)	34A	899 (4)	269 (3)	302 (2)	148 (14)
34B	956 (3)	350 (2)	350 (1)	91 (9)	34C	876 (4)	375 (2)	285 (2)	111 (11)
O3	880 (3)	573 (2)	264 (1)	104 (10)	O16	741 (3)	509 (2)	695 (1)	82 (8)
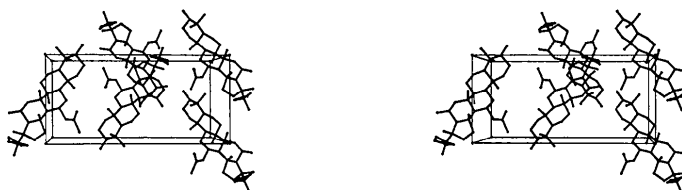
Fig. 2. Packing diagram. The direction of projection is **b**.

Spergulagenin A is thus a new migrated hopane-type triterpene with a methyl ketone in the E ring as a side chain. Fig. 1 produced by *ORTEP* (Johnson, 1965) shows the molecular conformation and demonstrates that all ring fusions are *trans*. The bond lengths and angles are shown in Fig. 1 and Table 3, respectively. All e.s.d.'s of the heavier-atom bond lengths and angles are ≤ 0.003 Å and $\leq 0.2°$ respectively except for bond lengths involving C(31) and C(32) which have e.s.d.'s of *ca* 0.004 Å. The values appear normal except for significant lengthening of some bonds involving C(8) and C(14). Since C(8) and C(14) both have four carbon atom substituents, it does not seem unlikely that overcrowding may be the explanation of the increases in bond lengths. Each of the A, B, C and D rings has a chair conformation and, as may be seen from the average torsion angles, a flattening of the cyclohexane rings, comparable with that found in steroids and calculated for cyclohexane itself by Hendrickson (1967), is observed. The conformation of the five-membered ring E is a distorted 18-envelope and can be described by the parameters, $\Delta = 18.4$ and $\varphi_m = 45.0$ (Altona, Geise & Romers, 1968). The torsion angles within each ring are given in Table 4.

Table 3. *Bond angles* (°)

C(2)—C(1)—C(10)	112·6	C(15)—C(14)—C(27)	106·1
C(3)—C(2)—C(1)	111·4	C(8)—C(14)—C(13)	107·3
C(4)—C(3)—C(2)	113·3	C(8)—C(14)—C(27)	110·8
C(4)—C(3)—O(3)	108·3	C(13)—C(14)—C(27)	111·9
C(2)—C(3)—O(3)	110·8	C(16)—C(15)—C(14)	116·0
C(5)—C(4)—C(3)	107·1	C(17)—C(16)—C(15)	107·4
C(5)—C(4)—C(23)	108·8	C(17)—C(16)—O(16)	113·9
C(5)—C(4)—C(24)	114·6	C(15)—C(16)—O(16)	107·2
C(3)—C(4)—C(23)	106·8	C(18)—C(17)—C(16)	110·6
C(3)—C(4)—C(24)	111·6	C(18)—C(17)—C(21)	107·2
C(23)-C(4)—C(24)	107·7	C(16)—C(17)—C(21)	122·0
C(6)—C(5)—C(4)	113·6	C(19)—C(18)—C(13)	114·8
C(6)—C(5)—C(10)	110·9	C(19)—C(18)—C(17)	99·0
C(4)—C(5)—C(10)	116·8	C(19)—C(18)—C(28)	107·3
C(7)—C(6)—C(5)	110·5	C(13)—C(18)—C(17)	106·1
C(8)—C(7)—C(6)	113·6	C(13)—C(18)—C(28)	113·9
C(9)—C(8)—C(7)	110·0	C(17)—C(18)—C(28)	114·9
C(9)—C(8)—C(14)	106·7	C(20)—C(19)—C(18)	104·1
C(9)—C(3)—C(26)	111·9	C(21)—C(20)—C(19)	107·5
C(7)—C(8)—C(14)	111·0	C(22)—C(21)—C(17)	111·1
C(7)—C(8)—C(26)	106·5	C(22)—C(21)—C(20)	108·6
C(14)-C(8)—C(26)	110·7	C(22)—C(21)—C(29)	109·2
C(10)-C(9)—C(8)	117·4	C(17)—C(21)—C(20)	102·3
C(10)-C(9)—C(11)	113·3	C(17)—C(21)—C(29)	113·5
C(8)—C(9)—C(11)	109·8	C(20)—C(21)—C(29)	111·8
C(25)-C(10)-C(1)	109·1	C(30)—C(22)—C(21)	113·9
C(25)-C(10)-C(5)	113·8	C(30)—C(22)—O(31)	109·2
C(25)-C(10)-C(9)	112·0	C(30)—C(22)—O(32)	109·4
C(1)—C(10)-C(5)	106·7	C(21)—C(22)—O(31)	109·7
C(1)—C(10)-C(9)	108·2	C(21)—C(22)—O(32)	109·5
C(5)—C(10)-C(9)	106·8	O(31)—C(22)—O(32)	104·8
C(12)-C(11)-C(9)	114·2	C(32)—C(31)—O(31)	107·5
C(13)-C(12)-C(11)	113·9	O(32)—C(32)—C(31)	104·1
C(13)-C(12)-O(12)	106·6	C(34)—C(33)—O(12)	111·3
C(11)-C(12)-O(12)	106·5	C(34)—C(33)—O(33)	124·2
C(14)-C(13)-C(12)	109·4	O(12)—C(33)—O(33)	124·4
C(14)-C(13)-C(18)	114·5	C(12)—O(12)—C(33)	118·1
C(12)-C(13)-C(18)	116·0	C(22)—O(31)—C(31)	108·6
C(15)-C(14)-C(8)	110·2	C(22)—O(32)—C(32)	108·1
C(15)-C(14)-C(13)	110·7		

Table 4. *The torsion angles* (φ) *within each ring*

Ring A		Ring B		Ring C	
Bond	φ	Bond	φ	Bond	φ
1—2	58·8°	5—6	63·1°	8—9	61·5°
2—3	−57·8	6—7	−57·4	9—11	−52·3
3—4	52·7	7—8	47·6	11—12	47·8
4—5	−53·2	8—9	−46·6	12—13	−52·3
5—10	54·1	9—10	51·6	13—14	45·6
10—1	−54·6	10—5	−58·0	14—8	−67·1
Average	55·2		54·1		54·4

Ring D		Ring E	
Bond	φ	Bond	φ
13–14	−45·6°	17–18	40·1°
14–15	45·2	18–19	−43·5
15–16	−54·9	19–20	32·5
16–17	65·2	20–21	−6·9
17–18	−65·5	21–17	−21·1
18–13	55·1		
Average	55·3		

A packing diagram viewed along the b axis is shown in Fig. 2. O(16) is involved in two hydrogen bonds as a donor and as an acceptor. Both bonds are linear within the e.s.d.'s. The formation of the bonds does not seem to have distorted ring D with respect to the other cyclohexane rings. The intramolecular hydrogen bond O(16)–H···O(32) is 2·697 Å long and controls the orientation of the ketal ring and the intermolecular bond O(3)–H···O(16) is 2·852 Å long and links the molecules along the c screw axis.

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