Ten New Labdane-Type Diterpenes from the Fruit of *Vitex rotundifolia*

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Ten new labdane-type diterpenes were isolated from the fruit of *Vitex rotundifolia* L. (Verbenaceae), along with a known diterpene, vitexilactone. Their chemical structures were determined on the bases of spectroscopic data.

Key words *Vitex rotundifolia*; labdane; diterpene; Verbenaceae; Viticis Fructus

Vitex rotundifolia L. (Verbenaceae) is widely distributed in Asia, and its fruit, Viticis Fructus, is used as a folk medicine for headaches, colds, migraine, eyepain, *etc*.[1] During the course of our research on the constituents of the genus *Vitex*, we have investigated the diterpene constituents of *V. trifolia* L.,[2] which is used as a substitute for the fruit of *V. rotundifolia*. In previous papers,[3—6] we reported the isolation and structural elucidation of iridoids, phenylpropanoids, a flavanone, lignanes, a diterpene glycoside and diterpenoids in the MeOH extract of the fruit of *V. rotundifolia*. As part of the continuing study of this fruit, we now describe the isolation and structural elucidation of ten new labdane-type diterpenes (**1**—**10**), along with a known labdane-type diterpene, vitexilactone (**11**)[7] from the MeOH extract.

The MeOH extract of the fruit of *Vitex rotundifolia* L. was purified by Diaion HP-20, silica gel, Sephadex LH-20 and Chromatorex ODS column chromatography, as well as by HPLC on ODS and silica gel to afford eleven labdane-type diterpenes (**1**—**11**).

Compound **1** was obtained as a colorless syrup. The EI-MS of **1** indicated the same intense fragment ion peak at *m*/*z* 318 $[M-CH_3COOH]^+$ as that of **11**. The molecular formula of **1** was determined to be $C_{22}H_{34}O_5$ by HR positive FAB-MS. The ^{1}H- and ^{13}C-NMR spectra of **1** were superimposable on those of **11** apart from the chemical shifts of signals due to the olefinic group [δ 7.13 (H-14), 135.0 (C-13), 144.0 (C-14) in **1**; δ 5.84 (H-14), 171.1 (C-13), 115.0 (C-14) in **11**], which exhibited the replacement of a β-substituted butenolide ring in **11** by an α-substituted butenolide ring.[8] Furthermore, the difference NOE spectra of **1** indicated correlations between the respective protons, as illustrated in Fig. 2. Consequently, **1** was elucidated to be (*rel* 5*S*,6*R*,8*R*,9*R*,10*S*)-6-acetoxy-9-hydroxy-13(14)-labden-16,15-olide.

Compound **2** was obtained as a colorless syrup, and its EI-MS showed the same dominant fragment ion peak at *m*/*z* 318 as those of **1** and **11**. The ^{1}H-NMR spectrum was closely analogous to that of **1** except for the splitting patterns and chemical shifts of the signals due to H-5 (δ 1.93, d, J=11.5 Hz) and H-6 (δ 5.08, ddd, J=5.0, 11.5, 11.5 Hz). The ^{13}C-NMR spectrum was similar to that of **1**, although the signals due to C-6, C-7, C-8, C-10, C-18 and C-20 were shifted by +2.0, +1.0, +3.6, +1.2, +2.9 and −1.4 ppm , respectively. Furthermore, in the difference NOE spectra, NOEs were observed between H_3-19 and H-6, as well as between H_3-20 and H-6, instead of the NOE correlation between H_3-18 and H-6 seen in **1**, and other NOE correlations were the same as those of **1**. Accordingly, **2** was defined as (*rel* 5*S*,6*S*,8*R*,9*R*,10*S*)-6-acetoxy-9-hydroxy-13(14)-labden-16,15-olide.

Compound **3** was obtained as a colorless syrup. The ^{1}H-NMR spectrum was similar to that of **1**, with the exception that the signal due to a methoxyl group appeared at δ 3.58, and the signal assignable to an H-15 disappeared. The EI-MS of **3** showed an intense fragment ion peak at *m*/*z* 348, which was 30 mass units [OCH_3-H] larger than that of **1**. These data suggested that **3** differed from **1** by the replacement of an H-15 in **1** by a methoxyl group. This suggestion was supported by the ^{13}C-NMR and difference NOE spectra. Comparing the ^{13}C-NMR spectrum of **3** with that of **1**, the signals due to C-13 and C-15 in **3** were shifted downfield by 4.2 and 32.3 ppm, respectively, whereas signals due to C-1, C-14 and C-16 were shifted upfield by 1.6, 2.5 and 3.0 ppm, respectively, and the other carbon signals were quite similar to those of **1**. The difference NOE spectra of **3** gave the same NOE correlations as those of **1**. Consequently, **3** was elucidated to be (*rel* 5*S*,6*R*,8*R*,9*R*,10*S*)-6-acetoxy-9-hydroxy-15-methoxy-13(14)-labden-16,15-olide. However, the configuration of the methoxyl group at C-15 was not determined.

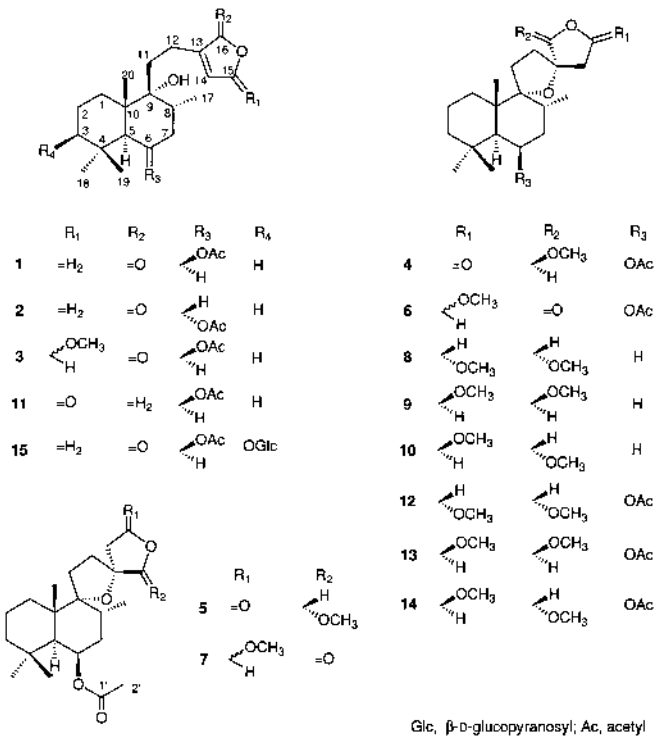

Fig. 1. Structures of **1**—**15**

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Table 1. ^{1}H-NMR Spectral Data for Compounds **1**—**3** and **11** (500 MHz, in $CDCl_3$)

H	1	2	3	11
1a	*ca.* 1.50	*ca.* 1.50	*ca.* 1.51	1.45 m
1b	*ca.* 1.50	*ca.* 1.50	*ca.* 1.44	*ca.* 1.36
2a	*ca.* 1.63	*ca.* 1.57	*ca.* 1.61	1.65 m
2b	1.44 m	*ca.* 1.47	*ca.* 1.49	*ca.* 1.50
3a	1.32 m	1.33 br d (13.0)	1.33 br d (13.5)	*ca.* 1.36
3b	1.18 ddd (3.0,13.5,13.5)	*ca.* 1.24	1.17 ddd (3.5,13.5,13.5)	1.17 ddd (3.0,13.5,13.5)
5	1.67 d (2.5)	1.93 d (11.5)	*ca.* 1.64	1.56 d (3.0)
6	5.39 ddd (2.5,2.5,2.5)	5.08 ddd (5.0,11.5,11.5)	5.38 ddd (2.5,2.5,2.5)	5.39 ddd (3.0,3.0,3.0)
7a	*ca.* 1.65	1.77 ddd (5.0,5.0,11.5)	*ca.* 1.64	*ca.* 1.59
7b	*ca.* 1.54	1.41 ddd (11.5,11.5,11.5)	*ca.* 1.55	*ca.* 1.50
8	2.11 m	1.97 m	2.10 m	2.14 m
11a	1.85 m	1.84 ddd (6.0,10.5,14.5)	1.85 m	1.98 ddd (6.0,10.5,15.0)
11b	1.78 m	*ca.* 1.66	1.75 m	1.75 ddd (6.0,10.5,15.0)
12a	2.43 ddddd (1.5,1.5,1.5,8.0,8.0)	*ca.* 2.38	2.43 br dd (7.5,7.5)	*ca.* 2.50
12b	2.43 ddddd (1.5,1.5,1.5,8.0,8.0)	*ca.* 2.38	2.43 br dd (7.5,7.5)	*ca.* 2.50
14	7.13 dddd (1.5,1.5,1.5,1.5)	7.10 br s	6.77 ddd (1.5,1.5,1.5)	5.84 dddd (1.5,1.5,1.5,1.5)
15a	4.79 ddd (1.5,1.5,1.5)	4.77 br s	5.73 ddd (1.5,1.5,1.5)	
15b	4.79 ddd (1.5,1.5,1.5)	4.77 br s		
16a				4.76 br s
16b				4.76 br s
17	0.93 d (6.5)	0.93 d (6.5)	0.92 dd (1.5,6.5)	0.90 d (6.5)
18	0.96 s	1.04 s	0.96 s	0.97 s
19	1.00 s	0.90 s	1.00 s	1.01 s
20	1.24 s	1.00 s	1.23 s	1.26 s
$COCH_3$	2.05 s	2.03 s	2.04 s	2.06 s
OCH_3			3.58 s	

δ in ppm from TMS (coupling constants (J) in Hz are given in parentheses). Assignments are based on ^{1}H–^{1}H COSY experiments.

Table 2. ^{13}C-NMR Spectral Data for Compounds **1**—**11** (in $CDCl_3$)

C	1	2	3	4	5	6	7	8	9	10	11
1	33.6	32.8[a)]	32.0[a)]	34.4	34.5	33.7	33.8	31.4[a)]	32.9	31.4[a)]	33.6
2	18.7	18.4	18.6	18.9	18.7	18.7	18.8	19.1	18.9	19.1	18.6
3	43.7	43.0	43.6	44.0	43.9	43.9	43.9	41.9[b)]	42.0	42.0[b)]	43.6
4	34.0	33.1	33.9	34.2	34.2	34.1	34.1	33.5	33.5	33.6	34.0
5	47.5	48.3	47.5	49.0	48.8	48.7	49.0	46.7	46.8	46.9	47.7
6	70.2	72.2	70.1	70.4	70.5	70.6	70.7	21.7	21.9	21.7	69.8
7	36.2	37.2	36.1	36.4	36.4	36.8	36.3	31.0[a)]	31.4	30.9[a)]	36.1
8	31.9	35.5	31.9	31.5	31.5	31.2	31.7	36.6	36.1	36.7	32.1
9	76.6	76.1	76.5	94.5	94.9	95.4	95.2	93.7	93.7	93.6	76.5
10	43.8	45.0	43.8	43.1	42.8	43.3	43.1	42.4	42.6	42.4	43.8
11	32.2	32.2[a)]	31.9[a)]	30.0	29.1	29.5	29.3	29.5	29.7	29.8	31.6
12	22.0	22.1	22.0	31.1	31.7	35.8	37.9	37.6	31.7	38.2	25.4
13	135.0	134.9	139.2	88.6	88.3	84.5	82.9	89.3	92.2	88.3	171.1
14	144.0	144.0	141.5	41.8	41.3	43.9	44.1	41.7[b)]	44.6	42.1[b)]	115.0
15	70.3	70.2	102.6	173.7	174.4	102.5	101.2	103.6	105.4	103.4	174.0
16	174.6	174.5	171.6	109.4	110.4	176.3	177.7	105.6	108.8	107.1	73.2
17	16.2	15.8	16.1	17.6	17.5	17.5	16.3	17.4[c)]	18.2	17.4[c)]	16.1
18	33.6	36.5	33.6	33.1	33.1	33.2	33.1	33.1	33.3	33.1	33.6
19	23.7	22.8	23.7	23.8	23.8	23.9	23.7	22.0	22.0	22.0	23.7
20	19.0	17.6	19.0	19.9	19.9	20.4	20.1	17.1[c)]	17.5	17.2[c)]	19.0
1′	170.5	170.5	170.5	170.4	170.5	170.6	170.4				170.4
2′	21.9	22.0	21.9	21.9	21.9	22.0	22.0				21.9
OCH_3			57.1	57.3	57.2	57.2	56.8	55.3	55.6	55.4	
OCH_3								54.6	55.2	54.8	

1—**3**, **6**—**11** at 125 MHz and **4**, **5** at 100 MHz. *a*, *b*, *c*) Assignments in each column may be interchangeable. Assignments are based on HMQC and HMBC spectra.

Compound **4** was obtained as a colorless syrup. The ^{1}H-NMR spectrum of **4** indicated signals due to three tertiary methyl groups (δ 1.22, 0.98, 0.95), one secondary methyl group (δ 0.83, d, J=6.5 Hz), one acetyl group (δ 2.04), one methoxyl group (δ 3.52), two oxygenated methine protons (δ 5.38, ddd, J=3.0, 3.0, 3.0 Hz; δ 5.33, s) and two methylene protons (δ 2.83, d, J=17.5 Hz; δ 2.67, d, J=17.5 Hz) adjacent to a carbonyl group. The ^{13}C-NMR spectrum of **4** gave 23 carbon signals, including two carbonyl carbons (δ 173.7, 170.4), one acetal carbon (δ 109.4), one methoxyl carbon (δ 57.3), one oxygenated methine carbon (δ 70.4) and two oxygenated quaternary carbons (δ 94.5, 88.6). In the EI-MS, **4** did not show a molecular ion peak but showed a base ion peak at m/z 348 $[M-CH_3COOH]^+$. These data suggested

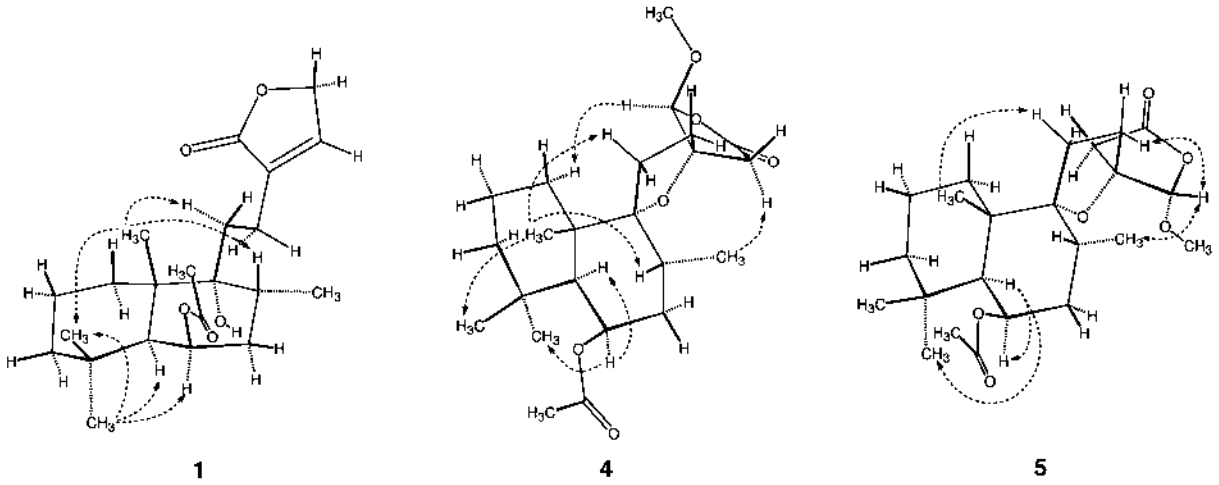

Fig. 2. Selected NOE Correlations Observed in the Difference NOE Spectra of **1**, **4** and **5**

that **4** was a labdane-type diterpene having one each of a spiro-tetrahydrofuran ring, γ-spiro-lactone ring, methoxyl group and acetoxy group. Furthermore, comparison of the ^{1}H- and ^{13}C-NMR data of **4** with those of (*rel* 5*S*,6*R*,8*R*,9*R*,10*S*,13*S*,15*S*,16*R*)-6-acetoxy-9,13;15,16-diepoxy-15,16-dimethoxylabdane (**12**) and (*rel* 5*S*,6*R*,8*R*,9*R*,10*S*,13*S*,15*R*,16*S*)-6-acetoxy-9,13;15,16-diepoxy-15,16-dimethoxylabdane (**13**), which were previously isolated from this fruit,[6] led to the assumption that **4** is a derivative among of **12**, **13** and C-13 epimers of **12** and **13**, in which the methoxyl group at C-15 was replaced by a carbonyl group. In the difference NOE spectra of **4**, NOEs were observed between the respective protons, as illustrated in Fig. 2, while, no correlation between H-16 and H-12 was detected. Compound **4** was therefore defined as (*rel* 5*S*,6*R*,8*R*,9*R*,10*S*,13*S*,16*S*)-6-acetoxy-9,13-epoxy-16-methoxy-labdan-15,16-olide.

Compound **5** was obtained as a colorless syrup, and it was recognized as an isomer at C-13 and/or C-16 of **4** by the NMR data and EI-MS. In the difference NOE spectra of **5**, correlations were as illustrated in Fig. 2, which indicated the configurations of C-13 and C-16 to be *R** and *S**, respectively. Consequently, **5** was concluded to be the C-13 epimer of **4**.

Compounds **6** and **7** were obtained as a colorless syrup. These compounds were determined to possess the same framework as those of **4** and **5**, except for an exchange of the positions of the carbonyl group and methoxyl group by considering the EI-MS and NMR data. In the difference NOE spectra of **6**, irradiation of the signal due to H_3-17 gave an NOE enhancement of the signal due to Ha-14, whereas, in the case of **7**, the NOE correlation between H_3-17 and H-14 was not detected. The other NOE correlations of **6** and **7** were the same as those of **4**. Furthermore, in the ^{1}H-NMR spectrum, the signal due to H_3-17 of **7**, which was deshielded by a carbonyl group, was observed downfield by 0.27 ppm compared with that of **6**. The structures of **6** and **7** were therefore defined as (*rel* 5*S*,6*R*,8*R*,9*R*,10*S*,13*S*)-6-acetoxy-9,13-epoxy-15-methoxy-labdan-16,15-olide 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, respectively. However, the configurations of the methoxyl groups at C-15 in **6** and **7** were not determined.

Compounds **8** and **9** were obtained as a colorless syrup, and **10** was obtained as colorless needles. Their EI-MS and NMR data indicated that **8**—**10** possess a common framework, differing only in the configurations of the methoxyl groups. Except for the absence of the acetoxy group, the ^{1}H-NMR spectra of **8**, **9** and **10** were similar to those of **12**, **13** and (*rel* 5*S*,6*R*,8*R*,9*R*,10*S*,13*S*,15*R*,16*R*)-6-acetoxy-9,13;15,16-diepoxy-15,16-dimethoxylabdane (**14**),[6] respectively. In particular, the signals due to two spiro-tetrahydrofuran rings were superimposable on those of **12**, **13** and **14**, respectively. Each difference NOE spectrum of **8**, **9** and **10** gave an NOE correlation between H_3-17 and Hb-14. In addition, the NOE correlation between Ha-12 and H-16 was observed in those spectra of **8** and **10**, but in the case of **9**, the NOE correlation was not detected. Accordingly, the structures of **8**, **9** and **10** were defined as deacetoxy derivatives of **12**, **13** and **14**, respectively.

Although the absolute configurations of **1**—**10** have not been confirmed, they are probably the same as that of viteoside A (**15**), previously isolated from this fruit,[5] from a biogenetic point of view. Compounds **3**—**10** might be artifacts produced from aldehydes during the extraction and/or isolation procedures.

Experimental

The melting point was determined on a Yanagimoto micromelting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DTP-1000 KUY digital polarimeter. ^{1}H-NMR spectra were recorded in $CDCl_3$ solution using a JEOL alpha 500 spectrometer at 500 MHz, and chemical shifts were given on a δ (ppm) scale with tetramethylsilane (TMS) as an internal standard. ^{13}C-NMR spectra were recorded in $CDCl_3$ solution using JEOL JNM-GX-400 and JEOL alpha 500 spectrometers at 100 MHz or 125 MHz, respectively. The MS were obtained on a JEOL JMS-DX-303HF instrument. Column chromatography was carried out with Diaion HP-20 (Mitsubishi Chemical Industries Co., Ltd.), silica gel 60 (Art. 7734 and Art. 9385, Merck), Sephadex LH-20 (Pharmacia Fine Chemicals) and Chromatorex ODS (Fuji Silysia Chemical Co., Ltd.). HPLC separation was run on a Micro pump LC-10AS (Shimadzu) with an RI-Detector RID-6A (Shimadzu). For HPLC column chromatography, a YMC-pack D-ODS-5 (250 mm×20 mm i.d., YMC Co., Ltd.), YMC-pack SIL-06 (250 mm×20 mm i.d., YMC Co., Ltd.), TSK-GEL ODS-120T (300 mm×21.5 mm i.d., Tosoh Co., Ltd.) and Inertsil ODS-3 (250 mm×4.6 mm i.d., GL Sciences Inc.) were used. The fruit of *Vitex rotundifolia* L. was purchased from Uchida Wakanyaku Co., Ltd. (Lot. 232418).

Extraction and Isolation The powdered fruit of *Vitex rotundifolia* L. (2914 g) was extracted with MeOH at room temperature, and the solvent was removed under reduced pressure to give a brown syrup (185.2 g). This ex-

Table 3. ^{1}H-NMR Spectral Data for Compounds **4**—**10** (500 MHz, in $CDCl_3$)

H	4	5	6	7	8	9	10
1a	1.42 dddd (3.0, 3.0, 3.0, 12.0)	*ca*. 1.39	*ca*. 1.81	1.41 m			
1b	*ca*. 1.32	*ca*. 1.32	1.32 m	*ca*. 1.31			
2a	*ca*. 1.63	*ca*. 1.62	*ca*. 1.60	1.65 ddddd (3.5, 3.5, 13.5, 13.5, 13.5)			
2b	1.51 ddddd (3.0, 3.0, 3.0, 3.0, 13.0)	*ca*. 1.49	*ca*. 1.54	*ca*. 1.48			
3a	*ca*. 1.32	*ca*. 1.31	*ca*. 1.27	*ca*. 1.31			
3b	1.17 ddd (3.0, 13.5, 13.5)	1.14 ddd (3.5, 13.5, 13.5)	1.20 ddd (4.0, 13.5, 13.5)	*ca*. 1.12			
5	1.45 d (3.0)	1.43 d (3.0)	1.50 d (3.0)	1.49 d (2.5)			
6	5.38 ddd (3.0, 3.0, 3.0)	5.37 ddd (3.0, 3.0, 3.0)	5.38 ddd (3.0, 3.0, 3.0)	5.41 ddd (2.5, 2.5, 2.5)			
7a	*ca*. 1.62	*ca*. 1.65	1.63 ddd (3.0, 14.0, 14.0)	*ca*. 1.79			
7b	1.48 ddd (3.0, 3.0, 14.0)	*ca*. 1.49	*ca*. 1.54	*ca*. 1.51			
8	*ca*. 2.13	*ca*. 2.12	*ca*. 2.13	2.13 m	1.69 m	1.70 m	1.69 m
11a	*ca*. 2.10	*ca*. 2.12	*ca*. 2.30	*ca*. 2.17	2.03 m	*ca*. 1.96	*ca*. 2.02
11b	1.72 ddd (2.5, 9.0, 13.5)	*ca*. 1.75	*ca*. 1.82	*ca*. 1.81	1.61 ddd (2.5, 9.5, 13.0)	1.62 ddd (4.0, 9.5, 13.0)	*ca*. 1.62
12a	2.48 ddd (2.5, 9.0, 13.5)	2.44 ddd (9.5, 9.5, 14.0)	*ca*. 2.30	2.36 m	1.90 ddd (2.5, 9.5, 13.0)	2.34 ddd (4.0, 9.5, 13.5)	*ca*. 2.02
12b	1.86 ddd (9.0, 9.0, 13.5)	*ca*. 1.77	*ca*. 2.11	*ca*. 2.17	1.80 ddd (9.5, 9.5, 13.0)	1.84 ddd (9.5, 9.5, 13.5)	*ca*. 2.02
14a	2.83 d (17.5)	2.89 d (17.0)	2.59 dd (5.5,13.5)	2.53 dd (6.0,13.0)	2.39 dd (6.0,13.0)	1.96 dd (4.5,13.5)	2.57 dd (6.5,13.0)
14b	2.67 d (17.5)	2.57 d (17.0)	2.15 dd (3.5,13.5)	2.20 d (13.0)	2.09 dd (6.0,13.0)	2.45 dd (5.5,13.5)	1.82 d (13.0)
15			5.45 dd (3.5,5.5)	5.34 d (6.0)	4.93 dd (6.0,6.0)	5.14 dd (4.5,5.5)	5.03 d (6.5)
16	5.33 s	5.29 s			4.25 s	4.91 s	4.34 s
17	0.83 d (6.5)	0.84 d (6.5)	0.84 d (6.5)	1.11 d (6.5)	0.80 d (6.5)	0.84 d (6.5)	0.81 d (6.5)
18	0.95 s	0.94 s	0.93 s	0.94 s	0.86 s	0.85 s[a)]	0.86 s[a)]
19	0.98 s	0.97 s	0.97 s	0.98 s	0.79 s	0.79 s	0.80 s
20	1.22 s	1.22 s	1.23 s	1.24 s	0.86 s	0.87 s[a)]	0.87 s[a)]
$COCH_3$	2.04 s	2.04 s	2.04 s	2.04 s			
OCH_3-15			3.53 s	3.47 s	3.42 s	3.43 s	3.36 s
OCH_3-16	3.52 s	3.53 s			3.44 s	3.41 s	3.42 s

δ in ppm from TMS (coupling constants (J) in Hz are given in parentheses). *a*) Assignments in each column may be interchangeable. Assignments are based on ^{1}H–^{1}H COSY experiments.

tract was partitioned between hexane and MeOH. The lower layer was filtered through absorbent cotton. The filtrate was evaporated under reduced pressure, and crude material (158 g) was subjected to Diaion HP-20 column chromatography with an H_2O–MeOH solvent system and acetone to give fractions (frs.) 1—4, in the order of elution. Fraction (fr.) 3 (36.1 g; 90 % MeOH and MeOH eluate) was chromatographed over silica gel (Art. 7734) with a gradient of hexane–AcOEt (1 : 0→0 : 1) and MeOH to afford frs. 5—10. Chromatography of fr. 5 (5.68 g) over Chromatorex ODS with a gradient of H_2O–MeOH (3 : 7→1 : 19) furnished frs. 11—21. Fraction 15 (638 mg) was subjected to silica gel (Art. 9385) column chromatography with a gradient of hexane–acetone (20 : 1→0 : 1) to give frs. 22—30. Fraction 21 (154 mg), fr. 26 (162 mg) and fr. 27 (143 mg) were each subjected to HPLC separation [column, YMC pack SIL-06; solv., hexane–EtOAc (10 : 1); flow rate, 4.0 ml/min] to give **10** (23 mg; t_R 28.4 min), **8** (11 mg; t_R 41.4 min) and frs. 31—35 from fr. 21, **7** (35 mg; t_R 86.8 min), **6** (21 mg; t_R 126.1 min) and frs. 36—38 from fr. 26, and **5** (10 mg; t_R 134.5 min) and **4** (26 mg; t_R 139.8 min) from fr. 27. Fraction 19 (1047 mg) was chromatographed over silica gel (Art. 9385) with a gradient of hexane–acetone (50 : 1→0 : 1) to afford frs. 39—43. HPLC [column, YMC pack SIL-06; solv., hexane–acetone (60 : 1); flow rate, 4.0 ml/min] of fr. 39 (705 mg) gave **9** (31 mg; t_R 29.2 min) and frs. 44—49. Fraction 7 (12.44 g) was subjected to Chromatorex ODS column chromatography eluted with a gradient of H_2O–MeOH (4 : 6→0 : 1) to furnish frs. 50—66. Fraction 58 (1248 mg) was subjected to Sephadex LH-20 column chromatography eluted with MeOH to give frs. 67—70. Fraction 67 (942 mg) was chromatographed over silica gel (Art. 9385) with a gradient of hexane–EtOAc (7 : 1→0 : 1) to give **11** (190 mg) and frs. 71—76. Fraction 73 (62 mg) was subjected to HPLC separation (column, YMC-pack D-ODS-5; solv., 80% MeOH; flow rate, 5.0 ml/min) to afford **2** (5 mg; t_R 30.5 min) and **1** (35 mg; t_R 32.3 min). Fraction 60 (1145 mg) was chromatographed over Sephadex LH-20 with MeOH to give fr. 77 and fr. 78. Fraction 78 (1015 mg) was subjected to silica gel (Art. 9385) column chromatography eluted with a gradient of hexane–EtOAc (4 : 1→5 : 2) to give frs. 79—81. Fraction 80 (780 mg) was subjected to HPLC separation [(column, TSK-GEL ODS-120T; solv., 80 % MeOH) and (column, Inertsil ODS-3; solv., 80% MeOH; flow rate, 1.0 ml/min) in turn] to afford **3** (14 mg; t_R 13.2 min).

(*rel* 5*S*,6*R*,8*R*,9*R*,10*S*)-6-Acetoxy-9-hydroxy-13(14)-labden-16,15-olide (1) Colorless syrup. $[\alpha]_D^{21}$ −10.0° (c=3.3, acetone). HR positive FAB-MS *m/z*: 401.2364 $[M+Na]^+$ (Calcd for $C_{22}H_{34}NaO_5$: 401.2304). Positive FAB-MS *m/z* (rel. int.): 401 (100) $[M+Na]^+$, 341 (70) $[M+Na-CH_3COOH]^+$. EI-MS *m/z* (rel. int.): 318 (34) $[M-CH_3COOH]^+$, 300 (15), 168 (100), 135 (45). ^{1}H- and ^{13}C-NMR: see Tables 1 and 2.

(*rel* 5*S*,6*S*,8*R*,9*R*,10*S*)-6-Acetoxy-9-hydroxy-13(14)-labden-16,15-olide (2) Colorless syrup. $[\alpha]_D^{26}$ +62.5° (c=0.4, acetone). HR positive FAB-MS *m/z*: 401.2285 $[M+Na]^+$ (Calcd for $C_{22}H_{34}NaO_5$: 401.2304). Positive FAB-MS *m/z* (rel. int.): 401 (51) $[M+Na]^+$, 341 (100) $[M+Na-CH_3COOH]^+$. EI-MS *m/z* (rel. int.): 318 (44) $[M-CH_3COOH]^+$, 168 (100), 135 (27). ^{1}H- and ^{13}C-NMR: see Tables 1 and 2.

(*rel* 5*S*,6*R*,8*R*,9*R*,10*S*)-6-Acetoxy-9-hydroxy-15-methoxy-13(14)-labden-16,15-olide (3) Colorless syrup. $[\alpha]_D^{28}$ −11.4° (c=1.6, acetone). HR positive FAB-MS *m/z*: 431.2482 $[M+Na]^+$ (Calcd for $C_{23}H_{36}NaO_6$: 431.2410). Positive FAB-MS *m/z* (rel. int.): 431 (100) $[M+Na]^+$, 371 (97) $[M+Na-CH_3COOH]^+$. EI-MS *m/z* (rel. int.): 348 (61) $[M-CH_3COOH]^+$, 198 (100), 135 (98). ^{1}H- and ^{13}C-NMR: see Tables 1 and 2.

(*rel* 5*S*,6*R*,8*R*,9*R*,10*S*,13*S*,16*S*)-6-Acetoxy-9,13-epoxy-16-methoxy-labdan-15,16-olide (4) Colorless syrup. $[\alpha]_D^{17}$ +27.2° (c=2.6, acetone). HR positive FAB-MS *m/z*: 431.2410 $[M+Na]^+$ (Calcd for $C_{23}H_{36}NaO_6$: 431.2410). Positive FAB-MS *m/z* (rel. int.): 431 (100) $[M+Na]^+$, 371 (25) $[M+Na-CH_3COOH]^+$, 348 (10) $[M-CH_3COOH]^+$. EI-MS *m/z* (rel. int.):

348 (100) $[M-CH_3COOH]^+$, 224 (21), 211 (34). ^{1}H- and ^{13}C-NMR: see Tables 2 and 3.

(*rel* 5*S*,6*R*,8*R*,9*R*,10*S*,13*R*,16*S*)-6-Acetoxy-9,13-epoxy-16-methoxylabdan-15,16-olide (5) Colorless syrup. $[\alpha]_D^{17}$ −31.2° (*c*=1.0, acetone). HR positive FAB-MS *m/z*: 431.2402 $[M+Na]^+$ (Calcd for $C_{23}H_{36}NaO_6$: 431.2410). Positive FAB-MS *m/z* (rel. int.): 431 (100) $[M+Na]^+$, 371 (22) $[M+Na-CH_3COOH]^+$, 348 (20) $[M-CH_3COOH]^+$. EI-MS *m/z* (rel. int.): 348 (100) $[M-CH_3COOH]^+$, 224 (18), 211 (34). ^{1}H- and ^{13}C-NMR: see Tables 2 and 3.

(*rel* 5*S*,6*R*,8*R*,9*R*,10*S*,13*S*)-6-Acetoxy-9,13-epoxy-15-methoxy-labdan-16,15-olide (6) Colorless syrup. $[\alpha]_D^{17}$ −65.4° (*c*=1.1, acetone). HR positive FAB-MS *m/z*: 431.2487 $[M+Na]^+$ (Calcd for $C_{23}H_{36}NaO_6$: 431.2410). Positive FAB-MS *m/z* (rel. int.): 431 (100) $[M+Na]^+$, 371 (49) $[M+Na-CH_3COOH]^+$, 348 (30) $[M-CH_3COOH]^+$. EI-MS *m/z* (rel. int.): 348 (100) $[M-CH_3COOH]^+$, 224 (14), 211 (49). ^{1}H- and ^{13}C-NMR: see Tables 2 and 3.

(*rel* 5*S*,6*R*,8*R*,9*R*,10*S*,13*R*)-6-Acetoxy-9,13-epoxy-15-methoxy-labdan-16,15-olide (7) Colorless syrup. $[\alpha]_D^{17}$ +37.1° (*c*=1.8, acetone). HR positive FAB-MS *m/z*: 431.2469 $[M+Na]^+$ (Calcd for $C_{23}H_{36}NaO_6$: 431.2410). Positive FAB-MS *m/z* (rel. int.): 431 (100) $[M+Na]^+$, 371 (28) $[M+Na-CH_3COOH]^+$, 348 (20) $[M-CH_3COOH]^+$. EI-MS *m/z* (rel. int.): 348 (100) $[M-CH_3COOH]^+$, 224 (13), 211 (39). ^{1}H- and ^{13}C-NMR spectral data: see Tables 2 and 3.

(*rel* 5*S*,8*R*,9*R*,10*S*,13*S*,15*S*,16*R*)-9,13;15,16-Diepoxy-15,16-dimethoxylabdane (8) Colorless syrup. $[\alpha]_D^{17}$ +24.0° (*c*=1.2, acetone). HR positive FAB-MS *m/z*: 389.2704 $[M+Na]^+$ (Calcd for $C_{22}H_{38}NaO_4$: 389.2668). Positive FAB-MS *m/z* (rel. int.): 389 (100) $[M+Na]^+$, 366 (9) $[M]^+$. EI-MS *m/z* (rel. int.): 367 (39) $[M+H]^+$, 306 (45) $[M-CH_3COOH]^+$, 248 (36), 227 (74), 191 (71), 167 (99), 69 (100). ^{1}H- and ^{13}C-NMR: see Tables 2 and 3.

(*rel* 5*S*,8*R*,9*R*,10*S*,13*S*,15*R*,16*S*)-9,13;15,16-Diepoxy-15,16-dimethoxylabdane (9) Colorless syrup. $[\alpha]_D^{16}$ −11.3° (*c*=3.3, acetone). HR positive FAB-MS *m/z*: 389.2571 $[M+Na]^+$ (Calcd for $C_{22}H_{38}NaO_4$: 389.2668). Positive FAB-MS *m/z* (rel. int.): 389 (100) $[M+Na]^+$, 366 (89) $[M]^+$. EI-MS *m/z* (rel. int.): 366 (100) $[M]^+$, 306 (96) $[M-CH_3COOH]^+$, 248 (40), 227 (35), 191 (50), 167 (46), 69 (65). ^{1}H- and ^{13}C-NMR: see Tables 2 and 3.

(*rel* 5*S*,8*R*,9*R*,10*S*,13*S*,15*R*,16*R*)-9,13;15,16-Diepoxy-15,16-dimethoxylabdane (10) Colorless needles (hexane–EtOAc). mp 104—105 °C. $[\alpha]_D^{17}$ −56.5° (*c*=2.4, acetone). HR positive FAB-MS *m/z*: 389.2657 $[M+Na]^+$ (Calcd for $C_{22}H_{38}NaO_4$: 389.2668). Positive FAB-MS *m/z* (rel. int.): 389 (100) $[M+Na]^+$, 366 (27) $[M]^+$. EI-MS *m/z* (rel. int.): 366 (40) $[M]^+$, 306 (60) $[M-CH_3COOH]^+$, 248 (32), 227 (36), 191 (37), 167 (50), 69 (100). ^{1}H- and ^{13}C-NMR: see Tables 2 and 3.

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