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A REARRANGED TAXANE FROM THE HIMALAYAN YEW *TAXUS WALLICHIANA**

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Key Word Index—*Taxus wallichiana*; Taxaceae; taxoids; 11(15 → 1)-abeotaxanes.

Abstract—The stem bark of *Taxus wallichiana* gave an abeobaccatin IV derivative, whose structure was established by spectral data and derivatization.

INTRODUCTION

The Himalayan yew (*Taxus wallichiana* [Zucc.] = *T. baccata* ssp. *wallichiana* Zucc Pilg) is a small medium sized evergreen tree growing in the temperate Himalayas at altitudes of 1800–3300 m and in the Khasia hills at an altitude of 1500 m. The plant is used in the Ayurvedic system of medicine [1] and its needles can be a good source of 10-deacetylbaccatin III [2], the starting material for the syntheses of the important anticancer drugs paclitaxel (=taxol®) and docetaxel (=taxotere®). Several other taxanes, rearranged taxanes [3–6] and apocarotenoid [7] have also been isolated from the Himalayan yew. As part of ongoing studies on the Himalayan yew, we report here the isolation of a new abeotaxane (**1**) from the stem bark of the plant.

RESULTS AND DISCUSSION

The amorphous compound **1** was obtained as a minor product (isolation yield 10 mg kg^{-1} of dried bark) from the chloroform-soluble fraction of an ethanolic extract of the stem bark. The ^1H NMR spectrum of the compound showed characteristic taxoid signals for four tertiary methyl groups, three acetoxy groups and one benzoyl group. The ^1H NMR spectrum of the compound showed broad peaks for other protons. Compound **1** underwent acetylation at room temperature, and the acetate (**2**) showed in its ^1H NMR spectrum sharp signals for all the protons at room temperature. The spectrum showed sharp signals for a 4-acetoxy-5-(20)-oxetane moiety, five acetoxy groups and the methine protons present in the molecule. The ^{13}C NMR spectrum of **2** showed a singlet at δ 75.48 (C-15) which suggested an 11 (15 → 1) abeotaxane structure [8]. Compounds of this type often produce a broad NMR spectrum [8] at room temperature and thus, the line broadening effect observed in the ^1H NMR spectrum of **1** also indicated an abeotaxane structure for **1**. Compound **2** exhibited signals for five acetoxy groups as compared to three in the original molecule and thus **1** has two acylable hydroxyl groups. Moreover, while the protons at δ 4.69 and one of the two protons at δ 5.97 of **1** underwent pronounced downfield shifts to δ 6.36 and 6.42, respectively, the remaining proton at δ 5.97 showed a marginal downfield shift to δ 6.16 on acetylation. This finding suggested that the benzoyl group was not at C-2 and it must be either at C-9 or C-10. This was also verified by the NOESY studies on **2** in which ROE peaks were observed between the aromatic proton at δ 8.0 *ortho* to the carbonyl and H-10 and H-9. The ^{13}C NMR spectrum and the chemical shifts and splitting pattern of the protons in the ^1H NMR spectrum of **2** were found to be identical with those reported for 13-acetyl-13-decinnamoyl taxchinin B and thus the acetate was characterized as 13-acetyl-13-decinnamoyl taxchinin B [5].

In order to assign the positions of the two hydroxyl groups in **1**, the connectivities of the protons in the taxoid skeleton were established by ^1H–^1H COSY, and the result showed that the C-9 and C-13 hydroxyls were not esterified. This was in accordance with the upfield resonances of H-9 and H-13 (δ 4.69 and 4.50, respectively) compared to δ 6.16 and 5.62 for the same protons in **2**. Thus, **1** was characterized as 13-decinnamoyl-9-deacetyl taxchinin B.

All 9,10-mono esters of abeotaxanes reported to date are 9-esters, [9,10]. Taxoid **1** represents the first example in which the ester group is at C-10. In order to prove that no acyl group migration has taken place during acetylation of **1** into **2** and to locate the benzoyl

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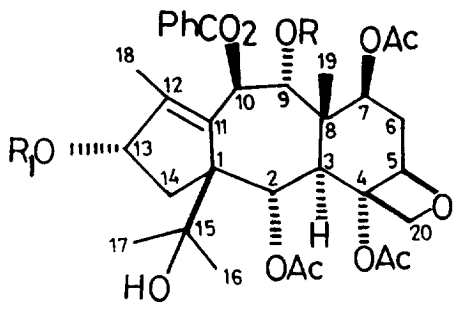

1 R = R_1 = H
2 R = R_1 = Ac

group at C-10, a NOESY* spectrum was run on **1** to inspect the generally observed ^1H–^1H NOESY correlations: H-9/H-19 and H-2, and H-10/H-3 and H-18 [11]. However, the above correlations were not observed. Instead, the following NOESY correlations were observed: 7/3; 2/H-19 and H-17; 5/6α, 6β; 3/14; 13/H-18. The relative stereochemistry of **1** was elucidated as shown in Fig. 1 on the basis of the above correlations.

EXPERIMENTAL

Plant material was collected in Arunachal Pradesh, India. A voucher specimen is kept at the herbarium of CIMAP.

Extraction and isolation. The dried and powdered bark (0.8 kg) was extracted with MeOH (4 × 3 l) at room temp. The combined extracts were concd (final vol. 200 ml), suspended in H_2O and extracted with $CHCl_3$ (3 × 0.5 l). Evapn of the $CHCl_3$ phase left a residue (19 g) that was sepd by CC (190 g silica gel, $CHCl_3$ containing increasing amounts of MeOH as eluent). Compound **1** was isolated from the $CHCl_3$–MeOH (49:1) eluate by repeated CC (silica gel) followed by prep. TLC (20 × 20 cm plate, toluene–Me_2CO, 3:1) as amorphous solid (8 mg).

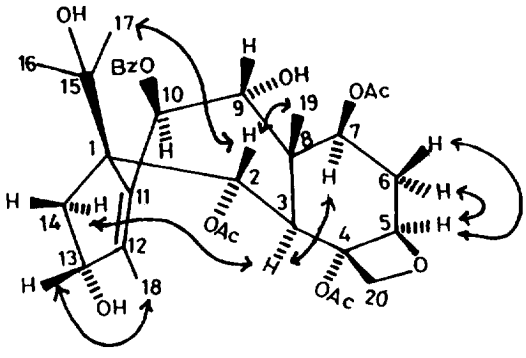

Fig. 1. Relative stereochemistry of **1**; arrows denote NOESY correlations.

*HMBC could not be run on **1** due to the paucity of material.

13-Decinnamoyl-9-deacetyl taxchinin B (**1**). UV λ_{max}^{MeOH} nm: 204, 228, 282 (hump); IR ν_{max}^{KBr} cm^{-1}: 3408, 1742–1719, 1240, 1026; FAB-MS *m/z*: 631 $[MH]^+$ $[C_{33}H_{42}O_{12}+H]^+$, 653 $[M+Na]^+$ $[C_{33}H_{42}O_{12}+Na]^+$, 613 $[MH-H_2O]^+$; ^1H NMR (300 MHz, $CDCl_3$, multiplicities after D_2O exchange): δ 5.97 (*br* signal, H-2, H-10), 3.19 (*br* signal, H-3), 4.92 (*d*, *J* = 7 Hz, H-5), 2.60 (*m*, *H*-6β), 1.90 (*m*, H-6α), 5.45 (*br.* signal, H-7), 4.69 (signal merged with HOD, H-9), 4.50 (merged signal, H-13, H-20), 2.13 (*m*, H-14β), 1.50 (*m*, H-14α), 1.25 (*s*, H-16), 1.22 (*s*, H-17), 2.17 (*s*, H-18), 1.74 (*s*, H-19), 2.04, 1.81, 1.74 (*s*, OAc).

REFERENCES

1. Kapoor, L. D. (1990) in *Handbook of Ayurvedic Medicinal Plants*, p. 317. CRC Press, Boca Raton, FL.
2. Appendino, G., Gariboldi, P., Gabetta, B., Pace, R., Bombardelli, E. and Viterbo, D. (1992) *J. Chem. Soc., Perkin Trans 1* 2925.
3. Appendino, G., Ozen, H. C., Gariboldi, P., Torregiani, E., Gabetta, B., Nizzola, R. and Bombardelli, E. (1993) *J. Chem. Soc., Perkin Trans 1* 1563.
4. Barboni, L., Gariboldi, P., Torregiani, E., Appendino, G., Gabetta, B. and Bombardelli, E. (1993) *Phytochemistry* **33**, 145.
5. Das, B., Padma Rao, S., Srinivas, K. V. N. S., Yadav, J. S. and Das, R. (1995) *Phytochemistry* **38**, 671.
6. Chattopadhyay, S. K., Sharma, R. P., Appendino, G. and Gariboldi, P. (1995) *Phytochemistry* **39**, 869.
7. Appendino, G., Ozen, H. C., Enriu, R., Barboni, L., Gabetta, B. and Zini, G. F. (1993) *Fitoterapia* **64**, 396.
8. Appendino, G., Barboni, L., Gariboldi, P., Bombardelli, E., Gabetta, B. and Viterbo, D. (1993) *J. Chem. Soc., Chem. Commun.* 1587.
9. Yue, Q., Fang, Q. C., Liang, X. T. and He, C. H. (1995) *Phytochemistry* **39**, 871.
10. Appendino, G. (1995) *Nat. Prod. Rep.* **12**, 349.
11. Fuji, K., Tanaka, K., Li, B., Shigu, T., Sun, H. and Taga, T. (1993) *J. Nat. Prod.* **56**, 1520.