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THREE NEW DITERPENOIDS FROM TAXUS CHINENSIS

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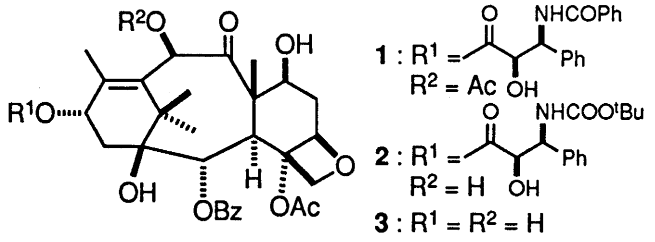
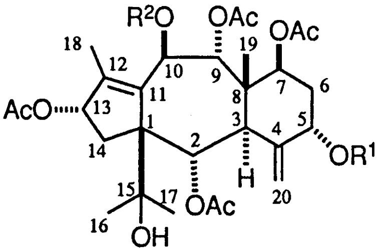
The structures of taxchinins D and G and taxchin A have been determined by means of NMR spectroscopy and confirmed by X-ray analyses. The former two possess a rearranged taxane skeleton found in taxchinin A, while the latter has a taxane skeleton.

KEYWORDS taxus chinensis; taxane; diterpenoid

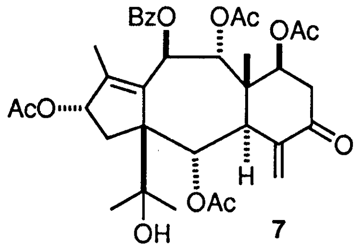
Although taxol (1) has evolved as a highly promising anticancer drug, the supply of this diterpenoid is limited due to its scarcity in natural sources.1) Semisynthesis from inactive but abundant taxanes has been actively investigated to solve this difficulty.2) Seach for new taxoids in natural sources 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.





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.



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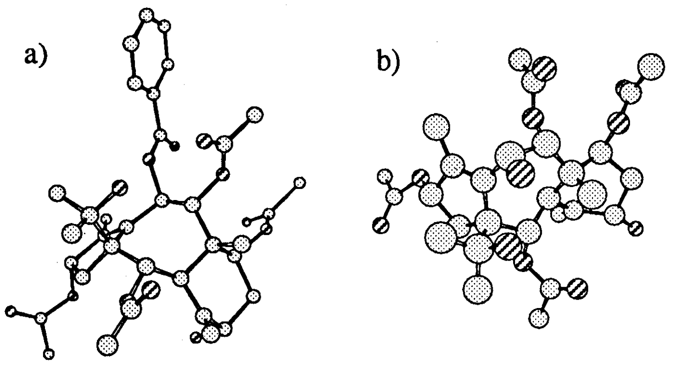
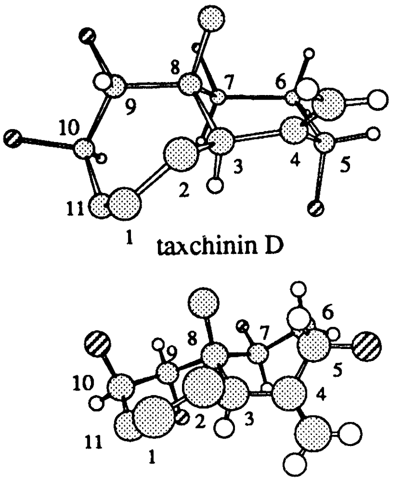


Fig. 1. Crystalline Structures. a) Taxchinin D. b) Taxchinin G

Taxchinin G (5) was isolated as colorless plates, mp 140-143°C (from ether) in 8x10^{-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.



taxchinin D

taxchinin G

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)

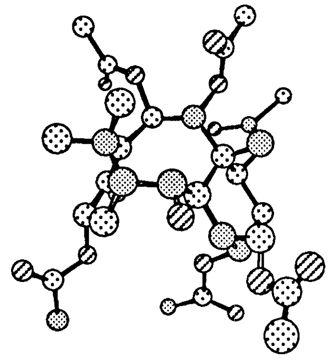
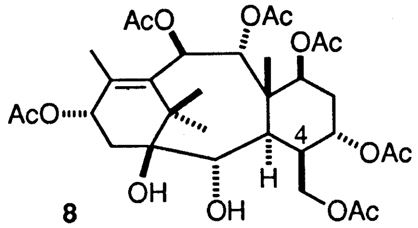


Fig. 3. Crystalline Structure of Taxchin A (8)



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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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