

Chemistry and Occurrence of Taxane Derivatives. Part 16.¹ Rearranged Taxoids from *Taxus × media* Rehd. cv *Hicksii*. X-Ray Molecular Structure of 9-*O*-Benzoyl-9,10-dide-*O*-acetyl-11(15 → 1)*abeo*-baccatin VI

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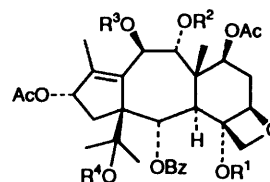
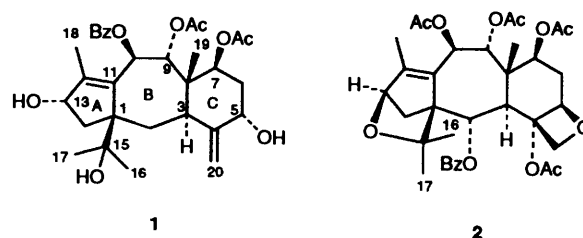
The roots of *Taxus × media* Rehd. cv *Hicksii* gave four new taxoids of the *abeo* 11(15 → 1)-type (2–5). Structures were elucidated by spectroscopic techniques, including X-ray analysis for compound 4. Compound 2 is conformationally fixed, whereas compounds 3–5 exist in solution as a mixture of rotamers, whose interconversion was investigated by variable-temperature NMR spectroscopy. Compound 2 has a C-13, C-15 oxygen bridge, and is the first natural taxoid with a β-oxygen function at C-13.

11(15 → 1)*abeo*-Taxanes are an emerging major structural type of taxoids.² Brevifoliol 1 was the first compound of this type isolated,³ but its rearranged structure was recognised only recently.^{2–4} Compound 1 is available in large amounts from the needles of *Taxus brevifolia* Nutt.,⁵ whereas the other compounds of this type isolated to date are only minor constituents of yew extracts. All 11(15 → 1)*abeo*-taxanes isolated to date bear a hydroxy group at C-15, whereas compounds of the Δ^{15,16}-type have been obtained only from the acid rearrangement of 1-hydroxylated taxanes.^{6–8} In spite of their widespread occurrence, 11(15 → 1)*abeo*-taxanes escaped detection for a long time, probably because of (i) their low concentration and (ii) some ambiguities in their NMR analysis. Indeed, the NMR spectra of *abeo*-taxanes are often very broad at room temperature, and of limited utility for structure elucidation.^{2,9} Furthermore, when sharp ¹H NMR spectra are observed, chemical shifts, multiplicities and NOE effects are similar to those of their corresponding taxanes, and a clear-cut distinction cannot be made without ¹³C NMR data.² As a result, several *abeo*-taxanes were originally reported as 1-hydroxylated taxanes.²

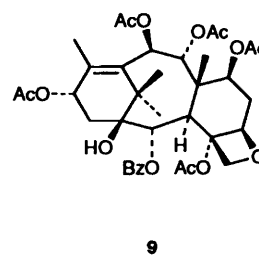
As part of an ongoing investigation into taxoids from various yew species, we report the isolation of four new *abeo*-taxanes from the roots of *Taxus × media* Rehd. cv *Hicksii*. This ornamental yew is popular as landscape material, and is extensively cultivated in nurseries.¹⁰ Previous studies had shown the presence of taxol and some related taxanes in this cultivar.^{11,12}

Results and Discussion

The crystalline compounds 2–5 were obtained after repeated chromatographic separation of fractions containing baccatin VI 9¹³ as the major constituent.† Compound 2 (C₃₅H₄₂O₁₂) showed sharp NMR spectra at room temperature. The presence of acetoxy groups at C-7, C-9, C-10 and of a benzyloxy group at C-2 was evident from the presence of diagnostic ¹H and ¹³C signals (Tables 1 and 2) and the detection of a long-range ¹H–¹³C correlation between the C-2 methine and the benzoate



- 3 R¹ = R⁴ = H, R² = R³ = Ac
 4 R¹ = Ac, R² = Bz, R³ = R⁴ = H
 5 R¹ = R³ = Ac, R² = Bz, R⁴ = H
 6 R¹ = R⁴ = Cl₃CCONHCO, R² = R³ = Ac
 7 R¹ = R³ = Ac, R² = Bz, R⁴ = Cl₃CCONHCO
 8 R¹ = R² = R³ = Ac, R⁴ = H



carbonyl. The signals of the 4-acetoxy-5(20)-oxetane moiety were also evident from the ¹H and ¹³C NMR spectra. A rearranged *abeo*-taxane structure (singlet at δ 67.1)² and two additional oxygenated carbons [δ 81.4 (d) and 78.6 (s), C-13 and C-15 respectively] were also present. Since compound 2

† Full spectroscopical data on baccatin VI are not available in the literature, and are reported in Tables 1 and 2.

Table 1 ^1H NMR spectra of compounds **2**, **3**, **7**, **9** (300 MHz; CDCl_3 ; δ_{H} in ppm from internal SiMe_4)

H	2	3^a	7	9
2	6.62 d (7.6)	6.60 d (8.0)	6.47 d (7.3)	5.85 d (6.2)
3	3.26 d (7.6)	2.38 d (8.0)	3.12 d (7.3)	3.16 d (6.2)
5	4.93 dd (9.9, 5.2)	4.72 dd (8.0, 2.7)	4.93 d (7.2)	4.95 br d (8.9)
6 α	2.46 m	2.37 m	2.68 m	2.48 m
6 β	2.00 m	1.97 m	1.80 m	1.84 m
7	5.32 dd (12.5, 5.5)	5.26 br s [20] ^b	5.55 dd (7.9, 7.2)	5.50 dd (9.7, 7.8)
9	5.00 d (5.7)	5.94 br s [40]	6.11 d (10.6)	5.98 d (11.5)
10	6.01 d (5.7)	6.18 d (9.3)	6.48 d (10.6)	6.20 d (11.5)
13	4.37 br d (1.8)	5.60 t (7.8)	5.75 br t (7.3)	6.14 dt (8.6, 1.4)
14 α	1.67 br d (8.2)	2.29 dd (14.0, 7.0)	2.04 dd (14.7, 7.4)	2.20 m
14 β	2.20 dd (8.2, 1.8)	2.49 dd (14.0, 7.3)	2.54 dd (14.7, 7.2)	
16	0.94 s	1.13 s	1.66 s	1.76 s
17	1.08 s	1.13 s	1.58 s	1.21 s
18	1.78 s	1.85 s	1.93 s	2.01 d (1.4)
19	1.74 s	1.69 s	1.79 s	1.58 s
20 α	4.25 d (7.8)	3.96 d (7.8)	4.16 d (7.3)	4.31 d (8.3)
20 β	4.56 d (7.8)	4.56 d (7.8)	4.38 d (7.3)	4.10 d (8.3)
MeCO	2.22, 2.17, 1.99, 1.98 s	2.15, 2.07, 2.03, 1.99 s	2.19, 2.18, 1.76, 1.62 s	2.27, 2.17, 2.09, 2.08, 1.98 s
4-OH		2.70 s		
15-OH		2.44 s		
2',6'	8.09 d (7.3)	7.95 d (7.8)	8.01 d (7.8), 7.97 d (7.8)	8.09 d (7.7)
3',5'	7.49 t (7.3)	7.46 t (7.8)	7.64 t (7.8), 7.62 t (7.8)	7.46 t (7.7)
4'	7.62 t (7.3)	7.59 t (7.8)	7.49 t (7.8), 7.48 t (7.8)	7.59 t (7.7)

^a 50 °C. ^b Values in square brackets are linewidths in Hz.**Table 2** ^{13}C NMR spectra of compounds **2**, **3**, **7**, **9** (75.43 MHz; CDCl_3 ; δ_{C} in ppm from internal SiMe_4)

C	2	3^a	7	9
1	67.1 s	67.9 s (24) ^b	67.9 s	78.8 s
2	65.8 d	69.8 d (15)	67.6 d	73.2 d
3	44.9 d	49.4 d (16)	44.1 d	47.2 d
4	82.0 s	73.7 s (26)	83.6 s	81.5 s
5	84.0 d	86.4 d	84.6 d	83.8 d
6	31.8 t	34.0 t (15)	34.8 t	34.5 t
7	70.5 d	70.8 d	70.4 d	71.7 d
8	43.4 s	43.3 s	43.8 s	45.7 s
9	73.2 d	76.2 d (18)	77.8 d	75.0 d
10	65.8 d	68.3 d	67.1 d	70.3 d
11	133.6 s	136.5 s (15)	135.1 s	133.6 s
12	148.0 s	146.3 s (65)	148.9 s	141.2 s
13	81.4 d	79.7 d	78.1 d	69.6 d
14	45.8 t	36.8 t	36.7 t	35.1 t
15	78.6 s	75.4 s	78.8 s	42.7 s
16	26.0 q	26.1 q (50)	22.5 q	22.2 q
17	28.6 q	28.0 q (12)	22.3 q	28.2 q
18	11.8 q	11.9 q	12.1 q	14.9 q
19	13.1 q	12.8 q	13.6 q	12.7 q
20	77.5 t	78.8 t (28)	74.3 t	76.3 t
MeCO	21.8 q, 21.2 q, 21.1 q, 20.6 q	21.1 q, 21.1 q, 20.6 q, 20.6 q	22.0 q, 21.7 q, 21.1 q, 20.6 q	22.7 q, 21.3 q, 21.2 q, 20.9 q, 20.7 q
MeCO	170.0 s, 169.9 s, 169.3 s, 168.7 s	170.9 s, 169.9 s, 169.4 s, 167.9 s	170.6 s, 170.0 s, 168.9 s, 168.9 s	170.4 s, 170.1 s, 169.8 s, 169.1 s, 168.8 s
1'	129.9 s	129.7 s	129.3, 128.7 s	129.2 s
2',6'	130.0 d	129.4 d	130.4, 129.7 d	130.1 d
3',5'	128.8 d	128.1 d	128.8, 128.6 d	128.6 d
4'	133.7 d	133.6 d	134.0, 134.0 d	133.6 d
7'	166.4 s	165.5 s	168.9, 165.9 s	166.9 s
acylcarbamate			159.3 s, 148.8 s, 91.0 s	

^a 50 °C. ^b Values in parentheses are linewidths in Hz.

had no hydroxy groups (IR spectroscopy) and one additional unsaturated degree had yet to be accounted for, the presence of an oxygen bridge between these two oxygenated carbons seemed likely. This was unambiguously confirmed by the detection of a long-range correlation between 13-H and C-15. Stereochemical constraints require a β -orientation for the

oxygen bridge, and thus 13-H is α , an observation consistent with its unusual splitting pattern (br *d*, *J* 1.8 Hz). Compound **2** is the first natural taxoid with a β -oxygenated function at C-13,¹⁴ and the oxygen bridge between C-13 and C-15 is presumably formed by $\text{S}_{\text{N}}2$ -type displacement of a 13α -oxygenated function by the tertiary C-15 hydroxy group. Ring **B** has a twist-chair

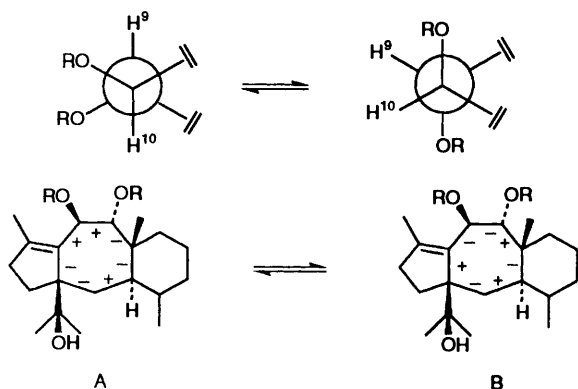


Fig. 1 Newman projection along C_{10} - C_9 and endocyclic torsion-angle sequence (Bucourt notation) of ring B in *abeo*-taxanes. A: twist-boat conformation; B: twist-chair conformation (ref. 15).

conformation in compound 2, with the oxygen function at C-9 and C-10 pseudoaxial and 9-H and 10-H pseudo-equatorial ($J_{9,10}$ 5.7 Hz) (Fig. 1).

This arrangement is different from that found in taxanes, where ring B has a twist-boat conformation and 9-H and 10-H are pseudoaxial ($J \sim 10$ Hz).⁹ In taxoids, values of $J_{9,10} \sim 5$ Hz can be misleading as regards the configuration at C-9 and C-10. Both *cis* and *trans* protons can in fact display values of this type, depending on the conformation of ring B.* In compound 2, a rotating frame NOE (ROESY) cross-peak between the C-19 methyl and 9-H and between the C-16 (*pro-R*)[†] methyl and the acetate at C-10 confirmed the *trans* relationship between 9-H and 10-H. The splitting pattern of 5-H in compound 2 (dd, J 9.0 and 5.2 Hz) is also somewhat unusual, since in oxetane-type taxoids this proton resonates as a broad doublet or as a doublet of narrow doublets.

The ^1H NMR spectrum of compound 3 ($\text{C}_{35}\text{H}_{44}\text{O}_{13}$) was rather broad at room temperature, but heating to 50 °C sharpened all signals with the exception of those for 7-H and 9-H. In the ^{13}C NMR spectrum taken at this temperature, only one set of lines was present, although some of them were rather broad (10–65 Hz).

Compound 3 was stable at 50 °C, and its NMR spectra could be fully assigned at this temperature by mono- and bi-dimensional techniques (COSY, ROESY, 1J and $^{2,3}J_{\text{C-H}}$ correlations). A singlet at δ 67.9 in the ^{13}C NMR spectrum indicated an *abeo*-taxane structure,² and multiplicity and coupling patterns of all protons and carbons were identical with those of *abeo*-baccatin VI 8.¹⁷ Comparison of the molecular formulae revealed that compounds 3 and 8 differ by the absence of one acetyl group in compound 3. All ester groups of compound 3 were bound to methine carbons (chemical-shift considerations and diagnostic $^3J_{\text{C-H}}$ correlations). Therefore C-15 and C-4 bear free hydroxy groups, and compound 3 is 4-*O*-deacetyl-*abeo*-baccatin VI. This was confirmed by the formation of a bis-carbamate 6 by *in situ* reaction with trichloroacetyl isocyanate (TAI).¹⁸ The downfield acylation shifts observed for 3-H, 5-H and 7-H ($\Delta\delta$ +0.78, +0.30 and

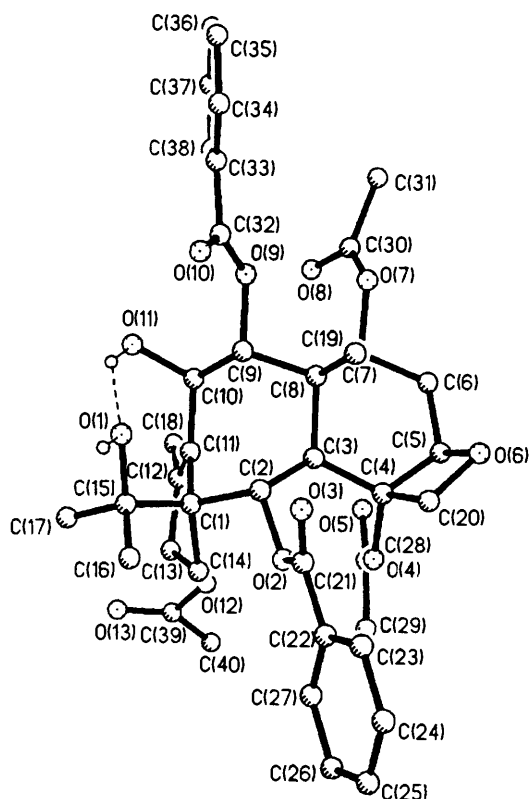


Fig. 2 Molecular structure of compound 4

+0.25 ppm, respectively) could be rationalised in terms of anisotropic deshielding from the newly introduced carbamate carbonyl at C-4, in the concave face of the molecule. Acetylation of the C-15 hydroxy group is instead responsible for the downfield shift of the *gem*-dimethyl groups ($\Delta\delta$ +0.48 and +0.51 for 16-H and 17-H, respectively). $J_{9,10}$ measured at 50 °C, under conditions of fast exchange, was 9.7 Hz, only slightly lower than normal (10–11 Hz). This indicates that the conformational equilibrium of compound 3 is highly biased, with a large predominance of the rotamer with ring B in a twist-boat conformation. The bis-carbamate derivative 6 displayed sharp NMR spectra at room temperature, suggesting that intramolecular hydrogen bonding plays a role in the conformational equilibration of compound 3 (see below).

Compound 4 ($\text{C}_{40}\text{H}_{46}\text{O}_{13}$) showed very broad NMR spectra at room temperature, where most signals were featureless humps. Upon cooling to -40 °C, a spectrum containing two sets of sharper signals was obtained, whereas heating to 120 °C was required to get fast exchange and one set of signals. The spectrum at low temperature was too complex, and compound 4 was not stable enough at 120 °C to allow thorough spectroscopic characterisation to be made. Eventually, crystals suitable for an X-ray analysis were obtained. The results showed that compound 4 is an *abeo*-baccatin VI derivative lacking the C-10 *O*-acetyl and with a benzoate in place of the acetate at C-9. The asymmetric unit is made up of two independent molecules having similar conformations. Only one of them is shown in Fig. 2. In the solid state, ring B adopts a twist-boat conformation and ring C an almost ideal 1,2-diplanar (= sofa) conformation. Both hydroxy groups are involved in hydrogen bonds: the one at C-10 acts as a donor toward that at C-15, which in turn acts as a donor toward the C-9 benzoate carbonyl of another molecule. A packing analysis showed that these are the only short contacts found in the structure.

Acetylation of compound 4 gave the monoacetyl derivative 5, identical with a compound isolated from the fractions

* A value of 5.5 Hz for $J_{9,10}$ was reported in a synthetic taxane having a *cis* 9,10-diol system (ref. 16).

† The numbering of the *gem*-dimethyls of *abeo*-taxanes is ambiguous; we suggest considering the methyl pointing toward ring B (*pro-R* methyl, when the hydroxy group is oriented toward the oxygen function at C-10) C-16, and the other, pointing toward ring A (*pro-S* methyl, when the hydroxyisopropyl side chain is oriented as above) C-17. This numbering maintains the topological relationship between the methyls and the rest of the diterpenoid core observed in taxanes, although prochirality descriptors are inverted, owing to changes in prochirality.

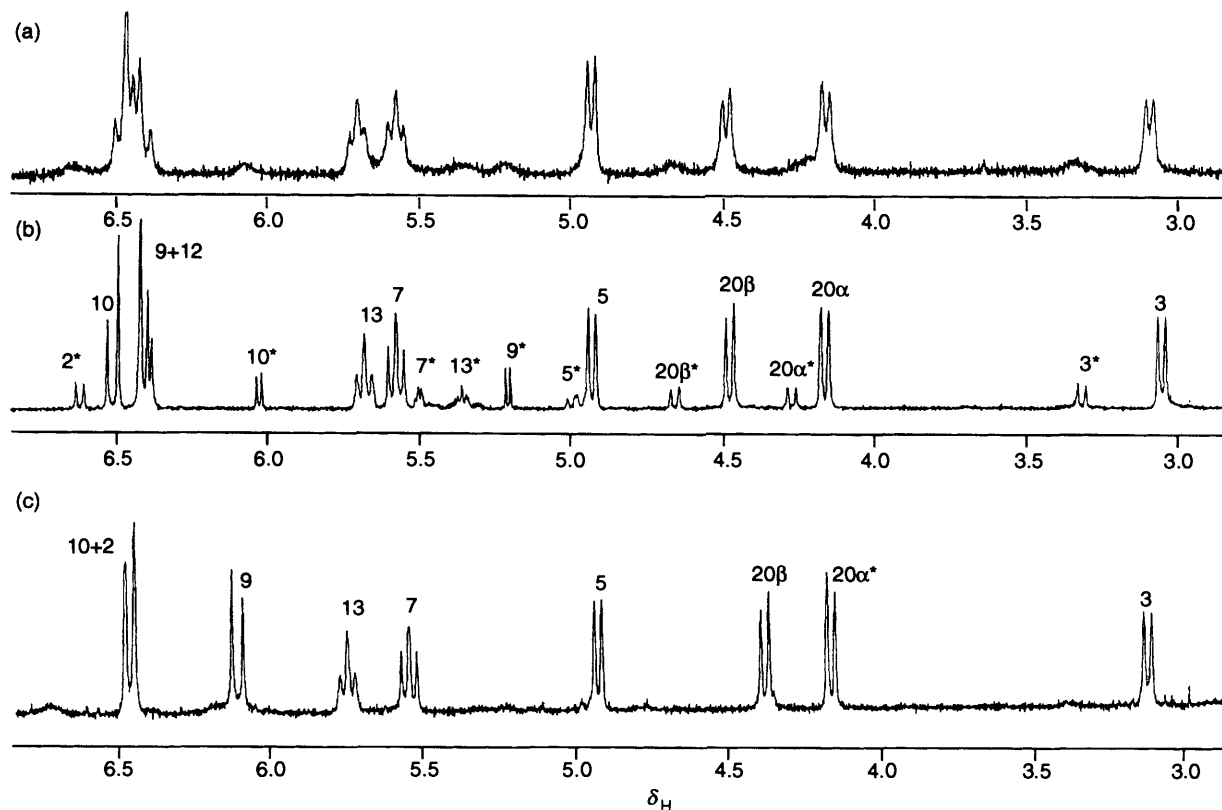


Fig. 3 ^1H NMR spectra of compound 5: (a) at room temperature; (b) at -20°C ; (c) after addition of TAI (*i.e.*, during formation of compound 7) (CDCl_3 ; 300 MHz). * Minor rotamer.

containing compounds 2–4. The ^1H NMR spectrum of tetraacetate 5 showed two sets of broad signals at room temperature, which sharpened upon cooling. At -20°C two sets of sharp signals in a $\sim 4:1$ ratio were observed (Fig. 3), and all signals could be assigned. The value of $J_{9,10}$ was 10.4 Hz in the major rotamer and 4.7 Hz in the minor one. Thus, ring B has a twist-boat conformation with diequatorial ester groups at C-9, C-10 in the major rotamer and a twist-chair conformation with these group diaxial in the minor rotamer. An *in situ* reaction of compound 5 and TAI gave the carbamate 7, whose NMR spectra were sharp at room temperature (Fig. 3) and could be fully assigned. $J_{9,10}$ (11.5 Hz) showed that ring B adopts a twist-boat conformation in carbamate 7.

The conformational features of *abeo*-taxanes 2–5 are different. Compound 2 is anancomeric (conformationally fixed)¹⁹ and adopts a ring B twist-chair conformation to avoid a severe steric interaction between the *pro-R* methyl at C-15 (16-H) and 9-H. Compounds 3–5 are instead each a mixture of rotamers, whose equilibration is governed by several factors, the major one being the formation of intramolecular hydrogen bonding between the hydroxy group at C-15 and the oxygen function at C-10. The α -hydroxyisopropyl group of *abeo*-taxane adopts a conformation that mimics the *gem*-dimethyl bridge of taxane: the *pro-S* methyl points towards ring A, and the other methyl towards ring B, allowing the formation of hydrogen bonding between the hydroxy group at C-15 and the C-10 oxygen. This arrangement is found in the solid-state conformation of both compound 4 and all the *abeo*-taxanes investigated by X-ray crystallography.^{2,20,21} Depending on the acylation state of the oxygen function at C-10, the hydroxy group at C-15 can act as a donor (acyloxy group at C-10) or as an acceptor (hydroxy at C-10) of hydrogen bonding. The existence of this arrangement also in solution is consistent with the ROE pattern of the geminal methyls and with the presence of an ROE correlation between 9-H and the 15-hydroxy proton.² The C-15 hydroxy

group and the oxygen at C-10 are much closer when ring B adopts a twist-chair conformation, to the point that an oxygen bridge can form between C-15 and C-10.^{1,8} Therefore, intramolecular hydrogen bonding between the oxygen functions at C-15 and C-10 is expected to stabilise the twist-chair conformation more than the twist-boat. Acylation of the C-15 hydroxy group gives anancomeric compounds, since this hydrogen bonding is not possible any more, and the twist-boat conformation, having diequatorial oxygen functions at C-9 and C-10, is the only detectable conformation in solution (*cf.* carbamates 6 and 7).

Since the *abeo*-taxane skeleton has a crowded topology, functionalities can strongly interact with each other, and the conformational equilibration of ring B is also affected by the formation of additional intramolecular hydrogen bonds as well as by the nature of the ester groups. Free hydroxy groups at C-4 and C-10, as in compounds 3 and 4, can act as hydrogen-bonding donors toward ester carbonyls at C-13 and C-9 respectively, and the phenyl ring of benzoate esters can be involved in lipophobic interactions. This subtle interplay of functionalities is responsible for the wide range of temperatures over which fast exchange is observed in *abeo*-taxanes (*e.g.*, 50°C for 3, 120°C for 4). In oxetane-type taxoids, ring C is conformationally biased on account of the presence of the oxetane ring. In brevifoliol-type *abeo*-taxanes, where a C-4–C-20 double bond is present, ring C is instead flexible and the conformational analysis of these compounds is therefore more complex. Our results suggest that the broad NMR spectra sometimes observed in *abeo*-taxanes are related to stabilisation of the 'unusual' twist-chair conformation of ring B by intramolecular hydrogen bonding between the tertiary hydroxy group at C-15 and the oxygen function at C-10. Acylation of the tertiary hydroxy group at C-15 gives anancomeric compounds, whose spectra are amenable to routine structure elucidation.

The isolation of baccatin VI 9 and the *abeo*-taxanes 2–4 from

T. × media confirms the trend, already observed in other yew species, that taxanes and *abeo*-taxanes generally show different acylation patterns. Benzoylation at C-9, as in compounds **4** and **5**, and deacylation at C-4, as in compound **3**, are in fact unprecedented within baccatin VI derivatives. Baccatin VI has been obtained from at least four different species of yew.^{13,21,22} *abeo*-Baccatin VI is still unknown as a natural product, since only partially deacylated or more benzoylated derivatives have been isolated. Migration of ester groups from O-9 to O-10 is documented in taxoids under conditions similar to the isolation procedure,²³ and compound **4** may thus be an extraction artefact derived from the corresponding C-10 benzoate, a hitherto unknown compound.

Experimental

M.p.s were determined on a Büchi SMP 20 apparatus; optical rotations were measured on a Perkin-Elmer 241 polarimeter; $[\alpha]_D$ -values are given in units of 10^{-1} deg $\text{cm}^2 \text{g}^{-1}$; UV spectra were recorded on a Beckmann DB-GT spectrophotometer, IR spectra on a Perkin-Elmer model 127 spectrophotometer, EIMS spectra on a VG EQ apparatus, and ^1H and ^{13}C NMR spectra on a Varian UNITY 300 spectrometer operating at 299.94 MHz for ^1H and 75.43 MHz for ^{13}C ; *J*-values are given in Hz. Silica gel LiChroprep Si 60 (15–25 μm , Merck) was used for medium-pressure (5–15 bar) column chromatography and silica gel 60 (70–230 mesh, Merck) for atmospheric-pressure column chromatography. HPLC purifications were carried out using a Hewlett-Packard series 1050 instrument equipped with an HP 1047 A refractive index detector; a Waters microporasil column (0.8 \times 30 cm) was used for compounds **2** and **3**, and a Waters Delta Pack C_{18} column (0.78 \times 30 cm) for compounds **4** and **5**.

Commercially available roots of *Taxus × media* Rehd. cv *Hicksii* were identified by Dr. U. Boni (Indena S.p.A); a voucher specimen is kept at the Indena labs, Milano, Italy.

Isolation of Compounds.—Finely ground roots (1200 kg) were stirred at room temp. with MeOH–water (1:1) and filtered. Counter-current extraction of the percolates with CH_2Cl_2 provided, after evaporation to dryness, a residue (28 kg), which was chromatographed on silica gel and eluted with toluene– Me_2CO (9:1). Three fractions [A (12 kg), B (3.9 kg) and C (8 kg)] were collected. Fraction B was chromatographed on silica gel and eluted with cyclohexane– Me_2CO (6:4); fractions D (0.5 kg) and E (0.4 kg) were obtained. A portion (20 g) of fraction E was chromatographed on silica gel (hexane containing increasing amounts of EtOAc as eluent). Fractions eluted with hexane–EtOAc (1:1) gave a mixture of taxoids (2.7 g), which was further separated by column chromatography to give baccatin VI **9** (290 mg) and a mixture of compounds **2** and **3**, which were separated by HPLC [hexane–EtOAc (6:4)] to give compounds **2** (42 mg) and **3** (36 mg).

13-Deacetoxy-13,15-epoxy-11(15 \rightarrow 1)abeo-13-epi-baccatin VI 2 (42 mg, 7×10^{-5} %), powder, m.p. 150 °C (decomp.); $[\alpha]_D^{20} + 23.9$ (*c* 0.58, CHCl_3) (Found: C, 64.4; H, 6.4. $\text{C}_{35}\text{H}_{42}\text{O}_{12}$ requires C, 64.2; H, 6.5%); $\lambda_{\text{max}}(\text{EtOH})/\text{nm}$ 230 and 265; $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1745, 1720, 1370, 1240, 1040, 995 and 710; *m/z* (negative ions) 654 (M^- , 100).

4-De-O-acetyl-11(15 \rightarrow 1)abeo-baccatin VI 3 (36 mg, 6×10^{-5} %), powder, m.p. 222 °C (decomp.); $[\alpha]_D^{20} - 73.1$ (*c* 0.33, CHCl_3) (Found: C, 62.4; H, 6.7. $\text{C}_{35}\text{H}_{44}\text{O}_{13}$ requires C, 62.5; H, 6.6%); $\lambda_{\text{max}}(\text{EtOH})/\text{nm}$ 230 and 268; $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3550, 1730, 1380, 1240, 1200, 980 and 720; *m/z* (negative ions) 672 (M^- , 100).

Baccatin VI 9 (290 mg, 4.8×10^{-4} %), m.p. 236–237 °C (from MeCN–water) (lit.,¹³ 244–245 °C); $[\alpha]_D^{20} - 8.7$ (*c* 0.92,

CHCl_3) (lit.,¹³ –5) (Found: C, 62.3; H, 6.7. Calc. for $\text{C}_{37}\text{H}_{46}\text{O}_{14}$: C, 62.2; H, 6.5%).

A portion (6 g) fraction D was chromatographed on a silica gel column (medium pressure) and eluted with CHCl_3 –MeOH (97:3). The first twenty fractions were collected (2.7 g) and chromatographed at medium pressure with hexane– Me_2CO (7:3) as eluent; a crude mixture (580 mg) containing compounds **4** and **5** was obtained. This mixture was chromatographed by HPLC [MeCN–water–MeOH (75:25:4)] to afford crude compounds **4** and **5**. After final purification by HPLC [MeCN–water–MeOH (70:30:4) and MeCN–water (7:3) for compounds **4** and **5**, respectively] the dibenzoates **4** (35 mg) and **5** (40 mg) were obtained.

9-O-Benzoyl-9,10-dide-O-acetyl-11(15 \rightarrow 1)abeo-baccatin VI 4 (35 mg, 2.4×10^{-4} %), m.p. 238 °C (from MeOAc–hexane); $[\alpha]_D^{20} - 30.5$ (*c* 0.91, CHCl_3) (Found: C, 65.3; H, 6.2. $\text{C}_{40}\text{H}_{46}\text{O}_{13}$ requires C, 65.4; H, 6.3%); $\lambda_{\text{max}}(\text{EtOH})/\text{nm}$ 232 and 265; $\nu_{\text{max}}(\text{Nujol})/\text{cm}^{-1}$ 3300, 1720, 1240, 1020 and 715; *m/z* (negative ions) 735 (M^- , 100).

9-O-Benzoyl-9-de-O-acetyl-11(15 \rightarrow 1)abeo-baccatin VI 5 (40 mg, 2.8×10^{-4} %), oil; $[\alpha]_D^{20} - 32.5$ (*c* 0.92, CHCl_3) (Found: C, 64.9; H, 6.3. $\text{C}_{42}\text{H}_{48}\text{O}_{14}$ requires C, 64.9; H, 6.2%); $\lambda_{\text{max}}(\text{EtOH})/\text{nm}$ 230 and 265; $\nu_{\text{max}}(\text{Nujol})/\text{cm}^{-1}$ 3290, 1720, 1240, 1025 and 720; *m/z* (negative ions) 777 (M^- , 100).

Reaction of Compounds 3 and 5 with TAI.—An excess TAI was added to an NMR tube containing a solution of substrate **3** or **5**. The formation of the carbamate derivatives was monitored by ^1H NMR spectroscopy, and the reaction was complete in 4 h. The solution of these carbamates was stable for several days.

X-Ray Analysis.—Diffraction data were collected with a Siemens P4 diffractometer equipped with a graphite monochromator. The intensities were measured by ω -scan with variable speed; the cell parameters were obtained and refined from 35 reflections. The intensities were corrected for background and Lorentz-polarisation effects, but no correction was applied for absorption. The structure was solved by direct methods using the SIR92 program.²⁴ All subsequent calculations were carried out by the SHELXTL IRIS system.²⁵ The structure was refined by full-matrix least-squares techniques. Not all non-hydrogen atoms could be assigned anisotropic thermal parameters because of the limited number of observed reflections, due to the poor quality of the crystals; the phenyl and methyl groups were thus treated as fixed groups with hydrogen atoms in calculated positions. Atomic co-ordinates, bond lengths, angles, torsion angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

Crystal data. $\text{C}_{40}\text{H}_{46}\text{O}_{13}$, *M* = 734.8, monoclinic, space group $P2_1$, *a* = 9.233(3), *b* = 19.819(7), *c* = 21.098(6) Å; β = 99.01(2)°; *Z* = 4, *D*_c = 1.282 (Mg m^{-3}); Mo–K α radiation, λ = 0.710 69 Å, μ = 0.096 mm^{-1} ; *R* = 0.104 for 3273 observed reflections having $F > 4.0\sigma(F)$.

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