

TAXOL RELATED DITERPENES FROM THE ROOTS OF *TAXUS*
YUNNANENSIS

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Abstract- Four new taxol related diterpenes were iso-
lated from the roots of *Taxus yunnanensis* together
with taxol, cephalomannine, 10-deacetyltaxol, and 10-
deacetylcephalomannine and their structures were eluci-
dated by spectroscopic means.

The natural product taxol (1)¹ has brought great promise for sufferers of ovarian and breast cancer, but its scarcity limits its application to small number of patients. The search for new compounds with similar bioactivity to taxol or semisynthetic precursors of taxol therefore is imperative. Our research on the roots of *Taxus yunnanensis* collected in the suburbs of Kunming, Yunnan, China led to the isolation of compound, taxuyunnanine A (2)² which showed comparable cytotoxicity to that of taxol (1). On further investigation, four new taxuyunnanine A related compounds were isolated together

with taxol (1),¹ 10-deacetyltaxol (3),³ cephalomannine (4),³ and 10-deacetylcephalomannine (5)³ from the ethereal extract of the roots of *T. yunnanensis*. This paper describes the structure elucidation of four new taxuyunnanine A related compounds,⁴ 10-deacetyltaxuyunnanine A (6), C₄₄H₅₅O₁₃N, [α]_D -50.9° (CHCl₃), 7-epi-taxuyunnanine A (7), C₄₆H₅₇O₁₄N, [α]_D -47.3° (CHCl₃), 7-epi-10-deacetyltaxuyunnanine A (8), C₄₄H₅₅O₁₃N, [α]_D -34.9° (CHCl₃) and 10-deacetyl-10-oxo-7-epi-taxuyunnanine A (9), C₄₄H₅₃O₁₃N, [α]_D -70.8° (CHCl₃), by spectroscopic means.

Metabolites (6, 7, 8 and 9) showed very similar ¹H- and ¹³C nmr spectra to those of taxuyunnanine A (2) (see Tables I and II). The ¹H nmr spectrum of 6 differed from that of 2 only in an upfield shift of the H-10 signal [δ _H 5.23 (1H, s)] and the disappearance of the acetyl signal at C-10, suggesting that 6 is a 10-deacetyl derivative of 2. Actually, the triacetate of 6 was identical with the diacetate of 2. Comparisons of the nmr data of 7 with those of 7-epi-taxol (10)^{5,6} revealed that 7 is 7-epi-taxuyunnanine A, since 7 possessed essentially the same chemical shifts and coupling patterns as those of 10 except signals of the side chain at C-13 of 2 but not those of 1. Likewise the ¹H nmr spectra of 8 and 7 show a parallel situation, that is, metabolite (8) differs from 7 only in lack of a 10-acetyl group, and this resulted in an upfield shift of the H-10 signal in 8. In fact, the triacetate of 8 was identical with the diacetate of 7. The ¹H nmr spectrum of 9 resembled that of 8. The coupling pattern of 5 α -H [δ _H 4.88 (1H, dd, J=7.8 and 4.4 Hz)] established the α -orientation of the 7-OH group but the singlet signal of H-10 disappeared. The ¹³C nmr spectrum of 9 showed a new signal at δ _C 188.73, suggesting that C-10 was oxidized to a carbonyl carbon. Actually, 9 showed the same characteristics in its ¹H- and ¹³C nmr spectra to those of 10-deacetyl-10-oxo-7-epi-taxol (11)^{5,7} except for the signals due to the side chain on C-13, which clearly indicated the presence of taxuyunnanine A type C-13-side chain in 9 instead of that of a

Table 1. ^1H nmr data for compounds (2, 6, 7, 8 and 9) in CDCl_3 (400 MHz, δ in ppm from TMS and J in Hz)

proton	2*	6	7	8	9
H-2	5.67 d (7.1)	5.67 d (7.1)	5.76 d (7.6)	5.74 d (7.6)	5.88 d (7.1)
H-3	3.78 d (7.1)	3.86 d (7.1)	3.90 d (7.6)	3.91 d (7.6)	3.99 d (7.1)
H-5	4.92 br dd (9.6, 2.3)	4.91 br d (9.8)	4.90 dd (8.8,3.9)	4.89 dd (8.8,4.4)	4.88 dd (7.6,4.2)
H α -6	2.52 ddd (14.8, 9.6, 6.6)	2.52 m	-2.40 m	-2.35 m	2.24 m
H β -6	1.87 ddd (14.8, 10.9, 2.3)	1.83 m	-2.25 m	-2.22 m	2.24 m
H-7	4.38 dd (6.6, 10.9)	4.20 m	3.69 dd (11.7,2.9)	3.67 dd (11.7,2.5)	3.83 br d (11.7)
H-10	6.28 s	5.23 s	6.79 s	5.43 s	
H-13	6.19 br t (8.4)	6.17 br t (8.8)	6.22 br t (8.8)	6.24 br t (8.3)	6.16 br t (9.0)
Ha-14	2.32 overlap	2.26 overlap	-2.40 m	-2.35 m	-2.41 m
Hb-14	2.29 overlap	2.26 overlap	-2.25 m	-2.22 m	-2.41 m
H ₃ -16	1.15 s	1.11 s	1.16 s	1.10 s	1.13 s
H ₃ -17	1.25 s	1.23 s	1.22 s	1.23 s	1.22 s
H ₃ -18	1.82 d (1.3)	1.80 s	1.81 s	1.78 s	1.78 s
H ₃ -19	1.67 s	1.73 s	1.66 s	1.72 s	1.73 s
Ha-20	4.27 ABd (8.3)	4.29 ABbr d (8.6)	4.38 br s	4.41 ABd (8.8)	4.46 ABd (8.8)
Hb-20	4.19 ABd (8.3)	4.19 ABbr d (8.6)	4.38 br s	4.38 ABd (8.8)	4.36 ABd (8.8)
H-2'	4.67 d (2.8)	4.69 br s	4.70 br s	4.68 br s	4.70 br s
H-3'	5.56 dd (9.1, 2.8)	5.56 dd (9.3, 4.4)	5.60 dd (9.3,2.5)	5.59 dd (9.3,2.4)	5.58 dd (9.2,2.5)
H ₂ -6'	2.18 t (7.3)	2.17 t (7.3)	2.19 t (8.3)	2.19 t (7.3)	2.19 t (7.8)
H ₂ -7'	1.56 m	1.55 m	1.55 m	1.55 m	1.55 m
H ₂ -8'	1.23 m	1.24 overlap	1.22 m	1.23 m	1.23 m
H ₂ -9'	1.23 m	1.24 overlap	1.22 m	1.23 m	1.23 m
H ₃ -10'	0.83 t (7.0)	0.83 t (6.8)	0.82 t (7.3)	0.82 t (7.3)	0.83 t (6.6)
<i>o</i> -ph1	8.10 dd (7.3, 1.3)	8.09 dd (7.3, 1.5)	8.15 br d (7.3)	8.15 br d (7.5)	8.16 br d (7.5)
<i>p</i> -ph1	7.60 br t (7.3)	7.61 br t (7.3)	7.62 br t (7.3)	7.62 br t (7.5)	7.64 br t (7.5)
<i>m</i> -ph1	7.49 br t (7.3)	7.32 br t (7.3)	7.52 br t (7.3)	7.53 br t (7.5)	7.54 br t (7.5)
<i>o</i> -ph2	7.38 m	7.38 m	7.41 m	7.39 m	~7.40 m
<i>m</i> -ph2	7.38 m	7.38 m	7.41 m	7.39 m	~7.40 m
<i>p</i> -ph2	7.32 m	7.37 m	7.35 m	7.34 m	7.35 m
1-OH	2.22 s	2.12 s		2.00 s	
7-OH	2.61 br d (3.9)		4.68 d (11.7)	4.73 d (11.7)	4.46 d (11.7)
10-OH		4.34 br s		4.14 br s	
2'-OH	3.78 br s	3.97 br s	3.53 br s	3.49 br d (4.4)	3.76 br s
3'-NH	6.36 d (9.1)	6.48 d (9.3)	6.29 d (9.3)	6.30 d (9.3)	6.42 d (9.2)
4-OAc	2.35 s	2.33 s	2.45 s	2.46 s	2.45 s
10-OAc	2.23 s		2.20 s		

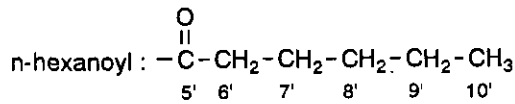
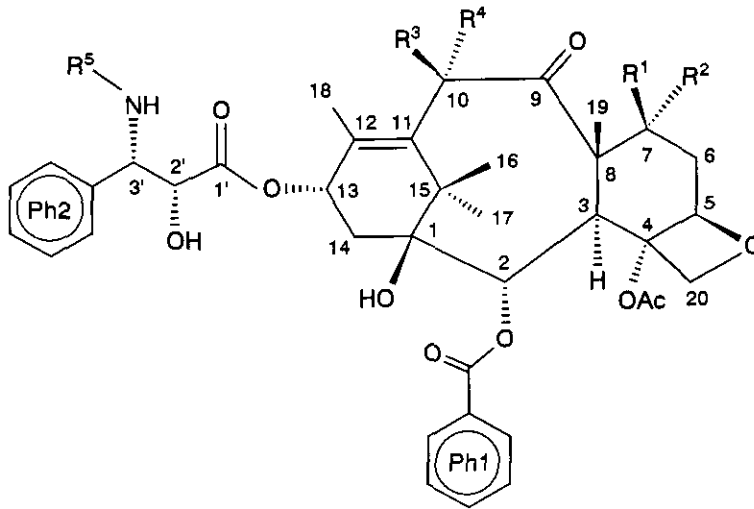
* Taken from reference 2.

Table II. ^{13}C nmr data^{a)} for compounds (2, 6, 7, 8 and 9) in CDCl_3 (100 MHz, δ in ppm from TMS)

carbon		2 ^{b)}	6	7	8	9
C-1	s	78.8	78.5	79.1	79.2	78.9
C-2	d	75.0	74.9	75.3	75.5	74.9
C-3	d	45.6	46.4	40.3	40.3	39.3
C-4	s	81.1	81.0	82.1	82.1	81.6
C-5	d	84.4	84.2	82.7	82.6	82.6
C-6	t	35.6	36.7	36.1	36.3	35.3
C-7	d	72.0	71.8	75.7	75.9	77.3
C-8	s	58.5	57.7	57.5	57.3	57.2
C-9	s	203.6	211.2	207.2	215.1	207.9
C-10		75.6d	74.5d	78.5d	77.9d	188.7 s
C-11	s	133.2	136.0	133.4	135.7	141.2
C-12	s	141.9	138.4	139.7	137.9	142.9
C-13	d	72.3	72.3	72.2	72.4	71.9
C-14	t	35.6	35.6	35.3	35.3	36.0
C-15	s	43.2	43.1	42.7	42.6	40.3
C-16	q	21.9	20.8	21.3	20.7	22.8
C-17	q	26.8	26.4	26.0	26.0	26.1
C-18	q	14.7	14.4	14.8	14.4	14.2
C-19	q	9.6	9.8	16.2	16.7	15.0
C-20	t	76.5	76.5	77.6	77.8	77.2
C-1'	s	172.8	173.3	172.8	172.7	172.7
C-2'	d	73.1	73.1	73.1	73.1	72.9
C-3'	d	54.5	54.4	54.4	54.4	54.5
C-5'	s	173.1	173.3	173.0	173.0	173.4
C-6'	t	36.5	36.4	36.6	36.6	36.5
C-7'	t	25.3	25.4	25.4	25.4	25.4
C-8'	t	31.3	31.3	31.3	31.3	31.3
C-9'	t	22.2	22.3	22.3	22.3	22.3
C-10'	q	13.8	13.9	13.8	13.8	13.8
q-ph1	s	129.2	129.2	129.3	129.3	129.2
o-ph1	d	130.2	130.2	130.3	130.3	130.2
m-ph1	d	128.7	128.7	128.9	128.8	128.8
p-ph1	d	133.6	133.7	133.7	133.7	133.8
C=O ph1	s	166.8	166.8	167.1	167.1	166.8
q-ph2	s	138.1	138.2	138.1	138.1	138.0
o-ph2	d	126.9	126.9	126.8	126.8	126.8
m-ph2	d	128.9	128.8	129.0	129.0	129.0
p-ph2	d	128.2	128.1	128.2	128.2	128.3
4-OAc Me	q	22.5	22.5	22.5	22.5	22.5
4-OAc C=O	s	170.2	170.3	172.2	172.4	172.2
10-OAc Me	q	20.8		20.9		
10-OAc C=O	s	171.2		169.4		

a) The assignments were based on noise decoupling, DEPT, ^1H - ^{13}C COSY, HMBC and comparisons of the data with related compounds.

b) Taken from reference 2.



	R ¹	R ²	R ³	R ⁴	R ⁵
(1)	OH	H	OAc	H	benzoyl
(2)	OH	H	OAc	H	n-hexanoyl
(3)	OH	H	OH	H	benzoyl
(4)	OH	H	OAc	H	tigloyl
(5)	OH	H	OH	H	tigloyl
(6)	OH	H	OH	H	n-hexanoyl
(7)	H	OH	OAc	H	n-hexanoyl
(8)	H	OH	OH	H	n-hexanoyl
(9)	H	OH	=O	H	n-hexanoyl
(10)	H	OH	OAc	H	benzoyl
(11)	H	OH	=O	H	benzoyl

taxol type. We thus elucidated the structures of **6**, **7**, **8** and **9** as 10-deacetyltaxuyunnanine A, 7-epi-taxuyunnanine A, 7-epi-10-deacetyltaxuyunnanine A and 10-deacetyl-10-oxo-7-epi-taxuyunnanine A.

Among the new compounds reported here, **9** is the third to possess a structure in which both C-9 and C-10 were oxidized to a carbonyl carbons.^{5,7}

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4. The yields of the new compounds are as follows: **6**, $3.2 \times 10^{-4}\%$; **7**, $3.3 \times 10^{-5}\%$; **8**, $4.4 \times 10^{-5}\%$; **9**, $6.8 \times 10^{-5}\%$.
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