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A TAXANE EPOXIDE FROM *TAXUS WALLICHIANA**

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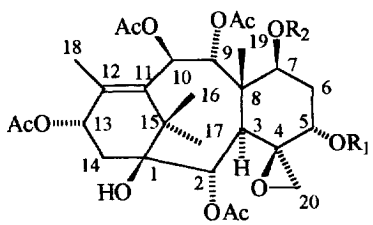
Abstract—The needles of the Himalayan yew gave a taxane epoxide identified as 5-deacetyl-1-hydroxybaccatin I. The structure of the compounds previously reported as the 5- and 7-deacetyl derivatives of 1-hydroxybaccatin I should be revised. © 1997 Elsevier Science Ltd. All rights reserved

INTRODUCTION

A taxane epoxide identified as 5-deacetyl-1-hydroxybaccatin I (**1**) was reported from the needles of the Chinese yew (*Taxus yunnanenis* Cheng et L. K. Fu) [2]. In the course of studies on the minor constituents of the Himalayan yew (*T. wallichiana* Zucc.) we isolated a compound having the spectroscopic features expected for **1**. However, the physical and NMR data of our epoxide did not match those reported for **1** [2], and were identical to those of an epoxide reported as 7-deacetyl-1-hydroxybaccatin I (**2**) [3]. We report here a spectroscopic study that has allowed us to settle this matter, and led to the structural revision of the epoxides originally reported as 5-deacetyl- and 7-deacetyl-1-hydroxylbaccatin I.

RESULTS AND DISCUSSION

Compound **1** was isolated as needles. The molecular formula ($C_{30}H_{42}O_{13}$, MS) and ^{13}C NMR spectra disclosed the presence of a taxane having five acetates and nine oxygenated carbons. Of these, two could be accounted for by an epoxide ring and five by the acetates, thus leaving two free hydroxyls. The presence of downfield signals ($\delta > 5.4$) for H-2, H-7, H-9, H-10 and H-13 showed that the acetates were located at these carbon positions, as confirmed by the inspection of long-range ^1H-^{13}C correlations (HMBC experiments). Thus, the free hydroxyls were at C-1 and C-5. The upfield chemical shift of H-5 (δ 3.00) is due to the magnetic anisotropy of the oxirane ring at C-4/C-20 [4], whereas the large separation of the geminal oxirane protons is in accordance with a β-orientation for the epoxide oxygen, as found in all the natural taxoids of this type reported to date [5]. Comparison of the NMR data of our epoxide and the compound reported as 5-deacetyl-1-hydroxybaccatin I [2], suggested that the epoxide from the Chinese yew differed from **1** in having the free secondary hydroxyl at C-7 rather than C-5, and is actually 7-deacetyl-1-hydroxybaccatin I (**2**) a compound isolated from the European yew [3] and the Pacific yew [6, 7]. The reported ^1H NMR data for 7-deacetyl-1-hydroxybaccatin I from these two sources are different, and the data of the compound isolated from the European yew are identical to those of our epoxide, suggesting that its structure should be revised. The most typical ^1H NMR feature of taxane epoxides is the upfield chemical shift of H-5 [4], and the incorrect assignment of this signal led to the wrong structure of **1** [2] and **2** [3], as it did for a compound reported as 1-acetoxy-5-deacetylbaccatin I, which is actually 1-hydroxybaccatin I [8].



	R_1	R_2
1	H	Ac
2	Ac	H

Deacetylation at C-5, as in **1**, is not uncommon in taxoids of the epoxide- and $\Delta^{4(20)}$-type [5, 9]. However, unlike compounds of the $\Delta^{4(20)}$-type, all taxanes of the oxetane- and epoxide type bear an oxygen function at C-2, though the ester residue is generally different (benzoate and acetate, respectively [5, 9]). The esterification pattern might have great relevance in the biogenesis of taxoids. One attractive possibility is that

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acetylation and benzoylation play a role in the trafficking of intermediates between cytosolic and membranous sites of biosynthesis [10]. The observation that taxoids of different structural types (oxetane, epoxide) generally also differ for their esterification pattern (benzoylation vs acetylation of the C-2 hydroxyl) is consistent with this intriguing hypothesis.

EXPERIMENTAL

General. CC: silica gel Merck 70–230 mesh; MPLC: silica gel Merck LiChroprep Si60 15–25 mm, 5–15 bra.

Plant material. Needles of *T. wallichiana* Zucc. were identified by U. Boni (Indena S.p.A.). A voucher specimen is kept at the Indena Laboratories, Settala, Milano.

Isolation of **1**. A sample (5 g) of the mother liquors from the crystallization of 10-deacetylbaccatin III was chromatographed on MPLC (hexane–EtOAc 7:3 as eluant) to give 408 mg of a fr. containing **1** as the major component. This was further purified by MPLC (iPrOH–hexane gradient, 1:9 to 1:4) to give an analytical sample of **1** (34 mg).

5-Deacetyl-1-hydroxybaccatin I (**1**). Needles from MeOAc–hexane, mp 208–210°, $[\alpha]_D^{25}+76$ (*c* 1.0, EtOAc). IR ν_{max}^{nujol} cm^{-1}: 3400, 1715, 1240, 730. Negative-ions MS 140 eV, *m/z* (rel. int.): 610 $[C_{30}H_{42}O_{13}]^-$ $[M]^-$ (100). ^1H NMR (300 MHz, $CDCl_3$, TMS as reference): δ 5.47 (1H, *d*, $J = 3.3$ Hz, H-2), 3.38 (1H, *d*, $J = 3.3$ Hz, H-3), 3.00 (1H, *t*, $J = 2.7$ Hz, H-5), 1.79 (1H, *m*, H-6a), 2.03 (1H, *m*, H-6b), 5.59 (1H, *dd*, $J = 11.9$, 4.6 Hz, H-7), 5.96 (1H, *d*, $J = 11.0$ Hz, H-9), 6.21 (1H, *d*, $J = 11.0$ Hz, H-10), 5.98 (1H, *dd*, $J = 10.1$, 4.9 Hz, H-13), 1.94 (1H, *dd*, $J = 15.8$, 4.9 Hz, H-14a), 2.50 (1H, *dd*, $J = 15.8$, 10.1 Hz, H-14b), 1.58 (3H, *s*, H-16), 1.11 (3H, *s*, H-17), 2.18 (3H, *br s*, H-18), 1.18 (3H, *s*, H-19), 2.23 (1H, *d*, $J = 5.2$ Hz, H-20a), 3.63 (1H, *d*, $J = 5.2$ Hz, H-20b), 2.09, 2.07, 2.04, 2.04, 1.97 (5×3H, *s*, Ac); ^{13}C NMR (75.5 MHz, $CDCl_3$, TMS as reference): δ 75.3 (*s*, C-1), 71.7 (*d*, C-2), 39.4 (*d*, C-3), 60.5 (*s*, C-4), 76.1 (*d*, C-5), 32.6 (*t*, C-6), 68.6 (*d*, C-7), 46.9 (*s*, C-8), 75.3 (*d*, C-9), 71.2 (*d*, C-10), 140.8 (*s*, C-11), 136.3 (*s*, C-12), 71.0 (*d*, C-13), 38.6 (*t*, C-14), 42.8 (*s*, C-15), 20.6 (*q*, C-16), 28.7 (*q*, C-17), 16.0 (*q*, C-18), 13.2 (*q*, C-19), 50.1 (*t*, C-20), 21.4, 20.9, 20.9, 20.8, 20.7 ($5 \times q$, Ac), 170.0, 169.8, 169.8, 169.5, 169.2 ($5 \times s$, Ac).

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