Pergamon

Tetrahedron Letters 39 (1998) 3417–3420

TETRAHEDRON LETTERS

Psorothamnone A: A Novel Heterocyclic Compound from *Psorothamnus junceus*

Xiaohua Li,[a] Hongbing Zhang,[a] Curtis Ashendel,[a] Phillip Fanwick[b] and Ching-jer Chang*[a]

[a] Department of Medicinal Chemistry and Molecular Pharmacology

and [b] Department of Chemistry, Purdue University, West Lafayette, Indiana, 47907

Received 9 February 1998; accepted 9 March 1998

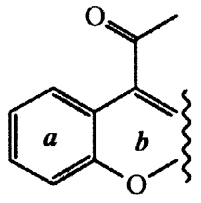
Abstract: A novel heterocyclic compound, psorothamnone A was isolated from *Psorothamnus junceus* and its structure was determined by spectroscopic methods.

Psorothamnus junceus (*Dalea juncea,* Rydb.) is a shrub that grows in the sandy washes and rocky slopes of the eastern side of the Sierra San Padro Martir.[1-2] Despite much previous phytochemical research on *Psorothamnus* species,[3-12] little attention has been paid thus far to the chemical constituents of *P. junceus.* During our search for potential antitumor agents and protein kinase C inhibitors from plants, we have examined the chemical constituents of *P. junceus.*[13] A novel heterocyclic compound, psorothamnone A (**1**), was discovered from the ethanol extract of the stem bark of *P. junceus* upon solvent partition and column chromatography on silica gel. Psorothamnone A exhibited modest inhibition of protein kinase C (IC_{50}: 12 μg/mL),[14] a Ca^{2+} and phospholipid-dependent protein kinase involved in the signal transduction of cell proliferation and differentiation.[15-18]

Psorothamnone A was recrystallized from ethyl acetate as orange needles, m. p. 247-248°C (decomp.). High resolution CIMS gave a $[MH]^+$ ion at m/z 337.0999 corresponding to the molecular formula of $C_{20}H_{17}O_5$ (calcd. 337.1076). IR absorptions at 1674, 1636 and 1607 cm^{-1} suggested an aromatic ketone system. UV absorptions at 465 (ε: 8.4 x 10^4 $Lmol^{-1}cm^{-1}$) and 230 nm (ε: 1.3 x 10^4 $Lmol^{-1}cm^{-1}$) indicated the existence of an extended conjugation. ^1H NMR spectrum revealed one singlet at δ_H 1.407 for two identical C-methyls in a relatively saturated environment, one singlet at δ_H 2.086 for a vinyl C-methyl, one singlet at δ_H 2.824 for an acetyl moiety, and signals for four aromatic protons at δ_H 7.50-8.35. Further 2D NMR experiments (COSY and NOESY) established the 1, 2-disubstituted benzene system for ring ***a***. HMQC and HMBC spectral correlation data established the connectivities for C4-H5, C4-H22, C9-H5 and C10-H8 , which revealed the basic skeleton of ring ***a*** and ***b*** and also allowed the placement of the acetyl group at C4 (ring ***b***).

0040-4039/98/$19.00
PII: S0040-4039(98)00581-4

Ring ***d*** was established by the HMBC correlation analyisis. Two C-methyls at δ_H 1.407 correlated with two ketone carbonyls at δ_C 193.9 (C14) and δ_C 199.3 (C16). In addition, the vinyl methyl at δ_H 2.068 correlated with C16 carbonyl and an oxygenated carbon at δ_C 165.8 (C12). Moreover, the carbon chemical shifts at δ_C 193.9, 194.6 (C21) and 199.3 suggested the presence of three distinct keto functional groups. Considering the above information, the following two structural components may be established.



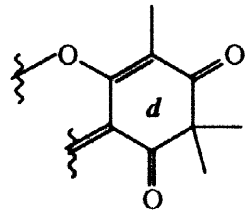
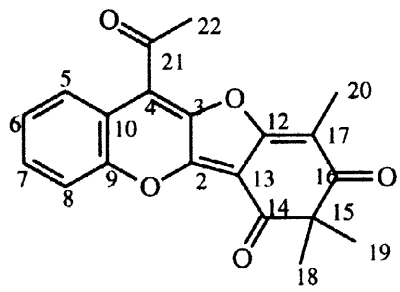


Table 1. 500 MHz ^{1}H-NMR Data in $CDCl_3$ and HMQC, HMBC (J=10Hz) Correlations of **1** [a]

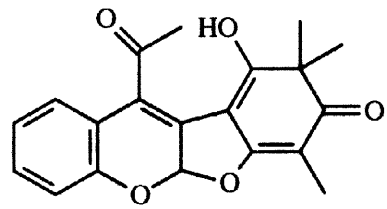
	H5	H6	H7	H8	H18,19	H20	H22
δ_H (J)	8.350 ddd (8.2;1.6;0.4 Hz)	7.348 ddd (8.2;7.1;1.5 Hz)	7.454 ddd (8.3;7.1;1.6 Hz)	7.501 ddd (8.3;1.5;0.4 Hz)	1.407 s	2.086 s	2.824 s
HMQC(δ_C)	C5 (127.0)	C6 (126.4)	C7 (129.9)	C8 (117.5)	C18,19 (23.7)	C20 (8.6)	C22 (32.9)
HMBC(δ_C)	C4 (113.4) C7 (129.9) C9 (150.0)	C8 (117.5) C10 (117.8)	C5 (127.0) C9 (150.0)	C6 (126.4) C9 (150.0) C10 (117.8)	C15 (56.8) C14 (193.9) C16 (199.3)	C12 (165.8) C16 (199.3) C17 (107.2)	C4 (113.4) C21 (194.6)

[a] Chemical shifts and coupling constants for H5-H8 were determined by spin simulation.

These structural formulae account for all oxygen and hydrogen atoms. On the basis of the total 13 degrees of unsaturation known to be present and all of the above-described spectral data, the most likely structure **1** can be envisioned for psorothamnone A (Fig. 1). The alternative linkages between the ring ***b*** and ring ***d*** (**2**) resulted in unaccepted enol functionality for one of the two keto groups (δ_C 199.3 and 193.9) of ring ***d***, and a cyclic acetal group.



1



2

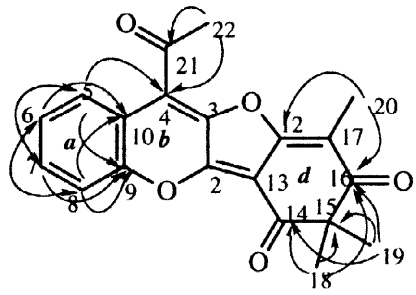


Fig. 1: Struture of **1,** showing HMBC correlations (J =10Hz).

The final structure of psorothamnone A was unambiguously determined by X-ray crystallography and the ORTEP structure is presented in Fig. 2.[19] The crystallographic model showed that the acetyl carbonyl was close to proton H5 while the acetyl methyl was away from proton H5. This explained the absence of cross peak between acetyl methyl and proton H5 in NOESY spectrum. The acetyl carbonyl may induce a strong anisotropic effect on H5 (δ_H 8.350). This new hetrocyclic natural product may serve as a lead compound for further synthesis of more potent protein kinase inhibitors.

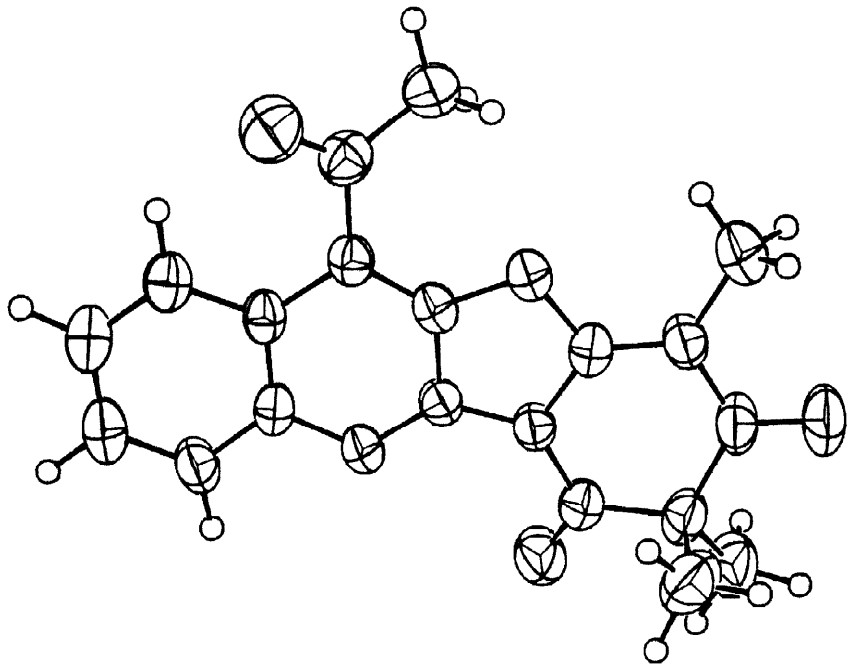


Fig. 2: **ORTEP** structure of **1**.

Acknowledgement

We would like to thank National Cancer Institute for financial support (U01 CA50743 and R01 CA 49632).

REFERENCES AND NOTES

1. Wiggins, I. L. *Contr. Dudley Herb.* **1940**, *3*, 41-55.
2. Shreve, F.; Wiggins, I. L. *Vegetation and Flora of the Sonoran Desert,* Vol. 1; Stanford University Press: Stanford, 1985; pp. 663.
3. Dreyer, D. L. ; Munderloh, K. P.; Thiessen, W. E. *Tetrahedron*, **1975**, *31*, 287-293.
4. Dreyer, D. L. *Phytochemistry,* **1978**, *17*, 585.
5. Roitman, J. N. ; Jurd, L. *Phytochemistry,* **1978**, *17*, 161-163.
6. Dominguez, X. A.; Franco, R.; Zamudio, A.; Barradas D., D. M.; Watson, W. H. ; Zabel, V.; Merijanian, A. *Phytochemistry,* **1980**, *19*, 1262-1263.
7. Dominguez, X. A.; Franco, R.; Marroquin, J.; Merijanian A.; Gonzalez, Q.; Juanita, A. *Rev. Latinoam. Quim.* **1982**, *13*, 39-40.
8. Manikumar. G.; Gaetano, K.; Wani, M. C.; Taylor, H.; Hughes, T. J.; Warner, J.; McGivney, R.; Wall, M. E. *J. Nat. Prod.* **1989**, *52*, 769-773.
9. Gonzalez, A. G.; Aguiar, Z. E.; Luis, J. G.; Rivera, A.; Calle, J.; Gallo, G. *Phytochemistry,* **1992**, *31*, 2565-2566.
10. Caffaratti , M.; Ortega, M. G.; Scarafia, M. E.; Ariza Espinar, L.; Juliani, H. R. *Phytochemistry,* **1994**, *36*, 1083-1084.
11. Ortega, M. G.; Scarafia, M. E.; Juliani, H. R. *Fitoterapia*, **1996**, *67*, 81.
12. Patil, A. D.; Freyer, A. J.; Eggleston, D. S.; Haltiwanger, R. C.; Tomcowicz, B.; Breen, A.; Johnson, R. K. *J. Nat. Prod.* **1997**, *60*, 306-308.
13. The stem bark of *P. junceus* was collected in Baja California, Mexico in April, 1989 by Richard Spjut and Richard Marin, World Botanical Association (Laurel, Maryland).
14. Protein kinase C inhibition assay was carried out as described in Reference 17.
15. Blumberg, P. M. *Cancer Res.* **1988**, *48*, 1-8.
16. Nishizuka, Y. *Nature*, **1988**, *334*, 661-665.
17. Jayatilake, G. S.; Jayasuriya, H.; Lee, E.-S.; Koonchanok, N. M.; Geahlen, R. L.; Ashendel, C. L.; McLaughlin, J. L.; Chang, C.-J. *J. Nat. Prod.* **1993**, *56*, 1805-1810.
18. Caponigro, F.; French, R. C.; Kaye, S. B. *Anti-Cancer Drugs*, **1997**, *8*, 26-33.
19. Crystal data for **1**, triclinic, space group P-1 (No. 2), a = 7.233 (1), b = 8.600 (1), c = 13.288 (1) Å, V = 805.4 A^3, for Z = 2, D_c = 1.39g cm^{-3}, λ = 0.71073 Å, T = 20°, F(000) = 352.0, R = 0.061, R_w = 0.0702. X ray spectrum was obtained by Enraf-Nonius CAD4 diffractometer. Crystal dimension 0.65 x 0.13 x 0.06 mm was mounted on a glass fiber in a random orientation. Data was collected by ω-2θ mode with ω scan width = 0.61 + 0.35 tan θ, take-off angle 3.2°, scan rate 2-20°/min. 2836 reflections measured, 2836 unique, giving 1603 with $I > 3.0\sigma$ (I). The structure was solved by direct methods using SHELX-86. All calculations were performed on a VAX computer using SDP/VAX.