Phytochemistry, Vol 28, No 10, pp 2846 2847, 1989
Printed in Great Britain

0031 9422/89 $3 00+0 00

SALVONITIN, A DITERPENE FROM *SALVIA PRIONITIS*

LONG-ZE LIN* and GEOFFREY A CORDELL†

Program for Collaborative Research in the Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago, Chicago, IL 60612, U S A

(*Received* 12 *January* 1989)

Key Word Index—*Salvia prionitis*, Labiateae, diterpenoid, salvonitin

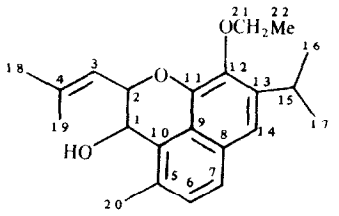
Abstract—From the roots of *Salvia prionitis* a new diterpenoid, salvonitin was isolated and its structure elucidated on the basis of its ^{1}H and ^{13}C NMR spectra

INTRODUCTION

In previous investigations of *Salvia prionitis* Hance (Labiateae), a plant native to the Southern Provinces of China and used in traditional Chinese medicine as an antibacterial, antitubercular and antiphlogistic drug, we reported the isolation and structure elucidation of several new diterpenoids [1–5] Most of these compounds were derived from the corresponding quinone methide abietane diterpenoids through acid-catalysed migration of the 10-methyl group to C-5 accompanied by fission of ring A [6] In this report, we present the isolation and structure elucidation of an additional new member of this subgroup of diterpenoids, salvonitin (**1**), which has a novel ether linkage between C-2 and C-11

RESULT AND DISCUSSION

Salvonitin (**1**), $C_{22}H_{28}O_3$ by HRMS, was obtained from the roots of *Salvia prionitis* (0.0006%, yield), and crystallized from acetone as yellowish needles, mp 123–124°, $[\alpha]_D$ +3° (MeOH, *c* 0.1). Intense absorptions in the UV spectrum were observed at 243, 300, 311 and 341 nm, suggesting a highly conjugated naphthalene system, and the IR spectrum showed absorption for a hydroxyl group (3316 cm^{-1}) The ^{1}H NMR spectrum indicated the presence of an isopropyl group (δ1.29, *d*, *J* =6.6 Hz, 1.34, *d*, *J*=6.6 Hz, 3.38, *sept*, *J*=6.6 Hz), an ethoxy group (δ1.22, *t*, *J*=7.2 Hz, 3.58, *m*, 3.75, *m*), an aromatic methyl (δ2.48), two olefinic methyls (δ1.59, 1.86), three aromatic protons (δ7.14, *d*, *J*=7.8 Hz; 7.61, *d*, *J*=7.8 Hz; 7.21, *s*) and a hydroxyl group (δ5.75, *s*, D_2O exchangeable) The homonuclear COSY spectrum showed that the coupling between H-2 (δ5.53, *dd*, *J*=1.8 and 8.7 Hz) and H-1 (δ 4.63, *d*, *J*=1.8 Hz), and the coupling constant between H-1 and H-2, indicated that the angle between the two protons was about 30° The COSY spectrum also showed long-range coupling between H-3 and each of two olefinic methyls



1

The ^{13}C NMR and APT spectra of the isolate exhibited six methyls, three aromatic methine carbons, an olefinic methine carbon, three aliphatic methine carbons and eight quaternary carbons. The methylene signal at δ63.75, and two methine signals at δ73.81 and 74.27, indicated that each of them was attached to an oxygen atom.

Determination of the carbon framework and substitution pattern of salvonitin (**1**) was made through a series of selective INEPT [7] and CSCM 1D [8] experiments, which also permitted the unambiguous assignment of the ^{13}C NMR spectrum CSCM 1D irradiation of the ^{13}C satellites of H-1 (δ4.63), H-2 (5.53), H-3 (4.88), H-6 (7.14), H-7 (7.61), H-14 (7.21), H-15 (3.38), H-16 (1.29), H-17 (1.34), H-18 (1.59), H-19 (1.86), H-20 (2.48) and H-22 (1.22) of **1** resulted in magnetization transfer to their corresponding carbon atoms appearing at δ73.81 (C-1), 74.27 (C-2), 120.45 (C-3), 126.50 (C-6), 127.54 (C-7), 115.70 (C-14), 27.71 (C-15), 22.15 (C-16), 22.91 (C-17), 18.66 (C-18), 25.66 (C-19), 18.24 (C-20) and 15.66 (C-22), respectively CSCM 1D experiments also led to the assignment of the methylene group of OCH_2Me H-21 at δ3.58, 3.75 and C-21 at 63.75

Selective INEPT irradiation of H-21 (δ3.58, 3.75) enhanced the signal at δ139.77 (C-12), indicating that the OCH_2Me group should be attached to C-12. Polarization transfer from H-15 enhanced C-12 and C-14, and irradiation of H-16 and H-17 enhanced C-13 (δ136.28), indicating the isopropyl group to be located at C-13. Irradiation of H-14 (δ7.21) enhanced C-12, C-15, C-7 and C-9 (110.81), whereas irradiation of H-20 enhanced C-6 and C-10 (122.36) and irradiation of H-6 enhanced C-8 (126.25), C-10 and C-20 Polarization transfer from H-7

*On leave from the Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, People's Republic of China

†Author to whom correspondence should be addressed

enhanced C-5 (δ132.91), C-9 and C-14, and selective INEPT irradiation of H-2 enhanced C-10, C-4 (138.56) and C-11 (139 77), indicating that C-2 and C-11 were attached to the same oxygen atom as part of a pyran ring. Furthermore, irradiation of the OH enhanced C-2 and irradiation of H-1 enhanced C-5, C-3, and C-9, supporting the view that this compound should have structure **1** Because of the conformational flexibility of the pyran ring system it was not possible to unambiguously assign the stereochemistry at C-1 and C-2. Salvonitin (1) represents a further new diterpene skeleton from *S prionitis* [2–5] and does not appear to be artefact.

EXPERIMENTAL

General Mp· uncorr. ^{1}H NMR, homonuclear COSY, ^{13}C NMR and APT spectra were recorded in $CDCl_3$, using TMS as int. standard. CSCM 1D and Selective INEPT NMR experiments were performed at 90.8 MHz using a Nicolet NMC-360 spectrometer Low resolution MS were obtained at 70 eV. Selective INEPT and CSCM 1D spectra were recorded on a Nicolet NMC 360 spectrometer Data sets of 16K covering a spectral width 10000 Hz were acquired Proton pulse widths were calibrated by using a sample of HOAc in 10% C_6D_6 ($^1J = 6.7$ Hz) in a 5-mm NMR tube. The radio frequency field strength for the soft pulse was on the order of 25 Hz in these experiment 6 or 8 Hz were used as the $^3J_{C-H}$ value for the aromatic protons, and 4 or 6 Hz for other protons

Plant material The plant material of *Salvia prionitis* Hance was collected in Jiang-Xi Province of China in June, 1986, and voucher specimens are deposited in the herbarium of Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, People's Republic of China

Isolation of salvonitin The air-dried powdered roots of *Salvia prionitis* (11 kg) were percolated with EtOH at room temp. and the EtOH extract conc *in vacuo* at 50° to afford a thick dark syrup, which was distributed between $CHCl_3$ and H_2O The organic layer was subjected to CC on silica gel eluting with $CHCl_3$, fractions containing **1** were subjected to repeated prep TLC using cyclohexane–CH_2Cl_2 (1 4) as a solvent system to afford yellow needles of **1** (70 mg, 0 00064%), mp 123–124°, $[\alpha]_D$ +3° (MeOH, *c* 0.1), UV λ_{max} (log ε)· 220 (4.02), 243 (4.24), 300 (3.22), 311 (3.22), 341 (3.09) nm; IR ν_{max}^{KBr} cm^{-1}: 3316, 2913, 1627, 1572, 1524, 1263, 1217, 1209, 1086 and 753, ^{1}H NMR ($CDCl_3$, 300 MHz)· δ4 63 (*d*, $J = 1$ 8 Hz, H-1), 5.53 (*dd*, $J = 1.8$, 8.7 Hz, H-2), 4.88 (*d*, $J = 8$ Hz, H-3), 7.14 (*d*, $J = 7$ 8 Hz, H-6), 7.61 (*d*, $J = 7.8$ Hz, H-7), 7.21 (*s*, H-14), 3.38 (*sep*, $J = 6.6$ Hz, H-15), 1.29 (*d*, $J = 6$ 6 Hz, H-16), 1 34 (*d*, $J = 6.6$ Hz, H-17), 1 59 (*s*, H-18), 1 86 (*s*, H-19), 2.48 (*s*, H-20), 3.58 (*m*, H-21α), 3.75 (*m*, H-21β), 1.22 (*t*, $J = 7$ 2 Hz, H-22) and 5.75 (*s*, OH, D_2O exch), ^{13}CNMR (75.6 MHz): δ73.81 (C-1), 74.27 (C-2), 120 45 (C-3), 138.56 (C-4), 132.91 (C-5), 126.50 (C-6), 127.54 (C-7), 126.25 (C-8), 110.81 (C-9), 122 36 (C-10), 139 77 (C-11), 139.77 (C-12), 136 28 (C-13), 115 70 (C-14), 27.71 (C-15), 22 15 (C-16), 22.91 (C-17), 18.66 (C-18), 25.66 (C-19), 18.24 (C-20), 63 75 (C-21) and 15.66 (C-22), MS (electron impact, 70 eV) *m/z* (rel. int)· 340 $[M]^+$ (19), 281 (15), 272 (11), 271 (61), 244 (18), 243 (100), 227 (11), 165 (4), 152 (4), 141 (4), 128 (5), 115 (4), 113 (5), 69 (4), 43 (5), 41 (15) and 29 (11); HRMS 340.2037 for $C_{22}H_{28}O_3$, calcd 340 2038

Acknowledgement—We would like to thank the Division of Cancer Treatment, National Cancer Institute, Bethesda, MD, for financial support, and the Research Resources Center of the University of Illinois at Chicago for the provision of NMR and mass spectroscopic facilities.

REFERENCES

1 Lin, L -Z., Wang, X.-M., Huang, X.-L., Huang, Y. and Yang, B.-J. (1988) *Acta Pharm. Sinica* **23**, 273.
2 Lin, L.-Z , Wang, X.-M , Huang, X -L., Huang, Y. and Yang, B -J (1988) *Planta Med* **54**, 443
3 Lin, L.-Z , Wang, X -M , Huang, X.-L. and Huang, Y (1989) *Acta Chim. Sinica* (in press).
4 Blaskó, G , Lin, L -Z. and Cordell, G. A. (1988) *J Org. Chem* **53**, 133
5 Lin, L -Z., Blaskó, G and Cordell, G. A. (1989) *Phytochemistry*, **28**, 177.
6 Karanatsios, D., Scarpa, J. S and Eugster, C H. (1966) *Helv Chim Acta*, **49**, 1151.
7. Bax, A. (1984) *J. Magn. Reson.* **57**, 314
8 Sarker, S K and Bax, A. (1985) *J Magn. Reson.* **62**, 109.