

Ferrubietolide: X-Ray Crystal Structure of a Novel Bis-diterpene from *Dysoxylum lenticellare*

Kay D. Onan,^{*a} Charles J. Kelley,^{*b} Chamnan Patarapanich,^b John D. Leary,^b and Adetunji J. Aladesanmi^c

^a Department of Chemistry, Northeastern University, Boston, MA 02115, U.S.A.

^b Department of Chemistry, Massachusetts College of Pharmacy and Allied Health Sciences, Boston, MA 02115, U.S.A.

^c Department of Pharmacognosy, University of Ife, Ile-Ife, Nigeria

Spectroscopic and X-ray diffraction analyses have established the structure and stereochemistry of ferrubietolide, a new bis-diterpene isolated from *Dysoxylum lenticellare*, which apparently arises as the result of a Diels–Alder condensation of two dissimilar diterpenes.

Recently we reported our studies of the alkaloids of *Dysoxylum lenticellare*.^{1,2} In addition, we have investigated the pentane soluble extract of the leaves of this plant and have found it to contain mainly diterpenes; indeed, the least polar chromatography fractions of the pentane extract contain almost exclusively diterpenes. Besides major quantities of the well-characterized diterpenes phyllocladene³ and 8 β -hydroxysandaracopimar-15-ene,⁴ minor quantities of ferruginol⁵ (1) and 10-nonacosanol were identified. Also isolated in small amounts was a new, unusual bis-diterpene.

This molecule, named ferrubietolide (2), m.p. 239–240 °C (from 1,2-dimethoxyethane, 1,2-DME), contains a γ -lactone carbonyl, ν_{\max} (KBr) 1797 cm⁻¹, and a single aromatic ring. The u.v. spectrum showed λ_{\max} (1,2-DME) 243 (ϵ 5 300), 284 (3 430), and 293 nm (3 150). The electron impact mass spectrum did not reveal the parent ion; rather two diterpenoid molecular ions of roughly equal intensity were observed (m/z 296.1726 calc. for C₂₀H₂₄O₂ and m/z 272.2517 calc. for C₂₀H₃₂). Further mass spectral investigation employing the field desorption technique revealed the true parent ion at m/z 568 (agreeing with C₄₀H₅₆O₂). The facile cleavage of the bis-diterpene suggested an electrocyclic fragmentation pathway such as a retro Diels–Alder or a McLafferty rearrangement.

The ¹H-n.m.r. spectrum (500 MHz, CDCl₃) revealed eight distinct C-methyl groups, δ 0.61–1.20, including a pair of diastereotopic methyl groups in an isopropyl group (δ 1.117 and 1.130). Other resolved features in the ¹H-n.m.r. spectrum included a dramatically shielded proton at δ 0.49 (dd, J 2, 10 Hz), single hydrogens at δ 1.97 (m), 2.22 (br. d, J 13 Hz), 2.46 (isopropyl septet), 2.72 (br. s), 5.52 (s, vinyl), 6.84 (s, aromatic broadened by benzylic coupling), and 6.93 (s), and a

two proton benzylic multiplet at δ 2.95. The remaining 22 aliphatic hydrogen atoms resonated in complex, overlapping multiplets between δ 0.8 and 1.85.

To define the complete structure and stereochemistry of this molecule an X-ray crystallographic study was undertaken.

Crystals of (2) are orthorhombic, space group $P2_12_12$, $Z = 4$, $a = 19.108(2)$, $b = 24.111(3)$, $c = 7.093(1)$ Å. Data were collected to $2\theta = 130^\circ$ on a Syntex P2₁ automated diffractometer using θ - 2θ scans and Cu- K_α radiation, $\lambda = 1.5418$ Å. The structure was solved using the MULTAN 80 direct methods programmes.⁶ Positional parameters and anisotropic thermal parameters for non-hydrogen atoms were refined by full-matrix least-squares. Hydrogen atoms were included in their calculated positions. Convergence was reached at $R = 0.054$ over 2539 statistically significant [$I \geq 2\sigma(I)$] reflections.†

Figure 1 shows the solid state conformation and numbering scheme of ferrubietolide, shown as is most probable, with the

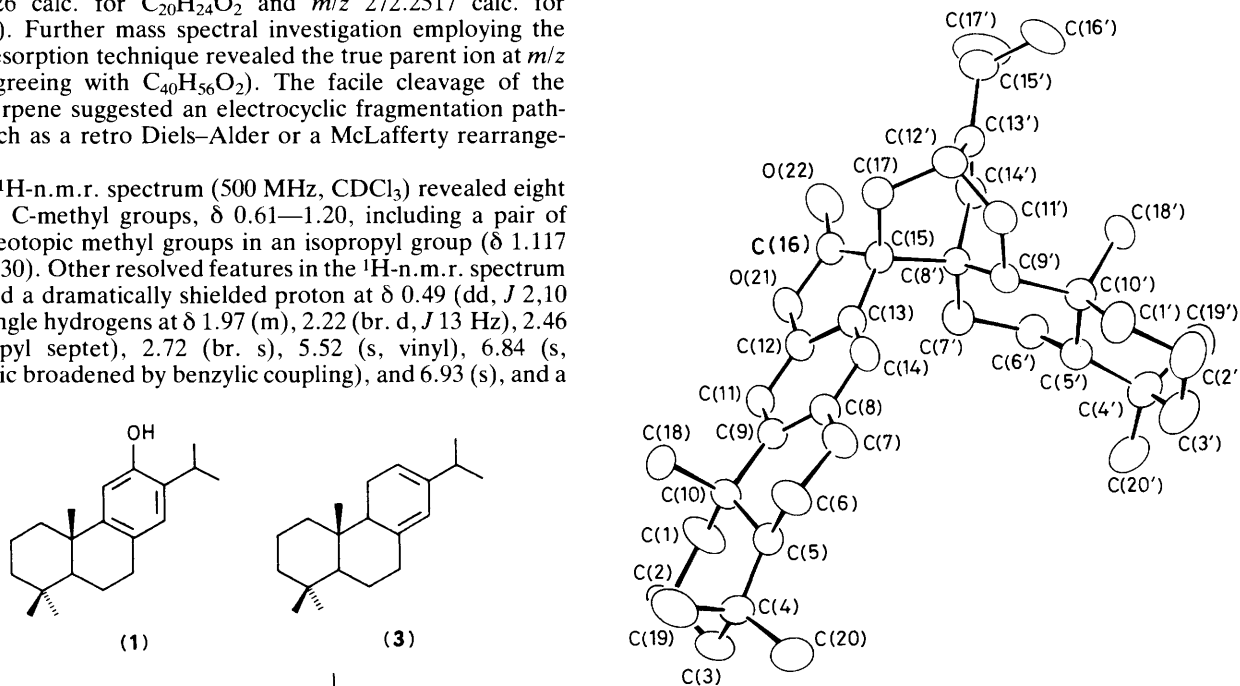
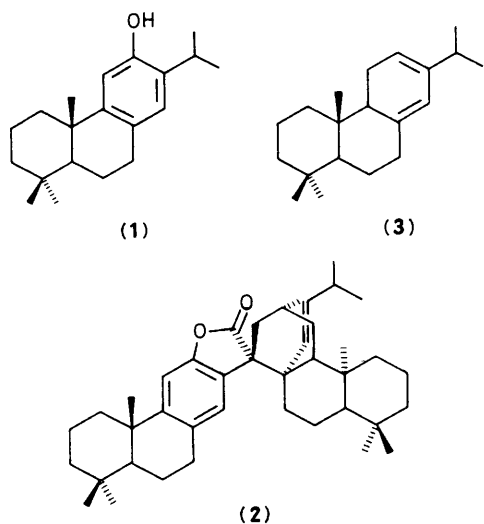


Figure 1. A view of the molecular structure of (2) with thermal ellipsoids at the 50% probability level (ORTEP) and the molecular numbering scheme. Hydrogen atoms have been omitted for clarity.

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



same absolute stereochemistry as ferruginol.⁵ Ferrubietolide has been formed *via* a Diels–Alder reaction of two *non-identical* diterpenes joined in an α -face to α -face union. This condensation involves the exocyclic methylene of ‘ferruginolide’ and the diene system of 8(14),12-abietadiene (**3**), and results in a relatively unstrained molecule. Except for the very long bond between the adjacent quaternary carbons C(15) and C(8') [1.611(4) Å], the molecular parameters are unexceptional.

Four other non-alkaloidal bis-diterpenes have been reported; all, however, are formed from two identical subunits. Maytenone,⁷ isolated from *Maytenus dispermus*, also arises *via* a Diels–Alder condensation while macrophylllic acid⁸ and podototarins,⁹ both from the *Podocarpus* genus, are dimers formed by oxidative coupling. Clerocidin (PR 1350),¹⁰ a bis-diterpene produced by the fungus *Oidiodendron truncatum*, arises through hemiacetal–acetal dimerization.

We thank Dr. C. E. Costello (M.I.T.) for mass spectra under a N.I.H. research grant and Mr. P. Demou (N.S.F. Northeast Regional N.M.R. Facility, Yale University) for a high field n.m.r. spectrum.

Received, 24th September 1984; Com. 1342

References

- 1 A. J. Aladesanmi, C. J. Kelley, and J. D. Leary, *J. Nat. Prod.*, 1983, **46**, 127.
- 2 A. J. Aladesanmi, C. J. Kelley, J. D. Leary, and K. D. Onan, *J. Chem. Res.*, 1984, (S) 108, (M) 1001.
- 3 W. Bottomley, A. R. H. Cole, and D. E. White, *J. Chem. Soc.*, 1955, 2624.
- 4 R. E. Corbett and R. A. J. Smith, *J. Chem. Soc. C*, 1967, 300.
- 5 W. P. Campbell and D. Todd, *J. Am. Chem. Soc.*, 1942, **64**, 928; G. R. Clark and T. N. Waters, *J. Chem. Soc. C*, 1970, 887.
- 6 P. Main, S. J. Fiske, S. E. Hall, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, MULTAN 80, Universities of York, England, and Louvain, Belgium, 1980.
- 7 C. P. Falshaw and T. J. King, *J. Chem. Soc., Perkin Trans. 1*, 1983, 1749.
- 8 S. M. Bocks, R. C. Cambie, and T. Takahashi, *Tetrahedron*, 1963, **19**, 1109.
- 9 R. C. Cambie, W. R. J. Simpson, and L. D. Colebrook, *Tetrahedron*, 1963, **19**, 209.
- 10 N. Rostrup Anderson and P. R. Rasmussen, *Tetrahedron Lett.*, 1984, 465; N. Rostrup Anderson, P. R. Rasmussen, C. P. Falshaw, and T. J. King, *Tetrahedron Lett.*, 1984, 469.