Structures of Croverin (*X*-Ray Analysis) and Dihydrocroverin, Two New Diterpene Lactones from *Croton verreauxii* Baill.

By EIICHI FUJITA,* MANABU NODE, KIYOHARU NISHIDE, MIDORI SAI, and KAORU FUJI
(*Institute for Chemical Research, Kyoto University, Uji, Kyoto-Fu* 611, *Japan*)

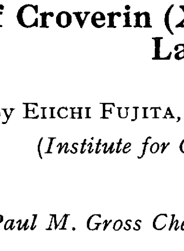
ANDREW T. MCPHAIL*
(*Paul M. Gross Chemical Laboratory, Duke University, Durham, North Carolina* 27706)

and JOHN A. LAMBERTON*
(*C.S.I.R.O. Division of Applied Organic Chemistry, P.O. Box* 4331, *Melbourne, Victoria* 3001, *Australia*)

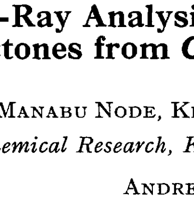
Summary The structures and stereochemistries of croverin and dihydrocroverin, two new diterpene lactones from *Croton verreauxii* Baill., have been elucidated by a combination of chemical, physical, and *X*-ray methods.

RECENT reports[1] on the structure of plaunol A (**1**), a new diterpene lactone from *Croton sublyratus* Kurz., prompt us to describe our investigations leading to the isolation and structural characterization of two new clerodane-type diterpenes from *Croton verreauxii* Baill. (Euphorbiaceae).

(1)



(2)



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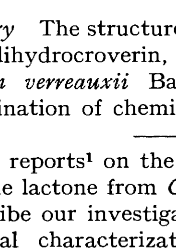

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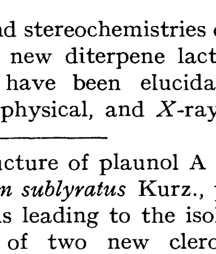

(5)

Croverin (**2**) {$C_{21}H_{22}O_6$, m.p. 151—153 °C, $[\alpha]_D^{25} - 26°$ ($CHCl_3$)} and a minor diterpene, dihydrocroverin (**5**) {$C_{21}H_{24}O_6$, m.p. 205—206 °C, $[\alpha]_D^{25} - 66°$ ($CHCl_3$)}, were both isolated from the methanol extracts of dry aerial parts of *C. verreauxii*. Hydrolysis of (**2**) with potassium hydroxide in aqueous tetrahydrofuran followed by methylation with diazomethane afforded the diester (**3**). The presence of a five-membered hemiacetal ring in (**3**) was confirmed by its conversion into the γ-lactone (**4**) [i.r. ($CHCl_3$) 1765 cm^{-1}] on oxidation with Collins reagent. These reactions and detailed examination of its spectral data [i.r. (KBr) 1736, 1710, 1645, and 1630 cm^{-1}; u.v. (MeOH) 210·5 (ϵ 13,500) and 283 nm (ϵ 1600); ^1H n.m.r. ($CDCl_3$): δ 7·41 (2H, d, *J* 1 Hz), 7·04 (1H, dd, *J* 5 and 3 Hz), 6·37 (1H, t, *J* 1 Hz), 5·65 (1H, s), 5·34 (1H, t, *J* 8 Hz), 4·91 (1H, s), 4·81 (1H, s), 3·76 (3H, s), 3·48 (1H, dt, *J* 13 and 4 Hz), and 2·53 (2H, d, *J* 8 Hz); ^{13}C n.m.r. ($CDCl_3$): C=O 170·8 and 166·5; furan ring 143·8, 139·2 (15-, 16-C), 126·9 (13-C), and 108·2 (14-C); C=C 149·2 (4-C), 140·6 (3-C), 132·4 (8-C), and 107·6 (17-C); quaternary C 50·1 and 46·6; CH 106·9 (20-C), 73·5 (12-C), and 48·3 (10-C); CH_2 39·1, 35·3, 31·9, 26·3, and 22·7; CH_3, 51·8 p.p.m.] led to the assignment of structure (**2**) to croverin with the stereochemistry at C(10), C(12), and C(20) still to be defined. A three-dimensional single-crystal *X*-ray analysis confirmed structure (**2**) and also provided the total relative stereochemistry for croverin.

Crystal data: $C_{21}H_{22}O_6$ (**2**), monoclinic, space group $P2_1$, $a = 8{\cdot}938(4)$, $b = 13{\cdot}061(6)$, $c = 7{\cdot}609(3)$ Å, $\beta = 90{\cdot}00(3)°$, $Z = 2$. Intensity data to $\theta = 67°$ were recorded on an Enraf-Nonius CAD-3 automated diffractometer (Ni-filtered Cu-K_α radiation, $\lambda = 1{\cdot}5418$ Å; θ–2θ scans). The structure was solved by direct methods by use of MULTAN.[2] Full-matrix least-squares refinement of atomic positional† and

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† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

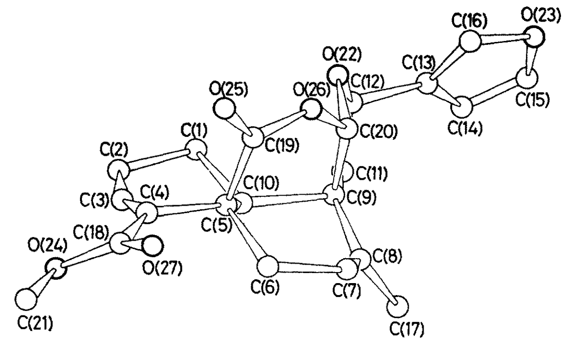

FIGURE. Structure and solid-state conformation of croverin (**2**).

thermal (anisotropic C, O; isotropic H) parameters converged at R 0·045 over 1082 statistically significant [$I > 2{\cdot}0\sigma(I)$] reflections. A view of the conformation‡ of (**2**) in the solid state is provided in the Figure. The cyclohexene ring lies closer to a 1β,10α-half-chair (C_2) form than to a 10α-envelope (C_s) form, the methylenecyclohexane ring has a flattened chair conformation, and the tetrahydrofuran ring adopts an envelope form. In the δ-lactone ring, the C–O–CO–C moiety is distinctly non-planar and this ring is best described as a flattened chair.

The ^{1}H n.m.r. spectrum of (**5**) lacked those peaks ascribed to the terminal methylene group (δ 4·91 and 4·81) in (**2**) but contained a new signal (δ 1·05, 3H, d, J 6 Hz) which indicated the presence of a secondary methyl group. Thus, the structure of dihydrocroverin is (**5**), with the relative configuration at C(8) tentatively assigned from biosynthetic considerations.

The crystallographic calculations, performed at the Triangle Universities Computation Center, Research Triangle Park, North Carolina, were supported by a grant of computer time from Duke University.

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‡ Endocyclic torsion angles, $\omega_{i,j}$(°), about bonds between atoms i and j are, for the cyclohexene ring: $\omega_{1,2}$ 40·7, $\omega_{2,3}$ −7·1, $\omega_{3,4}$ −4·4, $\omega_{4,5}$ −18·7, $\omega_{5,10}$ 52·2, $\omega_{1,10}$ −64·5; for the methylenecyclohexane ring: $\omega_{5,6}$ 53·7, $\omega_{6,7}$ −49·5, $\omega_{7,8}$ 52·1, $\omega_{8,9}$ −58·7, $\omega_{9,10}$ 61·6, $\omega_{5,10}$ −58·3; for the δ-lactone ring: $\omega_{5,10}$ 61·0, $\omega_{5,19}$ −37·4, $\omega_{9,10}$ −59·2, $\omega_{9,20}$ 33·4, $\omega_{20,26}$ −10·5, $\omega_{19,26}$ 12·3; for the tetrahydrofuran ring: $\omega_{9,11}$ −18·1, $\omega_{9,20}$ 32·3, $\omega_{11,12}$ −0·8, $\omega_{12,22}$ 21·9, $\omega_{20,22}$ −35·1.

[1] E. Kitazawa, A. Ogiso, S. Takahashi, A. Sato, M. Kurabayashi, H. Kuwano, T. Hata, and C. Tamura, *Tetrahedron Lett.*, 1979, 1117; E. Kitazawa, A. Sato, S. Takahashi, H. Kuwano, and A. Ogiso, *Chem. Pharm. Bull.*, 1980, **28**, 227.

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