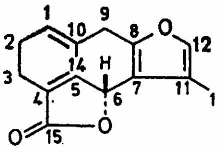
Crystal and Molecular Structure of the Germacrane Furanosesquiterpenoid Linderalactone

By **Hirozo Koyama** * and **Yoshiko Mizuno-Tsukuda**, Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-ku, Osaka, 553, Japan

The crystal structure of the title compound (I) has been determined by three-dimensional *X*-ray analysis from diffractometer data. Crystals are monoclinic, $a = 8.804(1)$, $b = 11.194(2)$, $c = 6.630(1)$ Å, $\beta = 105.6(2)°$, $Z = 2$, space group $P2_1$. The structure was solved by direct methods and refined by full-matrix least-squares calculations to a final R of 0.064 for 941 independent observed reflexions. Hydrogen atoms were located from a difference-Fourier synthesis. The molecule consists of a furan, γ-lactone, and ten-membered ring. The conformation of the ten-membered ring was similar to those previously observed in several other germacrane sesquiterpenoids. The transannular separation in the ten-membered ring is distinctly short [C(1) ··· C(4) 2.78 Å].

LINDERALACTONE, $C_{15}H_{16}O_3$, a germacrane furanosesquiterpenoid isolated[1] from the root of *Lindera strychnifolia*, was assigned[2,3] the structure (I) on the basis of chemical and spectroscopic investigations. In conjunction with this study, we have recently determined[4] the structure of lindenenol. The present *X*-ray crystal structure analysis was undertaken in order to elucidate the detailed stereochemistry of linderalactone (I).



(I)

EXPERIMENTAL

Crystals were prepared[5] and recrystallized from acetone–light petroleum as colourless prisms, m.p. 136—138 °C,

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elongated along the b axis. Preliminary cell data were determined from Weissenberg and precession photographs by use of Cu-K_α (λ 1.541 8 Å) radiation, and accurate unit-cell dimensions were obtained by least-squares refinement of the setting angles of 20 reflexions measured on the automatic diffractometer.

Crystal Data.—$C_{15}H_{16}O_3$, $M = 244.2$. Monoclinic, $a = 8.804(1)$, $b = 11.194(2)$, $c = 6.630(1)$ Å, $\beta = 105.6(2)°$, $U = 630.2$ Å^3, $D_m = 1.288$ (by flotation), $Z = 2$, $D_c = 1.287$ g cm^{-3}, $F(000) = 260$. Space group $P2_1$ (C_2^2) from systematic absences: $0k0$ when k is odd. Mo-K_α radiation, $\lambda = 0.710 7$ Å; μ(Mo-K_α) = 0.900 cm^{-1}.

Three-dimensional intensity data were collected on a Hilger and Watts automatic four-circle Y 290 diffractometer controlled by a PDP 8 computer. Integrated intensities were measured for $\theta < 27.5°$ by the θ—2θ scan technique with Mo-K_α radiation and a scintillation counter (with a Zirconium filter and pulse-height analyser). Each reflexion was integrated in 80 steps of intervals of 0.01°. A standard reflexion was monitored every 10 reflexions. The scan counts (P) and background counts (B_1, B_2) were combined to yield the integrated intensities $I = P - 2(B_1 + B_2)$.

In this way 1 526 independent reflexions were recorded, of which 941 were considered observed, having intensities $I > 3\sigma(I)$, and were used in the subsequent analysis. All intensities were corrected for Lorentz and polarization factors, and the normalized structure factors $|E|$ as well as structure amplitudes $|F|$ were derived. No absorption corrections were applied since the specimen was considered to be sufficiently small (0.25 × 0.31 × 0.27 mm).

Structure Analysis.—The structure was solved by direct methods, using the programme DIRECTER for automatic structure analysis, written [6] for the CDC 6600 computer.

TABLE 1

A simplified layout of the calculation

Start ⟶ Input data ⟶

- ⟶ Origin: (I), Definition (origin, enantiomorph); 3 kinds of origin sets
- ⟶ Symbol: (II), Calculation (phase relationships); starting sets (with additional symbols)
- ⟶ Tangent I: (III), Tangent refinement; select (best starting sets $\leqslant 5$). Criteria: R, Q, α,t
- ⟶ Tangent II: Phase recalculation (E maps by best sets)
- ⟶ E Map: (IV) 3-d E map; scan and sort (peak heights and co-ordinates); peaks, atoms
- ⟶ Figure: (V), Plot projection of molecule; equ. point bond distance; F, E, ϕ Table

This large program has been constructed from several others [7-11] in order to solve the crystal structure completely automatically. When the data are loaded, the program carries out the sequence of calculations listed (Table 1). Using 163 reflexions with $|E| > 1.50$, the programme automatically selects three kinds of origin sets and Σ_2 relationships were generated. This procedure yielded 364 starting sets as input to the tangent I formula.

Selection of the best five phase sets in tangent refinement I is based on the low values of R and Q, and the high values of α and t. On this basis, E maps were calculated and the atomic co-ordinates of 18 light atoms were found. The approximate co-ordinates of the 18 atoms were refined [12] isotropically by three cycles of full-matrix least-squares calculations to R 0.126, and anisotropically to R 0.077 using a CDC 6600 computer. At this stage, a three-dimensional difference-Fourier synthesis was calculated and the positions of the 16 hydrogen atoms were found. The final five cycles of full-matrix least-squares refinement decreased R to 0.064 for the 941 observed reflexions. In this refinement a weighting scheme of the type given by Cruickshank was applied, *i.e.* $w = (a + b|F_o| + c|F_o|^2)^{-1}$, where $a = 1.16$, $b = -0.09$, and $c = 0.025$. All hydrogen atoms were included in the final refinement with isotropic temperature factors (B values fixed at 2.50 Å^2).

Observed and calculated structure amplitudes and anisotropic thermal parameters are listed in Supplementary Publication No. SUP 21907 (4 pp., 1 microfiche).* Atomic scattering factors used in all calculations were taken from ref. 13 for non-hydrogen and from ref. 14 for hydrogen atoms. Final positional parameters with their estimated standard deviations are given in Tables 2 and 3.

RESULTS AND DISCUSSION

The absolute configuration of the molecule has already been determined [2,3] by a Cope rearrangement and n.m.r. spectral data. This results leads to the conclusion that the parameter of Tables 2 and 3 represent the left-hand co-ordinate system. The absolute configuration of the

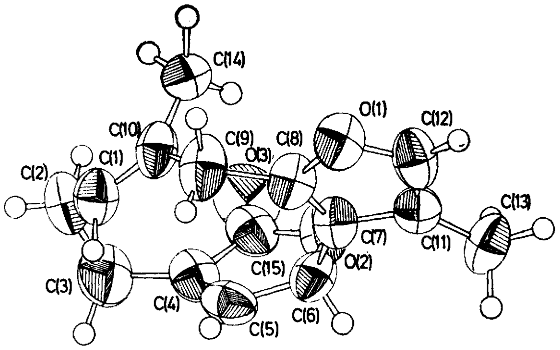

FIGURE 1 An ORTEP drawing of the linderalactone molecule viewed down the $-a$ axis

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* See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1976, Index issue.

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molecule of linderalactone is illustrated[15] in Figure 1. The molecule consists of the three rings, as predicted from the chemical evidence: a furan ring, a γ-lactone ring, and a ten-membered ring which contains two *trans* double bonds at the C(1)–C(10) and C(4)–C(5) positions. The hydrogen atom at C(6) lies on the β-face of the molecule. The conformation of the ten-membered ring resembles that of several other previously reported germacrane sesquiterpenoids.[16–24]

TABLE 2

Final fractional atomic co-ordinates ($\times 10^4$) with estimated standard deviations in parentheses

Atom	*x*	*y*	*z*
O(1)	6 971(5)	2 428(0)	2 389(7)
O(2)	5 823(6)	6 151(5)	3 792(8)
O(3)	7 342(8)	7 713(7)	5 224(10)
C(1)	9 313(9)	4 421(8)	8 748(12)
C(2)	9 600(12)	5 653(9)	9 536(14)
C(3)	8 041(12)	6 287(10)	9 404(15)
C(4)	6 887(9)	6 053(7)	7 315(10)
C(5)	6 031(9)	5 080(9)	6 783(11)
C(6)	5 327(8)	5 023(8)	4 527(11)
C(7)	5 821(8)	3 988(7)	3 389(10)
C(8)	7 002(8)	3 202(7)	3 966(12)
C(9)	8 335(11)	2 964(8)	5 900(14)
C(10)	9 208(8)	4 082(7)	6 800(10)
C(11)	4 949(8)	3 688(7)	1 311(10)
C(12)	5 719(9)	2 732(7)	778(11)
C(13)	3 521(9)	4 294(9)	8(15)
C(14)	9 888(11)	4 758(11)	5 299(14)
C(15)	6 774(10)	6 764(8)	5 458(11)

TABLE 3

Final fractional hydrogen atom co-ordinates ($\times 10^3$)

Atom	*x*	*y*	*z*
H(1)	860	395	940
H(2a)	1 011	610	867
H(2b)	1 022	558	1 078
H(3a)	824	714	948
H(3b)	749	610	1 053
H(5)	594	446	755
H(6)	422	493	435
H(9a)	798	253	672
H(9b)	915	251	553
H(12)	547	227	−52
H(13a)	254	415	63
H(13b)	301	386	−146
H(13c)	390	511	−32
H(14a)	1 074	435	459
H(14b)	908	521	436
H(14c)	1 071	516	603

Intramolecular bond distances and angles are given in Table 4, together with their estimated standard deviations computed from the least-squares residuals. Mean estimated standard deviations are *ca.* 0.01 Å and 0.7°. Most observed bond distances and angles are comparable to those found in other germacrane sesquiterpenoids.[18,20,21,23,24] Two or three differences which appear to be significant in terms of the estimated standard deviations are more likely to indicate a slight underestimation of errors.

Although the C–C single-bonds in the ten-membered ring vary over a wide range (1.472—1.526 Å), for the most part they do not differ significantly from their expected values.[25] The bond distances in the furan and γ-lactone rings are similar to those found in a recent structure determination.[4,21,23,24,26] The mean terminal Me bond distance at C(10) and C(11) is 1.491 Å, which is noticeably short. Bond distances involving hydrogen atoms are also given [Table 3(*c*)]; the means for C–H (0.96 Å) are less than the internuclear separations (1.08 Å) measured spectroscopically.

TABLE 4

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

(*a*) Bond distances

O(1)–C(8)	1.352(9)	C(4)–C(15)	1.447(11)
O(1)–C(12)	1.359(8)	C(5)–C(6)	1.460(10)
O(2)–C(6)	1.461(11)	C(6)–C(7)	1.508(12)
O(2)–C(15)	1.379(9)	C(7)–C(8)	1.337(10)
O(3)–C(15)	1.201(12)	C(7)–C(11)	1.428(8)
C(1)–C(2)	1.472(14)	C(8)–C(9)	1.515(10)
C(1)–C(10)	1.325(11)	C(9)–C(10)	1.506(12)
C(2)–C(3)	1.526(16)	C(10)–C(14)	1.495(14)
C(3)–C(4)	1.507(11)	C(11)–C(12)	1.362(12)
C(4)–C(5)	1.318(13)	C(11)–C(13)	1.486(10)

(*b*) Valency angles

C(8)–O(1)–C(12)	107.0(5)	O(1)–C(8)–C(7)	110.2(5)
C(6)–O(2)–C(15)	109.5(5)	O(1)–C(8)–C(9)	113.1(6)
C(2)–C(1)–C(10)	125.1(8)	C(7)–C(8)–C(9)	136.6(7)
C(1)–C(2)–C(3)	110.3(8)	C(8)–C(9)–C(10)	112.8(7)
C(2)–C(3)–C(4)	110.4(8)	C(1)–C(10)–C(9)	121.3(8)
C(3)–C(4)–C(5)	125.9(8)	C(1)–C(10)–C(14)	124.5(8)
C(3)–C(4)–C(15)	124.3(8)	C(9)–C(10)–C(14)	114.1(7)
C(5)–C(4)–C(15)	108.7(6)	C(7)–C(11)–C(12)	104.8(6)
C(4)–C(5)–C(6)	111.5(8)	C(7)–C(11)–C(13)	127.5(7)
O(2)–C(6)–C(5)	102.7(6)	C(12)–C(11)–C(13)	127.6(6)
O(2)–C(6)–C(7)	110.1(6)	O(1)–C(12)–C(11)	110.4(6)
C(5)–C(6)–C(7)	116.4(7)	O(2)–C(15)–O(3)	121.4(7)
C(6)–C(7)–C(8)	131.8(6)	O(2)–C(15)–C(4)	107.3(7)
C(6)–C(7)–C(11)	120.6(6)	O(3)–C(15)–C(4)	131.2(7)
C(8)–C(7)–C(11)	107.4(6)		

(*c*) Bond distances (Å) associated with hydrogen-atom positions

C(1)–H(1)	0.99	C(9)–H(9b)	0.95
C(2)–H(2a)	0.96	C(12)–H(12)	0.97
C(2)–H(2b)	0.86	C(13)–H(13a)	1.05
C(3)–H(3a)	0.97	C(13)–H(13b)	1.07
C(3)–H(3b)	1.01	C(13)–H(13c)	1.02
C(5)–H(5)	0.87	C(14)–H(14a)	1.08
C(6)–H(6)	0.95	C(14)–H(14b)	0.95
C(9)–H(9a)	0.84	C(14)–H(14c)	0.89

The bond angles in the furan ring and γ-lactone ring are close to their expected value.[4,25,26] The mean inter-

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bond angle in the ten-membered ring is 112.5° except for the angles at atoms C(1), C(4), C(5), C(7), C(8), and C(10), which are slightly, but not significantly, greater than the normal tetrahedral angle of 109.4°. Maximum distorsion of bond angles occurs at C(8) in the ten-membered ring. The angle C(7)–C(8)–C(9) of 136.6° gives an indication of the strain imposed at the juncture between the furan and the ten-membered ring. The torsion angles describing relationships within the ten-membered ring were calculated (Table 5). The endocyclic *trans* double-bonds in the ten-membered ring are generally subject to considerable strain, and in accord with this both the C(9)–C(10)–C(1)–C(2) and C(3)–C(4)–C(5)–C(6) torsion angles (−156.5 and −166.5°) differ significantly from the ideal unstrained value of 180°. These values are similar to the corresponding angles in other germacrane sesquiterpenoids.[16-18, 20] Deviations from the best plane through the various atom groups (Table 6) show the furan ring and methyl group to be quite planar. The γ-lactone ring is roughly planar, C(5) and C(6) being slightly displaced (by −0.02 and 0.02 Å) from the plane defined by O(2), O(3), C(4), and C(15). The dihedral angles between the plane of the ten-membered and the γ-lactone ring and the plane of the methyl group defined by C(1), C(9), C(10), C(14) are 75 and 83° respectively. The dihedral angle between the furan ring and the ten-membered ring is *ca.* 16°.

TABLE 5

Torsion angles (°) in the molecule

C(1)–C(2)–C(3)–C(4)	−45.1	C(2)–C(1)–C(10)–C(14)	22.1
C(2)–C(3)–C(4)–C(5)	79.9	C(15)–C(4)–C(5)–C(6)	2.4
C(3)–C(4)–C(5)–C(6)	−166.5	C(4)–C(5)–C(6)–O(2)	−2.9
C(4)–C(5)–C(6)–C(7)	117.5	O(1)–C(8)–C(7)–C(11)	1.1
C(5)–C(6)–C(7)–C(8)	−13.6	C(6)–C(7)–C(11)–C(13)	0.1
C(6)–C(7)–C(8)–C(9)	0.2	O(1)–C(8)–C(9)–C(10)	134.0
C(7)–C(8)–C(9)–C(10)	−46.0	O(2)–C(6)–C(7)–C(11)	−78.3
C(8)–C(9)–C(10)–C(1)	121.4	O(2)–C(6)–C(7)–C(8)	102.7
C(9)–C(10)–C(1)–C(2)	−156.5	C(5)–C(6)–C(7)–C(11)	165.2
C(10)–C(1)–C(2)–C(3)	93.5	C(3)–C(4)–C(15)–O(3)	−11.7
C(8)–C(9)–C(10)–C(14)	−57.3	C(5)–C(4)–C(15)–O(2)	−0.8

TABLE 6

Equations of planes and in square brackets displacements (Å) of the atoms from mean planes; X, Y, Z are orthogonal (Å) co-ordinates

Plane (I): O(2), O(3), C(4), C(15)

$$0.873\,0X - 0.465\,4Y - 0.145\,6Z = 0.336\,7$$

[O(2) −0.00, O(3) −0.00, C(3) 0.25, C(4) −0.00, C(5) −0.02, C(6) 0.02, C(7) 1.22, C(15) 0.00]

Plane (II): C(1), C(9), C(10), C(14)

$$0.793\,8X - 0.522\,6Y + 0.310\,8Z = 4.444\,0$$

[C(1) −0.00, C(2) −0.47, C(8) −1.18, C(9) −0.00, C(10) 0.00, C(14) −0.00]

Plane (III): O(1), C(7), C(8), C(11), C(12)

$$0.703\,5X + 0.613\,4Y - 0.358\,6Z = 5.142\,0$$

[O(1) 0.00, C(6) 0.00, C(7) 0.00, C(8) −0.00, C(9) −0.02, C(11) −0.00, C(12) 0.00, C(13) −0.01, H(12) −0.00]

Plane (IV): C(1)—(10)

$$0.361\,2X + 0.619\,6Y - 0.696\,8Z = 3.722\,9$$

[C(1) −0.32, C(2) 0.29, C(3) 0.06, C(4) 0.32, C(5) −0.50, C(6) 0.16, C(7) 0.20, C(8) −0.04, C(9) −0.48, C(10) 0.28]

In order to obtain detailed information on the molecular shape and the conformational features we have calculated the displacements from the plane through C(6)—(8) in the ten-membered ring (Figure 2). The stereochemistry of linderalactone is characterized by a *syn*-arrangement of the methyl group and γ-lactone ring and by the crossed orientation of two double bonds in the ten-membered ring. The ten-membered ring has the same flattened conformation as was found in other typical

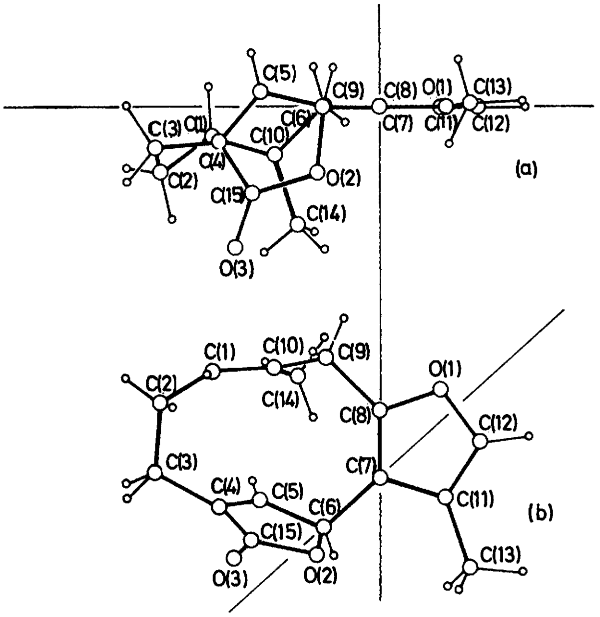

FIGURE 2 The molecule in projection (a) parallel to, and (b) on the C(6)—(8) plane

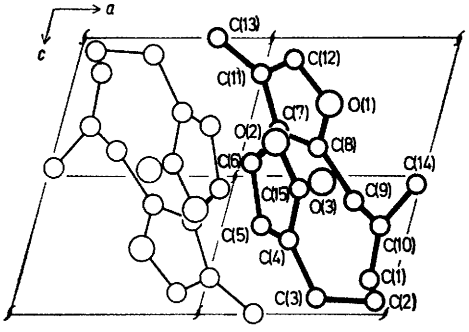

FIGURE 3 Packing of the structure viewed down the *b* axis

TABLE 7

Intermolecular distances (<3.6 Å)

O(2) ··· $C(12^{II})$	3.461	C(1) ··· $C(13^{I})$	3.578
O(3) ··· $C(6^{III})$	3.526	C(4) ··· $C(11^{III})$	3.594
O(3) ··· $C(7^{III})$	3.463	C(4) ··· $C(12^{III})$	3.455
O(3) ··· $C(14^{IV})$	3.428	C(7) ··· $C(15^{V})$	3.595

Roman numerals as superscripts refer to the following equivalent position relative to reference molecule at x,y,z:

I	$1 + x, y, 1 + z$	IV	$2 - x, \frac{1}{2} + y, 1 - z$
II	$1 - x, \frac{1}{2} + y, -z$	V	$1 - x, y - \frac{1}{2}, 1 - z$
III	$1 - x, \frac{1}{2} + y, 1 - z$		

germacrane sesquiterpenoids.[16-24] The methyl group at C(10) is α-oriented[3] and the two double bonds [C(1)–C(10) and C(4)–C(5)] are *trans*. The C(1) · · · C(4) and C(1) · · · C(5) non-bonded intramolecular separations in linderalactone are distinctly short (2.78 and 2.93 Å).

The molecular packing arrangement along the *b* axis is illustrated in Figure 3. The mean plane of the ten-membered ring is nearly parallel to the $(21\bar{1})$ plane. All intermolecular distances were calculated, and the most significant contacts (<3.60 Å) are given in Table 7. The packing is efficient with several contacts approaching the sum of the van der Waals radii, the shortest contact being O(3) · · · $C(14^{IV})$ 3.428 Å.

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