THREE NEW DITERPENOIDS FROM TAXUS CHINENSIS

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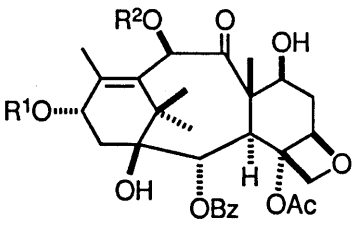
The structures of taxchinins D and G and taxchin A have been determined by means of NMR spectroscopy and confirmed by X-ray analyses. The former two possess a rearranged taxane skeleton found in taxchinin A, while the latter has a taxane skeleton.

KEYWORDS taxus chinensis; taxane; diterpenoid

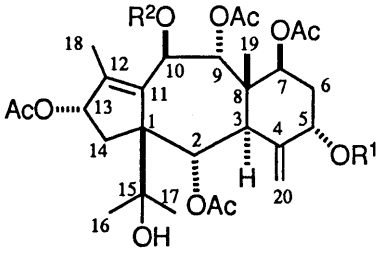
Although taxol (**1**) has evolved as a highly promising anticancer drug, the supply of this diterpenoid is limited due to its scarcity in natural sources.[1] Semisynthesis from inactive but abundant taxanes has been actively investigated to solve this difficulty.[2] Seach for new taxoids in natural sources is another method of choice for developing new therapeutic agents of this type. Over a hundred taxoids have been isolated to date,[3] and the number of new taxoids is increasing rapidly. As a part of our program to investigate new taxanes of antitumor activity and to find a plant source containing enough 10-deacetylbaccatin III (**3**), which is an important starting material for the partial synthesis of taxol (**1**) and unnatural taxotere (**2**),[1] we have isolated taxchinins A-C with a novel skeleton together with two taxane diterpenoids, 19-hydroxy-7-epi-baccatin III and 10-deacetyl-10-oxobaccatin V, from *Taxus chinensis*.[4,5] Further studies on the diterpenoid component of this plant led to isolation of ten new diterpenoid taxchinins D-K and taxchins A and B. Here we report the structures of diterpenoid taxchinins D and G and taxchin A.



1 : R^1 = O NHCOPh, Ph; R^2 = Ac, OH

2 : R^1 = O NHCOO^{t}Bu, Ph; R^2 = H, OH

3 : $R^1 = R^2 = H$



4 : R^1 = H, R^2 = Bz

5 : $R^1 = R^2 = H$

6 : R^1 = Ac, R^2 = Bz

Taxchinin D (**4**), mp 138-141°C (from hexane-acetone) was obtained as colorless plates in 1.84×10^{-3}% yield. Taxchinin D (**4**) showed broadened spectra in several kinds of deuterated solvents ($CDCl_3$, pyr-d_5, DMSO-d_6, and THF-d_8), and the unusual low signal-to-noise ratio in ^{13}C NMR spectrum suggested the slow conformational change of **4** on the NMR time scale. Acetylation of **4** afforded a product whose spectral data are identical with those of taxchinin A diacetate (**6**).[4,5] Obviously, taxchinins A and D possess a similar basic skeleton. Oxidation of **4** by pyridinium dichromate gave a product **7**, whose ^{13}C NMR signal at δ 197.7, 144.2 and 129.1 indicated the presence of an α,β-unsaturated keto unit. Thus, the position of a free hydroxyl group was established at C-5. The structure of taxchinin D (**4**) was confirmed unequivocally by an X-ray analysis as shown in Fig. 1a.

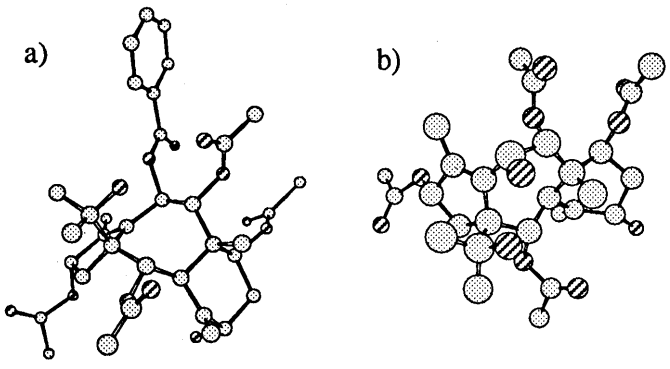
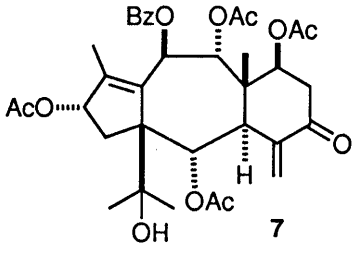


Fig. 1. Crystalline Structures. a) Taxchinin D. b) Taxchinin G



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Taxchinin G (**5**) was isolated as colorless plates, mp 140-143°C (from ether) in 8×10^{-5}% yield. Crystalline structure of taxchinin G (**5**) determined by an X-ray analysis is shown in Fig. 1b, which reveals that taxchinin G (**5**) is debenzoyl taxchinin D. Interestingly, the conformation of the B/C ring system is different. Two computer-generated diagrams are illustrated in Fig. 2 in order to emphasize their stereochemistries. Rings B and C of taxchinin D (**4**) exist in boat-like and chair conformation, respectively, and *vice versa* for taxchinin G (**5**). In order to study the conformation of taxchinin D (**4**) in solution, the low-temperature ^{1}H NMR spectra were measured. Signals for each proton appeared as two resonances at -10°C in $CDCl_3$, corresponding to two conformations, with the chair/boat and the boat/chair for the B/C ring. Table I compiles the ^{1}H NMR spectral assignments confirmed by HH-COSY experiment. The boat-like conformation of ring B can be easily determined by the large coupling constant (11 Hz) between H-9 and H-10. The smaller coupling constant (3.4 Hz) was observed for the chair-like conformation. Although ring B exists in a boat-like conformation in crystalline state, a chair-like conformation predominates in $CDCl_3$ with a 5:3 preference.

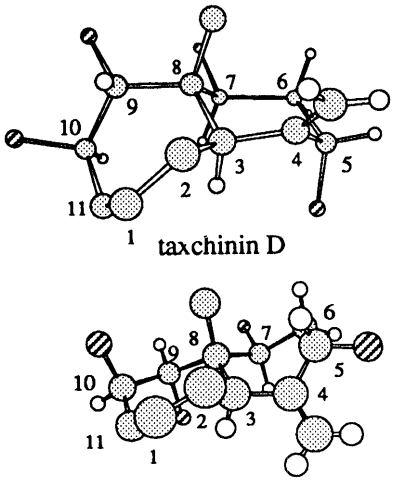


Fig. 2. The B/C Ring Conformation of Taxchinins D and G in Crystalline State

Table I. Pertinent ^{1}H NMR Data for Taxchinin D (**4**) at -10°C in $CDCl_3$

Proton	δ ppm (Hz)	
	Major	Minor
	B-ring chair	B-ring boat
H-2	5.90 (d, 9.5)	6.09 (d, 9.5)
H-3	3.03 (d, 9.5)	3.48 (d, 9.5)
H-5	4.78 (brt, 5.0)	4.33 (brs)
H-7	4.90 (t, 9.0)	5.55 (dd, 5.0, 9.0)
H-9	4.98 (d, 3.4)	6.03 (d, 11.0)
H-10	6.29 (d, 3.4)	6.71 (d, 11.0)
H- 13	5.56 (m)	5.50 (m)
αH-20	5.40 (s)	5.19 (s)
βH-20	4.84 (s)	4.60 (s)

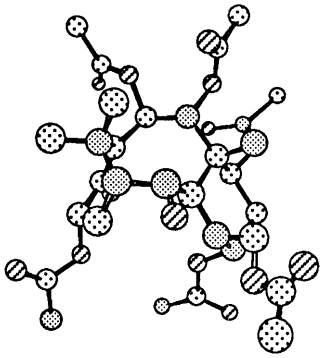
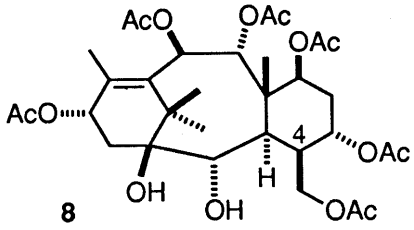


Fig. 3. Crystalline Structure of Taxchin A (**8**)



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Taxchin A (**8**), (3.2 x 10^{-4}%), mp 284-6°C (from hexane-acetone) possesses a normal taxane skeleton, the structure of which was unambiguously determined by a single crystalline X-ray analysis as shown above. Isolation of the taxane diterpenoid without any functionality at C-4 is the first example, because all of the known taxoids have an oxygen functionality or the sp^2-hybridized carbon at C-4.

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