TAXOL RELATED DITERPENES FROM THE ROOTS OF *TAXUS YUNNANENSIS*

Zhang Hongjie, Yoshio Takeda,* Takashi Matsumoto, Yoshinori Minami,[+] Kenichiro Yoshida,[+] Xiang Wei,[++] Mu Qing,[+++] and Sun Handong*,[+++]

Faculty of Integrated Arts and Sciences, The University of Tokushima, Tokushima 770, Japan; Taiho Pharmaceutical Co. Ltd.,[+] Tokushima 771-01, Japan; Yunnan Academy of Forestry,[++] Kunming 650204, Yunnan, China; Kunming Institute of Botany,[+++] Academia Sinica, Kunming 650204, Yunnan, China

Abstract- Four new taxol related diterpenes were isolated from the roots of *Taxus yunnanensis* together with taxol, cephalomannine, 10-deacetyltaxol, and 10-deacetylcephalomannine and their structures were elucidated 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 cytotoxity 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**), $C_{44}H_{55}O_{13}N$, $[\alpha]_D$ -50.9° ($CHCl_3$), 7-epi-taxuyunnanine A (**7**), $C_{46}H_{57}O_{14}N$, $[\alpha]_D$ -47.3° ($CHCl_3$), 7-epi-10-deacetyltaxuyunnanine A (**8**), $C_{44}H_{55}O_{13}N$, $[\alpha]_D$ -34.9° ($CHCl_3$) and 10-deacetyl-10-oxo-7-epi-taxuyunnanine A (**9**), $C_{44}H_{53}O_{13}N$, $[\alpha]_D$ -70.8° ($CHCl_3$), by spectroscopic means.

Metabolites (**6**, **7**, **8** and **9**) showed very similar ^1H- and ^{13}C 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 5α-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 ^{13}C 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 ^{13}C 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 I. ^{1}H 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)
Hα-6	2.52 ddd (14.8, 9.6, 6.6)	2.52 m	~2.40 m	~2.35 m	2.24 m
Hβ-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)
o-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)
p-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)
m-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)
o-ph2	7.38 m	7.38 m	7.41 m	7.39 m	~7.40 m
m-ph2	7.38 m	7.38 m	7.41 m	7.39 m	~7.40 m
p-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		

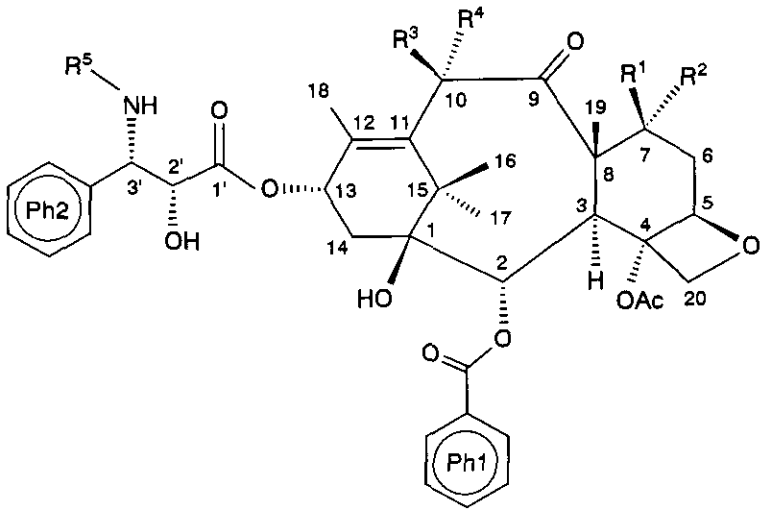
* Taken from reference 2.

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, ^{1}H-^{13}C COSY, HMBC and comparisons of the data with related compounds.

b) Taken from reference 2.



n-hexanoyl : $-\overset{\overset{O}{\|}}{C}-\underset{5'}{CH_2}-\underset{6'}{CH_2}-\underset{7'}{CH_2}-\underset{8'}{CH_2}-\underset{9'}{CH_2}-\underset{10'}{CH_3}$

	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		n-hexanoyl
(10)	H	OH	OAc	H	benzoyl
(11)	H	OH	=O		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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