Each of the three ring systems in the molecule is almost planar with a maximum deviation of 0·006 (4) Å from the least-squares plane. The imidazole ring, *A*, and the 2,4-dichlorophenyl ring, *B*, lie close to the same plane [dihedral angle 4·4 (2)°] whilst the *p*-chlorophenyl ring, *C*, is at an angle of 60·7 (4)° to that plane. This is a similar situation to that observed for miconazole except that ring *C* is found to be nearly perpendicular to the almost coplanar *A*,*B* ring system.

The absence of a Cl atom at C(19), compared to miconazole, allows several changes in conformation whereby ring *B* rotates through 180° such that Cl(14) is on the same side of the molecule as the *p*-chlorophenyl ring with the Cl atom adjacent to the ring nucleus. This situation confers a certain restriction on the degree of rotation of ring *C* about the O(16)–C(17) bond which is observed in the torsion angles C(7)–O(16)–C(17)–C(18), 67·0 (4)°, and O(16)–C(17)–C(18)–C(23), 34·2 (4)°, when compared to the values of −179·8 (8) and 0·9 (16)° found in miconazole. Whether these subtle conformational differences affect the pharmacological activity of the compound is difficult to assess, mainly because data obtained from *in vitro* experiments are derived from a number of differing techniques and test organisms. Recent experiments (Brasseur, Vandenbosch, Marichal, Van den Bossche & Ruysschaert, 1982) show that when imidazole derivatives are inserted in model lipid bilayers the two phenyl residues are maintained in the hydrophobic phase with the imidazole residue orientated towards the hydrophilic phase, which may partly be the mechanism by which they affect membrane fluidity.

Intra- and intermolecular distances and angles are within the values recorded for similar compounds.

References

BRASSEUR, R., VANDENBOSCH, C., MARICHAL, P., VAN DEN BOSSCHE, H. & RUYSSCHAERT, J.-M. (1982). *Arch. Int. Physiol. Biochim.* **90**, BP20–21.
DROUHET, E. (1978). *Antibiot. Chemother. (Basel)*, **25**, 253–288.
GILMORE, C. J. (1984). *J. Appl. Cryst.* **17**, 42–46.
GODEFROI, E. F., HEERES, J., VAN CUTSEM, J. & JANSSEN, P. A. J. (1969). *J. Med. Chem.* **12**, 784–791.
International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)
JOHNSON, C. K. (1976). *ORTEP.* Report ORNL-5138. Oak Ridge National Laboratory, Tennessee.
MALLINSON, P. R. & MUIR, K. W. (1985). *J. Appl. Cryst.* **18**, 51–53.
PEARSON, A., SHANKLAND, N., SALOLE, E. G. & JOHNSON, J. R. (1985). *J. Pharm. Pharmacol.* **37**(Suppl.), 59P.
PEETERS, O. M., BLATON, N. M. & DE RANTER, C. J. (1979). *Bull. Soc. Chim. Belg.* **88**, 265–272.
THIENPONT, D., VAN CUTSEM, J., VAN NUETEN, J. M., NIEMEGEERS, C. J. E. & MARSBOOM, R. (1975). *Arzneim. Forsch.* **25**, 224–230.

Structure of 5β,24-Cyclofriedelan-3-one, a Novel Hexacyclic Triterpenoid in Space Group P1

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Abstract. $C_{30}H_{48}O$, $M_r = 424\cdot7$, triclinic, $P1$, $a = 6\cdot259$ (3), $b = 7\cdot351$ (1), $c = 14\cdot382$ (3) Å, $\alpha = 85\cdot31$ (1), $\beta = 87\cdot25$ (2), $\gamma = 65\cdot89$ (2)°, $V = 601\cdot9$ Å³, $Z = 1$, $D_x = 1\cdot17$ g cm⁻³, Mo $K\alpha$, $\lambda = 0\cdot71069$ Å, $\mu = 0\cdot63$ cm⁻¹, $F(000) = 236$, $T = 291$ K, final $R = 0\cdot057$ for 1607 unique reflections. The molecule adopts an extended *S*, stretched, conformation for the chain of five six-membered rings. The

incorporation of a methyl group of a typical pentacyclic triterpenoid into a cyclopropane ring is uncommon and provides the first example of a cyclofriedelane. The elucidation of the crystal structure required the use of three distinct program packages.

Introduction. The triterpenoid ketone (1), m.p. 598 K, $[\alpha]_D$ +54·9°, was isolated from the leaves and stems of *Euphorbia nerifolia* (Anjaneyulu & Row, 1965). It was originally assigned (Anjaneyulu, Row, Subrahmanyam

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& Murty, 1973) the tentative structure 5(10)-gluten-1-one, but subsequent synthesis of this compound (Akiyama, Moriyama, Murae, Tsuyuki & Takahashi, 1978) revealed that it was different from the natural product. Further examination of the ^1H and ^{13}C NMR spectroscopic properties of (1) indicated that it is a hexacarbocyclic compound, including a cyclopropane ring, seven tertiary methyl groups and a ketonic carbonyl group. In view of the uncertainty about the nature of the carbon skeleton of (1) an X-ray analysis was undertaken.

(1)
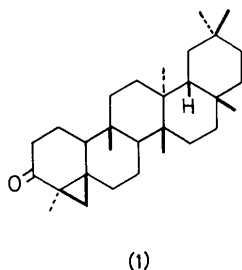
Experimental. Colourless, plate-shaped crystal, ca $0.1 \times 0.4 \times 0.5$ mm used in data collection, CAD-4 diffractometer. Preliminary Weissenberg photographs indicated crystals to be triclinic, and since the compound is an optically active natural product the space group is $P1$. D_m not measured. 2357 independent intensities, $\theta_{max} = 26°$, $\omega/2\theta$ scan. Two standard reflections gave $< 3\%$ variation in intensity. Least-squares technique based on 25 reflections, $\theta > 12°$, used to define lattice parameters. No absorption corrections; h 0 to 7, k -9 to 9, l -17 to 17. Structure solved by direct methods only with considerable difficulty. The inherent problem of solving a structure in the symmorphic space group $P1$ was compounded, in this case, by the existence of pseudo-translational overlap of the five almost regular six-membered rings, which led to E maps with chicken-wire patterns of peaks. Having the opportunity to work on the structure at a pre-meeting workshop in Torino (1985), we used the Italian direct-methods package, *SIR* (Cascarano, Giacovazzo, Polidori, Spagna & Viterbo, 1982), to produce a phase set with promising figures of merit derived from five symbols. The E maps, however, showed the same chicken-wire effect. Since the figures of merit had appeared encouraging and the best connected set of atoms involved the top 20 peaks, these coordinates were input to *DIRDIF* (Prick, Beurskens & Gould, 1983) in an attempt to break the pseudo-translational overlap. It should be acknowledged that standard recycling procedures failed miserably, usually by destroying the original fragment.

After two cycles of *DIRDIF* about 70% of the molecule, which gave the backbone of the structure, had been found. However, some degree of overlap still

Table 1. *Final positional parameters and equivalent isotropic thermal parameters (Å^2) with e.s.d.'s in parentheses*

$$U_{eq} = \tfrac{1}{3} \Sigma_i \Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i . \mathbf{a}_j.$$

	x	y	z	U_{eq}
O(1)	-0.4060(13)	-1.1331(11)	-1.3404(5)	0.097
C(1)	0.0778(14)	-1.2456(11)	-1.1832(5)	0.042
C(2)	-0.0615(16)	-1.2861(13)	-1.2544(6)	0.064
C(3)	-0.2555(15)	-1.1057(13)	-1.3002(6)	0.054
C(4)	-0.2703(14)	-0.9059(12)	-1.2915(5)	0.050
C(5)	-0.1667(12)	-0.8747(11)	-1.2020(5)	0.042
C(6)	-0.3007(13)	-0.6845(11)	-1.1565(5)	0.044
C(7)	-0.1679(12)	-0.6508(11)	-1.0781(5)	0.048
C(8)	-0.0939(11)	-0.8308(11)	-1.0084(5)	0.033
C(9)	0.0782(12)	-1.0209(10)	-1.0553(5)	0.031
C(10)	-0.0604(12)	-1.0578(11)	-1.1325(5)	0.034
C(11)	0.1481(12)	-1.1979(10)	-0.9811(5)	0.034
C(12)	0.2200(12)	-1.1606(10)	-0.8865(5)	0.036
C(13)	0.03371	-0.98057	-0.84198	0.027
C(14)	-0.0206(12)	-0.7922(10)	-0.9116(5)	0.033
C(15)	-0.2274(13)	-0.6127(11)	-0.8719(5)	0.042
C(16)	-0.2536(13)	-0.6125(11)	-0.7649(5)	0.044
C(17)	-0.0360(12)	-0.7396(11)	-0.7064(5)	0.042
C(18)	0.1211(11)	-0.9465(10)	-0.7470(5)	0.031
C(19)	0.1635(13)	-1.1210(10)	-0.6768(5)	0.038
C(20)	0.2399(13)	-1.1038(11)	-0.5793(5)	0.048
C(21)	0.0689(15)	-0.9047(11)	-0.5409(5)	0.053
C(22)	-0.1253(13)	-0.7795(12)	-0.6077(5)	0.048
C(23)	-0.4806(15)	-0.7383(13)	-1.3370(6)	0.070
C(24)	-0.0435(14)	-0.8704(12)	-1.2923(6)	0.056
C(25)	0.3015(12)	-1.0070(11)	-1.0970(5)	0.044
C(26)	0.1908(13)	-0.7338(11)	-0.9231(5)	0.044
C(27)	-0.1856(13)	-1.0285(12)	-0.8246(5)	0.043
C(28)	0.0957(14)	-0.6083(12)	-0.6945(6)	0.055
C(29)	0.4879(15)	-1.1141(13)	-0.5848(6)	0.068
C(30)	0.2385(17)	-1.2754(13)	-0.5162(6)	0.073

persisted; probably caused by one or more pseudo-related atoms being present from the original E map. Because of the limited time available at the workshop, structure elucidation was completed at Glasgow using the *GX* package (Mallinson & Muir, 1985) whence two incorrect atoms were identified and subsequent Fourier syntheses completed the structure. Interestingly, it was an F_o map which revealed the final three C atoms; ΔF maps failing to locate them. Full-matrix least-squares refinement on F of coordinates and anisotropic thermal parameters for all non-H atoms converged to R and wR of 0.057 and 0.067 with $w = 1/(\sigma_F^2)$. H-atom coordinates, obtained from a difference Fourier synthesis, included in final least squares but not refined. 1607 reflections, $I \geq 3.0\sigma_I$, used. $(\Delta/\sigma)_{max} = 0.31$; max. and min. heights in final difference Fourier synthesis 0.22 and -0.25 e Å^{-3}. Scattering factors from *International Tables for X-ray Crystallography* (1974).

Discussion. Final positional and equivalent isotropic thermal parameters are given in Table 1.* Bond lengths

Table 2. Bond distances (Å) and bond angles (°)

Bond	Distance	Bond	Distance
O(1)–C(3)	1·220 (11)	C(1)–C(2)	1·499 (12)
C(1)–C(10)	1·521 (11)	C(2)–C(3)	1·512 (13)
C(3)–C(4)	1·449 (12)	C(4)–C(5)	1·543 (11)
C(4)–C(23)	1·518 (12)	C(4)–C(24)	1·544 (12)
C(5)–C(6)	1·492 (11)	C(5)–C(10)	1·538 (11)
C(5)–C(24)	1·483 (11)	C(6)–C(7)	1·526 (11)
C(7)–C(8)	1·516 (11)	C(8)–C(9)	1·557 (10)
C(8)–C(14)	1·568 (10)	C(9)–C(10)	1·547 (10)
C(9)–C(11)	1·541 (10)	C(9)–C(25)	1·533 (10)
C(11)–C(12)	1·532 (10)	C(12)–C(13)	1·526 (7)
C(13)–C(14)	1·567 (7)	C(13)–C(18)	1·571 (7)
C(13)–C(27)	1·556 (8)	C(14)–C(15)	1·549 (10)
C(14)–C(26)	1·547 (10)	C(15)–C(16)	1·540 (12)
C(16)–C(17)	1·543 (11)	C(17)–C(18)	1·578 (10)
C(17)–C(22)	1·549 (11)	C(17)–C(28)	1·527 (11)
C(18)–C(19)	1·507 (10)	C(19)–C(20)	1·535 (11)
C(20)–C(21)	1·545 (11)	C(20)–C(29)	1·521 (12)
C(20)–C(30)	1·495 (12)	C(21)–C(22)	1·517 (11)

Angle	(°)	Angle	(°)
C(2)–C(1)–C(10)	113·6 (7)	C(1)–C(2)–C(3)	116·4 (7)
O(1)–C(3)–C(2)	117·8 (8)	O(1)–C(3)–C(4)	121·1 (8)
C(2)–C(3)–C(4)	121·0 (8)	C(3)–C(4)–C(5)	115·8 (7)
C(3)–C(4)–C(23)	115·4 (7)	C(3)–C(4)–C(24)	119·5 (7)
C(5)–C(4)–C(23)	120·6 (7)	C(5)–C(4)–C(24)	57·4 (5)
C(23)–C(4)–C(24)	115·9 (7)	C(4)–C(5)–C(6)	116·9 (7)
C(4)–C(5)–C(10)	116·6 (7)	C(4)–C(5)–C(24)	61·3 (6)
C(6)–C(5)–C(10)	113·7 (6)	C(6)–C(5)–C(24)	119·6 (7)
C(10)–C(5)–C(24)	118·9 (7)	C(5)–C(6)–C(7)	113·3 (7)
C(6)–C(7)–C(8)	108·9 (6)	C(7)–C(8)–C(9)	110·4 (6)
C(7)–C(8)–C(14)	113·9 (6)	C(9)–C(8)–C(14)	116·7 (6)
C(8)–C(9)–C(10)	106·5 (6)	C(8)–C(9)–C(11)	107·9 (6)
C(8)–C(9)–C(25)	114·8 (6)	C(10)–C(9)–C(11)	108·9 (6)
C(10)–C(9)–C(25)	110·0 (6)	C(11)–C(9)–C(25)	108·6 (6)
C(1)–C(10)–C(5)	111·1 (6)	C(1)–C(10)–C(9)	113·9 (6)
C(5)–C(10)–C(9)	112·1 (6)	C(9)–C(11)–C(12)	115·9 (6)
C(11)–C(12)–C(13)	113·2 (5)	C(12)–C(13)–C(14)	108·4 (4)
C(12)–C(13)–C(18)	110·7 (4)	C(12)–C(13)–C(27)	106·5 (4)
C(14)–C(13)–C(18)	110·1 (4)	C(14)–C(13)–C(27)	111·2 (4)
C(18)–C(13)–C(27)	110·0 (4)	C(8)–C(14)–C(13)	110·2 (5)
C(8)–C(14)–C(15)	108·3 (6)	C(8)–C(14)–C(26)	110·8 (6)
C(13)–C(14)–C(15)	109·0 (5)	C(13)–C(14)–C(26)	111·4 (5)
C(15)–C(14)–C(26)	107·1 (6)	C(14)–C(15)–C(16)	116·6 (6)
C(15)–C(16)–C(17)	117·9 (7)	C(16)–C(17)–C(18)	114·0 (6)
C(16)–C(17)–C(22)	107·0 (6)	C(16)–C(17)–C(28)	106·9 (6)
C(18)–C(17)–C(22)	108·7 (6)	C(18)–C(17)–C(28)	113·6 (6)
C(22)–C(17)–C(28)	106·2 (7)	C(13)–C(18)–C(17)	114·1 (5)
C(13)–C(18)–C(19)	111·4 (5)	C(17)–C(18)–C(19)	112·7 (6)
C(18)–C(19)–C(20)	116·9 (6)	C(19)–C(20)–C(21)	109·5 (6)
C(19)–C(20)–C(29)	109·5 (7)	C(19)–C(20)–C(30)	109·0 (7)
C(21)–C(20)–C(29)	110·5 (7)	C(21)–C(20)–C(30)	109·9 (7)
C(29)–C(20)–C(30)	108·5 (7)	C(20)–C(21)–C(22)	113·5 (7)
C(17)–C(22)–C(21)	113·7 (7)	C(4)–C(24)–C(5)	61·2 (5)

and angles are given in Table 2. An *ORTEP* (Johnson, 1976) diagram, Fig. 1, illustrates the numbering scheme for the molecule whilst a stereoview showing the structural conformation is in Fig. 2.

The molecule consists of five six-membered rings with the five methyl groups C(25)–C(28) and C(30), and the cyclopropane ring all axial. Ring *A* approximates a skew-boat conformation, owing to the torsional constraints of the cyclopropane group; rings *B* and *C* both adopt chair forms whereas the *cis*-decalin *D/E* system has the twist-boat boat conformation thus showing the characteristic stretched, *S*, form (Masaki, Niwa & Kikuchi, 1975) which is the generally preferred conformation for friedelane-type triterpenes (Rogers, Phillips, Balawant & Viswanathan, 1980), except those where a bulky substituent, *e.g.* at C(16α), may force the alternative *F*, folded, form to be adopted. Cyclopropane-ring formation involving a methyl group of a typical pentacyclic triterpenoid is rare in contrast to tetracyclic triterpenoid series, *e.g.* the cycloartanes. The only previous example is phyllanthol, 3β-hydroxy-13α,27-cycloursane (*Rodd's Chemistry of Carbon Compounds*, 1969). Participation of the C(4) axial methyl group in cyclopropane formation with C(5) has been observed previously in the diterpenoid field (Connolly, Gunn, McCrindle, Murray & Overton, 1967).
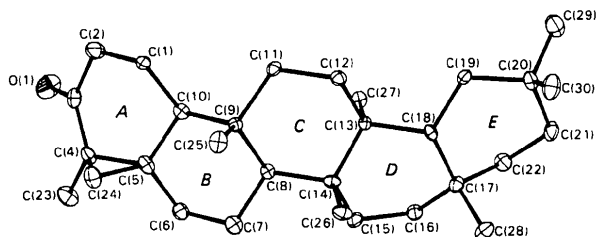
Fig. 1. Perspective view of the molecule showing the numbering scheme and vibrational ellipsoids (25% probability level).
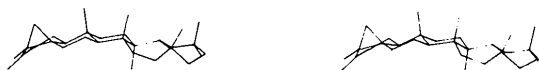

Fig. 2. Stereoview of the molecule showing the characteristic stretched conformation.

References

AKIYAMA, E., MORIYAMA, Y., MURAE, T., TSUYUKI, T. & TAKAHASHI, T. (1978). *Bull. Chem. Soc. Jpn*, 51, 2702–2704.
ANJANEYULU, A. S. R., ROW, L. R., SUBRAHMANYAM, C. & MURTY, K. S. (1973). *Tetrahedron*, 29, 3909–3914.
ANJANEYULU, V. & ROW, L. R. (1965). *Curr. Sci.* 34, 608–609.
CASCARANO, G., GIACOVAZZO, C., POLIDORI, G., SPAGNA, R. & VITERBO, D. (1982). *Acta Cryst.* A38, 663–670.
CONNOLLY, J. D., GUNN, D. M., MCCRINDLE, R., MURRAY, R. D. H. & OVERTON, K. H. (1967). *J. Chem. Soc. C*, 2, 668–674.
International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht).
JOHNSON, C. K. (1976). *ORTEP*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee.
MALLINSON, P. R. & MUIR, K. W. (1985). *J. Appl. Cryst.* 18, 51–53.
MASAKI, N., NIWA, M. & KIKUCHI, T. (1975). *J. Chem. Soc. Perkin Trans. 2*, pp. 610–614.
PRICK, P. A. J., BEURSKENS, P. I. & GOULD, R. O. (1983). *Acta Cryst.* A39, 570–576.
Rodd's Chemistry of Carbon Compounds (1969). Vol. II, Part C, edited by S. COFFEY, p. 451. Amsterdam: Elsevier.
ROGERS, D., PHILLIPS, F. L., BALAWANT, J. S. & VISWANATHAN, N. (1980). *J. Chem. Soc. Chem. Commun.* pp. 1048–1049.