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Triptotin A and B, Two Novel Diterpenoids from *Tripterygium wilfordii*

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Abstract: Two new diterpenoids, triptotin A and B have been isolated from the heartwood of the root of *Tripterygium wilfordii* Hook f., and their structures were established by spectroscopic studies and X-ray crystallography.

Since antileukemic diterpenoids were found in *Tripterygium wilfordii*,[1] a number of studies have been focused in China on the chemistry and pharmacology of *Tripterygium*. In our studies on the chemical components of *Tripterygium wilfordii* Hook f., two novel diterpenoids, 18(4→3)-abeo-1β,11α-epidioxy-11β-hydroxy-8,12-abietadiene-14-one-18,19-olide (**1**) and 1β, 11α-epidioxy -11β,19-dihydroxy-8,12-abietadiene-14-one (**2**), named triptotin A and B, were isolated. This paper describes the isolation and the structure elucidation of these two interesting compounds.

The ethanol extract obtained from the root heartwood was chromatographed to furnish triptotin A (8 mg), colorless prisms, mp187-188 °C(crystallized from MeOH), $[\alpha]_D^{23.5}$ +68.66° (c, 0.067, $CHCl_3$) and triptotin B (29 mg), amorphous powder, $[\alpha]_D^{23.5}$ +91.75° (c, 0.166, $CHCl_3$).

The molecular formula of (**1**), $C_{20}H_{22}O_6$, was assigned by HR-EI-MS (m/z 358.1428). The presence of a hydroxyl absorption (3425 cm^{-1}) and two carbonyls: an α,β-unsaturated-γ-lactone (1738 cm^{-1}) and a conjugate ketone (1653 cm^{-1}) was inferred from its IR spectrum. Its ^1H NMR spectrum revealed the presence of an isopropyl group [δ 0.93, 0.98 (each 3H, d, J = 6.9 Hz), 3.03 (1H, sept, J = 6.9Hz)], and one methyl group [δ1.49 (3H, s)]. The ^{13}C NMR

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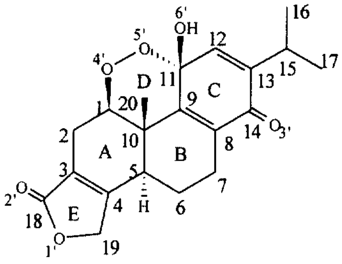
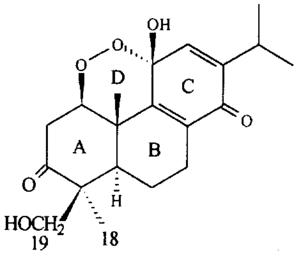
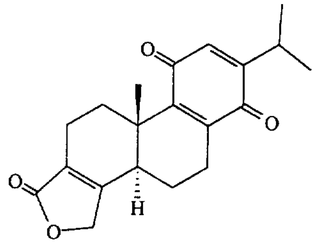
spectrum of (**1**) showed two carbonyl signals (δ 163.3,173.2) and two oxygenated carbons: one at δ 94.2 assignable to a doubly oxygenated cyclic ketal carbon and the other at δ 84.6 as a secondary carbon. Comparison of the ^{1}H and ^{13}C NMR spectral data for (**1**) with those of triptoquinone (**3**)[2] indicated the same abietane skeleton with an α,β unsaturated-γ-lactone, the



(**1**)



(**2**)



(**3**)

Table 1. NMR spectral Data of (**1**) and (**2**) [^{13}C(100MHz: δ in PPM)] [^{1}H(400MHz: δ in PPM, multiplicity, J in Hz)]

Assignment	δ_C		δ_H	
	1^{a}	2^{b}	1^{a}	2^{b}
1	84.6	83.0	4.67(dd, 6.1 and 11.3)	4.49(dd, 8.0 and 11.0)
2	22.7	37.5	2.41(m), 2.83(br d, 11.3)	2.43(m), 2.93(m)
3	*	214.4		
4	163.3	51.3		
5	41.3	48.3	2.64(br d, 12.4)	2.93(m)
6	17.9	17.3	1.68(m), 1.80(m)	1.71(m), 1.90(m)
7	23.3	24.2	2.41(m), 2.75(dd, 6.2 and 18.8)	2.21(m), 2.73(m)
8	129.5	130.9		
9	145.9	147.3		
10	37.3	37.8		
11	94.2	93.8		
12	*	133.8	6.70(s)	6.21(s)
13	*	146.7		
14	185.4	185.0		
15	27.0	26.5	3.03(sept, 6.9))	2.93(m)
16	21.7**	21.5**	0.98(3H, d, 6.9)**	1.05(3H, d, 6.8)**
17	21.5**	21.4**	0.93(3H, d, 6.9)**	1.01(3H, d, 6.8)**
18	173.2	24.3		1.16(3H, s)
19	70.8	65.7	4.83, 4.90(each 1H, AB q, 17.8)	3.69, 3.73(each 1H, AB q, 11.6)
20	14.0	13.9	1.49(3H, s)	1.35(3H, s)

* Signal is hidden by a solvent peak

** Assignments may be interchanged

a (**1**) in C_5D_5N b (**2**) in $CDCl_3$

difference between the two compounds being in rings A and C. Because (**1**) has only two carbonyl groups and has a hydroxyl whose chemical shift is at low field (δ9.95, br s), a hemiketal system was inferred to be at C_{11}. Its ^1H-^1H COSY spectrum showed cross-peaks between 2-H_2 and 19-H_2 and revealed the presence of one -$CHCH_2$- and a -$CHCH_2CH_2$- moiety in the molecule, assigned to H_1/H_2 and $H_5/H_6/H_7$, respectively. This suggested that these should be an oxygen atom connected to C_1. The formula required ten unsaturated equivalents. Five of them are accounted for by two carbonyl functionalities (δ 185.4 and δ 173.2) and its three double bonds, the remainder indicates its pentacyclic nature with a peroxide bridge between O_4 and O_5.

The structure, relative stereochemistry and probable absolute configuration of triptotin A were finally established by its X-ray analysis as depicted in the structure (**1**). Details of the X-ray analysis are given below.

Single crystal X-ray analysis of (**1**). Data were acquired with a Rigaku AFC7R diffractometer, Mo K_α radiation (λ = 0.71069 Å), graphite monochromator. $C_{20}H_{22}O_6$ (358.36), crystal size 0.20×0.20×0.30 mm, tetragonal, space group $P4_1$, 293K, a = 8.463(2) Å, c = 24.684(4) Å, V = 1767.7(5) $Å^3$, D_c= 1.347 g/cm^3, Z = 4, F(000) = 760.00, μ = 0.99 cm^{-1}. The data were collected at a temperature of 20±1 °C using the ω-2θ scan technique to a maximum 2θ value of 51.0°. Of the 3251 reflections which were collected, 3002 were unique (R_{int} = 0.031). The intensities of three representative reflections were measured after every 200 reflections. Over the course of data collection, the standards decreased by -1.6%. The structure was solved by direct methods (SHELXS-86)[3] and expanded using Fourier techniques.[4] The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically.

Triptotin B (**2**) was assigned the molecular formula $C_{20}H_{26}O_6$ (HRMS m/z 362.1713). Its IR spectrum showed two ketones (1700 cm^{-1} and 1650 cm^{-1}) and a hydroxyl group absorption (3423 cm^{-1}). Its ^{13}H NMR spectrum indicated the presence of an isopropyl group, two methyl groups and a hydroxyl methyl group (3.69, 3.73, AB q, J=11.6). A total of 20 carbon signals including two carbonyl signals and three oxygenated carbons (δ65.7, 83.0, 93.8) observed in the ^{13}C NMR spectrum of (**2**) were identified as CH_3×4, CH_2×4, CH×4, C×8 with the help of the DEPT spectrum. Based on a comparison of the ^1H and ^{13}C NMR spectral data of (**2**) with those of (**1**), (**2**) was assumed to be the similar type of abietane deterpenoid as (**1**) but not an α,β unsaturated-γ-lactone. In the 2D NOESY spectrum of (**2**), the proton signals at δ3.69 and 3.73

(each H-19) showed correlation with the proton signal at δ1.35 (H-20), thus, the configuration of the hydroxyl methyl group at C-4 was confirmed to be β. Finally 2D HMBC, HMQC, NOESY and ^{1}H-^{1}H COSY established the structure of (**2**) as indicated.

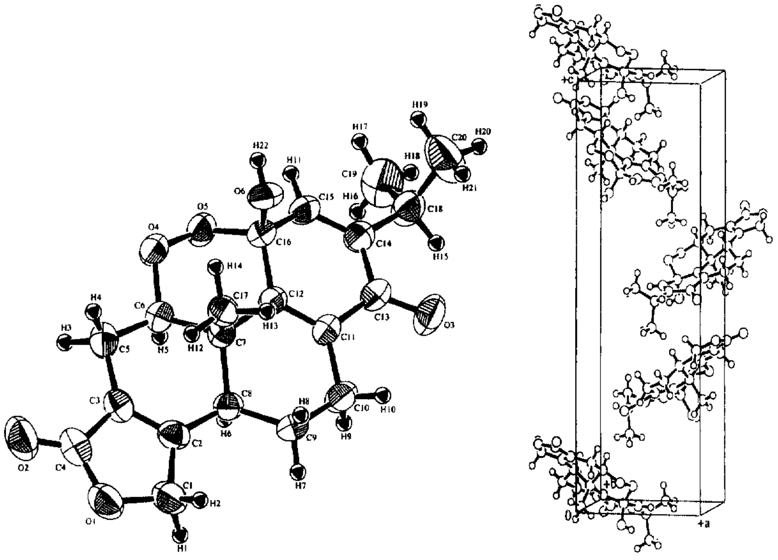


Fig. 1

- In figure 1, the numbering of C and H is different from (**1**).

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