Crystal and Molecular Structure of Goniothalamin [(+)-(6*S*)-5,6-Dihydro-6-styryl-2-pyrone]

By **Peter J. Clarke** *† and **Peter J. Pauling**, William Ramsay, Ralph Forster, and Christopher Ingold Laboratories, University College London, Gower Street, London WC1E 6BT

The crystal structure of goniothalamin has been determined from three-dimensional *X*-ray diffraction data. Crystals are monoclinic, with $a = 9{\cdot}710(3)$, $b = 9{\cdot}967(5)$, $c = 5{\cdot}691(3)$ Å, $\beta = 98{\cdot}72(3)°$, $Z = 2$, space group $P2_1$. The structure was solved by direct methods and refined by full-matrix least-squares to R 0·040 for 789 observed reflections. The planar styryl group adopts a pseudo-equatorial position on the lactone ring. and is inclined at 88·1° to the mean plane of it. The ester group of the unsaturated lactone is non-planar, and the lactone ring has a modified skew-boat conformation.

GONIOTHALAMIN [(+)-(6*S*)-5,6-dihydro-6-styryl-2-pyrone], an αβ-unsaturated δ-lactone, may be isolated from *Cryptocarya caloneura* (Scheff) Kostermans (Lauraceae) [1] and from certain species of the genus *Goniothalamus* (Annonaceae).[2] It has been shown to have antifungal and CNS activity.[2] The absolute configurations of goniothalamin and the structurally related natural product kawain [(+)-(6*R*)-5,6-dihydro-4-methoxy-6-styryl-2-pyrone] have been determined by degradation to malic acid.[1,3] These configurations are, however, only consistent with results of c.d. studies [4,5] if the styryl group adopts a pseudo-axial position on the lactone ring in goniothalamin and a pseudo-equatorial position in kawain. Such a difference between two closely related molecules would be rather unexpected. We have determined the crystal structure of goniothalamin in order to establish the conformation of the molecule in the solid state. Studies on the conformation of goniothalamin in solution will appear elsewhere.[6]

EXPERIMENTAL

Crystals of goniothalamin were grown from light petroleum. Crystal faces were {110}, {$\bar{1}$10}, {001} and (0$\bar{1}$0).

Crystal Data.—$C_{13}H_{12}O_2$, $M = 200{\cdot}08$. Monoclinic. $a = 9{\cdot}710(3)$, $b = 9{\cdot}967(5)$, $c = 5{\cdot}691(3)$ Å, $\beta = 98{\cdot}72(3)°$, $U = 544{\cdot}4$ Å^3, $D_m = 1{\cdot}23$ g cm^{-3} (by flotation), $Z = 2$, $D_c = 1{\cdot}22$ g cm^{-3}. Space group $P2_1$. Mo-K_α radiation, $\lambda = 0{\cdot}7107$ Å; μ(Mo-K_α) = 0·9 cm^{-1}.

Intensity Measurements.—*X*-Ray diffraction intensities with Bragg angles (θ) in the range 2·5—27·5° were measured with a computer-controlled [7] Stoe four-circle diffractometer by use of Mo-K_α radiation, a graphite monochromator, and a ω—2θ scan. Reflections were integrated over a peakwidth of 1·6° with steps of 0·02° in ω, and a counting time of 5 s per step. Of 1513 unique reflections, 789, having $I \geqslant 3\sigma(I)$ were considered observed. Intensities were corrected for Lorentz-polarisation effects, but not for absorption or extinction.

Structure Solution and Refinement.—The structure was solved by direct methods from intensities with $\theta \leqslant 22{\cdot}5°$ by use of the MULTAN program,[8] and refined by full-matrix least-squares. The *y* co-ordinate of C(2) was fixed to define the origin. Refinement of co-ordinates and isotropic temperature factors, for all observed unique reflections, reduced the *R* factor from 0·385 to 0·116, at which point all the hydrogen atoms were located from a difference-Fourier synthesis. These hydrogen atoms were included in the structure-factor calculations, and further refinement of co-ordinates and anisotropic temperature factors for the non-hydrogen atoms reduced *R* to 0·051. Subsequent refinement, including co-ordinates for the hydrogen atoms, gave a final *R* of 0·040. Atomic scattering factors for carbon and oxygen were taken from ref. 9, and for hydrogen from ref. 10. The function minimised was $\Sigma w(|F_o| - |F_c|)^2$ with $w = 1$ for all the data. Final atomic parameters are given for non-hydrogen atoms in Table 1 and for hydrogen atoms in Table 2. Interatomic distances and angles [11] are presented in Table 3, least-squares planes [12] in Table 4, and torsion angles in Table 5.

---

† *Present address:* Inorganic Chemistry Laboratory, South Parks Road, Oxford OX1 3QR.

[1] J. R. Hlubeck and A. V. Robertson, *Austral. J. Chem.*, 1967, **20**, 2199.

[2] K. Jewers, J. B. Davies, J. Dougan, A. H. Manchanda, G. Blunden, Aye Kyi, and S. Wetchapinan, *Phytochem.*, 1972, **11**, 2025.

[3] H. Achenbach and N. Theobald, *Chem. Ber.*, 1974, **107**, 735.

[4] A. F. Beecham, *Tetrahedron*, 1972, **28**, 5543.

[5] K. Jewers, Joint Meeting Phytochem. and Pharm. Soc., Chelsea College, London, January 1972.

[6] K. Jewers, J. B. Davies, J. Dougan, A. H. Manchanda, Aye Kyi, and S. Wetchapinan, to be published.

[7] W. R. Busing, R. D. Ellison, H. A. Levy, S. P. King, and R. T. Roseberry, U.S. Atomic Energy Commission, Oak Ridge, Tennessee, Report ORNL 4143, 1968.

[8] G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368.

[9] D. T. Cromer and J. T. Waber, *Acta Cryst.*, 1965, **18**, 104.

[10] 'International Tables for *X*-Ray Crystallography,' vol. 3, Kynoch Press, Birmingham, 1962.

[11] W. R. Busing, K. O. Martin, and H. A. Levy, U.S. Atomic Energy Commission, Oak Ridge, Tennessee, Report ORNL TM 306, 1964.

[12] W. C. Hamilton, *Acta Cryst.*, 1961, **14**, 185.

TABLE 1

Fractional co-ordinates (× 10^4) and thermal parameters * (× 10^4) for non-hydrogen atoms, with estimated standard deviations in parentheses

Atom	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(1)	4158(3)	167(6)	2481(5)	538(16)	692(19)	743(19)	85(16)	248(15)	128(18)
C(2)	5130(5)	600	1209(9)	745(33)	622(33)	730(33)	−29(26)	184(27)	−34(27)
C(3)	6531(5)	36(7)	1782(9)	567(29)	623(30)	778(32)	−106(25)	269(24)	−46(29)
C(4)	6897(5)	−733(7)	3600(10)	517(25)	818(40)	866(36)	24(26)	239(25)	50(33)
C(5)	5866(5)	−1141(9)	5150(10)	486(25)	1057(45)	846(37)	124(31)	170(24)	327(35)
C(6)	4406(4)	−1102(7)	3793(8)	530(23)	537(26)	667(28)	0(22)	236(20)	42(24)
C(7)	3296(4)	−1178(7)	5352(9)	493(23)	604(30)	787(31)	19(25)	162(21)	36(26)
C(8)	2274(4)	−2039(7)	5009(8)	477(24)	560(28)	698(32)	17(22)	118(22)	49(24)
C(9)	1123(4)	−2185(7)	6423(8)	445(23)	523(28)	688(31)	54(21)	100(20)	99(23)
C(10)	980(5)	−1361(8)	8311(9)	576(27)	744(37)	729(30)	−143(27)	174(23)	−20(27)
C(11)	−135(5)	−1536(8)	9596(10)	626(30)	913(42)	741(34)	−52(31)	171(26)	−14(29)
C(12)	−1108(5)	−2535(7)	8928(10)	435(25)	832(37)	844(36)	82(25)	186(24)	200(30)
C(13)	−965(5)	−3343(7)	7066(10)	524(28)	705(36)	914(40)	−75(26)	141(27)	50(32)
C(14)	131(5)	−3181(7)	5788(10)	569(28)	589(32)	815(35)	−15(25)	70(26)	−6(26)
O(2)	4804(5)	1453(7)	−251(9)	1041(30)	1044(32)	1117(32)	91(26)	332(24)	502(28)

* The temperature factor exponent takes the form: $[-2\pi^2(h^2a^{*2}U_{11}\cdots + 2hka^*b^*U_{12}\cdots)]$.

Observed and calculated structure factors are listed in Supplementary Publication No. SUP 21173 (3 pp.).*

DISCUSSION

Description of the Structure.—A perspective view of the goniothalamin molecule is given in Figure 1. In general, bond lengths and angles have their expected values. The bond angle C(7)–C(8)–C(9) is enlarged to 127·1(5)° by the non-bonded interaction between atoms C(7) and H(7) and C(10) and H(10), but there is no tendency to relieve this interaction by rotation about the C(8)–C(9) bond and the styryl group is planar (Table 4). The distances C(2)–O(2) (1·20 Å) and C(3)–C(4) (1·29 Å) are somewhat shorter than previously found (1·24 and 1·35—1·38 Å respectively) in αβ-unsaturated δ-lactones.[13-15] Indeed, the value for

TABLE 2

Fractional co-ordinates (× 10^3) for hydrogen atoms, with estimated standard deviations in parentheses

Atom	x	y	z
H(3)	715(6)	24(7)	79(10)
H(4)	789(5)	−101(7)	398(10)
H(5A)	598(6)	−59(6)	666(11)
H(5B)	612(6)	−208(7)	593(11)
H(6)	431(6)	−182(6)	252(10)
H(7)	331(6)	−37(6)	654(10)
H(8)	223(6)	−271(6)	356(11)
H(10)	157(6)	−62(7)	879(11)
H(11)	−23(6)	−88(7)	1091(10)
H(12)	−195(6)	−255(6)	993(10)
H(13)	−176(6)	−396(7)	654(10)
H(14)	16(6)	−379(8)	427(11)

For hydrogen, U_{iso} 0·076 Å^2.

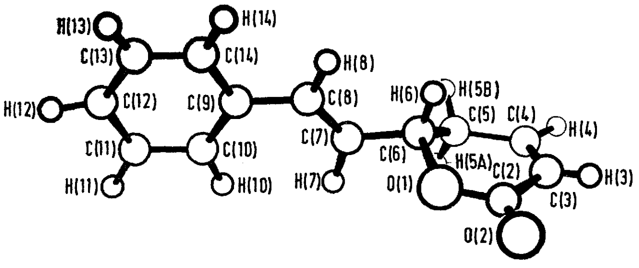

FIGURE 1 A perspective view of the molecule

TABLE 3

Interatomic distances (Å) and angles (°), with estimated standard deviations in parentheses

(*a*) Distances			
O(1)–C(2)	1·345(5)	C(12)–C(13)	1·355(7)
O(1)–C(6)	1·470(6)	C(13)–C(14)	1·387(7)
C(2)–O(2)	1·197(6)	C(3)–H(3)	0·91(6)
C(2)–C(3)	1·462(7)	C(4)–H(4)	0·99(5)
C(3)–C(4)	1·293(7)	C(5)–H(5A)	1·01(6)
C(4)–C(5)	1·488(6)	C(5)–H(5B)	1·05(7)
C(5)–C(6)	1·508(6)	C(6)–H(6)	1·01(6)
C(6)–C(7)	1·498(6)	C(7)–H(7)	1·05(6)
C(7)–C(8)	1·304(6)	C(8)–H(8)	1·06(6)
C(8)–C(9)	1·480(6)	C(10)–H(10)	0·95(6)
C(9)–C(10)	1·372(6)	C(11)–H(11)	1·01(6)
C(9)–C(14)	1·396(6)	C(12)–H(12)	1·07(6)
C(10)–C(11)	1·406(7)	C(13)–H(13)	1·00(6)
C(11)–C(12)	1·386(8)	C(14)–H(14)	1·06(7)
(*b*) Angles			
C(2)–O(1)–C(6)	118·4(3)	C(5)–C(4)–H(4)	120·7(34)
O(1)–C(2)–O(2)	117·9(5)	C(4)–C(5)–H(5A)	110·9(34)
O(1)–C(2)–C(3)	117·5(4)	C(4)–C(5)–H(5B)	111·1(32)
O(2)–C(2)–C(3)	124·5(5)	C(6)–C(5)–H(5A)	113·2(34)
C(2)–C(3)–C(4)	122·7(4)	C(6)–C(5)–H(5B)	112·4(34)
C(3)–C(4)–C(5)	120·6(5)	H(5A)–C(5)–H(5B)	97·8(46)
C(4)–C(5)–C(6)	110·7(4)	O(1)–C(6)–H(6)	104·5(33)
O(1)–C(6)–C(5)	110·5(4)	C(5)–C(6)–H(6)	109·2(32)
O(1)–C(6)–C(7)	105·5(4)	C(7)–C(6)–H(6)	113·1(32)
C(5)–C(6)–C(7)	113·6(4)	C(6)–C(7)–H(7)	113·6(30)
C(6)–C(7)–C(8)	122·9(5)	C(8)–C(7)–H(7)	122·5(30)
C(7)–C(8)–C(9)	127·1(5)	C(7)–C(8)–H(8)	118·3(31)
C(8)–C(9)–C(10)	122·6(4)	C(9)–C(8)–H(8)	114·5(32)
C(8)–C(9)–C(14)	118·6(4)	C(9)–C(10)–H(10)	124·4(35)
C(10)–C(9)–C(14)	118·7(4)	C(11)–C(10)–H(10)	114·9(35)
C(9)–C(10)–C(11)	120·6(5)	C(10)–C(11)–H(11)	118·1(33)
C(10)–C(11)–C(12)	119·5(5)	C(12)–C(11)–H(11)	122·2(32)
C(11)–C(12)–C(13)	119·7(5)	C(11)–C(12)–H(12)	114·3(31)
C(12)–C(13)–C(14)	121·2(5)	C(13)–C(12)–H(12)	125·9(31)
C(9)–C(14)–C(13)	120·2(5)	C(12)–C(13)–H(13)	116·1(34)
C(2)–C(3)–H(3)	116·9(38)	C(14)–C(13)–H(13)	122·1(34)
C(4)–C(3)–H(3)	120·4(38)	C(9)–C(14)–H(14)	121·0(34)
C(3)–C(4)–H(4)	118·6(34)	C(13)–C(14)–H(14)	118·6(34)

---

* See Notice to Authors No. 7, in *J.C.S. Perkin II*, 1974, Index issue.

[13] A. T. McPhail and G. A. Sim, *J. Chem. Soc.* (*B*), 1968, 1104.

[14] Y. Ogihara, Y. Iitaka, and S. Shibata, *Acta Cryst.*, 1968, **B24**, 1037.

[15] H. Lynton, *Canad. J. Chem.*, 1970, **48**, 307.

the C(2)–O(2) bond is closer to the range (1·18—1·22 Å) found for saturated δ-lactones.[16–19]

The styryl group adopts a pseudo-equatorial position on the lactone ring and is inclined at an angle of 88·0° to the mean plane of atoms O(1), O(2), C(2), and C(3), and of 86·5° to the mean plane of C(2)—(5). These latter groups of atoms are also planar. However, the ester group [plane (3), Table 4] is twisted, with torsion angle −18·8(6)°. Its non-planarity is due to the rigidity imparted to the lactone ring by the C(3)–C(4) double bond. Only C(6) is able to move far enough out of plane to relieve the severe angle strain which would otherwise result. Similar strain-relieving factors are responsible for the torsion angle of 169·3(6)° in the αβ-unsaturated system O(2)–C(2)–C(3)–C(4).

TABLE 4

Equations of least-squares planes relative to crystallographic axes. Deviations (Å) of atoms from the plane are given in square brackets, with estimated standard deviations in parentheses

Plane (1): C(6)—(14)

$$4{\cdot}4934x - 6{\cdot}3605y + 3{\cdot}0621z = 3{\cdot}8544$$

[C(6) −0·012(6), C(7) 0·014(6), C(8) −0·002(6), C(9) 0·007(5), C(10) −0·004(6), C(11) 0·000(7), C(12) −0·006(6), C(13) 0·002(6), C(14) 0·000(6)]

Plane (2): C(9)—(14)

$$4{\cdot}4717x - 6{\cdot}3559y + 3{\cdot}7061z = 3{\cdot}8645$$

[C(9) 0·002(5), C(10) −0·005(6), C(11) 0·003(7), C(12) −0·002(6), C(13) 0·002(6), C(14) −0·004(6)]

Plane (3): C(6), O(1), C(2), O(2), C(3)

$$1{\cdot}4312x + 6{\cdot}3842y + 4{\cdot}1124z = 1{\cdot}6266$$

[C(6) −0·140(6), O(1) 0·095(5), C(2) −0·012(4), O(2) −0·115(7), C(3) 0·063(6)]

Plane (4): O(1), O(2), C(2), C(3)

$$1{\cdot}4907x + 7{\cdot}1413y + 3{\cdot}6956z = 1{\cdot}6470$$

[O(1) 0·009(5), C(2) −0·007(4), O(2) 0·014(7), C(3) 0·010(6), C(6) −0·375(6)]

Plane (5): C(2)—(5)

$$1{\cdot}8048x + 7{\cdot}8964y + 3{\cdot}1091z = 1{\cdot}7741$$

[C(2) 0·001(3), C(3) −0·013(6), C(4) 0·011(7), C(5) −0·015(8), O(1) −0·120(5), O(2) 0·162(7), C(6) −0·670(6)]

Plane (6): O(1), O(2), C(2)—(6)

$$5{\cdot}7491x + 7{\cdot}1423y + 3{\cdot}8585z = 1{\cdot}2039$$

[O(1) 0·112(5), C(2) −0·014(4), O(2) 0·013(7), C(3) −0·116(6), C(4) 0·058(6), C(5) 0·305(8), C(6) −0·274(6)]

TABLE 5

Torsion angles (°), with estimated standard deviations in parentheses *

O(1)–C(2)–C(3)–C(4)	−7·9(7)	C(4)–C(3)–C(2)–O(2)	169·3(6)
O(1)–C(6)–C(5)–C(4)	−47·9(7)	C(4)–C(5)–C(6)–C(7)	−166·2(5)
O(1)–C(6)–C(7)–C(8)	110·5(5)	C(5)–C(6)–C(7)–C(8)	−128·3(6)
C(2)–O(1)–C(6)–C(5)	46·7(5)	C(6)–O(1)–C(2)–O(2)	163·8(5)
C(2)–O(1)–C(6)–C(7)	169·9(4)	C(6)–C(7)–C(8)–C(9)	−179·3(5)
C(2)–C(3)–C(4)–C(5)	3·2(8)	C(7)–C(8)–C(9)–C(10)	1·9(7)
C(3)–C(2)–O(1)–C(6)	−18·8(6)	C(7)–C(8)–C(9)–C(14)	−179·4(5)
C(3)–C(4)–C(5)–C(6)	25·4(8)		

* The sign convention is that given in W. Klyne and V. Prelog, *Experientia*, 1960, **16**, 521.

The conformation of the αβ-unsaturated δ-lactone ring may be regarded as a modified skew-boat, since atoms C(2)—(5) are coplanar, and atoms O(1) and C(6) lie on the same side of the plane but deviate from it by by different amounts (Table 4). Conformations almost identical to this have been observed in other αβ-unsaturated δ-lactones,[4] all in marked contrast to the situation in saturated δ-lactones[16–19] where the ester group is always planar and the atoms equivalent to C(4) and C(5) are generally disposed on opposite sides of the ester plane.

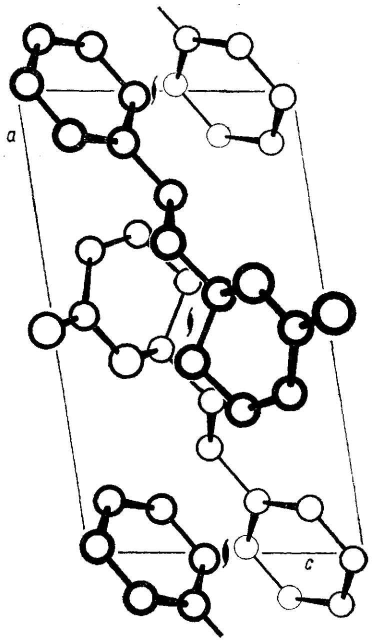

FIGURE 2 The crystal structure viewed normal to (010)

The molecular packing is shown in Figure 2 and is based on the usual van der Waals interaction. The closest intermolecular approach of 3·325(7) Å is between C(6) and O(2) [at $1 - x$, $y - \frac{1}{2}$, $\bar{z}$], and although the C–H ··· O angle is 153·2(45)°, the distance is too great for hydrogen bonding.

We thank the M.R.C for financial support, Dr. K. Jewers for the crystals of goniothalamin and for his useful criticisms of the original manuscript, and Miss P. Brennan for assistance.

[4/1568 *Received*, 29*th July*, 1974]

---

[16] M. Natsume and Y. Iitaka, *Acta Cryst.*, 1966, **20**, 197.

[17] G. Kartha and D. J. Haas, *J. Amer. Chem. Soc.*, 1964, **86**, 3630.

[18] A. T. McPhail and G. A. Sim, *J. Chem. Soc.* (*B*), 1966, 318.

[19] G. Ferguson and K. M. S. Islam, *J. Chem. Soc.* (*B*), 1969, 162.