Communications

A *seco*-Germacradienolide from *Liatris pycnostachya*

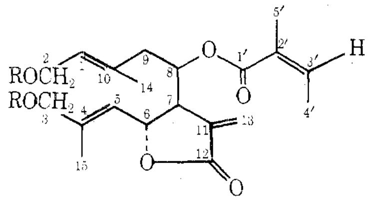
Summary: Discovery and structure determination of the first *seco*-germacradiene pycnolide, a 2,3-*seco*-1(10),4,5-germacradienolide from *Liatris pycnostachya* (Michx.) Kuntze, is reported.

Sir: Germacradienes play a crucial role in biogenetic schemes leading to many other classes of sesquiterpenes,[1] particularly those which, like the germacranes, are heavily represented in nature as sesquiterpene lactones. We now report discovery of the first *seco*-germacradiene pycnolide as a minor lactonic constituent of *Liatris pycnostachya* (Michx.) Kuntze.

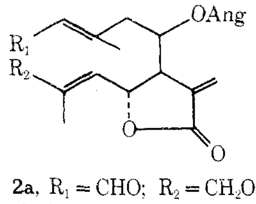
Pycnolide (**1a**), $C_{20}H_{28}O_6$[2] {$[\alpha]^{22}D$ +39.8° (c 1.1, $CHCl_3$), ir 3400, 1765, 1720 and 1650 cm^{-1}}, is an angeloyl ester (see characteristic peaks in Table I) and an α-methylene γ-lactone of the type shown in **1a** (typical signals for H-6, H-7, H-13a, and H-13b[3] whose relationship was established by spin decoupling). Other functional groups are two primary hydroxyls (AB quartet of H-2, two proton singlet of H-3, both shifted downfield on acetylation to **1b**), and two double bonds of type $-C(CH_3){=}CH-$ (two additional vinyl methyls, two vinyl proton signals at 5.30 and 5.52 ppm, the latter superimposed on the signal of a proton on the carbon carrying the angelate). The remaining two nmr signals revealed the presence of a methylene group (C-9); hence pycnolide contains no ring other than that of the lactone.

The above conclusions were corroborated by the ^{13}C nmr spectrum which exhibited the expected two carbonyl singlets (169.7, 166.8), four vinyl singlets (C-10, C-4, C-11, C-2′ at 142.7, 135.9, 132.3, 127.2), three vinyl doublets (C-3′, C-5, C-1 at 138.8, 128.9, 121.6), one vinyl triplet (C-13, 123.3), doublets of C-6 and C-8 (74.6, 71.3), triplets of C-3, C-2, and C-9 (66.3, 58.7, 41.9), doublet of C-7 (47.7), and four methyl quartets (20.3, 15.8, 15.6, 14.0).[4]

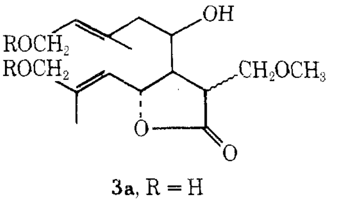
MnO_2 oxidation of **1a** gave the conjugated monoaldehydes **2a** and **2b** and the dialdehyde **2c**. The accompanying downfield shifts of H-1 (in **2a**) and H-5 (in **2b**) permitted unambiguous determination of the entire sequence C-3 through C-2 by double resonance, thus establishing the carbon skeleton as that of a 2,3-*seco*-1(10),4,5-germacradienolide. Hydrolysis of **1a** (NaOMe, MeOH, room temperature, 10–12 hr) furnished **3a** in whose nmr spectrum the H-8 multiplet, formerly at 5.52 ppm, had undergone the expected diamagnetic shift, whereas the signal near 5.3 ppm (H-6) had not been affected significantly and was still spin-coupled to H-5. Hence the lactone rings of **1a** and **3a** were closed to C-6.[6]



1a, R = H
b, R = Ac



2a, R_1 = CHO; R_2 = CH_2OH
b, R_1 = CH_2OH; R_2 = CHO
c, R_1, R_2 = CHO



3a, R = H
b, R = Ac

Table I: The 270-MHz Spectrum of Pycnolide ($CDCl_3$)[a]

H-1	5.30 tbr (6)	H-9b	2.16 dd (15, 6)
H-2	4.12 (AB)	H-13a	6.36 d (2.8)
H-3	4.06	H-13b	5.70 d (2.6)
H-5	5.52 dbr (9.5)	H-14	1.73 br[b]
H-6	5.35 dd (9.5, 5.3)	H-15	1.83 br[c]
H-7	3.10 m	H-3′	6.1 m
H-8	5.52 ddd (8.5, 6, 2)	H-4′	1.93 dq
H-9a	2.45 dd (15, 8.5)	H-5′	1.83 br

[a] Frequencies in ppm downfield from TMS. Figures in parentheses are coupling constants in Hz. [b] Coupled to H-1. [c] Coupled to H-5.

E stereochemistry around the 1,10 and 4,5 double bonds was evident, *inter alia*, from the chemical shifts of the aldehydic proton in **2b** (9.50 ppm)[7] and the C-10 methyl signal in **2a** (2.26 ppm).[8] The absolute configuration at C-8 was established as *R* by applying Horeau's method[9] to **3b** (14.2% optical yield). Since $J_{6,7}$ in **3a** and **3b** is 9 Hz, the lactone ring must be trans-fused (models). If the usual assumption is made that the C-7 side chain is β, H-6 is β as well. Thus the stereochemistry of pycnolide at C-6, C-7, and C-8 is the same as that deduced for all germacranolides and guaianolides isolated previously[10] from *Liatris* species.

It is interesting that, contrary to the situation prevailing in other classes of *seco*-terpenoids, the oxidation states of both C-2 and C-3 (or C-15[3]) of pycnolide are lower than what they must have been prior to ring cleavage.

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References and Notes

(1) W. Parker, J. S. Roberts, and R. Ramage, *Quart. Rev. Chem. Soc.*, **21**, 331 (1967); G. Rücker, *Angew. Chem.*, **85**, 895 (1973).
(2) Since all substances encountered in this study were difficult-to-analyze gums, composition was established by high resolution mass spectrometry and purity by tlc and ^1H and ^{13}C nmr criteria.
(3) Numbering reflects derivation from a germacradiene system. Either C-3 or C-15 of pycnolide could represent C-3 of the hypothetical germacradiene precursor.
(4) Tentative assignments on the basis of predicted chemical shifts, published information,[5] and ^{13}C nmr spectra of lactones of known structure in our files.
(5) N. S. Bhacca, F. W. Wehrli, and N. H. Fischer, *J. Org. Chem.*, **38**, 3618 (1973); N. S. Bhacca, R. A. Wiley, N. H. Fischer, and F. W. Wehrli, *J. Chem. Soc., Chem. Commun.*, 615 (1973).
(6) The relatively simple fragmentation of **1a** and its derivatives under electron impact is fully consonant with structure **1a** and will be discussed in our full publication.
(7) *E.g.*, K. C. Chan, R. A. Jewell, W. H. Nutting, and H. Rapoport, *J. Org. Chem.*, **33**, 3382 (1968); A. F. Thomas and M. Ozainne, *Chem. Commun.*, 47 (1969); U. Schwieter and S. Liaaen-Jensen, *Acta Chem. Scand.*, **23**, 1057 (1969).
(8) *E.g.*, P. B. Venuto and A. R. Day, *J. Org. Chem.*, **29**, 2735 (1964); K. T. Suzuki, N. Suzuki, and S. Nozoe, *Chem. Commun.*, 527 (1971).
(9) A. Horeau, *Tetrahedron Lett.*, 506 (1961); 965 (1962); A. Horeau and H. B. Kagan, *Tetrahedron*, **20**, 2431 (1964); W. Herz and H. B. Kagan, *J. Org. Chem.*, **32**, 216 (1967).
(10) S. M. Kupchan, V. H. Davis, T. Fujita, M. R. Cox, R. J. Restivo, and R. F. Bryan, *J. Org. Chem.*, **38**, 1853 (1973); W. Herz and I. Wahlberg, *Phytochemistry*, **13**, 1421 (1973); W. Herz and I. Wahlberg, *J. Org. Chem.*, **38**, 2485 (1973); W. Herz, J. Poplawski, and R. P. Sharma, *J. Org. Chem.*, **40**, 199 (1975); W. Herz and R. P. Sharma, *Phytochemistry*, in press.

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