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Structure of the Thermodynamic Benzenethiol 1,4 Adduct of the Cembranolide Crassin Alcohol,* $C_{26}H_{36}O_4S$

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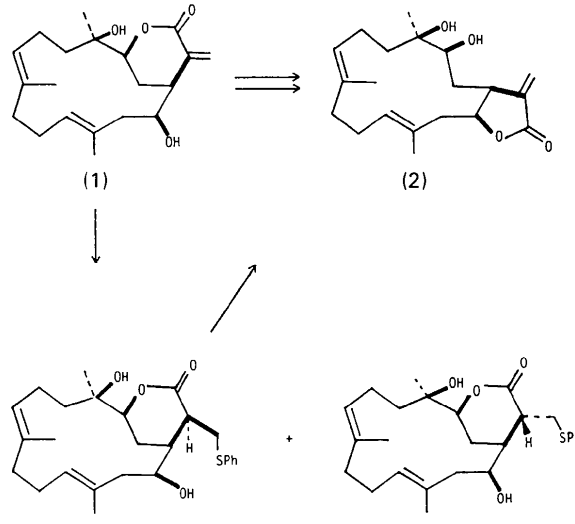
Abstract. $M_r = 444{\cdot}6$, orthorhombic, $P2_12_12_1$, $a = 9{\cdot}897$ (1), $b = 15{\cdot}367$ (4), $c = 15{\cdot}633$ (2) Å, $V = 2378$ (1) Å^3, $Z = 4$, $D_x = 1{\cdot}24$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71073$ Å, $\mu = 1{\cdot}57$ cm^{-1}, $F(000) = 960$, $T = 291$ K, final $R = 0{\cdot}040$ for 1202 observed reflections. The cyclotetradecadiene ring is in a 'flat' conformation and the condensed caprolactone adopts a sofa conformation. The angle between the average planes through these rings is 44·8 (4)°.

Introduction. We recently described a scheme for isomerizing a cembranolide 1,3-bridged α-methylene-δ-lactone (1) to a 1,2-fused α-methylene-γ-lactone (2) *via* conjugate addition of benzenethiol followed by translactonization and elimination of benzenethiol (Marshall, Karas & Coghlan, 1982). The conjugate addition reaction afforded two isomeric adducts in ratios which depended upon reaction conditions. A 'kinetic product' (3) was favored after short reaction times at low temperature whereas prolonged reaction times and higher temperature led to a 'thermodynamic isomer' (4). We expected the 'kinetic product' (3) to possess an axial CH_2SPh substituent which would provide the driving force for translactonization through relief of steric strain. While high-field ^{1}H NMR analysis supports the assigned stereochemistry the arguments require assumptions regarding restricted rotation and averaged conformations about carbon–carbon single bonds. Accordingly, additional evidence was sought from X-ray structure analysis.



(1) (2)

(3) (4)

Experimental. Crystals obtained by slow evaporation of an ethyl acetate–hexane solution over a period of several days; fragment of a bigger crystal ground to a sphere of radius 0·15 mm and mounted in a glass capillary; Enraf–Nonius CAD-4 diffractometer, graphite monochromator; 25 general reflections used for the orientation matrix and unit-cell measurements; $h00$ with h odd, $0k0$ with k odd, $00l$ with l odd absent; absorption corrections max. = min. = 1·00, $2\theta_{\max} = 48°$, hkl range 0–11, 0–17, 0–17, 3 standard reflections monitored every 2·5 h, maximum variation $3\sigma(I)$, no decay, 2152 reflections measured in ω–2θ scan mode, 1202 with $F > 3\sigma(F)$ used in refinement. Attempts to solve the structure with default *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980) input were not successful. Structure was solved by the multisolution tangent refinement program (Sheldrick, 1976) using 10 manually selected reflections and one phase determined by $\sum_1$ relationship obtained in the *MULTAN*80 runs. In the best E map (309 $E >$ 1·2) about $\frac{2}{3}$ of the molecule was readily recognized; the rest located in subsequent Fourier maps; calculated H-atom positions, updated during the refinement, were used except for methyl and hydroxyl groups which were located in difference Fourier maps but not refined; structure refined minimizing $\sum w(|F_o| - |F_c|)^2$, anisotropic thermal-motion parameters for non-H atoms and constrained phenyl geometry; elastic restraints on bond distances used in the initial stages of the refinement were waived in final cycles; $wR = 0{\cdot}041$, $S = 0{\cdot}90$ with $w = [\sigma^2(F) + 0{\cdot}0003F^2]^{-1}$, max. $\Delta/\sigma = 0{\cdot}08$, final difference Fourier map max. = 0·17, min. = −0·14 e Å^{-3}; atomic scattering factors and f', f'' values from *International Tables for X-ray Crystallography* (1974);

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* 2,12-Dihydroxy-4,8,12-trimethyl-16-(phenylthio)methyl-14-oxabicyclo[11.3.1]heptadeca-4,8-dien-15-one.

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data reduction and *MULTAN*80 runs done using *Enraf–Nonius Structure Determination Package* (Frenz, 1982); for structure solution and refinement *SHELX*76 (Sheldrick, 1976) was employed.

Discussion. The non-H atomic coordinates are listed in Table 1.* Important bond distances are in Table 2. The bond distances and angles are normal and show no unexpected values. An *ORTEP* (Johnson, 1970) drawing of the molecule is shown in Fig. 1. The enantiomorph conforming to the known absolute configuration of crassin *p*-iodobenzoate (Hossain & van der Helm, 1969) was selected. The structure confirms our earlier assignment of configuration of C(15) in (4).

The molecule consists of the thioether moiety and the crassin moiety which, except for the covalent link in the eclipsed conformation, do not have contacts smaller than the sum of the van der Waals radii. The conformation of the crassin moiety is essentially that found in crassin *p*-iodobenzoate (Hossain & van der Helm, 1969) with the maximum difference in the torsion angles 17° and the average 6°. This indicates that the crassin conformation found in both structures is stable and corresponds to a major minimum of the potential energy. It should be noted, however, that the related cembranolides peunicin (Chang, Ciereszko, Hossain & van der Helm, 1980) and lobophytolide (Karlsson, 1977) with the same arrangement of double bonds in the 14-membered ring have very different macrocycle conformations. The comparison of the torsion angles is presented in Table 3.

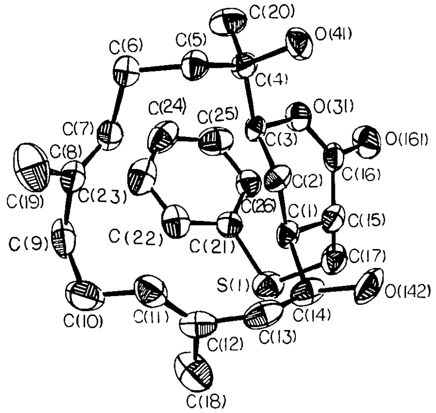

Fig. 1. An *ORTEP* (Johnson, 1970) drawing of the title molecule with the atom numbering scheme. The thermal ellipsoids are drawn at the 50% probability level. The phenyl ring does not have any contact with the 14-membered ring less than the sum of the van der Waals radii.

Table 1. *Atomic coordinates and equivalent isotropic thermal motion parameters with e.s.d.'s in parentheses*

$$B_{eq} = \tfrac{8}{3}\pi^2 \textstyle\sum_i \sum_j U_{ij} a^*_i a^*_j \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}(Å^2)
C(1)	0·0218 (6)	0·6232 (3)	0·4170 (3)	2·80
C(2)	0·0786 (6)	0·6946 (4)	0·3590 (3)	2·98
C(3)	0·2048 (6)	0·6605 (3)	0·3157 (3)	2·57
O(31)	0·3064 (3)	0·6359 (2)	0·3795 (2)	3·41
C(4)	0·2792 (6)	0·7242 (4)	0·2569 (3)	3·14
O(41)	0·3106 (5)	0·8026 (2)	0·3039 (2)	4·60
C(5)	0·1906 (6)	0·7578 (3)	0·1835 (3)	3·13
C(6)	0·1626 (6)	0·6969 (4)	0·1078 (3)	3·78
C(7)	0·0662 (6)	0·6224 (4)	0·1267 (3)	3·57
C(8)	−0·0588 (6)	0·6134 (4)	0·0990 (3)	3·39
C(9)	−0·1446 (7)	0·5372 (4)	0·1264 (4)	4·50
C(10)	−0·2707 (6)	0·5635 (5)	0·1764 (4)	5·50
C(11)	−0·2408 (6)	0·6212 (4)	0·2503 (4)	4·33
C(12)	−0·2569 (6)	0·6040 (4)	0·3325 (4)	4·08
C(13)	−0·2237 (6)	0·6727 (4)	0·3994 (4)	4·46
C(14)	−0·1110 (6)	0·6480 (4)	0·4608 (4)	3·76
O(142)	−0·0906 (4)	0·7156 (3)	0·5236 (2)	5·14
C(15)	0·1287 (6)	0·5997 (3)	0·4856 (3)	3·25
C(16)	0·2732 (6)	0·6081 (4)	0·4579 (3)	3·37
O(161)	0·3646 (4)	0·5950 (3)	0·5072 (2)	5·10
C(17)	0·1050 (6)	0·5123 (4)	0·5331 (3)	4·07
C(18)	−0·3098 (8)	0·5195 (5)	0·3681 (5)	6·81
C(19)	−0·1287 (7)	0·6782 (5)	0·0347 (4)	6·41
C(20)	0·4073 (6)	0·6840 (4)	0·2248 (4)	4·66
S(1)	0·0385 (2)	0·4236 (1)	0·4690 (1)	4·28
C(22)	0·2938 (4)	0·4025 (2)	0·3976 (2)	3·79
C(23)	0·3803 (4)	0·3882 (2)	0·3285 (2)	5·30
C(24)	0·3288 (4)	0·3860 (2)	0·2455 (2)	5·30
C(25)	0·1908 (4)	0·3981 (2)	0·2315 (2)	5·21
C(26)	0·1044 (4)	0·4124 (2)	0·3006 (2)	4·35
C(21)	0·1559 (4)	0·4146 (2)	0·3836 (2)	3·48

Table 2. *Bond lengths* (Å) *with e.s.d.'s in parentheses*

C(1)–C(2)	1·530 (7)	C(1)–C(14)	1·530 (8)
C(1) -C(15)	1·549 (8)	C(2)–C(3)	1·514 (8)
C(3)–O(31)	1·466 (6)	C(3)–C(4)	1·531 (8)
O(31)–C(16)	1·339 (6)	C(4)–O(41)	1·445 (7)
C(4)–C(5)	1·534 (7)	C(4)–C(20)	1·497 (8)
C(5)–C(6)	1·534 (7)	C(6)–C(7)	1·519 (9)
C(7)–C(8)	1·318 (8)	C(8)–C(9)	1·509 (9)
C(8)–C(19)	1·575 (9)	C(9)–C(10)	1·527 (9)
C(10)–C(11)	1·486 (9)	C(11)–C(12)	1·322 (9)
C(12)–C(13)	1·522 (9)	C(12)–C(18)	1·51 (1)
C(13)–C(14)	1·520 (9)	C(14)–O(142)	1·444 (7)
C(15)-C(16)	1·500 (8)	C(15)–C(17)	1·553 (7)
C(16)–O(161)	1·205 (7)	C(17)–S(1)	1·815 (6)
S(1)–C(21)	1·775 (4)		

Table 3. *Comparison of the torsion angles* (°) *in cembranolide* 7,11-*dienes*

Values for peunicin, crassin *p*-iodobenzoate and lobophytolide were obtained from the Cambridge Crystallographic Data File, May 1982 update (Allen *et al.*, 1979). The *R* factors for these structures are 0·038, 0·09 and 0·09, respectively.

Atom numbers	Peunicin	Crassin *p*-iodobenzoate	Crassin phenyl sulfide	Lobophytolide
1–2–3–4	−77·9	176·4	178·0 (4)	121·8
2–3–4–5	157·2	−57·0	−58·9 (6)	−176·5
3–4–5–6	22·4	−65·9	−75·7 (6)	−124·4
4–5–6–7	−80·7	81·6	72·4 (6)	65·1
5–6–7–8	179·3	99·4	108·7 (6)	−159·7
6–7–8–9	179·9	173·1	−177·4 (5)	−178·5
7–8–9–10	115·4	122·0	117·7 (6)	104·1
8–9–10–11	−67·3	−52·7	−52·5 (7)	65·2
9–10–11–12	119·6	−97·6	−114·5 (7)	83·5
10–11–12–13	173·3	179·2	−178·5 (6)	−149·1
11–12–13–14	41·1	−128·8	−117·7 (7)	−26·2
12–13–14–1	102·0	61·5	55·7 (7)	169·0
13–14–1–2	−31·4	52·8	57·5 (6)	−131·7
14–1–2–3	−75·1	−176·3	−176·8 (5)	62·3

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* Lists of structure factors, anisotropic thermal parameters H-atom parameters and bond angles have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39109 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

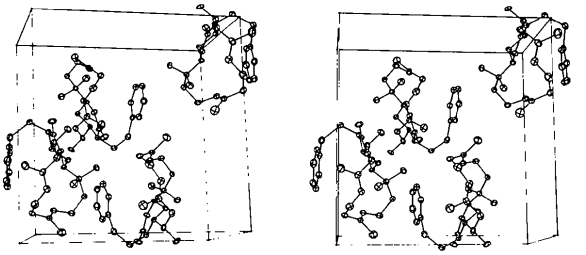

Fig. 2. The molecular packing viewed approximately along the *a* axis.

The Cremer–Pople (1975) puckering parameters for the pyran ring are: $q_2 = 0{\cdot}427$, $q_3 = 0{\cdot}316$ Å, $\varphi_2 = 239°$, $Q = 0{\cdot}531$ Å, $\theta = 53{\cdot}5°$. The torsion angles around the single bonds 6–7, 8–9, 10–11 and 12–13 flanking the double bonds in the 14-membered ring, which are of interest in relation to unsaturated-fatty-acid conformations, are 108·7 (6), 117·7 (6), −114·5 (7) and −117·7 (7)°, respectively.

The packing diagram is shown in Fig. 2. Intermolecular contacts are normal. Both hydroxyls form hydrogen bonds to the neighboring molecule related by a twofold screw axis along **a**.

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Structure of 3-Hydroxyimino-2-butanone Thiosemicarbazone, a Tridentate N—S Ligand, $C_5H_{10}N_4OS$

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Abstract. $M_r = 174{\cdot}23$, monoclinic, $P2_1/c$, $a = 11{\cdot}090\,(3)$, $b = 12{\cdot}691\,(4)$, $c = 6{\cdot}112\,(2)$ Å, $\beta = 104{\cdot}51\,(2)°$, $V = 832{\cdot}8\,(5)$ Å^3, $Z = 4$, $D_m = 1{\cdot}370$, $D_x = 1{\cdot}389$ Mg m^{-3}, $\lambda(\text{Mo } K\alpha) = 0{\cdot}7107$ Å, $\mu = 0{\cdot}335$ mm^{-1}, $F(000) = 368$, $T = 297$ K. Final $R = 0{\cdot}035$ for 1169 observed reflections. The molecule is in the fully extended form. Electron delocalization in the thiosemicarbazide and oxime moieties is observed. In packing, pairs of intermolecular N—H···S hydrogen bonds across centres of symmetry result in dimerization of the molecules. Intramolecular N—H···N hydrogen bonds lend conformational stability to the molecules.

Introduction. Antibacterial, antiviral and even antitumour activities have been observed in some N,S donor ligands such as substituted thiosemicarbazides and thiosemicarbazones (Johnson, Joyner & Perry, 1952; French & Blanz, 1965, 1966; Bauer, 1972; William, 1972). These activities are, in general, attributed to their ability to form metal chelates (Sorkin, Roth & Erlenmeyer, 1952; Cymerman, Willis, Rubbo & Edgar, 1955; Kirschner, Wei, Francis & Bergman, 1966) and their reductive capacities (Palenik, Rendle & Carter, 1974).

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