Triptowilfolide, a Novel Compound from *Tripterygium wilfordii*

by **Duqiang Luo**[a])[b]), **Xing Zhang**[a]), **Xuan Tian**[c]), and **Jikai Liu***[b])

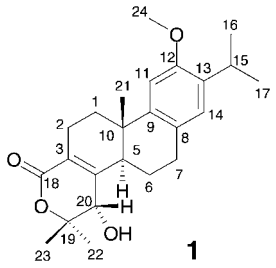
[a]) Biorational Pesticide Research Center, Northwest Sci-Tech University of Agriculture and Forestry, Yangling 712100, P. R. China

[b]) Kunming Institute of Botany, Chinese Academy of Sciences, Kuming 650204, P. R. China (e-mail: jkliu@mail.kib.ac.cn)

[c]) National Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, P. R. China

A novel diterpenoid-related compound, triptowilfolide (**1**), was isolated from the root bark of the *Tripterygium wilfordii*. Its structure was established by spectroscopic means.

Introduction. – The Thunder God Vine, *Tripterygium wilfordii* HOOK f., belongs to the Celastraceae family. Species of the Celastraceae have attracted a lot of attention, due to the range of biological activities [1]. *T. wilfordii* has been used as an anticancer drug and as an insecticide for hundreds of years in China [2]. Recently, some important pharmacological activities, including antifertility [3], antirheumatoid arthritis [4], immunosuppressive [5], and repair of burn wound [6], were found in *T. wilfordii*. A number of diterpenoides isolated from this plant have been reported [1][2][7–9]. As part of our studies on the insecticidally active constituents from plants, *T. wilfordii* was further investigated. This report deals with the characterization and structure elucidation of a novel diterpenoid-related compound, triptowilfolide (**1**), from the petroleum-ether extract of the root bark of *T. wilfordii*.



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Results and Discussion. – Compound **1** was obtained as colorless bulk crystals with a m.p. 194–196° (crystallized from petroleum ether/CH_2Cl_2) and $[\alpha]_D^{20} = -2.8$ ($c = 0.1$, $CHCl_3$). The molecular formula of **1**, $C_{24}H_{32}O_4$, was determined by HR-EI-MS (*m/z* 384.2328). Its IR spectrum showed characteristic absorption bands at 3416 (OH), 1729, 1664 (lactone), and 1564, 1483, 819 (substituted benzene).

The signals in the ^{13}C-NMR (DEPT) spectrum of **1** ($6 \times$ Me, $4 \times CH_2$, $5 \times$ CH and $9 \times$ C), included those of one MeO C-atom (60.5), one lactone C=O C-atom (173.1), two CH C-atoms (87.1, 42.5), six quarternary aromatic or olefinic C-atoms (127.4, 163.8,

Table. *^{1}H- and ^{13}C-NMR Data* (400 MHz, $CDCl_3$) *of* **1** (δ in ppm, J in Hz)

Position	^{13}C (DEPT)	^{1}H	H,H-COSY	HMBC
1	32.0 (CH_2)	2.50 (*m*)		H–C(5), H–C(21)
2	18.2 (CH_2)	2.50 (*m*)		
3	127.4 (C)			H–C(1), H–C(5)
4	163.8 (C)			H–C(2), H–C(6)
5	42.5 (CH)	2.50 (*m*)	H–C(6)	H–C(1), H–C(7), H–C(21)
6	20.7 (CH_2)	1.85 (*m*), 1.64 (*m*)	H–C(5), H–C(7)	
7	22.6 (CH_2)	3.01 (*m*)	H–C(6)	H–C(14)
8	128.4 (C)			H–C(7), H–C(11)
9	144.9 (C)			H–C(1), H–C(7), H–C(14), H–C(21)
10	36.7 (C)			H–C(2), H–C(6), H–C(11)
11	119.5 (CH)	7.11 (*s*)		
12	155.7 (C)			H–C(14), H–C(15), H–C(24)
13	139.3 (C)			H–C(11), H–C(15)
14	123.7 (CH)	7.11 (*s*)		H–C(15)
15	26.2 (CH)	3.31 (*sept.*, $J = 6.8$)	H–C(16), H–C(17), H–C(14)	
16	23.8 (Me)	1.22 (*d*, $J = 6.8$)	H–C(15)	
17	22.5 (Me)	1.25 (*d*, $J = 6.8$)	H–C(15)	
18	173.1 (C=O)			H–C(2)
19	72.3 (C)			
20	87.1 (CH)	4.84 (*s*)		H–C(22), H–C(23)
21	23.9 (Me)	1.04 (*s*)		
22	27.7 (Me)	1.12 (*s*)		H–C(20)
23	24.0 (Me)	1.35 (*s*)		H–C(20)
24	60.5 (Me)	3.75 (*s*)		

128.4, 144.9, 139.3, 155.7), and two aromatic or olefinic CH C-atoms (119.5, 123.7) (*Table*). The ^{1}H-NMR spectrum of **1** revealed the presence of an i-Pr group (δ 1.23, 1.25 (*d*, $J = 6.8$ Hz, each 3 H), and 3.31 (*sept.*, $J = 6.8$ Hz, 1 H)), four Me groups (δ 1.04 (*s*, 3 H), 1.12 (*s*, 3 H), 1.35 (*s*, 3 H), 3.75 (*s*, 3 H)), one CH group bearing the OH group (δ 4.84 (*s*, 1 H)). In the aromatic region, the usual signals for two *ortho*-coupled H-atoms for 1,2,3,4-tetrasubstituted aromatic benzene ring were not observed [7][8]; instead, the signals of two *p*-H-atoms appeared at δ 7.11 (*s*, 2 H). They were assigned to H–C(11) and H–C(14), not to H–C(11) and H–C(12). The signals at δ 3.75 (*s*, 3 H) in ^{1}H-NMR and at δ 60.5 in ^{13}C NMR were assigned to the MeO–C(12) H- and C-atoms, respectively.

The H,H-COSY spectrum showed cross-peaks between H–C(15), and H–C(16) and H–C(17), confirming the presence of an i-Pr group. The COSY interactions also revealed the presence of one $CHCH_2CH_2$ moiety, assigned to H–C(5)/H–C(6)/H–C(7). In the HMBC spectrum, the ^{13}C signal at δ(C) 173.1 (C(18)) was correlated with the ^{1}H resonance at δ(H) 2.50 (H–C(2)), and the ^{13}C signal at δ(C) 72.3 (C(19)) with the proton resonance at δ(H) 1.12, 1.35 (H–C(22), H–C(23)), and the ^{13}C signal at δ(C) 26.2 (C(15)) with the ^{1}H resonance at δ(H) 7.11 (H–C(14)). Taking all data into account, we could establish the structure of this novel compound as shown by the formula **1**. This structure was further confirmed by HMBC (*Table*). The configuration

at C(20) was determined by NOESY. To observe the NOE interactions between H–C(5) and H–C(20), the OH group at C(20) should be β-oriented. However, no NOE correlation peaks were observed between H–C(20) and H–C(5), indicating that the OH group at C(20) is α-oriented. At the same time the cross-peaks between H–C(20) and H–C(23) in NOESY spectrum also suggested a β-orientation for the OH group at C(20). No NOE interactions were observed between H–C(5) and H–C(20), suggesting a *trans* fusion at C(5) and C(10), as usual for this type compounds.

Experimental Part

General. M.p.: uncorrected. IR Spectra: *Nicolet AVATR360FT-IR* spectrometer, with KBr pellets. ^{1}H- and ^{13}C-NMR Spectra: *Bruker AM-400* spectrometer, TMS as internal standard. MS: *ZAB-HS* spectrometer.

Plant Material. The root bark of *Tripterygium wilfordii* HOOK f. was collected in Tanning County of Fujian Province, P. R. China, in November 2000, and air-dried. Dr. *X. L. He* identified it, and a voucher specimen was preserved in the Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. The dried root bark (20 kg) was finely powdered and extracted with petroleum ether (5 ×) at r.t. The solvent was evaporated, and the crude extract was partitioned between petroleum ether and MeOH (80% in H_2O). The petroleum-ether phase was evaporated to afford a deep brow gum. The residue was subjected to column chromatography (CC; silica gel) and eluted with petroleum ether/AcOEt (9:1, 8:2, 7:3, 6:4, 5:5 (*v*/*v*)). The fraction (3 g) eluted with petroleum ether/AcOEt (5:5 (*v*/*v*)) was further purified by repeated CC (silica gel; petroleum ether/Et_2O 1:1 and 1:4 (*v*/*v*)) and prep. TLC (petroleum ether/acetone 4:1) to afford **1** (14 mg).

Triptowilfolide (**1**). Colorless bulk crystals. M.p. 194–196° (petroleum ether/CH_2Cl_2), $[\alpha]_D^{20} = -2.8$ ($c = 0.1$, $CHCl_3$). IR: 3416, 3069, 2973, 2931, 2867, 1729, 1664, 1564, 1483, 1459, 1438, 1407, 1079, 1028, 1010, 819. ^{1}H- and ^{13}C-NMR: see *Table*. FAB-MS (pos.): 385 ($[M+1]^+$), 367, 327, 283, 227, 154, 136, 55.

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