New Sesquiterpenes from *Capsicum annuum*

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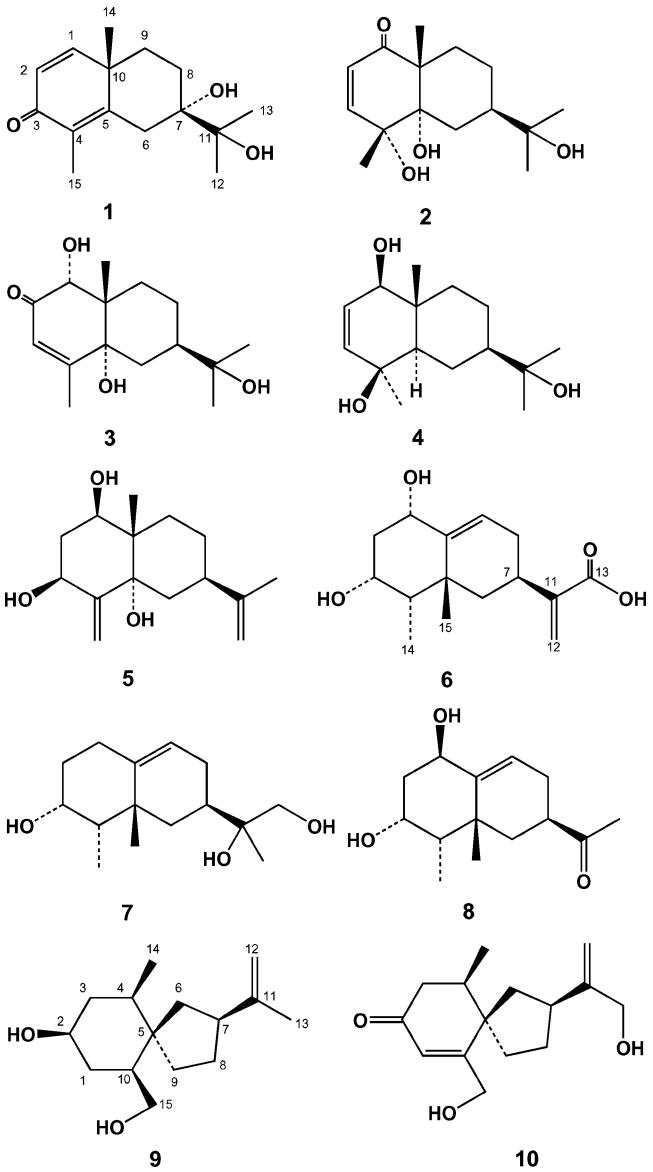
The ethyl acetate soluble fraction of a MeOH extract of the dried stems and roots of *Capsicum annum* gave 10 new sesquiterpenoids (**1**−**10**) and nine known compounds. The structures of the new compounds were elucidated on the basis of spectroscopic evidence. The isolated new compounds were evaluated for their cytotoxic activities.

Red pepper, *Capsicum annuum* (Solanaceae), is used as a spice all over the world. Red pepper is studied actively because its pungent principal component, capsaicin, has a dietary effect, analgesic activity, and antioxidant activity.[1] More than 16 other capsaicinoids have been found as minor components.[2] A dimer of capsaicin and dihydrocapsaicin has antioxidant activity the same as capsaicin, but is less pungent than capsaicin.[3] Numerous studies have been done on the red pepper fruit, but there are few studies on stems and roots.[4] So, as part of our study of the red pepper fruit, we initiated this study. We report herein the isolation and structure elucidation of 10 new compounds (**1**−**10**) from the stems and roots along with nine known compounds. None of the isolated compounds were cytotoxic.

Repeated column chromatography of the ethyl acetate soluble fraction from MeOH extracts of the stems and roots of *C. annuum* (*Himetougarashi* in Japanese) yielded 10 new sesquiterpenes, canusesnols A−J (**1**−**10**), and nine known compounds, capsidiol,[5] *N-cis*-feruloyltyramine,[6] *N-trans*-feruloyltyramine,[6] *N-p-cis*-coumaroyltyramine,[7] *N-p-trans*-coumaroyltyramine,[7] lariciresinol,[8] 13-hydroxycapsidiol,[9] lubiminol,[10] and drummondol.[11]

The IR spectrum of canusesnol A (**1**) indicated the presence of a hydroxyl group at 3419 cm^{-1} and a carbonyl group at 1657 cm^{-1}. The ^1H NMR spectrum of **1** showed the presence of an isopropyl group [δ 1.30 (6H, s)], two methyl groups [δ 1.91 (3H, s) and 1.25 (3H, s)], and two olefinic protons [δ 6.97 and 6.21 (each 1H, d, J = 9.7 Hz)]. The ^{13}C NMR spectrum (Table 1) of **1** showed 15 carbon signals due to one carbonyl carbon, four olefinic carbons, four methyl carbons, two quaternary carbons attached to an oxygen function, three methylenes, and one quaternary carbon. These observations agreed with the molecular formula of $C_{15}H_{22}O_3$, which was supported by HREIMS. The HMBC spectrum of **1** showed the correlations of H-1 to C-3 and C-5, H-6 to C-8 and C-11, H-13 to C-7, C-11, and C-12, H-14 to C-1, C-5, C-9, and C-10, and H-15 to C-3, C-4, and C-5. On the basis of these findings, compound **1** was assumed to be a eudesmane-type sesquiterpene. The α-, β-, and α′,β′-ketone could be placed at C-1 to C-5, and hydroxyl groups were placed at C-7 and C-11. The NOESY spectrum of **1** showed correlations of H-8β [(δ 2.09 (1H, ddd, J = 14.0, 14.0, 4.7 Hz)] to H_3-14 and H_2-12. This finding showed that the relative stereochemistries of hydroxyisopropyl and methyl groups at C-7 and C-14 are β. Thus, the structure of **1** was assigned as shown. Canusesnol B (**2**)



has a molecular formula of $C_{15}H_{24}O_4$ based on HRFABMS (*m/z* 267.1628 [M − H]$^-$). The ^{13}C NMR (Table 1) and ^1H NMR spectra of **2** showed the presence of an isopropyl group attached to an oxygen function, an α,β-unsaturated ketone (δ_C 206.8, 126.0, and 151.4), and two methyls [δ_H 1.22 and 1.44 (each 3H, s)]. The $^1H-^1H$ COSY spectrum of **2** showed the presence of partial structure $-CH_2CHCH_2-CH_2-$. The HMBC spectrum of **2** showed the correlations

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Table 1. ^{13}C NMR (CD_3OD) Data (δ) for Compounds **1**−**10**

	1	2	3	4	5	6	7	8	9	10
C-1	159.7	206.8	78.2	72.9	72.2	75.6	27.2	75.5	38.3	121.9
C-2	126.5	126.0	201.4	128.0	41.1	36.9	30.9	36.9	69.4	202.1
C-3	188.5	151.4	126.6	137.6	68.2	66.1	70.0	65.8	42.3	43.9
C-4	132.4	73.4	162.7	69.8	155.4	49.0	49.0	49.0	42.8	40.6
C-5	162.7	79.9	76.7	44.3	76.7	40.5	40.1	39.8	47.9	50.2
C-6	34.2	28.7	33.5	23.4	37.1	47.6	40.2	42.3	42.3	42.7
C-7	75.9	43.8	47.7	51.0	40.7	35.4	39.9	47.9	49.0	43.5
C-8	26.9	22.2	23.0	23.7	27.1	31.5	31.1	27.8	34.7	34.5
C-9	34.4	31.1	30.6	36.3	31.3	128.8	123.3	127.9	27.5	34.0
C-10	41.6	50.5	46.7	37.5	43.2	141.5	140.2	141.5	49.0	172.4
C-11	80.0	73.1	72.7	73.7	151.8	147.2	75.2	214.4	143.4	152.5
C-12	24.7	27.2	26.3	26.4	21.2	123.1	69.0	–	105.2	108.4
C-13	25.0	27.5	27.2	27.1	109.0	170.7	21.1	28.5	23.2	65.8
C-14	23.5	23.2	17.5	19.6	13.5	9.1	10.1	9.4	19.0	16.1
C-15	10.8	23.8	19.5	29.5	105.6	32.4	30.3	31.8	63.7	61.8

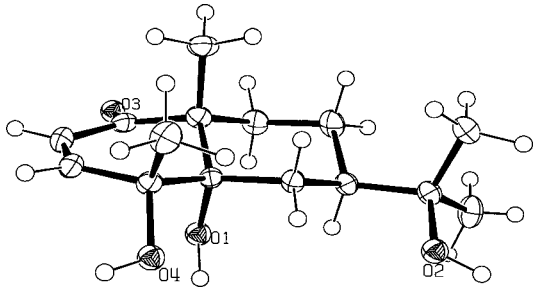

Figure 1. ORTEP drawing of compound **2**.

of H_3-14 to C-1 (δ 206.8) and C-10 (δ 50.5), H-2 to C-10, H_3-15 to C-4 (δ 73.4), and H_3-12 to C-7 (δ 43.8). These results showed the presence of hydroxyl groups on C-4, C-5, and C-11 and a ketone on C-1. The NOESY spectrum of **2** showed correlations of H-6β to H_3-12, H_3-14, and H_3-15. The structure of **2** was estimated to be as shown except for the configuration of the hydroxyl group on C-5. The configuration of this hydroxyl group was determined through X-ray crystallographic analysis, which confirmed that the configuration of the 5-hydroxyl was α.

Canusesnol C (**3**), $C_{15}H_{24}O_4$, has the same molecular formula as **2**. The ^{13}C NMR spectrum showed the presence of an α,β-unsaturated ketone (δ_C 126.6, 162.7, and 201.4). From comparison of the NMR data of **2** and **3**, compound **3** had the same partial structure as **2** from C-5 to C-14. The α,β-unsaturated ketone was placed at C-2 to C-4 because of a downfield shifted methyl on the double bond. The remaining methine was placed at C-1 by using HMBC. The proton signal at δ 1.26 (H_3-14) was correlated with the carbon signal at δ 78.2 (C-1), the proton signal at δ 4.45 (H-1) with the carbon signal at δ 201.4 (C-2), and the proton signal at δ 2.02 (H-15) with the carbon signals at δ 126.6 (C-3), 162.7 (C-4), and 76.7 (C-5). The NOESY spectrum of **3** showed the correlations of H-1 to H_3-14, H_3-14 to H-6β, and H-6β to H_3-12. These findings showed that the relative stereochemistry of C-11, C-14, and the hydroxyl group on C-1 is β, β, and α, respectively

Canusesnol D (**4**), $C_{15}H_{26}O_3$, showed the presence of one double bond (δ_C 128.0 and 137.6) hydroxy isopropyl, one methine (δ_C 72.9) attached to the oxygen function, and two quaternary carbons (δ 69.8 and 73.7) attached to oxygen functions in the ^{13}C NMR spectrum. From the $^1H-^1H$ COSY spectrum of **4**, the partial structures >CH−CH=CH− and >CH−CH_2−CH−CH_2−CH_2− were obtained. In the HMBC spectrum of **4**, the correlations of H_3-14 to C-1 (δ_C 72.9), H-1 to C-2, C-3, and C-5, H-2 to C-4 and C-10, H-3 to C-5, H_3-15 to C-3 and C-4, and H_3-12 to C-7 and C-11 were observed. These findings placed hydroxyl groups on C-1, C-4, and C-11, and the double bond at C-2−C-3. The NOESY spectrum of **4** showed correlations of H-1α to H-9α and H-5, H-5 to H-7, H-9β to H_3-14, and H_3-15 to H-5. Thus, the relative stereochemistry of the hydroxyl groups on C-1 and C-4 is β, and that of the hydroxy isopropyl group is also β.

Canusesnol E (**5**), $C_{15}H_{24}O_3$, showed the presence of four olefinic carbons (two methylenes at δ 105.6 and 109.0 and two quaternary olefinic carbons at δ 151.8 and 155.4), which indicated the presence of two exomethylenes. Three oxygenated carbons (two tertiary carbons at δ 68.2 and 72.2 and one quaternary carbon at δ 76.7) were also observed. The ^1H NMR spectrum of **5** contained two methyl signals (δ 0.76 and 1.77). The ^{13}C NMR spectral data of **5** were very similar to those of litneridanin A[12] (1β,3α,5α-trihydroxyeudesma-4(15),11-diene) except for the chemical shifts of C-3, C-4, and C-15. In the NOESY spectrum, correlations from H-1α to H-3α were obtained. From these results, the structure of **5** was determined to be 1β,3β,5α-trihydroxyeudesma-4(15),11-diene (C-3 epimer of litneridanin A).

Canusesnol F (**6**), $C_{15}H_{22}O_4$, showed the presence of carboxylic acid (IR 1696 cm^{-1}, ^{13}C NMR δ 170.7). The ^{13}C NMR spectrum of **6** was very similar to that of capsidiol (**11**) except for the chemical shifts of C-6, C-7, C-12, and C-13. The HMBC spectrum of **6** showed the following correlations: H-12 to C-13 (δ 170.7), C-11, and C-7, H-9 to C-7, C-8, and C-1 (δ 75.6), and H_3-14 to C-3 (δ 66.1) and C-5. These results clearly indicated the presence of a carboxylic acid group (C-11), hydroxyl groups on C-1 and C-3, and two double bonds at C-9−C-10 and C-11−C-12. The NOESY spectrum showed correlations of H_3-15 to H-1, H-3, and H-6β and of H-6α to H-7. The relative stereochemistry of compound **6** was similar to that of capsidiol[5] (**11**) except for C-1.

Canusesnol G (**7**), $C_{15}H_{26}O_3$, showed the presence of three methyls, one methylene attached to oxygen, four methylenes, one methine attached to the oxygen function, two methines, one double bond, one quaternary carbon attached to oxygen, and one quaternary carbon in the ^{13}C NMR spectrum. From the H−H COSY spectrum, the partial structures of CH_2−CH_2−CH(OH)CH(CH_3)− and −CH_2−CH−CH_2−CH=C< were obtained. Compound **7** was also estimated to be a capsidiol-type sesquiterpene. The HMBC spectrum of **7** showed the following correlations: H-4 to C-2, C-5, and C-10, H-9 to C-1 and C-7, H_3-15 to C-4, C-5, and C-6, H_3-14 to C-3 (δ 70.0), C-4, and C-5, and H_3-13 to C-7 and C-12 (δ 69.1). From these results, the hydroxyl groups were placed on C-3, C-11, and C-12. The NOESY spectrum showed correlations of H_3-15 to H-3β, H-4β, and H_3-13. Canusesnol H (**8**), $C_{14}H_{22}O_3$, showed 14 carbon signals including one double bond, a carbonyl carbon, two oxygenated tertiary carbons, and three methyls in the ^{13}C

NMR spectrum (Table 1). The ^{1}H NMR spectrum showed the presence of a double bond methine (δ 5.88), oxygenated methines at δ 4.50 and 4.27, and three methyls at δ_H 2.18 (3H, s), 1.35 (3H, s), and 0.89 (3H, d, J = 7.0 Hz). The chemical shifts of **8** were similar to those of capsidiol except for C-7, C-8 C-11, C-12, and C-13. The HMBC spectrum of **8** showed correlations of H-9 to C-1 and of H_3-13 (δ_H 2.18) to C-7 and C-11 (δ_C 214.4). Thus, the methyl ketone in compound **8** was placed at C-7. The NOESY spectrum of **8** indicated the same configuration as capsidiol.[5] Compound **8** is a rare 12-nor-sesquiterpene.

Canusesnol I (**9**), $C_{15}H_{26}O_2$, revealed the presence of two methyls [δ_H 1.74 (3H, s) and 0.94 (3H, d, J = 6.8 Hz)] and one methylene [δ_H 3.88 (1H, dd, J = 10.0, 3.1 Hz) and 3.24 (1H, t, J = 10.0 Hz)] attached to the oxygen function and one exomethylene [δ_H 4.70 and 4.67 (each 1H, s)] and one methine [δ_H 3.56 (1H, sept, J = 4.6 Hz)] attached to the oxygen function. The ^{13}C NMR data of **9** were similar to those of 15-dihydrolubimin[9] except for small chemical shift differences. The ^{1}H NMR data of **9** were also similar to those of 15-dihydrolubimin.[10] From the HMBC analysis, the structure of compound **9** was deduced to be the same as that of 15-dihydrolubimin except for the stereochemistry. The NOESY spectrum of **9** showed the following correlations: H_2-12 to H-8α, H-6α, and H_2-15; H-10β to H-2β; H-2β to H-4β; and H_3-14 to H-9β and H-8β. Thus, **9** was determined to be 4-epi-15-dihydrolubimin.

Canusesnol J (**10**), $C_{15}H_{22}O_3$, showed the presence of an α,β-unsaturated ketone (δ_C 121.9, 172.4, and 202.1), two methylenes (δ_C 61.8 and 65.8) attached to oxygen functions, one exomethylene (δ_C 108.4 and 152.5), and one methyl (δ_C 16.1) in the ^{13}C NMR spectrum. The following HMBC correlations were observed: H-1 to C-15 and C-5; H-12 to C-7 and C-13; H_2-13 to C-7 and C-11; H_3-14 to C-3, C-4, and C-5; and H_2-3 to C-2 (δ 202.1). From these results, the α,β-unsaturated ketone and two methylenes attached to the oxygen function were placed at C-10−12, C-10, and C-11, respectively.

Isolated compounds (**1**−**10** and the nine known compounds mentioned earlier) were assayed for cytotoxicity using a reported procedure.[13] Compounds **1**−**10** showed negligible activity as inhibitors of human tumor cell replication or anti-HIV activity.[14]

Experimental Section

General Experimental Procedures. Optical rotations were measured with a JASCO DIP-370 digital polarimeter. IR spectra were recorded on a JASCO Fourier transform infrared spectrometer (FT/IR-420). NMR (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR, both used TMS as internal standard) were measured on a Bruker AM 400 spectrometer, and MS on a JEOL JMSD-300 instrument. Column chromatography: silica gel 60 (Merck) and Toyopearl HW 40 (TOSOH). HPLC: GPC (Shodex GS-310 2G, MeOH), silica gel (YMC-pack SIL-06 SH-043-5-06, 250 × 20 mm, Merck Hibar RT 250-25 Si60).

Plant Material. The dried stems and roots of *C. annuum* (2.2 kg) were cultivated in October 2000 in the Medicinal Plant Garden of Tokushima University, from seeds purchased from Nakahara-saishujo Co., Japan. A voucher specimen was deposited in the Herbarium of the Faculty of Pharmaceutical Sciences, University of Tokushima, Japan.

Extraction and Isolation. The dried stem and root of *C. annuum* (2.2 kg) were extracted three times with MeOH at 60 °C. The MeOH extracts were concentrated to give a residue (255 g), which was partitioned between EtOAc and H_2O. The EtOAc layer was concentrated to give a residue (50.6 g), which was subjected to column chromatography on silica gel with solvents of increasing polarity (*n*-hexane−EtOAc) to give six fractions. Fraction 6 (1.4 g) was filtered off and washed with MeOH to give fraction 20 (50.0 mg). Fraction 3 (1.8 g) was applied to a Toyopearl HW-40 column with $CHCl_3$−MeOH (1:1) as an eluent to give four fractions (7−10). Fraction 8 (600 mg) was loaded on a silica gel column and eluted with solvents of increasing polarity ($CHCl_3$−MeOH) to give 13 fractions (11−23). Fraction 17 (64.7 mg) was crystallized to give capsidiol (15 mg) using EtOAc. Fraction 19 (159.1 mg) was subjected to GPC (MeOH) to give *N-cis*-feruloyltyramine (10.6 mg) and *N-trans*-feruloyltyramine (34.9 mg). Fraction 16 (53.9 mg) was subjected to GPC (MeOH) to give lariciresinol (3.0 mg). Fraction 20 (46.0 mg) was subjected to GPC (MeOH) to give lubiminol (6.7 mg). Fraction 21 (58.4 mg) was subjected to GPC (MeOH) to give *N-p-cis*-coumaroyltyramine (15.6 mg) and *N-p-trans*-coumaroyltyramine (30.1 mg). Fraction 4 (1.4 g) was applied to a Toyopearl HW-40 column with $CHCl_3$−MeOH (1:1) as an eluent to give four fractions (24−27). Fraction 25 (730.2 mg) was loaded on a silica gel column and eluted with different solvents of increasing polarity ($CHCl_3$−MeOH) to give 10 fractions (28−37). Fraction 30 (29.9 mg) was subjected to HPLC (silica gel, $CHCl_3$−MeOH, 95:5) to give six fractions (38−43). Fraction 39 (10.9 mg) was subjected to HPLC (silica gel, $CHCl_3$−MeOH, 99:1) to give **1** (3.6 mg). Fraction 35 (93.0 mg) was subjected to GPC (MeOH) to give 13-hydroxycapsidiol (35.5 mg). Fraction 32 (67.7 mg) was subjected to GPC (MeOH) to give drummondol (4.6 mg), **2** (11.9 mg), and **10** (4.8 mg). Fraction 33 (35.9 mg) was subjected to GPC (MeOH) to give **3** (10.6 mg). Fraction 31 (123.9 mg) was subjected to GPC (MeOH) to give six fractions (44−49). Fraction 45 (59.2 mg) was subjected to HPLC (ODS, MeOH−H_2O, 6:4) to give four fractions (50−53). Fraction 51 was **9** (5.7 mg). Fraction 53 (49.0 mg) was subjected to GPC (MeOH) to give five fractions (54−58). Fraction 56 (7.5 mg) subjected to PTLC ($CHCl_3$−MeOH, 95:5) to give two fractions (59 and 60). Fraction 60 (5.3 mg) was subjected to PTLC ($CHCl_3$−acetone, 7:3) to give **8** (3.2 mg). Fraction 36 (73.1 mg) was subjected to GPC (MeOH) to give **7** (4.7 mg) and **5** (14.3 mg). Fraction 34 (108.3 mg) was subjected to GPC (MeOH) to give 12 fractions (61−72). Fraction 61 was **4** (6.2 mg). Fraction 64 (18.5 mg) was subjected to HPLC (silica gel, $CHCl_3$−MeOH, 95:5) to give **6** (2.9 mg).

Canusesnol A (1): colorless oil; $[\alpha]_D$ −37.5° (*c* 0.1, MeOH); IR (KBr) ν_{max} 3419, 2931, 2360, 1657, 1385, 1135 cm^{-1}; ^{1}H NMR (CD_3OD) δ_H 6.97 (1H, d, J = 9.7 Hz, H-1), 6.21 (1H, d, J = 9.7 Hz, H-2), 3.00 (1H, d, J = 14.4 Hz, H-6α), 2.53 (1H, d, J = 14.4 Hz, H-6β), 2.09 (1H, ddd, J = 14.0, 14.0, 4.7 Hz, H-8β), 1.91 (3H, s, H-15), 1.76 (1H, m, H-9), 1.68 (1H, m, H-8), 1.65 (1H, m, H-9), 1.30 (6H, s, H-12,H-13), 1.25 (3H, s, H-14); ^{13}C NMR, see Table 1; HREIMS *m/z* 250.1578 [M]$^+$ (calcd for $C_{15}H_{22}O_3$, 250.1569).

Canusesnol B (2): colorless needles; mp >160 °C; $[\alpha]_D$ +3.6° (*c* 0.9, MeOH); IR (KBr) ν_{max} 3476, 3300, 2974, 2943, 1678, 1466, 1378, 1262, 1172, 1095, 1062 cm^{-1}; ^{1}H NMR (CD_3OD) δ_H 6.42 (1H, d, J = 10.3 Hz, H-3), 5.78 (1H, d, J = 10.3 Hz, H-2), 2.02 (1H, m, H-9), 1.86 (1H, m, H-6β), 1.84 (1H, m, H-7), 1.71 (1H, m, H-8), 1.62 (1H, m, H-9), 1.59 (1H, m, H-6α), 1.44 (3H, s, H-15), 1.30 (1H, m, H-8), 1.22 (3H, s, H-14), 1.20 (3H, s, H-12), 1.19 (3H, s, H-13); ^{13}C NMR, see Table 1; HRFABMS *m/z* 267.1628 [M − H]$^-$ (calcd for $C_{15}H_{23}O_4$, 267.1596).

Canusesnol C (3): colorless oil; $[\alpha]_D$ +33.6° (*c* 1.0, MeOH); IR (KBr) ν_{max} 3419, 2977, 2360, 1677, 1377, 1266, 1125, 1061, 1023 cm^{-1}; ^{1}H NMR (CD_3OD) δ_H 5.91 (1H, s, H-3), 4.45 (1H, s, H-1), 2.07 (1H, brd, J = ca. 13, H-6α), 2.02 (3H, s, H-15), 1.73 (1H, brd, J = 13.5 Hz, H-9), 1.58 (1H, m, H-8), 1.55 (1H, brt, J = ca. 13, H-6β), 1.26 (3H, s, H-14), 1.23 (1H, m, H-8), 1.20 (1H, m, H-9), 1.17 (6H, s, H-12, H-13), 1.08 (1H, m, H-7); ^{13}C NMR, see Table 1; HREIMS *m/z* 268.1674 [M]$^+$ (calcd for $C_{15}H_{24}O_4$, 268.1675).

Canusesnol D (4): colorless oil; $[\alpha]_D$ +165.0° (*c* 0.5, MeOH); IR (KBr) ν_{max} 3398, 2970, 2870, 2360, 1636, 1458, 1375, 1154, 1034 cm^{-1}; ^{1}H NMR (CD_3OD) δ_H 5.82 (1H, dd, J = 5.6, 9.9 Hz, H-2), 5.69 (1H, d, J = 9.9 Hz, H-3), 3.44 (1H, d, J = 5.6 Hz, H-1), 1.85 (1H, m, H-6), 1.79 (1H, m, H-9α), 1.71 (1H, m, H-8), 1.66 (1H, m, H-5), 1.36 (1H, m, H-7), 1.30 (1H, m, H-6), 1.25

(3H, s, H-15), 1.22 (1H, m, H-9β), 1.20 (6H, s, H-12, H-13), 0.94 (3H, s, H-14); ^{13}C NMR, see Table 1; HREIMS *m/z* 254.1873 $[M]^+$ (calcd for $C_{15}H_{26}O_3$, 254.1882).

Canusesnol E (5): colorless needles; mp 143−146 °C; $[\alpha]_D$ +62.7° (*c* 0 .5, MeOH); IR (KBr) ν_{max} 3408, 2931, 2360, 1715, 1456, 1009 cm^{-1}; ^{1}H NMR (CD_3OD) δ_H 5.19 (1H, s, H-15), 4.87 (1H, s, H-15), 4.75 (1H, s, H-13), 4.72 (1H, s, H-13), 4.63 (1H, dd, J = 6.1, 11.6 Hz, H-3α), 4.02 (1H, dd, J = 11.8, 4.8 Hz, H-1α), 2.53 (1H, m, H-7α), 2.14 (1H, m, H-2), 1.81 (1H, m, H-6),1.77 (3H, s, H-12), 1.75 (1H, m, H-9), 1.65 (1H, m, H-6), 1.65 (1H, m, H-9), 1.61 (1H, m, H-8), 1.52 (1H, m, H-2) 1.39 (1H, m, H-8) 0.76 (3H, s, H-14); ^{13}C NMR, see Table 1; HREIMS *m/z* 252.1656 $[M]^+$ (calcd for $C_{15}H_{24}O_3$, 252.1725).

Canusesnol F (6): colorless oil; $[\alpha]_D$ +35.6° (*c* 1.1, MeOH); IR (KBr) ν_{max} 3402, 2931, 1696, 1625, 1378, 1255, 1152, 1034, 1012 cm^{-1}; ^{1}H NMR (CD_3OD) δ_H 6.16 (1H, s, H-12), 5.92 (1H, d, J = 5.4 Hz, H-9), 5.53 (1H, s, H-12), 4.50 (1H, dt, J = 4.5, 12.3 Hz, H-3), 4.29 (1H, brs, H-1), 2.77 (1H, brt, J = ca. 13 Hz, H-7), 2.11 (1H, m, H-8), 1.96 (1H, m, H-8), 1.89 (1H, m, H-6α), 1.85 (1H, m, H-2), 1.68 (1H, m, H-4), 1.65 (1H, m, H-2), 1.35 (3H, s, H-15), 1.27 (1H, dd, J = 13.4, 13.4 Hz, H-6β) 0.96 (3H, d, J = 7.0 Hz, H-14); ^{13}C NMR, see Table 1; HREIMS *m/z* 266.1533 $[M]^+$ (calcd for $C_{15}H_{22}O_4$, 266.1518).

Canusesnol G (7): colorless oil; $[\alpha]_D$ +6.2° (*c* 0.3, MeOH); IR (KBr) ν_{max} 3371, 2935, 1459, 1384, 1262, 1094, 1040 cm^{-1}; ^{1}H NMR (CD_3OD) δ_H 5.58 (1H, d, J = 6.5, H-9), 4.17 (1H, dt, J = 12.0, 4.6 Hz, H-3β), 3.41 (2H, s, H-12), 2.33 (1H, m, H-8), 2.01 (1H, m, H-8), 2.01 (1H, m, H-1), 1.92 (1H, m, H-7), 1.84 (1H, m, H-6), 1.75 (1H, m, H-1), 1.68 (1H, m, H-4β), 1.68 (1H, m, H-2), 1.40 (1H, m, H-2), 1.29 (1H, m, H-6), 1.17 (3H, s, H-15) 1.08 (3H, s, H-13) 0.93 (3H, d, J = 7.0 Hz, H-14); ^{13}C NMR, see Table 1; HREIMS *m/z* 236.1750 $[M - H_2O]^+$ (calcd for $C_{15}H_{24}O_2$, 236.1776).

Canusesnol H (8): colorless needles; mp >160 °C; $[\alpha]_D$ +1.4° (*c* 0.3, MeOH); IR (KBr) ν_{max} 3420, 2931, 1699, 1456, 1386, 10323408, 2931, 2360, 1715, 1456, 1009 cm^{-1}; ^{1}H NMR (CD_3OD) δ_H 5.88 (1H, dd, J = 6.3, 2.2 Hz, H-9), 4.50 (1H, dt, J = 12.3, 4.4 Hz, H-3), 4.27 (1H, brt, J = 2.6 Hz, H-1), 2.72 (1H, m, H-7), 2.18 (3H, s, H-12), 2.17 (1H, m, H-8), 2.07 (1H, m, H-8), 1.96 (1H, m, H-6), 1.84 (1H, m, H-2), 1.74 (1H, m, H-4), 1.63 (1H, td, J = 12.8, 3.8 hzH-2), 1.44 (1H, m, H-6), 1.35 (3H, s, H-15), 0.89 (3H, d, J = 7.0 Hz, H-14); ^{13}C NMR, see Table 1; HREIMS *m/z* 238.1561 $[M]^+$ (calcd for $C_{14}H_{22}O_3$, 238.1569).

Canusesnol I (9): colorless needles; mp 119−121 °C; $[\alpha]_D$ +43.4° (*c* 0.4, MeOH); IR (KBr) ν_{max} 3364, 2951, 2359, 1645, 1457, 1372, 1038, 1012 cm^{-1}; ^{1}H NMR (CD_3OD) δ_H 4.70 (1H, s, H-12), 4.67 (1H, s, H-12), 3.88 (1H, dd, J = 10.0, 3.1 Hz, H-15), 3.56 (1H, sept, J = 4.6 Hz, H-2), 3.24 (1H, t, J = 10.0 Hz, H-15), 2.40 (1H, m, H-7), 2.24 (1H, m, H-1), 1.76 (1H, m, H-8), 1.74 (3H, s, H-13), 1.70 (1H, m, H-6), 1.64 (1H, m, H-3), 1.59 (1H, m, H-6), 1.48 (1H, m, H-4), 1.45 (1H, m, H-9) 1.40 (1H, m, H-10) 1.37 (1H, m, H-9), 1.35 (1H, m, H-8), 1.07 (1H, m, H-1), 1.04 (1H, m, H-3), 0.94 (3H, d, J = 6.8 Hz, H-14); ^{13}C NMR, see Table 1; HREIMS *m/z* 238.1931 $[M]^+$ (calcd for $C_{15}H_{26}O_2$, 238.1933).

Canusesnol J (10): colorless oil; $[\alpha]_D$ −25.3° (*c* 0.4, MeOH); IR (KBr) ν_{max} 3393, 2954, 1654, 1457, 1384, 1060 cm^{-1}; ^{1}H NMR (CD_3OD) δ_H 6.11 (1H, s, H-1), 5.06 (1H, s, H-12), 4.94 (1H, s, H-12), 4.31 (2H, s, H-15), 4.07 (2H, s, H-13), 2.79 (1H, m, H-3), 2.71 (1H, m, H-7), 2.28 (1H, m, H-6), 2.23 (1H, m, H-3), 2.21 (1H, m, H-4), 2.00 (1H, m, H-8), 1.93 (1H, m, H-9), 1.76 (1H, m, H-9), 1.66 (1H, m, H-8) 1.61 (1H, m, H-6) 1.01 (3H, d, J = 6.6 Hz, H-14); ^{13}C NMR, see Table 1; HREIMS *m/z* 250.1592 $[M]^+$ (calcd for $C_{15}H_{22}O_3$, 250.1569).

X-ray Crystallographic Analysis Data of 2. An orthorhombic crystal was obtained from MeOH. Crystal data: $C_{15}H_{24}O_4$, M_r = 268.35, orthorhombic. Crystal size: 0.1 × 0.1 × 0.1 mm. Cell parameters: a = 5.974(1) Å, b = 13.3867(7) Å, c = 17.3923(3) Å, V = 1390.9(2) Å^3, space group $P2_12_12_1$ (Z = 4). Data collection was performed on a Rigaku RAXIS imaging plate area detector with graphite-monochromated Mo Kα radiation, the structure was resolved by direct methods[15] (SIR92), and the final R and R_w values were 0.044 and 0.142 for 1832 observed reflections.[16]

References and Notes

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(16) Crystallographic data for the structure **2** reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

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