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Phytochemical Study on the Constitution of the Bark of Chinese Yew, *Taxus Mairei*

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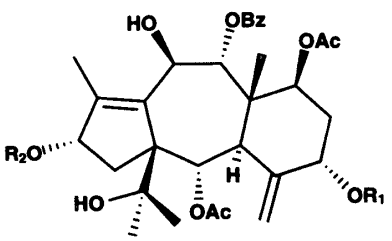
Summary

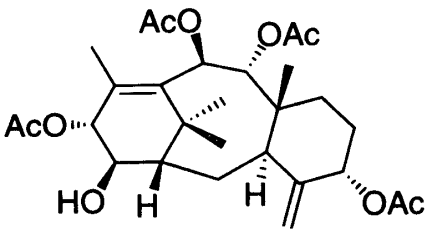
A phytochemical study on the constitution of the bark of Chinese yew, *Taxus mairei*, led to the isolation of five novel taxane diterpenoids with the rearranged skeleton. The structures of these new compounds were established unambiguously as 2α, 7β, 13α-triacetoxy-9β-benzoyloxy-11(15→1)-*abeo*taxa-4(20), 11-diene-5α, 10β, 15-triol (**1**), 2α, 7β-diacetoxy-9α-benzoyloxy-5α-cinnamoyloxy-11(15→1)-*abeo*taxa-4(20), 11-diene-10β, 13α, 15-triol (9-deacetyl-9-benzoyl-10-debenzoyl-5-cinnamoyl-taxchinin A) (**2**), 14β-hydroxytaxusin (**3**), 9α-benzoyloxy-4α, 7β-diacetoxy-5β, 20-epoxy-2α, 10β, 13α, 15-tetrahydroxy-11(15→1)-*abeo*taxane (**4**), and 2α, 7β-diacetoxy-9α-benzoyloxy-4α, 20-epoxy-11(15→1)-*abeo*tax-11-ene-5α, 10β, 13α, 15-tetraol (**5**) on the basis of 1D and 2D NMR spectra including ^{1}H NMR, ^{1}H-^{1}H COSY, ^{13}C NMR, DEPT, HMBC, HMQC, NOESY, and HR-FAB-MR analysis. In addition, more than thirty known compounds were also isolated, and their structures were determined with the aid of spectral data and by comparison with the data described in the literatures.

Taxol® (paclitaxel), a taxne diterpene original isolated from the bark of *Taxus brevifolia* (1), is one of the most exciting leads in cancer chemotherapy in the last 25 years. It can be used to treat developed ovarian and breast cancer, and showed promising effects in regard to a variety of other types of cancers, such as head and neck, lung, gastrointestinal, and bladder (2). Its unusual biological activity, mechanism of novel action *via* promoting the formation of microtubules to inhibit their disassembly by binding to B-tubulin, intriguing structure and scarcity in plants have spurred a flurry of investigation on the every part of all the species of this genus, and which has led to more than 250 natural taxanes being isolated in the last two decades (3, 4), there is still great interest in the isolation of new taxanes from various *Taxus* spp. In previous researching, the authors isolated a new compound from the heartwood of *T. cuspidata* (5); in order to



1 R_1=H R_2=Ac

2 R_1=cinn R_2=H



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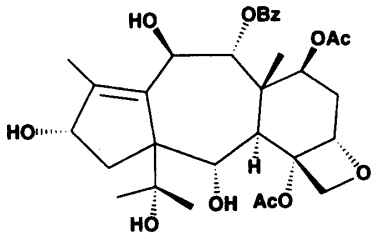

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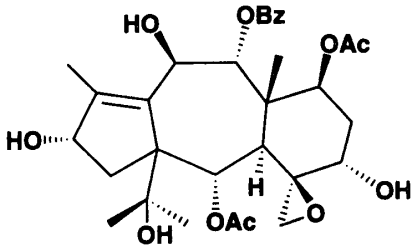

5

FIG. 1. The structures of compounds **1**-**5**.

continue this work, we investigated the constitution of the bark of *T. mairei*.

T. mairei, which is indigenous to China, is an evergreen and is mainly distributed in Jiangxi and Fujian Provinces in the south east of the People's Republic of China. Previous studies have led to the isolation of more than 20 new taxanes from this plant, most of which have the normal taxane skeletons with a 6/8/6 membered ring system (6-16). Recently, we re-examined the bark of this plant which was growing in a different area from those examined by other groups in search of new precursors fit for semisynthesis. In addition to taxol and other normal taxanes, five novel taxane diterpenoids were isolated from the bark of *T. mairei*, four of them with the rearranged 11 (15→1)-*abeo*taxane skeletons. 11(15→1)-*Abeo*taxanes, first reported in 1992 (17), were recognized as the rapidly growing family of taxoid diterpenes (18). Another one was a rare 14β-OH derivative of taxusin. In this communication, we will describe the isolation and structure elucidation of these novel taxane diterpeneoids from the bark of *T. mairei*.

Materials and Methods

General experimental

Silica gel 60 (Merck 100-200 mesh) was used for conventional CC. Thin layer chromatography (TLC) were conducted on precoated silica gel Kieselgel 60 F_{254} plates (0.2 mm thick), and the spots were detected by ultraviolet (UV) illumination and by spraying 10% H_2SO_4, followed by heating. The melting

points were measured on a MRK micro-melting point apparatus and were uncorrected. Optical rotations were recorded on a SEPA-300 polarimeter. The UV spectrum was recorded on a Shimadzu UV-1600 spectrophotometer. IR spectrum was recorded on a Jasco IR-810 spectrophotometer for chloroform solutions. Optical rotations were measured on a Horiba SEPA-300 polarimeter. MS were obtained on a JMS-Dx 305 HF mass spectrometer, using the FAB method and glycerol as a matrix. NMR spectra were taken on Varian GEMINI 2000/300 (300 MHz) and Varian Unity Inova 500 (500 MHz) spectrometers operating at 500 and 300 MHz for ^{1}H, and 125 MHz for ^{13}C respectively in $CDCl_3$ at ambient temperature, coupling constants (J values) are listed in hertz (Hz), Splitting patterns have been designated as following s (singlet), d (doublet), t (triplet), and m (multiplet), dd (double doublet), ddd (double double doublet), and ^{1}H chemical shifts data were expressed as parts per million downfield from tetramethylsilane (TMS) as internal reference. ^{1}H-^{1}H connectivities were determined *via* COSY experiments. ^{13}C shifts were based on the $CDCl_3$ signal at 77.0 ppm.

Plant material

The bark of *T. mairei* was collected from Jiangxi Province in the autumn of 1995. The plant material was authenticated by professor R. L. Liu of the Zhangzhou Forestry School, where a voucher specimen has been deposited (#950823). The material was maintained at 0°C until extraction.

Extraction and isolation

Air dried bark (13.25 kg) was extracted twice with MeOH at room temperature. The extracts were treated with activated charcoal and concentrated into a syrup under reduced pressure. This syrup was then diluted with water and the aqueous solution was extracted with EtOAc successively. The combined EtOAc extract, upon evaporation, was adsorbed onto silica gel and subjected to normal phase silica gel open column chromatography. Elution with hexane and hexane-EtOAc (2 : 1, 1 : 1, 1 : 2, 1 : 4 and EtOAc) gave six fractions, each of which was further purified by column chromatography and preparative TLC, separately, five new compounds along with more than thirty known compounds were produced.

Results and Discussion

The compound **1** was obtained as a white amorphous powder; m.p. 121-122°C, $[\alpha]_D^{24}$: +1.49° (c=0.70, $CHCl_3$). The FAB-MS spectrum gave ion peaks at m/z: 597 $[MH\text{-}H_2O]^+$. A combined analysis of the ^{1}H-NMR and the ^{13}C-NMR data, the molecular formula was determined as $C_{33}H_{42}O_{11}$. The ^{1}H-NMR spectrum showed the characteristic taxoid signals, including singlets for four methyl groups at 1.13, 1.27, 1.40 and 1.68 ppm, and a pair of doublets for an

exocyclic methylene group (4.86 ppm, 1H, br. s and 5.47 ppm, 1H, br. s). The presence of an exocyclic methylene group was verified further by two signals at 147.09 ppm and 113.26 ppm in the ^{13}C-NMR spectrum. The compound also showed to have two methylene groups, one methine group, six oxymethine groups, two quaternary carbons, one oxyquarternary carbon, three acetyl groups, one benzoyl group and two tetrasubstituted olefinic carbons besides an exocyclic methylene group in the ^{1}H and ^{13}C-NMR spectra.

This compound was distinguished from normal taxanes via the careful observation of the signals of their aromatic protons in the ^{1}H-NMR spectrum. The two ortho-protons of a benzoyl group of rearranged taxane resonated as a doublet in a region more upfield than 8.0 ppm (*ca.* 7.8 ppm), while those of normal taxane resonated in downfield region than this position (*ca.* 8.2 ppm) (4). The ortho-protons of the benzoyl group in **1** resonated as a doublet at 7.91 ppm, which suggested **1** as a 11(15→1)-*abeo*taxane: *i.e.* brevifoliol type taxane. The evidence for the brevifoliol skeleton for **1** was further supported by two key results: the first was the assignment of the ^{13}C-NMR signal at 76.03 ppm to C-15, which was confirmed *via* a correlation with the H-2 and H-14 signals in the HMBC spectrum. The downfield nature of this signal indicated that C-15 must be oxygenated. In addition, the C-1 signal, which correlated with H-3, H-10 and H-13 in the HMBC spectrum, resonated at an unusually lower field (66.76 ppm) than that in normal taxane (*ca.* 46 ppm). These two signals in the ^{13}C-NMR were used to distinguish 11(15→1)-*abeo*taxane from normal taxane. The other was that the lack of a diagnostic three-bond correlation from H-16 and H-17 to C-11 eliminated the normal taxane structure from consideration (19-22). A detailed analysis of its ^{1}H NMR, ^{13}C NMR, and HMBC led to its structure being established as a 2α, 7β, 13α-triacetoxy-9α-benzoyloxy-11(15→1)-*abeo*taxa-4 (20), 11-diene-5α, 10β, 15-triol (Fig. 1).

Compound **2** was isolated as a white powder, mp 148-149°C (MeOH, uncorrected), $[\alpha]_D^{24}$ −2.73° (c=1.10, $CHCl_3$). A HR-MR (FAB) analysis gave a molecular formula of $C_{40}H_{46}O_{11}$. All the ^{1}H-NMR signals of **2** were very broad at 40°C and 20°C; however, decreasing the temperature to 0°C resulted in convergence into a normal narrow line width of two components that appeared in a ratio of 2/1. Each spectrum showed the characteristic taxoid signals including two acetyls, one benzoyl and one cinnamoyl group along with one exo and one endo double bonds. Three hydroxy groups were also considered from the molecular formula. Unusual downfield shifts for the C-1 and the C-15 signals (65.92 and 76.00 ppms for the major one, and 67.85 and 76.13 ppms for the minor one) indicated that both C-15s were oxygenated and that these compounds had an 11(15→1)-*abeo*taxane skeleton. This was further supported by the HMBC correlation of H-10 with C-1. A determination of the relative configurations of both components was done using the ^{1}H-^{1}H coupling constants and observations of the

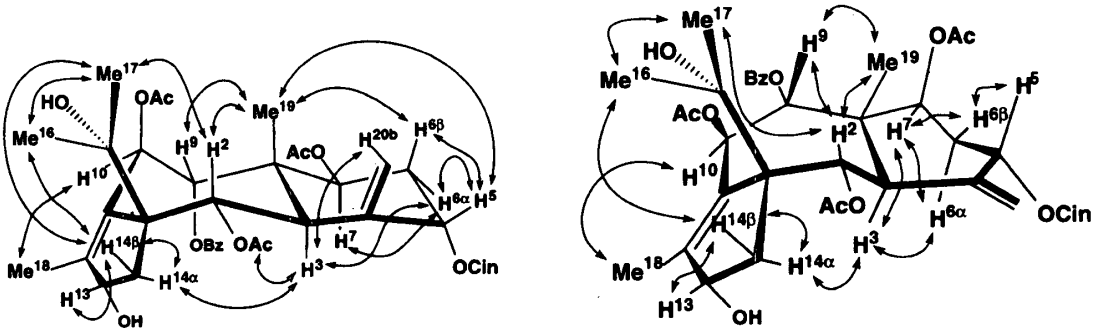

FIG. 2. The key NOEs observed for **2** (ROESY at 0°C)

NOEs (Fig. 2): 1β, 2β, 3α, 5α, 7β, 19β, 9α, 10β and 13α. The absolute configurations were assumed to be shown as **2** because the skeletons of all natural taxoids had the same absolute stereochemistry. These results showed that the two components were the conformational isomers that had slowly equilibrated at 40°C and 20°C. Consequently the structure of **2** was established as 2α, 7β-diacetoxy-9α-benzoyloxy-5α-cinnamoyloxy-11(15→1)-*abeo*taxa-4(20), 11-diene-10β, 13α, 15-triol (9-deacetyl-9-benzoyl-10-debenzoyl-5-cinnamoyl-taxchinin A). The slow equilibration between the two conformers was typical for 11(15→1)-*abeo*taxanes (21). A conformational analysis of these isomers was done as follow as the NOE was observed between H-2 and H-9, *i.e.*, these were brought so close together that the B ring of **2B** adopted a boat conformation. The conformational difference between the C rings of **2A** and **2B** was confirmed by the NOE relationships between H-5, 6α, 6β, 7 and 19. For **2B**; the NOEs between H-5 and H-6α, H-5 and H-19, and H-6β and H-19 (observed for **2A**) disappeared ; whereas, the NOE between H-6β and H-7 appeared . The proposed stereostructures for **2A** and **2B** are depicted in Fig. 2. The major conformer (**2A**) adopted a chair/half-chair conformation of B/C ring with a small coupling constant between H-9 and H-10 ($J_{9,10}=3.9$ Hz), while the minor one (**2B**) took boat/half-boat conformation ($J_{9,10}=10.3$ Hz). These results were in good accordance with those from previous studies (21).

Compound **3** was isolated as colorless crystals in 0.0001% yield. mp. 208-209°C (MeOH), $[\alpha]_D^{24}$ +7.64 ($c=0.48$, $CHCl_3$). Intensive infrared absorption at 3,460 cm$^-$ suggested there are free hydroxyl groups in **3**. The ^{1}H- and ^{13}C-NMR spectra (Table 1 and 2) showed that this compound consisted of a normal taxa-4(20), 11-diene skeleton with four acetoxy and one hydroxy groups. The molecular formula was determined to be $C_{28}H_{40}O_9$, as the FAB-MS spectrum gave the ion peaks at m/z 543 ($M+Na^+$) and 521 ($M+H^+$). The ^{1}H-NMR spectrum closely resembled that of taxusin ($C_{28}H_{40}O_8$) (23), and the appreciable difference was the absence of one H-14 proton (*ca.* 2.7 ppm) and a downfield shift of one H-14 proton (3.60 ppm). Base on the molecular formula and the ^{1}H-NMR spectrum, **3** seemed

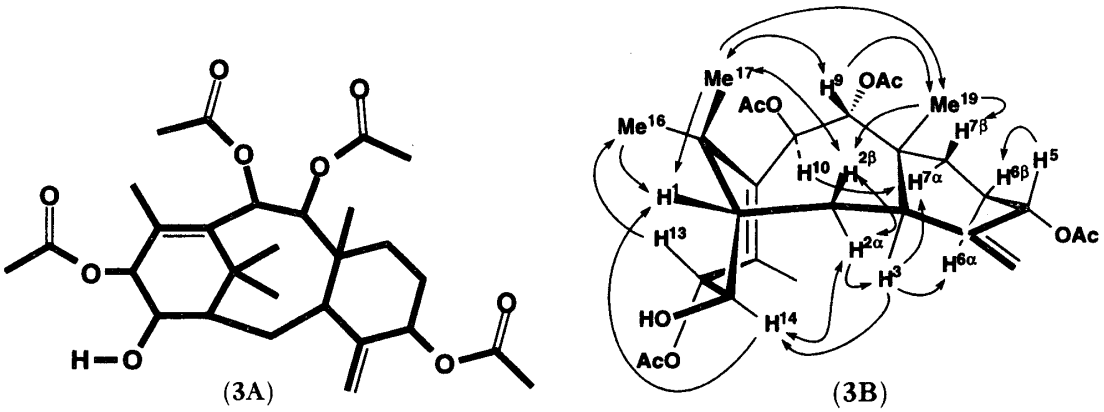

FIG. 3. HMBC (**3A**) and NOE (**3B**) correlations observed for **3**. Protons and carbons were correlated through bold bonds, most protons were ommitted for clarity.

to be a 14-hydroxylated derivative of taxusin. This was supported by the ^{1}H-^{1}H COSY coupling between H-14 and OH, and the HMBC correlation between C-1 and OH [Fig. 3 (**3A**)]. From a combined analysis of the ^{1}H-^{1}H-COSY, HMBC and NOE difference spectra [Fig. 3 (**3B**)], the positions and the configurations of the four acetoxy groups (5α, 9α, 10β and 13α) were deduced. The configuration of the 14-OH group was determined to be β because H-14 showed NOEs with H-2α and H-3. This β-orientation of the 14-OH group had the same configuration as those of other natural taxanes: baccatin III type, taiwanxan type, and austrotaxine type (3, 24, 25). The proposed conformation of **3** was illustrated in Fig. 3 (**3B**) by considering the observed NOEs. Finally, the structure of **3** was established as 14β-hydroxytaxusin [5α, 9α, 10β, 13α-tetraacetoxytaxa-4(20), 11-dien-14β-ol].

Compound **4** was isolated as a white gum in a 0.00004% yield from the dry material. IR absorptions at 3.370, 1.730, 1.718, 1.640, and 1.600 implied that **4** possessed hydroxy, ester, α, β-unsaturated ester, and benzene groups, respectively. FAB-MS gave the ion peaks at m/z 589 $(M+H)^+$. HR-FAB-MS analysis revealed the quasi-molecular formula to be $C_{31}H_{41}O_{11}$ (found 589.2665; calcd. 589.2646). Based on a combined analysis of the MS, and subsequent analysis on the ^{1}H-NMR and ^{13}C-NMR spectra, the molecular formula was determined as $C_{31}H_{40}O_{11}$. Its ^{1}H-NMR spectrum, tabulated in Table 1, showed the characteristic taxoid signals, including singlets for four methyl groups at 1.09, 1.55, 1.42, and 1.67 ppm. The chemical shift of the characteristic proton resonances due to the oxetane moiety were identical with two doublets at 4.17 (1H, d, $J=8.8$ Hz) and 3.97 (1H, d, $J=8.8$ Hz) ppm appeared as an AB system for the C-20 methylene bridge. **4** was also shown to have two methylene groups, one methine group, six oxymethine groups, two quaternary carbons, two oxyquarternary carbons, two acetyl groups, one benzoyl group and two fully substituted olefinic carbons in the

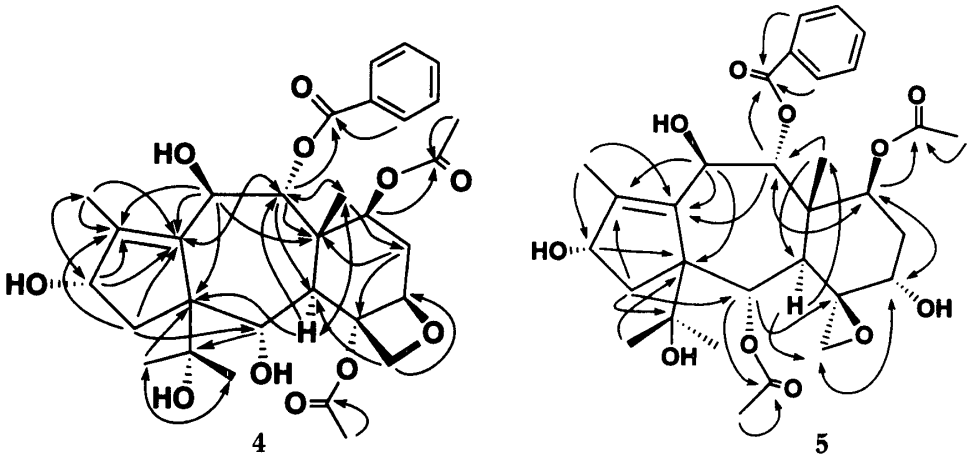

FIG. 4. Selected H/C correlations observed by HMBC spectra of **4** and **5**, most protons were not showed for clarity.

^{1}H- and ^{13}C-NMR spectra. The assignment of these and other groups on the taxane skeleton was made by an analysis of the ^{1}H-^{1}H COSY and HMBC spectra. A detailed interpretation of its NMR data showed that the structure of **4** was as 9α-benzoyloxy-4α, 7β-diacetoxy-5β, 40-epoxy-2α, 10β, 13α, 15-tetrahydroxy-11(15→1)-*abeo*taxane. A coupling constant between H-9β and H-10α of 4.3 Hz and the unusual chemical shifts of the H-3α, H-9β and H-19 methyl groups indicated that the B/C-rings of **4** were in the rare chair-chair conformations instead of the common chair-boat conformations, for which these values differ dramatically (21). A NOESY spectrum was run on **4** and only the following correlations were observed: H-6α/H-6β, 7α; H-9β/H-10α; H-14α/14β; H-2β/3α; H-20a/20b. This compound closely resembles taxchin L (15), which was isolated from the same plant, but **4** only has one conformation and the ^{1}H NMR spectrum showed sharp signals for all the protons at ambient temperatures, and some differences in the NMR data also observed.

Compound **5** was isolated as a white amorphous solid in a 0.00003% yield. mp 155-156°C, $[\alpha]_D^{24}$ −7.81°C (c=0.002, $CHCl_3$); UV λ_{max}^{MeOH} nm: 228 (1940); IR ν_{max} ($CHCl_3$) cm^{-1}: 3.350, 2.920, 1.740, 1.720, 1.700, 1.365, 1.278, 1.225, 1.062, 934, 750 and 708. FAB-MS gave the ion peaks at m/z 611 $(M+Na)^+$, 589 $(M+H)^+$, 545 $(M-COCH_3)^+$, 529 $(M+H-HOAc)^+$. HR-FAB-MS also gave the formula of $C_{31}H_{40}O_{11}Na$ (611.2465; calcd. 611.2468). From combined analyses of the MS, and subsequent works on the ^{1}H-NMR and ^{13}C-NMR spectra, the molecular formula was determined as $C_{31}H_{40}O_{11}$. Its ^{1}H-NMR spectrum showed the characteristic taxoid signals, including singlets for four methyl groups at 1.07, 1.25, 1.50 and 2.04 ppm. The upfield signals of 2.21 (1H, d, J=5.2 Hz) and 3.41 (1H, d, J=5.2 Hz) ppm appeared as an AB system, which is indicative of a terminal methylene group of the epoxide ring of baccatin I type (3, 22), which was further verified by two ^{13}C-NMR signals at 59.50 ppm and 49.67 ppm. **5** Also showed two

TABLE 1. *^1H NMR Data of Compounds 1-5 (300 MHz, $CDCl_3$)*

position	1	2a	3b	4	5
	^1H (mul. J)	^1H (mul. J)	^1H (mul. J)	^1H (mul. J)	^1H (mul. J)
1			1.78 (dd, 4.8, 2.4)		
2	5.86 (d, 8.5)	5.92 (d, 8.8)	1.84 (ddd, 15.6, 5.9, 2.4)	4.89 (d, 8.0)	5.95 (d, 6.5)
3	3.19 (d, 8.5)	3.30 (d, 8.8)	2.78 (d, 5.9)	2.55 (d, 8.0)	3.17 (d, 6.5)
5	4.71 (t, 2.2)	5.67 (br.t, 8.1)	5.35 (m)	3.95 (br.s)	3.12 (s)
6a	2.10 (m)	2.04 (m)	1.66 (m)	2.16 (dd, 13.7, 12.4)	1.89 (br.d, 13.0)
6b	1.88 (ddd, 14.5, 9.0, 2.0)	2.24 (m)	1.83 (br.d, 11.4)	1.81 (dt, 13.7, 3.3)	2.02 (m)
7	4.79 (t, 8.8)	4.89 (dd, 10.0, 8.3)	1.72 (m)	5.38 (dd, 12.4, 3.3)	5.45 (dd, 11.5, 5.0)
9	5.22 (d, 4.0)	5.25 (d, 3.9)	5.89 (d, 10.7)	5.21 (d, 4.3)	6.05 (d, 5.5)
10	4.94 (d, 4.0)	4.93 (d, 3.9)	6.05 (d, 10.7)	4.91 (d, 4.3)	4.72 (d, 5.5)
13	5.56 (m)	4.60 (m)	5.74 (dd, 4.9, 1.4)	4.55 (m)	4.62 (br.s)
14a	2.15 (m)	2.04 (m)	3.60 (d, 4.9)	1.94 (dd, 14.6, 6.8)	1.63 (dd, 14.2, 7.5)
14b	2.42 (dd, 14.7, 6.6)	2.36 (dd, 7.6, 7.1)		3.22 (dd, 14.6, 6.9)	2.27 (14.2, 6.0)
16	1.13 (s)	1.10 (s)	1.21 (s)	1.09 (s)	1.25 (s)
17	1.27 (s)	1.29 (s)	1.66 (s)	1.55 (s)	1.50 (s)
18	1.40 (s)	1.49 (s)	2.12 (s)	1.42 (s)	1.71 (s)
19	1.68 (s)	1.73 (s)	0.74 (s)	1.67 (s)	1.07 (s)
20a	4.86 (s)	5.33 (s)	5.22 (d, 1.1)	4.17 (d, 8.8)	2.21 (d, 5.2)
20b	5.47 (s)	5.00 (s)	4.89 (d, 1.6)	3.97 (d, 8.8)	3.41 (d, 5.2)
Ph-*o*	7.91 (d, 7.7)	7.92 (d, 7.1)		7.92 (br.d, 7.4)	8.00 (d, 7.5)
Ph-*m*	7.53 (m)	7.54 (m)		7.42 (m)	7.45 (t, 7.5)
Ph-*p*	7.56 (m)	7.54 (m)		7.53 (m)	7.56 (t, 9.0)
2-Ac	2.11 (s)	1.98 (s)			2.04 (s)
4-Ac				1.97 (s)	
5-Ac			2.02 (s)		
7-Ac	1.94 (s)	2.04 (s)		2.17 (s)	2.05 (s)
9-Ac			2.06 (s)		
10-Ac			2.16 (s)		
13-Ac	1.99 (s)		2.17 (s)		

a ^1H NMR data of cinnamoyl group: H-22, 6.44 (d, 16.1), H-23, 7.70 (d, 16.1), H-Ph, 7.38-7.46 (m).
b H-2b, 1.95 (dd, 156, 4.8), H-7b, 1.76 (m).

TABLE 2. *^{13}C NMR Data of Compounds 1-5 (500 MHz, $CDCl_3$).*

position	1	2*	3	4	5
1	66.76	65.92	50.45	64.67	65.83
2	70.04	69.41	27.26	68.52	69.89
3	45.04	44.95	39.01	34.97	37.27
4	147.09	141.19	148.09	73.29	59.50
5	65.83	68.36	76.30	69.39	75.80
6	35.59	32.30	29.68	29.70	29.67
7	71.35	71.16	27.18	70.01	68.90
8	43.92	43.39	42.94	44.21	44.48
9	76.03	75.54	77.20	75.77	81.10
10	68.03	68.10	72.27	69.39	66.98
11	137.32	134.59	137.31	133.19	138.37
12	144.11	147.64	134.76	146.15	145.84
13	80.13	77.43	81.28	78.13	75.62
14	37.95	40.36	79.12	39.78	40.23
15	76.03	76.00	39.39	75.58	76.65
16	27.05	27.73	31.04	28.70	27.92
17	26.89	27.00	27.20	29.02	29.69
18	13.09	12.86	14.90	12.78	11.13
19	14.49	14.52	17.48	13.46	14.10
20	113.28	114.69	144.37	72.09	49.67
Ph-*o*	128.36	133.21		120.39	130.29
Ph-*m*	129.47			128.55	129.77
Ph-*p*	133.27			134.62	128.39
Ph-*i*	128.71			129.54	133.00
PhC=O	164.96	165.05		164.54	167.70
2-AcO	21.80	21.47			21.63
	170.77	170.82			169.69
4-AcO				21.21	
				169.94	
5-AcO			21.44		
			169.77		
7-AcO	21.13	21.72		20.70	21.52
	170.03	170.13		170.08	171.69
9-AcO			20.99		
			170.34		
10-AcO			20.82		
			169.94		
13-AcO	20.97		21.79		
	170.91		172.78		

* ^{13}C NMR data of cinnamoyl group: 165.24 (C_{21}), 117.63 (C_{22}), 145.02 (C_{23}), 128.06, 128.51, 128.85, 129.32, 129.72, 130.36 (C-*Ph*)

methylene groups, one methine group, six oxymethine groups, two quaternary carbons, two oxyquarternary carbon, two acetyl groups, one benzoyl group and two fully substituted olefinic carbons in the ^{1}H- and ^{13}C-NMR spectra. The skeleton of compound **5** was deduced as an 11(15→1)-*abeo*taxane, *i.e.* brevifoliol type taxane by the careful observation of the signals in the ^{1}H-NMR spectrum (19-22). On the basis of the analysis of its 1D and 2D NMR spectra, the structure of **5** was established as 2α, 7β-diacetoxy-9α-benzoyloxy-4a (20)-epoxy-11(15→1)-*abeo*tax-11-ene-5α, 10β, 13α, 15-tetraol (Fig. 1). The HMBC spectra totally supported the entire carbon framework, as shown in Fig. 1. This was the second example of 11(15→1)-*abeo*taxane with an epoxidic ring at C-4 (20) (26). One interesting feature of both ^{1}H- and ^{13}C-NMR spectra observed in **5** was that the signals were very broad when the spectra were obtained at ambient temperature. Decreasing the temperature to 0°C, however, yielded normal narrow line widths, indicating that line broadening was due to a slow equilibrium between two or more conformatioal isomers. This has been previously observed in taxoids that were subsequently shown to have the brevifoliol skeleton (21, 22).

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