

Invited Review

The Taxane Diterpenoids

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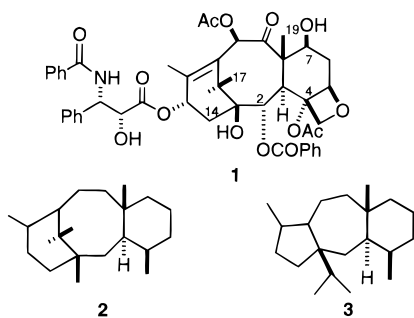
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The structures of over 350 taxane diterpenoids are classified and presented with information on their plant source, yield, melting point, and optical activity. The biotransformations and biosynthesis of the taxoids are also reviewed.

Introduction

The study of the taxane diterpenoids or taxoids has moved in the last twenty years from being a specialized subfield of natural products chemistry into something of a minor industry. The reason for this is, of course, the fact that the diterpenoid taxol (**1**), first isolated by Monroe Wall and Mansukh Wani from *Taxus brevifolia* Nutt. (Taxaceae),¹ as its formulated version Taxol,² is an effective anticancer drug for treatment of a variety of human cancers.³ This important discovery has spurred the isolation of many additional taxoids, in part with the hope of finding additional compounds with even better activity than taxol itself, in part as a byproduct of the large scale isolation of taxol for pharmaceutical use, and in part from sheer scientific curiosity.



The scope of this work can be documented by the large number of new compounds that have been isolated in the last six years. Thus in the 136 years between the first isolation of a "taxine" by Lucas⁴ and the completion of the literature survey for our previous review of this subject in 1992,⁵ approximately 100 taxoids had been isolated and characterized. In the seven years since 1992, over 250 additional taxoids have been isolated and characterized. The time is thus ripe for a comprehensive review of these fascinating compounds. This review will cover the structures and the biosynthesis of the taxoids; the chemistry of the taxoids will not be covered in this review, but a separate review covering this area is in preparation.⁶

Several reviews of the structures of the taxoids have appeared over the past few years. In addition to our review

Table 1. Systematics of the Genus *Taxus*

trivial name	botanical classification
European yew or English yew	<i>Taxus baccata</i> L.
Himalayan yew	<i>T. wallichiana</i> Zucc.
Chinese yew	<i>T. celebica</i> (Warburg) Li
Japanese yew	<i>T. cuspidata</i> Sieb. et Zucc.
Pacific yew	<i>T. brevifolia</i> Nutt.
Mexican yew	<i>T. globosa</i> Schlecht.
Florida yew	<i>T. floridana</i> Nutt.
Canadian yew	<i>T. canadensis</i> Marsh., <i>T. x media</i> Rehd., <i>T. x hunnewelliana</i> Rehd.

published in 1993,⁵ major comprehensive reviews have been published on the phytochemistry of the yew tree,⁷ on the taxine alkaloids,⁸ on naturally occurring taxoids,⁹ and on the chemical constituents of *Taxus* species.^{10,11} More specialized reviews have appeared on naturally occurring rearranged taxoids,¹² on oxetane-containing taxoids,¹³ on the structure elucidation of taxoids,¹⁴ on the detection and isolation of taxol,¹⁵ on the discovery and structure elucidation of taxol,¹⁶ and on the NMR spectra of taxane diterpenoids.¹⁷ The latter reference proposes several structural revisions of baccatin VI analogues and related compounds to the corresponding 11(15→1)-abeo-taxoids on the basis of their NMR spectra; for the most part these structural revisions have already been made by others.¹⁸

Taxonomy

As has been pointed out by Appendino,⁷ the taxonomy of the genus *Taxus* is difficult because yews look very much alike, and there is thus some confusion in the literature over the names of certain yews. In particular the Himalayan yew, *T. wallichiana* Zucc., is sometimes referred to as *T. baccata* L., while the Chinese yew, *T. celebica* (Warburg) Li is often considered as *T. chinensis* Rehd., *T. yunnanensis* Cheng et L. K. Fu, or *T. mairei* (Lemee and Lev.) Hu ex Liu. In this review no attempt has been made to correct or interpret the taxonomy assigned by the authors, and the sources are thus reported as recorded by the original authors. The botanical summary provided by Appendino⁷ is shown in Table 1; the botanical nomenclature follows the Krüssmann classification.¹⁹

Structures of the Taxane Diterpenoids

The structures of the taxane diterpenoids that have been reported in the literature through May 1999 are included

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in this review, together with short notes on any unusual features of chemical interest. The classification is basically the same as that used in our earlier review⁵ but with the addition of new tables to accommodate the new compound types that have been isolated since 1992. Each table gives the structure, name, molecular formula, molecular weight, optical rotation, melting point, plant source, plant part, and yield of each taxoid, insofar as these data are available in the original literature. The following code is used for the plant parts: lv, leaves; st, stems; rt, roots, hw, heartwood; tw, twigs; sd, seeds; cc, cell culture; bk, bark.

The basic structure for most of the taxoids consist of a pentamethyl [9.3.1.0]^{3,8} tricyclopentadecane skeleton (2), which is often called the normal taxane skeleton. Increasing numbers of taxoids with the 11(15→1) *abeo*-taxane skeleton (3) have been found in recent years, and several other skeletons that are obviously related to the normal taxane skeleton by rearrangement are also observed.

The confusion of names used for the taxoids makes the literature unnecessarily complex and confusing. The problem has been well discussed by Appendino,^{7,9} and we echo his plea that the discoverers of new taxoids name their compounds as derivatives of one of the known well-established taxoid structures wherever possible, rather than inventing additional trivial names. To assist this process, following Appendino⁹ we give below the structures of the baccatins and the taxinines whose structures were elucidated in the early days of the study of the taxoids, and whose names are thus well established (4–18).

Neutral Taxoids with a C-4(20) Double Bond (Table 2). This class is characterized by an exocyclic 4(20)-double bond and oxygenation at C-5. Oxygenation is also usually observed at C-9 and C-10 and often at C-1, C-2, and C-7. The oxygenated positions may be present either as hydroxyl groups or as acetate or occasionally other esters (Table 2). It has been suggested, primarily on the basis of NMR evidence, that the structures of several members of this class should be revised to the corresponding members of the class of 11(15→1)-*abeo*-taxoids with a C-4(20) double bond (Table 10).^{17,18} To minimize confusion, the structures of those compounds which are known to be incorrect are given in Table 1 with a footnote indicating that the structure has been corrected and that the correct structure will be found in Table 10.

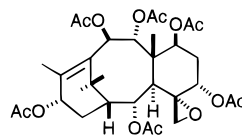
Basic Taxoids with a C-4(20) Double Bond (Table 3). This group of taxoids includes taxine B, one of the constituents of the crude "taxine" isolated by Lucas in 1856,⁴ and alkaloidal taxoids with basic properties are referred to collectively as taxine. Taxine is a powerful cardiotoxic agent and is the major toxic constituent of yew.²⁰ 2'-Deacetoxyaustrospicatin was the first basic taxoid isolated from the Himalayan yew, *T. wallichiana*.²¹

(+)-2 α -Acetoxy-2',7-dideacetoxy-1-hydroxyaustrospicatin, a new member of the austrospicatin class of taxoids, isolated from *T. baccata*, was reported earlier as a semi-synthetic compound.²² It shows activity as a pyrethroid synergist with the black vine weevil, *Otiorynchus sulcatus* Fab. (Curculionidae), which is a pest of several food and ornamental crops.

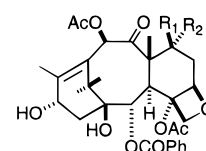
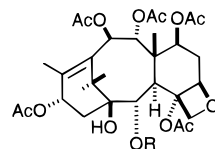
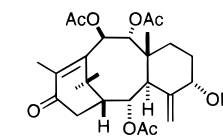
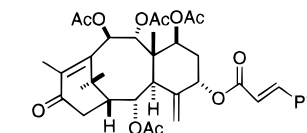
5-Cinnamoyl Taxoids with a C-4(20) Double Bond (Table 4). This important class of taxoids includes taxinine and 5-cinnamoyltaxicin I triacetate, two of the first taxoids whose structures were elucidated.^{23,24} The cinnamoyl group can be derived both formally and in practice by elimination of dimethylamine from basic taxoids such as taxine B (Table 3), but it is almost certain that the cinnamoyl

compounds also occur naturally since they can be isolated under conditions too mild to bring about elimination from taxine B.

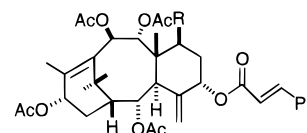
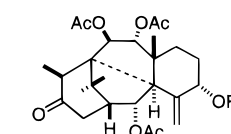
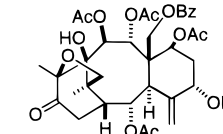
2-*O*-Acetyl-5-*O*-cinnamoyltaxicin I is reported to show fluxional behavior in its NMR spectra, similar to the brevifoliols which contain the (1→15)-*abeo*-taxane ring system. The corresponding 2-deacetoxy derivative is rigid. 2 α -Deacetyltaxinine J (taxuspinnanane G) showed weak cytotoxic activity against murine P-388 lymphocytic cells (IC₅₀ 3.9 μ g/mL).²⁵



4 Baccatin I

5 R₁ = OH, R₂ = H, Baccatin III
6 R₁ = H, R₂ = OH, Baccatin V7 R = Ac, Baccatin IV
8 R = C(=O)Ph, Baccatin VI
9 R = COC₅H₁₁, Baccatin VII10 R = OCCH=CHPh, Taxinine
11 R = H, Taxinine A
12 R = Ac, Taxinine H

13 Taxinine B

14 R = H, Taxinine E
15 R = OAc, Taxinine J16 R = H, Taxinine K
17 R = Ac, Taxinine L

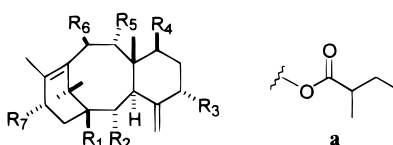
18 Taxinine M

Taxoids with a C-4(20) Double Bond and Oxygenation at C-14 (Table 5). Taxoids with a C-4(20) double bond and oxygenated at C-14 were only discovered relatively recently, and most of them have been found in the Chinese yew, *T. yunnanensis* or *T. chinensis* var. *mairii*. The C-14 hydroxyl group is invariably in the exo (or β) orientation, and C-13 is not oxygenated.

Taxoids with a C-12(16)-oxido Bridge and a C-4(20) Double Bond (Table 6). A small group of taxoids has members which are oxygenated at C-16, with the oxygen present as an oxido bridge to C-12. The taxoids 19-acetoxytaxagifine and taxezopidine L (Table 6) were recently reported independently and assigned the same structure.²⁶ However, their reported optical rotations are very different, and it is possible that one of the compounds has an alternate structure.

Taxoids with a C-4(20) Epoxide (Table 7). Taxoids of this class are related to baccatin I, one of the first taxoids to be elucidated structurally. The newer members of this group differ primarily in the number and position of acetyl groups on the hydroxyl groups around the periphery of the ring system.

1 β ,9 α -Dihydroxy-4 β ,20-epoxy-2 α ,5 α ,7 β ,10 β ,13 α -penta-acetoxytax-11-ene and 1 β ,7 β -dihydroxy-4 β ,20-epoxy-2 α ,5 α ,

Table 2. Neutral Taxoids with a C-4(20) Double Bond

name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	[α] _D	mp (°C)	plant source	plant part; % yield	refs
5α,9α,10β,13α-tetrahydroxy-4(20),11-taxadiene	C ₂₀ H ₃₂ O ₄	336	H	H	OH	H	OH	OH	OH	+134°	195–198	<i>T. baccata</i>	hw	<i>a</i>
1β,2α,5α,9α,10β,13α-hexahydroxy-4(20),11-taxadiene	C ₂₀ H ₃₂ O ₆	368	OH	OH	OH	H	OH	OH	OH	−5.6° (CHCl ₃)	120–121	<i>T. chinensis</i>	st, lv	<i>b</i>
taxezopidine C	C ₂₂ H ₃₂ O ₆	392	H	OH	OH	H	OAc	OH	=O	+17.3° (CHCl ₃)		<i>T. cuspidata</i>	sd, st; 5.2 × 10 ^{−4}	<i>c</i>
taxezopidine D	C ₂₂ H ₃₂ O ₆	392	H	OH	OH	H	OH	OAc	=O	+8.4° (CHCl ₃)		<i>T. cuspidata</i>	sd, st; 6.3 × 10 ^{−4}	<i>c</i>
7-debenzoyloxy-10-deacetyl-brevifoliol	C ₂₂ H ₃₄ O ₆	394	OH	H	OH	H	OAc	OH	OH	−24° (MeOH)	160–162	<i>T. wallichiana</i>	lv	<i>d</i>
taxuyunnanine D	C ₂₄ H ₃₄ O ₅	402	H	H	OAc	H	H	=O	OAc	−61.0° (CHCl ₃)		<i>T. yunnanensis</i>	rt	<i>e</i>
9α,10β-diacetoxy-5α,13α-dihydroxy-4(20),11-taxadiene	C ₂₄ H ₃₆ O ₆	420	H	H	OH	H	OAc	OAc	OH	+146°	235	<i>T. baccata</i>	hw; 3.8 × 10 ^{−4}	<i>f</i>
taxuspine G (2-deacetyltaxinine A)	C ₂₄ H ₃₄ O ₇	434	H	OH	OH	H	OAc	OAc	=O	+144.2° (CHCl ₃)	234–236	<i>T. mairei</i>	hw;	<i>g</i>
										+97° (CHCl ₃)		<i>T. cuspidata</i>	st, lv	<i>h</i>
										+147.8° (CHCl ₃)	295–298	<i>T. cuspidata</i>	lv, st	<i>i</i>
2α,5α,9α-trihydroxy-10β,13α-diacetoxytaxa-4(20),11-diene	C ₂₄ H ₃₆ O ₇	436	H	OH	OH	H	OH	OAc	OAc		186–188	<i>T. chinensis</i>	lv	<i>j</i>
2,10-di- <i>O</i> -acetyl-5-decinnamoyltaxinin I	C ₂₄ H ₃₄ O ₈	450	OH	OAc	OH	H	OH	OAc	=O	+30° (CHCl ₃)	165	<i>T. baccata</i>	lv	<i>k</i>
2α,9α-diacetoxy-1β,5α,10β,13α-tetrahydroxytaxa-4(20),11-diene	C ₂₄ H ₃₆ O ₈	452	OH	OAc	OH	H	OAc	OH	OH	−22° (CHCl ₃)	154	<i>T. baccata</i>	lv	<i>l</i>
5α-hydroxy-9α,10β,13α-triacetoxytaxa-4(20),11-diene	C ₂₆ H ₃₈ O ₇	462	H	H	OH	H	OAc	OAc	OAc	+266° (CHCl ₃)	204–206	<i>T. mairei</i>	tw	<i>m</i>
13-dehydro-5,13-deacetyl-2-deacetoxydecinnamoyltaxinine (taxuspinnanane K)	C ₂₆ H ₃₆ O ₈	476	H	H	OH	OAc	OAc	OAc	=O	+95.2° (CHCl ₃)		<i>T. cuspidata</i>	st; 1.0 × 10 ^{−4}	<i>n</i>
taxinine A	C ₂₆ H ₃₆ O ₈	476	H	OAc	OH	H	OAc	OAc	=O	+106° (CHCl ₃)	254–255	<i>T. cuspidata</i>	lv	<i>o</i>
											254–255	<i>T. chinensis</i>	lv; 4.0 × 10 ^{−4}	<i>p</i>
2-deacetyldecinnamoyltaxinine E	C ₂₆ H ₃₈ O ₈	478	H	OH	OH	H	OAc	OAc	OAc	+72° (CHCl ₃)		<i>T. baccata</i>	lv	<i>k</i>
triacetyl-5-decinnamoyltaxinin I	C ₂₆ H ₃₆ O ₉	492	OH	OAc	OH	H	OAc	OAc	=O	+54° (CH ₂ Cl ₂)	206–207	<i>T. baccata</i>	lv	<i>k</i>
(1-hydroxytaxinine A)														<i>ff</i>
7β,9α,10β-triacetoxy-2α,5α,13α-trihydroxy-4(20),11-taxadiene	C ₂₆ H ₃₈ O ₉	494	H	OH	OH	OAc	OAc	OAc	OH	+129° (CHCl ₃)		<i>Austrotaxus spicata</i>	bk; 7.0 × 10 ^{−4}	<i>q</i>
1β,7β,9α-trihydroxy-5α,10β,13α-triacetoxytaxa-4(20),11-diene (taxawallin G)	C ₂₆ H ₃₈ O ₉	494	OH	H	OAc	OH	OH	OAc	OAc		270	<i>T. wallichiana</i>	lv	<i>r</i>
5α,9α,10β,13α-tetraacetoxy-4(20),11-taxadiene (taxusin)	C ₂₈ H ₄₀ O ₈	504	H	H	OAc	H	OAc	OAc	OAc	+111°	126	<i>T. baccata</i>	hw; 1.3 × 10 ^{−1}	<i>f</i>
										+120° (CHCl ₃)	129–131	<i>T. baccata</i>	hw	<i>s</i>
										+95° (MeOH)	124–126	<i>T. mairei</i>	hw	<i>t</i>
										+168° (CHCl ₃)	124–126	<i>T. mairei</i>	hw; 5 × 10 ^{−2}	<i>g</i>
											131–132	<i>T. cuspidata</i>	hw; 4.0 × 10 ^{−1}	<i>u</i>
taxinine H	C ₂₉ H ₃₈ O ₉	518	H	OAc	OAc	H	OAc	OAc	=O	+96° (CHCl ₃)	166–167	<i>T. cuspidata</i>	lv	<i>o</i>
2-deacetoxy-5-decinnamoyltaxinine J	C ₂₈ H ₄₀ O ₉	520	H	H	OH	OAc	OAc	OAc	OAc	+112.9° (CHCl ₃)	178–180	<i>T. yunnanensis</i>	bk	<i>v</i>
										+114° (MeOH)	188–190	<i>T. wallichiana</i>	bk; 2.0 × 10 ^{−2}	<i>w</i>
										+113° (CHCl ₃)	185–187	<i>T. baccata</i>	lv	<i>k</i>
decinnamoyltaxinine E	C ₂₈ H ₄₀ O ₉	520	H	OAc	OH	H	OAc	OAc	OAc	+33.8° (CHCl ₃)		<i>T. chinensis</i>	sd; 2.8 × 10 ^{−3}	<i>x</i>
taxa-4(20),11-diene-5α-hydroxy-1β,7β,9α,10β-tetraacetate	C ₂₈ H ₄₀ O ₉	520	OAc	H	OH	OAc	OAc	OAc	H			<i>T. baccata</i>	rt	<i>y</i>
taxuspine F	C ₂₈ H ₃₈ O ₁₀	534	H	OAc	OH	OAc	OAc	OAc	=O	+50° (CHCl ₃)		<i>T. cuspidata</i>	st, lv; 1.0 × 10 ^{−3}	<i>z</i>

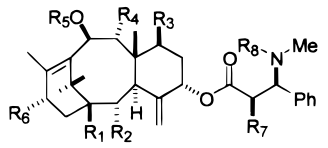
Table 2. (Continued)

name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	[α] _D	mp (°C)	plant source	plant part; % yield	refs
2α,5α-dihydroxy-7β,9α,10β,13α-tetraacetoxy-4(20),11-taxadiene	C ₂₈ H ₄₀ O ₁₀	536	H	OH	OH	OAc	OAc	OAc	OAc	+53° (CHCl ₃)		<i>Austrotaxus spicata</i>	lv; 4.4 × 10 ⁻⁴	aa
taxezopidine F	C ₂₈ H ₄₀ O ₁₀	536	H	OAc	OH	OAc	OAc	OAc	OH	-13.4° (CHCl ₃)		<i>T. cuspidata</i>	sd, st; 2.8 × 10 ⁻⁴	c
2α-(α-methylbutyryloxy)-5α,7β,10β-triacetoxy-4(20),11-taxadiene	C ₃₁ H ₄₆ O ₈	546	H	a	OAc	OAc	H	OAc	H	+45°	115	<i>T. baccata</i>	hw; 2.0 × 10 ⁻³	f
										+46.1° (CHCl ₃)	114–116	<i>T. mairei</i>	hw; 7.7 × 10 ⁻⁵	bb
2α-benzoyloxy-9α,10β-diacetoxy-1β,5α,13α-trihydroxy-4(20),11-taxadiene	C ₃₁ H ₄₀ O ₉	556	OH	OBz	OH	H	OAc	OAc	OH	+5° (CHCl ₃)	196–197	<i>T. chinensis</i>	st, lv	b
5α-hydroxy-2α-(α-methylbutyryloxy)-7β,9α,10β-triacetoxy-4(20),11-taxadiene	C ₃₁ H ₄₆ O ₉	562	H	a	OH	OAc	OAc	OAc	H	+63°	227–229	<i>T. baccata</i>	hw; 1.2 × 10 ⁻³	f
2α,5α,9α,10β,13α-pentaacetoxy-4(20),11-taxadiene	C ₃₀ H ₄₂ O ₁₀	562	H	OAc	OAc	H	OAc	OAc	OAc	+46°	165	<i>T. baccata</i>	hw; 3.5 × 10 ⁻⁴	f
5α,7β,9α,10β,13α-pentaacetoxy-4(20),11-taxadiene	C ₃₀ H ₄₂ O ₁₀	562	H	H	OAc	OAc	OAc	OAc	OAc	+92°	205–207	<i>T. baccata</i>	hw; 1.4 × 10 ⁻³	f
										+90.8° (CHCl ₃)	205–207	<i>T. mairei</i>	hw; 2.2 × 10 ⁻⁴	bb
5α-hydroxy-2α,7β,9α,10β,13α-tetraacetoxy-4(20),11-taxadiene (decinamoyl taxinine J)	C ₃₀ H ₄₂ O ₁₂	578	H	OAc	OH	OAc	OAc	OAc	OAc	+35° (CHCl ₃)	242–244	<i>T. brevifolia</i>	bk; 2.7 × 10 ⁻⁴	cc
												<i>Austrotaxus spicata</i>	lv; 2.6 × 10 ⁻⁴	aa
decinamoyl-1-hydroxy-taxinine J	C ₃₀ H ₄₂ O ₁₂	594	OH	OAc	OH	OAc	OAc	OAc	OAc	+44° (CHCl ₃)	213	<i>T. baccata</i>	lv	k
13-acetylbrevifoliol	C ₃₃ H ₄₂ O ₁₀	598	OH	H	OH	OBz	OAc	OAc	OAc	+8° (MeOH)		<i>T. wallichiana</i>		d
2α-benzoyloxy-9α,10β,13α-triacetoxy-1β,5α-dihydroxy-4(20),11-taxadiene	C ₃₃ H ₄₂ O ₁₀	598	OH	OBz	OH	H	OAc	OAc	OAc	+67.7° (CHCl ₃)	155–157	<i>T. chinensis</i>	st, lv	b
brevifoliol	C ₃₃ H ₄₂ O ₁₀	598	OH	H	OH	OAc	OAc	OBz	OH			<i>T. brevifolia</i>	lv	dd
2α-(α-methylbutyryloxy)-5α,7β,9α,10β-tetraacetoxy-4(20),11-taxadiene	C ₃₃ H ₄₈ O ₁₀	604	H	a	OAc	OAc	OAc	OAc	H	+56°	155–156	<i>T. baccata</i>	hw; 8.0 × 10 ⁻⁴	f
2α-acetoxybrevifoliol	C ₃₃ H ₄₂ O ₁₁	614	OH	OAc	OH	OBz	OAc	OAc	OH	-24° (CHCl ₃)	198	<i>T. baccata</i>	sd	ee

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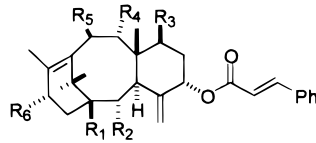
9α,10β,13α-pentaacetoxytax-11-ene provided the first examples of intramolecular transesterification in this family of taxane metabolites, and were found to isomerize readily via acyl migration between C-7 and C-9 under mild acid-catalyzed conditions, even when standing in CDCl₃.²⁷

Taxoids with an Oxetane Ring (Table 8). Taxoids of this group are related to baccatin III, important as the diterpenoid portion of taxol. Although most of them are substituted with the usual acetyl and benzoyl groups, some of them have more interesting esterification patterns with,

Table 3. Basic Taxoids with a C-4(20) Double Bond


name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	R ₈	[α] _D	mp (°C)	plant source	plant part; % yield	refs
2-deacetoxy-9-acetoxytaxine B	C ₃₃ H ₄₅ NO ₇	567	H	OH	H	OAc	H	=O	H	Me			<i>T. baccata</i>	lv	<i>a</i>
2-deacetoxy-10-acetyltaxine B	C ₃₃ H ₄₅ NO ₇	567	H	OH	H	OH	Ac	=O	H	Me			<i>T. baccata</i>	lv	<i>a</i>
taxine B	C ₃₃ H ₄₅ NO ₈	583	OH	OAc	H	OH	H	=O	H	Me	+116° (CH ₃ OH) +119° (CHCl ₃)	115 113	<i>T. baccata</i>	lv	<i>b</i> <i>c, d</i>
13-deoxo-13α-acetyloxy-1-deoxynortaxine B	C ₃₄ H ₄₇ NO ₈	597	H	OH	H	OH	Ac	OAc	H	H	+76° (CH ₂ Cl ₂)	165	<i>T. baccata</i>	lv;	<i>e</i> <i>f</i>
13-deoxo-13α-acetyloxy-1-deoxytaxine B	C ₃₅ H ₄₉ NO ₈	611	H	OH	H	OH	Ac	OAc	H	Me	+25° (CH ₂ Cl ₂)	192	<i>T. baccata</i>	lv;	<i>f</i> <i>f</i>
10-acetoxytaxine B	C ₃₅ H ₄₇ NO ₉	625	OH	OAc	H	OH	Ac	=O	H	Me			<i>T. baccata</i>	lv	<i>a</i>
9-acetoxytaxine B	C ₃₅ H ₄₇ NO ₉	625	OH	OAc	H	OAc	H	=O	H	Me			<i>T. baccata</i>	lv	<i>a</i>
13-deoxo-13α-acetyloxy-taxine B	C ₃₅ H ₄₉ NO ₉	627	OH	OH	H	OH	Ac	OAc	H	Me	+42° (CH ₂ Cl ₂)	119	<i>T. baccata</i>	lv;	<i>f</i> <i>f</i>
2'β,7β,9α-trisdeacetyl-austrospicatine	C ₃₅ H ₄₉ NO ₉	627	H	H	OH	OH	Ac	OAc	OH	Me	+41° (CHCl ₃)		<i>A. spicata</i>	lv;	<i>g</i> <i>g</i>
7,2'-didesacetoxy-austrospicatine	C ₃₇ H ₅₁ NO ₈	637	H	H	H	OAc	Ac	OAc	H	Me	+112.93° (CHCl ₃)	199–200	<i>T. walli-chiana</i>	bk	<i>h, i</i>
taxuspine Z	C ₃₇ H ₅₁ NO ₉	653	H	OH	H	OAc	Ac	OAc	H	Me	+31.2° (CHCl ₃)		<i>T. cuspidata</i>	st	<i>j</i>
comptonine	C ₃₇ H ₄₉ NO ₁₀	667	H	H	OAc	OAc	Ac	=O	OH	Me	+85° (CHCl ₃)		<i>A. spicata</i>	bk;	<i>k</i> <i>k</i>
2'-hydroxytaxine II	C ₃₇ H ₄₉ NO ₁₀	667	H	OAc	H	OAc	Ac	=O	OH	Me			<i>T. cuspidata</i>	lv;	<i>l</i> <i>l</i>
7β,9α-bisdeacetyl-austrospicatine	C ₃₇ H ₅₁ NO ₁₀	669	H	H	OH	OH	Ac	OAc	OAc	Me	+41° (CHCl ₃)		<i>A. spicata</i>	lv;	<i>g</i> <i>g</i>
2α-acetoxy-2',7-dideacetoxy-austrospicatine	C ₃₉ H ₅₃ NO ₁₀	695	H	OAc	H	OAc	Ac	OAc	H	Me	+33.7° (CHCl ₃)		<i>T. chinensis</i>	sd;	<i>e</i> <i>e</i>
2'β-deacetoxyaustrospicatine	C ₃₉ H ₅₃ NO ₁₀	695	H	H	OAc	OAc	Ac	OAc	H	Me	+71° (CH ₂ Cl ₂) +117° (CHCl ₃)		<i>A. spicata</i>	lv;	<i>g</i> <i>g</i>
13-deoxo-13α-acetyloxy-7β,9α-diacetyl-1,2-dideoxytaxine B	C ₃₉ H ₅₃ NO ₁₀	695	H	H	OAc	OAc	Ac	OAc	H	Me	+76.9° (MeOH)	162–164	<i>T. baccata</i>	bk	<i>n</i>
(+)-2α-acetoxy-2',7-dideacetoxy-1-hydroxyaustrospicatine	C ₃₉ H ₅₃ NO ₁₁	711	OH	OAc	H	OAc	Ac	OAc	H	Me	+60° (CHCl ₃)		<i>T. baccata</i>	lv	<i>o</i>
2'β-deacetylaustrospicatine	C ₃₉ H ₅₃ NO ₁₁	711	H	H	OAc	OAc	Ac	OAc	OH	Me	+56° (CH ₂ Cl ₂)	298–300	<i>A. spicata</i>	lv;	<i>g</i> <i>g</i>
2α-hydroxy-2'β-deacetoxy-austrospicatine	C ₃₉ H ₅₃ NO ₁₁	711	H	OH	OAc	OAc	Ac	OAc	H	Me	+50° (CHCl ₃)		<i>A. spicata</i>	lv;	<i>g</i> <i>g</i>
7β-deacetylaustrospicatine	C ₃₉ H ₅₃ NO ₁₁	711	H	H	OH	OAc	Ac	OAc	OAc	Me	+41° (CHCl ₃)		<i>A. spicata</i>	lv;	<i>g</i> <i>g</i>
austrospicatine	C ₄₁ H ₅₅ NO ₁₂	753	H	H	OAc	OAc	Ac	OAc	OAc	Me	+52° (CH ₂ Cl ₂)		<i>A. spicata</i>	lv;	<i>g</i> <i>g</i>
2α-acetoxy-2'β-deacetyl-austrospicatine	C ₄₁ H ₅₅ NO ₁₃	769	H	OAc	OAc	OAc	Ac	OAc	OH	Me	+19° (CHCl ₃)		<i>A. spicata</i>	lv;	<i>g</i> <i>g</i>
2α-acetoxy-2'-deacetyl-1-hydroxyaustrospicatine	C ₄₁ H ₅₅ NO ₁₄	785	OH	OAc	OAc	OAc	Ac	OAc	OH	Me	+42° (CHCl ₃)	120	<i>T. baccata</i>		<i>p</i>
2α-acetoxyaustrospicatine	C ₄₃ H ₅₇ NO ₁₄	811	H	OAc	OAc	OAc	Ac	OAc	OAc	Me	+37° (CHCl ₃)		<i>A. spicata</i>	lv;	<i>g</i> <i>g</i>

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Table 4. 5-Cinnamoyl Taxoids with a C-4(20) Double Bond

name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	[α] _D	mp (°C)	plant source	plant part; % yield	refs
<i>O</i> -cinnamoyltaxicin I	C ₂₉ H ₃₆ O ₇	496	OH	OH	H	OAc	OH	=O	+285° (CHCl ₃)	233–234	<i>T. baccata</i>	lv	<i>a</i>
5-cinnamoyl-10-acetyltaxicin II	C ₃₁ H ₃₈ O ₇	522	H	OH	H	OH	OAc	=O	+128° (CHCl ₃)	204–205	<i>T. baccata</i>	lv	<i>b</i>
2- <i>O</i> -acetyl-5- <i>O</i> -cinnamoyl taxicin I	C ₃₁ H ₃₈ O ₈	538	OH	OAc	H	OH	OH	=O	+182° (CH ₂ Cl ₂)	152–154	<i>T. baccata</i>	lv	<i>c</i>
5-cinnamoyl-10-acetyltaxicin I	C ₃₁ H ₃₈ O ₈	538	OH	OH	H	OH	OAc	=O	+185° (CHCl ₃)	145	<i>T. baccata</i>	lv	<i>b</i>
taxezopidine E	C ₃₁ H ₃₈ O ₈	538	H	OH	OH	OH	OAc	=O	+24° (CHCl ₃)		<i>T. cuspidata</i>	sd, st; 3.6 × 10 ⁻⁴	<i>d</i>
2-deacetoxy-7,9-dideacetyltaxinine J	C ₃₃ H ₄₂ O ₈	566	H	H	OH	OH	OAc	OAc	+82° (CHCl ₃)	238–240	<i>T. chinensis</i>	bk; 1.1 × 10 ⁻⁴	<i>e</i>
5α-cinnamoyloxy-2α,13α, dihydroxy-9α,10β-diacetoxy-4(20),11-taxadiene	C ₃₃ H ₄₆ O ₈	570	H	OH	H	OAc	OAc	OH	+4° (CHCl ₃)	104–106	<i>T. chinensis</i>	lv, st; 4.0 × 10 ⁻⁴	<i>f</i>
5-cinnamoyl-9,10-diacetyltaxicin I	C ₃₃ H ₄₀ O ₉	580	OH	OH	H	OAc	OAc	=O		185	<i>T. baccata</i>	lv	<i>g</i>
5α-cinnamoyloxy-9α,10β,13α-triacetoxytaxa-4(20),11-diene	C ₃₅ H ₄₄ O ₈	592	H	H	H	OAc	OAc	OAc	+118.5° (CHCl ₃)	165–166	<i>T. mairei</i>	hw	<i>h</i>
										175–177	<i>T. chinensis</i>	lv, st; 2.5 × 10 ⁻⁴	<i>f</i>
2-deacetoxytaxinine B	C ₃₅ H ₄₂ O ₉	606	H	H	OAc	OAc	OAc	=O	+71.7° (CHCl ₃)	240	<i>T. wallichiana</i>	lv, tw; 1.7 × 10 ⁻³	<i>i</i>
taxinine (<i>O</i> -cinnamoyltaxicin II triacetate)	C ₃₅ H ₄₂ O ₉	606	H	OAc	H	OAc	OAc	=O	+137° (CHCl ₃)	265–267	<i>T. baccata</i>	lv	<i>a, j, k</i>
									+128° (CHCl ₃)	266–267	<i>T. chinensis</i>	lv;	<i>l</i>
										264–265	<i>T. cuspidata</i>	lv; 8.8 × 10 ⁻²	<i>m, n</i>
										237–239	<i>T. mairei</i>	hw; 4.0 × 10 ⁻⁴	<i>o</i>
											<i>T. mairei</i>	tw	<i>p</i>
5α-(cinnamoyloxy)-7β-hydroxy-9α,10β,13α-triacetoxytaxa-4(20),11-diene	C ₃₅ H ₄₄ O ₉	608	H	H	OH	OAc	OAc	OAc	+20° (CHCl ₃)		<i>T. mairei</i>		
taxezopidine G	C ₃₅ H ₄₄ O ₉	608	H	OH	H	OAc	OAc	OAc	+25.2° (CHCl ₃)		<i>T. cuspidata</i>	sd, st; 1.5 × 10 ⁻⁴	<i>d</i>
taxezopidine H	C ₃₅ H ₄₄ O ₉	608	H	H	OAc	OAc	OAc	OH	+5.6° (CHCl ₃)		<i>T. cuspidata</i>	sd, st; 1.4 × 10 ⁻⁴	<i>d</i>
5α-cinnamoyloxy-10β-hydroxy-2α,9α,13α-triacetoxytaxa-4(20),11-diene	C ₃₅ H ₄₈ O ₉	612	H	OAc	H	OAc	OH	OAc	+29.6° (CHCl ₃)	110–112	<i>T. chinensis</i>	lv, st	<i>f</i>
<i>O</i> -cinnamoyltaxicin I triacetate	C ₃₅ H ₄₂ O ₁₀	622	OH	OAc	H	OAc	OAc	=O	+218° (CHCl ₃)	237–239	<i>T. baccata</i>	lv	<i>a</i>
											<i>T. cuspidata</i>	lv; 8.0 × 10 ⁻⁴	<i>m</i>
10-deacetyltaxinine B	C ₃₅ H ₄₂ O ₁₀	622	H	OAc	OAc	OAc	OH	=O	+45.2° (CHCl ₃)	245–248	<i>T. cuspidata</i>	lv, tw;	<i>q, r</i>
5α-cinnamoyloxy-2α,9α,10β,13α-tetraacetoxy-4(20),11-taxadiene (taxinine E)	C ₃₇ H ₄₆ O ₁₀	650	H	OAc	H	OAc	OAc	OAc	+225° (CHCl ₃)	231–233	<i>T. mairei</i>	hw; 3.1 × 10 ⁻⁴	<i>s</i>
											<i>T. cuspidata</i>	lv	<i>n</i>
2-deacetoxytaxinine J	C ₃₇ H ₄₆ O ₁₀	650	H	H	OAc	OAc	OAc	OAc	+50° (acetone)	171–172	<i>T. mairei</i>	bk	<i>t</i>
taxinine B	C ₃₇ H ₄₄ O ₁₁	664	H	OAc	OAc	OAc	OAc	=O	+93.8° (CHCl ₃)	265–266	<i>T. cuspidata</i>	lv	<i>n</i>
(7β-acetate- <i>O</i> -taxinine A)									+84.4° (CHCl ₃)	261–262	<i>T. mairei</i>	hw; 2.0 × 10 ⁻⁴	<i>s</i>
2α-deacetyltaxinine J (taxuspinnanane G)	C ₃₇ H ₄₆ O ₁₁	666	H	OH	OAc	OAc	OAc	OAc	-54.9° (CHCl ₃)		<i>T. cuspidata</i>	st	<i>u</i>
1-hydroxy-2-deacetoxytaxinine J (taxawallin A)	C ₃₇ H ₄₆ O ₁₁	666	OH	H	OAc	OAc	OAc	OAc	+64.0° (CHCl ₃)	112–114	<i>T. wallichiana</i>	bk	<i>v</i>
									+60.45° (CHCl ₃)	112–114	<i>T. wallichiana</i>	lv	<i>w</i>
2α-benzoyloxy-5α-cinnamoyloxy-9α,10β-diacetoxy-1β,13α-dihydroxy-4(20),11-taxadiene	C ₄₀ H ₄₆ O ₁₀	686	OH	OBz	H	OAc	OAc	OH	+6.5° (CHCl ₃)	212–214	<i>T. chinensis</i>	st, lv;	<i>x, y, z</i>

Table 4. (Continued)

name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	[α] _D	mp (°C)	plant source	plant part; % yield	refs
taxinine J	C ₃₉ H ₄₈ O ₁₂	708	H	OAc	OAc	OAc	OAc	OAc	+36° (CHCl ₃)	248–249	<i>T. mairei</i>	hw; 2.7 × 10 ⁻³	<i>aa</i>
										249–251	<i>T. cuspidata</i>	lv	<i>t</i>
										248–249	<i>T. mairei</i>	bk; 5.0 × 10 ⁻³	<i>bb</i>
									+137.1° (CHCl ₃)	284–286	<i>T. chinensis</i>	bk; 2.0 × 10 ⁻⁴	<i>cc</i>

^aBaxter, J. N.; Lythgoe, B.; Scales, B.; Scrowston, R. M.; Trippett, S. *J. Chem. Soc.* **1962**, 2964–2971. ^bAppendino, G.; Gariboldi, P.; Pisetta, A.; Bombardelli, E.; Gabetta, B. *Phytochemistry* **1992**, *31*, 4253–4257. ^cAppendino, G.; Ozen, H. C.; Gariboldi, P.; Gabetta, B.; Bombardelli, E. *Fitoterapia* **1992**, *64*(S1), 47–51. ^dWang, X.-X.; Shigemori, H.; Kobayashi, J. *J. Nat. Prod.* **1998**, *61*, 474–479. ^eLiang, J.-Y.; Huang, K.-S.; Gunatilaka, A. A. L. *Planta Med.* **1998**, *64*, 187–188. ^fZhang, Z.; Jia, Z. *Phytochemistry* **1991**, *30*, 2345–2348. ^gAppendino, G.; Cravotto, G.; Enriu, R.; Jakupovic, J.; Gariboldi, P.; Gabetta, B.; Bombardelli, E. *Phytochemistry* **1994**, *36*, 407–411. ^hYeh, M.-K.; Wang, J.-S.; Liu, L.-P.; Chen, F.-C. *Phytochemistry* **1988**, *27*, 1534–1536. ⁱShrestha, T. B.; Chetri, S. K. K.; Banskota, A. H.; Manandhar, M. D. *J. Nat. Prod.* **1997**, *60*, 820–821. ^jDukes, M.; Etre, D. H.; Harrison, J. W.; Scrowston, R. M.; Lythgoe, B. *J. Chem. Soc. C* **1967**, 448–452. ^kKurono, M.; Nakadaira, Y.; Onuma, S.; Sasaki, K.; Nakanishi, K. *Tetrahedron Lett.* **1963**, *30*, 2153–2160. ^lChiang, H. C. *Shih Ta Hsueh Pao* **1975**, *20*, 147–50. ^mChiang, H. C.; Woods, M. C.; Nakadaira, Y.; Nakanishi, K. *Chem. Commun.* **1967**, 1201–1202. ⁿWoods, M. C.; Chiang, H. C.; Nakadaira, Y.; Nakanishi, K. *J. Am. Chem. Soc.* **1968**, *90*, 522. ^oLiu, C.-L.; Lin, Y.-C.; Lin, Y.-M.; Chen, F.-C. *Taiwan K'ohsueh* **1984**, *38*, 119–125. ^pYang, S.-J.; Fang, J.-M.; Cheng, Y.-S. *Phytochemistry* **1996**, *43*, 839–842. ^qTong, X. J.; Fang, W. S.; Zhou, J. Y.; He, C. H.; Chen, W. M.; Fang, Q. C. *Yaoyue Xuebao* **1994**, *29*, 55–60. ^rTong, X. J.; Fang, W. S.; Zhou, J. Y.; He, C. H.; Chen, W. M.; Fang, Q. C. *Chin. Chem. Lett.* **1993**, *4*, 887–890. ^sYeh, M.-K.; Wang, J.-S.; Lui, L.-P.; Chen, F.-C. *J. Chin. Biochem. Soc.* **1988**, *35*, 309–313. ^tLiang, J.; Min, Z.; Niwa, M. *J. Huaxue Xuebao* **1988**, *46*, 1053–1054. ^uMorita, H.; Gonda, A.; Wei, L.; Yamamura, Y.; Wakabayashi, H.; Takeya, K.; Itokawa, H. *Planta Med.* **1998**, *64*, 183–186. ^vZhang, J.-Z.; Fang, Z.-C.; Liang, X.-T.; He, C.-H.; Kong, M.; He, W.-Y.; Jin, X.-L. *Phytochemistry* **1995**, *40*, 881–884. ^wZhang, J. Z.; Fang, Q. C.; Liang, X. T.; Kong, M.; He, W. Y. *Chin. Chem. Lett.* **1995**, *6*, 967–970. ^xJia, Z. J.; Zhang, Z. P. *Chin. Sci. Bull.* **1991**, *36*, 1174–1176. ^yZhang, Z.-P.; Jia, Z.-J.; Zhu, Z.-Q.; Cui, Y.-X.; Cheng, J.-L.; Wang, Q.-G. *Acta Chim. Sin.* **1991**, *49*, 1023–1027. ^zRevision of this structure to the corresponding 11(15→1)-*abeo*-taxoid skeleton has been suggested: Huang, K.; Liang, J.; Gunatilaka, A. A. L. *J. Chin. Pharm. University (Zhongguo Yaoke Daxue Xuebao)* **1998**, *29*, 259–266. ^{aa}Min, Z. D.; Jiang, H.; Liang, J. Y. *Acta Pharmacol. Sin.* (*Yaoyue Xuebao*) **1989**, *24*, 673–677. ^{bb}Liang, J.; Min, Z.; Niwa, M. *J. Huaxue Xuebao* **1988**, *46*, 1053–1054. ^{cc}Liang, J.-Y.; Huang, K.-S.; Gunatilaka, A. A. L.; Yang, L. *Phytochemistry* **1998**, *47*, 69–72.

for example, a 2,3-dihydroxy-3-phenylpropionyl group at the C-13 position of baccatin III in one example and a tigloyl substituent at C-2 in place of the more normal benzoyl group in another example. As with the taxoids of Table 2, it has been suggested that the structures of several members of this class should be revised to the corresponding members of the class of 11(15→1)-*abeo*-taxoids with an oxetane ring (Table 12).^{17,18} This reassignment of structure was supported by NMR evidence and in one case by an X-ray structure. To minimize confusion the structures of those compounds which are thought to be incorrect are given in Table 8 with a footnote indicating that the structure has been corrected.

13-Oxo-7,9-bisdeacetyl baccatin VI showed only very weak cytotoxic activity against P-388 lymphocytic cells (IC₅₀ 21 μg/mL).²⁵

Taxoids with an Oxetane Ring and a Phenylisoserine C-13 Side Chain (Table 9). Taxoids of this class include taxol and a number of related compounds differing in their ring substituents and also in the substituents on the N-3' position of the side chain. Side-chain hydroxylation at the 2'-position is always present as is oxidation at C-1 of the taxane ring. *N*-Methyl taxol C and taxcultine showed activity close to that of taxol in a tubulin assembly assay.²⁸

Taxoids with an Opened Oxetane or Oxirane Ring (Table 10). A number of taxoids have been isolated in recent years which can be derived formally by opening of the oxetane ring of a taxoid related to baccatin III or by opening of the oxirane ring of a taxoid related to baccatin I. Since oxirane rings can be opened fairly easily under basic conditions, and since the oxetane ring of baccatin III can be opened under a variety of conditions,²⁹ it is conceivable that some members of this class are artifacts of the isolation process, but it seems more probable that they are in fact genuine natural products.

11(15→1)-*abeo*-Taxoids with a C-4(20) Double Bond (Table 11). A growing number of taxoids have the 11(15→1)-

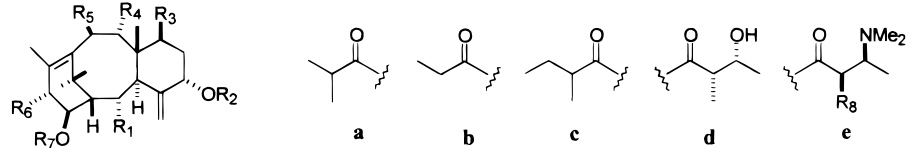
abeo-taxane skeleton. First encountered as a transformation product of taxol²⁹ this skeleton was then observed in the naturally occurring taxoid *brevifoliol*,³⁰ and then in an increasing number of taxoids. The NMR spectra of these compounds often show broad lines due to fluxional behavior of the B and C ring systems, which can adopt either B-twist-boat/C-chair or B-twist-chair/C-boat conformations.³¹ A few compounds of this type have been isolated with the epimeric β configuration at C-2 and C-9. Esterification at C-2 is usually acetate rather than benzoate in this series, and both cinnamate and β-aminophenylpropionate esters are observed at C-5.

(-)-2α-Acetoxy-2',7-dideacetoxy-1-hydroxy-11(15→1)-*abeo*-austrospicatin shows activity as a pyrethroid synergist with the black vine weevil.³²

11(15→1)-*abeo*-taxoids with an Oxetane Ring (Table 12). A large number of taxoids of this class has been isolated in recent years, primarily from *T. chinensis*, *T. yunnanensis*, and *T. wallichiana*. The C-2 ester group may be either benzoate or acetate, as is also the case with the C-7, C-9, and C-10 ester groups, if present. 9-Deacetyl-taxayuntin E showed very weak cytotoxic activity against P-388 lymphocytic leukemia cells, with an IC₅₀ of 44 μg/mL.³³

11(15→1)-*abeo*-Taxoids with an Opened Oxetane or Oxirane Ring (Table 13). The 11(15→)-*abeo*-taxoids correspond to *abeo*-taxoids which have undergone opening of an oxirane or oxetane ring, as observed also for a group of normal taxoids (Table 13). Taxuchin B, the first reported chlorine-containing taxoid, is a member of this class isolated from *T. chinensis*.

3,8-*seco*-Taxoids (Table 14). An interesting group of taxoids is bicyclic, with the normal ABC ring system replaced by an AB ring system comprising the usual six-membered A-ring and a 12-membered B-ring. Compounds of this class may have a cinnamoyl group at the C-4 position.

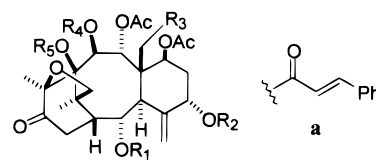
Table 5. Taxoids with a C-4(20) Double Bond and Oxygenation at C-14


name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	R ₈	[α] _D	mp (°C)	plant source	plant part; % yield	refs
taxuyunnanine J	C ₂₂ H ₃₄ O ₄	362	H	Ac	H	H	OH	H	H	NA	+71.3° (CHCl ₃)		<i>T. yunnanensis</i>	rt	<i>a</i>
2α,10β,14β-trihydroxy-5α-acetoxytaxa-4(20),11-diene	C ₂₂ H ₃₄ O ₅	378	OH	Ac	H	H	OH	H	H	NA	+39.2° (MeOH)	67–69	<i>T. yunnanensis</i>	cc	<i>b</i>
taxuyunnanine G	C ₂₄ H ₃₆ O ₆	420	OAc	Ac	H	H	OH	H	H	NA	+40.6° (CHCl ₃)		<i>T. yunnanensis</i>	rt	<i>a</i>
taxuyunnanine H	C ₂₅ H ₃₈ O ₆	434	OAc	H	H	H	OH	H	b	NA	+101.8° (CHCl ₃)		<i>T. yunnanensis</i>	rt	<i>a</i>
taxuyunnanine I	C ₂₆ H ₄₀ O ₆	448	OAc	H	H	H	OH	H	a	NA	+27.1° (CHCl ₃)		<i>T. yunnanensis</i>	rt	<i>a</i>
7β,9α-diacetoxy-5α,13α,14β-trihydroxy-10-oxotaxa-4(20),11-diene	C ₂₄ H ₃₄ O ₈	450	H	H	OAc	OAc	=O	OH	H	NA	+11° (CHCl ₃)		<i>A. spicata</i>	bk; 6.6 × 10 ⁻⁴	<i>c</i>
2α-hydroxy-5α,10β,14β-triacetoxytaxa-4(20),11-diene	C ₂₆ H ₃₈ O ₇	462	OH	Ac	H	H	OAc	H	Ac	NA	+28.7° (EtOH)	60–61	<i>T. yunnanensis</i>	cc	<i>b</i>
taxuyunnanine C	C ₂₈ H ₄₀ O ₈	504	OAc	Ac	H	H	OAc	H	Ac	NA	+41.1° (CHCl ₃)		<i>T. yunnanensis</i>	rt	<i>d</i>
(2α,5α,10β,14β-tetraacetoxytaxa-4(20),11-diene)											+31.95° (MeOH)	170	<i>T. chinensis</i>	cc	<i>f</i>
taxa-4(20),11-diene-10β-methoxy-2α,5α-diacetoxy-14β-(α-methyl)butyrate	C ₃₀ H ₄₆ O ₇	518	OAc	Ac	H	H	OMe	H	c	NA			<i>T. baccata</i>	rt	<i>e</i>
2α,5α,10β-triacetoxy-14β-propionyloxytaxa-4(20),11-diene	C ₂₉ H ₄₂ O ₈	518	OAc	Ac	H	H	OAc	H	b	NA	+41.37° (MeOH)	195	<i>T. chinensis</i>	cc	<i>f</i>
10-deacetylyunnanaxane	C ₂₉ H ₄₄ O ₈	520	OAc	Ac	H	H	OH	H	d	NA	-41.0° (CHCl ₃)		<i>T. media</i>	rt; 1.5 × 10 ⁻⁴	<i>g</i>
7β-hydroxy-2α,5α,10β,14β-tetraacetoxytaxa-4(20),11-diene	C ₂₈ H ₄₀ O ₉	520	OAc	Ac	OH	H	OAc	H	Ac	NA			<i>T. cuspidata</i>	cc; 1.4 × 10 ⁻²	<i>h</i>
14β-hydroxytaxusin (5α,9α,10β,13α-tetraacetoxytaxa-4(20),11-dien-14β-ol)	C ₂₈ H ₄₀ O ₉	520	H	Ac	H	OAc	OAc	OAc	H	NA	+76.4° (CHCl ₃)	208–209	<i>T. mairei</i>	bk; 1.0 × 10 ⁻⁴	<i>i</i>
2α,5α,10β-triacetoxy-14β-isobutyryloxytaxa-4(20),11-diene	C ₃₀ H ₄₄ O ₈	532	OAc	Ac	H	H	OAc	H	a	NA	+33.96° (MeOH)	183	<i>T. chinensis</i>	cc	<i>f</i>
2α,5α,10β-triacetoxy-14β-(2-methyl)butyryloxytaxa-4(20),11-diene	C ₃₁ H ₄₆ O ₈	546	OAc	Ac	H	H	OAc	H	c	NA	+36.96° (MeOH)	106	<i>T. chinensis</i>	cc	<i>f</i>
											+44.2° (CHCl ₃)	108.5	<i>T. baccata</i> <i>T. cuspidata</i>	rt hw	<i>e</i> <i>j</i>
9α-hydroxy-14β-(2-methylbutyryloxy)-2α,5α,10β-triacetoxytaxa-4(20),11-diene	C ₃₁ H ₄₆ O ₉	562	OAc	Ac	H	OH	OAc	H	c	NA	+65.8° (CHCl ₃)		<i>T. mairei</i>	tw	<i>k</i>
2α,5α,9α,10β,14β-pentaacetoxytaxa-4(20),11-diene	C ₃₀ H ₄₂ O ₁₀	562	OAc	Ac	H	OAc	OAc	H	Ac	NA	+26° (CHCl ₃)	132–133	<i>T. mairei</i>	tw	<i>k</i>
taiwanxan	C ₃₁ H ₄₆ O ₉	562	OAc	H	H	OAc	OAc	H	c	NA	+43.7° (CHCl ₃)	227–229	<i>T. mairei</i>	hw; 1.7 × 10 ⁻⁴	<i>l</i>
												227–230	<i>T. mairei</i> <i>T. yunnanensis</i>	hw rt	<i>m</i> <i>d</i>
taxuyunnanine B	C ₃₃ H ₄₈ O ₁₀	604	OAc	Ac	H	OAc	OAc	H	c	NA	+58.2° (CHCl ₃)		<i>T. yunnanensis</i>	rt	<i>d</i>
2′β,13α,14β-trisdeacetyl-austrotaxine	C ₃₅ H ₄₇ NO ₁₀	641	H	e	OAc	OAc	=O	OH	H	OH	-21° (CHCl ₃)		<i>A. spicata</i>	bk; 7.0 × 10 ⁻⁴	<i>c</i>
2′-deacetoxyaustrotaxine	C ₃₉ H ₅₁ NO ₁₁	709	H	e	OAc	OAc	=O	OAc	Ac	H	-37° (CHCl ₃)		<i>A. spicata</i>	lv; 3.3 × 10 ⁻⁴	<i>n</i>
2′-deacetylaustrotaxine	C ₃₉ H ₅₁ NO ₁₂	725	H	e	OAc	OAc	=O	OAc	Ac	OH	141° (CHCl ₃)		<i>A. spicata</i>	lv; 4.4 × 10 ⁻⁴	<i>n</i>
austrotaxine	C ₄₁ H ₅₃ NO ₁₃	767	H	e	OAc	OAc	=O	OAc	Ac	OAc	-49° (CHCl ₃)		<i>A. spicata</i>	lv; 4.8 × 10 ⁻⁴	<i>n</i>

Table 5. (Continued)

^aZhang, H.; Sun, H.; Takeda, Y. *J. Nat. Prod.* **1995**, *58*, 1153–1159. ^bCheng, K.; Fang, W.; Yang, Y.; Xu, H.; Meng, C.; Kong, M.; He, W.; Qicheng, F. *Phytochemistry* **1996**, *42*, 73–75. ^cEttouati, L.; Ahond, A.; Convert, O.; Poupat, C.; Potier, P. *Bull. Soc. Chim. Fr.* **1989**, *5*, 687–694. ^dZhang, H.; Takeda, Y.; Minami, Y.; Yoshida, K.; Matsumoto, T.; Xiang, W.; Mu, O.; Sun, H. *Chem. Lett.* **1994**, 957–960. ^eTopcu, G.; Sultana, N.; Akhtar, F.; Habib-ur-Rehman; Hussain, T.; Choudhary, M. I.; Atta-ur-Rahman. *Nat. Prod. Lett.* **1994**, *4*, 93–100. ^fMa, W.; Stahlhut, R. W.; Adams, T. L.; Park, G. L.; Evans, W. A.; Blumenthal, S. G.; Gomez, G. A.; Nieder, M. H.; Hylands, P. J. *J. Nat. Prod.* **1994**, *57*, 1320–1324. ^gGabetta, B.; Peterlongo, F.; Zini, G.; Barboni, L.; Rafaiiani, G.; Ranzuglia, P.; Torregiani, E.; Appendino, G.; Cravotto, G. *Phytochemistry* **1995**, *40*, 1825–1828. ^hFedoreyev, S. A.; Vasilevskaya, N. A.; Veselova, M. V.; Denisenko, V. A.; Dmitrenok, P. S.; Ozhigova, I. T.; Muzaeok, T. I.; Zhuravlev, Y. N. *Fitoterapia* **1998**, *69*, 430–432. ⁱShi, Q.-W.; Oritani, T.; Kiyota, H. *Nat. Prod. Lett.* **1998**, *12*, 85–90. ^jSugiyama, T.; Oritani, T.; Oritani, T. *Biosci., Biotechnol., Biochem.* **1994**, *58*, 1923–1924. ^kYang, S.-J.; Fang, J.-M.; Cheng, Y.-S. *Phytochemistry* **1996**, *43*, 839–842. ^lYeh, M. K.; Wang, J. S.; Yang, W. L.; Chen, F. C. *Proc. Natl. Sci. Counc. Repub. China, Part A: Phys. Sci. Eng.* **1988**, *12*, 89–90. ^mHo, T.-I.; Lin, Y.-C.; Lee, G.-H.; Peng, S.-M.; Yeh, M.-K.; Chen, F.-C. *Acta Crystallogr. Sect. C.* **1987**, *43*, 1380–1382. ⁿEttouati, L.; Ahond, A.; Convert, O.; Laurent, D.; Poupat, C.; Potier, P. *Bull. Soc. Chim. Fr.* **1988**, 749.

Table 6. Taxoids with a C-12(16)–Oxido Bridge and a C-4(20) Double Bond



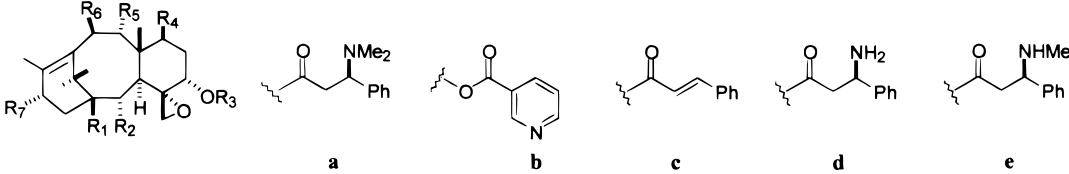
name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	[α] _D	mp (°C)	plant source	plant part; % yield	refs
2α-deacetyl-5α-decinnamoyltaxagifine	C ₂₆ H ₃₆ O ₁₁	524	H	H	H	Ac	H	+54.5° (CHCl ₃)	206–207	<i>T. chinensis</i>	lv, st; 3.5 × 10 ⁻⁴	a, b
5α-decinnamoyltaxagifine	C ₂₈ H ₃₈ O ₁₂	566	Ac	H	H	Ac	H	+4.6° (MeOH)	118–120	<i>T. chinensis</i>	lv, st; 1.7 × 10 ⁻³	c
5α-acetyl-5α-decinnamoyltaxagifine	C ₃₀ H ₄₀ O ₁₃	608	Ac	Ac	H	Ac	H	-7° (CHCl ₃)	261–263	<i>T. chinensis</i>	lv, st; 3.5 × 10 ⁻⁴	c
5-decinnamoyl-11-acetyl-19-hydroxytaxagifine	C ₃₀ H ₄₀ O ₁₄	624	Ac	H	OH	Ac	Ac	-12.1° (MeOH)	209–210	<i>T. yunnanensis</i>	bk	d
19-debenzoyl-19-acetyltaxinine M	C ₃₀ H ₄₀ O ₁₄	624	Ac	H	OAc	Ac	H	+2.8° (CHCl ₃)		<i>T. wallichiana</i>	lv	e
taxinine M	C ₃₅ H ₄₂ O ₁₄	686	Ac	H	OBz	Ac	H	-24° (MeOH)		<i>T. brevifolia</i>	bk	f
taxagifine	C ₃₇ H ₄₄ O ₁₃	696	Ac	a	H	Ac	H	-5.4° (CHCl ₃)	265–267	<i>T. cuspidata</i>	sd; 3.8 × 10 ⁻³	g
								+14.3° (MeOH)	265–267	<i>T. chinensis</i>	lv, st; 2.5 × 10 ⁻³	c
								+7.5° (MeOH)	265–267	<i>T. baccata</i>	lv; 5.0 × 10 ⁻³	h, i
taxuspine S	C ₃₇ H ₄₄ O ₁₄	712	Ac	a	OH	Ac	H	-4.4° (CHCl ₃)		<i>T. cuspidata</i>	st; 2.1 × 10 ⁻⁴	j
taxuspine T	C ₃₇ H ₄₄ O ₁₄	712	Ac	a	OAc	H	H	-13.4° (CHCl ₃)		<i>T. cuspidata</i>	st; 1.9 × 10 ⁻⁴	j
19-acetoxytaxagifine (taxezopidine L)	C ₃₉ H ₄₆ O ₁₅	754	Ac	a	OAc	Ac	H	-2.4° (MeOH)	106–108	<i>T. chinensis</i>	bk, tw, lv; 9.0 × 10 ⁻⁵	k
								+94° (CHCl ₃)		<i>T. cuspidata</i>	sd	l
taxacin	C ₄₄ H ₄₈ O ₁₅	816	Ac	a	OBz	Ac	H	-4.8° (CHCl ₃)	285–287	<i>T. cuspidata</i>	sd; 5.8 × 10 ⁻³	g

^aZhang, Z.; Jia, Z. *Phytochemistry* **1991**, *30*, 2345–2348. ^bZhang, Z. P.; Jia, Z. *J. Chin. Chem. Lett.* **1990**, *1*, 91–92. ^cZhang, Z.; Jia, Z.; Zhu, Z.; Cui, Y.; Cheng, J.; Wang, Q. *Planta Med.* **1990**, *56*, 293–294. ^dChen, W. M.; Zhang, P. L.; Zhou, J. Y. *Yaoxue Xuebao* **1994**, *29*, 207–214. ^eBarboni, L.; Gariboldi, P.; Torregiani, E.; Appendino, G.; Varese, M.; Gabetta, B.; Bombardelli, E. *J. Nat. Prod.* **1995**, *58*, 934–939. ^fBeutler, J. A.; Chmurny, G. M.; Look, S. A.; Witherup, K. M. *J. Nat. Prod.* **1991**, *54*, 893–897. ^gYoshizaki, F.; Fuduka, M.; Hisamichi, S.; Ishida, T.; In, Y. *Chem. Pharm. Bull.* **1988**, *36*, 2098–2102. ^hChauviere, G.; Guenard, D.; Pascard, C.; Picot, F.; Potier, P.; Prange, T. *J. Chem. Soc., Chem. Commun.* **1982**, 495. ⁱChauviere, G.; Guenard, D.; Picot, F.; Senilh, V.; Potier, P. *Acad. Sci. Paris, Ser. II* **1981**, *293*, 501–503. ^jWang, X.-X.; Shigemori, H.; Kobayashi, J. *Tetrahedron* **1996**, *52*, 12159–12164. ^kFukushima, M.; Takeda, J.; Fukamiya, N.; Okano, M.; Tagahara, K.; Zhang, S.-X.; Zhang, D.-C.; Lee, K.-H. *J. Nat. Prod.* **1999**, *62*, 140–142. ^lShigemori, H.; Sakurai, C. A.; Hosoyama, H.; Kobayashi, A.; Kajiyama, S.; Kobayashi, J. *Tetrahedron* **1999**, *55*, 2553–2558.

These taxoids may be formed from an initial verticillyl cation which does not undergo the proton shift needed to generate the normal taxane ring system, but instead is quenched at the bicyclic stage. An alternate possibility is that they arise by the pathway of Scheme 1, since it is unlikely that the enzymes responsible for hydroxylating the tricyclic taxoid skeleton would show a similar specificity for bicyclic taxoids. This consideration thus suggests that formation of the bicyclic skeleton occurs after hydroxylation, as indicated in Scheme 1.³⁴

Canadensene and its 5-epi derivative, novel *Taxus* metabolites with a pre-taxane structure in which rings B, C, and D are not yet formed, have been isolated from the leaves of *T. canadensis*.³⁵ Their structural similarity with the taxol skeleton makes these compounds intriguing possible intermediates for the biosynthesis of taxol.

Taxoids with a C-3(11) Bridge and a C-4(20) Double Bond (Table 15). It is not known whether 5-*O*-cinnamoyl-9-*O*-acetylphototaxacin I, which has been isolated in trace amounts from *T. baccata*, is a natural product or an artifact

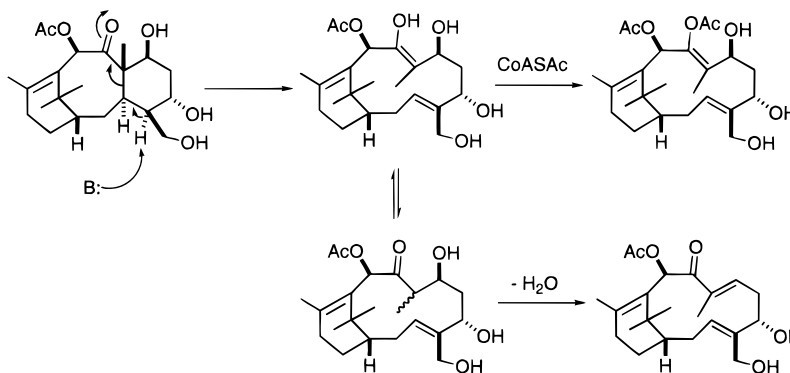
Table 7. Taxoids with a C-4(20) Epoxide


name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	[α] _D	mp (°C)	plant source	plant part; % yield	refs
2α,5α,9α-trihydroxy-10β,13α-diacetoxy-4β,20-epoxy-taxa-11-ene	C ₂₄ H ₃₆ O ₈	452	H	OH	H	H	OH	OAc	OAc		216–218	<i>T. chinensis</i>	lv	a, b
7β,9α,10β-tri-deacetyl-1β-hydroxybaccatin I, taxumairol C	C ₂₆ H ₃₈ O ₁₁	526	OH	OAc	Ac	OH	OH	OH	OAc	+78° (CHCl ₃)		<i>T. mairei</i>	rt	c
1-hydroxy-2,7,9-trideacetyl-baccatin I	C ₂₆ H ₃₈ O ₁₁	526	OH	OH	Ac	OH	OH	OAc	OAc	–52.9° (MeOH)	232–235	<i>T. yunnanensis</i>	bk	d
nicotaxine	C ₃₀ H ₃₇ NO ₉	555	H	OAc	H	H	b	OAc	=O	+112° (CHCl ₃)		<i>A. spicata</i>	bk; 6.3 × 10 ^{–5}	e
1β-hydroxy-7,9-deacetyl-baccatin I (2α,5α,10β,13α-tetraacetoxy-1β,7β,9α-trihydroxy-4β,20-epoxytax-11-ene), taxumairol B	C ₂₈ H ₄₀ O ₁₂	568	OH	OAc	Ac	OH	OH	OAc	OAc	+65.84° (CHCl ₃)		<i>T. canadensis</i>	4.0 × 10 ^{–3}	f
										+15° (MeOH)		<i>T. mairei</i>	rt	g
10β-deacetylspicatine	C ₃₃ H ₄₂ O ₉	582	H	OAc	c	H	OH	OH	OAc	+66° (CHCl ₃)		<i>A. spicata</i>	bk; 7.8 × 10 ^{–5}	e
5α-deacetyl-baccatin I	C ₃₀ H ₄₂ O ₁₂	594	H	OAc	H	OAc	OAc	OAc	OAc		256–258	<i>T. baccata</i>		h
1β,7β-dihydroxy-4β,20-epoxy-2α,5α,9α,10β,13α-penta-acetoxytax-11-ene	C ₃₀ H ₄₂ O ₁₃	610	OH	OAc	Ac	OH	OAc	OAc	OAc			<i>T. brevifolia</i>	bk	i
1β,9α-dihydroxy-4β,20-epoxy-2α,5α,7β,10β,13α-penta-acetoxytax-11-ene	C ₃₀ H ₄₂ O ₁₃	610	OH	OAc	Ac	OAc	OH	OAc	OAc			<i>T. brevifolia</i>	bk	i
1β-hydroxy-7β-deacetoxy-7α-hydroxybaccatin I	C ₃₀ H ₄₂ O ₁₃	610	OH	OAc	Ac	α-OH	OAc	OAc	OAc	+74° (CHCl ₃)	217–218	<i>T. baccata</i>	bk; 2.4 × 10 ^{–3}	j
1β-hydroxy-5α-deacetyl-baccatin I (taxuspine V)	C ₃₀ H ₄₂ O ₁₃	610	OH	OAc	H	OAc	OAc	OAc	OAc	+138.7° (CHCl ₃)	273–275	<i>T. yunnanensis</i>	lv, st; 4.3 × 10 ^{–4}	k
										+56° (CHCl ₃)	230–232	<i>T. cuspidata</i>	st	l
1β-hydroxy-10-deacetyl-baccatin I (10β-deacetyl-1β-hydroxy-baccatin I), taxumairol D	C ₃₀ H ₄₂ O ₁₃	610	OH	OAc	Ac	OAc	OAc	OH	OAc	+75° (CHCl ₃)		<i>T. yunnanensis</i>	rt	m
taxumairol F	C ₃₀ H ₄₂ O ₁₃	610	OH	OAc	Ac	OAc	OAc	OAc	OH	+13° (CHCl ₃)		<i>T. mairei</i>	rt	n
9α-acetyl-10β-deacetyl-spicateine	C ₃₅ H ₄₄ O ₁₀	624	H	OAc	c	H	OAc	OH	OAc	+17° (CHCl ₃)		<i>A. spicata</i>	bk; 4.7 × 10 ^{–5}	e
spicateine	C ₃₅ H ₄₄ O ₁₀	624	H	OAc	c	H	OH	OAc	OAc	+45° (CHCl ₃)		<i>A. spicata</i>	bk; 3.9 × 10 ^{–4}	e
baccatin I	C ₃₂ H ₄₄ O ₁₃	636	H	OAc	Ac	OAc	OAc	OAc	OAc	+86°	298	<i>T. baccata</i>		h
1β-hydroxybaccatin I	C ₃₀ H ₄₄ O ₁₄	652	OH	OAc	Ac	OAc	OAc	OAc	OAc	+102°	273	<i>T. baccata</i>		h
											257–262	<i>T. wallichiana</i>	lv, st, rt; 7.8 × 10 ^{–4}	o
												<i>T. mairei</i>	hw; 4.8 × 10 ^{–5}	p
1β-acetoxy-5α-deacetyl-baccatin I spicataxine	C ₃₂ H ₄₄ O ₁₄	652	OAc	OAc	H	OAc	OAc	OAc	OAc		240–241	<i>T. mairei</i>	bk; 5.0 × 10 ^{–3}	q
	C ₃₇ H ₅₁ NO ₁₀	669	H	OAc	a	H	OH	OAc	OAc	+67° (CHCl ₃)		<i>A. spicata</i>	bk; 1.4 × 10 ^{–3}	e
9α-acetyl-10β-deacetyl-spicataxine	C ₃₇ H ₅₁ NO ₁₀	669	H	OAc	a	H	OAc	OH	OAc	+43° (CHCl ₃)		<i>A. spicata</i>	bk; 5.8 × 10 ^{–4}	e
5α-O-(3'-amino-3'-phenylpropionyl)nicotaxine	C ₃₉ H ₄₆ N ₂ O ₁₀	702	H	OAc	d	H	b	OAc	=O	+93° (CHCl ₃)		<i>A. spicata</i>	bk; 1.2 × 10 ^{–4}	e
5α-O-(3'-methylamino-3'-phenylpropionyl)nicotaxine	C ₄₀ H ₄₈ N ₂ O ₁₀	716	H	OAc	e	H	b	OAc	=O	+103° (CHCl ₃)		<i>A. spicata</i>	bk; 1.9 × 10 ^{–4}	e
N-demethylnicaustrine	C ₄₂ H ₅₂ N ₂ O ₁₁	760	H	OAc	e	H	b	OAc	OAc	+93° (CHCl ₃)		<i>A. spicata</i>	bk; 1.1 × 10 ^{–4}	e
7β-acetoxy-9-acetylspicataxine	C ₄₁ H ₅₅ NO ₁₃	769	H	OAc	a	OAc	OAc	OAc	OAc	+56° (CHCl ₃)	212–213	<i>T. media</i>	rt	r
nicaustrine	C ₄₃ H ₅₄ N ₂ O ₁₁	774	H	OAc	a	H	b	OAc	OAc	+67° (CHCl ₃)		<i>A. spicata</i>	bk; 3.0 × 10 ^{–4}	e

Table 7. (Continued)

^aZhang, Z. P.; Wiedenfeld, H.; Roder, E. *Phytochemistry* **1995**, *38*, 667–670. ^bWiedenfeld, H.; Knoch, F.; Zhang, Z. P. *Acta Crystallogr. Sect. C: Cryst. Struct. Commun.* **1995**, *C51*, 2184–2186. ^cShen, Y.-C.; Chen, C.-Y. *Phytochemistry* **1997**, *44*, 1527–1533. ^dChen, W. M.; Zhang, P. L.; Zhou, J. Y. *Yaouxue Xuebao* **1994**, *29*, 207–214. ^eEttouati, L.; Ahond, A.; Convert, O.; Poupat, C.; Potier, P. *Bull. Soc. Chim. Fr.* **1989**, *5*, 687–694. ^fZamir, L. O.; Nedeia, M. E.; Zhou, Z.-H.; Belair, S.; Caron, G.; Sauriol, F.; Jacomain, E.; Jean, F. I.; Garneau, F.-X.; Mamer, O. *Can. J. Chem.* **1995**, *73*, 655–665. ^gShen, Y.-C.; Tai, H.-R.; Chen, C.-Y. *J. Nat. Prod.* **1996**, *59*, 173–176. ^hDella Casa de Marcano, D. P.; Halsall, T. G. *J. Chem. Soc. D* **1970**, 1381–1382. ⁱChu, A.; Davin, L. B.; Zajicek, J.; Lewis, N. G.; Croteau, R. *Phytochemistry* **1993**, *34*, 473–476. ^jSenilh, V.; Blechert, S.; Colin, M.; Guenard, D.; Picot, F.; Potier, P.; Varenne, P. *J. Nat. Prod.* **1984**, *47*, 131–137. ^kZhang, Z.; Jia, Z. *Phytochemistry* **1990**, *29*, 3673–3675. ^lHosoyama, H.; Inubushi, A.; Katsui, T.; Shigemori, H.; Kobayashi, J. *Tetrahedron* **1996**, *52*, 13145–13150. ^mZhang, H.; Mu, Q.; Xiang, W.; Yao, P.; Sun, H.; Yoshio, T. *Phytochemistry* **1997**, *44*, 911–915. ⁿShen, Y.-C.; Chen, C.-Y. *Planta Med.* **1997**, *63*, 569–570. ^oMiller, R. W.; Powell, R. G.; Smith, C. R., Jr.; Arnold, E.; Clardy, J. *J. Org. Chem.* **1981**, *46*, 1469–1474. ^pYeh, M.-K.; Wang, J.-S.; Lui, L.-P.; Chen, F.-C. *J. Chin. Biochem. Soc.* **1988**, *35*, 304–313. ^qLian, J.-Y.; Min, Z.-D.; Mizuno, M.; Tanaka, T.; Iinuma, M. *Phytochemistry* **1988**, *27*, 3674–3675. ^rAppendino, G.; Cravotto, G.; Enriu, R.; Gariboldi, P.; Barboni, L.; Torregiani, E.; Gabetta, B.; Zini, G.; Bombardelli, E. *J. Nat. Prod.* **1994**, *57*, 607–613.

Scheme 1. Proposed Biosynthetic Pathway for Bicyclic Taxoids



formed from the corresponding alkaloidal taxane by loss of dimethylamine during the repeated chromatographic separations required for its separation.³⁶ The same comments could also apply to the other cinnamoyl derivatives in Table 15.

2-(3→20)-abeo-Taxoids (Table 16). Taxoids of this class are presumably formed from a different transannular cyclization of an intermediate verticilladiene than that involved in normal taxoid biosynthesis.³⁷ The alkaloid taxine A, a component of the original “taxine”, is a member of this class.

Miscellaneous Taxoids (Table 17). A variety of taxoids which do not fit any simple structural grouping are incorporated into Table 17. 13-Deacetoxy-13,15-epoxy-11(15→1)-abeo-13-epi-baccatin VI is reported to be anancomeric (conformationally fixed) and is the first natural taxoid with a β -oxygenated function at C-13.³⁸ A proposal for the biogenetic pathway of taxuchin is given in the original paper.³⁹ Taxuspine D has a taxol-like biological activity,⁴⁰ and a compound with the wallifoliol skeleton was obtained from the rearrangement of a 9,10-dioxotaxane.⁴¹

Biotransformations of Taxoids

A number of investigations have been carried out on the biotransformation of taxol and related taxoids, with a view either to increasing the availability of precursors to taxol or of preparing metabolites that would be inaccessible by simple chemical transformations. In the former class are studies of the site-specific enzymatic hydrolysis of taxanes. Thus two different strains of *Nocardioides* produced specific 13-deacylase and 10-deacetylase enzymes which could be used to convert various taxoid precursors to 10-deacetyl-baccatin III or related compounds;⁴² the problem of the removal of the 7 β -xylosyl group in some precursors was solved by the isolation of a xylosidase from *Moraxella* sp.⁴³ This work has been reviewed.⁴⁴

Several workers have investigated nonmammalian biotransformations of taxol and related compounds. Taxol

itself is metabolized in the presence of *Eucalyptus perriniana* cells to baccatin III, 10-deacetyl-baccatin III, and 2-debenzoyltaxol.⁴⁵ 10-Deacetyl-7-epitaxol and 1 β -hydroxy-baccatin I are both metabolized by fungi isolated from the inner bark of *T. yunnanensis*, and interestingly 10-deacetyl-7-epitaxol is converted in part into 10-deacetyl-taxol.⁴⁶ The conversion of taxol into 10-epitaxol can occur readily under certain conditions,⁴⁷ so the fact that this reaction can be reversed under biological conditions is interesting and potentially useful. Another fungus isolated from *T. yunnanensis* carried out a simple deacetylation of taxa-4(20),11-diene-2 α ,5 α ,10 β ,14 β -tetrol tetracetate (sinenxan H) to its corresponding 5,10-deacetyl derivative.⁴⁸

Perhaps more interesting are the various oxidative transformations that have been observed on certain taxoids, since these can give some hints as to the biosynthetic oxidations that must also occur. Thus, the taxadiene **19** was metabolized by *Absidia coerulea* and other fungi into the three metabolites **20–22**,⁴⁹ while two different 14 β -hydroxytaxadienes were hydroxylated by *Cunninghamella echinulata*.⁵⁰ These conversions thus indicate that microbial metabolism is a viable route to the preparation of new taxoids.

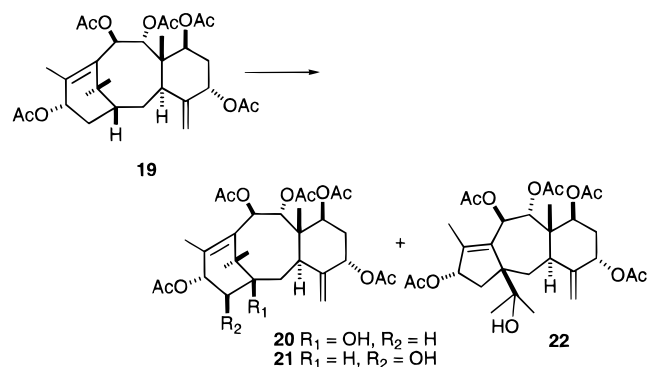
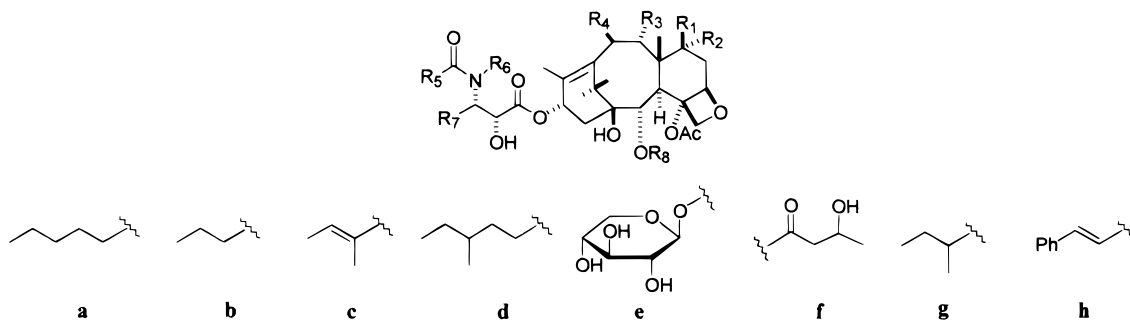


Table 8. (Continued)

name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	R ₈	R ₉	[α] _D	mp (°C)	plant source	plant part; % yield	refs
9-dihydro,13-acetyl-baccatin III	C ₃₃ H ₄₂ O ₁₂	630	OH	OBz	OAc	OH	OH	OAc	OAc	H	H		221	<i>T. canadensis</i>	lv	w
10-(β-hydroxybutyryl)-10-deacetyl-baccatin I	C ₃₃ H ₄₂ O ₁₂	630	OH	OBz	OAc	OH	=O	d	OH	H	H			<i>T. baccata</i>	lv	x
7,9-deacetyl-baccatin VI	C ₃₃ H ₄₃ O ₁₂	631	OH	OBz	OAc	OH	OH	OAc	OAc	H	H			<i>T. canadensis</i>	lv, st; 1.4 × 10 ⁻²	n
1β-dehydroxybaccatin IV	C ₃₂ H ₄₄ O ₁₃	636	H	OAc	OAc	OAc	OAc	OAc	OAc	H	H	+5° +99° (CHCl ₃)	286 259–260	<i>T. mairei</i>	hw; 2.2 × 10 ⁻²	y z
baccatin IV	C ₃₂ H ₄₄ O ₁₄	652	OH	OAc	OAc	OAc	OAc	OAc	OAc	H	H	+19°	254–255			y
9-deacetyl-baccatin VI	C ₃₅ H ₄₄ O ₁₃	672	OH	OBz	OAc	OAc	OH	OAc	OAc	H	H			<i>T. yunnanensis</i>	rt	aa
10-deacetyl-baccatin VI	C ₃₅ H ₄₄ O ₁₃	672	OH	OBz	OAc	OAc	OAc	OH	OAc	H	H			<i>T. yunnanensis</i>	rt	aa
13-deacetyl-baccatin VI	C ₃₅ H ₄₄ O ₁₃	672	OH	OBz	OAc	OAc	OAc	OH	H	H	H	-38° (MeOH)	225–226	<i>T. wallichiana</i>	lv; 2.1 × 10 ⁻²	bb
7-xylosyl-10-deacetyl-baccatin III	C ₃₄ H ₄₄ O ₁₄	676	OH	OBz	OAc	g	=O	OH	OH	H	H	-26.9° (MeOH)	244–246	<i>T. yunnanensis</i>	bk	cc
1β-dehydroxybaccatin VI	C ₃₇ H ₄₆ O ₁₃	698	H	OBz	OAc	OAc	OAc	OAc	OAc	H	H	-21.2° (CHCl ₃)	220–221	<i>T. mairei</i>	hw; 1.6 × 10 ⁻²	z
baccatin VII	C ₃₆ H ₅₂ O ₁₄	708	OH	h	OAc	OAc	OAc	OAc	OAc	H	H	+9°	270			y
baccatin VI	C ₃₇ H ₄₆ O ₁₄	714	OH	OBz	OAc	OAc	OAc	OAc	OAc	H	H	-5° (CHCl ₃)	248–250	<i>T. baccata</i>	bk; 4.0 × 10 ⁻⁴	k
												-5° (CHCl ₃)	244–245			y
												-9° (CHCl ₃)	239–241	<i>T. mairei</i>	hw; 3.2 × 10 ⁻³	z
deaminoacylcinnamoyltaxol, taxuspinanane J (baccatin III-13-cinnamate)	C ₄₀ H ₄₄ O ₁₂	716	OH	OBz	OAc	OH	=O	OAc	e	H	H	-43.8° (CHCl ₃)		<i>T. cuspidata</i>	st;	dd
												-75.7° (CHCl ₃)		<i>T. mairei</i>	tw	ee
10-hydroxyacetyl-baccatin VI	C ₃₇ H ₄₆ O ₁₅	730	OH	OBz	OAc	OAc	OAc	b	OAc	H	H			<i>T. canadensis</i>		i
13(2',3'-dihydroxy-3'-phenyl)-propionyl-baccatin III, yunnanxol	C ₄₀ H ₄₆ O ₁₄	750	OH	OBz	OAc	OH	=O	OAc	a	H	H	-75.2° (CHCl ₃)	154–157	<i>T. yunnanensis</i>	bk	ff
2α,7β-dibenzoxy-5β,20-epoxy-1β-hydroxy-4α,9α,10β,13α-tetraacetoxytax-11-ene	C ₄₂ H ₄₈ O ₁₄	776	OH	OBz	OAc	OBz	OAc	OAc	OAc	H	H			<i>T. brevifolia</i>	bk	gg
2α,10β-dibenzoxy-5β,20-epoxy-1β-hydroxy-4α,7β,9α,13α-tetraacetoxytax-11-ene	C ₄₂ H ₄₈ O ₁₄	776	OH	OBz	OAc	OAc	OAc	OBz	OAc	H	H			<i>T. brevifolia</i>	bk	gg
5β,20-epoxy-1β-hydroxy-4α,7β,13α-triacetoxy-2α,9α,10β-tribenzoxytax-11-ene	C ₄₇ H ₅₀ O ₁₄	838	OH	OBz	OAc	OAc	OBz	OBz	OAc	H	H			<i>T. brevifolia</i>	bk	gg
taxuspine N	C ₄₆ H ₅₇ NO ₁₄	847	OH	OAc	OAc	OAc	OAc	OBz	f	H	H	-6.0° (CHCl ₃)		<i>T. cuspidata</i>	st; 7.3 × 10 ⁻⁴	hh

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Table 9. Taxoids with an Oxetane Ring and a Phenylisoserine C-13 Side Chain

name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	R ₈	[α] _D	mp (°C)	plant source	plant part; % yield	refs
<i>N</i> -debenzoyl- <i>N</i> -propanoyl-10-deacetylpaclitaxel	C ₄₁ H ₄₉ NO ₁₃	763	OH	H	=O	OH	Et	H	Ph	Bz		245	<i>T. baccata</i>		<i>a</i>
<i>N</i> -debenzoyl- <i>N</i> -butanoyl-10-deacetylpaclitaxel	C ₄₂ H ₅₁ NO ₁₃	777	OH	H	=O	OH	b	H	Ph	Bz		244	<i>T. baccata</i>		<i>a</i>
10-deacetylcephalomannine	C ₄₃ H ₅₁ NO ₁₃	789	OH	H	=O	OH	c	H	Ph	Bz			<i>T. wallichiana</i>	rt, st, lv; 3.8 × 10 ⁻³	<i>b</i>
(10-deacetyltaxol B)											-2° (pyridine)		<i>T. baccata</i>	bk; 3.4 × 10 ⁻³	<i>c</i>
10-deacetyl-10-oxo-7-epitaxuyunnaninane A	C ₄₄ H ₅₃ NO ₁₃	803	H	OH	=O	=O	a	H	Ph	Bz	-70.8° (CHCl ₃)		<i>T. yunnanensis</i>	rt	<i>d</i>
10-deacetyltaxuyunnaninane A	C ₄₄ H ₅₅ NO ₁₃	805	OH	H	=O	OH	a	H	Ph	Bz	-50.9° (CHCl ₃)		<i>T. yunnanensis</i>	rt	<i>d</i>
7-epi-10-deacetyltaxol, taxuspinanane E (7-epi-10-deacetyl-taxuyunnaninane A)	C ₄₄ H ₅₅ NO ₁₃	805	H	OH	=O	OH	a	H	Ph	Bz	-22.9° (MeOH)		<i>T. cuspidata</i>	st	<i>e</i>
10-deacetyl-10-oxo-7-epitaxol	C ₄₅ H ₄₇ NO ₁₃	809	H	OH	=O	=O	Ph	H	Ph	Bz	-34.9° (CHCl ₃)		<i>T. yunnanensis</i>	rt	<i>d</i>
10-deacetyltaxol	C ₄₅ H ₄₉ NO ₁₃	811	OH	H	=O	OH	Ph	H	Ph	Bz	-60.4° (MeOH)		<i>T. brevifolia</i>	bk; 1.2 × 10 ⁻³	<i>f</i>
													<i>T. wallichiana</i>	rt, st, lv; 2.1 × 10 ⁻³	<i>b</i>
											-3° (pyridine)		<i>T. baccata</i>	bk; 2.9 × 10 ⁻³	<i>c</i>
taxcultine	C ₄₄ H ₅₃ NO ₁₄	819	OH	H	=O	OAc	b	H	Ph	Bz	-7.54° (MeOH)	155	<i>T. baccata</i>	cc	<i>g</i>
(<i>N</i> -debenzoyl- <i>N</i> -butanoyl-taxol; taxol D)											-16° (CHCl ₃)	206–208	<i>T. x media</i>	rt	<i>h</i>
cephalomannine	C ₄₅ H ₅₃ NO ₁₄	831	OH	H	=O	OAc	c	H	Ph	Bz	-41° (MeOH)	181–184	<i>T. baccata</i>	bk; 6.4 × 10 ⁻³	<i>c</i>
(taxol B)											-41° (MeOH)	184–186	<i>T. wallichiana</i>	lv, st, rt; 1.6 × 10 ⁻³	<i>i, j</i>
												180–183	<i>T. baccata</i>	bk; 3.0 × 10 ⁻⁵	<i>k</i>
2-debenzoyl-2-tigloyltaxol (isocephalomannine)	C ₄₅ H ₅₃ NO ₁₄	831	OH	H	=O	OAc	Ph	H	Ph	c	-44° (MeOH)	232	<i>T. x media</i>	rt	<i>l</i>
7-epicephalomannine	C ₄₅ H ₅₃ NO ₁₄	831	H	OH	=O	OAc	c	H	Ph	Bz	-7.32° (MeOH)	210	<i>T. x media</i>	lv	<i>m</i>
<i>N</i> -debenzoyl- <i>N</i> -(2-methylbutyryl)taxol	C ₄₅ H ₅₅ NO ₁₄	833	OH	H	=O	OAc	g	H	Ph	Bz	-48° (MeOH)	226	<i>T. x media</i>	rt; 1.4 × 10 ⁻⁵	<i>l</i>
taxuyunnaninane	C ₄₆ H ₅₇ NO ₁₄	847	OH	H	=O	OAc	a	H	Ph	Bz	-45.4° (MeOH)		<i>T. yunnanensis</i>	rt	<i>n</i>
<i>N</i> -debenzoyl- <i>N</i> -hexanoyl-taxol, taxol C											-64.7° (CHCl ₃)	204–205	<i>T. x media</i>	rt	<i>o</i>
7-epitaxuyunnaninane A	C ₄₆ H ₅₇ NO ₁₄	847	H	OH	=O	OAc	a	H	Ph	Bz	-47.3° (CHCl ₃)		<i>T. yunnanensis</i>	rt	<i>d</i>
10-deacetyl-10-dehydro-7-acetyltaxol A	C ₄₇ H ₄₉ NO ₁₄	851	OAc	H	=O	=O	Ph	H	Ph	Bz	-57° (MeOH)	226–230	<i>T. x media</i>	rt; 1.5 × 10 ⁻³	<i>p</i>
taxol (paclitaxel)	C ₄₇ H ₅₁ NO ₁₄	853	OH	H	=O	OAc	Ph	H	Ph	Bz	-49° (MeOH)	213–216	<i>T. brevifolia</i>	bk; 2.0 × 10 ⁻²	<i>q</i>
											-54° (MeOH)	194–197	<i>T. brevifolia</i>	bk; 2.9 × 10 ⁻⁴	<i>r</i>
											-42° (MeOH)	198–203	<i>T. wallichiana</i>	st, rt	<i>j</i>
											-42° (MeOH)	198–203	<i>T. wallichiana</i>	lv, st, rt; 1.1 × 10 ⁻³	<i>i</i>
											-54° (MeOH)	205–208	<i>T. baccata</i>	bk; 1.6 × 10 ⁻²	<i>c</i>
											-21° (pyridine)				
7-epitaxol	C ₄₇ H ₅₁ NO ₁₄	853	H	OH	=O	OAc	Ph	H	Ph	Bz	-32.3° (MeOH)	168–171	<i>T. brevifolia</i>	bk	<i>f</i>
9-deoxo-9α-hydroxytaxol	C ₄₇ H ₅₃ NO ₁₄	855	OH	H	OH	OAc	Ph	H	Ph	Bz	-13.1° (CHCl ₃)	174–176	<i>T. yunnanensis</i>	bk	<i>s</i>

Table 9. (Continued)

name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	R ₈	[α] _D	mp (°C)	plant source	plant part; % yield	refs
<i>N</i> -methyltaxol C	C ₄₇ H ₅₉ NO ₁₄	861	OH	H	=O	OAc	a	Me	Ph	Bz	-52.7° (CHCl ₃) -16.52° (MeOH)	225–228 134	<i>T. x media</i> <i>T. baccata</i>	rt cc	<i>o</i> <i>g</i>
taxuspinanane A	C ₄₇ H ₅₉ NO ₁₄	861	OH	H	=O	OAc	d	H	Ph	Bz	-40.2° (MeOH)		<i>T. cuspidata</i>	st; 2.0 × 10 ⁻³	<i>t</i>
<i>N</i> -methylpaclitaxel, taxuspinanane I	C ₄₈ H ₅₃ NO ₁₄	867	OH	H	=O	OAc	Ph	Me	Ph	Bz	-71° (CHCl ₃)		<i>T. cuspidata</i>	st;	<i>u</i>
10-(β-hydroxybutyryl)-10-deacetylcephalomannine	C ₄₇ H ₅₇ NO ₁₅	875	OH	H	=O	f	c	H	Ph	Bz			<i>T. baccata</i>	bk; 1.8 × 10 ⁻³	<i>c</i>
<i>N</i> -debenzoyl- <i>N</i> -cinnamoyl-taxol	C ₄₉ H ₅₃ NO ₁₄	879	OH	H	=O	OAc	h	H	Ph	Bz	-16.6° (MeOH)	180	<i>T. x media</i>	rt	<i>l</i>
10-(β-hydroxybutyryl)-10-deacetyltaxol	C ₄₉ H ₅₅ NO ₁₅	897	OH	H	=O	f	Ph	H	Ph	Bz			<i>T. baccata</i>	bk; 2.6 × 10 ⁻³	<i>c</i>
7-(β-xyloxy)-10-deacetyltaxol D	C ₄₇ H ₅₉ NO ₁₇	909	e	H	=O	OH	b	H	Ph	Bz	-14.3° (MeOH)		<i>T. baccata</i>	bk	<i>v</i>
7-(β-xyloxy)-10-deacetyltaxol C	C ₄₉ H ₆₃ NO ₁₇	937	e	H	=O	OH	a	H	Ph	Bz	+3° (pyridine)	215–217	<i>T. baccata</i>	bk; 2.8 × 10 ⁻³	<i>c</i>
7-(β-xyloxy)-10-deacetyltaxol	C ₅₀ H ₅₇ NO ₁₇	943	e	H	=O	OH	Ph	H	Ph	Bz	-2° (pyridine)	246–248	<i>T. baccata</i>	bk; 2.2 × 10 ⁻²	<i>c</i>
7-(β-xyloxy)cephalomannine	C ₅₀ H ₆₁ NO ₁₈	963	e	H	=O	OAc	c	H	Ph	Bz	-26° (pyridine)		<i>T. baccata</i>	bk; 3.9 × 10 ⁻³	<i>c</i>
7-(β-xyloxy)taxol C	C ₅₁ H ₆₅ NO ₁₈	979	e	H	=O	OAc	a	H	Ph	Bz	-4° (pyridine)	229–231	<i>T. baccata</i>	bk; 2.9 × 10 ⁻³	<i>c</i>
7-(β-xyloxy)taxol	C ₅₂ H ₅₉ NO ₁₈	985	e	H	=O	OAc	Ph	H	Ph	Bz	-23° (pyridine)	236–238	<i>T. baccata</i>	bk; 5.8 × 10 ⁻³	<i>c</i>

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Taxol Biosynthesis

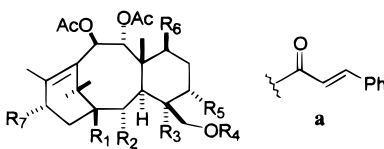
Knowledge of the biosynthesis of taxol has made significant advances over the past few years, driven in part by the desire to increase the yield of taxol production. Taxol production has been observed not only in various *Taxus* species, but also in the endophytic fungi *Taxomyces andreanae*,⁵¹ and in a number of unrelated fungal endophytes including *Fusarium*, *Alternaria*, *Pithomyces*, and others.⁵² In another study *Alternaria alternata* ssp. *Taxus hicksii*, was found to be the preferred source of taxol, with fermentation yielding 116 mg of taxol per liter.⁵³ Plant tissue culture production of taxol is also being investigated by several groups, with yields of up to 55 mg of taxol per liter per week;⁵⁴ the subject has been reviewed recently.⁵⁵ These yields could presumably be significantly enhanced by genetic engineering based on a knowledge of the biosynthetic pathway of taxol and on the key enzymes involved in it.

The first studies of the biosynthesis of taxol were carried out by feeding studies using labeled acetate, mevalonate, and phenylalanine with *T. canadensis*⁵⁶ although the incorporations were low, ranging from 0.02 to 0.12%. The best incorporation of mevalonate was found with new growth *T. canadensis* leaves. Incorporation of taxol formed

from [³H]-L-phenylalanine and [¹⁴C]mevalonate gave a product with a ³H/¹⁴C ratio of 4.4, which was reduced to 1.75 by removal of the side chain. This indicated that the phenylalanine was incorporated into both the side chain and also into the 2-benzoate group.

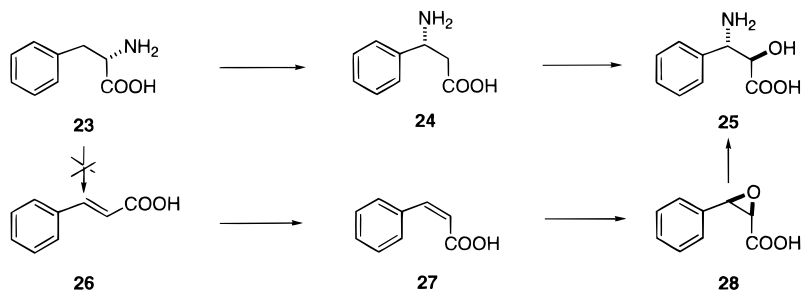
More specific information on the biosynthesis of the taxol side chain came from work by Floss and his collaborators using variously labeled putative side chain precursors.⁵⁷ Benzoic acid was incorporated primarily into the side chain (88% of total label) versus the 2-position (11% of the label). More significantly, ring-deuterated α-phenylalanine, β-phenylalanine, and phenylisoserine were all efficiently incorporated, while neither *trans*-cinnamic acid (**26**) nor its *cis*-isomer (**27**) nor its epoxide (**28**) were incorporated. This result indicates that the rearrangement of α-phenylalanine (**23**) to β-phenylalanine (**24**) cannot proceed via cinnamic acid or its epoxide, and must thus go by an intramolecular rearrangement of α-phenylalanine to β-phenylalanine and thence to phenylisoserine (**25**) (Scheme 2). Interestingly, the intact *N*-benzoyl side chain was not incorporated directly, since a ring perdeuterated precursor (²H₁₀) only gave pentadeuterated taxol.

Further information on the mode of attachment of the side chain to baccatin III came from studies with [10-acetyl-

Table 10. Taxoids with an Opened Oxetane Ring


name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	[α] _D	mp (°C)	plant source	plant part; % yield	refs
5α,7β,9α,10β,13α-pentaacetoxy-2α-20-dihydroxytax-11-ene, taxumairol E	C ₃₀ H ₄₄ O ₁₂	596	H	OH	H	H	OAc	OAc	OAc	+54.9° (CHCl ₃)		<i>T. mairei</i>	rt	<i>a</i>
taxuspine L	C ₃₂ H ₄₆ O ₁₃	638	H	OAc	H	H	OAc	OAc	OAc	+108° (CHCl ₃)		<i>T. cuspidata</i>	st; 1.4 × 10 ⁻⁴	<i>b</i>
taxchin A	C ₃₂ H ₄₆ O ₁₃	638	H	OH	H	Ac	OAc	OAc	OAc		284–286	<i>T. chinensis</i>	3.2 × 10 ⁻⁴	<i>c</i>
taxuspine R	C ₃₂ H ₄₇ O ₁₄	655	OH	OH	H	Ac	OAc	OAc	OAc	+68° (CHCl ₃)		<i>T. cuspidata</i>	st; 2.6 × 10 ⁻⁴	<i>d</i>
5α,7β,9α,10β,13α-pentaacetoxy-2α-benzoyloxy-4α,20-dihydroxytax-11-ene	C ₃₇ H ₄₈ O ₁₄	716	H	OBz	OH	H	OAc	OAc	OAc	-30° (CHCl ₃)	114–115	<i>T. mairei</i>	hw	<i>e</i>
7β,9α,10β,13α,20-pentaacetoxy-2α-benzoyloxy-4α,5α-dihydroxytax-11-ene	C ₃₇ H ₄₈ O ₁₄	716	H	OBz	OH	Ac	OH	OAc	OAc	-37° (CHCl ₃)	122–123	<i>T. mairei</i>	hw	<i>e</i>
5α,7β,9α,10β,13α-pentaacetoxy-20-(benzoyloxy)-2α,4α-dihydroxytax-11-ene, taxumairol A	C ₃₇ H ₄₈ O ₁₄	716	H	OH	OH	Bz	OAc	OAc	OAc	+46° (MeOH)		<i>T. mairei</i>	rt	<i>f</i>
taxchin B	C ₄₁ H ₅₂ O ₁₄	768	H	OAc	H	a	OAc	OAc	OAc	+39.74° (CHCl ₃)	124–126	<i>T. chinensis</i>	st, lv; 8.3 × 10 ⁻⁵	<i>g</i>

^a Shen, Y.-C.; Chen, C.-Y. *Phytochemistry* **1997**, *44*, 1527–1533. ^b Wang, X.-X.; Shigemori, H.; Kobayashi, J. *Tetrahedron* **1996**, *52*, 2337–2342. ^c Li, B.; Tanaka, K.; Fujii, K.; Sun, H.; Taga, T. *Chem. Pharm. Bull.* **1993**, *41*, 1672–1673. ^d Wang, X.-X.; Shigemori, H.; Kobayashi, J. *Tetrahedron* **1996**, *52*, 12159–12164. ^e Liang, J.; Kingston, D. G. I. *J. Nat. Prod.* **1993**, *56*, 594–599. ^f Shen, Y.-C.; Tai, H.-R.; Chen, C.-Y. *J. Nat. Prod.* **1996**, *59*, 173–176. ^g Tanaka, K.; Fujii, K.; Yokoi, T.; Shingu, T.; Li, B.; Sun, H. *Chem. Pharm. Bull.* **1994**, *42*, 1539–1541.

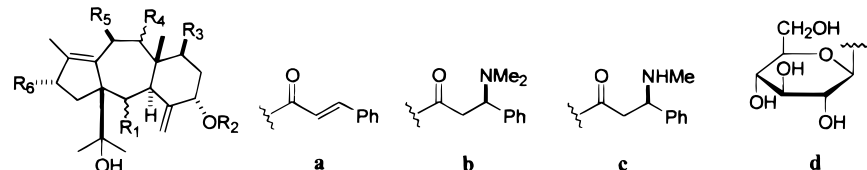
Scheme 2. Biosynthetic Pathway of the Taxoid Phenylisoserine Side Chain

²H₃,13-²H]baccatin III and [13-³H]baccatin III.^{57a} Incorporation of all four deuterium atoms from the first baccatin III indicated that it is not hydrolyzed to 10-deacetyl baccatin III prior to incorporation. An experiment with [benzoyl-¹⁴C]-labeled side chain showed that the *N*-benzoyl group was not significantly hydrolyzed under the conditions of the incorporation. This confirmed that the earlier failure to incorporate intact side chain was not due to its rapid hydrolysis and, thus, that intact side chain is not a precursor to taxol. Indeed, [²H₈]-*N*-debenzoyltaxol was largely incorporated intact into taxol, confirming its intermediacy in the biosynthetic pathway. Although the phenylisoserine side chain was incorporated intact in these experiments, β-phenylalanine was incorporated even more efficiently, and it is thus not clear at this point whether hydroxylation at the 2'-position occurs before or after attachment of the side chain.⁵⁸

The intact incorporation of baccatin III noted above is consistent with results on the cell-free acetylation of 10-deacetyl baccatin III by crude extracts from the roots of *T. baccata* saplings.⁵⁹ Very recently, the enzyme acetyl-coenzyme A:10-hydroxytaxane *O*-acetyltransferase has

been purified and characterized from cell suspensions of *T. chinensis*.⁶⁰

The formation of the tetracyclic diterpenoid moiety of the taxane diterpenoids was surprisingly found *not* to arise from mevalonate, despite the incorporation of [¹⁴C]mevalonate into taxol observed by Zamir et al.⁵⁶ The evidence for the nonmevalonoid nature of the taxoid skeleton came from studies of the incorporation of [U-¹³C₆]glucose and [1,2-¹³C₂]acetate into the taxoid taxayunnanin in *T. chinensis* (Scheme 3).⁶¹ [1,2-¹³C₂]Acetate was incorporated efficiently into the four acetate groups of taxayunnanin C but not into the skeleton itself. Since mevalonic acid is formed from acetate, this lack of incorporation of acetate suggests that mevalonic acid is not a precursor to taxayunnanin C. Definitive proof of this came from the experiment with [U-¹³C₆]glucose, which clearly showed the incorporation of an intact 3-carbon precursor from glucose, ruling out mevalonic acid which is formed from the 2-carbon precursor acetate. The presumed isopentenyl pyrophosphate precursor to the geranylgeranyl diphosphate building block must thus arise by condensation of 2-carbon unit and a 3-carbon unit, as proposed by Rohmer

Table 11. 11(15→1)-*abeo*-Taxoids with a C-4(20) Double Bond


The image shows the general structure of a taxoid core with substituents R₁ through R₆ and OR₂. It also shows four specific substituents labeled a, b, c, and d. Structure a is a cinnamoyl group. Structure b is a 3-(dimethylamino)propyl group. Structure c is a 3-(N-methylamino)propyl group. Structure d is a 2,3,4-trihydroxybutyl group.

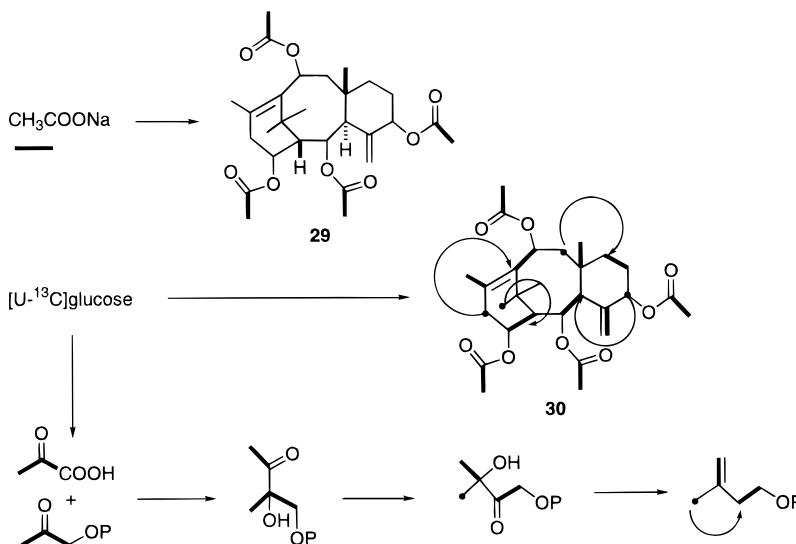
name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	[α] _D	mp (°C)	plant source	plant part: % yield	refs
7-debenzoyloxy-10-deacetylbrevifoliol	C ₂₂ H ₃₄ O ₆	394	H	H	H	α-OAc	OH	OH	−24° (MeOH)	160–162	<i>T. wallichiana</i>	lv	a
taxacustone	C ₂₄ H ₃₄ O ₈	450	β-OAc	H	H	β-OAc	OH	=O	−14.6° (CHCl ₃)	268–271	<i>T. cuspidata</i>	lv, st	b
13-acetyl-2-deacetoxy-10-debenzoyltaxchinin A, taxawallin F	C ₂₆ H ₃₈ O ₉	494	H	H	OAc	α-OAc	OH	OAc		124–125	<i>T. wallichiana</i>	lv	c
10-acetyl-2-deacetoxy-10-debenzoyltaxchinin A, taxawallin H	C ₂₆ H ₃₈ O ₉	494	H	H	OAc	α-OAc	OAc	OH		72–74	<i>T. wallichiana</i>	lv	c
taxuspine O	C ₂₆ H ₃₆ O ₁₀	508	α-OAc	H	OH	α-OAc	OAc	=O	+79.7° (MeOH)		<i>T. cuspidata</i>	st	d
10-debenzoyl-2α-acetoxybrevifoliol	C ₂₆ H ₃₈ O ₁₀	510	α-OAc	H	OAc	α-OAc	OH	OH	+32.6° (MeOH)	180	<i>T. wallichiana</i>	lv	e
9-deacetyl-9-benzoyl-10-debenzoylbrevifoliol	C ₂₉ H ₃₈ O ₈	514	H	H	OAc	α-OBz	OH	OH	+18° (CHCl ₃)	152	<i>T. brevifolia</i>		f
teixidol	C ₂₈ H ₄₀ O ₁₀	536	α-OAc	H	H	α-OAc	OAc	OAc	−15.91° (CHCl ₃)	159	<i>T. baccata</i>	lv	g
taxchinin G	C ₂₈ H ₄₀ O ₁₁	552	α-OAc	H	OAc	α-OAc	OH	OAc		140–143	<i>T. chinensis</i>		h
taxuspine Y	C ₃₁ H ₃₈ O ₉	554	α-OAc	H	H	α-OAc	OBz	=O	−25.4° (CHCl ₃)		<i>T. cuspidata</i>	8.0 × 10 ^{−5} st;	i
9-deacetyl-9-benzoyl-10-debenzoyltaxchinin A	C ₃₁ H ₄₀ O ₁₀	572	α-OAc	H	OAc	α-OBz	OH	OH	+19.4° (MeOH)		<i>T. baccata</i>	2.0 × 10 ^{−4} bk;	j
5,10,13-triacetyl-10-debenzoylbrevifoliol	C ₃₀ H ₄₂ O ₁₁	578	H	Ac	OAc	α-OAc	OAc	OAc	−50° (CHCl ₃)		<i>T. wallichiana</i>	2.3 × 10 ^{−3} lv	k
brevifoliol	C ₃₁ H ₄₀ O ₉	556	H	H	OAc	α-OAc	OBz	OH		200–203	<i>T. brevifolia</i>	lv	l
13-acetylbrevifoliol	C ₃₃ H ₄₂ O ₁₀	598	H	H	OAc	α-OAc	OBz	OAc	+8° (MeOH)		<i>T. wallichiana</i>		a
9-benzoyl-2-deacetoxy-9-deacetyl-10-debenzoyl-10,13-diacetyltaxchinin A, taxawallin D	C ₃₃ H ₄₂ O ₁₀	598	H	H	OAc	α-OBz	OAc	OAc		122–124	<i>T. wallichiana</i>	lv	c
taxuspinanane B	C ₃₃ H ₄₀ O ₁₁	612	α-OAc	H	OAc	α-OAc	OBz	=O	+26.6° (MeOH)		<i>T. cuspidata</i>	3.0 × 10 ^{−3} st;	m
taxchinin A	C ₃₃ H ₄₂ O ₁₁	614	α-OAc	H	OAc	α-OAc	OBz	OH	−34.62° (CH ₂ Cl ₂)	208–210	<i>T. chinensis</i>	4.7 × 10 ^{−3} lv, st;	n
									−34.62° (CH ₂ Cl ₂)	208–210	<i>T. chinensis</i>	lv, st	o
13-acetyl-9-deacetyl-9-benzoyl-10-debenzoyltaxchinin A	C ₃₃ H ₄₂ O ₁₁	614	α-OAc	H	OAc	α-OBz	OH	OAc	+14.9° (CHCl ₃)	121–122	<i>T. chinensis</i>	1.9 × 10 ^{−6} bk; lv;	p
2α-acetoxybrevifoliol	C ₃₃ H ₄₂ O ₁₁	614	α-OAc	H	OAc	α-OAc	OBz	OH	−24° (CHCl ₃)	198	<i>T. baccata</i>	sd	q
taxuspine M	C ₃₅ H ₄₄ O ₁₀	624	H	a	OAc	α-OAc	OH	OAc	+35° (CHCl ₃)		<i>T. cuspidata</i>	1.6 × 10 ^{−4} st;	r
taxchinin D	C ₃₅ H ₄₄ O ₁₂	656	α-OAc	H	OAc	α-OAc	OBz	OAc		138–141	<i>T. chinensis</i>	1.8 × 10 ^{−3} st, lv	h
taxuspine J	C ₃₇ H ₄₆ O ₁₁	666	H	a	OAc	α-OAc	OAc	OAc			<i>T. cuspidata</i>	lv	s
taxamedin A	C ₃₇ H ₄₆ O ₁₁	666	α-OAc	a	H	α-OAc	OAc	OAc			<i>T.x media</i>	lv	t
taxchinin H	C ₄₀ H ₄₆ O ₁₀	686	H	a	OAc	α-OAc	OBz	OH	−65.29° (CHCl ₃)	115–118	<i>T. chinensis</i>	1.1 × 10 ^{−3} st, lv;	u
5-cinnamoylbrevifoliol (13-deacetyltaxuspine A, 5-cinnamoyl-2-deacetoxytaxchinin A, taxawallin C)	C ₄₀ H ₄₆ O ₁₀	686	H	a	OAc	α-OAc	OBz	OH	−41.5° (CHCl ₃)		<i>T. wallichiana</i>	lv	e
(−)-2α-acetoxy-2',7-dideacetoxy-1-hydroxy-11(15→1)- <i>abeo</i> -austrospicatin	C ₃₉ H ₅₃ NO ₁₁	711	α-OAc	b	H	α-OAc	OAc	OAc	−46° (CHCl ₃)		<i>T. baccata</i>	lv	v
5α-O-(β-D-glucopyranosyl)-10β-benzoyltaxacustone	C ₃₇ H ₄₈ O ₁₄	716	β-OAc	d	H	β-OAc	OBz	=O	−92.6° (CHCl ₃)	178–180	<i>T. cuspidata</i>	lv, st	b
taxuspine A (10β-benzoyloxy-5α-cinnamoyloxy-1β-hydroxy-7β,9α,13α-triacetoxy-11(15→1)- <i>abeo</i> -taxa-4(20),11-diene)	C ₄₂ H ₄₈ O ₁₁	728	H	a	OAc	α-OAc	OBz	OAc	−3.4° (CHCl ₃)		<i>T. cuspidata</i>	st;	w
											<i>T. brevifolia</i>	1.7 × 10 ^{−3} lv	l
taxchinin E	C ₄₂ H ₄₈ O ₁₂	744	α-OAc	H	OAc	α-OAc	OBz	a	−17.49° (CHCl ₃)	134–136	<i>T. chinensis</i>	1.8 × 10 ^{−4} st, lv;	u
10β-benzoyloxy-1β-hydroxy-5α-(3'-methylamino-3'-phenyl)propanoxy-7β,9α,13α-triacetoxy-11(15→1)- <i>abeo</i> -taxa-4(20),11-diene	C ₄₃ H ₅₃ O ₁₁	745	H	c	OAc	α-OAc	OBz	OAc			<i>T. brevifolia</i>	lv	l

Table 11. (Continued)

name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	[α] _D	mp (°C)	plant source	plant part; % yield	refs
10β-benzoyloxy-5α-(3'-dimethylamino-3'-phenyl)propanoxy-1β-hydroxy-7β,9α,13α-triacetoxy-11 (15→1)-abeo-taxa-4(20),11-diene	C ₄₄ H ₅₅ O ₁₁	759	H	b	OAc	α-OAc	OBz	OAc			<i>T. brevifolia</i>	lv	1
2-deacetyl-2α-benzoyl-5,13-diacetyl-taxachinin A	C ₄₂ H ₄₈ O ₁₃	760	α-OBz	Ac	OAc	α-OAc	OBz	OAc	-21.5°	200–203	<i>T. brevifolia</i>	bk; 2.0 × 10 ⁻⁴	x

^a Barboni, L.; Pierluigi, G.; Torregiani, E.; G., A.; Gabetta, B.; Zini, G.; Bombardelli, E. *Phytochemistry* **1993**, *33*, 145–150. Structure corrected to the 11(15→1)-abeo-taxoid skeleton by: Appendino, G.; Barboni, L.; Gariboldi, P.; Bombardelli, E.; Gabetta, B.; Viterbo, D. *J. Chem. Soc., Chem. Commun.* **1993**, 1587–1589. ^b Tong, X.-J.; Fang, W.-S.; Zhou, J.-Y.; He, C.-H.; Chen, W.-M.; Fang, Q.-C. *J. Nat. Prod.* **1995**, *58*, 233–238. ^c Zhang, J. Z.; Fang, Q. C.; Liang, X. T.; Kong, M.; Yi He, W. *Chin. Chem. Lett.* **1995**, *6*, 971–974. ^d Kobayashi, J.; Hosoyama, H.; Katsui, T.; Yoshida, N.; Shigemori, H. *Tetrahedron* **1996**, *52*, 5391–5396. ^e Barboni, L.; Gariboldi, P.; Torregiani, E.; Appendino, G.; Varese, M.; Gabetta, B.; Bombardelli, E. *J. Nat. Prod.* **1995**, *58*, 934–939. ^f Chen, R.; Kingston, D. G. I. *J. Nat. Prod.* **1994**, *57*, 1017–1021. ^g Soto, J.; Fuentes, M.; Castedo, L. *Phytochemistry* **1996**, *43*, 313–314. ^h Li, B.; Tanaka, K.; Fuji, K.; Sun, H.; Taga, T. *Chem. Pharm. Bull.* **1993**, *41*, 1672–1673. ⁱ Shigemori, H.; Wang, X.-X.; Yoshida, N.; Kobayashi, J. *Chem. Pharm. Bull.* **1997**, *45*, 1205–1208. ^j Guo, Y.; Diallo, B.; Jaziri, M.; Vanhaelen-Fastre, R.; Vanhaelen, M. *J. Nat. Prod.* **1996**, *59*, 169–172. ^k Chattopadhyay, S. K.; Tripathi, V.; Sharma, R. P.; Shawl, A. S.; Joshi, B. S.; Roy, R. *Phytochemistry* **1999**, *50*, 131–133. ^l Balza, F.; Tachibana, S.; Barrios, H.; Towers, G. H. N. *Phytochemistry* **1991**, *30*, 1613–1614. ^m Chu, A.; Furlan, M.; Davin, L. B.; Zajicek, J.; Towers, G. H. N.; Soucy-Breau, C. M.; Rettig, S. J.; Croteau, R.; Lewis, N. G. *Phytochemistry* **1994**, *36*, 975–985. Structure corrected to the 11(15→1)-abeo-taxoid skeleton by: Appendino, G.; Barboni, L.; Gariboldi, P.; Bombardelli, E.; Gabetta, B.; Viterbo, D. *J. Chem. Soc., Chem. Commun.* **1993**, 1587–1589. ⁿ Morita, H.; Gonda, A.; Wei, L.; Yamamura, Y.; Takeya, K.; Itokawa, H. *J. Nat. Prod.* **1997**, *60*, 390–392. ^o Fuji, K.; Tanaka, K.; Li, B.; Shingu, T.; Sun, H.; Taga, T. *Tetrahedron Lett.* **1992**, *33*, 7915–7916. ^p Fuji, K.; Tanaka, K.; Li, B.; Shingu, T.; Sun, H.; Taga, T. *J. Nat. Prod.* **1993**, *56*, 1520–1531. ^q Shi, Q.-W.; Oritani, T.; Sugiyama, T.; Kiyota, H. *Planta Med.* **1998**, *64*, 766–769. ^r Appendino, G.; Tagliapietra, S.; Ozen, H.-C.; Gariboldi, P.; Gabetta, B.; Bombardelli, E. *J. Nat. Prod.* **1993**, *56*, 514–520. Revision of structure suggested by: Appendino, G.; Barboni, L.; Gariboldi, P.; Bombardelli, E.; Gabetta, B.; Viterbo, D. *J. Chem. Soc., Chem. Commun.* **1993**, 1587–1589. ^s Wang, X.-X.; Shigemori, H.; Kobayashi, J. *Tetrahedron* **1996**, *52*, 2337–2342. ^t Kobayashi, J.; Inubushi, A.; Hosoyama, H.; Yoshida, N.; Sasaki, T.; Shigemori, H. *Tetrahedron* **1995**, *51*, 5971–5978. ^u Gao, Y.-L.; Zhou, J.-Y.; Ding, Y.; Fang, Q.-C. *Chin. Chem. Lett.* **1997**, *8*, 1057–1058. ^v Tanaka, K.; Fuji, K.; Yokoi, T.; Shingu, T.; Li, B.; Sun, H. *Chem. Pharm. Bull.* **1994**, *42*, 1539–1541. ^w Doss, R. P.; Carney, J. R.; Shanks, C. H., Jr.; Williamson, R. T.; Chamberlain, J. D. *J. Nat. Prod.* **1997**, *60*, 1130–1133. ^x Kobayashi, J.; Ogiwara, A.; Hosoyama, H.; Shigemori, H.; Yoshida, N.; Sasaki, T.; Li, Y.; Iwasaki, S.; Naito, M.; Tsuruo, T. *Tetrahedron* **1994**, *50*, 7401–7416. ^y Rao, K. V.; Juchum, J. *Phytochemistry* **1998**, *47*, 1315–1324.

Scheme 3. Incorporation of Glucose and Acetate into the Taxayunnanine Skeleton

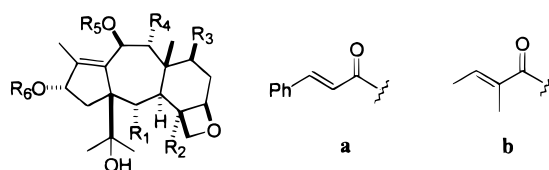


et al.⁶² for the formation of isoprenoids in eubacteria (Scheme 3). Although a comparable experiment has not been performed on taxol, it seems likely that taxol is also biosynthesized by the same pathway.

The first committed step in the biosynthesis of taxol has been elucidated by Croteau and his collaborators⁶³ as the cyclization of geranylgeranyl diphosphate (**31**) to taxa-4(5),11(12)-diene (**35**, Scheme 4). The previously unknown taxadiene **35** was first observed as a radioactive intermediate formed from [1-³H]geranylgeranyl diphosphate by a cell-free preparation from sapling yew stems. It was then shown that it was further converted by stem sections into 10-deacetylbaaccatin III and into taxol. Its structure was elucidated after a larger quantity (1 mg) was isolated by radiochemically guided fractionation of the radioactive intermediate in a mixture with a hydrocarbon fraction from

750 kg of *T. brevifolia* bark! The low cyclization activity in *T. brevifolia* stems, together with the low levels of **35** found in the bark, suggest that the cyclization of geranylgeranyl diphosphate to **35** is slow relative to subsequent oxygenations and is thus an important step for genetic manipulation.

The formation of taxa-4(5),11(12)-diene **35** as the initial cyclization product was surprising, since the isomeric taxa-4(20),11(12)-diene **36** had been assumed to be the initial cyclization product on the basis of the common occurrence of taxoids with a 4(20)-double bond. The mechanism of the cyclization was thus investigated in more detail⁶⁴ and it was shown that neither the diene **36** nor casbene (**37**) nor verticillene (**38**) served as intermediates. Cyclization thus must occur via the transient verticillyl intermediate **32**, which transfers the C-11α proton via an enzyme-bound

Table 12. 11(15→1)-*abeo*-Taxoids with an Oxetane Ring

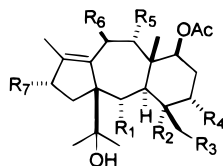
name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	[α] _D	mp (°C)	plant source	plant part; % yield	refs
7,13-dideacetyl-9,10-debenzoyltaxchinin C	C ₂₉ H ₃₈ O ₁₀	546	OBz	OAc	OH	OH	H	H	-15° (CHCl ₃)	162	<i>T. brevifolia</i>		<i>a</i>
taxacustin (10,13-deacetyl- <i>abeo</i> -baccatin IV)	C ₂₈ H ₄₀ O ₁₂	568	OAc	OAc	OAc	OAc	H	H	-38.4° (MeOH)	225–227	<i>T. cuspidata</i>	lv, tw	<i>b, c</i>
9α-(benzoyloxy)-2α,4α-diacetoxy-5β,20-epoxy-1β,7β,10β,13α-tetrahydroxy-11(15→1)- <i>abeo</i> -taxene, taxumairol K	C ₃₁ H ₄₀ O ₁₁	588	OAc	OAc	OH	OBz	H	H	-34° (MeOH)	220–222	<i>T. wallichiana</i>	lv	<i>d</i>
9α-(benzoyloxy)-2α,4α-diacetoxy-5β,20-epoxy-1β,7β,9α,13α-tetrahydroxy-11(15→1)- <i>abeo</i> -taxene, taxumairol K	C ₃₁ H ₄₀ O ₁₁	588	OAc	OAc	OH	OH	Bz	H	-8.5° (MeOH)	242–243	<i>T. brevifolia</i>	bk; 4.0 × 10 ⁻³	<i>e</i>
10β-benzoyloxy-2α,4α-diacetoxy-5β,20-epoxy-1β,7β,9α,13α-tetrahydroxy-11(15→1)- <i>abeo</i> -taxene (7,9-dideacetyl taxayuntin)	C ₃₁ H ₄₀ O ₁₁	588	OBz	OAc	OAc	OH	H	H	-23.2° (CHCl ₃)	266–268	<i>T. yunnanensis</i> <i>T. cuspidata</i>	bk st	<i>g</i> <i>h</i>
9-deacetyl taxayuntin E, taxuspinnanane F	C ₃₁ H ₄₀ O ₁₁	588	OAc	OAc	OBz	OH	H	H	+25.1° (CHCl ₃)	225–228	<i>T. yunnanensis</i>	bk	<i>i</i>
2α-debenzoyl-2α-acetyl taxayuntin A, taxayuntin B	C ₃₁ H ₄₀ O ₁₁	588	OBz	OAc	OH	OH	H	Ac	-26° (CHCl ₃)		<i>T. baccata</i>	lv	<i>j</i>
7,9,10-trideacetyl- <i>abeo</i> -baccatin VI taxayuntin H	C ₃₀ H ₄₂ O ₁₃	610	OAc	OAc	OAc	OAc	Ac	H	-66.7° (CHCl ₃)	249–250	<i>T. yunnanensis</i>	bk	<i>k</i>
taxuyunnanine F	C ₃₀ H ₄₂ O ₁₃	610	OAc	OAc	OAc	OAc	H	Ac	-22.6° (CHCl ₃)		<i>T. yunnanensis</i>	rt	<i>l</i>
13-decinnamoyl-9-deacetyl taxchinin B taxayuntin E	C ₃₃ H ₄₂ O ₁₂	630	OAc	OAc	OAc	OH	Bz	H	+8.7° (MeOH)	185–186	<i>T. yunnanensis</i>	lv, st	<i>n</i>
taxayuntin F (taxchinin L)	C ₃₃ H ₄₂ O ₁₂	630	OAc	OAc	OAc	OBz	H	H	-19.0° (MeOH)	185–186	<i>T. yunnanensis</i>	lv, st	<i>n</i>
taxuspine Q	C ₃₃ H ₄₆ O ₁₃	650	OAc	OAc	OAc	OAc	b	H	-40° (CHCl ₃)	263–264	<i>T. chinensis</i>	lv, st; 1.3 × 10 ⁻⁴	<i>o</i>
4α,7β,9α-trideacetyl-2α,7β-dibenzoyl-10β-debenzoyltaxayuntin, taxayuntin A	C ₃₆ H ₄₂ O ₁₁	650	OBz	OAc	OBz	OH	H	H	-8.2° (CHCl ₃)	160–163	<i>T. yunnanensis</i>	st; 2.9 × 10 ⁻⁴	<i>p</i>
4-deacetyl-11(15→1)- <i>abeo</i> -baccatin VI	C ₃₅ H ₄₄ O ₁₃	672	OBz	OH	OAc	OAc	Ac	Ac	± 0° (CHCl ₃)		<i>T. yunnanensis</i>	bk	<i>i</i>
4-deacetyl-11(15→1)- <i>abeo</i> -baccatin VI (taxayunnansin A) taxayuntin	C ₃₅ H ₄₄ O ₁₃	672	OBz	OH	OAc	OAc	Ac	Ac	-73.1° (CHCl ₃)	222	<i>T. x media</i>	rt; 6.0 × 10 ⁻⁵	<i>q</i>
13-deacetyl baccatin VI (taxayunnansin A) taxayuntin	C ₃₅ H ₄₄ O ₁₃	672	OAc	OAc	OAc	OAc	OBz	H	-38° (MeOH)	225–226	<i>T. wallichiana</i>	lv; 2.1 × 10 ⁻²	<i>r</i>
taxchinin M	C ₃₅ H ₄₄ O ₁₃	672	OAc	OAc	OAc	OAc	Bz	H	-53.3° (MeOH)	249–250	<i>T. yunnanensis</i>	rt	<i>l</i>
4α,7β-diacetoxy-2α,9α-dibenzoyloxy-5β,20-epoxy-10β,13α,15-tri-hydroxy-11(15→1)- <i>abeo</i> -taxene	C ₃₈ H ₄₄ O ₁₂	692	OAc	OAc	OAc	OBz	H	H	-19.6° (CHCl ₃)	239–242	<i>T. chinensis</i>	lv, st; 2.0 × 10 ⁻⁵	<i>o</i>
13-acetyl-13-decinnamoyl taxchinin B	C ₃₇ H ₄₆ O ₁₄	718	OAc	OAc	OAc	OAc	Bz	Ac	-8° (CHCl ₃)		<i>T. baccata</i>	lv; 6.0 × 10 ⁻³	<i>t</i>
9- <i>O</i> -benzoyl-9,10-dide- <i>O</i> -acetyl-11(15→1)- <i>abeo</i> -baccatin VI (taxchinin I)	C ₄₀ H ₄₆ O ₁₃	734	OBz	OAc	OAc	OBz	H	Ac	-54° (CHCl ₃)	243–244	<i>T. baccata</i>	lv	<i>v</i>
taxchinin J	C ₄₂ H ₄₈ O ₁₃	760	OBz	OAc	OAc	OBz	H	a	-30.5° (CHCl ₃)	238	<i>T. x media</i>	rt; 2.4 × 10 ⁻⁴	<i>q</i>
9- <i>O</i> -benzoyl-9-de- <i>O</i> -acetyl-11(15→1)- <i>abeo</i> -baccatin VI	C ₄₂ H ₄₈ O ₁₄	776	OBz	OAc	OAc	OBz	Ac	Ac	-6.08° (CHCl ₃)	235–237	<i>T. chinensis</i>	st, lv; 6.1 × 10 ⁻⁴	<i>w</i>
2α,7β-dibenzoyloxy-5β,20-epoxy-1β-hydroxy-4α,9α,10β,13α-tetraacetoxytax-11-ene	C ₄₂ H ₄₈ O ₁₄	776	OBz	OAc	OBz	OAc	OAc	Ac	+23.36° (CHCl ₃)	238–240	<i>T. chinensis</i>	st, lv; 3.4 × 10 ⁻⁴	<i>w</i>
2α-deacetyl-2α-benzoyl-13α-acetyl taxayuntin,	C ₄₂ H ₄₈ O ₁₄	776	OBz	OAc	OAc	OAc	Bz	Ac	-32.5° (CHCl ₃)		<i>T. x media</i>	rt; 2.8 × 10 ⁻⁴	<i>q</i>
	C ₄₂ H ₄₈ O ₁₄	776	OBz	OAc	OAc	OAc	Bz	Ac		226–230	<i>T. yunnanensis</i>	bk	<i>i</i>

Table 12. (Continued)

name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	[α] _D	mp (°C)	plant source	plant part; % yield	refs
taxayuntin C (2α,10β-dibenzoxy-5β,20-epoxy-1β-hydroxy-4α,7β,9α,13α-tetraacetoxytax-11-ene)											<i>T. brevifolia</i>	bk	<i>x</i>
2,7-dideacetyl-2,7-dibenzoyl-taxayunnanin F	C ₄₂ H ₄₈ O ₁₄	776	OBz	OAc	OBz	OAc	H	Ac		203–205	<i>T. brevifolia</i>	bk;	<i>y</i>
taxchinin K	C ₄₂ H ₄₈ O ₁₄	776	OAc	OAc	OAc	OBz	Bz	Ac	−30.0° (CHCl ₃)	217–219	<i>T. chinensis</i>	1.1 × 10 ^{−3} st, lv;	<i>w</i>
7-deacetyl-taxayuntin D	C ₄₅ H ₄₈ O ₁₃	796	OBz	OAc	OH	OBz	Bz	Ac		164–166	<i>T. brevifolia</i>	bk;	<i>y</i>
7-deacetyl-7-benzoyltaxchinin I	C ₄₅ H ₄₈ O ₁₃	796	OBz	OAc	OBz	OBz	H	Ac		255	<i>T. brevifolia</i>	2.0 × 10 ^{−3} bk;	<i>y</i>
taxchinin B	C ₄₄ H ₅₀ O ₁₄	802	OAc	OAc	OAc	OAc	Bz	a	+7.40° (CH ₂ Cl ₂)	176–178	<i>T. chinensis</i>	3.2 × 10 ^{−3} lv, st	<i>z</i>
7-deacetyl-7-benzoyl-taxayuntin C	C ₄₇ H ₅₀ O ₁₄	838	OBz	OAc	OBz	OAc	Bz	Ac		234–236	<i>T. brevifolia</i>	bk;	<i>y</i>
9-deacetyl-9-benzoyl-taxayuntin C, taxayuntin D	C ₄₇ H ₅₀ O ₁₄	838	OBz	OAc	OAc	OBz	Bz	Ac	−40.4° (MeOH)	210–214	<i>T. yunnanensis</i>	1.1 × 10 ^{−4} bk	<i>i</i>
taxchinin C (5β,20-epoxy-1β-hydroxy-4α,7β,13α-triacetoxo-2α,9α,10β-tribenzoxytax-11-ene)	C ₄₇ H ₅₀ O ₁₄	838	OBz	OAc	OAc	OBz	Bz	Ac	−45.6° (CH ₂ Cl ₂)	212–214	<i>T. chinensis</i>	lv, st	<i>z</i>
											<i>T. brevifolia</i>	bk	<i>x</i>

^a Chen, R.; Kingston, D. G. I. *J. Nat. Prod.* **1994**, *57*, 1017–1021. ^bTong, X. J.; Fang, W. S.; Zhou, J. Y.; He, C. H.; Chen, W. M.; Fang, Q. C. *Yaouxue Xuebao* **1994**, *29*, 55–60. ^cTong, X. J.; Fang, W. S.; Zhou, J. Y.; He, C. H.; Chen, W. M.; Fang, Q. C. *Chin. Chem. Lett.* **1993**, *4*, 887–890. ^dChattopadhyay, S. K.; Sharma, R. P.; Appendino, G.; Gariboldi, P. *Phytochemistry* **1995**, *39*, 869–870. ^eShen, Y.-C.; Chen, C.-Y.; Kuo, Y.-H. *J. Nat. Prod.* **1998**, *61*, 838–840. ^fRao, K. V.; Bhakuni, R. S.; Hanuman, J. B.; Davies, R.; Johnson, J. *Phytochemistry* **1996**, *41*, 863–866. ^gZhong, S.-Z.; Hua, Z.-X.; Fan, J.-S. *J. Nat. Prod.* **1996**, *59*, 603–605. ^hMorita, H.; Gonda, A.; Wei, L.; Yamamura, Y.; Wakabayashi, H.; Takeya, K.; Itokawa, H. *Planta Med.* **1998**, *64*, 183–186. ⁱChen, W. M.; Zhou, J. Y.; Zhang, P. L.; Fang, Q. C. *Chin. Chem. Lett.* **1993**, *4*, 695–698. ^jAppendino, G.; Cravotto, G.; Enriu, R.; Jakupovic, J.; Gariboldi, P.; Gabetta, B.; Bombardelli, E. *Phytochemistry* **1994**, *36*, 407–411. ^kZhou, J.-Y.; Zhang, P.-L.; Chen, W.-M.; Fang, Q.-C. *Phytochemistry* **1998**, *48*, 1387–1389. ^lZhang, H.; Tadedo, Y.; Sun, H. *Phytochemistry* **1995**, *39*, 1147–1151. ^mChattopadhyay, S. K.; Saha, G. C.; Sharma, R. P.; Kumar, S.; Roy, R. *Phytochemistry* **1996**, *42*, 787–788. ⁿYue, Q.; Fang, Q.-C.; Liang, X.-T.; He, C.-H. *Phytochemistry* **1995**, *39*, 871–873. ^oTanaka, K.; Fujii, K.; Yokoi, T.; Shingu, T.; Li, B.; Sun, H. *Chem. Pharm. Bull.* **1996**, *44*, 1770–1774. ^pWang, X.-x.; Shigemori, H.; Kobayashi, J. *Tetrahedron* **1996**, *52*, 12159–12164. ^qBarboni, L.; Gariboldi, P.; Torregiani, E.; Appendino, G.; Cravotto, G.; Bombardelli, E.; Gabetta, B.; Viterbo, D. *J. Chem. Soc., Perkin Trans. I* **1994**, 3233–3238. ^rBarboni, L.; Pierluigi, G.; Torregiani, E.; G., A.; Gabetta, B.; Zini, G.; Bombardelli, E. *Phytochemistry* **1993**, *33*, 145–150. Structure revision to the corresponding 11(15→1)-abeo-taxoid by: Appendino, G.; Barboni, L.; Gariboldi, P.; Bombardelli, E.; Gabetta, B.; Viterbo, D. *J. Chem. Soc., Chem. Commun.* **1993**, 1587–1589. ^sRao, C.; Zhou, J. Y.; Chen, W. M.; Lu, Y.; Zheng, Q. T. *Chin. Chem. Lett.* **1993**, *4*, 693–694. ^tRao, K. V.; Johnson, J. H. *Phytochemistry* **1998**, *49*, 1361–1364. ^uGuo, Y.; Vanhaelen-Fastre, R.; Diallo, B.; Vanhaelen, M.; Jaziri, M.; Homes, J.; Ottinger, R. *J. Nat. Prod.* **1995**, *58*, 1015–1023. ^vDas, B.; Rao, S. P.; Srinivas, K. V. N. S.; Yadav, J. S.; Das, R. *Phytochemistry* **1995**, *38*, 671–674. ^wTanaka, K.; Fujii, K.; Yokoi, T.; Shingu, T.; Li, B.; Sun, H. *Chem. Pharm. Bull.* **1994**, *42*, 1539–1541. ^xChu, A.; Zajicek, J.; Davin, L. B.; Lewis, N. G.; Croteau, R. B. *Phytochemistry* **1992**, *31*, 4249–4252. Structure revision to the corresponding 11(15→1)-abeo-taxoid by: Huang, K.; Liang, J.; Gunatilaka, A. A. L. *J. Chin. Pharm. University (Zhongguo Yaoke Daxue Xuebao)* **1998**, *29*, 259–266. ^yRao, K. V.; Juchum, J. *Phytochemistry* **1998**, *47*, 1315–1324. ^zFujii, K.; Tanaka, K.; Li, B.; Shingu, T.; Sun, H.; Taga, T. *J. Nat. Prod.* **1993**, *56*, 1520–1531.

Table 13. 11(15→1)-abeo-Taxoids with an Opened Oxetane Ring

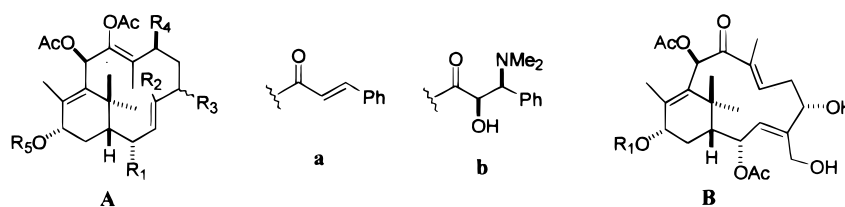


name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	[α] _D	mp (°C)	plant source	plant part; % yield	refs
taxayuntin G	C ₂₈ H ₄₂ O ₁₂	570	OAc	H	OH	OAc	OAc	OH	OH	+56° (MeOH)	205–206	<i>T. yunnanensis</i>	lv, st	<i>a</i>
taxayuntin J	C ₃₀ H ₄₄ O ₁₃	612	OH	H	OAc	OAc	OAc	OAc	OH	−54° (MeOH)	125–127	<i>T. yunnanensis</i>	bk	<i>b</i>
taxumain A	C ₃₀ H ₄₄ O ₁₃	612	OAc	H	OAc	OAc	OAc	OH	OH	−11.1° (CHCl ₃)	284–286	<i>T. mairei</i>	tw	<i>c</i>
taxuchin B	C ₃₁ H ₄₁ O ₁₁ Cl	624.5	OAc	OH	Cl	OH	OBz	OH	OH			<i>T. chinensis</i>	tw, lv	<i>d</i>
taxumain B	C ₃₂ H ₄₆ O ₁₄	654	OAc	H	OAc	OAc	OAc	OH	OAc	−15.2° (CHCl ₃)		<i>T. mairei</i>	tw	<i>c</i>
yunantaxusin A	C ₃₅ H ₄₆ O ₁₄	690	OH	OH	OAc	OAc	OAc	OBz	OH			<i>T. yunnanensis</i>	lv, st	<i>e</i>

^a Yue, Q.; Fang, Q. C.; Liang, X. T. *Chin. Chem. Lett.* **1995**, *6*, 225–228. ^bZhou, J.-Y.; Zhang, P.-L.; Chen, W.-M.; Fang, Q.-C. *Phytochemistry* **1998**, *48*, 1387–1389. ^cYang, S.-J.; Fang, J.-M.; Cheng, Y.-S. *Phytochemistry* **1999**, *50*, 127–130. ^dFang, W. S.; Fang, Q. C.; Liang, X. T.; Lu, Y.; Wu, N.; Zheng, Q. T. *Chin. Chem. Lett.* **1997**, *8*, 231–232. ^eZhang, S.; Lee, C. T.-L.; Kashiwada, Y.; Chen, K. J. *Nat. Prod.* **1994**, *57*, 1580–1583.

intermediate to the C-7 position to give the intermediate **33**, which then undergoes transannular B/C ring closure to the taxenyl cation **34** and proton loss to **35**. The

intramolecular transfer of the C-11α proton to C-7 was demonstrated by the use of [10-²H]geranylgeranyl diphosphate.

Table 14. Bicyclic Taxoids

name	molecular formula	MW	structure	R ₁	R ₂	R ₃	R ₄	R ₅	[α] _D	mp (°C)	plant source	plant part; % yield	refs
(3 <i>E</i> ,7 <i>E</i>)-2α,10β-diacetoxy-5α,13α,20-trihydroxy-3,8- <i>sec</i> -taxa-3,7,11-trien-9-one	C ₂₄ H ₃₄ O ₈	450	B	H	NA	NA	NA	NA	-155° (CHCl ₃)		<i>T. chinensis</i>	lv	<i>a</i>
(3 <i>E</i> ,7 <i>E</i>)-2α,10β,13α-triacetoxy-5α,20-dihydroxy-3,8- <i>sec</i> -taxa-3,7,11-trien-9-one	C ₂₆ H ₃₆ O ₉	492	B	Ac	NA	NA	NA	NA	-60° (CHCl ₃)	77–78	<i>T. chinensis</i>	lv	<i>a</i>
7-deacetylcanadensene	C ₂₈ H ₄₀ O ₁₁	552	A	OAc	CH ₂ OH	α-OH	OH	OAc	+5.3° (CHCl ₃)	95–96	<i>T. mairei</i>	lv	<i>b</i>
13-deacetylcanadensene	C ₂₈ H ₄₀ O ₁₁	552	A	OAc	CH ₂ OH	α-OH	OAc	H	+4.5° (CHCl ₃)	98–99	<i>T. mairei</i>	lv; 3.5 × 10 ⁻⁴	<i>b</i>
taxuspine U	C ₂₈ H ₄₀ O ₁₁	552	A	OH	CH ₂ OH	α-OAc	OH	Ac	+18° (MeOH)		<i>T. cuspidata</i>	st; 1.7 × 10 ⁻⁵	<i>c</i>
canadensene	C ₃₀ H ₄₂ O ₁₂	594	A	OAc	CH ₂ OH	β-OH	OAc	Ac			<i>T. canadensis</i>	lv	<i>d</i>
5-epicanadensene	C ₃₀ H ₄₂ O ₁₂	594	A	OAc	CH ₂ OH	α-OH	OAc	Ac			<i>T. canadensis</i>	lv	<i>e</i>
2-deacetylaxachitriene A	C ₃₀ H ₄₂ O ₁₂	594	A	OH	CH ₂ OAc	α-OH	OAc	Ac	-51° (CHCl ₃)	82–83	<i>T. chinensis</i>	lv	<i>a</i>
5-deacetylaxachitriene B	C ₃₀ H ₄₂ O ₁₂	594	A	OH	CH ₂ OH	α-OH	OAc	Ac	+67.7° (MeOH)	96–98	<i>T. chinensis</i>	lv	<i>f</i>
taxachitriene A	C ₃₂ H ₄₄ O ₁₃	636	A	OAc	CH ₂ OAc	α-OH	OAc	Ac	-9.9° (CHCl ₃)	99–101	<i>T. chinensis</i>	lv	<i>g</i>
taxachitriene B	C ₃₂ H ₄₄ O ₁₃	636	A	OH	CH ₂ OH	α-OAc	OAc	Ac	+29° (MeOH)	225–227	<i>T. chinensis</i>	lv	<i>g</i>
taxuspine X	C ₄₁ H ₅₀ O ₁₄	766	A	OAc	CH ₂ OAc	α-O-a	OAc	Ac	+31.7° (CHCl ₃)		<i>T. cuspidata</i>	st; 1.4 × 10 ⁻⁴	<i>h</i>
(2' <i>S</i> ,3' <i>R</i>)-5-(<i>N,N</i> -dimethyl-3'-phenylisoseryl)-taxachitriene A	C ₄₇ H ₅₇ NO ₁₅	875	A	OAc	CH ₂ OAc	α-O-b	OAc	Ac	+22.3° (CHCl ₃)	93–95	<i>T. chinensis</i>	bk, lv	<i>i</i>

^aShi, Q.-W.; Oritani, T.; Sugiyama, T.; Kiyota, H. *J. Nat. Prod.* **1998**, *61*, 1437–1440. ^bShi, Q.-W.; Oritani, T.; Sugiyama, T. *Phytochemistry* **1999**, *50*, 633–636. ^cHosoyama, H.; Inubushi, A.; Katsui, T.; Shigemori, H.; Kobayashi, J. *Tetrahedron* **1996**, *52*, 13145–13150. ^dZamir, L. O.; Zhou, Z. H.; Caron, G.; Nedeau, M. E.; Sauriol, F.; Mamer, O. *J. Chem. Soc., Chem. Commun.* **1995**, 529–530. (Stereochemistry at C-5 established in 1998, see ref *e*.) ^eZamir, L. O.; Zhang, J.; Kutterer, K.; Sauriol, F.; Mamer, O.; Khat, A.; Boulanger, Y. *Tetrahedron* **1998**, *54*, 15845–15860. ^fFang, W.-S.; Fang, Q.-C.; Liang, X.-T. *Planta Med.* **1996**, *62*, 567–569. ^gFang, W.-S.; Fang, Q.-C.; Liang, X.-T.; Lu, Y.; Zheng, Q.-T. *Tetrahedron* **1995**, *51*, 8483–8490. ^hShigemori, H.; Wang, X.-X.; Yoshida, N.; Kobayashi, J. *Chem. Pharm. Bull.* **1997**, *45*, 1205–1208. ⁱShi, Q.-W.; Oritani, T.; Sugiyama, T.; Kiyota, H. *Planta Med.* **1998**, *64*, 766–769.

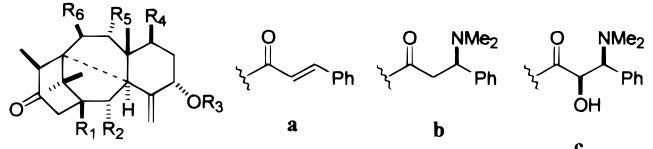
The importance of taxadiene synthase as the probable key rate-controlling enzyme for taxol biosynthesis led to a successful effort to purify it and to isolate and express its corresponding cDNA. The enzyme was localized primarily in the bark and adhering cambium cells of *T. brevifolia*, and was purified to homogeneity by chromatographic and electrophoretic methods. The purified enzyme was shown to be a monomer of about 79 kDa, and was also characterized with regard to pH optimum, kinetic constants, and metal ion cofactors, with Mg²⁺ being preferred.⁶⁵

The genes encoding taxadiene synthase were found by constructing DNA primers based on homologous sequences of terpenoid cyclases thought to be related to taxadiene synthase.⁶⁶ Amplification of two of these primers by the polymerase chain reaction (PCR) yielded a DNA fragment of 83 base pairs whose sequence was homologous to that of a cyclase. Screening of a cDNA library of *T. brevifolia* DNA led to the isolation of a hybridizing cDNA fragment which was then expressed in *Escherichia coli*. The protein produced by this engineered *E. coli* was the desired taxadiene synthase, which was found to have 862 amino acid residues corresponding to a molecular weight of about 98 000. Comparison with terpenoid synthases from higher plants, and especially with those of gymnosperms, showed

significant similarities, supporting the idea of a common ancestry for this class of enzymes.

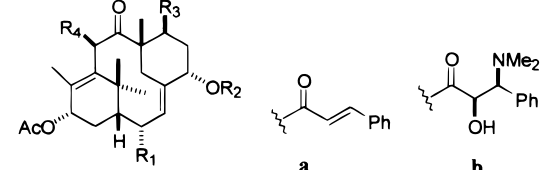
Although earlier results suggested that the formation of taxa-4(5),11(12)-diene from geranylgeranyl diphosphate was the rate-limiting step in the biosynthesis of taxol,⁶⁴ a study of taxadiene synthase activity in *T. canadensis* suspension cell cultures showed that it exceeded that needed for the maximum rate of taxol accumulation in vivo.⁶⁷ This result suggests that the real rate-limiting step in taxol biosynthesis lies further down the biosynthetic pathway.

The conversion of taxa-4(5),11(12)-diene (**35**) to taxol requires that it undergo oxygenation at eight distinct sites. The fact that almost all known taxoids are oxygenated at C-5 suggested that this was the first oxygenation site, and so it proved to be. Incubation of (20-²H₃)taxa-4(5),11(12)-diene with microsomal preparations from extracts of *T. brevifolia* stems or *T. cuspidata* suspension-cultured cells gave a product in 4–14% yield which was identified as taxa-4(20),11(12)-dien-α-ol (**39**), in which the endocyclic 4(5)-double bond has migrated to the familiar 4(20)-exo position, with concomitant oxygenation at C-5.⁶⁸ The structure and stereochemistry of **39** were established unambiguously by synthesis, and the reaction was shown

Table 15. Taxoids with a C-3(11) Bridge and a C-4(20) Double Bond


name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	[α] _D	mp (°C)	plant source	plant part; % yield	refs
taxinine K	C ₂₆ H ₃₆ O ₈	476	H	OAc	H	H	OAc	OAc		167–168	<i>T. cuspidata</i>	lv; 2.0 × 10 ⁻⁵	<i>a</i>
5-cinnamoylphototaxin II	C ₂₉ H ₃₆ O ₆	480	H	OH	a	H	OH	OH			<i>T. baccata</i>	lv	<i>b</i>
taxinine L	C ₂₈ H ₃₈ O ₉	518	H	OAc	Ac	H	OAc	OAc		159–160	<i>T. cuspidata</i>	lv; 1.2 × 10 ⁻⁵	<i>a</i>
5- <i>O</i> -cinnamoyl-9- <i>O</i> -acetyl-phototaxin I	C ₃₁ H ₃₈ O ₈	538	OH	OH	a	H	OAc	OH	+3.2° (CH ₂ Cl ₂)	78–80	<i>T. baccata</i>	lv	<i>c</i>
2,9-diacetyl-5-cinnamoyl-phototaxin II	C ₃₃ H ₄₀ O ₈	564	H	OAc	a	H	OAc	OH			<i>T. canadensis</i>		<i>d</i>
2,10-diacetyl-5-cinnamoyl-phototaxin II	C ₃₃ H ₄₀ O ₈	564	H	OAc	a	H	OH	OAc			<i>T. canadensis</i>		<i>d</i>
2,10-diacetyl-5-cinnamoyl-7β-hydroxyphototaxin II	C ₃₃ H ₄₀ O ₉	580	H	OAc	a	OH	OH	OAc			<i>T. canadensis</i>		<i>d</i>
taxuspine C	C ₃₅ H ₄₂ O ₉	606	H	OAc	a	H	OAc	OAc	+7.4° (CHCl ₃)		<i>T. cuspidata</i>	st; 1.7 × 10 ⁻³	<i>e</i>
taxuspine H	C ₃₇ H ₄₉ NO ₉	651	H	OAc	b	H	OAc	OAc	+6.8° (CHCl ₃)		<i>T. cuspidata</i>	st, lv	<i>f</i>
spicaledonine	C ₃₇ H ₄₉ NO ₁₀	667	H	OAc	c	H	OAc	OAc	+29° (CHCl ₃)		<i>A. spicata</i>	bk; 9.3 × 10 ⁻⁵	<i>g</i>

^a Chiang, H. C.; Woods, M. C.; Nakadaira, Y.; Nakanishi, K. *Chem. Commun.* **1967**, 1201–1202. ^bSoto, J.; Castedo, L. *Phytochemistry* **1998**, *47*, 817–819. ^cAppendino, G.; Ozen, H. C.; Gariboldi, P.; Gabetta, B.; Bombardelli, E. *Fitoterapia* **1992**, *64*(S1), 47–51. Zamir, L. O.; Zhang, J.; Kutterer, K.; Sauriol, F.; Mamer, O.; Khiat, A.; Boulanger, Y. *Tetrahedron* **1998**, *54*, 15845–15860. ^dKobayashi, J.; Ogiwara, A.; Hosoyama, H.; Shigemori, H.; Yoshida, N.; Sasaki, T.; Li, Y.; Iwasaki, S.; Naito, M.; Tsuruo, T. *Tetrahedron* **1994**, *50*, 7401–7416. ^eKobayashi, J.; Inubushi, A.; Hosoyama, H.; Yoshida, N.; Sasaki, T.; Shigemori, H. *Tetrahedron* **1995**, *51*, 5971–5978. ^fEttouati, L.; Ahond, A.; Convert, O.; Poupat, C.; Potier, P. *Bull. Soc. Chim. Fr.* **1989**, *5*, 687–694.

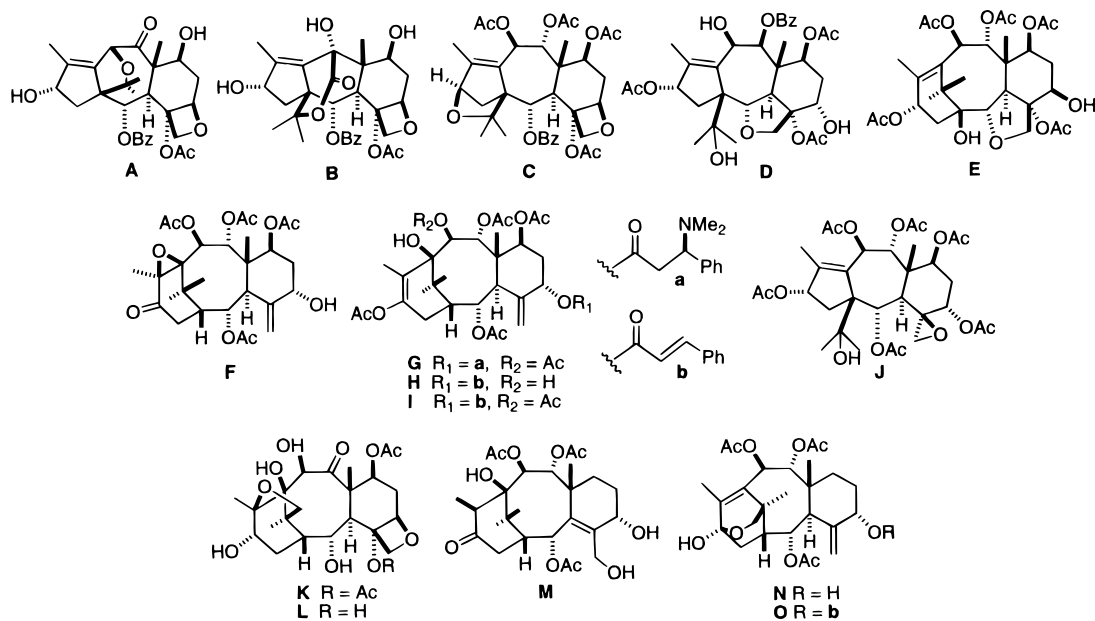
Table 16. 2(3–20)-*abeo*-Taxanes


name	molecular formula	MW	R ₁	R ₂	R ₃	R ₄	[α] _D	mp (°C)	plant source	plant part; % yield	refs
deaminoacyltaxine A	C ₂₄ H ₃₄ O ₈	450	OAc	H	OH	OH			<i>T. baccata</i>	lv	<i>a</i>
2-deacetyltaxine B	C ₂₆ H ₃₆ O ₉	492	OH	H	OAc	OAc	–218.2° (CHCl ₃)	178–179	<i>T. yunnanensis</i>	lv, st	<i>b</i>
2α,7β,13α-triacetoxy-5α,10β-dihydroxy-9-keto-2(3–20)- <i>abeo</i> -taxane (taxuspine W)	C ₂₆ H ₃₆ O ₉	492	OAc	H	OAc	OH	–147° –94.7 (MeOH)	172–174	<i>T. x media</i> <i>T. cuspidata</i>	lv; 5.0 × 10 ⁻³ st	<i>c</i> <i>d</i>
taxine B	C ₂₈ H ₃₈ O ₁₀	534	OAc	H	OAc	OAc	–239.5° (CHCl ₃)	166–167	<i>T. yunnanensis</i>	lv, st	<i>b</i>
taxuspinanane H, deaminoacyl-cinnamoyltaxine A	C ₃₃ H ₄₀ O ₉	580	OAc	a	OH	OH	–42° (CHCl ₃)		<i>T. cuspidata</i>	st;	<i>e</i>
2-deacetyltaxine A (taxine C)	C ₃₃ H ₄₅ NO ₉	599	OH	b	OH	OH	–106° (CHCl ₃)		<i>T. baccata</i>	lv	<i>f</i>
taxuspine B	C ₃₅ H ₄₂ O ₁₀	622	OAc	a	OAc	OH	–73° (MeOH)	220–221	<i>T. baccata</i>	lv	<i>g</i>
taxine A	C ₃₅ H ₄₇ O ₁₀	641	OAc	b	OH	OH	–40.6° (CHCl ₃)			st;	<i>h</i>
7- <i>O</i> -acetyltaxine A	C ₃₇ H ₄₉ NO ₁₁	683	OAc	b	OAc	OH	–140° (CHCl ₃)	204–206	<i>T. baccata</i>	lv	<i>i, j</i>
							–96° (CHCl ₃)	178–180	<i>T. baccata</i>		<i>g</i>

^a Appendino, G.; Cravotto, G.; Enriu, R.; Jakupovic, J.; Gariboldi, P.; Gabetta, B.; Bombardelli, E. *Phytochemistry* **1994**, *36*, 407–411. ^bYue, Q.; Fang, Q.-C.; Liang, X.-T.; He, C.-H.; Jing, X.-L. *Planta Med.* **1995**, *61*, 375–377. ^cRao, K. V.; Reddy, G. C.; Juchum, J. *Phytochemistry* **1996**, *43*, 439–442. ^dHosoyama, H.; Inubushi, A.; Katasui, T.; Shigemori, H.; Kobayashi, J. *Tetrahedron* **1996**, *52*, 13145–13150. ^eMorita, H.; Gonda, A.; Wei, L.; Yamamura, Y.; Wakabayashi, H.; Takeya, K.; Itokawa, H. *Phytochemistry* **1998**, *48*, 857–862. ^fPoupat, C.; Ahond, A.; Potier, P. *J. Nat. Prod.* **1994**, *57*, 1468–1469. ^gBarboni, L.; Gariboldi, P.; Appendino, G.; Enriu, R.; Gabetta, B.; Bombardelli, E. *Liebigs Ann.* **1995**, 345–349. ^hKobayashi, J.; Ogiwara, A.; Hosoyama, H.; Shigemori, H.; Yoshida, N.; Sasaki, T.; Li, Y.; Iwasaki, S.; Naito, M.; Tsuruo, T. *Tetrahedron* **1994**, *50*, 7401–7416. ⁱGraf, E.; Bertholdt, H. *Pharmazeut. Zent.* **1957**, *96*, 385–395. ^jGraf, E.; Kirfel, A.; Wolff, G.-J.; Breitmaier, E. *Liebigs Ann. Chem.* **1982**, 376–381.

to be due to mixed function cytochrome P₄₅₀ dependent hydroxylase with molecular oxygen as the oxidant.

Compound **39** was shown to be an intermediate on the pathway to taxol by incubation with *T. brevifolia* stem disks

Table 17. Miscellaneous Taxoids

name	molecular formula	MW	structure	$[\alpha]_D$	mp (°C)	plant source	plant part; % yield	refs
4-deacetyltaxagifine III	$\text{C}_{22}\text{H}_{32}\text{O}_{10}$	456	L	+38.1° (MeOH)	221–223	<i>T. chinensis</i>	lv, st; 2.0×10^{-4}	<i>a</i>
taxezopidine A	$\text{C}_{26}\text{H}_{36}\text{O}_9$	492	N	+5° (CHCl ₃)		<i>T. cuspidata</i>	sd	<i>b</i>
taxagifine III	$\text{C}_{24}\text{H}_{34}\text{O}_{11}$	498	K	+31.4° (MeOH)	246–247	<i>T. chinensis</i>	lv, st; 1.5×10^{-4}	<i>a, c</i>
taxezopidine B	$\text{C}_{26}\text{H}_{38}\text{O}_{10}$	510	M	+10.4° (CHCl ₃)		<i>T. cuspidata</i>	sd, st; 2.5×10^{-4}	<i>d</i>
10,15-epoxy-11(15→1)-abeo-10-deacetylbaccatin III	$\text{C}_{29}\text{H}_3\text{O}_{49}$	526	A	–18° (CH ₂ Cl ₂)		<i>T. wallichiana</i>	lv	<i>e</i>
wallifoliol	$\text{C}_{29}\text{H}_{34}\text{O}_{10}$	542	B	–10.8° (MeOH)		<i>T. wallichiana</i>	lv	<i>f</i>
decinnamoyltaxinine B	$\text{C}_{28}\text{H}_{38}\text{O}_{11}$	550	F	+14° (CHCl ₃)	160	<i>T. yunnanensis</i>	lv, st	<i>g</i>
taxuspine K	$\text{C}_{30}\text{H}_{42}\text{O}_{13}$	610	E	+48° (CHCl ₃)		<i>T. cuspidata</i>	st; 1.7×10^{-4}	<i>h</i>
taxezopidine J	$\text{C}_{35}\text{H}_{42}\text{O}_{10}$	622	O	+48° (CHCl ₃)		<i>T. cuspidata</i>	sd	<i>i</i>
taxuyunnanine E	$\text{C}_{33}\text{H}_{42}\text{O}_{12}$	630	D	+3.3° (CHCl ₃)		<i>T. yunnanensis</i>	rt	<i>j</i>
taxuchin A	$\text{C}_{32}\text{H}_{44}\text{O}_{14}$	652	J	–64.8° (MeOH)	248–250	<i>T. chinensis</i>	bk; 6.2×10^{-4}	<i>k</i>
13-deacetoxy-13,15-epoxy-11(15→1)-abeo-13-epi-baccatin VI	$\text{C}_{35}\text{H}_{42}\text{O}_{12}$	654	C	+23.9° (CHCl ₃)	150	<i>T. x media</i>	rt	<i>l</i>
taxezopidine K	$\text{C}_{37}\text{H}_{46}\text{O}_{12}$	682	H	+53° (CHCl ₃)		<i>T. cuspidata</i>	sd	<i>i</i>
taxuspine D	$\text{C}_{39}\text{H}_{48}\text{O}_{13}$	724	I	–32.2° (MeOH)		<i>T. cuspidata</i>	st; 4.4×10^{-3}	<i>m</i>
taxuspine P	$\text{C}_{41}\text{H}_{55}\text{NO}_{13}$	769	G	+32.7° (MeOH)		<i>T. cuspidata</i>	st	<i>n</i>

^aZhang, Z.; Jia, Z. *Phytochemistry* **1991**, *30*, 2345–2348. ^bWang, X.-X.; Shigemori, H.; Kobayashi, J. *Tetrahedron Lett.* **1997**, *38*, 7587–7588. ^cZhang, Z. P.; Jia, Z. *J. Chin. Chem. Lett.* **1990**, *1*, 91–92. ^dWang, X.-X.; Shigemori, H.; Kobayashi, J. *J. Nat. Prod.* **1998**, *61*, 474–479. ^eAppendino, G.; Ozen, H. C.; Gariboldi, P.; Torregiani, E.; Gabetta, B.; Nizzola, R.; Bombardelli, E. *J. Chem. Soc., Perkin Trans I* **1993**, 1563–1566. ^fVander Velde, D. G.; Georg, G. I.; Gollapudi, S. R.; Jampani, H. B.; Liang, X.-Z.; Mitscher, L. A.; Ye, Q.-M. *J. Nat. Prod.* **1994**, *57*, 862–867. ^gYue, Q.; Fang, Q.-C.; Liang, X.-T. *Phytochemistry* **1996**, *43*, 639–642. ^hWang, X.-X.; Shigemori, H.; Kobayashi, J. *Tetrahedron* **1996**, *52*, 2337–2342. ⁱShigemori, H.; Sakurai, C. A.; Hosoyama, H.; Kobayashi, A.; Kajiyama, S.; Kobayashi, J. *Tetrahedron* **1999**, *55*, 2553–2558. ^jZhang, H.; Tateda, Y.; Sun, H. *Phytochemistry* **1995**, *39*, 1147–1151. ^kZhang, S.; Lee, C. T.-L.; Kashiwada, Y.; Zhang, D.-C.; McPhail, A. T.; Lee, K.-H. *J. Chem. Soc., Chem. Commun.* **1994**, 1561–1562. ^lBarboni, L.; Gariboldi, P.; Torregiani, E.; Appendino, G.; Cravotto, G.; Bombardelli, E.; Gabetta, B.; Viterbo, D. *J. Chem. Soc., Perkin Trans. I* **1994**, 3233–3238. ^mKobayashi, J.; Hosoyama, H.; Shigemori, H.; Koiso, Y.; Iwasaki, S. *Experientia* **1995**, *51*, 592–595. ⁿKobayashi, J.; Hosoyama, H.; Katsui, T.; Yoshida, N.; Shigemori, H. *Tetrahedron* **1996**, *52*, 5391–5396.

and isolation of taxol as well as other taxoids. Radiochemically guided fractionation of a large extract of dried *T. brevifolia* bark showed that **39** and its esters are present in the bark, but at low levels, again suggesting that this oxygenation step of taxol biosynthesis is a slow one.⁶⁸

The next step in the biosynthetic pathway is probably

acylation at C-5, and this reaction has been observed with a soluble enzyme preparation from *T. canadensis*. The enzyme preparation catalyzed the acetylation of **39** to **40** but did not catalyze the benzylation of **39**.⁶⁹

Subsequent steps in the biosynthesis of taxol are as yet undetermined, but it has been predicted, based on the

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