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THE STRUCTURE OF CROTOFOLIN E, A NOVEL TRICYCLIC DITERPENE FROM *Croton corylifolius**

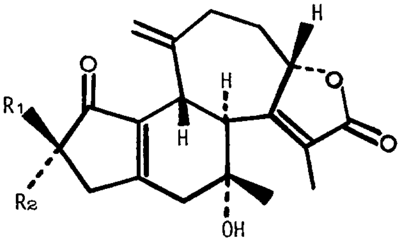
Basil A. Burke, Wilfred R. Chan and Keith O. Pascoe
Chemistry Department, University of the West Indies,
Mona, Jamaica
and
John F. Blount and Percy S. Manchand
Chemical Research Department, Hoffmann-La Roche Inc.,
Nutley, New Jersey 07110, U.S.A.

Abstract. A novel and highly functionalized crotofolane diterpene, crotofolin E (4), has been isolated from *Croton corylifolius* L. (Euphorbiaceae) and its stereostructure determined from spectral and X-ray crystallographic analyses.

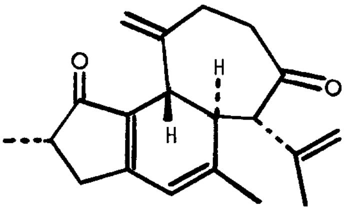
The Jamaican plant *Croton corylifolius* L. (Euphorbiaceae)[1] has been shown by us to contain the unusual tricyclic diterpenes crotofolins A (1),[2] B (2),[2] and C (3),[3] whose novel carbon skeleton (crotofolane) was revealed by X-ray crystallography. Also isolated from this plant was the clerodane diterpene corylifuran.[4] In continuation of our studies on C. *corylifolius* we report the isolation and structural elucidation of crotofolin E (4), a highly functionalized member of the crotofolanes, which contains the rare[5] (for diterpenes) pseudo acid moiety.

Crotofolin E (4), $C_{20}H_{22}O_5$ (M^+ m/e 342), m.p. 208-211° (dec.), $[\alpha]_D^{25}$-65° ($CHCl_3$, C=1.00), $\lambda_{max.}$(EtOH) 215 nm (ε=15,700), had i.r. (KBr, cm^{-1}) absorptions attributed to the following functional groups: OH (3515, 3417), α,β-unsaturated cyclopentenone (1698), and terminal methylene (1670, 905).

The ^1H n.m.r. spectrum ($CDCl_3$, δ) of 4 showed the presence of a secondary methyl group (1.21, d, J=7 Hz, $C\underline{H}_3$-19), a methyl group on a fully substituted carbon atom bearing an oxygen function (1.31, s, $C\underline{H}_3$-20), a vinylic methyl group (1.93, s, $C\underline{H}_3$-17), and a terminal methylene group (4.46 and 4.91, d, J=1 Hz, $C\underline{H}_2$-18). Absorption due to the proton on C-5 appeared as a singlet at 3.16. In addition, the Fourier transform ^{13}C n.m.r. spectrum[6] ($CDCl_3$, p.p.m. from Me_4Si) of crotofolin E was in accord with structure **4** with absorptions at 9.5 (q, C-20), 16.8 (q, C-19), 19.6 (q, C-17), 34.3 (t, C-10), 35.7 (t, C-11), 39.4 (d, C-7), 40.0 (d, C-13), 41.2 (t, C-3), 52.2 (d, C-2), 53.7 (d, C-5), 59.2 (s, C-6), 107.9 (s, C-9), 111.7 (t, C-18), 128.4 (s, C-12), 143.6 (s, C-15), 146.1 (s, C-14), 159.1 (s, C-8), 165.8 (s, C-4), 169.7 (s, C-16), and 206.6 (s, C-1). Assignments are based on chemical shifts and off-resonance decoupled spectra, and are tentative for C-10 and C-11.



1, R_1=OH, R_2=CH_3
2, R_1=CH_3, R_2=OH



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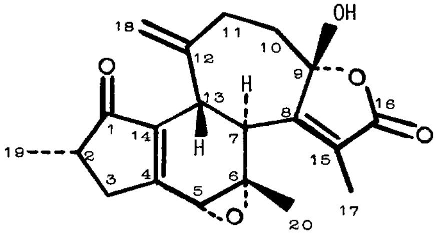


Crotofolin E (**4**)

Owing to the paucity of material that was isolated, and because the preceding spectral evidence did not differentiate between a crotofolane and a daphnetoxin-type[7] diterpene, we decided to determine the structure of crotofolin E by single-crystal X-ray analysis using direct methods.

A crystal (approximate size 0.15 x 0.25 x 0.30 mm) of **4**, ex CH_3OH, belongs to space group $P2_1,2_1,2_1$, with a = 10.907 (1) Å, b = 10.921 (2) Å, c = 15.827 (2) Å, and Z = 4;

d_{calcd} was 1.269 g cm^{-3}. Of a total of 1467 independent reflections, which were measured on a computer-controlled four-circle diffractometer (θ-2θ scans, Ni-filtered CuKα radiation, μ CuKα = 7.8 cm^{-1}), 1348 were considered observed [$I > 2.5\sigma$ (I)]. Application of a multiple solution procedure[8] with full-matrix least squares refinement (anisotropic and isotropic thermal parameters were used for non-hydrogen and hydrogen atoms, respectively) led to the final discrepancy indices of R = 0.035 and wR = 0.042. The final difference map had no peaks > ± 0.2 eA^{-3}. Although the hydrogen atoms were included in the structure factor calculation their parameters were not refined.[9] A stereoscopic ORTEP drawing of a molecule of 4 (relative stereochemistry) is shown in the Figure.

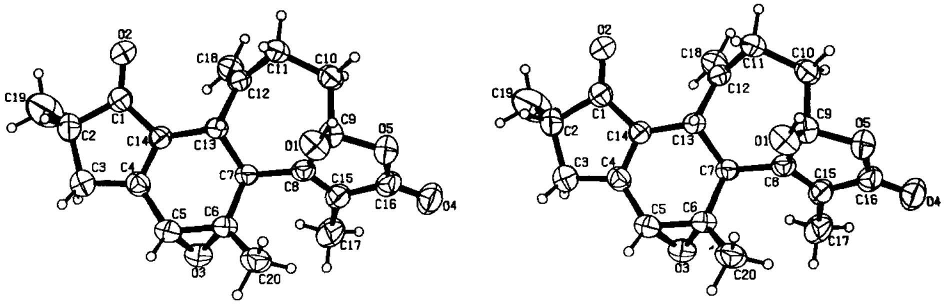
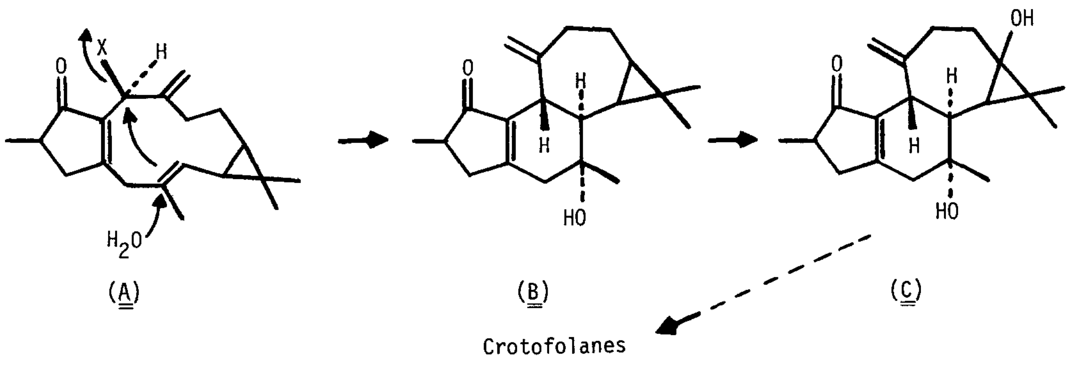


Figure: A stereoscopic view of crotofolin E (4) (relative stereochemistry).

The isolation of crotofolin E substantiates the hypothesis[2,10] that the crotofolanes are probably derived from a lathyrane-type precursor (A), as indicated below:



References and Notes

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3. W.R. Chan, E.C. Prince, J.F. Blount, and P.S. Manchand (unpublished results). Also isolated by us is crotofolin D, whose structure is related to 3.
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6. Recorded at 25.2 M Hz on a Varian XL-100 instrument by Mr. Ross Pitcher (Hoffmann-La Roche, Nutley), to whom we are most grateful.
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9. Listings of atomic parameters, final anisotropic thermal parameters, bond lengths, bond angles and torsion angles for 4 may be obtained from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England. [see Tetrahedron Letts., 3081 (1978)].
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* Correspondence may be directed to B.A.B., W.R.C., or P.S.M. The present address of W.R.C. is: Department of Chemistry, University of the West Indies, St. Augustine, Trinidad, West Indies.

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