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TEIXIDOL, AN *ABEO*-TAXANE FROM EUROPEAN YEW, *TAXUS BACCATA**

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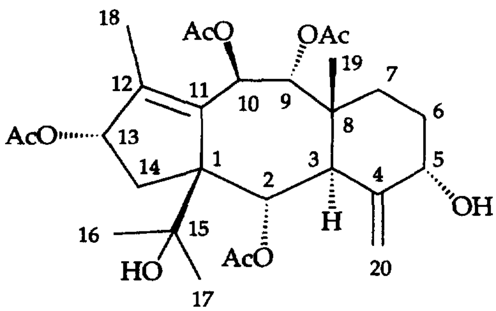
Key Word Index—*Taxus baccat*; Taxaceae; diterpenoids; 11(15→1)*abeo*-taxanes.

Abstract—A new taxoid, teixidol, was isolated from the leaves of *Taxus baccata*. Its structure, which features an 11(15→1)*abeo*-taxane skeleton consisting of a 5/7/6 membered ring system, was established by spectroscopic analysis. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

In our search for novel, potent and more selective antitumour agents, we have recently investigated the taxoid contents of the leaves of a Galician specimen of *Taxus baccata*. In addition to the known taxoids 10-deacetylbaccatine III [1], baccatine III [2], taxuspine F [3], decinnamoyl-1-hydroxytaxinine J [4], 5-cinnamoyl-10-acetyltaxine I [5] and deaminoacyltaxine A [6], we also isolated a new 11(15→1) *abeo*-taxane [7], teixidol (**1**). This new taxoid is the 10,13-diacetylated derivative of a taxoid originally assigned a baccatine structure [8] and more recently shown to have a 11(15→1)*abeo*-taxane skeleton [9].



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RESULTS AND DISCUSSION

A methanolic extract of *T. baccata* leaves collected at Santiago de Compostela provided, in addition to several known taxoids, a new member of the 11(15→1)*abeo*-taxane family that we have named teixidol (**1**).

Compound **1** was obtained as an amorphous white solid of mp 159°. A molecular formula of $C_{28}H_{40}O_{10}$ was established on the basis of its ^{13}C NMR spectrum and an EI mass spectral peak for $[M - 2xAc]^+$ at m/z 418. IR bands at 3600–3400 and 1730 cm^{-1} revealed the presence of hydroxyl and ester groups. ^1H and ^{13}C NMR signals were assigned by DEPT, HMQC, COSY and NOE techniques, and are indicated in Table 1. The ^{13}C NMR and DEPT spectra showed signals due to six oxygenated, four secondary (one sp^2 and three sp^3), eight primary, one tertiary and five quaternary (three sp^2 and two sp^3) carbons, and to four ester carbonyl groups. The presence of three quaternary signals at δ 68.7, 42.4 and 75.4 is characteristic of an 11(15→1)*abeo*-taxane skeleton [7, 9]. The ^1H NMR spectrum showed singlets for four methyl groups at δ 0.93, 1.15, 1.17 and 1.84, and singlets for four acetyl methyls at δ 1.97, 1.98, 2.0 and 2.05. The protonated carbons were identified by HMQC and COSY experiments. The relative sterochemistry was elucidated by means of a NOESY experiment [10] (Fig. 1).

The structures of the other six taxoids isolated were determined by comparing their physical and spectral data with those reported in the literature [1–6].

EXPERIMENTAL

General. Mps: uncorr. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ and CD_3OD on Bruker AMX-300 and AMX-500 spectrometers with TMS as int. standard; the NOE data and 2D ^1H–^1H and ^{13}C–^1H correlation spectra were obtained using standard Bruker software. EIMS: direct inlet, 70 ev. UV: Hewlett Packard 8452A diode array spectrophotometer. IR: Midac Prospect spectrophotometer. HPLC: Waters 600 E system controller and Waters 490 UV detector.

*Dedicated to Prof. Antonio González González in celebration of his half-century of contribution to natural product chemistry.

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Table 1. ^{1}H and ^{13}C NMR data of teixidol (**1**) (300 MHz, $CDCl_3$, δ values with TMS as internal standard, J in Hz)

No.	^{13}C	^{1}H
1	68.74 *s*	
2	68.58 *d*	5.90 *d* (9.2)
3	43.65 *d*	3.42 *d* (9.2)
4	146.55 *s*	
5	75.50 *d*	4.23 *s br*
6	37.51 *t*	1.6 *m br*
7	30.38 *d*	1,73 *m br*
8	42,40 *s*	
9	76.89 *d*	5.73 *d* (10)
10	69.10 *d*	6,15 *d* (10)
11	146.83 *s*	
12	136.02 *s*	
13	79.23 *d*	5.5 *t* (7.15)
14	36.81 *t*	2.35 *dd* (7.5; 15)
		1.9 *dd* (7.4; 15)
15	75.37 *s*	
16	25.37 *q*	1.17 *s*
17	27.65 *q*	1.15 *s*
18	11.09 *q*	1.84 *s*
19	17.05 *q*	0.93 *s*
20	111.30 *t*	5.08 *s*
		4.44 *s*
Ac	171.11 *s*	
	170.93 *s*	
	169.88 *s*	
	168.55 *s*	
Ac	21.73 *t*	2.05 *s*
	21.11 *t*	2.0 *s*
	20.79 *t*	1.98 *s*
	20,65 *t*	1.97 *s*

Plant material. Taxus baccatas leaves were collected at Santiago de Compostela in March 1992.

Extraction and separation. Leaves (5 kg) were extracted with MeOH (16 L) at room temp. The methanolic extract was partitioned between CH_2Cl_2 and H_2O, and the solvent was evapd from the organic fr. under red. pres. to give a residue (164 g) that was suspended in MeOH–H_2O and loaded on to a reversed-phase chromatography column (Merck Lichroprep RP-18, 25–40 μm) that was then successively eluted with MeOH–H_2O (1 : 1), MeOH and CH_2Cl_2 to give frs I, II and III, respectively.

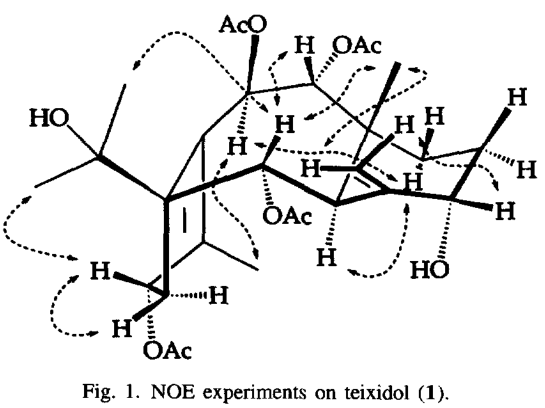

Fig. 1. NOE experiments on teixidol (**1**).

Fr. I (60 g) was subjected to flash CC on an 8 × 25 cm column of Merck 230–400 silica gel with a CH_2CL_2–MeOH (1 : 0–1 : 1) gradient as eluent; 9 frs were collected. Fr. I-7 (8.6 g) was diluted with CH_3CN and left for 72 hr. The yellow amorphous ppt (500 mg) was filtered out and crystallized from MeCN–MeOH to give 356 mg 10-deacetylbaccatine III. Fr. I-2 (6.3 g) was sepd by reversed-phase HPLC (Zorbax ODS, 250 × 20 mm; flow rate 6.0 ml min^{-1}; UV detection at 230 nm; 7 : 3–0 : 100 H_2O-CH_3CN gradient) to give frs I–2a (706 mg, R_t 23 min) and I-2b (762 mg, R_t 32 min). preparative TLC of I-2a (Merck GF-254 silica gel; CH_2Cl_2–MeOH, 19 : 1) gave 280 mg deaminoacyltaxine A. Prep. TLC of I-2b (Merck GF-254 silica gel; CH_2Cl_2–*i*-PrOH, 49 : 1) gave 15 mg baccatine III, 20 mg taxuspine F, 31 mg decinnamoyl-1-hydroxytaxinine J and 22 mg **1**. Reversed-phase HPLC of fr. I-9 (5.8 g) (Zorbax ODS 250 × 20 mm; flow rate 6.0 ml min^{-1}; UV detection at 230 nm; 1 : 1–0 : 100 H_2O–MeCN gradient) gave fr. I-9a (153 mg, R_t 28 min.), which by prep. TLC (Merck GF-254 silica gel; CH_2Cl_2–*n*-BuOH, 19 : 1) afforded 5-cinnamoyl-10-acetyltaxicine I (75 mg).

Teixidol (**1**). Amorphous solid; mp 159° $[\alpha]_D^{20}$ −15.91 (*c* 0.77, $CHCl_3$). Positive EIMS *m/z*: 418 $[M-2xAcO]^+$. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400, 3600, 2931, 1734. UV $\lambda_{max}^{CHCl_3}$ nm: 274. ^{1}H–^{1}H COSY correlations ($CDCl_3$, H/H): 2/3, 9/10, 13/14, 13/14′, 14/14′. NOESY correlations ($CDCl_3$, H/H): 2/9, 2/16, 2/17, 2/19, 3/7, 3/14′, 5/6, 5/20, 7/10, 9/19, 10/18, 13/14, 13/16, 13/17, 13/18, 14/14′, 19/20′, 20/20′.

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