

## Three Novel Bicyclic Taxoids from the Needles of the Chinensis yew, *Taxus chinensis* var *mairei*

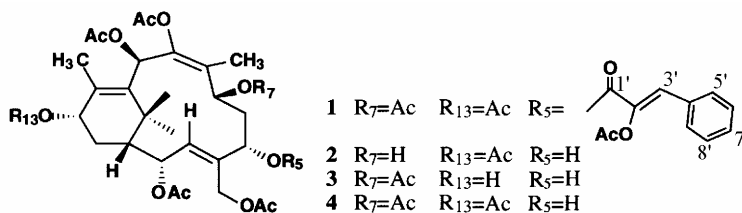
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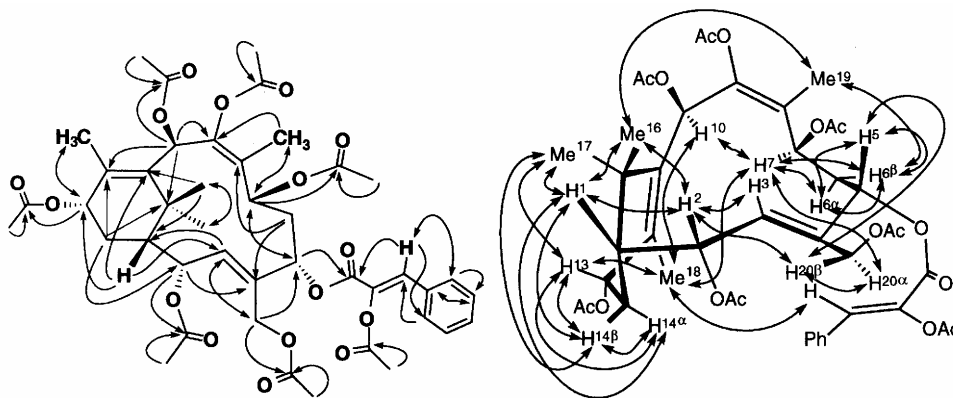
**Abstract:** Three novel bicyclic taxane diterpenoids with the rare 6/12-membered rings were isolated from the needles of *Taxus chinensis* var. *mairei*. The structures were established with the help of 1D and 2D NMR spectral analysis.

**Keywords:** *Taxus chinensis* var. *mairei*; Taxaceae; taxoids; bicyclic taxanes.

Phytochemical investigation on the needles of *Taxus chinensis* var. *mairei* resulted in the isolation of three new bicyclic taxoids **1**–**3** along with taxachitriene A **4**<sup>1</sup>. Compound **1**,  $[\alpha]_D^{26} +14.5$  (c 0.001, CHCl<sub>3</sub>), was isolated as a colorless gummy substance. The IR spectrum showed the acetoxy and  $\alpha,\beta$ -unsaturated carbonyl system bands at 1730 and 1650 cm<sup>-1</sup>. HR-FAB-MS analysis at *m/z* 847.3152 established the quasi-molecular formula as C<sub>43</sub>H<sub>52</sub>O<sub>16</sub>Na ([M+Na]<sup>+</sup>,  $\Delta(B-0.1)$  mmu). Its <sup>1</sup>H-NMR spectrum (**Table 1**) showed the characteristic signals of four tertiary methyl groups of taxoids, and seven acetyl groups and a mono-substituted benzene group. Meanwhile, <sup>13</sup>C-NMR spectrum also demonstrated four additional double bonds and a signal due to an  $\alpha,\beta$ -unsaturated carbonyl carbon (161.55 ppm) in the structure of **1**. From these observations together with the unsaturation numbers, **1** was deduced as a bicyclic taxane derivative with 6/12-membered rings (3,8-secotaxane), as represented by taxachitriene A **4**<sup>1</sup>. This was in good agreement with the following features of **1**. Compound **1** lacked a characteristic signal due to H-3a, which was usually appeared at 2.5–4.1 ppm with a coupling constant of ca 2.0–9.5 Hz in the 6/8/6 or 5/7/6-membered three-rings taxoids<sup>2</sup>. The signals of H-20a and H-20 $\beta$  in **1** appeared with a relatively larger  $\Delta\delta$  and bigger coupling constant (H-20a, 4.91 ppm, d, J=12.94 Hz; H-20b, 4.43 ppm, d, J=12.94 Hz).



**Figure 1.** H-C Long-range correlations (left) observed from the HMBC spectrum and relative stereochemistry (right) deduced from the NOE correlations of **1**.



The chemical shift of H-20a and H-20b implied that 20-OH was acetylated, which was confirmed by the HMBC spectrum (**Figure 1**). Detailed analysis of the 1H-1H COSY spectrum revealed the connectivities of C<sub>13</sub>-C<sub>14</sub>-C<sub>1</sub>-C<sub>2</sub>-C<sub>3</sub>, C<sub>5</sub>-C<sub>6</sub>-C<sub>7</sub>. Of them, C<sub>13</sub>, C<sub>2</sub> and C<sub>7</sub> attached to acetoxy groups as revealed by the HMBC spectrum. The signal at 7.27 ppm (1H, br.s) was H-10 and an acetoxy group attached to C-10 as demonstrated by the HMBC spectrum. C-9, as a tetrasubstituted carbon, exhibited cross peaks with H-10 and 19-CH<sub>3</sub> in the HMBC spectrum, appeared at an unusual downfield shift (143.68 ppm), suggesting that C-9 was an olefinic carbon and attached to an acetoxy group. Both 1H- and <sup>13</sup>C-NMR spectra showed that there was a substituted cinnamoyl group in **1**. A singlet signal (7.55 ppm, 1H, s) showed correlations with an α,β-unsaturated carbonyl carbon (161.55 ppm) as well as two *ortho*-carbons of benzene group in the HMBC spectrum and assigned to an olefinic β-H of the cinnamoyl moiety. The remaining acetoxy group, which was connected to a tetrasubstituted carbon as deduced from the HMBC spectrum, should be attached to α-C of cinnamoyl group. This was further supported by the prominent fragment ion at *m/z* 189 in both EI-MS and FAB-MS, which was analyzed for C<sub>11</sub>H<sub>9</sub>O<sub>3</sub> by HR-EI-MS. The HMBC spectrum revealed the α-substituted cinnamoyl group was connected to C-5. Taking the above analysis and the subsequent work on the NOESY experiments into consideration, the structure of **1** was determined as shown in the above chart. α-Substituted cinnamoyl group is much rare in the nature. The relative stereochemistry of **1** was deduced from NOESY spectrum as shown in **Figure 1**. The regiochemistry of the 12-membered ring part was determined to be 3E and 8E from observation of NOEs between H-2 and H-20b, H-7 and H-10, respectively. The NOESY correlation between H-13 and 17-CH<sub>3</sub> revealed that the ring A had a boat conformation and H-13 was β-oriented, while the correlations between H-2 and 16-CH<sub>3</sub>, H-5 and H-20β indicated the β-orientations of H-2 and H-5. NOESY cross-peaks between H-7 and 18-CH<sub>3</sub>, H-10 and 18-CH<sub>3</sub> revealed that the relative configurations of H-7 and H-10 were α-oriented.

**Table 1.**  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectral data of compound **1** (500 MHz,  $\text{CDCl}_3$ ).

position	$\delta^{13}\text{C}$	$\delta^1\text{H}$	$J(\text{Hz})$	$^1\text{H}$ - $^1\text{H}$ COSY
1	46.30	1.80m	4.64, 10.50	H-2, H-14 $\alpha$ , 14 $\beta$
2	68.79	5.79dd	10.50	H-1, H-3
3	125.28	5.83br.d		H-2
4	132.02			
5	71.19	5.75br.s		H-6 $\alpha$ , H-6 $\beta$
6 $\alpha$	35.50	2.10m		H-5, H-6 $\beta$ , H-7
6 $\beta$		2.62ddd	2.93, 1079, 16.11	H-5, H-6 $\alpha$ , H-7
7	66.56	5.58br.d	10.79	H-6 $\alpha$ , 6 $\beta$ , H-10
8	124.43			
9	143.68			
10	68.31	7.27br.s		H-7, 18- $\text{CH}_3$ , 19- $\text{CH}_3$
11	136.81			
12	136.27			
13	69.45	5.20br.d	8.79	H-14 $\alpha$ , 14 $\beta$ , 18- $\text{CH}_3$
14 $\alpha$	25.12	2.04m		H-1, 13, 14 $\beta$
14 $\beta$		2.49ddd	7.57, 8.79, 16.11	H-1, 13, 14 $\alpha$
15	36.17			
16	33.17	1.10s		
17	25.45	1.30s		
18	17.24	2.21br.s		H-10, 13
19	12.32	1.66br.s		H-10
20 $\alpha$	59.73	4.91d	12.94	H-20b
20 $\beta$		4.43d	12.94	H-20a
1'	161.55			
2'	135.27			
3'	128.65	7.75s		
4'	131.92			
5', 9'	130.32	7.55m		H-6', 7', 8'
6', 8'	129.02	7.42m		H-5', 7', 9'
7'	130.28	7.42m		H-5', 6', 8', 9'
2-OAc	169.81			
	21.17	2.22s		
7-OAc	169.29			
	20.09	2.08s		
9-OAc	168.43			
	20.87	2.05s		
10-OAc	167.98			
	20.79	2.01s		
13-OAc	170.92			
	20.75	1.96s		
20-OAc	170.68			
	20.47	1.79s		
2'-OAc	167.98			
	21.86	2.34s		

Compound **2** showed the pseudo-molecular ion peak at  $m/z$  617 ( $\text{M}+\text{Na}$ ) $^+$  in the FAB-MS spectrum, and the molecular formula was determined as  $\text{C}_{30}\text{H}_{42}\text{O}_{12}$  by HR-FAB-MS ( $m/z$   $\text{C}_{30}\text{H}_{42}\text{O}_{12}\text{Na}$ , 617.2577,  $\Delta+0.3$  mmu). The  $^1\text{H}$ -NMR spectrum of **2** closely resembled that of taxachitriene A **4**<sup>1</sup> with the exception of H-7 shifted upfield from 5.07 ppm to 4.40 ppm and signal for one acetyl group absent. Therefore, the structure was proposed as 7-deacetyltaxachitriene A [(3E, 8E)-2 $\alpha$ ,9,10 $\beta$ ,13 $\alpha$ ,20-pentaacetoxy-3,8-seco-taxa-3,8,11-trien-5 $\alpha$ ,7 $\beta$ -diol]

**Table 2.** <sup>1</sup>H-NMR spectral data of compounds **2** and **3** (300 MHz, CDCl<sub>3</sub>)

Position	2		3	
	δ <sup>1</sup> H(J, Hz)	<sup>1</sup> H- <sup>1</sup> H COSY	δ <sup>1</sup> H(J, Hz)	<sup>1</sup> H- <sup>1</sup> H COSY
1	1.81 m	H-2	1.78 br.t (5.8)	H-2
2	5.79 dd (11.2, 4.4)	H-1,3	5.76 dd (10.8, 4.4)	H-1, 3
3	4.4)	H-2	6.42 b.br.d (10.8)	H-2
5	6.22 br.d (11.2)	H-6α, 6β, 20	4.47 br.s	H-6α, 6β, 20
6α	4.52 br.s	H-5, 6β, 7	2.55 m	H-5, 6β, 7
6β	2.38 m	H-5, 6α, 7	2.05 m	H-5, 6α, 7
7	2.00 m	H-6α, 6β	5.13 br.d (8.2)	H-6α, 6β
10	4.40 br.d (7.2)	19-CH <sub>3</sub>	6.97 d (1.1)	19-CH <sub>3</sub>
13	6.99 d (1.4)	H-14β, 18-CH <sub>3</sub>	4.18 br.d (8.8)	H-14β, 18-CH <sub>3</sub>
14α	5.32 br.d (9.2)	H-14β	2.24 m	H-14β
14β	2.12 m	H-1, 13, 14α	2.47 m	H-1, 13, 14α
16	2.55 m		1.25 s	
17	1.27 s		1.09 s	
18	1.12 s	H-13	2.04 br.s	H-13
19	2.01 br.s	H-10	1.63 s	H-10
OAc	1.60 br.s		2.22 s	
	2.22 s		2.09 s	
	2.14 s		2.03 s	
	2.03 s		1.96 s	
	2.02 s		2.18 s	
	1.98 s			

Compound **3** had a molecular formula of C<sub>30</sub>H<sub>42</sub>O<sub>12</sub> as elucidated by HR-FAB-MS (m/z C<sub>30</sub>H<sub>42</sub>O<sub>12</sub>Na, 617.2572, Δ-0.2 mmu) analysis. The <sup>1</sup>H-NMR spectrum of **3** also closely resembled that of taxachitriene A **4**<sup>1</sup> with the exception of H-13 shifted upfield from 5.27 ppm to 4.18 ppm with concomitant absence of one acetyl group. Therefore, the structure of **3** was proposed as 13-deacetyltaxachitriene A [(3E,8E)-2α,7β,9,10β,20-pentaacetoxy-3,8-secotaxa-3,8,11-trien-5α,13α-diol]

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