

Taccalonolides W–Y, Three New Pentacyclic Steroids from *Tacca plantaginea*

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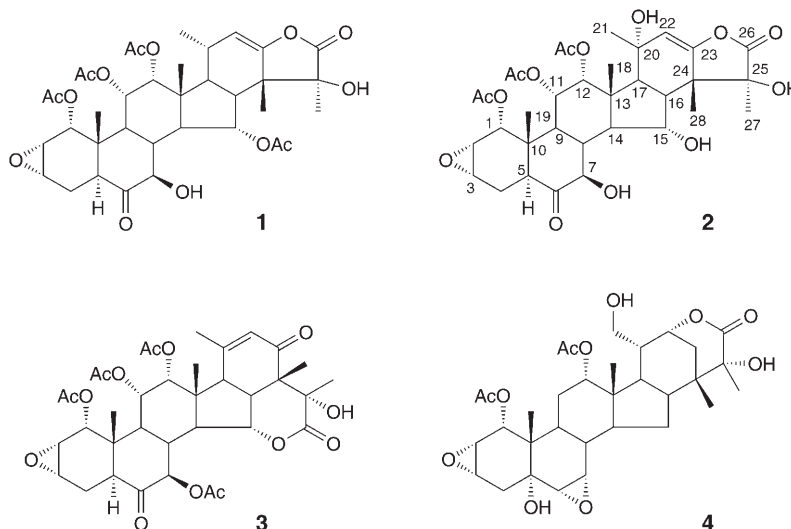
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Three new pentacyclic steroids, taccalonolides W–Y (**2–4**, resp.), have been isolated from the whole plants of *Tacca plantaginea*. Their structures were elucidated on the basis of spectroscopic methods including extensive 1D- and 2D-NMR experiments.

Introduction. – Plants of the genus *Tacca* are phenomenal resources of taccalonolide steroids, which possess a special pentacyclic steroidal skeleton, and some of which show antitumor activity [1][2]. Up to now, the 22 taccalonolides A–V have been isolated from *T. plantaginea*, *T. subflaellata*, and *T. paxiana* [1][3–9]. The rhizome of *Tacca plantaginea* has long been used in China as folk medicine for analgesic, antipyretic, anti-inflammatory, and incised wounds [10]. Previous chemical investigation of this plant led to the isolation of four new steroidal saponins, and five new withanolides, plantagiolides A–E [11–13], as well as 13 taccalonolides A–M [1][3–6]. As part of our continuing work to search for novel compounds, three new taccalonolides W–Y (**2–4**, resp.) were isolated from the species besides the known taccalonolide A. The isolation and structure elucidation of compounds **2–4** are the subject of this report.

Results and Discussion. – The CHCl₃-soluble part of the extract from the whole plants of *T. plantaginea* using 95% EtOH was subjected to repeated column chromatography on silica gel and semi-preparative HPLC to afford taccalonolides A, W, X, and Y (**1–4**).

Taccalonolide W (**2**) was obtained as a white powder. The molecular formula of **2** was deduced to be C₃₄H₄₄O₁₄ from HR-ESI-MS at *m/z* 699.2618 ([*M* + Na]⁺; calc. 699.2629), indicating 13 degrees of unsaturation. The IR spectrum showed absorptions at 3420, 1818, 1745, and 1693 cm⁻¹, which implied the presence of OH groups, an enol γ -lactone, Ac groups, and C=C bonds, respectively. The ¹H-NMR spectrum of **2** (Table 1) exhibited characteristic resonances similar to those of taccalonolides, including five Me groups at δ (H) 0.83, 1.05, 1.35, 1.37, and 1.74, and an olefinic H-atom at 5.26. A detailed comparison of the ¹H- and ¹³C-NMR and DEPT spectroscopic data (Tables 1 and 2) of **2** with those of taccalonolide B [1] revealed the absence of a doublet for Me(21) in the ¹H-NMR spectrum, and a missing CH signal for C(20) in the



^{13}C -NMR spectrum, but instead the presence of a Me *singlet* at $\delta(\text{H})$ 1.35 for Me(21) in the ^1H -NMR spectrum, and a quaternary oxygenated C-atom at $\delta(\text{C})$ 72.7 in the ^{13}C -NMR spectrum for C(20) in **2**. This was confirmed by HMBC correlations of the C-atom at $\delta(\text{C})$ 72.7 (*s*, C(20)) with the H-atoms at $\delta(\text{H})$ 2.48–2.52 (*m*, H–C(16)), 2.44–2.48 (*m*, H–C(17)), 1.35 (*s*, Me(21)), and 5.26 (*br. s*, H–C(22)). The relative configuration of **2** was determined by the analysis of a ROESY experiment, in which correlations of Me(18)/H–C(11) and H–C(12), Me(19)/H–C(1) and H–C(11) indicated that the AcO groups at C(1), C(11), and C(12) are in α -orientation, while the correlations of H–C(1)/H–C(2) and H–C(2)/H–C(3) confirmed the β -orientation of H–C(2) and H–C(3). The observed ROESY correlations for H–C(14)/H–C(7) and H–C(17), Me(18)/H–C(16), Me(21), and Me(28), and H–C(17)/Me(27) suggested that HO–C(7), HO–C(25), Me(21), and Me(28) were in the β -orientation. The H–C(5) and HO–C(15) were assigned α on the basis of ROESY correlations for H–C(5)/H–C(7) and H–C(15)/Me(18). From the above analysis, the structure of **2** was unequivocally determined as shown and named taccalonolide W.

Taccalonolide X (**3**) was isolated as a colorless powder. Its molecular formula, $\text{C}_{36}\text{H}_{44}\text{O}_{14}$ was determined by HR-ESI-MS at m/z 723.2626 ($[M + \text{Na}]^+$; calc. 723.2629), corresponding to 15 degrees of unsaturation. The UV spectrum of **3** showed an absorption maximum at 244 nm, indicating the presence of a conjugated enone system, while the absorptions in the IR spectrum at 3439, 1813, 1745, and 1659 cm^{-1} suggested the presence of OH groups, a δ -lactone, an Ac group, and C=C bonds, respectively. The ^{13}C -NMR spectrum indicated 36 C-atom resonances as required by the HR-ESI-MS. There were two signals for C=O groups at $\delta(\text{C})$ 202.4 and 198.0, five ester C=O groups at 170.9, 170.6, 169.7, 169.6, and 169.2, one trisubstituted C=C bond at 160.9 and 130.0, nine Me groups, one CH_2 group, 13 CH groups, thereof seven oxygenated, four quaternary C-atoms, thereof one oxygenated. The general NMR characteristics indicated that **3** is quite similar in structure to taccalonolide C [3]. The major

Table 1. $^1\text{H-NMR}$ Data of Compounds **2–4**. δ in ppm, J in Hz.

	2^{a)}	3^{a)}	4^{b)}
H–C(1)	4.72 (<i>d</i> , $J=5.4$)	4.73 (<i>d</i> , $J=5.5$)	4.79 (<i>d</i> , $J=5.2$)
H–C(2)	3.51 (<i>dd</i> , $J=3.7, 5.4$)	3.46 (<i>dd</i> , $J=3.7, 5.5$)	3.82 (<i>d</i> , $J=5.2$)
H–C(3)	3.40 (<i>br. s</i>)	3.37–3.38 (<i>m</i>)	3.50 (<i>br. s</i>)
CH ₂ (4)	2.08–2.10 (<i>m</i>), 2.20–2.26 (<i>m</i>)	2.00–2.11 (<i>m</i>), 2.17–2.20 (<i>m</i>)	2.03–2.05 (<i>m</i>), 2.30–2.33 (<i>m</i>)
H–C(5)	2.79 (<i>dd</i> , $J=6.1, 11.0$)	2.84–2.88 (<i>m</i>)	–
H–C(6)	–	–	2.88 (<i>d</i> , $J=3.4$)
H–C(7)	4.16 (<i>d</i> , $J=10.8$)	5.28 (<i>d</i> , 11.5)	3.13 (<i>br. s</i>)
H–C(8)	1.78–1.83 (<i>m</i>)	2.06–2.13 (<i>m</i>)	1.70–1.72 (<i>m</i>)
H–C(9)	2.72–2.77 (<i>m</i>)	2.87–2.92 (<i>m</i>)	2.34–2.36 (<i>m</i>)
H–C(11) or CH ₂ (11)	5.31 (<i>d</i> , $J=2.4$)	5.38 (<i>dd</i> , $J=2.6, 11.5$)	1.48–1.50 (<i>m</i>), 1.56–1.59 (<i>m</i>)
H–C(12)	5.28 (<i>br. s</i>)	5.43 (<i>d</i> , $J=2.6$)	5.06 (<i>br. s</i>)
H–C(14)	2.08–2.11 (<i>m</i>)	2.50–2.53 (<i>m</i>)	2.60–2.62 (<i>m</i>)
H–C(15) or CH ₂ (15)	4.43 (<i>dd</i> , $J=8.0, 9.1$)	5.06 (<i>dd</i> , $J=2.0, 8.5$)	1.40–1.43 (<i>m</i>), 2.62–2.65 (<i>m</i>)
H–C(16)	2.48–2.52 (<i>m</i>)	2.48–2.50 (<i>m</i>)	1.90–1.93 (<i>m</i>)
H–C(17)	2.44–2.48 (<i>m</i>)	3.76 (<i>d</i> , $J=12.8$)	2.21–2.25 (<i>m</i>)
Me(18)	1.05 (<i>s</i>)	1.06 (<i>s</i>)	0.87 (<i>s</i>)
Me(19)	0.83 (<i>s</i>)	0.83 (<i>s</i>)	0.71 (<i>s</i>)
H–C(20)	–	–	2.03–2.05 (<i>m</i>)
Me(21) or CH ₂ (21)	1.35 (<i>s</i>)	1.93 (<i>s</i>)	3.85–3.88 (<i>m</i>), 4.01–4.03 (<i>m</i>)
H–C(22)	5.26 (<i>br. s</i>)	5.84 (<i>s</i>)	5.30 (<i>br. s</i>)
CH ₂ (23)	–	–	1.43 (<i>d</i> , $J=4.8$), 2.20–2.22 (<i>m</i>)
Me(27)	1.74 (<i>s</i>)	1.63 (<i>s</i>)	1.45 (<i>s</i>)
Me(28)	1.37 (<i>s</i>)	1.25 (<i>s</i>)	1.15 (<i>s</i>)
Ac	2.00 (<i>s</i>), 2.10 (<i>s</i>), 2.16 (<i>s</i>)	2.02 (<i>s</i>), 2.12 (<i>s</i>), 2.12 (<i>s</i>), 2.16 (<i>s</i>)	1.96 (<i>s</i>), 2.03 (<i>s</i>)

^{a)} In CDCl₃. ^{b)} In (D₅)pyridine.

differences in the $^{13}\text{C-NMR}$ spectrum for **3** were the disappearance of signals for one CH and one CH₂ group each, and the presence of a signal for one trisubstituted C=C bond. The location of the C=C bond was deduced from the HMBC spectrum, which indicated important correlations of the CH H-atom at $\delta(\text{H})$ 2.48–2.50 (*m*, H–C(16)) to the C-atom at $\delta(\text{C})$ 160.9 (*s*, C(20)), of the methine H-atom at $\delta(\text{H})$ 3.76 (*d*, H–C(17)) to the C-atoms at $\delta(\text{C})$ 21.5 (*q*, C(21)), 160.9 (*s*, C(20)), and 130.0 (*d*, C(22)), and of the methine H-atom at $\delta(\text{H})$ 5.84 (*s*, H–C(22)) to the C-atoms at $\delta(\text{C})$ 21.5 (*q*, C(21)), 44.4 (*d*, C(17)), 198.0 (*s*, C(23)), and 47.6 (*s*, C(24)). These correlations indicated that the C=C bond connects C(20) with C(22). Extensive interpretation of the ROESY spectrum correlations, combined with comparison of the data with those of taccalonolide C, established the configuration of **3** as follows: H–C(1), H–C(2), H–C(3), H–C(11), H–C(12), H–C(15), Me(27), and Me(28) possess β -configuration, while H–C(5) and H–C(7) possess α -configuration. Consequently, the structure of **3** was unambiguously established and named taccalonolide X.

Table 2. ^{13}C -NMR Data of Compounds **2**–**4**. δ in ppm.

	2 ^{a)}	3 ^{a)}	4 ^{b)}		2 ^{a)}	3 ^{a)}	4 ^{b)}
C(1)	72.5 (<i>d</i>)	72.4 (<i>d</i>)	72.6 (<i>d</i>)	C(19)	13.1 (<i>q</i>)	12.8 (<i>q</i>)	16.3 (<i>q</i>)
C(2)	49.8 (<i>d</i>)	49.5 (<i>d</i>)	51.8 (<i>d</i>)	C(20)	72.7 (<i>s</i>)	160.9 (<i>s</i>)	48.1 (<i>d</i>)
C(3)	52.0 (<i>d</i>)	52.1 (<i>d</i>)	55.6 (<i>d</i>)	C(21)	26.1 (<i>q</i>)	21.5 (<i>q</i>)	60.1 (<i>t</i>)
C(4)	21.4 (<i>t</i>)	21.2 (<i>t</i>)	33.6 (<i>t</i>)	C(22)	115.7 (<i>d</i>)	130.0 (<i>d</i>)	76.5 (<i>d</i>)
C(5)	42.4 (<i>d</i>)	42.7 (<i>d</i>)	70.6 (<i>s</i>)	C(23)	153.1 (<i>s</i>)	198.0 (<i>s</i>)	40.4 (<i>t</i>)
C(6)	208.5 (<i>s</i>)	202.4 (<i>s</i>)	56.9 (<i>d</i>)	C(24)	51.0 (<i>s</i>)	47.6 (<i>s</i>)	40.2 (<i>s</i>)
C(7)	75.6 (<i>d</i>)	76.7 (<i>d</i>)	54.7 (<i>d</i>)	C(25)	79.2 (<i>s</i>)	77.2 (<i>s</i>)	77.5 (<i>s</i>)
C(8)	42.5 (<i>d</i>)	38.0 (<i>d</i>)	36.3 (<i>d</i>)	C(26)	174.9 (<i>s</i>)	170.9 (<i>s</i>)	180.3 (<i>s</i>)
C(9)	39.3 (<i>d</i>)	40.8 (<i>d</i>)	29.7 (<i>d</i>)	C(27)	21.6 (<i>q</i>)	23.3 (<i>q</i>)	27.6 (<i>q</i>)
C(10)	43.2 (<i>s</i>)	42.7 (<i>s</i>)	40.6 (<i>s</i>)	C(28)	25.4 (<i>q</i>)	22.3 (<i>q</i>)	22.4 (<i>q</i>)
C(11)	70.2 (<i>d</i>)	70.2 (<i>d</i>)	25.4 (<i>t</i>)	Ac	170.9 (<i>s</i>)	170.6 (<i>s</i>)	170.9 (<i>s</i>)
C(12)	73.9 (<i>d</i>)	73.0 (<i>d</i>)	75.5 (<i>d</i>)		170.0 (<i>s</i>)	169.7 (<i>s</i>)	170.5 (<i>s</i>)
C(13)	44.5 (<i>s</i>)	44.0 (<i>s</i>)	46.5 (<i>s</i>)		170.0 (<i>s</i>)	169.6 (<i>s</i>)	20.8 (<i>q</i>)
C(14)	57.0 (<i>d</i>)	57.3 (<i>d</i>)	44.1 (<i>d</i>)		21.0 (<i>q</i>)	169.2 (<i>s</i>)	20.5 (<i>q</i>)
C(15)	71.5 (<i>d</i>)	78.4 (<i>d</i>)	25.6 (<i>t</i>)		21.3 (<i>q</i>)	21.1 (<i>q</i>)	
C(16)	44.8 (<i>d</i>)	46.0 (<i>d</i>)	52.4 (<i>d</i>)		20.5 (<i>q</i>)	20.8 (<i>q</i>)	
C(17)	49.6 (<i>d</i>)	44.4 (<i>d</i>)	41.1 (<i>d</i>)			20.6 (<i>q</i>)	
C(18)	15.2 (<i>q</i>)	14.8 (<i>q</i>)	12.9 (<i>q</i>)			20.5 (<i>q</i>)	

^{a)} In CDCl_3 . ^{b)} In $(\text{D}_5)\text{pyridine}$.

Taccalonolide **Y** (**4**) was obtained as a white powder. Its positive FAB-MS indicated the pseudomolecular ion at m/z 605 ($[M + \text{H}]^+$), and the HR-ESI-MS indicated the molecular formula $\text{C}_{32}\text{H}_{44}\text{O}_{11}$ with eleven degrees of unsaturation. The IR spectrum showed characteristic absorptions at 3448, 1730, and 1635 cm^{-1} which indicated the presence of OH and Ac groups, as well as a δ -lactone. The ^1H -NMR showed signals for six Me groups, four epoxy H-atoms, one $\text{HO}-\text{CH}_2$, and three downfield-shifted H-atoms. As for taccalonolides **A**, **W**, and **X** (**1**–**3**), the basic skeleton of taccalonolide **Y** (**4**) was that of a pentacyclic steroid, except that the side chain was enlarged from C_5 to C_6 , and ring *B* contained an epoxy group. According to the ^1H - and ^{13}C -NMR spectral data, **4** was very similar to the known compound taccalonolide **Q** [8], except for the lack of a COOH group and the presence of a $\text{HO}-\text{CH}_2$ ($\delta(\text{C})$ 60.1) connected to C(20) ($\delta(\text{C})$ 48.1). Thus, it was supposed that the COOH group at C(20) of taccalonolide **Q** was reduced to a $\text{HO}-\text{CH}_2$ group, which was confirmed by the mass difference of 14 amu and the HMBC spectrum. In the HMBC spectrum, cross-peaks between $\delta(\text{H})$ 2.21–2.25 (*m*, $\text{H}-\text{C}(17)$) with $\delta(\text{C})$ 44.1 (*d*, C(14)), 52.4 (*d*, C(16)), 12.9 (*q*, C(18)), 48.1 (*d*, C(20)), 60.1 (*t*, C(21)), and 76.5 (*d*, C(22)), and between $\delta(\text{H})$ 5.30 (*br. s*, $\text{H}-\text{C}(22)$) and $\delta(\text{C})$ 41.1 (*d*, C(17)), 60.1 (*t*, C(21)), 40.4 (*t*, C(23)), 40.2 (*s*, C(24)), and 180.3 (*s*, C(26)) were observed. The relative configuration was determined by a ROESY experiment with cross-peaks between Me(18)/ $\text{H}-\text{C}(12)$ and $\text{H}-\text{C}(16)$, $\text{H}-\text{C}(16)/\text{H}-\text{C}(22)$, $\text{H}-\text{C}(22)/\text{H}-\text{C}(20)$ and Me(28)/Me(27), and Me(19)/ $\text{H}-\text{C}(1)$, $\text{H}-\text{C}(2)$, $\text{H}-\text{C}(3)$, $\text{H}-\text{C}(6)$, and $\text{H}-\text{C}(7)$. Therefore, the structure of **4** was assigned as shown and named taccalonolide **Y**.

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Experimental Part

General. Semiprep. HPLC: *Agilent 1100* apparatus equipped with a *Zorbax SB-C-18* column (*Agilent*, 9.4 mm × 25 cm). Column chromatography (CC): silica gel (SiO₂) (200–300 mesh; *Qingdao Marine Chemical Inc.*, China) or SiO₂ *H* (10–40 μm, *Qingdao Marine Chemical Inc.*), and *Lichroprep RP-18* (43–63 μm, *Merck*). Fractions were monitored by TLC, and spots were visualized by heating SiO₂ plates sprayed with 10% H₂SO₄ in EtOH. Optical rotations: *Jasco DIP-370* digital polarimeter. UV Spectra: *Shimadzu UV-2401 PC* spectrophotometer; λ_{max} in nm. IR Spectra: *Bio-Rad FTS-135* infrared spectrophotometer with KBr pellets. 1D- and 2D-NMR Spectra: *Bruker AM-400* and *DRX-500* instruments using Me₄Si as the internal standard; δ in ppm rel. to solvent signals. ESI-MS and HR-ESI-MS Spectra: *API Qstar Pulsar LC/TOF* spectrometer; in *m/z* (rel. %).

Plant Material. The whole plants of *Tacca plantaginea* were collected in Guilin, Guangxi Zhuang Autonomous Region, P. R. China, in August 1999, and identified by Professor *De-Ding Tao*, Kunming Institute of Botany, the Chinese Academy of Sciences (CAS). The voucher was deposited with the Herbarium of Kunming Institute of Botany, CAS.

Extraction and Isolation. The powdered air-dried plants of *T. plantaginea* (30 kg) were exhaustively extracted three times with 400 l of 95% EtOH under reflux. After evaporation of the solvent, the resulting residue (1.5 kg) was successively extracted with CHCl₃ and BuOH. The CHCl₃ extract (700 g) was subjected to CC (SiO₂) eluting with a petroleum ether/AcOEt gradient (1:0, 10:1, 5:1, 7:1, 1:1) to give five fractions. *Fr. 4* (150 g) was repeatedly chromatographed on SiO₂ (CHCl₃/MeOH, 100:1) and semiprep. HPLC (MeCN/H₂O, 30:70) to afford **1** (1.1 g), **2** (20 mg), **3** (4 mg), and **4** (21 mg).

Taccalonolide W (= (1*S*,5*S*,5*aS*,6*R*,7*R*,8*aS*,9*aS*,10*aS*,11*R*,11*aR*,12*S*,13*R*,13*aR*)-11,12,13-Tris(acetyloxy)-5,5*a*,5*b*,6,6*a*,6*b*,7,8*a*,9,9*a*,10*a*,11,11*a*,11*b*,12,13,13*a*,13*b*-octadecahydro-1,5,6,7-tetrahydroxy-1,5,5*a*,11*a*,13*a*-pentamethyl-1*H*-oxireno[6,7]naphtho[1',2':7,8]fluoreno[2,1-*b*]furan-4,8-dione; **2**). White powder. [α]_D²⁰ = +39.5 (*c* = 0.50, CHCl₃). IR (KBr): 3420, 2975, 2930, 1818, 1745, 1693, 1434, 1375, 1250, 1126, 1091, 1041, 751. ¹H- and ¹³C-NMR: *Tables 1* and *2*. FAB-MS: 677 (4, [M + H]⁺). HR-EI-MS: 699.2618 ([M + Na]⁺, C₃₄H₄₄NaO₁₄; calc. 699.2629).

Taccalonolide X (= (3*aS*,4*S*,6*aR*,7*R*,8*aS*,9*aS*,10*aS*,11*R*,11*aR*,12*S*,13*R*,13*aR*)-7,11,12,13-Tetrakis(acetyloxy)-3*a*,4,6*a*,6*b*,6*c*,7,8*a*,9,9*a*,10*a*,11,11*a*,11*b*,12,13,13*a*,13*b*,13*c*-octadecahydro-4-hydroxy-1,3*a*,4,11*a*,13*a*-pentamethyl-3*H*-oxireno[6,7]naphtho[1',2':7,8]fluoreno[9,1-*bc*]pyran-3,5,8-trione; **3**). Colorless powder. [α]_D²⁰ = +23.8 (*c* = 0.13, MeOH). UV (CHCl₃): 244. IR (KBr): 3439, 2926, 2854, 1813, 1745, 1659, 1438, 1376, 1248, 1124, 1040, 761. ¹H- and ¹³C-NMR: *Tables 1* and *2*. ESI-MS: 723 (100, [M + Na]⁺). HR-EI-MS: 723.2626 ([M + Na]⁺, C₃₆H₄₄NaO₁₄; calc. 723.2629).

Taccalonolide Y (= (1*aS*,1*bR*,2*aS*,3*aS*,4*R*,4*aS*,6*S*,6*aS*,7*R*,8*R*,11*R*,12*S*,13*cS*)-4,6-Bis(acetyloxy)icosahydro-1*b*,11-dihydroxy-7-(hydroxymethyl)-4*a*,6*a*,11,12-tetramethyl-8,12-methanobisoxireno[3',4':6',7']naphtho[2',1':4,5]indeno[1,2-*d*]joxocin-10(2*H*)-one; **4**): White powder. [α]_D²⁰ = +7.7 (*c* = 0.23, MeOH). IR (KBr): 3448, 2976, 2941, 1730, 1635, 1378, 1254, 1131, 1032. ¹H- and ¹³C-NMR: *Tables 1* and *2*. FAB-MS: 605 (49, [M + H]⁺), 545 (100, [M – AcOH]⁺), 527 (70, [M – AcOH – H₂O]⁺). HR-EI-MS: 627.2778 ([M + Na]⁺, C₃₂H₄₄NaO₁₁; calc. 627.2781).

REFERENCES

- [1] Z. L. Chen, B. D. Wang, M. Q. Chen, *Tetrahedron Lett.* **1987**, 28, 1673.
- [2] T. L. Tinley, D. A. Randall-Hlubek, R. M. Leal, E. M. Jackson, J. W. Cessac, J. C. Quada, T. K. Hemscheidt, S. L. Mooberry, *Cancer Res.* **2003**, 63, 3211.
- [3] Z. L. Chen, B. D. Wang, J. H. Shen, *Phytochemistry* **1988**, 27, 2999.
- [4] J. H. Shen, Z. L. Chen, Y. S. Gao, *Chin. J. Chem.* **1991**, 1, 92.
- [5] J. H. Shen, Z. L. Chen, Y. S. Gao, *Phytochemistry* **1996**, 42, 891.

- [6] Z. L. Chen, J. H. Shen, Y. S. Gao, M. Wichtl, *Planta Med.* **1997**, 63, 40.
- [7] A. Mühlbauer, M. Gehling, R. Velten, W. Andersch, C. Erdelen, A. Harder, P. Marczok, R. Nauen, A. Turberg, V. S. Tran, G. Adam, J. K. Liu, Int. Pat. WO 01/04256 to *Bayer AG* Germany, 2001.
- [8] Y. Huang, J. K. Liu, A. Mühlbauer, T. Henkel, *Helv. Chim. Acta* **2002**, 85, 2553.
- [9] A. Mühlbauer, S. Seip, A. Nowak, V. S. Tran, *Helv. Chim. Acta* **2003**, 86, 2065.
- [10] Jiangsu New Medical College, 'The Dictionary of Traditional Chinese Medicines', Shanghai Science and Technology Press, Shanghai, 1977, p. 524.
- [11] H. Y. Liu, C. X. Chen, *Chin. Chem. Lett.* **2002**, 13, 633.
- [12] H. Y. Liu, W. Ni, X. J. Hao, C. X. Chen, *J. Asian Nat. Prod.* **2006**, 8, 293.
- [13] H. Y. Liu, W. Ni, B. B. Xie, L. Y. Zhou, X. J. Hao, X. Wang, C. X. Chen, *Chem. Pharm. Bull.* **2006**, 54, 992.

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