

that the functional OH group of the compound is involved in an intricate network of hydrogen bonds in the crystal.

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Raspacionin, a New Tetracyclic Triterpenoid from the Sponge *Raspaciona aculeata*: a Structure Containing Disordered Solvent

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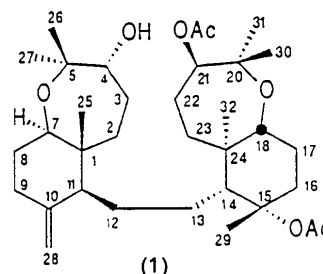
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Abstract. 6-[2-(3-Hydroxy-2,2,5a-trimethyl-7-methylenedecahydro-1-benzoxepin-6-yl)ethyl]-2,2,5a,7-tetramethyldecahydro-1-benzoxepin-3,7-diyl diacetate, $C_{34}H_{56}O_7$, $M_r = 576.8$, orthorhombic, $P2_12_1$, $a = 7.117$ (1), $b = 19.757$ (2), $c = 27.156$ (4) Å, $V = 3819$ (1) Å³, $Z = 4$, $D_x = 1.003$ Mg m⁻³, $\lambda(\text{Cu } K\alpha) = 1.54178$ Å, $\mu(\text{Cu } K\alpha) = 0.52$ mm⁻¹, $F(000) = 1264$, room temperature, final $R = 0.050$ for 2839 reflections with $I \geq 2.5\sigma(I)$ and 371 variables (not including solvent). The structural analysis revealed a new squalene-derived triterpenoid skeleton, characterized by two *trans*-perhydrobenzoxepine systems linked by an equatorial ethylene bridge. In the crystal, raspacionin molecules are connected by a hydrogen bond between the hydroxyl group and a carbonyl O atom and form channels parallel to **a**, filled with partially disordered solvent.

Introduction. Marine organisms are a very rich source of substances with interesting pharmacological or biological activities, often correlated to unusual structural features. As part of a program (Cimino, Gavagnin, Sodano, Puliti, Mattia &

Mazzarella, 1988; Mattia, Mazzarella, Puliti, Riccio & Minale, 1988; Cimino, Mattia, Mazzarella, Puliti, Scognamiglio, Spinella & Trivellone 1989; Puliti, De Rosa, Mattia & Mazzarella, 1990) on the structural and biological investigation of marine metabolites, we now present the crystal structure of raspacionin (1), the main metabolite of the Mediterranean sponge *Raspaciona aculeata*.



The tetracyclic skeleton of (1), which is structurally related to sipholane and siphonellane metabolites (Carmely & Kashman, 1983; Carmely, Loya & Kashman, 1983), presents a unique feature in nature

and adds to the small group of known triterpenoids from sponges (Faulkner 1990).

Experimental. The title compound (1) has been recently isolated (Cimino, Crispino, Mattia, Mazzarella, Puliti, Trivellone & Uriz, 1990) by silica-gel chromatography from the diethyl ether soluble fraction of the acetonic extract from the sponge *R. aculeata*, collected along the northeast Iberian coast. Single crystals were obtained by slow evaporation from *n*-heptane in the form of small prisms. A 0.37 × 0.15 × 0.11 mm sample was employed for the crystallographic analysis. Enraf-Nonius CAD-4F diffractometer, monochromated Cu K α radiation, room temperature, cell dimensions from 25 reflections ($20 < \theta < 23^\circ$); ω - 2θ scan, as suggested by peak-shape analysis. Three standard reflections monitored every 4 h (4% variation); 4438 independent reflections with $\theta \leq 75^\circ$, $0 \leq h \leq 8$, $0 \leq k \leq 24$, $0 \leq l \leq 34$, 2839 considered observed, with $I \geq 2.5\sigma(I)$; Lp correction, absorption ignored. The structure was solved by *MULTAN82* (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982) and difference Fourier syntheses. Anisotropic full-matrix refinement (on *F*). H atoms from geometrical considerations and ΔF suggestions (for hydroxyl and methyl groups), not refined, their isotropic thermal parameters set equal to the B_{eq} of the parent atoms. At convergence ($R = 0.087$), the difference Fourier map revealed a continuous region of approximately constant electron density ($0.9 \text{ e } \text{\AA}^{-3}$), parallel to the *a* axis and centered on the screw axis. The residual density was ascribed to disordered molecules of solvent (*n*-heptane) and this interpretation was confirmed by an NMR spectrum measured on the crystalline material dissolved in chloroform. Using the program *FRODO* (Jones, 1982) on an Evans & Sutherland PS390, the residual electron density was satisfactorily fitted by a disordered model consisting of two randomly alternating heptane molecules, related by the screw axis parallel to *a*. The heptane model was first refined for a few cycles using bond-length and valency-angle restraints, and was successively held fixed with occupancy factor 0.5 and $B = 25 \text{ \AA}^2$. Full-matrix refinement of the non-H atoms of the raspacionin molecule converged to the final $R = 0.050$, $wR = 0.057$. Function minimized $\sum w(\Delta F)^2$, $w^{-1} = [\sigma^2(F_o) + (0.02F_o)^2 + 1]$ (Killeen & Lawrence, 1969) and σ from counting statistics. A correction for secondary extinction was refined [$g = 6.6(3) \times 10^{-7}$], $S = 0.57$; final $(\Delta/\sigma)_{\max} = 0.01$; maximum and minimum heights in final $\Delta\rho$ map 0.27 and $-0.19 \text{ e } \text{\AA}^{-3}$. Scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV), Enraf-Nonius *SDP* software (B. A. Frenz & Associates, Inc., 1985) and a MicroVAX 3100 computer. Final atomic parameters for the non-H atoms are

Table 1. Fractional coordinates and equivalent isotropic thermal parameters (\AA^2) with e.s.d.'s in parentheses

$$B_{eq} = (4/3)\sum_i\sum_j\beta_{ij}a_i \cdot a_j.$$

	x	y	z	B_{eq}
O6	0.8652 (5)	0.3416 (1)	0.02614 (9)	4.31 (6)
O19	0.2898 (5)	0.3674 (2)	0.3690 (1)	5.84 (8)
O33	0.8107 (5)	0.4775 (2)	0.0896 (1)	5.67 (8)
O34	0.5317 (5)	0.1601 (1)	0.3260 (1)	5.14 (7)
O35	0.1603 (5)	0.4447 (2)	0.2716 (1)	6.10 (8)
O38	0.3990 (7)	0.0630 (2)	0.3508 (2)	9.4 (1)
O41	0.1972 (8)	0.5445 (2)	0.2354 (2)	9.6 (1)
C1	0.7227 (6)	0.2969 (2)	0.1010 (1)	3.77 (8)
C2	0.5876 (7)	0.3580 (2)	0.1085 (2)	4.6 (1)
C3	0.5521 (7)	0.4048 (2)	0.0644 (2)	5.0 (1)
C4	0.7148 (7)	0.4493 (2)	0.0479 (2)	4.7 (1)
C5	0.8541 (7)	0.4124 (2)	0.0145 (2)	4.6 (1)
C7	0.9036 (6)	0.3225 (2)	0.0765 (1)	3.78 (9)
C8	1.0606 (7)	0.2702 (2)	0.0742 (2)	4.9 (1)
C9	1.1046 (7)	0.2418 (2)	0.1256 (2)	5.2 (1)
C10	0.9269 (7)	0.2152 (2)	0.1487 (2)	4.4 (1)
C11	0.7741 (6)	0.2676 (2)	0.1533 (1)	3.88 (8)
C12	0.6026 (7)	0.2455 (2)	0.1830 (2)	4.7 (1)
C13	0.6368 (7)	0.2368 (2)	0.2387 (1)	4.40 (9)
C14	0.4552 (7)	0.2474 (2)	0.2691 (1)	4.14 (9)
C15	0.3806 (7)	0.1807 (2)	0.2919 (2)	4.7 (1)
C16	0.1982 (7)	0.1940 (2)	0.3196 (2)	5.5 (1)
C17	0.2123 (8)	0.2518 (2)	0.3565 (2)	5.5 (1)
C18	0.2767 (7)	0.3169 (2)	0.3310 (2)	4.6 (1)
C20	0.2158 (9)	0.4344 (2)	0.3589 (2)	6.2 (1)
C21	0.2882 (8)	0.4635 (2)	0.3110 (2)	5.9 (1)
C22	0.4874 (8)	0.4420 (2)	0.2973 (2)	6.2 (1)
C23	0.5059 (8)	0.3720 (2)	0.2728 (2)	5.5 (1)
C24	0.4680 (7)	0.3090 (2)	0.3053 (2)	4.40 (9)
C25	0.6276 (8)	0.2426 (2)	0.0695 (2)	5.2 (1)
C26	0.7811 (9)	0.4127 (3)	-0.0378 (2)	5.8 (1)
C27	1.0501 (8)	0.4438 (3)	0.0168 (2)	6.0 (1)
C28	0.9110 (9)	0.1510 (2)	0.1618 (2)	6.5 (1)
C29	0.3536 (8)	0.1268 (2)	0.2524 (2)	5.8 (1)
C30	0.0019 (9)	0.4331 (3)	0.3617 (2)	8.0 (2)
C31	0.2941 (9)	0.4758 (3)	0.4020 (2)	8.4 (2)
C32	0.6270 (8)	0.3015 (2)	0.3434 (2)	5.7 (1)
C36	0.5242 (9)	0.1036 (3)	0.3523 (2)	6.8 (1)
C37	0.6960 (9)	0.0962 (3)	0.3830 (2)	8.5 (2)
C39	0.1296 (9)	0.4892 (3)	0.2360 (2)	6.5 (1)
C40	-0.0007 (9)	0.4620 (3)	0.1981 (2)	8.8 (2)
Solvent				
C1s	0.0951	0.1539	0.4856	25.0
C2s	0.2770	0.1746	0.5123	25.0
C3s	0.3253	0.2490	0.5008	25.0
C4s	0.5393	0.2698	0.5042	25.0
C5s	0.5871	0.3328	0.4890	25.0
C6s	0.7772	0.3553	0.5106	25.0
C7s	0.9289	0.3015	0.5005	25.0

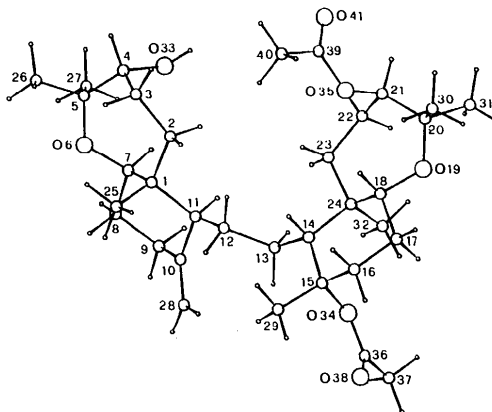


Fig. 1. Drawing of the molecule of raspacionin oriented at optimal viewing. Labels for H atoms have been omitted for clarity.

Table 2. Selected bond lengths (Å), bond angles (°) and torsion angles (°) with e.s.d.'s in parentheses

O6—C5	1.436 (5)	C10—C11	1.507 (6)
O6—C7	1.444 (5)	C10—C28	1.322 (6)
O19—C18	1.436 (5)	C11—C12	1.526 (6)
O19—C20	1.451 (6)	C12—C13	1.543 (6)
O34—C15	1.476 (6)	C13—C14	1.548 (6)
O35—C21	1.453 (6)	C14—C15	1.550 (6)
C1—C2	1.557 (6)	C14—C24	1.566 (6)
C1—C7	1.535 (6)	C15—C16	1.522 (7)
C1—C11	1.577 (5)	C16—C17	1.525 (7)
C2—C3	1.533 (6)	C17—C18	1.531 (6)
C3—C4	1.522 (7)	C18—C24	1.539 (7)
C4—C5	1.529 (6)	C20—C21	1.513 (7)
C7—C8	1.524 (6)	C21—C22	1.526 (8)
C8—C9	1.535 (6)	C22—C23	1.540 (7)
C9—C10	1.506 (7)	C23—C24	1.550 (6)
C5—O6—C7	118.2 (3)	C11—C12—C13	115.0 (4)
C18—O19—C20	118.4 (3)	C12—C13—C14	112.1 (4)
C2—C1—C7	108.6 (3)	C13—C14—C15	112.6 (4)
C7—C1—C11	108.5 (3)	C15—C14—C24	115.5 (3)
C1—C2—C3	117.8 (4)	C14—C15—C16	110.0 (4)
C2—C3—C4	116.9 (4)	C15—C16—C17	113.5 (4)
C3—C4—C5	113.1 (4)	C16—C17—C18	110.6 (4)
O6—C5—C4	111.7 (3)	O19—C18—C24	109.8 (4)
O6—C7—C1	109.8 (3)	C17—C18—C24	112.7 (4)
C1—C7—C8	114.1 (3)	O19—C20—C21	112.6 (4)
C7—C8—C9	111.2 (4)	C20—C21—C22	114.8 (4)
C8—C9—C10	109.5 (4)	C21—C22—C23	115.7 (4)
C9—C10—C11	113.7 (4)	C22—C23—C24	117.3 (4)
C1—C11—C10	110.1 (3)	C14—C24—C18	108.2 (4)
C10—C11—C12	115.1 (3)	C18—C24—C23	109.3 (4)
C10—C11—C12—C13	69.5 (4)	C11—C12—C13—C14	153.5 (3)
O33—C4—C5—C27	-30.1 (4)	C30—C20—C21—O35	-34.4 (5)
C12—C13—C14—C15	109.6 (4)		

listed in Table 1* and the atomic numbering scheme is given in Fig. 1.

Discussion. The structural analysis revealed a novel tetracyclic framework (see Fig. 1), characterized by two substituted *trans*-decahydrobenzoxepine systems, linked to each other by an equatorial ethylene bridge. A *trans*-decahydrobenzoxepine moiety has previously been found in some metabolites (Carmely, Loya & Kashman, 1983), from the red sponge *Siphonochalina siphonella*, and in these cases it is linked by an ethylene bridge, to a *cis*-octahydroazulene moiety (sipholenol) or to a substituted cyclohexene group (siphonellinol). As the absolute configuration could not be determined by X-ray data, the configuration for raspacionin was chosen to be in agreement with the one proposed by Carmely & Kashman (1983) for sipholanes.

In raspacionin, the two bicyclic systems are not chemically identical (see Fig. 1); however, the two systems show a remarkable degree of geometrical similarity and the two moieties are related by a pseudo-twofold axis, intersecting the bond

* Lists of structure factors, anisotropic thermal parameters, H-atom parameters and the complete molecular geometries have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54289 (21 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

C12—C13. On superposition the r.m.s deviation of sixteen pairs of corresponding atoms is only 0.06 Å. The largest deviation, 0.14 (1) Å, is associated with the atoms C10 and C15 which exhibit different hybridization in the two systems.

A few relevant geometrical parameters involving non-H atoms are given in Table 2. Bond lengths and bond angles agree with the generally accepted values and most of the discrepancies between the two halves of the molecule are within the experimental errors, except for those determined by the different stereochemistry at C10 and C15, resulting from short intramolecular contacts which are present in only one system.

The two cyclohexane rings adopt very similar chair conformations, only slightly distorted, as shown by the puckering parameters (Cremer & Pople, 1975), $Q = 0.569$ (6) and 0.554 (7) Å, $\theta = 2.4$ (8) and 4.8 (8)°. The mean values of the endocyclic torsion angles are 55.5 (4) and 53.9 (4)°; the conformation of the two oxepane rings can be described as a twisted chair (Hendrickson, 1961), with an approximate twofold axis through C5 (or C20) and the bond C1—C2 (or C23—C24): the deviations from ideal C_2 symmetry

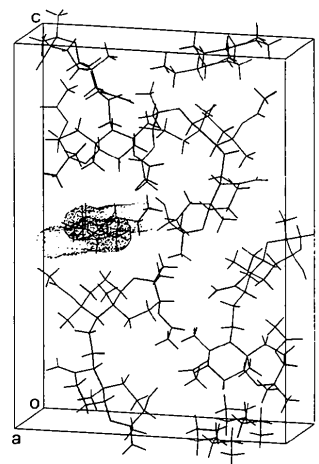


Fig. 2. Crystal packing. The channel parallel to *a*, filled with solvent density, is also shown.

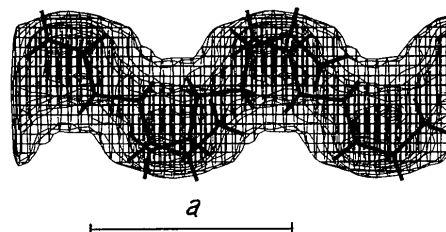


Fig. 3. Residual solvent density, contour levels at 0.25, 0.50 and $0.75 \text{ e } \text{Å}^{-3}$, projected approximately onto the *ab* plane. Two translated molecules of *n*-heptane are shown with a screw-related molecule.

can be measured by ΔC_2 (for C5) = 18.2° and ΔC_2 (for C20) = 15.8° (Duax, Weeks & Rohrer, 1976). The acetoxy groups are planar and the carbonyl O atoms are eclipsed to the intracyclic atoms (C15 and C21 respectively).

In the crystal, molecules of raspacionin, related by a screw axis parallel to **b**, are linked by an intermolecular hydrogen bond, which involves the hydroxyl group and the O38($1 - x, \frac{1}{2} + y, \frac{1}{2} - z$) carbonyl O atom at a distance 2.775 (5) Å. As shown in Fig. 2, the packing is characterized by channels parallel to **a** and centered on the screw axis, with a sinusoidal shape (Fig. 3) and an approximate cross section of $3.5 \times 6 \text{ \AA}^2$. The identity period *a* and the channel cross section are compatible with the presence of only one bent heptane molecule roughly in a *11g* conformation (Fig. 3). All distances between successively translated molecules are greater than 3.0 Å. This minimal parameter model of the disordered 'guest' structure satisfactorily fitted the residual density. The resulting heptane molecule is roughly planar, with a maximum displacement of 0.32 Å from the mean molecular plane, which is parallel to the *ab* plane. In relation to the 'host' lattice, the heptane molecules are loosely packed and no interactions are below 3.9 Å.

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Structure of Bulbocarpine

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Abstract. $C_{19}H_{19}NO_4$, $M_r = 325.36$, orthorhombic, $P2_12_12_1$, $a = 8.293$ (5), $b = 8.462$ (5), $c = 22.80$ (1) Å, $V = 1600$ (1) Å³, $Z = 4$, $D_x = 1.350 \text{ Mg m}^{-3}$,

$\lambda(\text{Mo K}\alpha) = 0.7107 \text{ \AA}$, $\mu = 0.088 \text{ mm}^{-1}$, $F(000) = 688$, $T = 293$ (1) K, $R = 0.063$ for 1523 reflections with $I > 3.5\sigma(I)$. The asymmetric C atom C5 has an

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