explain the disorder are approximately related by rotation about the C–H bond. The elongation of the atoms in the molecule in the *ORTEP* drawing (Fig. 1*b*) is consistent with this disordered model. The bond lengths and angles for chloroform are given in Table 4.

We thank Professor G. A. Jeffrey for suggesting this research problem. We thank Dr C. S. Yoo for his assistance in obtaining the second set of data. We gratefully acknowledge the use of computing facilities at the University of Pittsburgh.

References

ALCOCK, N. W. (1970). *Crystallographic Computing*, edited by F. R. AHMED, pp. 271–278. Copenhagen: Munksgaard.
BUGG, C. E., THOMAS, J. M., SUNDARALINGAM, M. & RAO, S. T. (1971). *Biopolymers*, **10**, 175–219.
CHAPMAN, T. (1979). Private communication.
GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* A**27**, 368–376.
HARRIS, D. R. & MACINTYRE, W. M. (1964). *Biophys. J.* **4**, 203–225.

International Tables for X-ray Crystallography (1968). Vol. III, 2nd ed. Birmingham: Kynoch Press.
JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.
KONNERT, J. H. (1976). *Acta Cryst.* A**32**, 614–617.
RAHMAN, A. & WILSON, H. R. (1972). *Acta Cryst.* B**28**, 2260–2270.
SAENGER, W. & SUCK, D. (1971). *Acta Cryst.* B**27**, 2105–2112.
SCHAEFER, W. P. & MARSH, R. E. (1969). *Acta Cryst.* B**25**, 1675–1682.
SHIONO, R. (1970). Tech. Rep. No. 48. Crystallography Department, Univ. of Pittsburgh, USA.
STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.
SUCK, D., SAENGER, W. & ROHDE, W. (1974). *Biochim. Biophys. Acta*, **361**, 1–10.
SUNDARALINGAM, M. (1975). *Ann. N.Y. Acad. Sci.* **255**, 3–42.
SUNDARALINGAM, M. & JENSEN, L. H. (1965). *J. Mol. Biol.* **13**, 930–943.
WILSON, A. J. C. (1942). *Nature (London)*, **150**, 151–152.
YOUNG, D. W., TOLLIN, P. & WILSON, H. R. (1969). *Acta Cryst.* B**25**, 1423–1432.

Salignone-D

BY VOLKER ZABEL AND WILLIAM H. WATSON*

FASTBIOS Laboratory, Department of Chemistry, Texas Christian University, Fort Worth, Texas 76129, USA

MARIO SILVA AND MAGALIS BITTNER

Laboratorio de Productos Naturales, Departamento de Botánica, Universidad de Concepción, Concepción, Chile

AND DAVID A. LANGS

Medical Foundation of Buffalo, 73 High Street, Buffalo, NY, USA

Abstract

$C_{18}H_{20}O_5$, $M_r = 316.36$, is monoclinic, $P2_1$, with $a = 13.928$ (4), $b = 9.218$ (2), $c = 6.119$ (2) Å, $\beta = 97.45$ (3)°, $V = 779.0$ (4) Å^3, $Z = 2$, $d_c = 1.349$ Mg m^{-3}, λ(Cu $K\alpha$) $= 1.54178$ Å. Full-matrix least-squares refinement (nonhydrogen atoms anisotropic, H atoms isotropic) based on 1441 reflexions led to a final R of 0.057. Salignone-D is a bisnorditerpene dilactone. The A and B rings are *trans* fused and exhibit flattened-chair and 1,2-diplanar conformations, respectively. The conformation of the δ-lactone ring is best described as 1,3-diplanar, while the five-membered γ-lactone is in an envelope conformation with C(5) as the flap. The molecule also contains a *cis*-fused epoxide function.

Introduction

Nor- and bisnorditerpene dilactones, isolated from *Podocarpus* species, exhibit a variety of biological activities. Hallactone A and B (Russell, Fenemore & Singh, 1973) and nagilactone A (Hirotsu, Higuchi, Shimada, Hayashi & Sakan, 1975) are toxic to housefly larvae; sellowin-A (Cambie & Russell, 1973) and podolactones A and B (Galbraith, Horn & Sasse, 1971) inhibit growth of pea stem hook segments; inumakilactone-A glucoside is an inhibitor of expansion

---

and mitosis of plant cells (Hayashi, Kakisawa, Ito, Chen & Hsu, 1972); and podolide (Kupchan, Baxter, Ziegler, Smith & Bryan, 1975) and the nagilactones (Hayashi, Matsumoto, Yuki & Sakan, 1977; Hayashi, Matsumoto & Sakan, 1978; Hembre et al., 1979) exhibit cytotoxic and antileukemic activity. This class of terpenoids has been difficult to characterize chemically and spectroscopically and most of the original structural formulae have been modified by subsequent X-ray studies (Arora, Bates & Chou, 1976). In addition, many Podocarpus species have been found to contain insect-moulting hormones (Galbraith & Horn, 1966; Nakanishi, Korreda, Sasaki, Chang & Hsu, 1966; Nakanishi, Chang & Hsu, 1968; Imai, Fujioka, Murata, Sasakawa & Nakanishi, 1968). The great variety of secondary metabolities and their substitution patterns have been used in chemosystematic and chemotaxonomic investigations of the Podocarpus genus (Alpin, Cambie & Rutledge, 1963; Lowry, 1968, 1972).

Podocarpus saligna D. Don is one of the three species of Podocarpus native to Chile. The leaves do not elicit insect-moulting-hormone behavior; however, the plant has not been screened for other types of activity. Earlier work (Bhakuni, Bittner, Sammes & Silva, 1974) reported the identification of β-sitosterol, n-nonacosane, daucosterin and the diterpenes fern-9(11)-ene and isofernene. Subsequent extractions of the roots indicated the presence of at least eight nor- and bisnorditerpene dilactones. The compounds are difficult to purify with co-crystallization being a common phenomenon in this series. Only small quantities of pure sample are available for characterization. We report the structure of one component, salignone-D (1), determined by an X-ray diffraction investigation.

Structure determination and refinement

A crystal of dimensions 0·3 × 0·25 × 0·5 mm was used to collect intensity data on a Syntex $P2_1$ diffractometer by the $\theta : 2\theta$ scanning technique using a variable scan speed, a graphite monochromator and Cu $K\alpha$ radiation ($\lambda = 1\cdot54178$ Å). Room-temperature lattice parameters were refined by a least-squares procedure utilizing 15 reflexions whose angles were measured by a centering routine associated with the Syntex diffractometer. Systematic absences were consistent with space group $P2_1$. A periodically monitored reflexion showed no significant change in intensity. Of the 1559 independent reflexions measured ($2\theta < 140°$), 112 had intensities less than $2\sigma(I)$ and were not used in the refinement. An additional six reflexions showed significant secondary extinction and were dropped from the final refinement. Lorentz and polarization corrections were applied, but no absorption corrections were made.

The direct-methods program QTAN (Langs & DeTitta, 1975) was used to generate and select triples and negative quartets within the set of 191 $|E|$'s ≥ 1·5. Cosine-invariant estimation procedures (Hauptman, 1972) were used to remove aberrant triple-phase relationships from the tangent-formula determination. Tangent refinement extended the starting set, which defined 30 ambiguities, to 243 phases. The lowest NQEST (DeTitta, Edmonds, Langs & Hauptman, 1975) indicated the correct set and an E map calculated with these phases revealed the positions of all nonhydrogen atoms. The structure was refined isotropically to $R = 0\cdot122$ and anisotropically to $R = 0\cdot078$. A difference Fourier map yielded the coordinates of all H atoms.

Table 1. Atomic positional parameters ($\times 10^4$; $\times 10^3$ for H) and U_{eq} values ($\text{Å}^2 \times 10^3$; $\text{Å}^2 \times 10^2$ for H) for salignone-D

	x	y	z	U_{eq}
C(1)	2438 (2)	7935 (3)	8668 (4)	57 (1)
C(2)	3094 (2)	9042 (4)	7757 (6)	62 (2)
C(3)	4121 (2)	8523 (4)	7687 (5)	57 (2)
C(4)	4262 (2)	6975 (3)	7098 (3)	36 (1)
C(5)	3522 (1)	5922 (3)	7850 (3)	39 (1)
C(6)	3677 (2)	4592 (3)	6468 (4)	52 (1)
O(6)	3867 (1)	5191 (3)	4359 (3)	50 (1)
C(7)	2853 (2)	3532 (3)	6223 (5)	51 (1)
O(7)	2707 (1)	2954 (2)	8333 (3)	62 (1)
C(8)	1964 (2)	3855 (3)	7145 (4)	46 (1)
C(9)	1828 (2)	5327 (3)	8102 (3)	38 (1)
C(10)	2470 (1)	6500 (*)	7424 (3)	38 (1)
C(11)	1084 (2)	5450 (4)	9259 (4)	55 (1)
C(12)	463 (2)	4227 (4)	9640 (5)	62 (2)
O(12)	−34 (2)	4177 (4)	11108 (5)	110 (1)
O(13)	457 (1)	3091 (3)	8285 (4)	67 (1)
C(14)	1015 (2)	3095 (3)	6425 (4)	38 (1)
C(15)	1121 (2)	1523 (4)	5796 (6)	44 (2)
C(16)	1113 (4)	1091 (5)	3776 (8)	48 (2)
C(18)	5311 (2)	6560 (4)	8070 (4)	48 (2)
C(19)	4194 (2)	6586 (4)	4677 (3)	47 (1)
O(19)	4420 (2)	7284 (4)	3179 (3)	64 (1)
C(20)	2075 (2)	6762 (4)	4959 (4)	53 (1)
H(1a)	180 (3)	845 (6)	833 (7)	6 (1)
H(1b)	281 (2)	779 (4)	1029 (6)	4 (1)
H(2a)	312 (3)	1008 (6)	832 (6)	6 (1)
H(2b)	272 (2)	933 (5)	607 (6)	5 (1)
H(3a)	454 (3)	920 (6)	678 (7)	6 (1)
H(3b)	452 (3)	861 (7)	925 (8)	7 (1)
H(5)	369 (2)	578 (3)	938 (4)	3 (1)
H(6)	429 (3)	430 (6)	715 (7)	6 (1)
H(7)	285 (3)	318 (8)	491 (9)	9 (1)
H(11)	92 (4)	632 (8)	974 (9)	7 (1)
H(14)	63 (3)	361 (5)	532 (7)	5 (1)
H(15)	115 (4)	66 (8)	710 (9)	8 (1)
H(16a)	130 (4)	−3 (6)	317 (8)	6 (1)
H(16b)	129 (8)	155 (17)	254 (18)	14 (4)
H(18a)	551 (5)	667 (9)	982 (11)	9 (2)
H(18b)	552 (4)	560 (7)	758 (8)	6 (1)
H(18c)	575 (5)	724 (10)	755 (10)	8 (2)
H(20a)	132 (3)	714 (5)	481 (7)	5 (1)
H(20b)	246 (2)	768 (4)	410 (5)	4 (1)
H(20c)	200 (4)	576 (7)	405 (9)	7 (1)

* Fixed during the refinement.

Further least-squares refinement led to a final R of 0·057, where $R = \sum ||F_o| - |F_c||/\sum |F_o|$. The function minimized in the refinement was $\sum w(|F_o| - |F_c|)^2$ where $w = 1$. $\sigma(I)$ was determined from counting statistics. H-atom thermal parameters were refined isotropically.

During the last cycle of refinement the maximum shift in a nonhydrogen positional parameter was 0·8σ. A final difference map showed no peak larger than 0·30 e Å^{-3}. Atomic scattering factors and anomalous-

Table 2. Interatomic distances (Å)

C(1)—C(2)	1·523 (4)	C(8)—C(9)	1·500 (4)
C(1)—C(10)	1·530 (3)	C(8)—C(14)	1·512 (3)
C(2)—C(3)	1·515 (4)	C(9)—C(10)	1·496 (3)
C(3)—C(4)	1·491 (4)	C(9)—C(11)	1·333 (3)
C(4)—C(5)	1·529 (3)	C(10)—C(20)	1·556 (3)
C(4)—C(18)	1·552 (3)	C(11)—C(12)	1·458 (5)
C(4)—C(19)	1·515 (3)	C(12)—O(12)	1·204 (4)
C(5)—C(6)	1·521 (4)	C(12)—O(13)	1·335 (4)
C(5)—C(10)	1·550 (3)	O(13)—C(14)	1·459 (4)
C(6)—C(7)	1·500 (4)	C(14)—C(15)	1·512 (5)
C(6)—O(6)	1·459 (3)	C(15)—C(16)	1·298 (6)
C(7)—C(8)	1·455 (3)	O(6)—C(19)	1·370 (4)
C(7)—O(7)	1·435 (4)	C(19)—O(19)	1·195 (4)
C(8)—O(7)	1·448 (3)		
C(1)—H(1a)	1·00 (4)	C(14)—H(14)	0·94 (4)
C(1)—H(1b)	1·07 (3)	C(15)—H(15)	1·12 (7)
C(2)—H(2a)	1·02 (6)	C(16)—H(16a)	1·14 (6)
C(2)—H(2b)	1·13 (3)	C(16)—H(16b)	0·93 (13)
C(3)—H(3a)	1·06 (5)	C(18)—H(18a)	1·08 (6)
C(3)—H(3b)	1·05 (4)	C(18)—H(18b)	1·00 (6)
C(5)—H(5)	0·94 (3)	C(18)—H(18c)	0·96 (8)
C(6)-H(6)	0·94 (4)	C(20)—H(20a)	1·10 (4)
C(7)—H(7)	0·86 (6)	C(20)—H(20b)	1·16 (4)
C(11)—H(11)	0·89 (7)	C(20)—H(20c)	1·07 (7)

Table 3. Valence angles (°)

C(10)C(1)C(2)	109·8 (2)	C(9)C(8)C(14)	112·5 (2)
C(1)C(2)C(3)	114·4 (3)	C(8)C(9)C(10)	115·8 (2)
C(2)C(3)C(4)	117·6 (2)	C(8)C(9)C(11)	115·6 (2)
C(3)C(4)C(5)	114·8 (2)	C(10)C(9)C(11)	128·3 (2)
C(3)C(4)C(18)	106·9 (2)	C(9)C(10)C(5)	106·9 (1)
C(3)C(4)C(19)	118·0 (2)	C(9)C(10)C(20)	103·4 (2)
C(5)C(4)C(18)	111·4 (2)	C(9)C(10)C(1)	115·5 (2)
C(5)C(4)C(19)	100·7 (2)	C(1)C(10)C(5)	107·6 (2)
C(18)C(4)C(19)	104·6 (2)	C(1)C(10)C(20)	108·6 (2)
C(4)C(5)C(6)	101·2 (2)	C(5)C(10)C(20)	115·1 (2)
C(4)C(5)C(10)	113·0 (2)	C(9)C(11)C(12)	122·5 (3)
C(6)C(5)C(10)	112·5 (2)	C(11)C(12)O(13)	117·6 (3)
C(5)C(6)C(7)	114·8 (2)	C(11)C(12)O(12)	124·0 (3)
C(5)C(6)O(6)	104·0 (2)	O(13)C(12)O(12)	118·4 (3)
C(7)C(6)O(6)	112·5 (2)	C(12)O(13)C(14)	121·4 (3)
C(6)C(7)C(8)	120·4 (2)	O(13)C(14)C(8)	108·0 (2)
C(6)C(7)O(7)	110·3 (2)	O(13)C(14)C(15)	106·0 (3)
O(7)C(7)C(8)	60·1 (2)	C(8)C(14)C(15)	114·1 (2)
C(7)O(7)C(8)	60·6 (2)	C(14)C(15)C(16)	123·2 (4)
C(7)C(8)O(7)	59·3 (2)	C(6)O(6)C(19)	109·0 (2)
C(7)C(8)C(9)	119·6 (2)	O(6)C(19)C(4)	109·8 (2)
C(7)C(8)C(14)	123·2 (2)	O(6)C(19)O(19)	120·8 (3)
O(7)C(8)C(14)	114·9 (2)	C(4)C(19)O(19)	129·3 (3)
O(7)C(8)C(9)	116·2 (2)		

Table 4. Endocyclic torsion angles (°)

1—2—3—4	37·6 (4)	5—6—7—8	4·0 (3)
2—3—4—5	−32·5 (3)	6—7—8—9	7·4 (3)
3—4—5—10	43·7 (2)	7—8—9—10	18·4 (3)
4—5—10—1	−59·0 (2)	8—9—10—5	−51·4 (2)
5—10—1—2	62·8 (2)	9—10—5—6	62·6 (2)
10—1—2—3	−53·0 (3)	10—5—6—7	−39·4 (3)
8—9—11—12	2·1 (3)	6—O(6)—19—4	1·5 (3)
9—11—12—O(13)	−20·0 (4)	O(6)—19—4—5	−24·7 (2)
11—12—O(13)—14	−2·8 (4)	19—4—5—6	36·5 (2)
12—O(13)—14—8	37·9 (3)	4—5—6—O(6)	−37·0 (2)
O(13)—14—8—9	−53·1 (3)	5—6—O(6)—19	22·8 (2)
14—8—9—11	35·1 (3)		

dispersion corrections were taken from *International Tables for X-ray Crystallography* (1974). Atomic positional parameters are given in Table 1, while interatomic distances, valence and torsion angles are presented in Tables 2, 3 and 4.*

Discussion

Fig. 1. is an *ORTEP* drawing (Johnson, 1965) of salignone-D. The interatomic distances, valence angles and torsion angles may be most closely compared with those of podolide (2) (Bryan & Smith, 1975), sellowin-B (3) (Arora, Bates & Chou, 1976) and podolactone A (4) (Poppleton, 1975). The *A* ring of salignone-D exhibits a flattened-chair conformation while the *B*-ring conformation is 1,2-diplanar. The maximum deviation of torsion angles in the *B* ring of salignone-D from the average obtained from the reference structures is 1·8°. The conformation of the *B* ring in these structures is determined by the
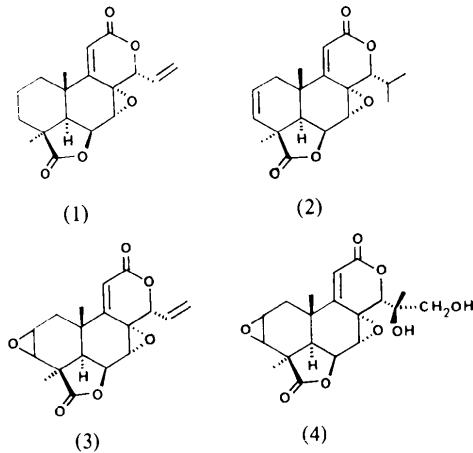
(1)

(2)

(3)

(4)
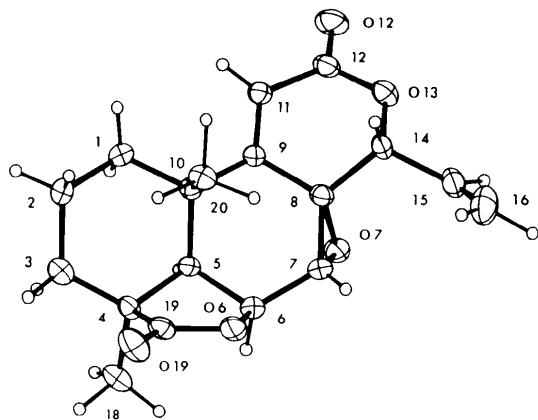
Fig. 1. *ORTEP* drawing of salignone-D. Thermal ellipsoids are drawn at the 35% probability level while H atoms are represented by spheres of arbitrary size.

C(9)=C(11) double bond, the C(7)—C(8) *cis*-fused epoxide and the axial fusion of the γ-lactone ring at C(4) and C(6). The C(4)C(19)O(6)C(6) torsion angle of 1·5 (3)° indicates planarity of this part of the γ-lactone ring while C(5) lies significantly out of the plane, C(19)O(6)C(6)C(5) = 22·8 (2) and O(6)C(19)-C(4)C(5) = −24·7 (2)°. Torsion angles around the γ-lactone ring differ from the average values of the three reference structures by less than 1°. The C(20) methyl group occupies an axial site at the juncture of the *A* and *B* rings with H(20c)—O(6) = 2·63 (5), H(20b)—C(7) = 2·60 (3) and H(20b)—O(7) = 2·88 (4) Å. The δ-lactone ring exhibits a 1,3-diplanar conformation while the reference structures are intermediate between 1,2- and 1,3-diplanar. The torsion angles C(9)C(11)C(12)O(13), C(11)C(12)O(13)C(14) and C(12)O(13)C(14)C(8) of the δ-lactone ring of salignone-D differ from the average values of the reference structures by 4·4, 8·9 and 3·7°.

References

ALPIN, R. T., CAMBIE, R. C. & RUTLEDGE, P. S. (1963). *Phytochemistry*, 2, 205–214.

ARORA, S. K., BATES, R. B. & CHOU, P. C. C. (1976). *J. Org. Chem.* 41, 2458–2461.

BHAKUNI, D. S., BITTNER, M., SAMMES, P. G. & SILVA, M. (1974). *Ref. Latinoam. Quim.* 5, 163–168.

BRYAN, R. F. & SMITH, P. M. (1975). *J. Chem. Soc. Perkin Trans.* 2, pp. 1482–1486.

CAMBIE, R. C. & RUSSELL, G. B. (1973). *Phytochemistry*, 12, 2057.

DETITTA, G. T., EDMONDS, J. W., LANGS, E. A. & HAUPTMAN, H. (1975). *Acta Cryst.* A31, 472–479.

GALBRATIH, M. N. & HORN, D. H. S. (1966). *J. Chem. Soc. Chem. Commun.* pp. 905–906.

GALBRAITH, M. N., HORN, D. H. S. & SASSE, J. M. (1971). *J. Chem. Soc. Chem. Commun.* pp. 1362–1363.

HAUPTMAN, H. (1972). *Crystal Structure Determination: The Role of the Cosine Seminvariants.* New York: Plenum.

HAYASHI, Y., KAKISAWA, H., ITO, S., CHEN, Y. P. & HSU, H. Y. (1972). *Tetrahedron Lett.* pp. 3785–3388.

HAYASHI, Y., MATSUMOTO, T. & SAKAN, T. (1978). *Heterocycles*, 10, 123–131.

HAYASHI, Y., MATSUMOTO, T., YUKI, Y. & SAKAN, T. (1977). *Tetrahedron Lett.* pp. 4215–4218.

HEMBRE, J. A., CHANG, C. J., McLAUCHLIN, J. L., CASSADY, J. M., WATTS, D. J., WENKERT, E., FONSECA, S. F. & DE PAIVA CAMPELLO, J. (1979). *Phytochemistry*, 18, 1691–1694.

HIROTSU, K., HIGUCHI, T., SHIMADA, A., HAYASHI, Y. & SAKAN, T. (1975). *Bull. Chem. Soc. Jpn*, 48, 1157–1162.

IMAI, S., FUJIOKA, S., MURATA, E., SASAKAWA, Y. & NAKANISHI, K. (1968). *Tetrahedron Lett.* pp. 3887–3890.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press.

JOHNSON, C. K. (1965). *ORTEP.* Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.

KUPCHAN, S. M., BAXTER, R. C., ZIEGLER, M. G., SMITH, P. M. & BRYAN, R. F. (1975). *Experientia*, 31, 137–138.

LANGS, D. A. & DETITTA, G. T. (1975). *Acta Cryst.* A31, S16.

LOWRY, J. B. (1968). *Phytochemistry*, 7, 1897–1898.

LOWRY, J. B. (1972). *Phytochemistry*, 11, 725–731.

NAKANISHI, K., CHANG, M. & HSU, H. Y. (1968). *Tetrahedron Lett.* pp. 1105–1110.

NAKANISHI, K., KORREDA, M., SASAKI, S., CHANG, M. L. & HSU, H. Y. (1966). *J. Chem. Soc. Chem. Commun.* pp. 915–917.

POPPLETON, B. J. (1975). *Cryst. Struct. Commun.* 4, 101–106.

RUSSELL, G. B., FENEMORE, P. G. & SINGH, P. (1973). *J. Chem. Soc. Chem. Commun.* pp. 166–167.