Daphnane-Type Diterpenoids from the Flower Buds of *Daphne genkwa*

by **Ling-Zhi Li**[a]), **Pin-Yi Gao**[a]),**Ying Peng**[b]), **Li-Hui Wang**[b]), **Jing-Yu Yang**[b]), **Chun-Fu Wu**[b]), **Yan Zhang**[a]), and **Shao-Jiang Song***[a])

[a]) School of Traditional Chinese Materia Medica, Key Laboratory of Structure-Based Drug Design & Discovery, Shenyang Pharmaceutical University, Shenyang 110016, P. R. China (phone: +86-24-23986510; e-mail: songsj99@yahoo.com.cn)

[b]) School of Pharmacy, Shenyang Pharmaceutical University, Shenyang 110016, P. R. China

Three new daphnane-type diterpenoids, genkwanines M–O (**1**–**3**, resp.), together with seven known daphnane-type diterpenoids, genkwanines D and H, genkwaine F, genkwadaphnine, yuanhuatine, yuanhuafine, and yuanhuapine (**4**–**10**, resp.), were isolated from the flower buds of *Daphne genkwa* during a phytochemical investigation. The structures of the new compounds were elucidated on the basis of spectroscopic analyses, especially 2D-NMR spectra (HSQC, HMBC, and NOESY).

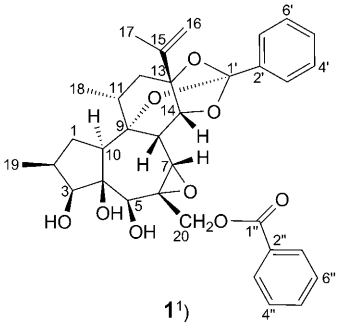
Introduction. – *Daphne genkwa* SIEB. et ZUCC., indigenous to the provinces along both the Yangtze River and the Yellow River of China, is a member of the family Thymelaeaceae. It is used as a folk medicine in China mainly for diuretic, antitussive, expectorant, and antitumors purposes. Previous studies on the chemical constituents of *Daphne genkwa* led to the isolation of a series of diverse compounds, including flavonoids, lignins, coumarins, caffeotannic acids, and diterpenoids [1–3]. Numerous species of the families Thymelaeaceae and Euphorbiaceae are known to contain toxic daphnane-type diterpene esters. So far, more than 80 daphnane-type diterpenoids were isolated from these families [4–7]. Those diterpenoids show a pleiotropic and partly overlapped pattern of biological activities, such as antitumor properties [6–9], potent antifertility activities [10–12], and, independently, neurotrophic [13] or irritant activities [14][15]. In the course of our search for biologically active compounds from plants, we were interested in the genus *Daphne* and began a study of the chemical components of *Daphne genkwa*.

In this article, we describe the isolation and structure elucidation of three new compounds of the polyfunctional daphnane type, named genkwanines M–O[1]) (**1**–**3**, resp.), along with the seven known daphnane-type diterpenoids genkwanines D and H, genkwaine F, genkwadaphnin, yuanhuatine, yuanhuafine, and yuanhuapine (**4**–**10**, resp.) from the flower buds of *Daphne genkwa*.

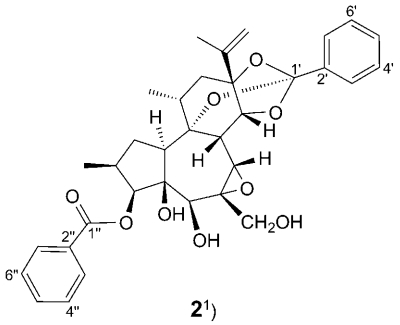
Results and Discussion. – 1. *Isolation and Structure Elucidation.* Column chromatography of 95% EtOH extracts obtained from the flower buds of *Daphne genkwa* yielded the three new diterpenoids **1**–**3**, along with seven known diterpenoids **4**–**10**.

---

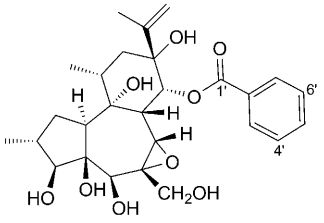
[1]) Arbitrary atom numbering; for systematic names, see *Exper. Part.*



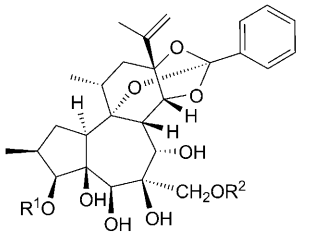
1[1])



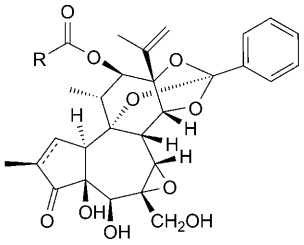
2[1])



3[1])



	R^1	R^2
4	Bz	H
5	H	Bz
6	H	$Me(CH_2)_4(CH=CH)_2C(O)$



	R	$\Delta^{1,2}$
7	Ph	$\Delta^{1,2}$
8	Ph	
9	Me	$\Delta^{1,2}$
10	Me	

Genkwanine M (**1**) was obtained as a white amorphous powder. In the HR-ESI-MS, the $[M+Na]^+$ ion peak appeared at *m*/*z* 613.2407, and the molecular formula was determined as $C_{34}H_{38}O_9$. The IR spectrum showed absorptions at 3452 (OH), 1720 (C=O), and 1645 (C=C). In the ^{1}H-NMR spectrum (600 MHz, $CDCl_3$) of **1** (*Table 1*), typical signals of the diterpene unit can be identified. The presence of one tertiary Me group at δ(H) 1.84 (*s*, Me(17)) and two secondary Me groups at δ(H) 1.31 (*d*, $J=$ 6.6 Hz, Me(18)) and 1.05 (*d*, $J=6.6$ Hz, Me(19)) were revealed. Four CH–O signals resonated at δ(H) 4.52 (*d*, $J=3.0$ Hz, H–C(14)), 3.83 (*s*, H–C(5)), 3.86 (*d*, $J=4.6$ Hz, H–C(3)), and 3.43 (*s*, H–C(7)). One CH_2 group showed up at δ(H) 5.09 (*d*, $J=$ 12.0 Hz, H–C(20)) and 4.02 (*d*, $J=12.0$ Hz, H′–C(20)), suggesting it to be attached to an O-function. The olefinic H-atoms appeared to be at a terminal C=C bond (δ(H) 5.07 (*s*, H–C(16)) and 4.93 (*s*, H′–C(16))), while an overlapping *m* at δ(H) 1.79–1.59 (3 H) was assigned to CH_2(1) and H–C(2). The ^{1}H-NMR spectrum further showed *m*s

Table 1. *^{1}H- and ^{13}C-NMR Data* (600 and 150 MHz, resp.; $CDCl_3$) *of* **1** *and* **2**[1]). δ in ppm, J in Hz.

	1		**2**	
	δ(H)	δ(C)	δ(H)	δ(C)
H_β–C(1)	1.79–1.80 (*m*)	34.3	1.98–2.00 (*m*)	36.1
H_α–C(1)	1.55–1.59 (*m*)		1.86–1.88 (*m*)	
H–C(2)	1.65–1.67 (*m*)	36.7	1.83–1.85 (*m*)	36.5
H–C(3)	3.86 (*d*, *J* = 4.6)	78.3	4.84 (*d*, *J* = 4.2)	82.9
C(4)		80.1		81.8
H–C(5)	3.83 (*s*)	71.3	4.13 (*s*)	74.7
C(6)		60.2		60.7
H–C(7)	3.43 (*s*)	64.2	3.44 (*s*)	64.2
H–C(8)	3.05 (*d*, *J* = 3.0)	36.5	2.95 (*d*, *J* = 2.4)	36.6
C(9)		80.0		80.5
H–C(10)	2.77 (*dd*, *J* = 13.2, 5.4)	48.6	2.88 (*dd*, *J* = 13.2, 5.4)	48.8
H–C(11)	2.36–2.38 (*m*)	35.3	2.46–2.51 (*m*)	35.5
H_β–C(12)	2.22 (*dd*, *J* = 13.8, 7.8)	35.8	2.16 (*dd*, *J* = 14.4, 7.8)	36.3
H_α–C(12)	1.80 (*d*, *J* = 13.8)		1.76 (*d*, *J* = 14.4)	
C(13)		84.3		84.6
H–C(14)	4.52 (*d*, *J* = 3.0)	82.5	4.49 (*d*, *J* = 2.4)	82.7
C(15)		146.5		146.6
CH_2(16)	5.07 (*s*), 4.93 (*s*)	111.2	5.03 (*s*), 4.90 (*s*)	111.4
Me(17)	1.84 (*s*)	19.2	1.81 (*s*)	19.4
Me(18)	1.31 (*d*, *J* = 6.6)	20.8	1.35 (*d*, *J* = 6.6)	21.2
Me(19)	1.05 (*d*, *J* = 6.6)	13.0	1.14 (*d*, *J* = 6.0)	13.6
CH_2(20)	5.09 (*d*, *J* = 12.0), 4.02 (*d*, *J* = 12.0)	68.4	3.86 (*d*, *J* = 12.0), 3.81 (*d*, *J* = 12.0)	66.3
C(1′)		117.0		117.6
C(2′)		136.1		136.4
H–C(3′)	7.74–7.75 (*m*)	126.1	7.75–7.76 (*m*)	126.3
H–C(4′)	7.34–7.35 (*m*)	127.9	7.37–7.38 (*m*)	128.2
H–C(5′)	7.34–7.35 (*m*)	129.2	7.37–7.38 (*m*)	129.5
H–C(6′)	7.34–7.35 (*m*)	127.9	7.37–7.38 (*m*)	128.2
H–C(7′)	7.74–7.75 (*m*)	126.1	7.75–7.76 (*m*)	126.3
C(1″)		166.6		168.8
C(2″)		129.8		130.0
H–C(3″)	8.06–8.07 (*m*)	129.8	8.06–8.07 (*m*)	130.2
H–C(4″)	7.43–7.45 (*m*)	128.4	7.49–7.51 (*m*)	128.9
H–C(5″)	7.55–7.57 (*m*)	133.2	7.62–7.64 (*m*)	133.9
H–C(6″)	7.43–7.57 (*m*)	128.4	7.49–7.51 (*m*)	128.9
H–C(7″)	8.06–8.07 (*m*)	129.8	8.06–8.07 (*m*)	130.2

of ten aromatic H-atoms at δ(H) 8.06–7.34 indicating the presence of two Ph moieties, one of them belonging to the 9,13,14-orthobenzoate moiety and the other to a benzoyloxy group. The ^{13}C-NMR spectrum (150 MHz, $CDCl_3$) of **1** (*Table 1*) exhibited 34 C-atom resonances, including three Me, four CH_2, and eighteen CH groups, and nine quaternary C-atoms, in which three Me groups (δ(C) 20.8 (C(18)), 19.2 (C(17)), and 13.0 (C(19))) and one terminal C=C bond (δ(C) 146.5 (C(15)) and 111.2 (C(16))) were distinguishable. Two O-bearing C-atoms at δ(C) 60.2 (C(6)) and 64.2 (C(7)) were shifted upfield compared with compounds **4**–**6** [6], suggesting the presence of a 6,7-epoxy unit instead of a 6,7-dihydroxy pattern. This change can also be verified by the

shifted H–C(7) at δ(H) 3.43. A quaternary C-atom at δ(C) 117.0 revealed the typical orthoester unit of daphnane-type diterpenoids. Analysis of the ^{1}H- and ^{13}C-NMR and HSQC data helped us to allot the H- to their bonded C-atoms, and the HMBC experiment further demonstrated the planar structure of **1**. In the HMBC spectrum (*Fig. 1*), the signals at δ(H) 5.09 and 4.02 (CH_2(20)) were correlated with the C(1″)=O group at δ(C) 166.6; accordingly the ester linkage site of the benzoyloxy group was deduced to be C(20). The signal at δ(C) 117.0 (quaternary C(1′)) showing correlation with H–C(14) authenticated the presence of an orthoester group in **1**. Other main connectivities displayed in this spectrum were: H–C(7)/C(8), C(9), C(14), and C(20), and H–C(10)/C(4), C(5), and C(11). The configuration of **1** was asserted by the ^{1}H-NMR coupling constants and the correlations in its NOESY plot (*Fig. 2*). The vicinal coupling constant J(2,3) of 4.6 Hz suggested a *cis* relation between the protons H–C(2) and H–C(3), and indicated that H–C(2) and H–C(3) were both in the α-configuration. Moreover, the significant NOESY cross-peaks H–C(2)/H–C(3), H–C(2)/H–C(10), and H–C(10)/H–C(5) permitted the assignment of H–C(5) and H–C(10) in the α-configuration. The absence of cross-peaks between δ(H) 2.77 (H–C(10)) and δ(H) 2.37 (H–C(11)) indicated that H–C(11) is in β-configuration. H–C(8) was correlated with H–C(11), H–C(7), and H–C(14), which showed that H–C(8), H–C(7), and H–C(14) are all in β-configuration; the configuration of H–C(7) was also supported by the *s* at δ(H) 3.43 (H–C(7)). If the H–C(7) was α-oriented, the coupling constant J(7,8) would be expected to be *ca.* 10 Hz. Therefore, the structure of genkwanine M (**1**) was elucidated as (2β,3β,6α,7α)-3-deoxo-6,7-epoxy-1,2,5,6-tetrahydro-3,5-dihydroxyresiniferonol 20-benzoate 9,13,14-orthobenzoate[1]).

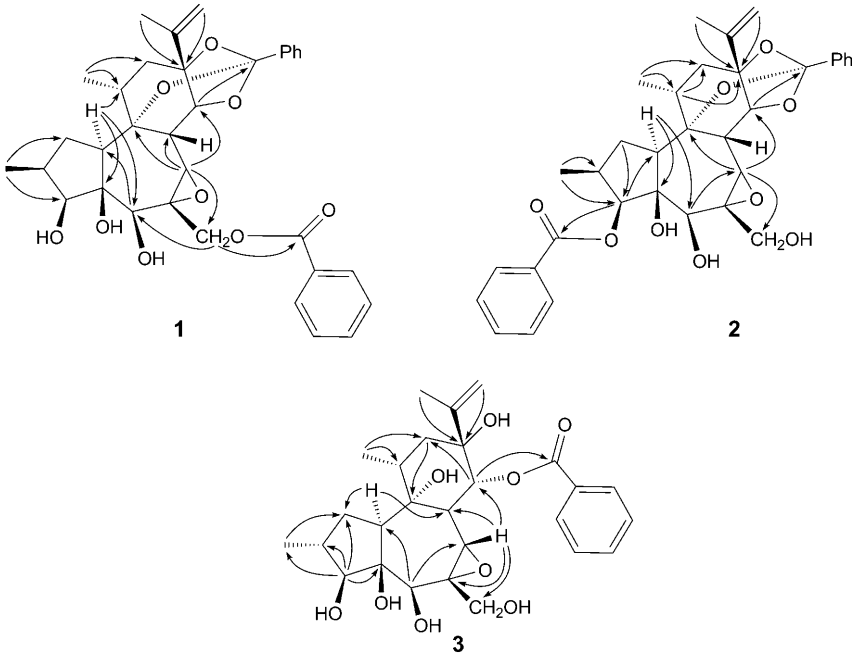


Fig. 1. *Key HMBC interactions* (H → C) *for* **1**, **2**, *and* **3**

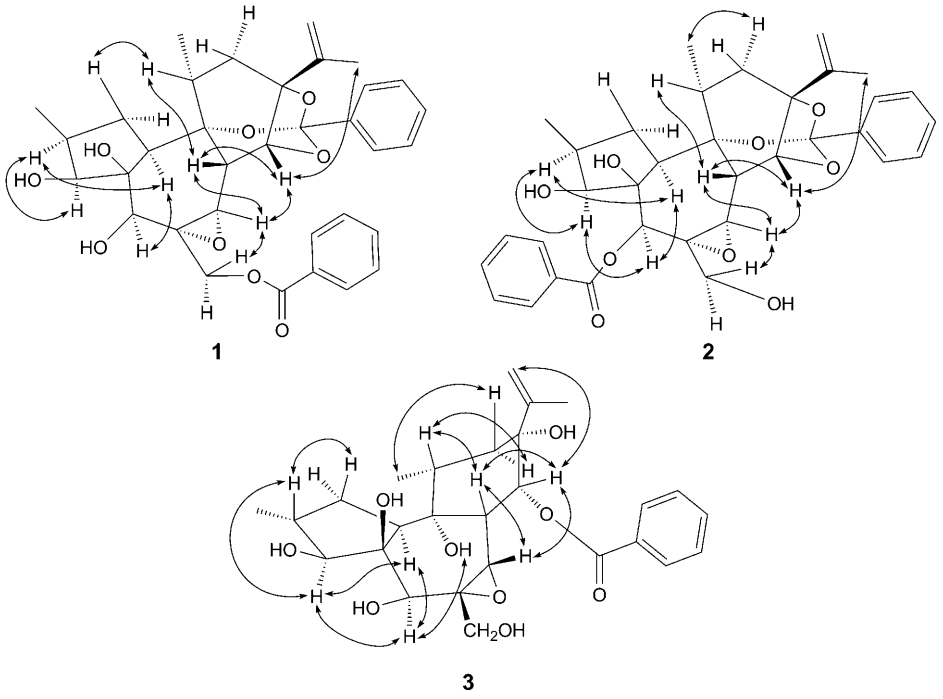


Fig. 2. *Key NOE correlations* (H ↔ H) *of* **1**–**3**

Genkwanine N (**2**), a white amorphous powder, has a molecular formula $C_{34}H_{38}O_9$ as determined by HR-ESI-MS with the $[M+Na]^+$ ion peak at *m/z* 613.2406. The IR spectrum showed bands of OH (3441 cm^{-1}), ester C=O (1708 cm^{-1}), C=C (1645 cm^{-1}), aromatic C=C (1602 cm^{-1}), and C–O–C moieties (1178 cm^{-1}). The HR-MS of **2** and **1** provided the same molecular formula $C_{34}H_{38}O_9$, indicating that **2** and **1** are regioisomeric diterpene esters. The ^{1}H- and ^{13}C-NMR data (600 and 150 MHz, resp.; $CDCl_3$) of **2** (*Table 1*) closely resembled those of **1**. They suggested the presence of the same daphnane-type skeleton, and the positions of the H- and C-atoms were almost identical in the NMR spectra; however, interestingly, the acylation position of the benzoyloxy linkages differed. As judged by visual inspection, the *s* at δ(H) 4.84 (*d*, $J = 4.2$ Hz, H–C(3)) was severely shifted downfield compared with that of **1**, thus suggesting the benzoyloxy was attached to C(3), which was also confirmed by the correlation between the C(1″)=O group at δ(C) 168.8 and the H-atom at δ(H) 4.84 (H–C(3)) in the HMBC spectrum (*Fig. 1*). A clearly distinguishable *s* at δ(C) 117.6 (quaternary C(1′)) in the ^{13}C-NMR spectrum suggested the presence of a 9,13,14-orthobenzoate unit. Further, the NOE cross-peaks (H–C(2)/H–C(3), H–C(3)/H–C(5), and H–C(5)/H–C(10) were consistent with an α-configuration of these H-atoms, as shown in *Fig. 2*. Additionally, H–C(8) had strong NOE correlations with H–C(7) and H–C(14), as well as H–C(11), indicating that these H-atoms are in β-configuration. The above-described spectral interpretations support the relative structure of compound **2** as (2β,3β,5β,6α,7α)-3-deoxo-6,7-epoxy-1,2,6,7-tetrahydro-

3,5-dihydroxyresiniferonol 3-benzoate 9,13,14-orthobenzoate[1]). All H- and C-atom signals in the NMR spectra of **2** were completely assigned by the interpretation of its HSQC, HMBC, and NOESY data.

Genkwanine O (**3**), an optically active white amorphous powder, displayed the $[M+Na]^+$ ion peak at *m/z* 527.2258 in the HR-ESI-MS, in accord with the molecular formula $C_{27}H_{36}O_9$, indicating the presence of ten degrees of unsaturation. The IR spectrum of **3** indicated the presence of OH (3452 cm^{-1}), ester C=O (1711 cm^{-1}), C=C (1642, 1600, and 1580 cm^{-1}), and C−O−C moieties (1178 cm^{-1}). The basic analysis of the ^{1}H- and ^{13}C-NMR spectra (600 and 150 MHz, resp.; $CDCl_3$; *Table 2*) implied that **3** had a similar diterpenoid core as that of **1**. In the ^{1}H-NMR, the signals of three Me, one CH_2O, and four CH−O groups, two olefinic H-atoms at a terminal C=C bond as well as a group of aromatic H-atoms were distinguishable. In the ^{13}C-NMR, compared with **1**, the C-atoms at δ(C) 73.5 (C(9)), 73.7 (C(13)), and 77.2 (C(14)) were severely upfield-shifted; this indicated the presence of a 9,13-dihydroxy-14-(acyloxy)daphnane, which was confirmed by the absence of a typical quaternary C-atom for a 9,13,14-orthoester moiety. The benzoyloxy group was located at C(14) by the data from the HMBC spectrum (*Fig. 1*), in which the C(1′)=O group at δ(C) 167.1 showed correlations with signals at δ(H) 5.95 (*s*, H−C(14)) and 8.11–8.12 (H−C(3′,7′)). In the NOESY plot (*Fig. 2*), the strong correlations H−C(3)/H−C(5), H−C(5)/H−C(10), and H−C(10)/H−C(3) indicated that H−C(3), H−C(5), and H−C(10) are in α-configuration. The coupling constant *J*(2,3) of **3** was determined as 10.2 Hz, indicating that H−C(2) and H−C(3) must be in a *trans*-diaxial orientation from which can be inferred the β-configuration of H−C(2). Moreover, H−C(2) had no NOE correlation with H−C(10), which confirmed the configuration of H−C(2). Thus, the structure of **3** was assigned as (2α,3β,5β,6α,7α)-3-deoxo-6,7-epoxy-1,2,6,7-tetrahydro-3,5-dihydroxyresiniferonol 14-benzoate.

Table 2. *^{1}H- and ^{13}C-NMR Data* (600 and 150 MHz, resp.; $CDCl_3$) *of* **3**[1]). δ in ppm, *J* in Hz.

	δ(H)	δ(C)		δ(H)	δ(C)
H_β−C(1)	1.81–1.84 (*m*)	35.1	H−C(14)	5.95 (*s*)	77.2
H_α−C(1)	1.32–1.35 (*m*)				
H−C(2)	2.21–2.26 (*m*)	31.4	C(15)		144.9
H−C(3)	4.13 (*d*, *J* = 10.2)	75.5	CH_2(16)	5.17 (*s*), 5.14 (*s*)	114.0
C(4)		79.8	Me(17)	1.87 (*s*)	18.9
H−C(5)	4.52 (*s*)	76.7	Me(18)	1.00 (*d*, *J* = 6.6)	15.4
C(6)		64.5	Me(19)	0.96 (*d*, *J* = 7.2)	15.7
H−C(7)	3.24 (*s*)	67.3	CH_2(20)	4.01 (*d*, *J* = 12.0), 3.28 (*d*, *J* = 12.0)	68.0
H−C(8)	3.05 (*d*, *J* = 3.0)	39.5	C(1′)		167.1
C(9)		73.5	C(2′)		130.0
H−C(10)	1.83–1.85 (*m*)	54.4	H−C(3′)	8.11–8.12 (*m*)	129.9
H−C(11)	1.37–1.41 (*m*)	36.1	H−C(4′)	7.44–7.46 (*m*)	128.5
H_β−C(12)	2.11 (*t*, *J* = 13.2)	33.9	H−C(5′)	7.55–7.57 (*m*)	133.2
H_α−C(12)	1.59 (*d*, *J* = 13.2)		H−C(6′)	7.44–7.46 (*m*)	128.5
C(13)		73.7	H−C(7′)	8.11–8.12 (*m*)	129.9

The known compounds were identified as genkwanine D (**4**), genkwanine H (**5**), genkwaine F (**6**), genkwadaphnin (**7**), yuanhuatine (**8**), yuanhuafine (**9**), and yuan-

huapine (**10**), by comparing their physico-chemical properties and NMR data with those reported in the literature [6][16][17].

Compared with compounds **1** and **2**, compounds **4**–**6** bear a 6,7-dihydroxy unit instead of the 6,7-epoxy group. Compounds **7**–**10** all possess substituents at C(12), and an oxo group at C(3). Compound **3**, sharing the core part of the daphnane-type skeleton, is structurally different from compounds **1**, **2**, and **4**–**10** due to the absence of the 9,13,14-orthobenzoate moiety. Also, the relative configuration at the stereogenic center C(2) of compound **3** is changed. Thus, compound **3** is the first member of daphnane-type diterpenoids with β-configuration of H–C(2).

This work was financially supported by the *National Natural Science Foundation of China* (Grant No. 30973868). We are grateful to Prof. *Qishi Sun*, Department of Traditional Chinese Materia Medica, Shenyang Pharmaceutical University, for the identification of the plant material.

Experimental Part

General. TLC: Precoated *Si-gel-GF$_{254}$* plates (*Qingdao Marine Chemical Factory*, Qingdao, P. R. China). Column chromatography (CC): silica gel (SiO_2; 200–300 mesh; *Qingdao Marine Chemical Factory*, Qingdao, P. R. China); *Sephadex LH-20* (*Greenherbs Science and Technology Development Co., Ltd.*, P. R. China); *MCI* gel *(CHP20P*, 75–150 μm; *Mitsubishi Chemical Corporation*, Japan); reversed-phase C_{18} silica gel (60–80 μm; *Merck*, Germany). Prep. reversed-phase HPLC: *Hitachi* (*Japan Analytical Industry Co., Ltd.*), column *YMC ODS-A* (5 μm; 250 × 10 mm; *YMC*, Japan). Optical rotations: *Perkin-Elmer-214-MC* polarimeter. IR Spectra: *Bruker* spectrometer; $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: *Bruker-ARX-600* spectrometer; at 600 (^{1}H) and 150 MHz (^{13}C) in $CDCl_3$; δ in ppm, *J* in Hz. HR-ESI-MS: *MicroTOF* spectrometer (*Bruker Daltonics*); in *m*/*z*.

Plant Material. The flower buds (6 kg) of *Daphne genkwa* were collected in August 2006 from the Sichuan Mianyang area, P. R. China, and authenticated by Prof. *Qishi Sun*, Department of Traditional Chinese Materia Medica, Shenyang Pharmaceutical University. A voucher specimen is kept in the Nature Products Laboratory of Shenyang Pharmaceutical University, Shenyang, P. R. China.

Extraction and Isolation. Air-dried flower buds of *Daphne genkwa* (6 kg) were extracted extensively with 95% EtOH (25 l) at r.t. for 20 d. The EtOH filtrate was then concentrated affording a brownish-dark crude extract (638 g) which was dissolved in H_2O (10 l) to form a suspension, and partitioned with $CHCl_3$ to afford a $CHCl_3$-soluble fraction (250 g). The latter fraction was subjected to CC (SiO_2, petroleum ether/AcOEt 100:1 → 2:1): *Fractions A–F* (monitored by TLC). *Fr. D* (17 g) was further separated by CC (SiO_2, $CHCl_3$/MeOH 100:1 → 2:1): *Frs. D1–D6*. *Fr. D2* (1 g) was purified by CC (*Sephadex LH-20*, MeOH) and then by CC (SiO_2, $CHCl_3$/MeOH 30:1): **6** (12 mg). *Frs. D4* (5 g) and *D5* (2 g) were each applied to CC (*MCI* gel) to give major fractions. Having removed of a large amount of chlorophyll, these major fractions from *Frs. D4* and *D5* were combined (TLC monitoring) and finally subjected to reversed-phase HPLC (MeOH/H_2O 70:30 → 90:10): **1** (7 mg), **2** (17 mg), **4** (4 mg), **5** (5 mg), **7** (40 mg), **8** (35 mg), **9** (25 mg), and **10** (18 mg). The purification of *Fr. F* (22 g) was carried out by reversed-phase (CC C_{18} silica gel, MeOH/H_2O 60:40 → 80:20): **3** (12 mg).

Genkwanine M (= rel-*(2*R,*3a*S,*3b*R,*3c*R,*4a*S,*5*R,*5a*S,*6*R,*7*R,*8a*S,*8b*S,*9*S,*10a*S*)-4a-[(Benzoyloxy)-methyl]dodecahydro-7,9-dimethyl-10a-(1-methylethenyl)-2-phenyl-5a*H*-2,8b-epoxyoxireno[6,7]azuleno[5,4-*e*]-1,3-benzodioxole-5,5a,6-triol*; **1**): White amorphous powder. IR (KBr): 3452, 1720, 1645. ^{1}H- and ^{13}C-NMR: *Table 1*. HR-ESI-MS: 613.2407 ($[M + Na]^+$, $C_{34}H_{38}NaO_9^+$; calc. 613.2408).

Genkwanine N (= rel-*(2*R,*3a*S,*3b*R,*3c*R,*4a*S,*5*R,*5a*R,*6*R,*7*R,*8a*S,*8b*S,*9*S,*10a*S*)-Dodecahydro-4a-(hydroxymethyl)-7,9-dimethyl-10a-(1-methylethenyl)-2-phenyl-5a*H*-2,8b-epoxyoxireno[6,7]azuleno[5,4-*e*]-1,3-benzodioxole-5,5a,6-triol 6-Benzoate*; **2**): White amorphous powder. IR (KBr): 3441, 1708, 1645, 1602, 1178. ^{1}H- and ^{13}C-NMR: *Table 1*. HR-ESI-MS: 613.2406 ($[M + Na]^+$, $C_{34}H_{38}NaO_9^+$; calc. 613.2408).

Genkwanine O (= rel-*(1*R,*3*R,*4*R,*4a*S,*4b*S,*5a*R,*6*S,*6a*R,*7*S,*8*R,*9a*S,*9b*R*)-Dodecahydro-5a-(hydroxy-methyl)-1,8-dimethyl-3-(1-methylethenyl)benz[7,8]azuleno[5,6-*b*]oxirene-3,4,6,6a,7,9b-hexol 4-Benzoate*;

3): White amorphous powder. $[\alpha]_D^{21} = -57.3$ ($c = 1.2$, $CHCl_3$). IR (KBr): 3452, 1711, 1642, 1600, 1580, 1178. ^{1}H- and ^{13}C-NMR: *Table 2*. HR-ESI-MS: 527.2258 ($[M+Na]^+$, $C_{27}H_{36}NaO_9^+$; calc. 527.2252).

REFERENCES

[1] Z. W. Xie, *Acta Pharm. Sin.* **1958**, *6*, 356.
[2] H. Kai, T. Koine, M. Baba, T. Okuyama, *Yakugaku Zasshi* **2004**, *124*, 349.
[3] L. Z. Li, S. J. Song, P. Y. Gao, *Shenyang Yaoke Daxue Xuebao* **2007**, *24*, 587.
[4] W. D. He, M. Cik, G. Appendino, L. V. Puyvelde, J. E. Leysen, N. D. Kimpe, *Mini-Rev. Med. Chem.* **2002**, *2*, 185.
[5] Y.-M. Zheng, W.-J. Zuo, M.-G. Sun, M. He, Q.-H. Wang, J.-H. Wang, X. Li, *Helv. Chim. Acta* **2009**, *92*, 1273.
[6] Z.-J. Zhan, C.-Q. Fan, J. Ding, J.-M. Yue, *Bioorg. Med. Chem.* **2005**, *13*, 645.
[7] S. Zhang, X. Li, F. Zhang, P. Yang, X. Gao, Q. Song, *Bioorg. Med. Chem.* **2006**, *14*, 3888.
[8] R. Kasal, K.-H. Lee, H.-C. Huang, *Phytochemistry* **1981**, *20*, 2592.
[9] I. H. Hall, R. Kasai, R. Y. Wu, K. Tagahara, K. H. Lee, *J. Pharm. Sci.* **1982**, *71*, 1263.
[10] W. C. Wang, S. R. Shen, *Reprod. Contracept.* **1988**, *8*, 60.
[11] C. R. Wang, B. N. Zhou, *Reprod. Contracept.* **1989**, *9*, 9.
[12] Z. P. Gu, C. R. Wang, Z. Y. Liang, L. J. Lin, R. F. Lu, S. X. Zhao, B. N. Zhou, *Reprod. Contracept.* **1989**, *9*, 48.
[13] W. D. He, M. Cik, A. Lesage, I. Van der Linden, N. De Kimpe, G. Appendino, J. Bracke, S. G. Mathenge, F. P. Mudida, J. E. Leysen, L. Van Puyvelde, *J. Nat. Prod.* **2000**, *63*, 1185.
[14] D. Wu, B. Sorg, W. Adolf, E. H. Seip, E. Hecker, *Phytother. Res.* **1991**, *5*, 163.
[15] D. Wu, B. Sorg, E. Hecker, *Phytother. Res.* **1994**, *8*, 95.
[16] B. H. Hu, H. Sha, C. R. Wang, D. F. Yu, X. C. Wu, X. G. Yu, *Acta Chim. Sin.* **1985**, *43*, 460.
[17] B. H. Hu, H. Sha, Z. W. He, X. C. Wu, *Acta Chim. Sin.* **1986**, *44*, 843.

Received July 31, 2009