Pergamon

0031-9422(95)00962-0

Phytochemistry, Vol. 42, No. 3, pp. 907–908, 1996

0031-9422/96 $15.00 + 0.00

NOTHAPODYTINES A AND B FROM *NOTHAPODYTES FOETIDA*

TIAN-SHUNG WU,* YU-YI CHAN, YANN-LII LEU, CHING-YUH CHERN and CHIEH-FU CHEN†

Department of Chemistry, National Cheng Kung University, Tainan, Taiwan, R.O.C.; †National Research Institute of Chinese Medicine, Taipei, Taiwan, R.O.C.

(*Received in revised form* 27 *November* 1995)

Key Word Index—*Nothapodytes foetida*; Icacinaceae; alkaloids; nothapodytines A and B.

Abstract—Two new naturally occurring alkaloids, nothapodytines A and B, were isolated and characterized from the stems of *Nothapodytes foetida*.

INTRODUCTION

Nothapodytes foetida is the only species of *Nothapodytes* native to Orchid island and is cultivated in Taiton County, Taiwan [1, 2]. As we reported previously [3], the ethanol extract of stems of *N. foetida* showed significant cytoxicity in a human KB tissue culture assay. In the course of our continuing search for novel bioactive natural products, we have succeeded in isolating two new alkaloids, nothapodytines A and B, from stems of this species.

RESULTS AND DISCUSSION

Nothapodytine A (**1**) was isolated and recrystallized from $CHCl_3$ as pale yellowish needles, mp 235 ~ 238°. Its high resolution mass spectrum (*m/z* 334.1317) indicated the molecular formula $C_{20}H_{18}N_2O_3$ $[M]^+$. The UV spectrum, with absorption at 220, 260, 321 and 363 nm, was consistent with the typical spectra of complex alkaloids with quinoline and pyridone chromophores [4]; these absorptions also resembled those of 9-methoxycamptothecine (**3**) [3]. The presence of amide and α,β-unsaturated ketone moieties in the molecule could be explained rationally by the IR absorption bands at 1651 and 1694 cm^{-1}, respectively. In the ^1H NMR spectrum of **1**, three mutually coupled protons at δ 6.95 (1H, *d*, $J = 7.6$ Hz), 7.71 (1H, *dd*, $J = 8.8$ and 7.6 Hz) and 7.77 (1H, *d*, $J = 8.8$ Hz) were characteristic signals for the H-10, H-11 and H-12 resonances of ring A. Two singlet signals at δ 8.82 and 7.26, together with a methylene proton at δ 5.29, were attributed to H-7, H-14 and H_2-5, respectively. On the basis of the above observations, the partial structure of **1** was similar to that of rings A–D of **3**. Furthermore, the ^1H NMR spectrum of **1** differed from that of **3** only in the presence of a singlet signal at δ 2.25 (3H) for a methyl group and at δ 1.24 (3H) and 2.90 (2H) for a 1-oxopropyl group instead of the E ring of **3** [3]. The presence of a 1-oxopropyl group in **1** was also supported by the fragment ion at *m/z* 278 $[M - C_3H_5O]^+$. The arrangement of these two substituents on positions C-16 and C-15 is based on the NOESY spectrum [5]. In the NOESY experiment of **1** (Fig. 1), only the 1-oxopropyl (δ 1.24 and 2.90) group is within nOe distance from H-14 (δ 7.26), indicating that the methyl and 1-oxopropyl groups should be located at C-16 and

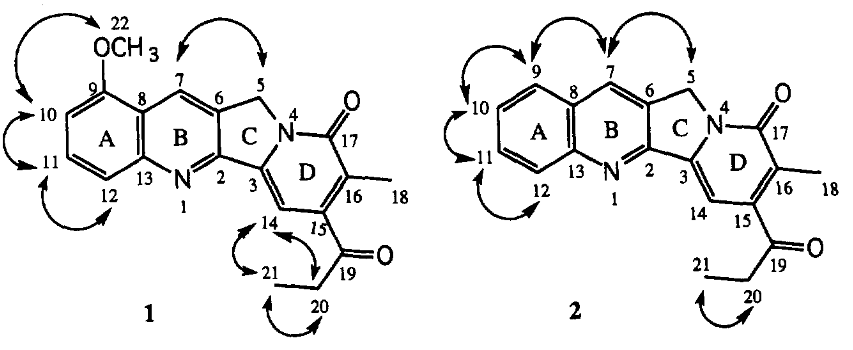
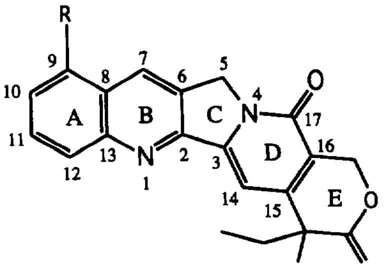


Fig. 1. NOESY correlations of compounds **1** and **2**.

---

*Author to whom correspondence should be addressed.



3 R = OMe
4 R = H

C-15, respectively. To conclude from the above results, the structure of nothapodytine A could be assigned as **1**.

The identity of nothapodytine B (**2**) was established by comparison of its physical properties (IR, UV, NMR and mass spectrum) with those of **1**. Both compounds showed similar carbonyl absorption and UV spectrum. Compound **2** has the same degree of unsaturation as **1**, suggesting that the two alkaloids have the same skeleton. The ^{1}H NMR signals of **2** showed four mutually coupled aromatic protons at δ 8.20 (1*H*, *dd*, $J = 8.8$ and 1.4 Hz), 7.92 (1H, *dd*, $J = 8.8$ and 1.4 Hz), 7.82 (1H, *ddd*, $J = 8.8$, 8.8 and 1.4 Hz) and 7.65 (1H, *ddd*, $J = 8.8$, 8.8 and 1.4 Hz). This indicates that there is no substituent on ring A. To confirm this result, a NOESY experiment was conducted (Fig. 1). The results obtained showed that H-9 had correlation with both H-10 and H-7, H-10 with H-9 and H-11, and H-11 with H-12. In addition, the high resolution mass spectrum showed a molecular formula of $C_{19}H_{16}N_2O_2$, which corresponds to be one methoxyl group less than **1**. Including all of the above results, the structure of nothapodytine B is represented as **2**.

EXPERIMENTAL

General. Mps: uncorr. ^{1}H NMR (400 MHz) spectra were recorded in $CDCl_3$. Chemical shift values are shown in ppm (δ) with TMS as int. standard. MS were recorded using a direct inlet system. UV were determined in MeOH, and IR recorded in KBr discs.

Plant material. N. foetida was collected from Taiton County, Taiwan, in July 1989, and its identity verified by Prof. C. S. Kuoh. A voucher specimen is deposited in the Herbarium of Cheng Kung University, Tainan, Taiwan [3].

Extraction and separation. This is the same procedure as described previously [3].

Nothapodytine A (**1**). Pale yellowish needles ($CHCl_3$), mp 235–238°. UV λ_{max} nm: 220, 260, 321, 363. IR ν_{max} cm^{-1}: 1694, 1651, 1478, 1441, 1405, 1192, 1173, 722. ^{1}H NMR: δ 1.24 (3H, *t*, $J = 7.2$ Hz, $-CH_2C\underline{H}_3$), 2.25 (3H, *s*, CH_3), 2.90 (2H, *q*, $J = 7.2$ Hz, $-C\underline{H}_2CH_3$), 4.06 (3H, *s*, 9-OMe), 5.29 (2H, *s*, H-5), 6.95 (1H, *d*, $J = 7.6$ Hz, H-10), 7.26 (1H, *s*, H-14), 7.71 (1H, *dd*, $J = 8.8$, 7.6 Hz, H-11), 7.77 (1H, *d*, $J = 8.8$ Hz, H-12), 8.82 (1H, *s*, H-7). EIMS *m/z* (rel. int.): 334 ([M]$^+$, 100), 319 (42), 306 (25), 291 (12), 278 (41), 263 (13), 249 (17), 234 (19), 206 (15), 103 (11), 55 (10); HREIMS: calc. for $C_{20}H_{18}N_2O_3$, *m/z* 334.1317 [M]$^+$, found 334.1317.

Nothapodytine B (**2**). Pale yellowish needles ($CHCl_3$), mp 210–215°. UV λ_{max} nm: 220, 254, 368. IR ν_{max} cm^{-1}: 1700, 1650, 1600, 1382, 1230, 1142, 760, ^{1}H NMR: δ 1.25 (3H, *t*, $J = 7.2$ Hz, $-CH_2C\underline{H}_3$), 2.30 (3H, *s*, CH_3), 2.91 (2H, *q*, $J = 7.2$ Hz, $-C\underline{H}_2CH_3$), 5.30 (2H, *s*, H-5), 7.26 (1H, *s*, H-14), 7.65 (1H, *ddd*, $J = 8.8$, 8.8, 1.4 Hz), H-10), 7.82 (1H, *ddd*, $J = 8.8$, 8.8, 1.4 Hz, H-11), 7.92 (1H, *dd*, $J = 8.8$, 1.4 Hz, H-9), 8.20 (1H, *dd*, $J = 8.8$, 1.4 Hz, H-12), 8.38 (1H, *s*, H-7). EIMS *m/z* (rel. int.): 304 (M]$^+$, 100), 289 (29), 276 (18), 248 (43), 219 (30), 191 (7), 140 (7), 109 (8). HREIMS calc. for $C_{19}H_{16}N_2O_2$, *m/z* 304.1211 [M]$^+$, found 304.1210.

Acknowledgement—We thank the National Research Institute of Chinese Medicine for financial support.

REFERENCES

1. Li, H. L. (1977) *Flora of Taiwan*, Vol. 3, p. 648. Epoch Publishing Co., Taipei, Taiwan.
2. Liu, Y. C. (1972) *Ligneous Plants of Taiwan*, p. 500. National Chung-Shing University, Taiwan.
3. Wu, T. S., Leu, Y. L., Hsu, H. C., Ou, L. F., Chen, C. C., Chen, C. F., Ou, J. C. and Wu, Y. C. (1995) *Phytochemistry* **39**, 383.
4. Cordell, G. A. (1981) *Introduction to Alkaloids: a Biogenetic Approach*, p. 665. John Wiley & Sons, New York.
5. Ernst, R. R., Bodenhansen, G. and Wokaun, A. (1987) *Principles of Nuclear Magnetic Resonance in One and Two Dimensions*, p. 490–538. Oxford