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Structure and Absolute Configuration of Two *ent*-Atisane Diterpenes from *Euphorbia fidjiana*

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Abstract. *ent*-(13*S*)-Hydroxyatis-16-en-3,14-dione, $C_{20}H_{28}O_3$, $M_r = 316\cdot4$, orthorhombic, $P2_12_12_1$, $a = 7\cdot335$ (2), $b = 12\cdot539$ (1), $c = 18\cdot325$ (1) Å, $V = 1685\cdot4$ Å^3, $Z = 4$, $D_x = 1\cdot247$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 0\cdot80$ cm^{-1}, $F(000) = 688$, $R = 0\cdot042$ for 1626 observed data $[I > 2\cdot5\sigma(I)]$ at room temperature. *ent*-16α-Hydroxy-3-oxoatisan-17-yl 4-bromobenzoate, $C_{27}H_{35}BrO_4$, $M_r = 503\cdot5$, orthorhombic, $P2_12_12_1$, $a = 7\cdot029$ (2), $b = 11\cdot642$ (3), $c = 28\cdot626$ (6) Å, $V = 2342\cdot5$ Å^3, $Z = 4$, $D_x = 1\cdot427$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 17\cdot8$ cm^{-1}, $F(000) = 1056$, $R = 0\cdot034$ for 1801 observed data $[I > 3\sigma(I)]$ at 170 K. These compounds are new diterpenoids whose stereochemistry has been determined.

Introduction. The Euphorbiaceae family is known as a source of antileukaemic and cocarcinogenic compounds (Kupchan, Uchida, Branfman, Dailey & Fei, 1976). Preparations of *Euphorbia fidjiana*, a Fijian plant known locally as vasa damu, have been used locally for the treatment of a variety of ailments. Extracts of the heartwood of *E. fidjiana* have yielded 15 diterpenoid compounds with atisane or seco-

atisane skeletons (Lal, Cambie, Rutledge & Woodgate, 1990). The structure of two of these, *ent*-(13*S*)-hydroxyatis-16-en-3,14-dione (I) and *ent*-16α,17-dihydroxyatisan-3-one as the *p*-bromobenzoate (II), along with the NMR spectra establish the stereochemistry of the whole series. In addition the absolute configuration of (II) establishes the absolute stereochemistry of all of the compounds.

Experimental. Suitable single crystals were obtained from slow evaporation of hexane solutions. Crystal samples of dimensions $0\cdot4 \times 0\cdot3 \times 0\cdot2$ mm (I) and $0\cdot5 \times 0\cdot2 \times 0\cdot2$ mm (II) were mounted in random orientations on an Enraf–Nonius CAD-4 diffractometer. The lattice parameters and orientation matrix were obtained from 25 reflections in the range $22 < 2\theta < 26°$. The Laue symmetry is *mmm* and the space groups were uniquely determined by the systematic absences. The intensity data were collected using Zr-filtered Mo $K\alpha$ radiation (II) using the ω–2θ scan technique. Three reflections monitored every hour showed no non-statistical variations in intensity. Unique data sets were collected for each structure. The number of reflections surveyed was 2352 in the range $2 < 2\theta < 56°$ with *h, k, l* ranges 10, 17, 25 (I) and 2480 in the range $2 < 2\theta < 50°$ with *h, k, l* ranges

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9, 14, 35 (II). Calculations were carried out on a PDP11/34 computer using the *SDP* software (Enraf–Nonius, 1979) for data reduction and on an IBM-4341 computer using *SHELXS*86 (Sheldrick, 1986) for structure solution and *SHELX*76 (Sheldrick, 1976) for refinement. Absorption corrections applied to (II) were by the empirical φ-scan technique (North, Phillips & Mathews, 1968) with transmission factors in the range 0·761 to 0·763.

Structure solution was by direct methods using *SHELXS*86 for (I) and conventional Patterson and Fourier techniques for (II). Full-matrix least-squares refinement on F was carried out using anisotropic thermal parameters for non-hydrogen atoms. Scattering factors were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV). The hydrogen-atom positions including those of the hydroxyl groups were obtained from difference Fourier maps and were included in the least-squares calculations with isotropic thermal parameters fixed at $U = 0·05$ and $0·025$ Å^2 for (I) and (II) respectively. Refinement converged to conventional R (wR) 0·042 (0·048) for 1626 data (I) and 0·034 (0·029) for 1801 data (II). Least-squares weights were $a/[\sigma^2(F) + bF^2]$, values of a and b being 1·0 and 0·0767 for (I) and 1·2 and 0·00018 for (II). At convergence maximum shift/e.s.d. was 1·1. These shifts were in the hydrogen coordinates which tended to oscillate about their mean position. Maxima and minima in the final electron density maps were approximately 0·5 e Å^{-3}, randomly distributed in space. Tables 1 and 2 give the final atomic parameters for (I) and (II) respectively.* Refinement of (II) as the opposite
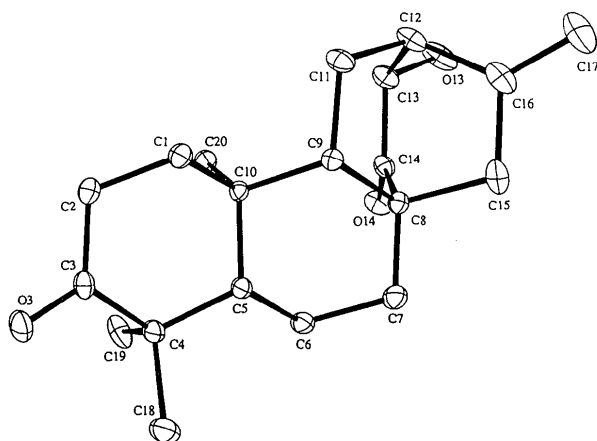

Fig. 1. The molecular geometry and numbering for *ent*-(13*S*)-hydroxyatis-16-en-3,14-dione. Atoms are presented as 50% probability ellipsoids.

Table 1. *Atomic coordinates and equivalent isotropic thermal parameters for* (I), C$_{20}$H$_{28}$O$_3$

$$B_{eq} = (\tfrac{8}{3}\pi^2)\Sigma_i\Sigma_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}(Å^2)
C1	0·2862 (4)	0·4484 (3)	0·5016 (2)	2·9
C2	0·2681 (5)	0·5623 (3)	0·4724 (2)	3·3
C3	0·0842 (4)	0·6093 (2)	0·4795 (2)	2·7
C4	−0·0333 (4)	0·5838 (2)	0·5464 (2)	2·7
C5	0·0086 (4)	0·4708 (2)	0·5777 (2)	2·3
C6	−0·0839 (4)	0·4509 (3)	0·6519 (2)	2·8
C7	−0·0807 (4)	0·3323 (3)	0·6703 (2)	3·1
C8	0·1108 (4)	0·2864 (4)	0·6702 (1)	2·3
C9	0·2161 (4)	0·3150 (2)	0·5986 (2)	2·2
C10	0·2111 (4)	0·4359 (2)	0·5798 (1)	2·0
C11	0·4092 (5)	0·2644 (3)	0·6004 (2)	3·1
C12	0·4373 (5)	0·1974 (2)	0·6707 (2)	3·3
C13	0·4176 (5)	0·2721 (3)	0·7357 (2)	3·1
C14	0·2234 (4)	0·3164 (2)	0·7366 (1)	2·5
C15	0·1005 (5)	0·1619 (2)	0·6738 (2)	3·5
C16	0·2929 (6)	0·1139 (3)	0·6736 (2)	3·5
C17	0·3246 (1)	0·0099 (3)	0·6744 (3)	5·4
C18	−0·2348 (5)	0·5879 (4)	0·5225 (2)	4·4
C19	0·0012 (7)	0·6761 (3)	0·6012 (2)	4·2
C20	0·3273 (4)	0·5018 (3)	0·6330 (2)	2·8
O3	0·0277 (4)	0·6730 (2)	0·4345 (1)	3·9
O13	0·4550 (4)	0·2161 (2)	0·8011 (1)	4·7
O14	0·1646 (3)	0·3645 (2)	0·7886 (1)	3·6

Table 2. *Atomic coordinates and equivalent isotropic thermal parameters for* (II), C$_{27}$H$_{35}$BrO$_4$

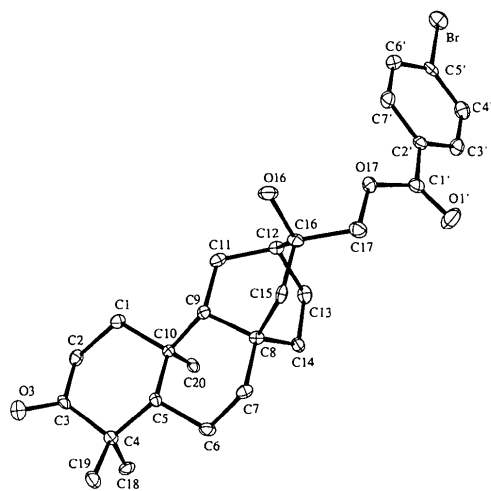$$B_{eq} = (\tfrac{8}{3}\pi^2)\Sigma_i\Sigma_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}(Å^2)
Br	1·2254 (1)	0·1159 (1)	0·1986 (0)	2·2
C1	0·2954 (9)	0·3926 (5)	0·5489 (2)	1·4
C2	0·2904 (9)	0·4466 (5)	0·5983 (2)	1·5
C3	0·0950 (8)	0·4896 (5)	0·6091 (2)	1·2
C4	0·0114 (8)	0·5789 (5)	0·5753 (2)	1·2
C5	0·0288 (8)	0·5250 (5)	0·5253 (3)	1·0
C6	−0·0536 (8)	0·6013 (5)	0·4861 (2)	1·4
C7	−0·0840 (8)	0·5302 (5)	0·4420 (2)	1·2
C8	0·0933 (8)	0·4694 (5)	0·4244 (2)	1·1
C9	0·1937 (8)	0·4048 (5)	0·4654 (2)	1·1
C10	0·2259 (9)	0·4768 (5)	0·5108 (2)	1·1
C11	0·3695 (9)	0·3405 (5)	0·4462 (2)	1·5
C12	0·3905 (8)	0·3579 (5)	0·3932 (2)	1·1
C13	0·4120 (9)	0·4874 (6)	0·3837 (2)	1·6
C14	0·2280 (9)	0·5503 (5)	0·3977 (2)	1·3
C15	0·0358 (8)	0·3749 (6)	0·3886 (2)	1·2
C16	0·2108 (8)	0·3137 (4)	0·3686 (2)	1·2
C17	0·2202 (9)	0·3337 (6)	0·3160 (2)	1·8
C18	−0·1989 (8)	0·5973 (6)	0·5870 (2)	1·5
C19	0·1146 (9)	0·6943 (6)	0·5822 (2)	1·7
C20	0·3806 (9)	0·5696 (5)	0·5040 (2)	1·4
C1′	0·4700 (9)	0·3332 (5)	0·2599 (2)	1·7
C2′	0·6553 (8)	0·2787 (5)	0·2468 (2)	1·3
C3′	0·7704 (9)	0·3372 (5)	0·2160 (2)	1·8
C4′	0·9424 (8)	0·2915 (5)	0·2012 (2)	1·9
C5′	0·9930 (8)	0·1839 (5)	0·2184 (2)	1·4
C6′	0·8800 (8)	0·1235 (6)	0·2499 (2)	1·6
C7′	0·7093 (9)	0·1722 (5)	0·2638 (2)	1·8
O1′	0·3952 (6)	0·4111 (4)	0·2389 (2)	3·0
O3	0·0022 (6)	0·4531 (3)	0·6418 (1)	1·9
O16	0·1852 (6)	0·1935 (3)	0·3770 (2)	1·8
O17	0·3932 (5)	0·2839 (3)	0·2981 (2)	1·7

enantiomorph gave conventional R (wR) 0·059 (0·057) confirming the absolute configuration.

Discussion. The structure of (I) is shown in Fig. 1 and interatomic distances and angles are given in Table 3. The junction between rings A and B is *trans* as is the junction between rings B and C. The length of the exocyclic bond C16—C17 is 1·324 (5) Å which together with the proton geometry confirms the presence of the double bond. Likewise the C3—O3 and

Table 3. *Interatomic distances (Å) and angles (°) for (I), $C_{20}H_{28}O_3$*

C2—C1	1·531 (5)	C15—C8	1·565 (4)
C10—C1	1·543 (4)	C10—C9	1·555 (4)
C3—C2	1·478 (5)	C11—C9	1·552 (4)
C4—C3	1·532 (4)	C20—C10	1·537 (4)
O3—C3	1·221 (4)	C12—C11	1·551 (4)
C5—C4	1·559 (4)	C13—C12	1·522 (4)
C18—C4	1·542 (5)	C16—C12	1·490 (5)
C19—C4	1·553 (5)	C14—C13	1·529 (5)
C6—C5	1·540 (4)	O13—C13	1·416 (4)
C10—C5	1·549 (4)	O14—C14	1·208 (3)
C7—C6	1·526 (4)	C16—C15	1·534 (6)
C8—C7	1·518 (4)	C17—C16	1·324 (5)
C9—C8	1·563 (4)	C14—C8	1·518 (4)
C10—C1—C2	112·8 (2)	C11—C9—C8	109·9 (2)
C3—C2—C1	114·9 (3)	C11—C9—C10	115·1 (2)
C4—C3—C2	120·1 (2)	C5—C10—C1	106·9 (2)
O3—C3—C2	120·8 (3)	C9—C10—C1	107·3 (2)
O3—C3—C4	119·1 (3)	C9—C10—C5	107·7 (2)
C5—C4—C3	111·9 (2)	C20—C10—C1	109·7 (2)
C18—C4—C3	107·8 (3)	C20—C10—C5	113·3 (2)
C18—C4—C5	108·9 (3)	C20—C10—C9	111·7 (2)
C19—C4—C3	105·7 (3)	C12—C11—C9	111·1 (3)
C19—C4—C5	114·0 (2)	C13—C12—C11	107·7 (2)
C19—C4—C18	108·3 (3)	C16—C12—C11	108·4 (3)
C6—C5—C4	112·6 (2)	C16—C12—C13	109·7 (3)
C10—C5—C4	117·1 (2)	C14—C13—C12	108·7 (3)
C10—C5—C6	110·8 (2)	O13—C13—C12	109·9 (3)
C7—C6—C5	110·3 (2)	O13—C13—C14	110·6 (3)
C8—C7—C6	112·5 (2)	C13—C14—C8	114·1 (2)
C9—C8—C7	111·9 (2)	O14—C14—C8	124·2 (3)
C14—C8—C7	114·1 (2)	O14—C14—C13	121·5 (3)
C14—C8—C9	110·3 (2)	C16—C15—C8	110·3 (3)
C15—C8—C7	109·5 (2)	C15—C16—C12	112·2 (3)
C15—C8—C9	106·8 (2)	C17—C16—C12	124·6 (4)
C15—C8—C14	103·8 (2)	C17—C16—C15	123·2 (4)
C10—C9—C8	113·4 (2)		

Table 4. *Interatomic distances (Å) and angles (°) for (II), $C_{27}H_{35}BrO_4$*

C5'—Br	1·902 (6)	C20—C10	1·545 (8)
C2—C1	1·547 (8)	C12—C11	1·535 (9)
C10—C1	1·547 (8)	C13—C12	1·539 (9)
C3—C2	1·495 (9)	C16—C12	1·536 (8)
C4—C3	1·536 (8)	C14—C13	1·539 (9)
O3—C3	1·217 (7)	C16—C15	1·533 (8)
C5—C4	1·568 (7)	C17—C16	1·526 (8)
C18—C4	1·531 (8)	O16—C16	1·431 (6)
C19—C4	1·540 (8)	O17—C17	1·440 (8)
C6—C5	1·544 (8)	C2'—C1'	1·497 (8)
C10—C5	1·551 (8)	O1'—C1'	1·209 (7)
C7—C6	1·525 (8)	O17—C1'	1·348 (7)
C8—C7	1·519 (8)	C3'—C2'	1·376 (8)
C9—C8	1·562 (8)	C7'—C2'	1·385 (8)
C14—C8	1·539 (8)	C4'—C3'	1·387 (9)
C15—C8	1·556 (8)	C5'—C4'	1·393 (8)
C10—C9	1·562 (7)	C6'—C5'	1·391 (8)
C11—C9	1·547 (8)	C7'—C6'	1·386 (9)
C10—C1—C2	112·4 (5)	C20—C10—C9	111·9 (4)
C3—C2—C1	110·2 (5)	C12—C11—C9	111·4 (5)
C4—C3—C2	116·7 (5)	C13—C12—C11	108·3 (5)
O3—C3—C2	122·3 (5)	C16—C12—C11	109·3 (5)
O3—C3—C4	121·0 (5)	C16—C12—C13	109·1 (5)
C5—C4—C3	105·9 (4)	C14—C13—C12	109·7 (5)
C18—C4—C3	109·0 (4)	C13—C14—C8	110·8 (5)
C18—C4—C5	109·4 (4)	C16—C15—C8	111·5 (4)
C19—C4—C3	109·2 (5)	C15—C16—C12	109·4 (4)
C19—C4—C5	115·5 (5)	C17—C16—C12	111·5 (5)
C19—C4—C18	107·7 (5)	C17—C16—C15	109·4 (5)
C6—C5—C4	113·8 (5)	O16—C16—C12	110·7 (4)
C10—C5—C4	117·3 (4)	O16—C16—C15	106·9 (5)
C10—C5—C6	110·4 (4)	O16—C16—C17	108·7 (4)
C7—C6—C5	109·9 (5)	O17—C17—C16	109·0 (5)
C8—C7—C6	114·4 (5)	O1'—C1'—C2'	124·8 (5)
C9—C8—C7	110·2 (4)	O17—C1'—C2'	111·9 (5)
C14—C8—C7	112·6 (5)	O17—C1'—O1'	123·3 (6)
C14—C8—C9	113·0 (4)	C3'—C2'—C1'	117·6 (5)
C15—C8—C7	109·5 (4)	C7'—C2'—C1'	121·9 (5)
C15—C8—C9	105·8 (4)	C7'—C2'—C3'	120·5 (5)
C15—C8—C14	105·4 (4)	C4'—C3'—C2'	121·2 (6)
C10—C9—C8	115·6 (4)	C5'—C4'—C3'	117·4 (5)
C11—C9—C8	109·0 (4)	C4'—C5'—Br	119·2 (4)
C11—C9—C10	116·1 (5)	C6'—C5'—Br	118·3 (4)
C5—C10—C1	108·8 (4)	C6'—C5'—C4'	122·5 (5)
C9—C10—C1	107·0 (4)	C7'—C6'—C5'	118·3 (6)
C9—C10—C5	106·7 (4)	C6'—C7'—C2'	120·2 (6)
C20—C10—C1	108·0 (5)	C1'—O17—C17	117·0 (4)
C20—C10—C5	114·2 (5)		

Fig. 2. The molecular geometry, absolute configuration, and numbering for ent-16α-hydroxy-3-oxoatisan-17-yl 4-bromobenzoate. Atoms are represented as 50% probability ellipsoids.

C14—O14 distances are 1·221 (4) and 1·208 (3) Å respectively confirming the ketonic nature of these groups. All other distances and angles are within the normally accepted range.

The structure of (II) is shown in Fig. 2 and interatomic distances are given in Table 4. This structure has the same ring conformation as (I) with *trans* fused junctions between the *A* and *B* rings and between the *B* and *C* rings. The bond length C3—O3

is 1·217 (7) Å which confirms the ketonic nature of the bond. All other bond lengths and angles are within the normally accepted range. The measured optical rotation for (I) is $[\alpha]_D^{25°C} = +44°$. The amount of (II) available was insufficient to determine the rotation but the parent alcohol has $[\alpha]_D^{25°C} = -86°$. The absolute configuration is that illustrated in the diagram and confirms the absolute stereochemistry of (I) through normal biosynthetic pathways.

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