New Dimeric Monoterpenes and Dimeric Diterpenes from the Heartwood of *Chamaecyparis obtusa* var. *formosana*

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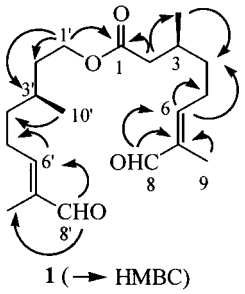
Two dimeric monoterpenes obtusal A and B, and two dimeric diterpenes obtusanol A and B, along with (−)-(*S*)-citronellol, (−)-(*S*)-citronellic acid, (+)-borneol, (+)-sugiol, and (−)-6,12-dihydroxyabieta-5,8,11,13-tetraen-7-one, have been isolated from the heartwood of *Chamaecyparis obtusa* var. *formosana* and were characterized by spectroscopic means, including 2D-NMR techniques and chemical methods. Synthesis of (−)-obtusal A and (+)-obtusal B were carried out.

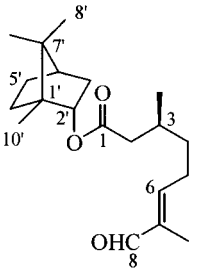
1. Introduction. – Among seven species, only two species of *Chamaecyparis* (Cupressaceae) are indigenous to Taiwan. *C. formosensis* and *C. obtusa* var. *formosana* (Taiwan hinoki) are important building materials and found in the central mountains of Taiwan at 1300 – 2800 m above sea level. The *C. obtusa* var. *formosana* possesses a high resistance against termites and can live over 1000 years. Its timber is yellow-red with a distinguished purple-pink streak together with a huge body. Based on the above features, the value of *C. obtusa* var. *formosana* is higher than *C. formosensis*. In previous papers on chemical studies of the heartwood of *C. obtusa* var. *formosana*, we reported the structural elucidation of novel diterpenes and lignans [1 – 4]. Further detailed re-investigation of the same extract from the heartwood of this plant yielded two new dimeric monoterpenes, obtusal A (**1**) and B (**2**), and two new dimeric diterpenes, obtusanol A (**3**) and B (**4**), together with (−)-citronellol (**5**) [5], (−)-citronellic acid (**6**) [6], (+)-borneol (**7**) [7], (+)-sugiol (**8**) [8], and (−)-6,12-dihydroxyabieta-5,8,11,13-tetraen-7-one (**9**) [8]. The structures of these new dimeric compounds were elucidated on the basis of the spectral evidence and chemical methods. Optically pure (−)-obtusal A (**1**) and (+)-obtusal B (**2**) were synthesized from (−)-citronellol (**5**), (−)-citronellic acid (**6**), and (+)-borneol (**7**).

2. Results and Discussion. – Compound **1**, called obtusal A, has been isolated as a liquid. HR-EI-MS Experiments revealed **1** to have the formula $C_{20}H_{32}O_4$. The IR spectrum indicated the presence of ester (1734, 1248, and 1073 cm^{-1}), conjugated aldehyde (2716 and 1690 cm^{-1}), and olefinic (1674 cm^{-1}) groups. The UV absorption band at λ_{Max}^{MeOH} 229 nm confirmed the presence of the conjugated system. By means of ^{1}H- and ^{13}C-NMR (*Table 1*) analysis and 2D techniques (including HMQC, HMBC, COSY, and NOESY methods), the structure of obtusal A (**1**) was judged to be a dimeric monoterpene with an ester linkage and not as a diterpene.

The alcohol moiety exhibited two Me signals at δ 0.94 (*d*, $J = 6.7$ Hz) and 1.72 (*s*, attached on C=C bond), on olefinic H-atom at δ 6.44 (*t*, $J = 7.3$ Hz), and an aldehyde



1 (→ HMBC)



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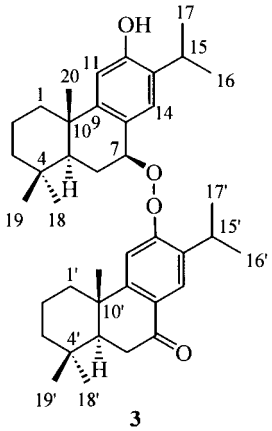

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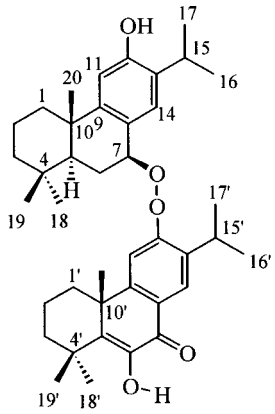

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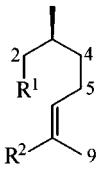
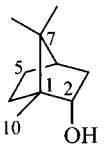


5 R^1=CH_2OH, R^2=Me
6 R^1=CO_2H, R^2=Me
10 R^1= CH_2OH, R^2=CHO
11 R^1=CO_2H, R^2=CHO
12 R^1=COCl, R^2=CHO



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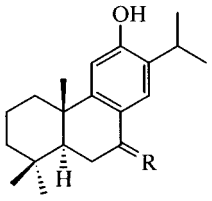
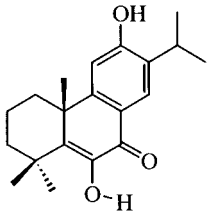


8 R=O
13 R=β-OH, α-H



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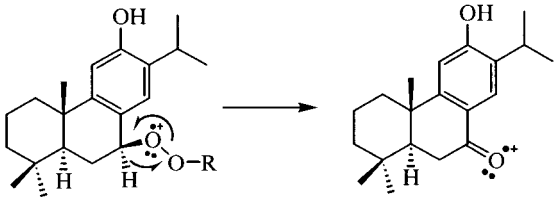

3 *m/z* 600 (3%) **8** *m/z* 300 (100%)

Table 1. *^{1}H-NMR Data* ($CDCl_3$, 400 MHz) *of Compounds* **1**–**4**. δ in ppm, J in Hz.

	1	**2**		**3**	**4**
H_a–C(2)	2.15 (*dd*, *J* = 14.8, 7.7)	2.18 (*dd*, *J* = 14.7, 7.5)	H_β–C(1)	2.22 (br. *d*, *J* = 13.6)	2.24 (br. *d*, *J* = 13.4)
H_b–C(2)	2.29 (*dd*, *J* = 14.8, 6.3)	2.30 (*dd*, *J* = 14.7, 6.5)	H_α–C(7)	5.38 (*dd*, *J* = 9.1, 2.6)	5.41 (*dd*, *J* = 9.0, 2.5)
H–C(3)	1.98 (*m*)	2.01 (*m*)	H–C(11)	6.68 (*s*)	6.68 (*s*)
CH_2(4)	1.57 (*m*), 1.61 (*m*)	1.38 (*m*), 1.53 (*m*)	H–C(14)	7.03 (*s*)	7.18 (*s*)
CH_2(5)	2.36 (*m*)	2.36 (*m*)	H–C(15)	3.01 (*sept.*, *J* = 6.9)	3.00 (*sept.*, *J* = 6.9)
H–C(6)	6.44 (*t*, *J* = 7.3)	6.44 (*tq*, *J* = 7.3, 1.1)	Me(16)	1.10 (*d*, *J* = 6.9)	1.11 (*d*, *J* = 6.9)
H–C(8)	9.37 (*s*)	9.37 (*s*)	Me(17)	1.12 (*d*, *J* = 6.9)	1.16 (*d*, *J* = 6.9)
Me(9)	1.72 (*s*)	1.72 (*d*, *J* = 1.1)	Me(18)	0.96 (*s*)	1.02 (*s*)
Me(10)	0.96 (*d*, *J* = 6.7)	0.98 (*d*, *J* = 6.6)	Me(19)	0.93 (*s*)	0.98 (*s*)
CH_2(1′)	4.10 (*m*)		Me(20)	1.21 (*s*)	1.27 (*s*)
H_a–C(2′)	1.38 (*m*)	4.87 (*ddd*, *J* = 10.0, 3.4, 2.2)	HO–C(12)	4.58 (br. *s*)	4.60 (br. *s*)
H_b–C(2′)	1.53 (*m*)		H_β–C(1′)	2.32 (br. *d*, *J* = 13.8)	2.40 (br. *d*, *J* = 13.6)
H_a–C(3′)	1.57 (*m*)	0.92 (*dd*, *J* = 13.7, 10.0)	H–C(5′)	1.92 (*dd*, *J* = 13.2, 4.3)	
H_b–C(3′)		2.34 (*m*)	H_a–C(6′)	2.58 (*dd*, *J* = 18.1, 4.3)	
H_a–C(4′)	1.51 (*m*)	1.65 (br. *t*, *J* = 4.5)	H_b–C(6′)	2.67 (*dd*, *J* = 18.1, 4.3)	
H_b–C(4′)	1.67 (*m*)		H–C(11′)	6.76 (*s*)	6.77 (*s*)
H_a–C(5′)	2.36 (*m*)	1.20 (*m*)	H–C(14′)	7.93 (*s*)	8.03 (*s*)
H_b–C(5′)	2.36 (*m*)	1.72 (*m*)	H–C(15′)	3.29 (*sept.*, *J* = 6.8)	3.33 (*sept.*, *J* = 6.9)
H_a–C(6′)	6.44 (*t*, *J* = 7.3)	1.29 (*m*)	Me(16′)	1.19 (*d*, *J* = 6.8)	1.20 (*d*, *J* = 6.9)
H_b–C(6′)		1.89 (*m*)	Me(17′)	1.21 (*d*, *J* = 6.8)	1.25 (*d*, *J* = 6.9)
H–C(8′)	9.37 (*s*)		Me(18′)	0.98 (*s*)	1.46 (*s*)
Me(8′)		0.88 (*s*)	Me(19′)	1.02 (*s*)	1.42 (*s*)
Me(9′)	1.72 (*s*)	0.84 (*s*)	Me(20′)	1.37 (*s*)	1.48 (*s*)
Me(10′)	0.94 (*d*, *J* = 6.7)	0.80 (*s*)	HO–C(6′)		7.15 (*s*)

H-atom at δ 9.37 (*s*). The olefinic and aldehyde H-atom demonstrated a NOESY correlation, which establishes the (*E*)-form of the C=C bond. A *m* CH_2 signal at δ 4.10 (CH_2(1′)) was considered to be attached on the O-terminal of the ester function. The C(3′) is a stereogenic center causing the two H-atoms at C(1′) to be nonequivalent. The COSY correlations (H–C(2′) (δ 1.53, 1.38)/H–C(3′) (δ 1.57); H–C(3′)/H–C(10′), H–C(4′) (δ 1.51, 1.67); H–C(5′) (δ 2.36)/H–C(4′–6′)) confirmed the proton sequence. ^{1}H- and ^{13}C-NMR data of this moiety are similar to those of (*E*)-2,6-dimethyl-8-hydroxyoct-2-enal (**10**) [5] except for the data of C(1′) and H–C(1′) (δ(H) 4.10 (*m*), in **1** and 3.72 (*m*) in **10**; δ(C) 62.5 in **1** and 60.8 in **10**). The acid moiety also showed signals of secondary Me (δ 0.96 (*d*, *J* = 6.7 Hz)), vinyl Me (δ 1.72 (*s*)], aldehyde (δ 9.37 (*s*)), and olefinic H-atoms (δ 6.44 (*t*, *J* = 7.3 Hz)). The signals of the two CH_2 H-atoms vicinal to the C=O group of ester were observed at δ 2.29 (*dd*, *J* = 14.8, 6.3 Hz, 1 H) and 2.15 (*dd*, *J* = 14.8, 7.7 Hz, 1 H). COSY Correlations δ 2.29/δ 1.98; δ 1.98/δ 1.57, 1.61; δ 1.61/δ 2.36, and δ 2.36/δ 6.44 allowed identification of contiguous protons. The (*E*)-configuration of the C=C bond was revealed from the NOESY correlation between δ 6.44 and 9.37. The above evidence established the structure of obtusal A (**1**) as an ester condensed from **10** and **11**. HMBC (Structure **1**) and ^{13}C-NMR (*Table 2*) also confirmed the structure. The specific rotation of **1** is $[\alpha]_D^{25} = -8.2$. The biosynthetic pathway was proposed from the condensation of (−)-(*S*)-**10** and (−)-(*S*)-**11**, which were derived from (−)-(*S*)-**5** and (−)-(*S*)-**6**, respectively. The total synthesis of **1** was carried out as follows. The oxidation of (−)-citronellol (**5**) with SeO_2 in EtOH under reflux yielded (−)-**10** [9]. Compound (−)-**11** was obtained from (−)-citronellic acid (**6**) under the same

Table 2. *^{13}C-NMR Data* ($CDCl_3$, 100 MHz) *of Compounds* **1**–**4**. δ in ppm.

	1	**2**		**3**	**4**		**3**	**4**
C(1)	172.8	173.1	C(1)	41.1	41.1	C(1′)	38.2	33.7
C(2)	41.6	41.9	C(2)	18.7	18.8	C(2′)	18.8	17.6
C(3)	30.0	30.2	C(3)	42.5	42.4	C(3′)	41.3	37.7
C(4)	35.3	35.0	C(4)	33.3	37.7	C(4′)	34.8	35.9
C(5)	26.4	26.5	C(5)	47.4	47.3	C(5′)	49.7	141.1
C(6)	154.4	154.1	C(6)	34.3	34.2	C(6′)	36.0	143.8
C(7)	139.4	139.5	C(7)	102.5	102.4	C(7′)	198.8	179.8
C(8)	195.2	195.2	C(8)	142.7	142.6	C(8′)	125.2	120.9
C(9)	9.2	9.2	C(9)	146.2	146.1	C(9′)	156.0	154.2
C(10)	19.5	19.5	C(10)	41.2	41.4	C(10′)	38.3	40.7
C(1′)	62.5	48.7	C(11)	114.0	114.1	C(11′)	108.4	109.8
C(2′)	35.0	79.9	C(12)	149.4	149.4	C(12′)	159.0	158.5
C(3′)	29.6	36.9	C(13)	133.0	133.1	C(13′)	136.3	137.2
C(4′)	35.3	44.9	C(14)	120.9	120.8	C(14′)	126.1	125.1
C(5′)	26.4	28.0	C(15)	26.8	26.9	C(15′)	27.5	27.4
C(6′)	154.0	27.1	C(16)	21.7	21.7	C(16′)	22.5	22.6
C(7′)	139.5	47.8	C(17)	21.8	21.8	C(17′)	22.5	22.6
C(8′)	195.2	18.8	C(18)	33.7	33.7	C(18′)	32.6	27.6
C(9′)	9.2	19.7	C(19)	22.6	22.5	C(19′)	21.4	28.0
C(10′)	19.2	13.5	C(20)	23.4	23.2	C(20′)	23.2	35.0

conditions. By means of *Mitsunobu* reaction [10], the condensed product from (−)-**10** and (−)-**11** could be identified as obtusal A (**1**) with a specific rotation $[\alpha]_D^{25} = -5.8$.

Compound **2**, obtusal B, has been isolated as an oil and has the molecular formula $C_{20}H_{32}O_3$ based on its exact mass and ^{13}C-NMR spectrum (*Table 2*). As compound **1**, obtusal B (**2**) contained ester and conjugated aldehyde groups attributed to the IR absorption bands at 2710, 1735, 1695, and 1630 cm^{-1}, and UV absorption band at λ_{Max}^{MeOH} 229 nm. By analysis of ^{1}H- and ^{13}C-NMR spectra, **2** was not identified as a diterpene but as a dimeric monoterpene linked by ester group as in **1**. The ^{1}H-NMR data (δ 0.98 (3 H, d, $J = 6.6$ Hz), 1.72 (3 H, *d*, $J = 1.1$ Hz), 2.18 (1 H, *dd*, $J = 14.7$, 7.5 Hz, H−C(2a)), 2.30 (1 H, *dd*, $J = 14.7$, 6.5 Hz, H−C(2b)), 6.44 (1 H, *tq*, $J = 7.3$, 1.1 Hz), 9.37 (1 H, s) are almost the same as in the acid moiety of compound **1**. The alcohol moiety exhibited three Me *singlets* at δ 0.80, 0.84, and 0.88, and the signal of CH H-atom attached to the ester at δ 4.87 (*ddd*, $J = 10.0$, 3.4, 2.2 Hz). Comparison of ^{1}H-NMR data of alcohol moiety of **2** with those of (+)-borneol (**7**) showed only a difference for the signal of H−C(2′) in **2** located at lower field than in **7**. The coupling constant of H−C(2′) of **2** with 10 Hz revealed the *endo*-orientation of the 2′-ester group. Compound **2** exhibited a specific rotation $[\alpha]_D^{25} = +26.5$. Compound **2** was proposed to form by condensation of (+)-borneol (**7**) (1*R*,2*S*) and (−)-**11**. To confirm this proposal, the following reaction was carried out. Oxidation of (−)-citronellic acid (**6**) with SeO_2 yielded compound **11**. Acid chloride **12**, prepared from **11** by treatment with $SOCl_2$, reacted with (+)-borneol (**7**) in CH_2Cl_2 to give a product that was identified as **2** by comparison of its physical and spectroscopic data. The specific rotation of the synthesized compound **2** ($[\alpha]_D^{25} = +27.3$) was in good agreement with that of the natural product.

Obtusanol A (**3**) had the molecular formula $C_{40}H_{56}O_4$ on the basis of exact mass (HR-EI-MS) at *m*/*z* 600.4178. It showed OH (3373 cm^{-1}), aromatic (3051, 1598,

1490 cm^{-1}), and conjugated C=O (1654 cm^{-1}) absorptions in its IR spectrum. The UV spectrum indicated a PhCO functionality (λ_{Max}^{MeOH} 224 and 278 nm). The ^{1}H-NMR spectrum showed two sets of dehydroabietane signals as follows: one set of signals are δ 1.10, 1.12 (each 3 H, *d*, $J = 6.9$ Hz, Me(16), Me(17)), 2.22 (1 H, br. *d*, $J = 13.6$ Hz, H_β–C(1), characteristic signal for dehydroabietane) [10][11]), 3.01 (1 H, *sept.*, $J =$ 6.9 Hz, H–C(15)), 4.58 (1 H, br. *s*, exchangeable, HO–C(12)), 5.38 (1 H, *dd*, $J = 9.1$, 2.6 Hz, H_α–C(7)), 6.68, 7.03 (each 1 H, *s*, H–C(11, 14)); the second set of signals are δ 0.98, 1.02, 1.37 (each 3 H, *s*, Me(18′), Me(19′), Me(20′)), 1.19, 1.21 (each 3 H, *d*, $J =$ 6.8 Hz, Me(16′), Me(17′)), 2.32 (1 H, br. *d*, $J = 13.8$ Hz, H_β–C(1′)), 3.29 (1 H, *sept.*, $J =$ 6.8 Hz, H–C(15′)), 6.76, 7.93 (each 1 H, *s*, H–C(11′), H–C(14′)). The signal at δ 5.38 was assigned to H–C(7) due to HMBC correlations to C(6), C(8), and C(14). The second set of signals of **3** are like those of sugiol (**8**), the signal of H–C(14′) of **3** also appears at lower field due to deshielding from the C(7′)=O group. On account of the O-atom number from formula $C_{40}H_{56}O_4$, the remaining two O-atoms were present as a peroxide, which links C(7) with C(12′) to form compound **3**. The signals of H–C(7) and C(7) of **3** at lower field in comparison with **13** are in agreement with the peroxide influence of **3**. The base peak at *m*/*z* 300 from the mass-fragmentation pattern of **3** is consistent with a peroxide structure. Catalytic hydrogenolysis of **3** with 10% Pd/C in MeOH yielded two products, (+)-sugiol (**8**) and (+)-7β-hydroxyferrugiol (**13**)[1]).

The IR spectrum of obtusanol B (**4**) indicated the presence of OH (3382 cm^{-1}), aromatic (3062, 1598, 1493 cm^{-1}), and conjugated C=O (1646 cm^{-1}) groups. The molecular formula $C_{40}H_{54}O_5$ was established by HR-EI-MS. By the analysis of ^{1}H- and ^{13}C-NMR data together with two dimensional NMR technique, compound **4** was established as a dimer of two dehydroabietane diterpene with peroxide linkage and not as a tetraterpene. A semimoiety is a 7-oxygenated ferrugiol, which was revealed from its ^{1}H- and ^{13}C-NMR data (*Tables 1* and *2*). The 7β-hydroxyferrugiol moiety showed three Me *singlets*, and signals of an exchangeable phenolic H-atom, and i-Pr group attached to phenyl, two *p*-phenyl H-atom, a typical H_β–C(1) proton of dehydroabietane, and a CH H-atom (δ(H) 5.41, *dd*, $J = 9.0$, 2.5 Hz) located at C(7) (δ(C) 102.4), which is connected to a peroxide group. The ^{1}H-NMR data are similar to those of compound **3**. The other semimoiety also showed three Me *singlets* and signals of a typical H_β–C(1) of dehydroabietane, an i-Pr group attached to a phenyl group, two *p*-phenyl H-atoms (one at δ 8.03, which is deshielded from C(7) carbonyl), one exchangeable H-atom (δ 7.15, HO–C(6′) with a strong H-bond to C(7′)=O group). This semimoiety is revealed as 6,12-dihydroxyabieta-5,8,11,13-tetraen-7-one by comparison of its ^{1}H- and ^{13}C-NMR data with those of **9**. Therefore, in obtusanol (**4**) C(7) of ferrugiol and C(12′) of 6-hydroxyabieta-5,8,11,13-tetraen-7-one were connected with peroxide. The base peak of the mass spectrum of **4** is also found at *m*/*z* 300, which confirmed the assigned structure. The hydrogenolysis of **4** under the above-mentioned conditions yielded (–)-**9** and (–)-**13**. The occurrence of hydroperoxide and endoperoxide compounds in nature is very high, but disubstituted peroxides occur very seldomly.

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[1]) Compound **13** is a new compound, which was prepared from (+)-sugiol by reduction with $NaBH_4$ in MeOH solution (see *Exper. Part*).

Experimental Part

General. Extracts were chromatographed on silica gel (*Merck* 70–230 mesh, 230–400 mesh, ASTM) and purified with a semi-prep. normal-phase HPLC column (250 × 10 nm, 7 μm, *LiChrosorb Si 60*) taken on *LDC Analytical-III*. M.p.: *Yanagimoto* micro-melting-point apparatus; uncorrected. Specific rotations: *Jasco DIP-180* digital polarimeter. IR Spectra: *Perkin-Elmer 983 G* spectrophotometer. ^{1}H- and ^{13}C-NMR spectra: *Bruker DMX-400* spectrophotometer. EI-MS: *JEOL JMS-HX 300* mass spectrometer.

Plant Material. The heartwood of *C. obtusa* var. *formosana* was collected from Taichung, Taiwan, in 1996. Mr. *Muh-Tsuen*, formerly of the Department of Botany, National Taiwan University, identified the plant. A voucher specimen has been deposited at the Herbarium of Department of Botany, National Taiwan University, Taipei, Taiwan.

Extraction and Isolation. The dried heartwood of *C. obtusa* var. *formosana* (11 kg) was extracted with Me_2CO (120 l) at r.t. (7 d × 2). To the evaporated Me_2CO extract, H_2O was added to bring the total volume to 1 l. This phase was extracted with AcOEt (1 l × 3). The combined AcOEt layers afforded, after evaporation, a black syrup (680 g), which was purified by silica-gel chromatography and HPLC (normal phase on *Lichrosorb Si 60*), repeatedly, with hexane/AcOEt. Compounds **1** (13 mg), **2** (15 mg), **5** (25 mg), **8** (13 mg), **9** (15 mg), **3** (10 mg), **4** (9 mg), **7** (51 mg), and **6** (25 mg) were eluted with 10, 10, 10, 10, 10, 25, 25, 25, and 25% AcOEt in hexane, respectively.

*(3*S*,6*E*)-8-Formyl-3,7-dimethyloct-6-en-1-yl (3*S*,6*E*)-8-Formyl-3,7-dimethyloct-6-en-1-oate* (= *Obtusal A*; **1**). Liquid. $[\alpha]_D^{25} = -8.2$ ($c = 0.48$, $CHCl_3$). UV (MeOH): 229 (4.48). IR (film): 2716, 1734, 1690, 1674, 1248, 1073. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. EI-MS: 336 (7, M^+), 165 (68), 152 (40), 139 (41), 121 (81), 109 (68), 95 (100), 81 (76), 69 (52). HR-EI-MS: 336.2303 ($C_{20}H_{34}O_4^+$; calc. 336.2300).

*(1*R*,2*S*)-1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl (3*S*,6*E*)-8-Formyl-3,7-dimethyloct-6-en-1-oate* (= *Obtusal B*; **2**). Liquid. $[\alpha]_D^{25} = +26.5$ ($c = 0.79$, $CHCl_3$). UV (MeOH): 229 (3.98). IR (film): 2710, 1735, 1695, 1630, 1195, 1158, 1115, 1025. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. EI-MS: 320 (7, M^+), 167 (31), 136 (91), 121 (76), 109 (35), 93 (87), 81 (100), 71 (34). HR-EI-MS: 320.2356 ($C_{20}H_{32}O_3^+$; calc. 320.2351).

12-Hydroyabieta-8,11,13-trien-7β-yl 7-Oxoabieta-8,11,13-trien-12-yl Peroxide (= *Obtusanol A*; **3**). M.p. 158–159°. $[\alpha]_D^{25} = -12.5$ ($c = 0.37$, $CHCl_3$). UV (MeOH): 224 (4.06), 278 (3.89). IR (film): 3373, 3051, 1654, 1598, 1490, 1303, 1263, 1175. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. EI-MS: 600 (3, M^+), 318 (78), 300 (100), 217 (27). HR-EI-MS: 600.4187 ($C_{40}H_{56}O_4^+$; calc. 600.4179).

12-Hydroxyabieta-8,11,13-trien-7β-yl 6-Hydroxy-7-oxoabieta-5,8,11,13-tetraen-12-yl Peroxide (= *Obtusanol B*; **4**). Amorphous solid. $[\alpha]_D^{25} = -26.4$ ($c = 0.55$, $CHCl_3$). UV (MeOH): 222 (4.01), 246 (3.73), 278 (3.74), 333 (3.51). IR (film): 3382, 3062, 1646, 1598, 1493, 1260, 1248, 1176. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. EI-MS: 614 (9, M^+), 313 (20), 300 (100), 204 (27), 188 (23). HR-EI-MS: 614.3973 ($C_{40}H_{54}O_5^+$; calc. 614.3971).

Oxidation of (−)-Citronellol (**5**) *with SeO_2. (−)-Citronellol* (**5**) (455.3 mg) and SeO_2 (0.95 g) in 20 ml of 95% EtOH was refluxed for 20 h. The mixture was filtered through *Celite*, and the filtrate was purified by chromatography on silica gel to yield **10** (421.2 mg). Liquid. $[\alpha]_D^{25} = -8.2$ ($c = 0.48$, $CHCl_3$). UV (MeOH): 229 (4.48). IR (film): 2716, 1734, 1690, 1248, 1073. ^{1}H- and ^{13}C-NMR: see [9].

Oxidation of (−)-Citronellic acid (**6**) *with SeO_2*. The oxidation of (−)-*citronellic* acid (**6**) (485.3 mg) with SeO_2 (0.93 g) was performed in the same way as described above. The product **11** (446.4 mg) was isolated after purification by chromatography on silica gel. Liquid. $[\alpha]_D^{25} = -4.6$ ($c = 0.48$, $CHCl_3$). UV (MeOH): 228 (4.0). IR (film): 3200–2500, 2717, 1711, 1686, 1653. ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.00 (*d*, $J = 6.6$, 3 H); 1.73 (*s*, 3 H); 1.44, 1.58 (*m*, each 1 H, CH_2(4)), 2.21 (*dd*, $J = 15.1$, 7.5, H_a–C(2)); 2.38 (*dd*, $J = 15.1$, 6.6, H_b–C(2)); 2.38 (*m*, CH_2(5)); 6.46 (*t*, $J = 7.2$, H–C(6)); 9.37 (*s*, H–C(8)). ^{13}C-NMR ($CDCl_3$, 100 MHz): 9.1 (C(9)); 19.4 (C(10)); 26.4 (C(4)); 29.8 (C(3)); 34.9 (C(5)); 41.2 (C(2)); 139.5 (C(7)); 154.1 (C(6)); 178.7 (C(1)); 195.3 (C(8)). EI-MS: 184 (5, M^+), 166 (24), 122 (20), 109 (26), 97 (100), 85 (25), 69 (32). HR-EI-MS: 184.1091 ($C_{10}H_{16}O_3^+$; calc. 184.1099).

Synthesis of **1** *from* **10** *and* **11** *by* Mitsunobu *Reaction*. To a THF (20 ml) soln. of **10** (138.3 mg, 0.89 mmol), **11** (151.5 mg, 0.89 mmol), and Ph_3P (280.0 mg, 1.068 mmol) was added dropwise diethyl azodicarboxylate (185.8 mg, 1.068 mmol) at −20°, and the mixture was allowed to warm slowly to r.t. After 8 h, the mixture was concentrated at reduced pressure, and the products were purified by silica-gel chromatography (10% AcOEt in hexane) to provide **1** (260.3 mg, 87%). $[\alpha]_D^{25} = -5.8$ ($c = 0.62$, $CHCl_3$).

Synthesis of **2** *from (+)-Borneol* (**7**) *and (−)-***11**. To a CH_2Cl_2 (10 ml) soln. of (−)-**11** (80.0 mg, 0.44 mmol) was added $SOCl_2$ (104.7 mg, 0.88 mmol). After 1 h, the solvent was removed under reduced pressure to obtain the acid chloride. To the acid chloride, a soln. of *(+)-borneol* (**7**) (68.0 mg, 0.44 mmol) and Et_3N (50.2 mg,

0.53 mmol) in CH_2Cl_2 (5 ml) were added. The mixture was stirred for 1 h and then poured into 10 ml of H_2O. The aq. soln. was extracted with AcOEt to yield, after evaporation of the solvent, the crude product, which was purified by silica-gel chromatography (10% AcOEt in hexane) to provide **2** (107.1 mg, 76%). $[\alpha]_D^{20} = -27.3$ ($c = 0.45$, $CHCl_3$).

Reduction of Sugiol (**8**) *with NaBH4 in MeOH*. An excess of $NaBH_4$ (85.3 mg) was added in small portions to a soln. of **8** (8.4 mg) in MeOH (1 ml), and the mixture was stirred for 6 h. After removing the solvent under reduced pressure, 10 ml of H_2O was added, and the aq. soln. was extracted with AcOEt to yield the crude product. After purification by silica-gel chromatography, **13** (8.2 mg) was obtained.

Data of **13**. M.p. 181–182°. $[\alpha]_D^{25} = +28.3$ ($c = 0.21$, $CHCl_3$). UV (MeOH): 232 (4.03), 285 (2.25). IR (KBr): 3264, 2962, 2925, 1615, 1583, 1512, 1424, 1239, 1029. ^{1}H-NMR (400 MHz, CD_3OD): 0.95 (*s*, Me(19)); 0.96 (*s*, Me(18)); 1.19 (*d*, $J = 6.9$, Me(16)); 1.20 (*d*, $J = 6.9$, Me(17)); 1.25 (*s*, Me(20)); 1.33 (*d*, $J = 12.9$, H–C(5)); 2.14 (*dd*, $J = 13.4$, 7.1, H_α–C(6)); 2.21 (br. *d*, $J = 12.9$, 2 H–C(1)); 3.20 (*sept*., $J = 6.9$, H–C(15)); 4.66 (*dd*, $J = 10.2$, 7.1, H–C(7)); 6.60 (*s*, H–C(11)); 7.26 (*s*, H–C(14)). ^{13}C-NMR (100 MHz, CD_3OD): 18.3 (C(2)); 20.1 (C(19)); 21.1 (C(16)); 21.1 (C(17)); 23.6 (C(20)); 25.9 (C(15)); 29.0 (C(6)); 31.7 (C(18)); 32.1 (C(4)); 37.3 (C(10); 38.2 (C(1)); 40.6 (C(3)); 48.8 (C(5)); 69.7 (C(7)); 109.1 (C(11)); 124.3 (C(14)); 128.2 (C(13)); 131.6 (C(9)); 147.5 (C(8)); 152.7 (C(12)). EI-MS: 302 (4, M^+), 284 (86), 269 (26), 213 (54), 202 (100), 185 (26), 159 (28), 128 (8), 83 (11). HR-EI-MS: 320.4514 ($C_{20}H_{30}O_2^+$; calc. 320.4510).

Catalytic Hydrogenolysis of **3** *and* **4** *with 10% Pd/C*. Compound **3** (10.2 mg) was hydrogenated in MeOH (5 ml) with 10% Pd–C (10.5 mg) as catalyst. After 5 h, **8** (4.1 mg) and **13** (4.1 mg) were obtained. By means of the same conditions, **9** (4.3 mg) and **13** (4.3 mg) were obtained from compound **4** (10.3 mg).

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REFERENCES

[1] Y. H. Kuo, C. H. Chen, S. L. Huang, *Chem. Pharm. Bull.* **1998**, *46*, 181.
[2] Y. H. Kuo, C. H. Chen, S. L. Huang, *J. Nat. Prod*. **1998**, *61*, 829.
[3] Y. H. Kuo, C. H. Chen, *Tetrahedron Lett*. **2001**, *42*, 2985.
[4] Y. H. Kuo, C. H. Chen, Y. M. Chiang, *Tetrahedron Lett*. **2001**, *42*, 6731.
[5] M. Hirama, T. Noda, S. Ito, *J. Org. Chem*. **1985**, *50*, 127.
[6] J. D. White, J. C. Amedio, S. Gut, S. Ohira, L. R. Jayasinghe, *J. Org. Chem*. **1992**, *57*, 2270.
[7] F. Bohlmann, R. Zeisberg, *Org. Magn. Reson.* **1975**, *7*, 426.
[8] W. C. Su, J. M. Fang, Y. S. Cheng, *Phytochemistry* **1994**, *35*, 1279.
[9] T. Miyase, C. Akahori, H. Kohsaka, A. Ueno, *Chem. Pharm. Bull*. **1991**, *39*, 2944.
[10] O. Mitsunobu, *Synthesis* **1981**, 1.
[11] Y. H. Kuo, M. H. Yeh, *Phytochemistry* **1998**, *49*, 2453.
[12] Y. H. Kuo, M. T. Yu, *J. Nat. Prod*. **1997**, *60*, 648.

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