Tetrahedron Letters No. 43, pp 3675 - 3676, 1975. Pergamon Press. Printed in Great Britain.

STRUCTURE AND STEREOCHEMISTRY OF VERNODESMINE, A NOVEL PHENYL BEARING SESQUITERPENE LACTONE FROM *VERNONIA PECTORALIS* BAKER

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(Received in USA 15 August 1975; received in UK for publication 15 September 1975)

Previous studies[1] have established that the germacranolides vernolide(1) and pectorolide (2) occur as the major sesquiterpenoid components of *Vernonia pectoralis* Baker. Further examination of the plant material has now yielded a unique new sesquiterpene lactone, vernodesmine(3), which proves to be the first known example of a naturally-occurring sesquiterpenoid bearing a phenyl substituent.

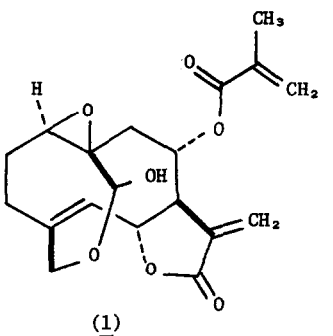
Vernodesmine(3), $C_{25}H_{28}O_7$, m.p. 190-194°, $[\alpha]_D$ +27° (c 0.58, acetone), λ_{max}(EtOH) 210 nm (ε 31300), two conjugated carbonyl groups, 252 and 257 nm (ε 500 and 480), aromatic ring; λ_{max}(Nujol) 3560, 3460 $cm.^{-1}$ (two hydroxy groups), 1745, 1725 $cm.^{-1}$ (γ-lactone and unsaturated ester, 750, 700 $cm.^{-1}$ (phenyl); m/e 440(M^+), 422(M^+-18), 336(M^+-18-18-86), 69 and 41, in accord with the presence of two hydroxy groups and a methacrylate ester. NMR decoupling experiments (240 MHz) led to the following assignment of protons consistent with structure (3): δ($CHCl_3$/pyridine-d_5) 7.15-7.35 (5H, m, phenyl), 6.08 (1H, br. s, H-18), 5.91 (1H, d, J = 3 Hz, H-13), 5.83 (1H, dt, J = 10 and 5.5 Hz, H-8), 5.62 (1H, br. s, H-18), 5.49 (1H, d, J = 4 Hz, H-15), 5.40 (1H, d, J = 2.5 Hz, H-13), 5.06 (1H, t, J = 10 Hz, H-6), 3.81 (1H, m, H-1), 2.77 (1H, m, H-7), 2.32 (1H, d, J = 10 Hz, H-5), 1.95(3H, s, vinyl methyl).

The constitution and relative stereochemistry (3) were elucidated by *X*-ray single crystal analysis. Vernodesmine crystallizes in the monoclinic system, space group $P2_1$, a = 11.94(1), b = 6.68(1), c = 14.17(1) Å, β = 108.48(10)°, U = 1072 $Å^3$, D_m(flotation) = 1.35 $g.cm.^{-3}$, Z = 2, D_c = 1.365 $g.cm.^{-3}$ The structure was solved by direct non-centrosymmetric phase-determining

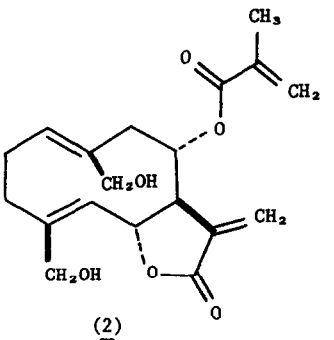
methods using MULTAN[2]. Atomic positional and thermal parameters (anisotropic C,O; isotropic H) were refined by full-matrix least-squares calculations to R 0.052 over 1548 statistically significant [$I > 2\sigma(I)$] reflections measured on an Enraf-Nonius CAD 3 automated diffractometer (Ni-filtered Cu-K_α radiation, λ = 1.542 Å) operating in the θ-2θ scanning mode.

The origin of the phenyl substituent presents a biogenetically intriguing problem. The relative stereochemistries at all the asymmetric centers in vernodesmine, coupled with its co-occurrence with (1) and (2), suggests that it arises from (1) through a nucleophilic attack at C_4 by a suitably modified phenyl substituent precursor with concerted C_5-C_{10} bond formation and opening of the epoxide ring. Subsequent steps will then occur to transform the nucleophile into the phenyl moiety found in (3).

Acknowledgement We thank Schering Research Corporation for partial support of this work.



(1)



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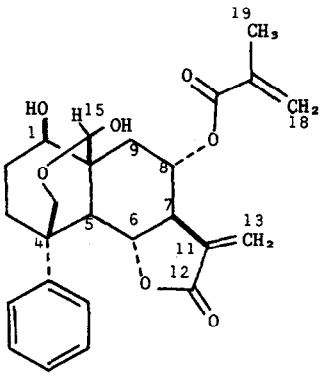

(3)

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