Cathepsin B Inhibitory Tetraene Lactones from the Fungus *Talaromyces wortmannii*

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Wortmannilactones E–H (**1**–**4**), four new cathepsin B inhibitors, were produced and isolated from the culture of the soil filamentous fungus *Talaromyces wortmannii*. Their structures and relative configurations were elucidated on the basis of 1D- and 2D-NMR techniques, three of them (**1**, **2**, and **4**) posses an oxabicyclo[2.2.1]heptane moiety. Compounds **1**–**4** showed inhibitory activities against cathepsin B with IC_{50} values of 4.3, 6.5, 13.0, and 6.0 μM, respectively.

Introduction. – Cathepsins, known as a class of lysosomal protein-degrading enzymes, play significant roles in specific physiological activities [1]. Among them, cathepsin B has been documented to be important in many metastatic tumors and the inhibition of its activity resulted in a decreased invasiveness of tumor cells [2]. Therefore, cathepsin B is a possible therapeutic target for the control of tumor progression. In anticipation of the usefulness of cathepsin B inhibitors, we screened against the enzyme new compounds isolated from filamentous fungi, which have been proved to be important sources of significant biological activities [3][4]. As a result, a fungus *Talaromyces wortmannii* from the soil of Chuxiong, in China's Yunnan Province, showed potent activity. Bioassay-guided fractionation afforded four novel tetraene lactones (wortmannilactones; **1**–**4**), three of them (**1**, **2**, and **4**) posses an oxabicyclo[2.2.1]heptane moiety in their structures. Recently, several oxabicyclo[2.2.1]heptane compounds with inducing neuritogenesis against neuroblastoma and anticoccidial activities have been reported [5–8].

A few previous chemical investigations of *Talaromyces wortmannii* and its asexual stage *Penicillium wortmannii* have been described. These studies resulted in the isolation of some quinones [9–11], wortmannolone [12], wortmannin, which showed phosphatidylinositol 3-kinase inhibition activities [13], and wortmannilactones A–D with *in vitro* antitumor activities [14]. In this work, we report the details of the isolation, structure elucidation, and preliminary biological evaluation of compounds **1**–**4** for cathepsin B.

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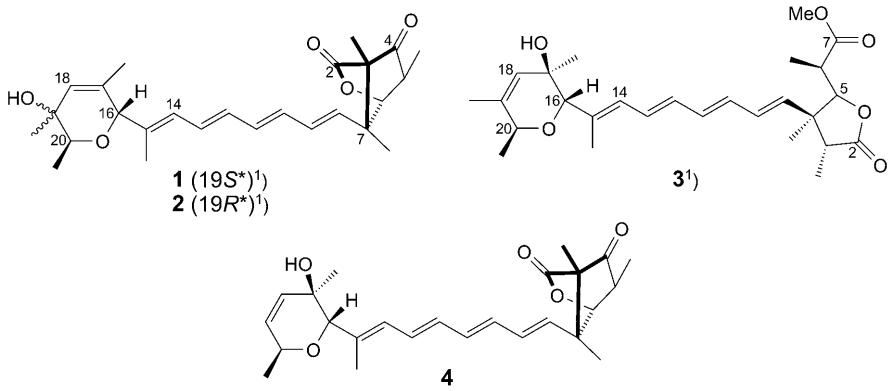

Results and Discussion. – *T. wortmannii* was cultured in solid-state medium for 14 days. The cultures were extracted with AcOEt, and the extract was separated by sequential chromatography on silica gel and reverse phase HPLC to afford compounds **1**–**4**.

The molecular formula of wortmannilactone E (**1**) was determined as $C_{26}H_{34}O_5$ by high-resolution FAB-MS, requiring 10 degrees of unsaturation. The UV spectrum of **1** in MeOH exhibited absorption bands at 297, 312 and 326 nm, indicating the presence of a conjugated tetraene moiety [15]. ^{13}C-NMR (CD_3OD) and DEPT spectra confirmed the presence of 26 C-atoms, including a keto CO group, an ester CO group, ten olefinic CH groups, four quaternary C-atoms, three sp^3 CH groups, and seven Me groups. ^{1}H-NMR (CD_3OD) and HMQC spectra of **1** displayed resonances for 33 H-atoms, including six *singlet* Me groups and one *doublet* Me group, four CH groups, and eight olefinic H-atoms. The H-atoms of **1** were assigned unambiguously to their respective C-atoms *via* the HMQC spectrum.

The constitutional formula of **1** was established by straightforward analysis of ^{1}H- and ^{13}C-NMR, COSY, HMQC, and HMBC spectra (*Table 1*). Analyses of the ^{1}H- and ^{13}C-NMR spectra revealed a partial structure, which contained an oxabicyclo[2.2.1]-heptane substructure [7]. The ^{1}H-NMR, COSY, and HMBC data led to the identification of a conjugated tetraene substructure (C(8) to C(15)[1])) which was substituted by a Me group at C(15). The ^{1}H- and ^{13}C-NMR data, together with the HMBC observed between H–C(16)/C(18) and C(20), H–C(18)/C(16) and C(20), and H–C(20)/C(16) showed the presence of a dihydropyrane ring which was the same as that of prugosene A1. Connection of the three fragments was established through HMBC correlations from H–C(6)/C(8), H–C(9)/C(7), and H–C(16)/C(14), respectively.

Wortmannilactone F (**2**) was shown to have the same molecular formula as that of **1** provided by HR-FAB-MS. Closer inspection of the ^{1}H- and ^{13}C-NMR spectra of **2** and comparison with those of **1** revealed a number of similarities. In particular signals for the oxabicyclo[2.2.1]heptane and tetraene moieties were identical to **1**. The COSY,

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[1]) Arbitrary numbering. For systematic names, see *Exper. Part.*

Table 1. *^{1}H-NMR* (500 Hz) *and ^{13}C-NMR* (125 Hz) *Data of Wortmannilactone E* (**1**) *and Wortmannilactone F* (**2**) (in CD_3OD). δ in ppm, J in Hz.

	1				**2**		
	δ(H)	δ(C)	HMBC (H → C)	NOESY	δ(H)	δ(C)	NOESY
2		173.4 (*s*)				173.4 (*s*)	
3		70.8 (*s*)				70.8 (*s*)	
4		209.5 (*s*)				209.5 (*s*)	
5	2.81 (*qd*, *J* = 7, 2)	44.4 (*d*)	4, 5-Me	6, 5-Me, 7-Me	2.82 (*qd*, *J* = 7, 2)	44.4 (*d*)	6, 5-Me, 7-Me
6	4.95 (*d*, *J* = 2.5)	86.3 (*d*)	2, 3, 4, 5, 8	5, 5-Me	4.97 (*d*, *J* = 2.5)	86.3 (*d*)	5, 9, 5-Me
7		59.5 (*s*)				59.5 (*s*)	
8	5.71 (*d*, *J* = 15)	131.3 (*d*)	3, 6, 7, 10, 7-Me	9, 3-Me, 7-Me	5.71 (*d*, *J* = 15)	131.2 (*d*)	9
9	6.38 (*dd*, *J* = 15, 11)	135.5 (*d*)	7, 11	6, 7-Me	6.40 (*dd*, *J* = 15, 11)	135.6 (*d*)	6
10	6.23 (*dd*, *J* = 15, 11)	133.5 (*d*)	8, 10		6.26 (*dd*, *J* = 15, 11)	133.4 (*d*)	
11	6.36 (*dd*, *J* = 15, 11)	134.9 (*d*)	12, 13		6.38 (*dd*, *J* = 15, 11)	134.9 (*d*)	
12	6.23 (*dd*, *J* = 15, 11)	134.8 (*d*)	10, 11, 14		6.23 (*dd*, *J* = 15, 11)	134.8 (*d*)	
13	6.50 (*dd*, *J* = 15, 11)	130.4 (*d*)			6.52 (*dd*, *J* = 15, 11)	130.7 (*d*)	15-Me
14	5.84 (*d*, *J* = 11)	130.4 (*d*)	12, 16, 15-Me	16	5.97 (*d*, *J* = 11)	130.5 (*d*)	16,17-Me
15		136.0 (*s*)				136.4 (*s*)	
16	4.26 (*s*)	81.5 (*d*)	14, 15, 17, 18, 20, 15-Me, 17-Me	14, 15-Me, 17-Me, 20-Me	4.22 (*s*)	81.8 (*d*)	14, 20-Me, 15-Me, 17-Me
17		135.6 (*s*)				134.3 (*s*)	
18	5.53 (*d*, *J* = 1.5)	130.9 (*d*)	16, 19, 20, 17-Me, 19-Me	17-Me, 19-Me	5.52 (*d*, *J* = 1.5)	132.4 (*d*)	17-Me, 19-Me
19		68.1 (*s*)				69.8 (*s*)	
20	3.47 (*q*, *J* = 6.5)	73.1 (*d*)	16, 19, 19-Me, 20-Me	19-Me, 20-Me	3.58 (*q*, *J* = 6.5)	72.5 (*d*)	19-OH, 20-Me
3-Me	1.01 (*s*)	5.0 (*q*)	2, 3, 4, 7	8	1.01 (*s*)	5.0 (*q*)	8
5-Me	1.12 (*d*, *J* = 7)	11.7 (*q*)	4, 5, 6	5, 6	1.13 (*d*, *J* = 7)	11.7 (*q*)	5
7-Me	1.09 (*s*)	16.9 (*q*)	3, 6, 7	5, 8, 9	1.10 (*s*)	16.9 (*q*)	5, 9
15-Me	1.80 (br. *s*)	15.7 (*q*)	14, 15, 16	16, 20	1.82 (br. *s*)	15.8 (*q*)	13, 16
17-Me	1.55 (br. *s*)	20.1 (*q*)	16, 17, 18	14, 16, 18	1.52 (br. *s*)	19.8 (*q*)	14, 16, 18
19-Me	1.07 (*s*)	25.6 (*q*)	18, 19, 20	20	1.05 (*s*)	22.0 (*q*)	18
19-OH[a])					3.16 (*s*)		20
20-Me	1.09 (*d*, *J* = 5.5)	14.4 (*q*)	19, 20	16, 20	1.03 (*d*, *J* = 6)	14.7 (*q*)	16, 20

[a]) Data were recorded in (D_6)DMSO.

HMQC, and HMBC data led to the unambiguous assignments of the ^{1}H and ^{13}C signals, which revealed the constitution of **2** to be the same as that of **1**. Thus **2** was considered to be a stereoisomer of **1**.

The assignment of the relative configuration in **1** and **2** arose from the NOESY spectral data. The relative NOESY correlations of H–C(5)/*Me*–C(7)[1]), H–C(8)/*Me*–C(3), and H–C(5)/H–C(6) revealed that the relative configuration of the oxabicyclo[2.2.1]heptane moiety is (3*S**,5*R**,6*S**,7*R**) which is consistent with that of prugosene A(1–3) with the exception of the C(7) position [8]. The four C=C bonds in the two compounds were all assigned the (*E*) geometry on the basis of the well-resolved H-atom coupling constants ($J = 15.0$ Hz). The difference of 1D-NMR chemical shift between **1** and prugosene A1 in the dihydropyran moiety suggests that they have a different relative configuration at C(19). H–C(16) showed a NOESY correlation with H–C(14) and *Me*–C(20), whereas *Me*–C(15) in the *trans* position of the H–C(14) exhibited a NOESY correlation with H–C(20), indicating that H–C(16) and *Me*–C(20) should be *cis* disposed (*Fig. 1*). The presence of NOESY relationships between H–C(20) and *Me*–C(19) in **1** and H–C(20) and HO–C(19) in **2** (in (D_6)DMSO) indicated that the *Me*–C(19) and *Me*–C(20) were *trans* in **1** and *cis* in **2**. Therefore, the relative configuration at the three stereogenic centers of the dihydropyran moiety of **1** and **2** was identified as (16*S**,19*S**,20*S**) and (16*S**,19*R**,20*S**), respectively.

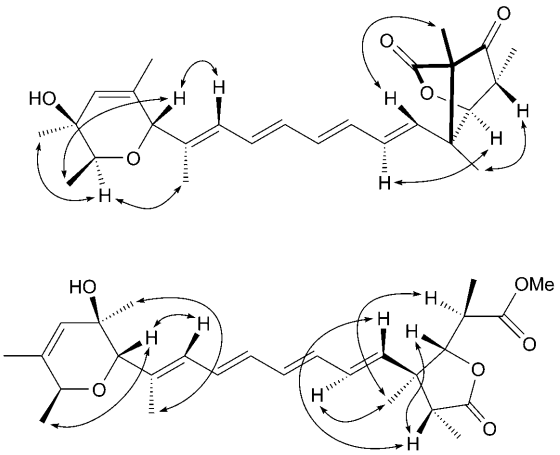

Fig. 1. *Key NOE correlations of compounds* **1** (*top*) *and* **3** (*bottom*)

The molecular formula of wortmannilactone G (**3**) was established as $C_{27}H_{38}O_6$ on the basis of HR-FAB-MS data. The UV spectrum and NMR data showed the presence of a tetraene group, the (*E*) configurations of the C=C bonds were deduced from their large coupling constant ($J = 15$ Hz) with the exception that the signals of H–C(11)[1]) and H–C(12) were overlapped. The NMR data, together with HMBC correlations of H–C(3) to C(2), C(8), and *Me*–C(4), H–C(5) to C(8), H–C(16) to C(18), C(20), *Me*–C(15), and *Me*–C(17), and *Me*–C(17) to C(16) and C(18) showed the presence of a 2,3-dimethylated γ-lactone substituted with a 1-carboxyethyl group in γ-position (at C(5)) and of a dihydropyran moiety, which was the same as in prugosene B2 (*Table 2*). In the NOESY experiment, the *Me*–C(4) showed correlations with H–C(6) and H–C(9), whereas H–C(8) exhibited a correlation with H–C(3) and H–C(5).

Table 2. *^{1}H-NMR* (500 Hz) *and ^{13}C-NMR* (125 Hz) *Data of Wortmannilactone G* (**3**) *and Wortmannilactone H* (**4**) (in CD_3OD). δ in ppm, J in Hz.

	3				**4**	
	δ(H)	δ(C)	HMBC (H → C)	NOESY	δ(H)	δ(C)
2		179.1 (*s*)				173.4 (*s*)
3	2.75 (*q*, *J* = 7)	47.9 (*d*)	2, 4, 8, 3-Me, 4-Me	5, 8, 3-Me		70.8 (*s*)
4		49.5 (*s*)				209.5 (*s*)
5	4.36 (*d*, *J* = 11)	87.2 (*d*)	6, 7, 8, 4-Me	3, 8, 6-Me	2.82 (*qd*, *J* = 7, 2)	44.4 (*d*)
6	2.71 (*dd*, *J* = 11, 7)	42.4 (*d*)	5, 7, 6-Me	4-Me, 6-Me	4.96 (*d*, *J* = 2.5)	86.3 (*d*)
7		175.9 (*s*)				59.5 (*s*)
8	5.72 (*d*, *J* = 15)	136.7 (*d*)	9	3, 5, 6-Me	5.68 (*d*, *J* = 15)	130.5 (*d*)
9	6.19 (*dd*, *J* = 15, 11)	132.6 (*d*)	10	4-Me	6.39 (*dd*, *J* = 15, 11)	136.0 (*d*)
10	6.33 (*dd*, *J* = 15, 11)	135.1 (*d*)	9, 11		6.22 (*dd*, *J* = 15, 11)	133.2 (*d*)
11	6.20 – 6.25 (*m*)[a])	132.6 (*d*)	10		6.39 (*dd*, *J* = 15,11)	135.0 (*d*)
12	6.20 – 6.25 (*m*)[a])	133.3 (*d*)	14		6.22 (*dd*, *J* = 15, 11)	132.5 (*d*)
13	6.53 (*dd*, *J* = 15, 11)	130.7 (*d*)	15		6.55 (*dd*, *J* = 15, 11)	131.0 (*d*)
14	6.12 (*d*, *J* = 11)	128.0 (*d*)	12, 16, 15-Me	16	6.13 (*d*, *J* = 11)	127.9 (*d*)
15		137.8 (*s*)				138.0 (*s*)
16	3.98 (*s*)	78.8 (*d*)	14, 15, 17, 18, 20, 15-Me, 17-Me	14, 15-Me, 20-Me	3.96 (*s*)	78.8 (*d*)
17		71.2 (*s*)				71.1 (*s*)
18	5.29 (*dd*, *J* = 2)	130.8 (*d*)	16, 20, 19-Me	17-Me, 19-Me	5.29 (*d*, *J* = 1.5)	130.7 (*d*)
19		137.3 (*s*)				137.3 (*s*)
20	4.12 (*q*, *J* = 7)	74.0 (*d*)	16, 18, 19, 20-Me	19-Me, 20-Me	4.12 (*q*, *J* = 7)	74.0 (*d*)
3-Me	0.90 (*d*, *J* = 7)	7.6 (*q*)	2, 4	3	1.01 (*s*)	5.0 (*d*)
4-Me (5-Me in **4**)	0.98 (*s*)	11.9 (*q*)	4, 5, 8	6, 9	1.12 (*d*, *J* = 7)	11.7 (*q*)
6-Me (7-Me in **4**)	1.02 (*d*, *J* = 7)	14.3 (*q*)	5, 6, 7	5, 6, 8	1.10 (*s*)	16.9 (*q*)
7-Me	3.64 (*s*)	52.5 (*q*)	7			
15-Me	1.83 (*s*)	16.1 (*q*)	14, 15, 16	13, 16, 17-Me	1.83 (br. *s*)	16.0 (*q*)
17-Me	0.96 (*s*)	22.8 (*q*)	16, 17,18	18, 15-Me	0.96 (br. *s*)	22.7 (*q*)
19-Me	1.58 (*s*)	19.3 (*q*)	18, 19, 20	18, 20	1.52 (*s*)	19.2 (*q*)
20-Me	1.24 (*d*, *J* = 6.5)	17.5 (*q*)	19, 20	16, 20	1.24 (*d*, *J* = 6)	17.4 (*q*)

[a]) Overlapping signals.

This, together with the large coupling constant ($J = 11$ Hz) between H–C(5) and H–C(6), suggesting that H–C(3)/*Me*–C(4), *Me*–C(4)/H–C(5), and H–C(5)/H–C(6) were *trans*, respectively. In addition, NOESY correlations from H–C(16) to H–C(14), *Me*–C(20) as well as from *Me*–C(15) to *Me*–C(17) provided evidence that H–C(16)/*Me*–C(17) and H–C(16)/H–C(20) were *trans* disposed (*Fig. 1*). Thus, the structure of G was assigned as **3**, having (3*R**,4*R**,5*S**,6*S**,16*S**,17*R**,20*S**) relative configuration.

Wortmannilactone H (**4**) was assigned the molecular formula as $C_{26}H_{34}O_5$ on the basis of HR-FAB-MS. The IR, ^{1}H- and ^{13}C-NMR spectral data of **4** were closely related to those of **1** in the bicyclic ketolactone moiety and **3** in the dihydropyran ring moiety. The remaining signals also showed the presence of a tetraene, which was consistent with those of **1**, **2**, and **3**, respectively. The (*E*) geometry was assigned for the C=C bonds on the basis of the large coupling constant ($J = 15$ Hz). On the basis of these data, the structure **4** is proposed for wortmannilactone H (*Table 2*).

Biosynthetic studies showed that the 2,3-dimethylated γ-lactone moiety of prugosene B2 could be the product of hydrolytic opening of the lactone ring in the oxabicyclo[2.2.1]heptane substructure [8]. The *cis* disposed *Me*–C(3)/*Me*–C(4) suggested that **3** should not be the product of cleaving the C(3)/C(4) bond in **4**, the biosynthetic pathway of **3** may be different from that of prugosene B2.

As the initial step of evaluating the biological properties of the compounds isolated in this study, compounds **1**–**4** were screened for cathepsin B inhibitory activity. The IC_{50} values of compounds **1**–**4** against cathepsin B were 4.3, 6.5, 13.0, and 6.0 μM, respectively. Leupeptin, the positive control substance, had an IC_{50} value of 7.5 μM (*Fig. 2*).

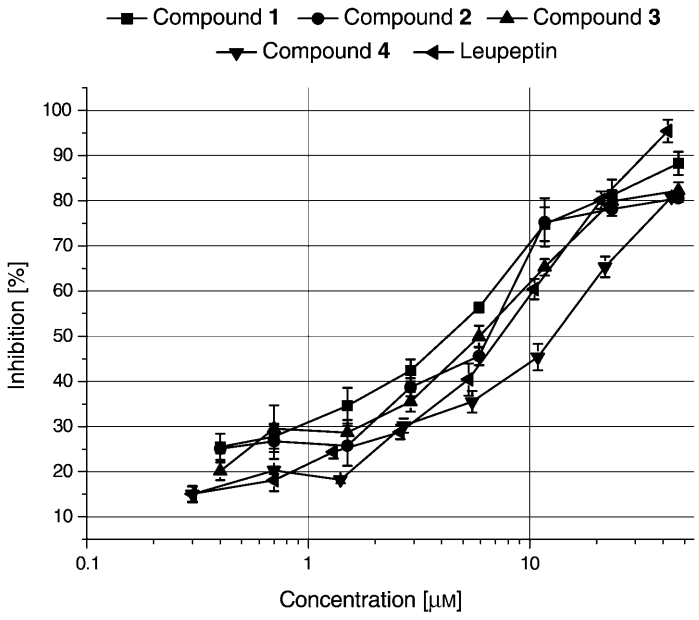

Fig. 2. *Inhibitory activities of compounds* **1**–**4** *against cathepsin B* (leupeptin as positive control)

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Experimental Part

General. HPLC: *Waters* HPLC system equipped with a photo-diode array (PDA) detector. Optical rotations: *Perkin-Elmer 241* polarimeter at the sodium D line (589 nm). IR Spectra: *Nicolet Magna-IR 550* instrument. UV Spectra: *Pharmacia Ultrospec 2100 Pro* instrument. 1D- and 2D-NMR spectra: *Varian Inova-500* spectrometer using standard VARIAN pulse sequences. Mass Spectra: *Waters LC-MS ZQ 2000* (ESI mode) or *Bruker Daltonics Apex II* mass spectrometer (FAB mode).

Fungal Material. The fungus was isolated from a soil sample collected in Chuxiong of Yunnan Province, China (May, 2001). The strain was identified as *Talaromyces wortmannii* according to *Pitt*'s description [16]. The strain was deposited with the *North China Pharmaceutical Group Ltd*. New Drug R&D Center with accession number F 01Z0195.

Fermentation and Isolation of Wortmannilactones. T. wortmannii was fermented and the four new tetraene lactones were isolated using a procedure similar to previous work [14]. Briefly, after two stage solid-state fermentation, the solid culture (4 kg) was extracted with AcOEt (4.0 l). The AcOEt layer was evaporated under reduced pressure to yield a residue (20.5 g). The tetraene macrolides were isolated by initial column chromatography on silica gel using $CHCl_3$ with increasing proportions of MeOH, followed by prep. RP-HPLC, using 80% MeCN/H_2O at a flow rate of 6 ml/min and UV detection at 312 nm to afford **1** (12.8 mg), **2** (8.2 mg), **3** (5.4 mg), and **4** (4.8 mg).

Bioassay. The cathepsin B assays were carried out in triplicate according to a published method [17] with modification: 50 µl of reaction buffer (100 mM AcONa, 1 mM EDTA, 4 mM dithiothreitol, pH 5.5) containing 0.0025 units of cathepsin B and 2 µl of compounds dissolved in DMSO were added to each well of a 96 well plate. After pre-incubation for 15 min at r.t., 50 µl of reaction buffer (100 µM Z-Arg-Arg-7-amido-4-methylcoumarin) was added and incubated for 30 min at r.t. Fluorescence was measured using a microplate reader (*Wallac 1420 Victor*^{2}, *Perkin-Elmer Ex 355*, Em 460 nm). The IC_{50} value was defined as the concentration of sample necessary to inhibit the cathepsin B activity to 50% of the control. Leupeptin was used as a positive control substance.

Wortmannilactone E (=*(4*S*,7*R*)-7-{(1*E*,3*E*,5*E*,7*E*)-8-[(2*S*,5*S*,6*S*)-5,6-Dihydro-5-hydroxy-3,5,6-trimethyl-2*H*-pyran-2-yl]nona-1,3,5,7-tetraen-1-yl}-4,6,7-trimethyl-2-oxabicyclo[2.2.1]heptane-3,5-dione*; **1**). Amorphous powder. $[\alpha]_D^{25} = -38.0$ ($c = 0.125$, MeOH). UV (MeOH): 297 (4.12), 312 (4.35), 326 (4.08). IR (KBr): 3300, 1800 (C=O), 1754 (C=O), 1390, 970. ^{1}H-NMR (500 MHz, CD_3OD) and ^{13}C-NMR (125 MHz, CD_3OD): *Table 1*. ESI-MS (pos.): 449 ($[M+Na]^+$). ESI-MS (neg.): 425 ($[M-H]^-$). HR-FAB-MS (pos.): 449.2298 ($[M+Na]^+$, $C_{26}H_{34}NaO_5^+$; calc. 449.2304).

Wortmannilactone F (=*(4*S*,7*R*)-7-{(1*E*,3*E*,5*E*,7*E*)-8-[(2*S*,5*R*,6*S*)-5,6-Dihydro-5-hydroxy-3,5,6-trimethyl-2*H*-pyran-2-yl]nona-1,3,5,7-tetraen-1-yl}-4,6,7-trimethyl-2-oxabicyclo[2.2.1]heptane-3,5-dione*; **2**). Amorphous powder. $[\alpha]_D^{25} = -65.0$ ($c = 0.178$, MeOH). UV (MeOH): 297 (4.12), 312 (4.36), 326 (4.08). IR (KBr): 3300, 1800 (C=O), 1755 (C=O), 1390, 970. ^{1}H-NMR (500 MHz, CD_3OD) and ^{13}C-NMR (125 MHz, CD_3OD): *Table 1*. ESI-MS (pos.): 449 ($[M+Na]^+$). ESI-MS (neg.): 425 ($[M-H]^-$). HR-FAB-MS (pos.): 449.2292 ($[M+Na]^+$, $C_{26}H_{34}NaO_5^+$; calc. 449.2304).

Wortmannilactone G (=*Methyl (2*R*)-2-[(3*R*,4*R*)-3-{(1*E*,3*E*,5*E*,7*E*)-8-[(2*S*,3*R*,6*S*)-3,6-Dihydro-3-hydroxy-3,5,6-trimethyl-2*H*-pyran-2-yl]nona-1,3,5,7-tetraen-1-yl}-3,4-dimethyl-5-oxotetrahydrofuran-2-yl]propanoate*; **3**). Amorphous powder. $[\alpha]_D^{25} = -26.0$ ($c = 0.159$, MeOH). UV (MeOH): 297 (4.08), 312 (4.32), 326 (4.18). IR (KBr): 3300, 2920, 1680 (C=O), 1390, 970. ^{1}H-NMR (500 MHz, CD_3OD) and ^{13}C-NMR (125 MHz, CD_3OD): *Table 2*. ESI-MS (pos.): 459 ($[M+H]^+$). ESI-MS (neg.): 457 ($[M-H]^-$). HR-FAB-MS (pos.): 459.2758 ($[M+H]^+$, $C_{27}H_{39}O_6^+$; calc. 459.2747).

Wortmannilactone H (=*(4*S*,7*R*)-7-{(1*E*,3*E*,5*E*,7*E*)-8-[(2*S*,3*R*,6*S*)-3,6-Dihydro-3-hydroxy-3,6-dimethyl-2*H*-pyran-2-yl]nona-1,3,5,7-tetraen-1-yl}-4,6,7-trimethyl-2-oxabicyclo[2.2.1]heptane-3,5-dione*;

4). Amorphous powder. $[\alpha]_D^{25} = -46.0$ ($c = 0.198$, MeOH). UV (MeOH): 297 (4.11), 312 (4.36), 326 (4.09). IR (KBr): 3300, 1801 (C=O), 1754 (C=O). ^{1}H-NMR (500 MHz, CD_3OD) and ^{13}C-NMR (125 MHz, CD_3OD): *Table 2*. ESI-MS (pos.): 449 ($[M+Na]^+$). ESI-MS (neg.): 425 ($[M-H]^-$). HR-FAB-MS (pos.): 449.2289 ($[M+Na]^+$, $C_{26}H_{34}NaO_5^+$; calc. 449.2304).

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