Acta Cryst. (1989). C**45**, 748–750

The Structure of Ganervosin B, $C_{22}H_{30}O_6$, a New Diterpenoid from *Rabdosia nervosa*: an X-ray Study

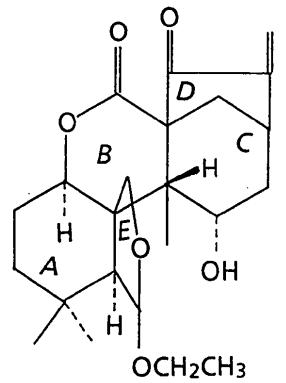
BY SU-MING HUA,* QI-GUANG WANG, GUANG BAI AND YAO-ZU CHEN

Department of Chemistry, Lanzhou University, Lanzhou, People's Republic of China

(*Received* 15 *March* 1988; *accepted* 31 *October* 1988)

Abstract. $C_{22}H_{30}O_6$, $M_r = 390{\cdot}5$, orthorhombic, $P2_12_12_1$, $a = 7{\cdot}714$ (2), $b = 9{\cdot}555$ (3), $c = 26{\cdot}78$ (1) Å, $V = 1973$ (1) Å^3, $Z = 4$, $D_x = 1{\cdot}313$ g cm^{-3}, λ(Mo $K\alpha$) $= 0{\cdot}7107$ Å, $\mu = 0{\cdot}884$ cm^{-1}, $F(000) = 840$, $R = 0{\cdot}042$ for 1646 diffraction data at room temperature. This compound is a new diterpenoid, ganervosin B (20,1-epoxymethano-21-ethoxy-11α-hydroxy-2,2-dimethyl-6-oxa-18,19-dinor-16-karene-7,15-dione), which has internal strain in the *D* ring. This compound is expected to have anti-tumor activity.

Introduction. In recent years, the chemical ingredients of *Rabdosia* have widely been studied, because some diterpenoids isolated from the plants of this genus have anti-tumor activity (Fujita & Node, 1984). The crystal structures of some anti-tumor drug molecules isolated from *Rabdosia* have been studied by means of X-ray diffractometry. It is found that the existence of interior stress in the molecule leads to an increase in the chemical reactivity of these drugs and probably bears a close relation to their anti-tumor activity (Chen, Wu & Cheng, 1987). Here, we report an X-ray study on the structure of ganervosin B, (1), a derivative of kaurane, a new diterpenoid from *Rabdosia nervosa* (Hemsl.), a species collected from the Wen Xian district of south Gansu province (Bai, 1987).



(1)

Experimental. Single crystals of the title compound were slowly grown from acetone as colorless parallelepipeds. A crystal sample, of approximate dimensions $0{\cdot}3 \times 0{\cdot}3 \times 0{\cdot}1$ mm, was mounted in a random orientation on an Enraf–Nonius CAD-4 diffractometer for data collection. The lattice parameters and orientation matrix were obtained from 25 reflections ($2 \leq \theta \leq 25°$). The Laue symmetry was *mmm* and its space group was determined clearly by three 2_1 screw axes along **a, b** and **c** respectively. The intensity data (room temperature) were measured by the ω–2θ scan technique with Mo $K\alpha$ radiation from a graphite monochromator. Monitor reflections were measured every hour, no significant intensity decay observed. 2047 reflections were measured, of which 1646 were observed with $I > 3{\cdot}0\sigma(I)$, and h, k, l range: 0 to 9, 0 to 11 and 0 to 31. Max. $\theta = 25°$. All of the calculations were carried out on a PDP11/44 computer, using the *SDP* software package (B. A. Frenz & Associates, Inc., 1982). Empirical absorption corrections were made with the ψ-scan technique (North, Phillips & Mathews, 1968), transmission factors 0·962 to 0·998.

The structure was solved by direct methods with *MULTAN*82 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982). The refinement was carried out with anisotropic thermal parameters for all non-H atoms (253 parameters). Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974). The positions of H atoms apart from H27, H28 and H29 were revealed from a difference Fourier synthesis. These atomic positions were included in the calculation of structure factors but not refined. At the end of refinement on F, the value of the conventional R (wR) was 0·042 (0·045) for 1646 data. $w = 1/\sigma^2(F)$. The largest parameter shift (S) was $0{\cdot}24\sigma$ and highest electron density (max. $\Delta\rho$) was 0·221 e Å^{-3}. Table 1 gives the final atomic parameters and their equivalent isotropic thermal factors.†

* To whom correspondence should be addressed.

† Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51564 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

0108-2701/89/050748-03$03.00

Table 1. *Fractional coordinates and equivalent isotropic temperature factors*

	x	*y*	*z*	*B**(Å²)
O(1)	0·0679 (4)	0·0214 (4)	0·7987 (1)	3·77 (7)
O(2)	−0·1694 (4)	0·1405 (3)	0·8127 (1)	2·98 (6)
O(3)	0·0729 (4)	−0·2044 (4)	0·8703 (1)	4·04 (7)
O(4)	−0·5858 (4)	−0·1143 (3)	0·8052 (1)	3·02 (6)
O(5)	−0·4931 (4)	−0·1175 (3)	0·9624 (1)	3·18 (6)
O(6)	−0·3037 (4)	0·0730 (4)	0·9632 (1)	3·31 (7)
C(1)	−0·3521 (5)	0·1350 (5)	0·8278 (2)	2·50 (8)
C(2)	−0·4153 (6)	0·2850 (5)	0·8314 (2)	2·97 (9)
C(3)	−0·6013 (6)	0·2802 (5)	0·8513 (2)	3·17 (9)
C(4)	−0·6088 (5)	0·2259 (5)	0·9048 (2)	2·58 (8)
C(5)	−0·5354 (5)	0·0736 (4)	0·9062 (1)	2·23 (8)
C(6)	−0·3649 (5)	0·0489 (4)	0·8761 (1)	2·08 (7)
C(7)	−0·3342 (5)	−0·1067 (4)	0·8613 (2)	2·20 (8)
C(8)	−0·1774 (5)	−0·1152 (4)	0·8229 (2)	2·25 (8)
C(9)	−0·0830 (5)	0·0193 (5)	0·8112 (2)	2·72 (8)
C(10)	−0·2349 (6)	−0·1898 (5)	0·7741 (2)	2·91 (9)
C(11)	−0·2729 (6)	−0·3384 (5)	0·7937 (2)	3·24 (9)
C(12)	−0·4426 (6)	−0·3357 (5)	0·8246 (2)	3·21 (9)
C(13)	−0·4936 (6)	−0·1884 (4)	0·8432 (2)	2·62 (8)
C(14)	−0·1159 (6)	−0·3639 (5)	0·8258 (2)	3·4 (1)
C(15)	−0·0525 (6)	−0·2256 (5)	0·8439 (2)	3·04 (9)
C(16)	−0·0324 (7)	−0·4806 (6)	0·8347 (3)	5·6 (1)
C(17)	−0·2267 (5)	0·0912 (5)	0·9144 (2)	2·77 (9)
C(18)	−0·4790 (6)	0·0287 (5)	0·9583 (2)	3·04 (9)
C(19)	−0·5213 (7)	0·3315 (5)	0·9401 (2)	3·9 (1)
C(20)	−0·8016 (6)	0·2157 (5)	0·9199 (2)	3·7 (1)
C(21)	−0·4461 (7)	−0·1719 (6)	1·0111 (2)	4·2 (1)
C(22)	−0·4334 (8)	−0·3276 (6)	1·0073 (2)	5·1 (1)

* $B_{eq} = \frac{4}{3}[a^2\beta(1,1) + b^2\beta(2,2) + c^2\beta(3,3) + ab\cos\gamma\beta(1,2) + ac\cos\beta\beta(1,3) + bc\cos\alpha\beta(2,3)]$.

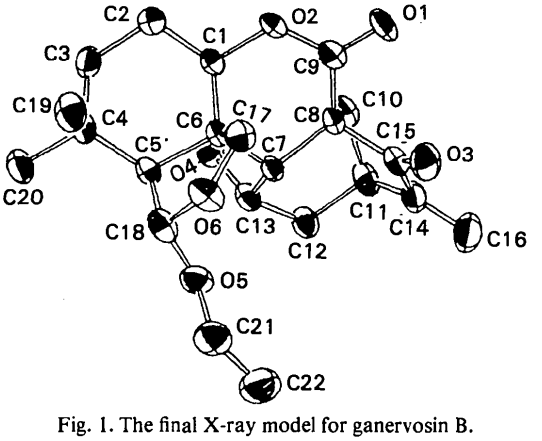


Fig. 1. The final X-ray model for ganervosin B.

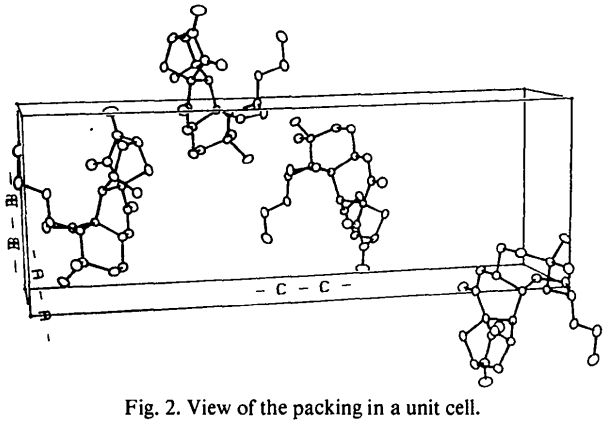


Fig. 2. View of the packing in a unit cell.

Table 2. *Bond lengths* (Å) *and angles* (°)

O(1)–C(9)	1·211 (5)	C(5)–C(6)	1·561 (5)
O(2)–C(1)	1·467 (5)	C(5)–C(18)	1·524 (6)
O(2)–C(9)	1·337 (5)	C(6)–C(7)	1·557 (6)
O(3)–C(15)	1·214 (5)	C(6)–C(17)	1·534 (6)
O(4)–C(13)	1·429 (5)	C(7)–C(8)	1·590 (5)
O(5)–C(18)	1·405 (6)	C(7)–C(13)	1·534 (6)
O(5)–C(22)	1·451 (5)	C(8)–C(9)	1·509 (6)
O(6)–C(17)	1·445 (5)	C(8)–C(10)	1·555 (6)
O(6)–C(18)	1·423 (5)	C(8)–C(15)	1·535 (6)
C(1)–C(2)	1·517 (6)	C(10)–C(11)	1·542 (7)
C(1)–C(6)	1·537 (6)	C(11)–C(12)	1·548 (6)
C(2)–C(3)	1·531 (6)	C(11)–C(14)	1·504 (6)
C(3)–C(4)	1·526 (6)	C(12)–C(13)	1·544 (6)
C(4)–C(5)	1·562 (6)	C(14)–C(15)	1·490 (7)
C(4)–C(19)	1·539 (7)	C(14)–C(16)	1·309 (7)
C(4)–C(20)	1·544 (6)	C(21)–C(22)	1·494 (8)

C(1)–O(2)–C(9)	117·1 (3)	C(7)–C(8)–C(10)	110·6 (3)
C(18)–O(5)–C(22)	114·0 (3)	C(7)–C(8)–C(15)	105·9 (3)
C(17)–O(6)–C(18)	110·1 (3)	C(9)–C(8)–C(10)	110·6 (3)
O(2)–C(1)–C(2)	107·0 (3)	C(9)–C(8)–C(15)	111·0 (3)
O(2)–C(1)–C(6)	108·3 (3)	C(10)–C(8)–C(15)	100·0 (3)
C(2)–C(1)–C(6)	115·5 (4)	O(1)–C(9)–O(2)	118·2 (4)
C(1)–C(2)–C(3)	107·2 (4)	O(1)–C(9)–C(8)	122·3 (4)
C(2)–C(3)–C(4)	111·9 (4)	O(2)–C(9)–C(8)	119·4 (3)
C(3)–C(4)–C(5)	109·1 (3)	C(8)–C(10)–C(11)	100·8 (3)
C(3)–C(4)–C(19)	109·8 (4)	C(10)–C(11)–C(12)	109·1 (4)
C(3)–C(4)–C(20)	107·7 (4)	C(10)–C(11)–C(14)	101·0 (4)
C(5)–C(4)–C(19)	115·9 (4)	C(12)–C(11)–C(14)	112·2 (4)
C(5)–C(4)–C(20)	106·5 (3)	C(11)–C(12)–C(13)	113·8 (4)
C(19)–C(4)–C(20)	107·6 (4)	O(4)–C(13)–C(7)	111·9 (3)
C(4)–C(5)–C(6)	115·7 (3)	O(4)–C(13)–C(12)	110·4 (3)
C(4)–C(5)–C(18)	112·8 (3)	C(7)–C(13)–C(12)	111·2 (3)
C(6)–C(5)–C(18)	101·0 (3)	C(11)–C(14)–C(15)	107·9 (4)
C(1)–C(6)–C(5)	114·1 (3)	C(11)–C(14)–C(16)	129·6 (5)
C(1)–C(6)–C(7)	106·7 (3)	C(15)–C(14)–C(16)	122·3 (5)
C(1)–C(6)–C(17)	112·2 (3)	O(3)–C(15)–C(8)	126·8 (4)
C(5)–C(6)–C(7)	113·8 (3)	O(3)–C(15)–C(14)	126·8 (4)
C(5)–C(6)–C(17)	101·5 (3)	C(8)–C(15)–C(14)	106·5 (4)
C(7)–C(6)–C(17)	108·5 (3)	O(6)–C(17)–C(6)	106·8 (3)
C(6)–C(7)–C(8)	109·2 (3)	O(5)–C(18)–O(6)	111·2 (4)
C(6)–C(7)–C(13)	116·4 (3)	O(5)–C(18)–C(5)	109·2 (3)
C(8)–C(7)–C(13)	112·3 (3)	O(6)–C(18)–C(5)	105·7 (3)
C(7)–C(8)–C(9)	117·3 (3)	O(5)–C(21)–C(22)	108·2 (4)

Discussion. The structure of a single molecule of ganervosin B is shown in Fig. 1. The junction between the *A* and *B* rings has *trans* geometry, and ring *C* is fused to *B* in the *cis* configuration. The bond lengths C14–C16, C15–O3 and C9–O1 are 1·309 (7), 1·214 (5) and 1·211 (5) Å, respectively, suggesting that these are all double bonds. Atoms C9, C14 and C15 are sp^2 hybridized, with bond angles around C14 and C15 of C11–C14–C15 107·9 (4), C15–C14–C16 123·3 (4), C11–C14–C16 129·6 (5), C8–C15–O3 126·8 (4), O3–C15–C14 126·8 (4) and C14–C15–C8 106·5 (4)°, all of which deviate from the normal value of 120°. The other three bond angles in five-membered ring *D* are also less than the normal value of 107° by *ca* 7°. These data indicate that this portion of the molecule has much interior stress which would confer high chemical reactivity on the C14–C16 and C15–O3 double bonds.

As compared with some diterpenoids having antitumor activities, such as rabdophyllin G (Chen, Wu & Cheng, 1984), macrocalin A (Chen, Yao, Xu & Cheng,

1985), 1-acetoxyrubescensine A (Chen, Lin, Zhang & Li, 1983) and trichorabdal F acetate (Kashyap, Watson, Grossie, Node, Sai, Fujita & Fuji, 1984), it is found that these compounds all possess a 2-methylene-cyclopentanone fragment, the structural data of which are quite similar. In addition, this fragment of ganervosin B is located on the side of molecule with no steric hindrance (see Fig. 1), so it would react with other compounds more easily. This compound, therefore, would be expected to have anti-tumor activity.

Fig. 2. gives the packing view in a unit cell. The principal bond lengths and bond angles in ganervosin B are shown in Table 2.

References

B. A. FRENZ & ASSOCIATES, INC. (1982). *SDP Structure Determination Package.* College Station, Texas, USA, and Enraf–Nonius, Delft, The Netherlands.

BAI, G. (1987). MS thesis, Department of Chemistry, Lanzhou University, Lanzhou, China.

CHEN, Y. ZH., LIN, Y. J., ZHANG, T. M. & LI, J. CH. (1983). *J. Struct. Chem.* **2**, 21–24.

CHEN, Y. ZH., WU, Z. W. & CHENG, P. Y. (1984). *Acta Chim. Sin.* **42**, 645–649.

CHEN, Y. ZH., WU, Z. W. & CHENG, P. Y. (1987). *Youji Huaxue*, **1**, 21–28.

CHEN, Y. ZH., YAO, W. X., XU, B. J. & CHENG, P. Y. (1985). *Kexue Tongbao*, **22**, 1709–1713.

FUJITA, E. & NODE, M. (1984). *Progress in the Chemistry of Organic Natural Products*, Vol. 46, edited by W. HERZ, H. GRISEBACH, G. W. KIRBY & CH. TAMM, p. 78. Berlin: Springer-Verlag.

International Tables for X-ray Crystallography (1974). Vol. IV, Table 2.2B. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

KASHYAP, R. P., WATSON, W. H., GROSSIE, D. A., NODE, M., SAI, M., FUJITA, E. & FUJI, K. (1984). *Acta Cryst.* C**40**, 515–517.

MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DERCLERCQ, J.-P. & WOOLFSON, M. M. (1982). *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.

NORTH, A. C. T., PHILLIPS, D. C. & MATHEWS, F. S. (1968). *Acta Cryst.* A**24**, 351–359.

Acta Cryst. (1989). C**45**, 750–754

Structure of Methyl (*E*)-*p*-[3,3,3-Trifluoro-2-(2,2,4,4-tetramethyl-6-thiochromanyl)-1-propenyl]benzoate

BY X. JI AND D. VAN DER HELM

Department of Chemistry, University of Oklahoma, Norman, OK 73019, *USA*

AND K. D. BERLIN AND L. W. SPRUCE

Department of Chemistry, Oklahoma State University, Stillwater, OK 74078, *USA*

(*Received* 24 *March* 1988; *accepted* 3 *November* 1988)

Abstract. Methyl (*E*)-*p*-[3,3,3-trifluoro-2-(2,2,4,4-tetramethyl-6-thiochromanyl)-1-propenyl]benzoate, $C_{24}H_{25}F_3O_2S$, $M_r = 434{\cdot}52$, monoclinic, $P2_1/n$, $a = 16{\cdot}475\ (9)$, $b = 16{\cdot}519\ (6)$, $c = 8{\cdot}024\ (4)$ Å, $\beta = 101{\cdot}84\ (5)°$, $V = 2137{\cdot}27$ Å^3, $Z = 4$, $D_x = 1{\cdot}35$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å, $\mu = 1{\cdot}52$ cm^{-1}, $F(000) = 912$, $T = 138\ (2)$ K, $R = 0{\cdot}035$ for 3869 data. The configuration about the C(11)–C(13) double bond is such that the thiochromanyl group and the benzoate group are *cis* to each other. The sulfur-containing ring is closer to a half-chair than a sofa conformation. The conformations and bond distances of nine differently substituted thiochromans are discussed. It is concluded that the difference in S–C(sp^2) and S–C(sp^3) distances occurs when the sulfur atom is not substituted but that this difference is not present when the ring is oxidized to a sulfone.

0108-2701/89/050750-05$03.00

Introduction. Retinoids (vitamin A and derivatives thereof), arotinoids (molecules with an aryl ring fused to the saturated ring of a retinoid) and heteroarotinoids (molecules with a heteroatom in the saturated ring of an arotinoid) are of current interest in anticancer-drug design (Waugh, Berlin, Ford, Holt, Carrol, Schomber, Thompson & Schiff, 1985). Many of these compounds have the ability to inhibit the induction of epidermal ornithine decarboxylase (ODC) by the tumor promotor 12-*O*-tetradecanoylphorbol-13-acetate (TPA). Moreover, toxicity studies have indicated that heteroarotinoids are less toxic than the retinoids and the arotinoids (Dawson, Hobbs, Derdzinshki, Chan, Gruber, Chao, Smith, Thies & Schiff, 1984; Metra, Schiff, Moore, Buckley & Dawson, 1986). The heteroarotinoid ethyl (*E*)-*p*-[2-(4,4-dimethyl-6-thiochromanyl)propenyl]benzoate, (I), has been synthesized and