PERGAMON

Phytochemistry 50 (1999) 131–133

PHYTOCHEMISTRY

A brevifoliol analogue from the Himalyan yew *Taxus wallichiana*☆

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Revised 20 May 1998

Abstract

The needles of *Taxus wallichiana* gave a new brevifoliol derivative whose structure was established by spectral data.

Keywords: *Taxus wallichiana*; Taxaceae; Taxoids; 11(15 → 1) Abeotaxanes

1. Introduction

After the discovery of the anticancer drug paclitaxel from the pacific yew *Taxus brevifolia*, almost all the species of genus *Taxus* including the Himalayan yew (*Taxus wallichiana*, Zucc.) were chemically investigated for the occurrence of paclitaxel, its important precursors and other naturally occurring analogues (Appendino, 1995). The needles (Barboni et al., 1993; Appendino, 1995; Chattopadhyay, Sharma, Appendino, & Gariboldi, 1995), stem bark (Chattopadhyay, Tripathi, Thakur, Sharma, & Jain, 1994; Chattopadhyay & Sharma, 1995; Chattopadhyay, Saha, Sharma, Kumar, & Roy, 1996), heartwood (Chattopadhyay, Kulshrestha, Saha, Sharma, & Jain, 1996) and roots (Chattopadhyay et al., 1997) of *Taxus wallichiana* were separately investigated, yielding several structurally unique taxoids. As part of an ongoing research program on the isolation of paclitaxel analogues/precursors from the Himalayan yew, we have isolated a new abeotaxane (**1**) from the needles of the plant. Another taxoid (**2**) has also been isolated from the needles of this plant. This compound is known (Appendino, Ozen, Gariboldi, Gabetta, & Bombardelli, 1993; Appendino et al., 1993), but had not previously been isolated from the Himalayan yew.

2. Results and discussion

Compound **1** was isolated as an oil from the chloroform soluble fraction of the methanol extract of the needles of *T. wallichiana*. The FAB-MS of the compound exhibited its molecular formula $C_{30}H_{42}O_{11}$. Compound **1** showed a ^{1}H NMR spectrum at room temperature which was sharp enough to be analyzed both by one dimensional and two dimensional NMR spectroscopy. The ^{1}H NMR of the compound showed characteristic taxoid signals for four methyl groups, five acetoxy groups and a C-4(20)-exocyclic methylene group (Barboni et al., 1993). Taxoid **1** did not undergo acetylation at room temperature, thus it did not have any acylable hydroxyl group. The ^{13}C NMR spectrum of **1** showed a down field signal (δ 62.7) for one of the quaternary aliphatic nonoxygenated carbons (C-1) suggesting that it had a abeotaxane skeleton (Appendino et al., 1993). Full assignments of ^{1}H NMR and ^{13}C NMR spectrum of **1** were made by a combination of ^{1}H–^{1}HCOSY, DEPT, HMQC and HMBC techniques (Table 1). The results show that compound **1** is an 11 (15 → 1) abeotaxane related to brevifoliol having five ace oxyt groups at C-5, C-7, C-9, C-10 and C-13 positions. Thus compound **1** was characterized as 10-debenzoyl-5,10,13-acetyl-brevifoliol.

Brevifoliol type taxoids have the functionalization pattern of the taxinine J taxanes. In such taxoids 5-

☆ CIMAP Communication No. 98-20J.

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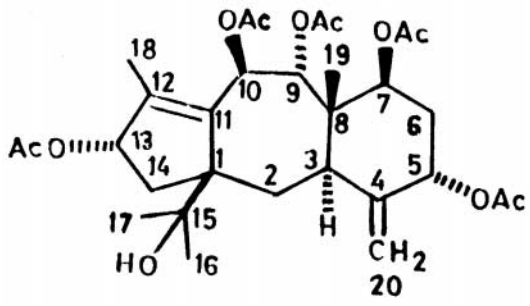
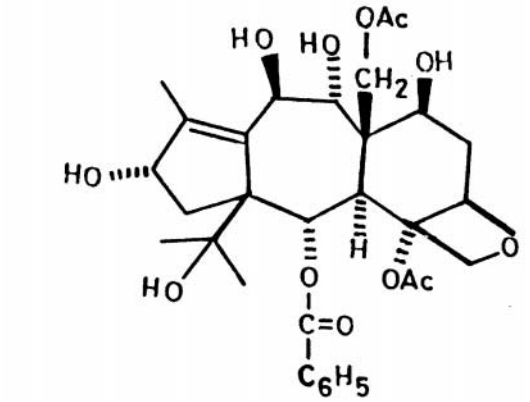
0031-9422/98/$ - see front matter
PII: S0031-9422(98)00461-0



(1)



(2)

and 13-hydroxyls are rarely esterified (Appendino, 1995).

3. Experimental

The needles of *T. wallichiana* were collected in Kashmir, India. A voucher specimen is kept at the herbarium of CIMAP regional centre at Bonera, Kashmir.

The dried needles (60 kg) were extracted with MeOH (600 l). The extract was concentrated and the concentrate (15.70 kg) thus obtained was suspended in H_2O (200 l) and extracted with hexane (3×200 l) and $CHCl_3$ (3×200 l) successively. Evaporation of the $CHCl_3$ phase left a residue (2000 g). A portion (300 g) of $CHCl_3$ concentrate was chromatographed on silica gel (1800 g) eluting sequentially with $CHCl_3$, Me_2CO–$CHCl_3$ (5:95), MeOH–$CHCl_3$ (2:98) (fraction A), MeOH–$CHCl_3$ (5:95) (fraction B) and MeOH–$CHCl_3$ (10:90) (fraction C). Concentration of fractions A and C gave 5 g and 7 g residues, respectively; fraction A was rechromatographed on silica gel using $CHCl_3$–MeOH (99:1) as eluant; fractions containing **1** were combined. Final purification of **1** was achieved by prep. TLC (silica gel PF 254 E Merck) using solvent system C_6H_6–Me_2CO (80:20). Compound **1** was obtained as an oil (25 mg).

Fraction C was rechromatographed over silica gel using EtoAc–hexane (1:1) as the eluent. Fractions, containing **2** were combined and subjected to prep.

Table 1
NMR data of 5,10,13-acetyl-10-debenzoyl brevifoliol (**1**)

Position	δ H[a]	δ C[b]	^{1}H–^{1}HCOSY	HMBC[c]
(1)	–	62.7		
(2)	α 1.41 (br. d, 14.4) β 2.35 (dd, 14.4, 9.0)	29.2	H-2β, 7	C-3, 4, 8
(3)	2.64 (d, 9.0)	38.6	H-2β, 20A, 20B	C-2, 4, 5, 8, 20
(4)	–	145.2		
(5)	5.37, br.s.	74.0	–	C-4, 6, 7, 20
(6)	α 1.99 (m) β 1.70 (m)	33.8		
(7)	5.41 (dd, 5.4, 11.1)	69.6	H-9	C-8, 9, $OCOCH_3$
(8)	–	44.7		
(9)	5.86 (d, 10.2)	76.6	H-7	C-7, 19, $OCOCH_3$
(10)	6.36 (d, 10.5)	69.2		
(11)	–	136.6		
(12)	–	146.3		
(13)	5.55 (br.t, 6.3)	79.3	H-14α, 14β	C-11, 12, 14, $OCOCH_3$
(14)	α 1.20 (dd, 13.5, 8.0)	44.0		
	β 2.50 (dd, 13.8, 7.5)		H-14α, 13	C-11, 12, 13, 15
(15)	–	75.3		
(16)	1.13 (s)	24.7	–	C-1, 15, 17
(17)	1.32 (s)	29.6	–	C-1, 15, 16
(18)	1.92 (s)	11.6		
(19)	0.88 (S)	12.8	–	C-3, 7, 8, 9
(20)	α 5.46 (br.s)	114.2	H-3, 20β	C-3, 5
	β 4.87 (br.s)		H-3, 20α	C-3, 5
$OCOCH_3$	1.97 (s), 1.99 (s)	20.7, 20.9		
	2.01 (s)	20.8		
	2.06 (s), 2.07 (s)	21.1, 21.3		
		167.8, 169.5 169.8, 169.7 170.5		

[a] ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm); multiplicity and apparent coupling constants (*J*) in parenthesis.
[b] ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm); ^{13}C NMR assignments of protonated carbons were confirmed by a HMQC experiments and carbon types were assigneed by A DEPT experiments.
[c] The HMBC experiment was performed with the second delay in the *J* filter segment set for $J = 7$ Hz; H-20α and H-20β were assigned by ROESY.

TLC (silica gel PF 254 E Merck) using solvent system C_6H_6–Me_2CO (1:1); **2** was obtained as an amorphous solid (75 mg).

5,10,13-acetyl-10-debenzoyl brevifoliol (**1**). Oil; $[\alpha]_D$-50° (1.0 $CHCl_3$); IR ν_{max} cm^{-1}; 3553, 2928, 1746, 1438, 1373, 1236, 1161, 1032, 962, 912, 758: FAB-MS *m*/*z*: 601 $[M + Na]^+$ $[C_{30}H_{42}O_{11} + Na]^+$.

Acknowledgements

The authors from CIMAP are grateful to the director, CIMAP, for providing necessary facilities.

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