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A REARRANGED TAXANE FROM THE HIMALAYAN YEW

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

Abstract—The needles of *Taxus wallichiana* gave an *abeo*baccatin IV derivative, whose structure was established by spectroscopical data.

INTRODUCTION

The Himalayan yew (*Taxus wallichiana Zucc.* (= *T. baccata* ssp. *wallichiana* [Zucc.] Pilg.)) is a tree or a large shrub growing on either sides of the Himalayas, from Afganistan to Burma [1]. In contrast to the European yew (*T. baccata* L.), the Himalayan yew has a remarkable history of medicinal use [2], and is also employed as a colouring matter and as incense [3]. The needles of *T. wallichiana* can be a good source of 10-deacetylbaccatin III [4], the starting material for the synthesis of the important antitumour drugs taxol and taxotere. The plant has thus received considerable attention [4–11], and important differences between the secondary metabolites of *T. baccata* and *T. wallichiana* have emerged. Indeed, C-13, C-14 oxygenated taxoids [4, 5] and apocarotenoids [11] have been isolated only from the Himalayan yew. Furthermore, taxine, a mixture of basic alkaloids responsible for the poisonous properties of the European yew, has not yet been detected in *T. wallichiana*, as a result of a lower concentration or of an easier degradation during storing. Differences in the acylation pattern of *abeo*taxanes have also been observed, since the compounds of this type isolated from *T. wallichiana* generally bear an acetyl and not a benzoyl at C-2 [12]. As part of ongoing studies on plants from the genus *Taxus*, we report the isolation of a further *abeo*taxane from the needles of the Himalayan yew.

RESULTS AND DISCUSSION

The crystalline compound **1** was obtained from the brevifoliol [7]-containing fraction of a needle extract. The isolation yield (*ca* 16 mg kg^{-1} of dried needles) compares with that of other oxetane-type *abeo*taxanes [12]. A singlet at δ66.9 suggested a rearranged 11 (15 → 1) *abeo*taxane structure [13]. Compounds of this type often show broad NMR spectra at room temperature [13], but line-broadening in the spectra of **1** was moderate, and full assignment of the ^{1}H and ^{13}C NMR spectra by 1D and 2D techniques (H–H COSY, ^1J ^3J and ^{1}H–^{13}C correlations) could be achieved already at room temperature. The results showed that **1** is an *abeo*baccatin IV derivative with the allylic hydroxyls non esterified. This was in accordance with the upfield resonance of H-10 and H-13 (δ4.36 and 4.30, respectively) and with the lack of long-range (^3J) heterocorrelation between these protons and the acetate carbonyls.

The large value of $J_{9,10}$ (10.0 Hz) shows that the major rotamer in solution is the one with ring B in the twist-boat conformation and the oxygen functions at C-9 and C-10 pseudoequatorial.

EXPERIMENTAL

Plant material. *Taxus wallichiana* was collected in Himachal Pradesh (India), and was identified by S. P. Jain, CIMAP, India. A voucher specimen is kept at the herbarium of CIMAP.

Isolation of **1**. Dried, powdered needles (5 kg) were extracted with MeOH (4 × 25 l) at room temp. The combined extracts were concd (final vol. 1 l), suspended in water and successively extracted with hexane and CHCl$_3$ (3 × 2 l). Evapn of the CHCl$_3$ phase left a residue (60 g that was sepd by CC (600 g silica gel, CHCl$_3$ containing increasing amounts of MeOH as eluant). Frs eluted with CHCl$_3$–MeOH (96 : 4) contained **1** and brevifoliol, which were further sepd by CC using CHCl$_3$–MeOH, 49:1 as eluant. The final yield was 200 mg for brevifoliol and 80 mg for **1**.

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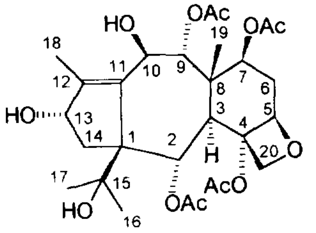

1

10,13-*Deacetyl*abeo*baccatin* IV (**1**). Crystals, mp 220–222°, $[\alpha]_D^{25}$ -34 (MeOH, *c* 1.0); IR ν_{max}^{KBr} cm^{-1}: 3620, 3480, 3420, 1745, 1735, 1718, 1480, 1445; CIMS (NH_3) 586 $[M + 18]^+$ $[C_{28}H_{40}O_{12} + NH_4]^+$ (100); ^1H NMR (300 MHz, DMSO-d_6, multiplicities after D_2O exchange): δ5.78 (*d*, $J = 7.6$ Hz, H-2), 2.83 (*d*, $J = 7.6$ Hz, H-3), 4.87 (*br*, *d*, $J = 7.6$ Hz, H-5), 2.28 (*m*, H-6α), 1.60 (*m*, H-6β), 5.24 (*br t*, $J = 8.0$ Hz, H-7), 5.61 (*d*, $J = 10.0$ Hz, H-9), 4.36 (*d*, $J = 10.0$ Hz, H-10), 4.30 (*br*, *t*, $J = 7.0$ Hz, H-13), 1.48 (*m*, H-14α), 1.92 (*m*, H-14β), 0.96 (*s*, H-16), 0.86 (*s*, H-17), 1.65 (*s*, H-18), 1.43 (*s*, H-19), 4.14 (*d*, $J = 7.8$ Hz, H-20α), 4.32 (*d*, $J = 7.8$ Hz, H-20β), 2.08, 2.06, 2.00, 1.94 (*s*, OAc); ^{13}C NMR (75 MHz, DMSO-d_6): δ66.9 (*s*, C-1), 68.0 (*d*, C-2), 44.8 (*d*, C-3), 78.4 (*s*, C-4), 84.2 (*d*, C-5), 35.1 (*t*, C-6), 70.3 (*d*, C-7), 43.0 (*s*, C-8), 79.2 (*d*, C-9), 65.5 (*d*, C-10), 136.9 (*s*, C-11), 145.9 (*s*, C-12), 75.6 (*d*, C-13), 38.8 (*t*, C-14), 75.0 (*s*, C-15), 25.1 (*q*, C-16), 28.0 (*q*, C-17), 11.3 (*q*, C-18), 12.6 (*q*, C-19), 73.9 (*t*, C-20), 171.3, 170.5, 170.1, 169.8 (*s*, OAc), 22.2, 21.9, 21.8, 21.5 (*q*, OAc).

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