Three New Pregnane Alkaloids from *Veratrum taliense*

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Three new alkaloids, 3-*O*-acetylveralkamine (**1**), veralkamine 3-(*β*-D-glucopyranoside) (**2**), and 6,7-epoxyverdine (**3**), together with five known alkaloids, veramitaline, veralkamine (**4**), angeloylzygadenine, veratroylzygadenine, and veramiline 3-(*β*-D-glucopyranoside), were isolated from the whole plants of *Veratrum taliense*. Their structures were elucidated on the basis of spectroscopic analysis, and the NMR data of veralkamine (**4**) are given for the first time. In addition, the cytotoxic activities of all isolated compounds, except for veramitaline, were tested.

Introduction. – The *Veratrum taliense* species is a kind of herbaceous plants, from the family Liliaceae, genus *Veratrum* [1]. In China, it is also named Dalililu, Qixiancao, or Jiejingzhixuecao. In spite of its poison, this plant has been used medicinally for centuries, functioning as an emetic, antihemorrhagic, and analgesic. The previous studies on the genus *Veratrum* had shown that plants of this genus contained complex and bioactive steroidal alkaloids [2–5]. Verazine and jervine alkaloids are the typical steroidal alkaloids of this species, which usually have all kinds of substituents, such as acetyloxy groups or saccharide moieties. The jervine alkaloids have a furan ring fused onto a piperidine ring system forming an ether bridge. And some alkaloids displayed significant cytotoxic activities (for example, cyclopamine). Our research for bioactive substances from *V. taliense* now led to the isolation of three new alkaloids (*Fig. 1*), 3-*O*-acetylveralkamine (**1**), veralkamine 3-(*β*-D-glucopyranoside) (**2**), and 6,7-epoxyverdine (**3**), together with five known alkaloids, veramitaline [6], veralkamine (**4**), angeloylzygadenine [7], veratroylzygadenine [8], and veramiline 3-(*β*-D-glucopyranoside) [9]. Moreover, the NMR data of compound **4** are given here for the first time.

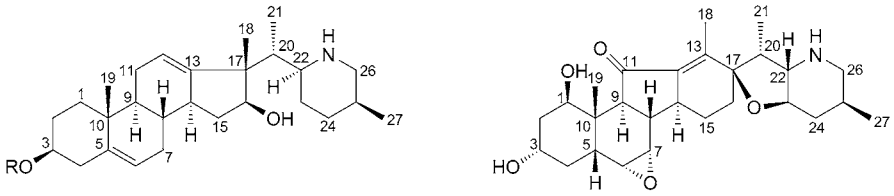

Fig. 1. *Structures of compounds* **1**–**4**, *isolated from* Veratrum taliense

Results and Discussion. – Compound **1** was isolated as a white powder. It was determined to have the molecular formula $C_{29}H_{45}NO_3$ by HR-EI-MS (*m/z* 456.3417) and NMR data. The ^{1}H-NMR spectrum (*Table 1*) exhibited the presence of five Me groups at δ(H) 0.96 (*s*, Me(18)), 0.96 (*s*, Me(19)), 0.82 (*d*, $J = 7.2$ Hz, Me(21)), 0.97 (*d*, $J = 8.7$ Hz, Me(27)), and 2.03 (*s*, Ac). In the ^{13}C-NMR spectrum (*Table 2*), the

Table 1. *^{1}H-NMR Data* ($CDCl_3$) *of Compounds* **1**–**4**. δ in ppm, *J* in Hz.

H-Atom	**1**	**2**	**3**	**4**
CH_2(1) or H–C(1)	1.73–1.78[a]), 1.17–1.22 (*m*)	1.63–1.71[a]), 0.99–1.09[a])	3.91–3.95 (*m*)	1.70–1.74[a]), 1.11–1.24 (*m*)
CH_2(2)	1.83–1.93[a]), 1.55–1.61 (*m*)	1.80–1.84 (*m*), 1.40–1.49[a])	1.95–2.07[a]), 1.48–1.60[a])	1.91–1.91[a]), 1.48–1.52[a])
H–C(3)	4.56–4.66 (*m*)	3.43–3.51 (*m*)	3.97–4.03 (*m*)	3.51–3.54 (*m*)
CH_2(4)	2.25–2.41[a]), 2.25–2.41[a])	2.32–2.42[a]), 2.08–2.17[a])	1.92–1.99[a]), 1.52–1.61[a])	2.09–2.42[a]), 2.09–2.42[a])
H–C(6)	5.30–5.40 (*m*)	5.20–5.29 (*m*)	4.01–4.11 (*m*)	5.33–5.34 (*m*)
CH_2(7) or H–C(7)	2.20–2.32[a]), 1.63–1.74[a])	2.24–2.15[a]), 1.58–1.66[a])	3.26–3.34 (*m*)	2.19–2.24[a]), 1.61–1.69[a])
H–C(8)	1.19–1.30[a])	1.13–1.21[a])	1.45–1.56[a])	1.17–1.25[a])
H–C(9)	1.78–1.87[a])	1.67–1.75[a])	2.02–2.14[a])	1.65–1.70[a])
CH_2(11) or H–C(11)	2.07–2.20[a]), 1.95–2.04[a])	2.04–2.11[a]), 1.88–1.97[a])		2.05–2.15[a]), 1.95–2.04[a])
H–C(12)	5.21–5.27 (*m*)	5.24 (*m*)		5.25–5.26 (*m*)
H–C(14)	1.63–1.74[a])	1.51–1.58[a]);	1.96–2.10[a])	1.61–1.69[a])
H–C(15)	2.04–2.15[a]), 1.19–1.30[a])	1.86–1.94[a]), 1.06–1.15[a])	1.91–2.00[a]), 1.29–1.39[a])	2.08–2.16[a]), 1.22–1.29[a])
H–C(16) or CH_2(16)	3.96–4.03 (*m*)	3.91 (*dd*, $J = 5.9, 11.2$)	1.48–1.60[a]), 1.21–1.32[a])	3.97–4.01 (*m*)
Me(18)	0.96 (*s*)	0.84 (*s*)	2.19 (*s*)	0.95 (*s*)
Me(19)	0.96 (*s*)	0.88 (*s*)	1.28 (*s*)	0.95 (*s*)
H–C(20)	1.36–1.42 (*m*)	3.09–3.16 (*m*)	2.49–2.55 (*m*)	1.28–1.37 (*m*)
Me(21)	0.82 (*d*, $J = 7.2$)	0.79 (*d*, $J = 7.2$)	0.97 (*d*, $J = 11.0$)	0.82 (*d*, $J = 7.2$)
H–C(22)	2.75–2.82[a])	2.64–2.71[a])	2.68–2.75 (*m*)	2.74–2.86[a])
CH_2(23) or H–C(23)	1.63–1.74[a]), 1.19–1.30[a])	1.44–1.53[a]), 1.07–1.15[a])	3.46–3.52 (*m*)	1.61–1.69[a]), 1.22–1.26[a])
CH_2(24)	1.74–1.83[a]), 1.63–1.74[a])	1.65–1.73[a]), 1.48–1.56[a])	2.18–2.27[a]), 1.22–1.32[a])	1.74–1.82[a]), 1.61–1.69[a])
H–C(25)	1.82–1.92[a])	1.62–1.69[a])		1.64–1.75[a])
CH_2(26)	2.75–2.82[a]), 2.75–2.82[a])	2.69–2.75[a]), 2.63–2.69[a])		3.05–3.11 (*m*), 2.29–2.37 (*m*)
Me(27)	0.97 (*d*, $J = 8.7$)	0.96 (*d*, $J = 7.2$)	0.95 (*d*, $J = 6.7$)	
H–C(1′)		4.21 (*d*, $J = 7.8$)		
H–C(2′)		2.86–2.94 (*m*)		
H–C(3′)		3.00–3.08[a])		
H–C(4′)		3.00–3.08[a])		
H–C(5′)		3.09–3.16 (*m*)		
CH_2(6′)		3.64 (*d*, $J = 11.3$)		
Ac	2.03 (*s*)			

[a]) Overlapped.

Table 2. *^{13}C-NMR Data of Compounds* **1**–**4**. δ in ppm.

C-Atom	**1**	**2**	**3**	**4**
C(1)	36.6 (*t*)	36.4 (*t*)	72.4 (*d*)	36.9 (*t*)
C(2)	27.6 (*t*)	29.2 (*t*)	32.2 (*t*)	32.1 (*t*)
C(3)	73.6 (*d*)	76.8 (*d*)	65.5 (*d*)	71.4 (*d*)
C(4)	37.9 (*t*)	38.2 (*t*)	30.6 (*t*)	42.1 (*t*)
C(5)	139.6 (*s*)	140.5 (*s*)	35.5 (*d*)	140.8 (*s*)
C(6)	121.9 (*d*)	120.7 (*d*)	61.0 (*d*)	121.0 (*d*)
C(7)	32.0 (*t*)	31.8 (*t*)	59.3 (*d*)	24.7 (*t*)
C(8)	35.0 (*d*)	34.7 (*d*)	39.1 (*d*)	35.0 (*d*)
C(9)	45.8 (*d*)	45.5 (*d*)	54.4 (*d*)	45.9 (*d*)
C(10)	36.7 (*s*)	36.4 (*s*)	36.0 (*s*)	36.6 (*s*)
C(11)	24.7 (*t*)	24.3 (*t*)	206.4 (*s*)	32.1 (*t*)
C(12)	115.3 (*d*)	114.7 (*d*)	136.4 (*s*)	115.4 (*d*)
C(13)	150.9 (*s*)	151.1 (*s*)	146.0 (*s*)	150.8 (*s*)
C(14)	45.5 (*d*)	45.4 (*d*)	43.9 (*d*)	45.2 (*d*)
C(15)	34.9 (*t*)	35.2 (*t*)	23.6 (*t*)	34.8 (*t*)
C(16)	71.0 (*d*)	70.4 (*d*)	32.3 (*t*)	71.0 (*d*)
C(17)	50.3 (*s*)	50.7 (*s*)	85.6 (*s*)	50.2 (*s*)
C(18)	22.1 (*q*)	22.2 (*q*)	12.0 (*q*)	22.1 (*q*)
C(19)	18.9 (*q*)	18.8 (*q*)	19.4 (*q*)	19.0 (*q*)
C(20)	45.1 (*d*)	44.7 (*d*)	39.1 (*d*)	45.4 (*d*)
C(21)	8.8 (*q*)	9.1 (*q*)	10.4 (*q*)	8.8 (*q*)
C(22)	56.2 (*d*)	56.1 (*d*)	65.9 (*d*)	56.2 (*d*)
C(23)	25.4 (*t*)	25.1 (*t*)	75.8 (*d*)	25.4 (*t*)
C(24)	30.5 (*t*)	30.6 (*t*)	38.4 (*t*)	30.5 (*t*)
C(25)	26.3 (*d*)	26.5 (*d*)	31.0 (*d*)	26.3 (*d*)
C(26)	51.2 (*t*)	50.0 (*t*)	53.9 (*t*)	51.2 (*t*)
C(27)	16.1 (*q*)	16.4 (*q*)	18.4 (*q*)	16.1 (*q*)
C(1′)		100.8 (*d*)		
C(2′)		73.5 (*d*)		
C(3′)		76.6 (*d*)		
C(4′)		70.1 (*d*)		
C(5′)		76.8 (*d*)		
C(6′)		61.1 (*t*)		
Me–*C*=O	170.6 (*s*)			
Me–C=O	21.4 (*q*)			

characteristic signals of a skeleton similar to that of verazine (=(3β,20*S*)-20-[(5*S*)-2,4,5,6-tetrahydro-5-methylpyridin-2-yl]pregn-5-en-3-ol) were present: five Me groups (δ(C) 22.1, 18.9, 8.8, 16.1, and 21.4), nine CH_2 groups (δ(C) 36.6, 27.6, 37.9, 32.0, 24.7, 34.9, 25.4, 30.5, and 51.2), ten CH groups (δ(C) 73.6, 121.9, 35.0, 45.8, 115.3, 45.5, 71.0, 45.1, 56.2, and 26.3), and five quaternary C-atoms (139.6, 36.7, 150.9, 50.3, and 170.6). Moreover, considering the abundance of pregnane alkaloids in the *Veratrum* genus, **1** was proposed to have the basic skeleton of veraexamine (=(3β,16β,17α,20*S*)-17-methyl-20-[(2*S*,5*S*)-5-methylpiperidin-2-yl]-18-norpregna-5,12-diene-3,16-diol; **4**), the latter being derived from a verazine-type alkaloid. Comparison of the spectroscopic data of **1** and **4** revealed similarities, except for the replacement of a OH group of **4** by an AcO group in **1**, which was supported by the downfield chemical shift of C(3) (δ(C)

73.6 for **1** and 71.4 for **4**). HMBC Cross-peaks (*Fig. 2*) of H–C(3) (δ(H) 4.56–4.66)/Me–*C*=O (δ(C) 170.6), H–C(4) (δ(H) 2.25–2.41)/C(3) (δ(C) 73.6), C(5) (δ(C) 139.6), and C(6) (δ(C) 121.9), H–C(16) (δ(H) 3.96–4.03)/C(14) (δ(C) 45.5) and C(15) (δ(C) 34.9), and H–C(12) (δ(H) 5.21–5.27)/C(14) and C(17) (δ(C) 50.3) further supported the assignment. Besides, the orientation of the substituent groups were determined by the ROESY correlations H_α–C(1)/H–C(9) and H_α–C(2), H_α–C(3)/H_α–C(1) and H_α–C(2), and H_α–C(16)/H_α–C(15). All of the substituents had the same orientations as those in **4**. Therefore, **1** was elucidated as 3-*O*-acetylveralkamine.

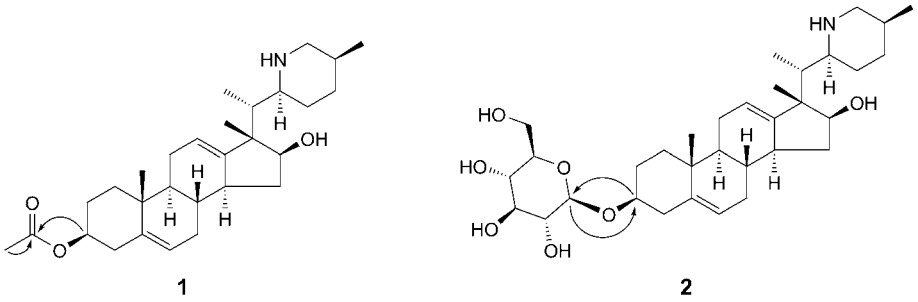

Fig. 2. *Key HMBC* (H → C) *correlations of* **1** *and* **2**

Compound **2** had the molecular formula $C_{33}H_{53}NO_7$, as determined by HR-EI-MS (*m*/*z* 575.3818). Its NMR data (*Tables 1* and *2*) showed that **2** had the same skeleton as compound **4**, except for a saccharide moiety at C(3) of **2**. This was supported by the downfield chemical shift of C(3) (δ(C) 76.8 (*d*)) and the upfield shifts of C(2) (δ(C) 29.2 (*t*)) and C(4) (δ(C) 38.2 (*t*)) in **2**, compared with those of C(3) (δ(C) 71.4 (*d*)), C(2) (δ(C) 32.1 (*t*)), and C(4) (δ(C) 42.1 (*t*)) in **4**. HMBC Cross-peaks H–C(3) (δ(H) 3.43–3.51)/C(1′) (δ(C) 100.8) of the saccharide moiety (*Fig. 2*), CH_2(2) (δ(H) 1.80–1.84 and 1.40–1.49)/C(3), and CH_2(4) (δ(H) 2.32–2.42 and 2.08–2.17)/C(3) further supported the assignment. Besides, the product of the acid hydrolysis of compound **2**, which was analyzed by gas chromatography (GC), showed that the sugar moiety of **2** was D-glucose. The β-orientation of the substituting groups at C(3) and C(16) were deduced from the ROESY correlations H_β–C(1)/H–C(19), H_α–C(1)/H_α–C(2), H_α–C(3)/H_α–C(1) and H_α–C(2), and H_α–C(16)/H_α–C(15). Hence, the structure of **2** was assigned as veralkamine 3-(β-D-glucopyranoside).

The molecular formula of compound **3** was inferred as $C_{27}H_{39}NO_5$ by HR-EI-MS (*m*/*z* 457.2820) and NMR data (*Tables 1* and *2*). The ^{1}H-NMR spectrum of **3** showed characteristic signals at δ(H) 2.19 (*s*, Me(18)), 1.28 (*s*, Me(19)), 0.97 (*d*, J = 11.0 Hz, Me(21)), and 0.95 (*d*, J = 6.7 Hz, Me(27)). In addition, the ^{13}C-NMR and DEPT experiments showed signals for four Me groups, six CH_2 groups, twelve CH groups (including five oxygenated CH at δ(C) 72.4, 65.5, 61.0, 59.3, and 75.8), and four quaternary C-atoms (including a C=O at δ(C) 206.4, and two olefinic C-atoms at δ(C) 136.4 and 146.0). Compound **3** was proposed to have a basic skeleton similar to that of jervine (=(2′*R*,3*S*,3′*R*,3′a*S*,6′*S*,6a*S*,6b*S*,7′a*R*,11a*S*,11b*R*)-2,3,3′a,4,4′,5′,6,6′,6a,6b,7,7′,7′a,8,11a,11b-hexadecahydro-3-hydroxy-3′,6′,10,11b-tetramethylspiro[9*H*-benzo[*a*]fluor-

ene-9,2(3′*H*)-foro[3,2-*b*]pyridin]-11(1*H*)-ones). Comparison of the spectroscopic data of **3** and the known compound verdine (=(1*R*,2′*R*,3*S*,3′*R*,3′a*S*,4a*R*,5*S*,6′*S*,6a*S*,6b-*S*,7′a*R*,11a*S*,11b*S*)-2,3,3′a,4,4′,4a,5,5′,6,6′,6a,6b,7,7′,7′a,8,11a,11b-octadecahydro-1,3,5-trihydroxy-3′,6′,10,11b-tetramethylspiro[9*H*-benzo[*a*]fluorene-9,2′(3′*H*)-furo[3,2-*b*]pyridin]-11(1*H*)-one) [10] revealed similarities, except for the substituents at C(6) and C(7). The downfield chemical shift of C(6) (δ(C) 61.0 (*d*)) and C(7) (δ(C) 59.3 (*d*)) suggested that there were oxygenated substituents at C(6) and C(7). In addition, the chemical shift of C(6) of **3** was more upfield than that of C(6) (δ(C) 69.2 (*d*)) of verdine. Combined with the molecular formula of **3**, it was determined that C(6) and C(7) were linked by an O-atom. Besides, the correlations H–C(1) (δ(H) 3.91–3.95)/C(10) (δ(C) 36.0) and C(2) (δ(C) 32.2), H–C(2) (δ(H) 1.48–1.60)/C(3) (δ(C) 65.5), H–C(6) (δ(H) 4.01–4.11)/C(4) (δ(C) 30.6), C(5) (δ(C) 35.5), and C(6), and H–C(7) (δ(H) 3.26–3.34)/C(6) also supported this conclusion (*Fig. 3*). The β-orientation of OH–C(1), the α-orientations of OH–C(3) and the epoxy bridge between C(6) and C(7) were confirmed by the ROESY correlations H_α–C(1)/H_α–C(2), H_β–C(2)/H–C(3), H–C(3)/H_β–C(6), and H_β–C(6)/H_β–C(7) and Me(19). So **3** was characterized as 6,7-epoxyverdine.

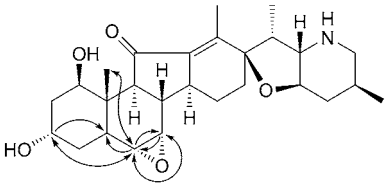

Fig. 3. *Key HMBC* (H → C) *and ROESY* (H ↔ H) *correlations of* **3**

For the cytotoxic activities, see the *Exper. Part.*

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Experimental Part

General. Optical rotations: *Horiba-SEAP-300* spectropolarimeter. NMR Spectra: *Bruker-AV-400* or *-DRX-500* instruments; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. MS: *VG-Autospec-3000* spectrometer; in *m*/*z* (rel. %).

Plant Material. The whole plants were collected in Dali Prefecture, Yunnan Province, China, in August 2009, and identified by Prof. *Xi-Wen Li*, Kunming Institute of Botany, Chinese Academy of Science, where a voucher specimen is deposited.

Extraction and Isolation. The air-dried and chipped whole plants of *V. taliense* (6.9 kg) were extracted with 95% EtOH (3 × 25 l), and the extracts were concentrated to afford a residue (560 g). This residue was suspended in 2% AcOH and the suspension filtered. The aq. filtrate was rendered basic with $NH_3 \cdot H_2O$ (pH 11) and then extracted with $CHCl_3$ (3 × 2 l). The org. layer was concentrated to give the crude alkaloid fraction (40 g), which was fractionated by CC (SiO_2 (200–300 mesh), $CHCl_3$/MeOH 1:0 → 0:1): *Fractions A1–A5*. *Fr. A1* was purified by repeated CC (SiO_2, $CHCl_3$/acetone 20:1; then *Sephadex LH-20*, MeOH): *veramitaline* (8 mg), **4** (19 mg), and *angeloylzygadenine* (31 mg). *Fr. A2* was also purified by repeated CC (SiO_2, $CHCl_3$/acetone 15:1; then *Sephadex LH-20*, MeOH): **1** (12 mg), **3**

(15 mg), and *veratroylzygadenine* (22 mg). *Fr. A3* was purified by repeated CC (SiO_2, $CHCl_3$/MeOH 25:1): **2** (85 mg) and **3** (40 mg). *Fr. A4* was purified by repeated CC (SiO_2, $CHCl_3$/MeOH 20:1): *angeloylzygadenine* (18 mg) and *veratroylzygadenine* (8 mg). *Fr. A5* was purified by repeated CC (Al_2O_3 (200–300 mesh), $CHCl_3$/MeOH 20:1; then SiO_2, $CHCl_3$/ MeOH 20:1): *veramiline 3-(β-*D*-glucopyranoside)* (160 mg).

3-O-*Acetylveralkamine* (*=(3β,16β,17α,20*S*)-17-Methyl-20-[(2*S,5S*)-5-methylpiperidin-2-yl]-18-norpregna-5,12-diene-3,16-diol 3-Acetate*; **1**): White powder. $[\alpha]_D^{20} = -158.0$ ($c = 0.37$). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. ESI-MS (pos.): 456 ($[M+H]^+$). HR-EI-MS: 455.3417 (M^+, $C_{29}H_{45}NO_3^+$; calc. 455.3399).

*Veralkamine 3-(β-*D*-Glucopyranoside)* (*=(3β,16β,17α,20*S*)-16-Hydroxy-17-methyl-20-[(2*S,5S*)-5-methylpiperidin-2-yl]-18-norpregna-5,12-dien-3-yl β-*D*-Glucopyranoside*; **2**): White powder. $[\alpha]_D^{20} = -109.5$ ($c = 0.86$). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. ESI-MS (pos.): 576 ($[M+H]^+$). HR-EI-MS: 575.3818 (M^+, $C_{33}H_{53}NO_7^+$; calc. 575.3822).

6,7-Epoxyverdine (*=(1a*R*,1b*R*,2′*R*,3*S*,3′*R*,3′a*S*,5*R*,5a*S*,5b*S*,6′*S*,7′a*R*,10a*S*,10b*S*,10c*S*)-1a,1b,23′a,4,4′,5,5′,5a,5b,6′,7′,7′a,9,10,10a,10b,10c-Octadecahydro-3,5-dihydroxy-3′,5a,6′,7-tetramethylspiro[8*H*-benzo[1,2]fluoreno[3,4-*b*]oxirene-8,2′(3′*H*)-furo[3,2-*b*]pyridin]-6(3*H*)-one*; **3**): White powder. $[\alpha]_D^{20} = -51.2$ ($c = 0.92$).^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. ESI-MS (pos.): 458 ($[M+H]^+$). HR-EI-MS: 457.2820 (M^+, $C_{27}H_{39}NO_5^+$; calc. 457.2828).

Veralkamine (*=(3β,16β,17α,20*S*)-17-Methyl-20-[(2*S,5S*)-5-methylpiperidin-2-yl]-18-norpregna-5,12-diene-3,16-diol*; **4**): White powder. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. FAB-MS (pos.): 414 (45, $[M+H]^+$), 211 (13), 127 (30), 97 (70), 57 (100).

Sugar Analysis. Compound **2** (3 mg) in 1N HCl/MeOH 1:1 (2 ml) was heated at 90° for 6 h in a water bath. After cooling to r.t., the mixture was neutralized with Ag_2CO_3 and then filtrated. The filtrate was extracted with $CHCl_3$ (3 × 2 ml). The aq. layer was concentrated and the residue dissolved in pyridine (0.5 ml). After that, L-cysteine methyl ester hydrochloride (0.5 mg) was added, and the mixture was heated at 60° for 1 h. The trimethylsilylation reagent 1-(trimethylsilyl)-1*H*-imidazole (0.5 ml) was added, and heating at 60° was continued for another 30 min. The precipitate was centrifuged off, and the supernatant (6 µl) was subjected to GC analysis (*Shimadzu-GC-17A* gas chromatographe, with an H_2 flame-ionization detector; *DB-1* column (15 m × 0.25 mm (*i.d.*), film thickness 0.25 µm); oven temp. 120–250°, programmed temp. increase of 8°/min, injection-port temp. 250°, detector temp. 280°; carrier gas N_2, 10 psi; injection volume 6 µl, split ratio 1/30): D-glucose, t_R 9.82 min.

Cytotoxicity Assay. All isolated compounds, except for varamitaline, were tested for their cytotoxic activity against five human-tumor cell lines, *viz.*, HL-60, SMMC-7721, A-549, MCF-7, and SW480, by using the improved MTT (= 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2*H*-tetrazolium bromide) method as previously described [11], with cisplatin as the positive control. Compound **1** was cytotoxic for all the tested cell lines, with the IC_{50} values 10.02, 17.05, 16.51, 6.40, and 5.61 µM, resp. Besides, compounds **2** and **4** showed selective cytotoxicity against some of the cells (*Table 3*). The other compounds showed no inhibitory activity against the tumor cells tested with IC_{50} values greater than 40 µM.

Table 3. *Cytotoxic Activities of Compounds* **1**, **2**, *and* **4**. IC_{50} values in µM.

Compound	HL-60	SMMC-7721	A-549	MCF-7	SW480
1	10.02	17.05	16.51	6.40	5.61
2	4.07	> 40	21.01	13.48	19.04
4	10.69	> 40	19.08	8.29	11.53
Cisplatin	0.97	14.75	13.61	17.13	15.56

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