Five New Diterpenoids, Viteagnusins A—E, from the Fruit of *Vitex agnus-castus*

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Two new halimane-type diterpenoids, viteagnusins A and B, and three new labdane-type diterpenoids, viteagnusins C, D, and E, were isolated from the fruit of *Vitex agnus-castus* L. (Chasteberry, Verbenaceae) along with two known diterpenoids. Their chemical structures were determined on the basis of spectroscopic data.

Key words *Vitex agnus-castus*; Verbenaceae; chasteberry; halimane; labdane; diterpenoid

Vitex agnus-castus L. (Verbenaceae) is a shrub that grows widely throughout Central Asia, the Mediterranean region, and Southern Europe. The fruit (Chasteberry) of this plant is used as a dietary supplement for the treatment of hormone-imbalance syndrome in women.[1)] This fruit has been reported to contain essential oils, iridoids, flavonoids, and diterpenoids.[1—9)] Further, linoleic acid isolated from this fruit was identified as an estrogenic compound.[10)] In the course of our study on the constituents of Verbenaceae plants,[11—14)] we have investigated the constituents of the fruit of *V. agnus-castus*. The present paper describes the isolation and structural elucidation of five new diterpenoids along with two known diterpenoids.

The hexane extract of the fruit of *V. agnus-castus* was successively subjected to silica gel, Chromatorex octadecyl silica (ODS), and HPLC on ODS to yield seven diterpenoids (**1**—**7**).

Compounds **6** and **7** were identified as 8-*epi*-sclareol[15)] and (*rel* 5*S*,6*R*,8*R*,9*R*,10*S*,13*R*)-6-acetoxy-9,13-epoxy-15-methoxy-labdan-16,15-olide,[16)] respectively, based on the comparison of their physical and spectral data with previously reported samples (Fig. 1).

Compound **1**, called viteagnusin A, was obtained as an amorphous powder. The positive FAB-MS of **1** exhibited an $[M+Na]^+$ ion peak at *m/z* 371; the molecular formula of **1** was determined to be $C_{22}H_{36}O_3$ by high-resolution (HR)-positive FAB-MS. The ^{1}H-NMR spectrum (in $CDCl_3$) of **1** exhibited signals due to four tertiary methyl groups (δ 1.28, 1.03, 1.01, 0.79), one secondary methyl group [δ 0.78 (d, J=6.0 Hz)], one acetyl group (δ 2.05), one vinylic group [δ 5.88 (dd, J=11.0, 17.0 Hz), 5.20 (d, J=17.0 Hz), 5.05 (d, J=11.0 Hz)], one olefinic proton [δ 5.46 (br s)], and one oxygenated methine proton [δ 4.44 (dd, J=3.5, 11.5 Hz)]. The ^{13}C-NMR spectrum of **1** exhibited signals due to one carbonyl carbon (δ 170.7), one tri-substituted olefinic bond (δ 143.9, 118.0), one vinylic group (δ 145.3, 111.8), one oxygenated methine carbon (δ 79.7), and one oxygenated quaternary carbon (δ 73.5). These ^{1}H- and ^{13}C-NMR signals were assigned using the ^{1}H–^{1}H correlation spectroscopy (COSY), heteronuclear multiple-quantum coherence (HMQC), and heteronuclear multiple-bond correlation (HMBC) techniques, as shown in Tables 1 and 2, and the planar structure of **1**, a halimane-type diterpenoid possessing one 3-hydroxy-3-methyl-1-propenyl group and one acetyl group, could be determined, as shown in Fig. 2. The relative stereostructure was defined on the basis of nuclear Overhauser and exchange spectroscopy (NOESY) spectra, which were carried out in $CDCl_3$ and C_5D_5N, and the values of the coupling constants of the signal due to H-3 in the ^{1}H-NMR spectrum. In the NOESY spectra of **1**, key nuclear Overhauser effects (NOEs) were observed between the respective protons, as shown in Fig. 3, and the values of the coupling constants (dd, J=3.5, 11.5 Hz) of the signals due to H-3 indicated the hydroxyl group at C-3 to have a β-configuration. Moreover, the ^{13}C-NMR data of the B-ring moiety in **1** were not in agreement with those of nosyberkol (**8**).[17)] The structure of **1** was thus concluded to be (*rel* 3*R*,8*R*,9*R*,10*R*)-3-acetoxy-5(6),14-halimadien-13-ol (Fig. 3). Further, in the ^{13}C-NMR spectra of **1** obtained by measurements using $CDCl_3$, C_5D_5N, and CD_3OD as solvents, the peak height of 11 signals, which were assigned to C-2—C-7, C-9, C-11, C-12, C-19, and C-20, was found to be fairly low and a signal due to C-1 could not be detected (Table 2). A similar phenomenon, which was ascribable to short spin–spin relaxation times, was reported in the case of the ^{13}C-NMR signals for sclareol (**9**).[18)]

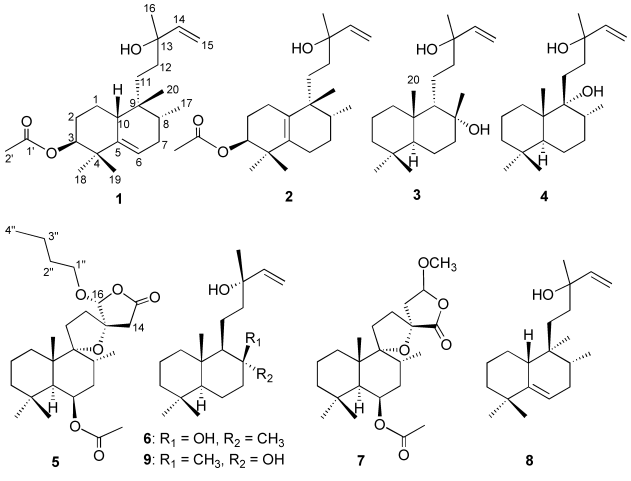

Fig. 1. Structures of **1**—**9**

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Table 1. ^{1}H-NMR Data for **1**—**5** (500 MHz)

	1[a)]	**2**[a)]	**3**[a)]	**3**[b)]	**4**[a)]	**5**[a)]
1a	*ca.* 1.74	*ca.* 2.09	*ca.* 1.56	*ca.* 1.90	*ca.* 1.46	*ca.* 1.64
1b	1.16 dddd (3.5, 13.5, 13.5, 13.5)	*ca.* 2.09	*ca.* 1.11	1.17 dddd (3.0, 3.0, 3.0, 12.5)	*ca.* 1.46	*ca.* 1.30
2a	1.87 dddd (3.5, 3.5, 3.5, 12.0)	1.78 m	1.67 m	1.66 m	*ca.* 1.57	*ca.* 1.66
2b	*ca.* 1.56	1.71 m	1.42 m	1.36 m	*ca.* 1.46	1.45 m
3a	4.44 dd (3.5, 11.5)	4.74 dd (3.0, 10.5)	1.36 ddd (3.0, 3.0, 13.0)	*ca.* 1.29	1.34 ddd (3.0, 3.0, 13.0)	*ca.* 1.31
3b			1.14 ddd (4.0, 13.0, 13.0)	1.10 ddd (4.0, 13.0, 13.0)	1.14 ddd (3.5, 13.0, 13.0)	*ca.* 1.20
5			1.04 dd (2.5, 12.5)	1.23 dd (2.0, 12.5)	1.42 dd (3.0, 12.5)	1.58 d (2.5)
6a	5.46 br s	2.03 m	*ca.* 1.55	1.51 m	1.52 m	5.40 ddd (2.5, 2.5, 2.5)
6b		1.91 m	1.25 m	*ca.* 1.33	*ca.* 1.28	
7a	*ca.* 1.70	*ca.* 1.54	*ca.* 1.55	*ca.* 1.86	*ca.* 1.47	1.69 m
7b	*ca.* 1.70	*ca.* 1.42	*ca.* 1.55	1.75 m	*ca.* 1.25	1.50 ddd (3.0, 3.0, 15.0)
8	*ca.* 1.61	*ca.* 1.44			1.74 m	2.08 m
9			*ca.* 1.11	*ca.* 1.28		
10	1.96 br d (11.0)					
11a	*ca.* 1.43	1.50 m	1.76 m	2.46 m	1.70 m	2.14 m
11b	*ca.* 1.20	*ca.* 1.30	*ca.* 1.55	*ca.* 1.82	*ca.* 1.47	1.75 dd (11.0, 13.0)
12a	*ca.* 1.49	*ca.* 1.55	*ca.* 1.61	2.05 ddd (4.0, 12.0, 12.0)	*ca.* 1.66	*ca.* 2.06
12b	*ca.* 1.40	*ca.* 1.37	*ca.* 1.49	*ca.* 1.86	*ca.* 1.63	1.95 ddd (11.0, 11.0, 13.0)
14a	5.88 dd (11.0, 17.0)	5.87 dd (11.0, 17.0)	5.94 dd (11.0, 17.0)	6.29 dd (11.0, 17.0)	5.89 dd (11.0, 17.0)	3.11 d (17.0)
14b						2.37 d (17.0)
15a	5.20 d (17.0)	5.18 dd (1.0, 17.0)	5.22 dd (1.0, 17.0)	5.60 dd (2.0, 17.0)	5.22 dd (1.0, 17.0)	
15b	5.05 d (11.0)	5.06 dd (1.0, 11.0)	5.03 dd (1.0, 17.0)	5.13 dd (2.0, 11.0)	5.05 dd (1.0, 11.0)	
16	1.28 s	1.26 s	1.28 s	1.53 s	1.27 s	4.90 s
17	0.78 d (6.0)	0.93 d (6.0)	1.45 s	1.67 s	0.85 d (6.5)	0.82 d (6.5)
18	1.01 s	0.98 s	0.86 s	0.80 s	0.87 s	0.96 s
19	1.03 s	1.03 s	0.78 s	0.78 s	0.83 s	0.99 s
20	0.79 s	0.97 s	1.06 s	1.10 s	0.92 s	1.22 s
2′	2.05 s	2.07 s				2.05 s
1″a						3.81 ddd (7.0, 7.0, 10.0)
1″b						3.50 ddd (7.0, 7.0, 10.0)
2″						*ca.* 1.64
3″						1.40 m
4″						0.93 t (7.5)

δ in ppm from tetramethylsilane (TMS) (coupling constants (J) in Hz are given in parentheses). *a*) In $CDCl_3$. *b*) In C_5D_5N.

Table 2. ^{13}C-NMR Data for **1**–**5** (125 MHz)

	1[a)]	**1**[b)]	**1**[c)]	**2**[a)]	**3**[a)]	**3**[b)]	**4**[a)]	**5**[a)]
C-1	—	—	—	23.3	36.6	36.9	32.4	32.5
C-2	27.8	28.2	28.9	24.1[d)]	18.6	19.0	18.8	18.9
C-3	79.7	79.8	81.4	78.4	42.3	42.5	41.8	43.8
C-4	41.0	41.4	42.1	38.5	33.0	33.0	33.4	34.1
C-5	143.9	144.5	145.5	134.5	46.3	46.8	46.4	48.7
C-6	118.0	118.2	119.2	24.3[d)]	21.0[d)]	21.0	21.7	70.5
C-7	31.1	31.4	32.2	28.2	38.0	38.4	31.5	36.4
C-8	32.8	33.2	34.2	38.4	74.2	72.6	36.8	31.5
C-9	35.6	35.9	36.6	39.7	61.2	62.3	76.8	94.8
C-10	39.9	40.3	41.4	132.0	39.0	39.2	43.6	42.8
C-11	29.7	30.1	30.8	29.3	20.8[d)]	22.0	28.0	28.7
C-12	36.1	36.9	37.2	38.8	45.1	46.9	37.5	37.0
C-13	73.5	72.7	74.2	73.4	73.7	73.1	73.5	86.1
C-14	145.3	147.5	146.4	145.1	146.1	147.6	145.4	39.3
C-15	111.8	111.3	112.2	111.9	111.2	110.8	111.7	173.9
C-16	27.8	28.8	27.9	27.7	27.6	28.7	27.9	107.2
C-17	14.5	14.8	14.9	16.5	32.1	32.5	16.6	16.9
C-18	24.6	24.9	25.2	25.2	33.2	33.2	33.8	33.1
C-19	21.0	21.2	21.6	22.0	21.4	21.5	22.0	23.7
C-20	22.2	22.5	22.8	27.3	24.8	25.1	16.3	19.7
C-1′	170.7	170.5	172.7	171.0				170.4
C-2′	21.3	21.2	21.1	21.4				21.9
C-1″								69.5
C-2″								31.5
C-3″								19.3
C-4″								13.8

δ in ppm from TMS. *a*) In $CDCl_3$. *b*) In C_5D_5N. *c*) In CD_3OD. *d*) Assignments may be interchangeable in each column. —, signal not recorded.

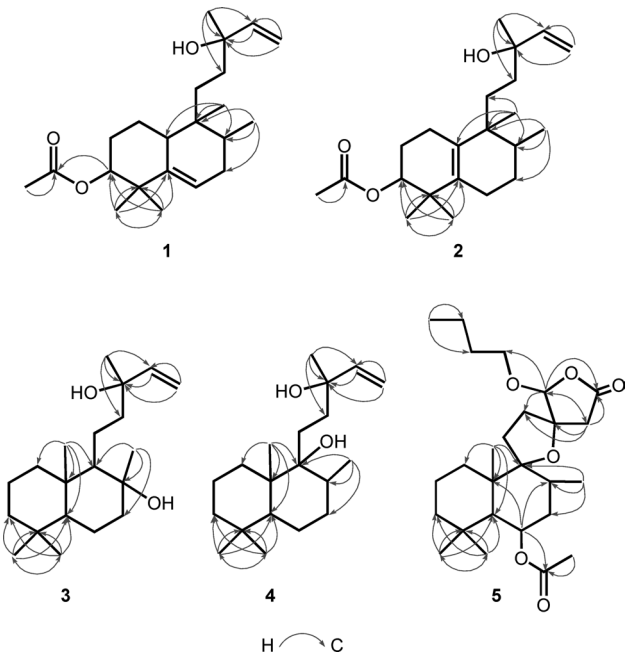

Fig. 2. HMBC Correlations for **1**—**5**

Compound **2**, called viteagnusin B, was obtained as an amorphous powder, and its positive FAB-MS indicated the same $[M+Na]^+$ ion peak as that of **1**. The ^{1}H- and ^{13}C-NMR spectra of **2** were similar to those of **1**, except for the absence of signals due to one olefinic proton and one olefinic methine carbon, and the presence of a signal due to one olefinic quaternary carbon. In a manner similar to that in the case of **1**, these ^{1}H- and ^{13}C-NMR signals were examined in detail, and the planar structure of **2** was determined, as shown in Fig. 2.

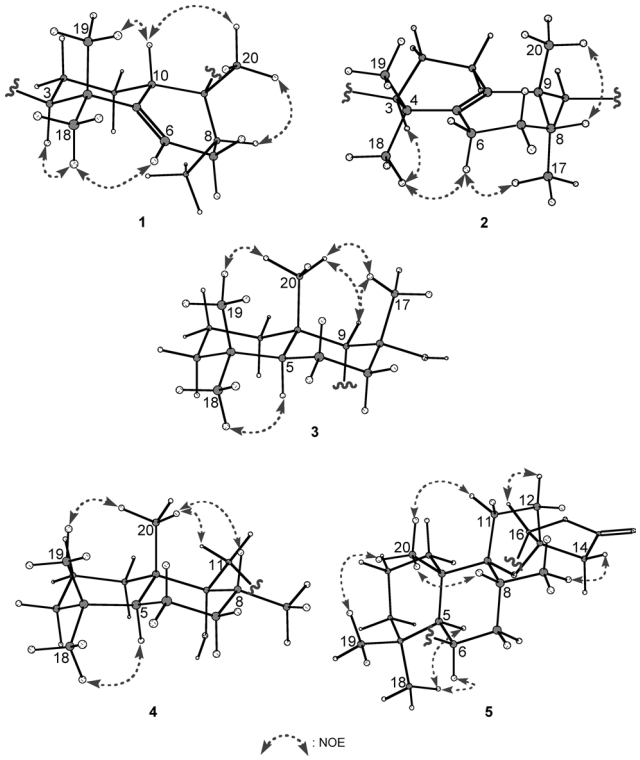

Fig. 3. Key NOE Correlations for **1**—**5**

The relative configurations at C-3, C-8, and C-9 were characterized on the basis of the NOESY and the difference NOE spectra of **2**, in which key NOEs were observed between respective protons, as shown in Fig. 3, and by the comparison of the ^{13}C-NMR data of the B-ring moiety between **2** and the related 5(10)-halimene-type diterpenoids.[19] Thus, the structure of **2** was concluded to be (*rel* 3*R*,8*R*,9*R*)-3-acetoxy-5(10),14-halimadien-13-ol.

Compound **3**, called viteagnusin C, was obtained as an amorphous powder, and its molecular formula was determined to be $C_{20}H_{36}O_2$ by using HR-positive FAB-MS. The ^{1}H- and ^{13}C-NMR spectra of **3** were analogous to those of **6**, and the planar structure of **3** was determined to be same as that of **6** by using 2D-NMR techniques similar to those used for **1**. In the NOESY spectra of **3** (in $CDCl_3$ and C_5D_5N), key NOEs were observed between H-5 and H_3-18, H-9 and H_3-17, H-9 and H_3-20, H_3-17 and H_3-20, and H_3-19 and H_3-20. Furthermore, the ^{13}C-NMR data of **3** were different from those of **9** and the 13-epimer of **9**.[20] Consequently, the structure of **3** was concluded to be (*rel* 5*S*,8*R*,9*S*,10*S*)-8,13-dihydroxy-14-labden (Fig. 1).

Compound **4**, called viteagnusin D, was obtained as an amorphous powder. The molecular formula of **4** was determined to be same as that of **3** by using HR-positive FAB-MS. The ^{1}H- and ^{13}C-NMR spectra of **4** were also similar to those of **3**, although signals due to one secondary methyl group were present and signals due to one tertiary methyl group were absent. These NMR signals were assigned by using 2D-NMR techniques similar to those used for **1**, and the planar structure of **4** was determined, as shown in Fig. 2. The stereostructure of **4** was characterized on the basis of the NOESY and the difference NOE spectra of **4**, in which key NOEs were observed between the respective protons, as shown in Fig. 3. The structure of **4** was therefore concluded to be (*rel*

5*S*,8*R*,9*R*,10*S*)-8,13-dihydroxy-14-labden (Fig. 1).

Compound **5**, called viteagnusin E, was obtained as an amorphous powder. The HR-positive FAB-MS of **5** revealed its molecular formula of **5** to be $C_{26}H_{42}O_6$. The ^{1}H-NMR spectrum of **5** exhibited signals due to three tertiary methyl groups (δ 1.22, 0.99, 0.96), one secondary methyl group [δ 0.82 (d, J=6.5 Hz)], one primary methyl group [δ 0.93 (t, J=7.5 Hz)], one acetyl group (δ 2.05), two oxygenated methine protons [δ 5.40 (ddd, J=2.5, 2.5, 2.5 Hz), 4.90 (s)], two oxygenated methylene protons [δ 3.81 (ddd, J=7.0, 7.0, 10.0 Hz), 3.50 (ddd, J=7.0, 7.0, 10.0 Hz)], and two methylene protons [δ 3.11 (d, J=17.0 Hz), 2.37 (d, J=17.0 Hz)] adjacent to a carbonyl group. The ^{13}C-NMR spectrum of **5** exhibited 26 carbon signals, comprising two carbonyl carbons (δ 173.9, 170.4), one acetal carbon (δ 107.2), one oxygenated methylene carbon (δ 69.5), one oxygenated methine carbon (δ 70.5), and two oxygenated quaternary carbons (δ 94.8, 86.1). These NMR signals were assigned by using techniques similar to those used for **1**, and the planar structure of **5**, which was a labdane-type diterpenoid possessing one each of spiro-tetrahydrofuran ring, γ-spiro-lactone ring, acetoxy group, and butoxy group, could be determined. The relative stereostructure of **5** was examined using its NOESY spectrum, and key NOEs were observed, as shown in Fig. 3. Consequently, the structure of **5** was concluded to be (*rel* 5*S*,6*R*,8*R*,9*R*,10*S*,13*S*,16*R*)-6-acetoxy-9,13-epoxy-16-butoxy-labdan-15,16-olide (Fig. 1).

Compounds **1**—**5** are new diterpenoids, and the isolation of **6** and **7** from *Vitex agnus-castus* has been described here for the first time. However, the configurations of the hydroxyl group at C-13 of **1**—**4** and the absolute configurations of **1**—**5** have not yet been confirmed.

Experimental

All instruments and materials used were the same as cited in previous reports[14] unless otherwise specified.

Plant Material The fruit of *Vitex agnus-castus* L. was purchased in May 2006 from Charis Seijo Co., Ltd., a commercial supplier of herbs in Tokyo, Japan and identified by Prof. Toshihiro Nohara, Faculty of Pharmaceutical Sciences, Sojo University. A voucher specimen has been deposited at the laboratory of Natural Products Chemistry, School of Agriculture, Tokai University.

Extraction and Isolation The powdered fruit of *V. agnis-castus* (1994 g) was percolated with hexane, acetone, and MeOH at room temperature, and each solvent was removed under reduced pressure to yield hexane extract (188.4 g), acetone extract (36.9 g), and MeOH extract (113.4 g), respectively. The hexane extract was subjected to silica gel (Merck, Art. 1.07734) with a gradient of mixtures of hexane–acetone (20 : 1, 10 : 1, 3 : 1, 1 : 1, 0 : 1) to yield fractions 1—9. The chromatography of fraction 6 (26.9 g) on a Chromatorex ODS column with a gradient of mixtures of H_2O–MeOH (70% MeOH, 75% MeOH, 80% MeOH, 85% MeOH, 90% MeOH, 95% MeOH, and 100% MeOH) yielded fractions 10—24. Fraction 15 (2498 mg) was chromatographed on silica gel (Merck, Art. 1.09385) with a gradient of mixtures of hexane–acetone (15 : 1, 10 : 1, 5 : 1, 3 : 1, 1 : 1) to yield fractions 25—36. Fraction 29 (161 mg) was subjected to HPLC (column, COSMOSIL 5C18 AR-II, 250 mm×20 mm i.d., Nacalai Tesque Inc.; solv., 80% MeOH) to yield **7** (10 mg), **1** (17 mg), **5** (18 mg), **4** (13 mg), and **2** (7 mg). Similar HPLC (75% MeOH) of fraction 31 (117 mg) to fraction 29 afforded **3** (5 mg) and **6** (10 mg).

Viteagnusin A (**1**): Amorphous powder, $[\alpha]_D^{26}$ −62.0° (c=1.7, $CHCl_3$). Positive FAB-MS m/z: 371 $[M+Na]^+$, HR-positive FAB-MS m/z: 371.2555 (Calcd for $C_{22}H_{36}O_3Na$: 371.2562). ^{1}H-NMR spectral data (in $CDCl_3$): see Table 1. ^{13}C-NMR spectral data (in $CDCl_3$, C_5D_5N, and CD_3OD): Table 2. ^{1}H-NMR spectral data (in C_5D_5N) δ: 6.20 (1H, dd, J=11.0, 17.0 Hz, H-14), 5.57 (1H, dd, J=1.0, 17.0 Hz, H-15a), 5.46 (1H, dd, J=3.5, 3.5 Hz, H-6), 5.17 (1H, dd, J=1.0, 11.0 Hz, H-15b), 4.69 (1H, dd, J=4.5, 11.5 Hz, H-3), 2.05 (3H, s, $COCH_3$), 1.96 (1H, m, H-2a), *ca.* 1.70 (H-2b), 1.58 (1H, m, H-8), 1.51 (3H, s, H_3-16), 1.15 (3H, s, H_3-19), 1.08 (3H, s, H_3-18), 0.81 (3H, d, J=7.0 Hz, H_3-17), 0.79 (3H, s, H_3-20). ^{1}H-NMR spectral data (in CD_3OD) δ: 5.85 (1H, dd, J=11.0, 17.0 Hz, H-14), 5.50 (1H, dd, J=3.0, 3.0 Hz, H-6), 5.16 (1H, dd, J=1.0, 17.0 Hz, H-15a), 5.01 (1H, dd, J=1.0, 11.0 Hz, H-15b), 4.38 (1H, dd, J=5.0, 11.5 Hz, H-3), 2.03 (3H, s, $COCH_3$), 1.23 (3H, s, H_3-16), 1.07 (3H, s, H_3-19), 1.01 (3H, s, H_3-18), 0.82 (3H, s, H_3-20), 0.81 (3H, d, J=6.5 Hz, H_3-17).

Viteagnusin B (**2**): Amorphous powder, $[\alpha]_D^{26}$ +10.0° (c=0.3, $CHCl_3$). Positive FAB-MS m/z: 371 $[M+Na]^+$. ^{1}H- and ^{13}C-NMR spectral data: see Tables 1 and 2.

Viteagnusin C (**3**): Amorphous powder, $[\alpha]_D^{26}$ −4.2° (c=0.5, $CHCl_3$). Positive FAB-MS m/z: 331 $[M+Na]^+$, HR-positive FAB-MS m/z: 331.2615 (Calcd for $C_{20}H_{36}O_2Na$: 331.2613). ^{1}H- and ^{13}C-NMR spectral data: see Tables 1 and 2.

Viteagnusin D (**4**): Amorphous powder, $[\alpha]_D^{26}$ +9.8° (c=1.4, $CHCl_3$). Positive FAB-MS m/z: 331 $[M+Na]^+$, HR-positive FAB-MS m/z: 331.2615 (Calcd for $C_{20}H_{36}O_2Na$: 331.2613). ^{1}H- and ^{13}C-NMR spectral data: see Tables 1 and 2.

Viteagnusin E (**5**): Amorphous powder, $[\alpha]_D^{26}$ −16.1° (c=1.6, $CHCl_3$). Positive FAB-MS m/z: 473 $[M+Na]^+$, HR-positive FAB-MS m/z: 473.2877 (Calcd for $C_{26}H_{42}O_6Na$: 473.2880). ^{1}H- and ^{13}C-NMR spectral data: see Tables 1 and 2.

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References

1) Li S. H., Zhang H. J., Qiu S. X., Niu X. M., Santarsiero B. D., Mesecar A. D., Fong H. H. S., Farnsworth N. R., Sun H. D., *Tetrahedron Lett.*, **43**, 5131—5134 (2002).
2) Wollenweber E., Mann K., *Planta Med.*, **48**, 126—127 (1983).
3) Görler K., Oehlke D., Soicke H., *Planta Med.*, **51**, 530—531 (1985).
4) Hirobe C., Qiao Z., Takeya K., Itokawa H., *Phytochemistry*, **46**, 521—524 (1997).
5) Hoberg E., Orjala J., Meier B., Sticher O., *Phytochemistry*, **52**, 1555—1558 (1999).
6) Sørensen J. M., Katsiotis S. T., *Planta Med.*, **66**, 245—250 (2000).
7) Kurüzüm-Uz A., Ströch K., Demirezer L. Ö., Zeeck A., *Phytochemistry*, **63**, 959—964 (2003).
8) Jarry H., Spengler B., Wuttke W., Christoffel V., *Maturitas*, **55S**, S26—S36 (2006).
9) Hajdú Z., Hohmann J., Forgo P., Martinek T., Dervarics M., Zupkó I., Falkay G., Cossuta D., Máthé I., *Phytother. Res.*, **21**, 391—394 (2007).
10) Liu J., Burdette J. E., Sun Y., Deng S., Schlecht M., Zheng W., Nikolic D., Mahady G., van Breemen R. B., Fong H. H. S., Pezzuto J. M., Bolton J. L., Farnsworth N. R., *Phytomedicine*, **11**, 18—23 (2004).
11) Yamasaki T., Kwabata T., Masuoka C., Kinjo J., Ikeda T., Nohara T., Ono M., *J. Nat. Med.*, **62**, 47—51 (2008).
12) Ono M., Oda E., Tanaka T., Iida Y., Yamasaki T., Masuoka C., Ikeda T., Nohara T., *J. Nat. Med.*, **62**, 101—106 (2008).
13) Yamasaki T., Masuoka C., Nohara T., Ono M., *J. Nat. Med.*, **61**, 318—322 (2007).
14) Ono M., Tsuru T., Abe H., Eto M., Okawa M., Abe F., Kinjo J., Ikeda T., Nohara T., *J. Nat. Prod.*, **69**, 1417—1420 (2006).
15) Torrenegra R., Pedrozo J., Robles J., Waibel R., Achenbach H., *Phytochemistry*, **31**, 2415—2418 (1992).
16) Ono M., Yamamoto M., Yanaka T., Ito Y., Nohara T., *Chem. Pharm. Bull.*, **49**, 82—86 (2001).
17) Rudi A., Aknin M., Gaydou E., Kashman Y., *J. Nat. Prod.*, **67**, 1932—1935 (2004).
18) Almqvist S., Enzell C. R., Wehrli F. W., *Acta Chem. Scand.*, **B29**, 695—702 (1975).
19) Hara N., Asaki H., Fujimoto Y., Gupta Y. K., Singh A. K., Sahai M., *Phytochemistry*, **38**, 189—194 (1995).
20) Forester P. G., Ghisalberti E. L., Jefferies P. R., *Phytochemistry*, **24**, 2991—2993 (1985).