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Studies on the Sesquiterpenoids of *Panax ginseng* C. A. MEYER. Isolation and Structure Determination of Sesquiterpene Alcohols, Panasinsanols A and B

HISAKATSU IWABUCHI,*,[a] MASAHIRO YOSHIKURA,[a] YOSHITOMI IKAWA,[a] and WASUKE KAMISAKO[b]

SAN-EI Chemical Industries, Ltd.,[a] 1–1–11, Sanwa-cho, Toyonaka, Osaka 561, Japan and Faculty of Pharmaceutical Sciences, Mukogawa Women's University,[b] 4–16, Edagawa-cho, Nishinomiya, Hyogo 663, Japan

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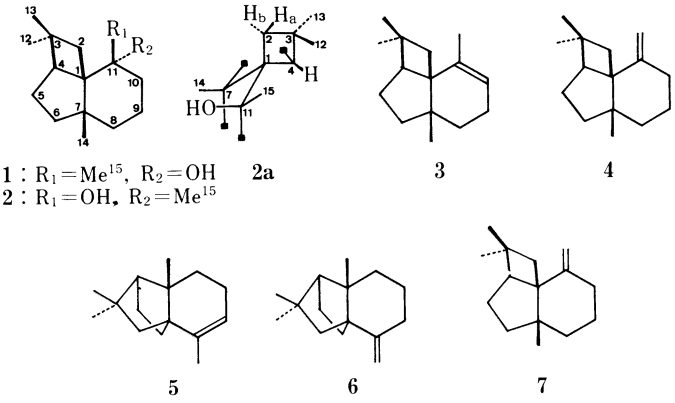
Two sesquiterpene alcohols, panasinsanol A (**1**) and panasinsanol B (**2**), were isolated from the rootlets of *Panax ginseng* C. A. MEYER (Araliaceae) together with known sesquiterpene hydrocarbons, α-panasinsene (**3**), β-panasinsene (**4**), α-neoclovene (**5**), and β-neoclovene (**6**). The structures of **1** and **2** were established by spectral evidence, chemical correlations to congener hydrocarbons (**3**, **4**, **5**, and **6**), and finally by their syntheses from (−)-β-caryophyllene. This is the first isolation of **1** from a natural source, and **2** is a novel panasinsane-type sesquiterpene.

Keywords——*Panax ginseng*; Araliaceae; *Panax* spp.; sesquiterpenoid; panasinsanol A; panasinsanol B

The roots and rootlets of *Panax ginseng* C. A. MEYER (Araliaceae) are a well-known and very important crude drug in the prescriptions of traditional oriental medicine. In the previous paper,[1] we reported methoxy- and alkylpyrazines from the basic fraction of the ethereal extract of *P. ginseng*. Many reports on saponins of this crude drug have been published,[2a,b] but only a few chemical studies have been done on the constituents other than these compounds.[2b–d,3a] During our study of the constituents of this crude drug,[1] the results of gas chromatography-mass spectrometry (GC-MS) indicated that many sesquiterpenoids were contained in the neutral fraction of the ethereal extract. Thus far, several sesquiterpenoids have been reported,[2d,3a] but no investigation of sesquiterpenoids other than these compounds has yet been made in detail. We therefore investigated the oxygen-containing sesquiterpenoids and have now isolated two sesquiterpene alcohols, named panasinsanols A and B, together with the related known sesquiterpene hydrocarbons, α-panasinsene, β-panasinsene, α-neoclovene, and β-neoclovene.[3a] In this paper, we wish to report the structural elucidation of panasinsanols A and B, as well as some findings obtained by the comparative analyses of the neutral volatile oils of *Panax* spp., *P. ginseng*, *P. japonicum*, *P. quinquefolium*, and *P. notoginseng*.

The neutral fractions[1] were chromatographed on a silica-gel column using hexane, hexane–ether, ether and acetone as eluants. From the hexane–ether (4:1) fractions, panasinsanols A and B were isolated by further silica-gel column chromatography and preparative high-performance liquid chromatography (HPLC). The least polar fractions eluted with hexane were further chromatographed on a silver nitrate ($AgNO_3$)-impregnated silica-gel column, followed by preparative HPLC at low temperature, yielding four analytically pure sesquiterpene hydrocarbons. These compounds were identified as α-panasinsene (**3**), β-panasinsene (**4**), α-neoclovene (**5**), and β-neoclovene (**6**) by comparisons of the spectral data with reported values.[3a–d]



1 : R_1=Me[15], R_2=OH
2 : R_1=OH, R_2=Me[15]

2a 3 4

5 6 7

Chart 1

Panasinsanol A (**1**) was isolated as a minor compound, colorless oil, $[\alpha]_D^{25}$ −51.9° ($CHCl_3$). The molecular formula $C_{15}H_{26}O$ of **1** was determined from the high-resolution mass spectrum (HR-MS) together with the carbon-13 nuclear magnetic resonance (^{13}C-NMR) data, which indicated the presence of three degrees of unsaturation. The infrared (IR) absorption at 3630 cm^{-1} and a dehydration ion at *m/z* 204 ($M^+ - 18$, H_2O) in the MS of **1** indicated the presence of a hydroxy group, and a quaternary carbon signal at δ 72.6 in the ^{13}C-NMR spectrum indicated the hydroxy group to be tertiary. The IR absorptions at 1375 and 1380 cm^{-1} and fragment ion at *m/z* 166 ($M^+ - 56$, C_4H_8) suggested that two of four methyl groups were assignable to a geminal dimethyl group.[4] The proton nuclear magnetic resonance (^{1}H-NMR) spectrum showed signals due to four tertiary methyl groups at δ 0.91 (6H, s), 1.12, 1.20 (each 3H, s), and a methine proton at δ 2.26 (1H, m), and its ^{13}C-NMR spectrum showed no sp^2 carbon. These observations suggest that panasinsanol A is a saturated tricarbocyclic sesquiterpenoid possessing a tertiary hydroxy group and a geminal dimethyl group.

Dehydration of **1** with thionyl chloride ($SOCl_2$) in pyridine gave two olefins which were identified as **3** and **4** by comparisons of the MS and retention times on GC with those of authentic samples.[3a] From the above results, two formulas (**1** and **2**) were suggested for the structure of panasinsanol A. One of them, **1**, has been previously synthesized as a key intermediate in the total syntheses of sesquiterpene hydrocarbons (**4**, **5**),[3c,d] and the chemical shift values of methyl signals in the ^{1}H-NMR spectrum and optical rotation of our **1** were similar to those of the reported **1**.[3c,d] McKillop and his collaborators have reported that this alcohol was converted to **5** by treatment with concentrated sulfuric acid (H_2SO_4) in anhydrous ether.[3c] Indeed, on similar treatment of our **1**, two different olefins were formed. These compounds were directly identified as **5** and **6** by comparisons of the MS and retention times on GC with those of the authentic samples.[3a] All these results indicate that the structure of panasinsanol A is represented by formula **1**, whose relative configuration at the carbinol center is as shown by Johnson and Meanwell.[3d] To our knowledge, this is the first isolation of **1** from a natural source.

Panasinsanol B (**2**) was obtained as a colorless oil, $[\alpha]_D^{25}$ −44.3° ($CHCl_3$). The molecular formula $C_{15}H_{26}O$ of **2** was determined from the HR-MS together with the ^{13}C-NMR data, which indicated the presence of three degrees of unsaturation, and its MS showed a similar fragmentation to that of **1**. By analogy with **1**, the IR absorption at 3630 cm^{-1} and dehydration ion at *m/z* 204 ($M^+ - 18$, H_2O) in the MS of **2** indicated the presence of a hydroxy group, and a quaternary carbon signal at δ 73.2 (s) in the ^{13}C-NMR spectrum indicated the hydroxy group to be tertiary. Also the IR absorptions at 1370 and 1380 cm^{-1} and a fragment

ion at m/z 166 ($M^+ - 56$, C_4H_8) suggested that two of four methyl groups were assignable to a geminal dimethyl group.[4] The ^{1}H-NMR spectrum of **2** showed signals due to four tertiary methyl groups at δ 0.95, 1.04, 1.16, 1.41 (each 3H, s), and a methine proton at δ 2.08 (1H, m), and the ^{13}C-NMR spectrum showed no sp^2 carbon. Furthermore, in the ^{1}H-NMR spectrum, signals were observed as A and B parts of an ABX system at δ 1.62 (1H, br d, J=12.9 Hz) and 1.92 (1H, dd, J=2.1 and 12.9 Hz). These observations are similar to those in the case of **1**. Hence, it is suggested that panasinsanol B is a similar saturated tricarbocyclic sesquiterpenoid to **1**.

Dehydration of **2** with $SOCl_2$ in pyridine gave two olefins and these compounds were identified as **3** and **4** by comparisons of the spectral data, optical rotations and retention times on GC with those of authentic samples.[3a-d] On treatment of **2** with concentrated H_2SO_4 in anhydrous ether as described for **1**,[3c] three compounds were obtained. The major product was identified as **5** by comparisons of the spectral data, optical rotation and retention time on GC with those of an authentic sample.[3a-c,5] The second product was directly identified as **6** by comparisons of the MS and retention time on GC with those of an authentic sample.[3a] The remaining product appeared to be a new alcoholic compound. From the chemical evidence, the formula **2** was suggested for the structure of panasinsanol B.

To confirm the structure of **2**, ^{1}H-NMR studies on **2**, including proton spin decoupling, proton spin decoupling difference, and nuclear Overhauser effect (NOE) difference experiments, were undertaken. In the ^{1}H-NMR spectrum of **2**, a methyl signal at δ 1.41 was assignable to the equatorial carbinol methyl group (15-H_3) from its chemical shift value. In the spin decoupling experiments, irradiation at the frequency of a double doublet at δ 1.92 (2-H_a) collapsed a broad doublet at δ 1.62 (2-H_b) to a broad singlet and a multiplet at δ 2.08 (4-H) to a broad doublet. Irradiation at the frequency of the multiplet at δ 1.62 (2-H_b) collapsed the double doublet at δ 1.92 (2-H_a) to a doublet and slightly influenced the multiplet at δ 2.08 (4-H). Also, irradiation with the frequency of the multiplet at δ 2.08 (4-H) collapsed the signals at δ 1.62 (2-H_b) and 1.92 (2-H_a) to AB-type signals. In the proton spin decoupling difference experiments, long-range coupling between two methyl signals at δ 0.95 (13-H_3) and 1.16 (12-H_3) was found, supporting the presence of a geminal dimethyl group. In the NOE experiments on the geminal dimethyl group, irradiation at the frequency of the methyl signal at δ 0.95 (13-H_3) resulted in NOE enhancement of the signal at δ 1.62 (2-H_b), and irradiation at the frequency of the methyl signal at δ 1.16 (12-H_3) resulted in NOE enhancements of the signals at δ 1.41 (15-H_3), 1.92 (2-H_a), and 2.08 (4-H). Also, irradiation at the frequency of the methyl signal at δ 1.41 (15-H_3) resulted in NOE enhancements of the signals at δ 1.16 (12-H_3), 1.92 (2-H_a), and 2.08 (4-H). Irradiation at the frequency of the methyl signal at δ 1.04 (14-H_3) resulted in NOE enhancement of the signal at δ 1.62 (2-H_b). These NOE findings are indicated by the double-headed arrows in Fig. 1. These observations are consistent with the partial structure **2a**. Hence, all these results indicate that the structure of panasinsanol B is represented by formula **2**. Furthermore, this result indirectly supports the relative con-

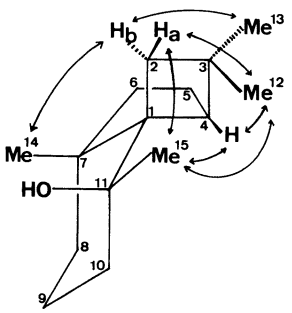


Fig. 1. NOE Findings for **2** (400 MHz)

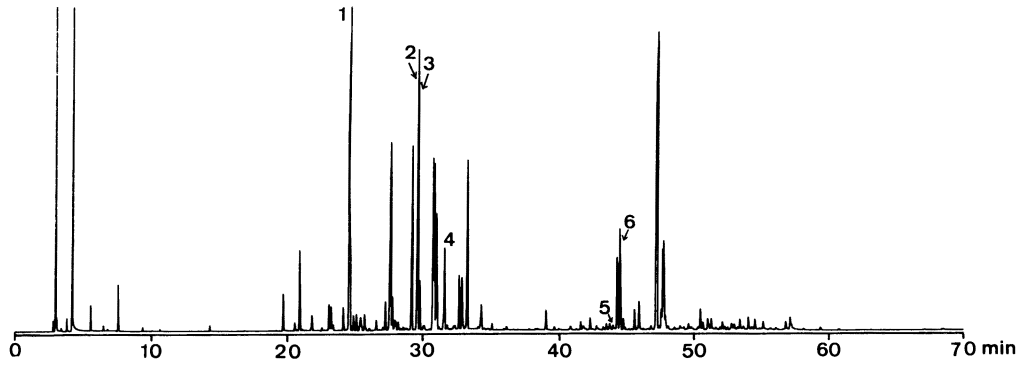


Fig. 2. Gas Chromatogram of the Neutral Volatile Oil of *P. ginseng* C. A. MEYER

Peak 1, β-panasinsene (**4**); peak 2, α-panasinsene (**3**); peak 3, α-neoclovene (**5**); peak 4, β-neoclovene (**6**); peak 5, panasinsanol A (**1**); peak 6, panasinsanol B (**2**).

figuration at the carbinol methyl group in **1** as axial, a choice so far based on the result of a ^{1}H-NMR experiment on this alcohol using a shift reagent, and the ^{13}C-NMR and IR spectra of its related compounds.[3d]

Finally, the stereostructures of **1** and **2** were confirmed by total syntheses from the tricarbocyclic ketone (**7**), which was obtained from (−)-β-caryophyllene of known absolute configuration[3e] by a method similar to that reported by McKillop and his collaborators.[3c] Treatment of **7** with methyl lithium produced a 11 : 1 mixture of the desired two tertiary alcohols (**1** and **2**) in good yield.[3f] The spectral data, optical rotations and retention times on GC of these synthetic alcohols were in good agreement with those of naturally occurring **1** and **2**. Thus, the structures of panasinsanols A and B were established as (4*S*,7*R*,11*R*)-(**1**) and (4*S*,7*R*,11*S*)-3,3,7,11-tetramethyltricyclo[5,4,0,$0^{1,4}$]undecan-11-ol (**2**) respectively.

It has been reported by Yoshihara and Hirose that there was little difference between the gas chromatograms of the volatile oils obtained from dried rootlets of *P. ginseng* collected in Japan and in Korea.[3a] Indeed, it was proved by detailed analyses by GC and GC-MS that these materials all contained not only **3**—**6** but also **1** and **2**. Furthermore, it was also proved that white and red ginsengs both contained **1**—**6**. A typical gas chromatogram of the neutral volatile oil of the rootlets collected in Japan is shown in Fig. **2**. On the other hand, the GC analyses clearly showed that the constituents of the neutral volatile oils obtained from dried roots of other *Panax* spp., *P. japonicum* C. A. MEYER (chikusetsu-ninjin), *P. quinquefolium* L. (American ginseng) and *P. notoginseng* (BURK) F. H. CHEN (sanchi-ginseng), were different from those of *P. ginseng*. Detailed GC-MS analyses showed that trace amounts of **3**, **4** and **5** were contained only in *P. quinquefolium*. Also, **1**, **2** and **6** could not be found in any *Panax* spp. other than *P. ginseng*.

P. ginseng contains other sesquiterpenoids which are under investigation in our laboratories.

Experimental

^{1}H- and ^{13}C-NMR spectra were measured with tetramethylsilane (TMS) as an internal reference. Chemical shifts are expressed in ppm downfield from TMS and coupling constants (J) in Hz. Abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. ^{1}H-Gated decoupling measurements without NOEs were employed to confirm the number of carbon atoms. Intensive nuclei enhanced by polarization transfer and single frequency off-resonance decoupling measurements were also employed to delineate the ^{13}C signals. The following instruments were used: IR spectra, Shimadzu IR-410 IR spectrometer; ^{1}H-NMR spectra, JEOL FX-100, FX-200, and GX-400 FT NMR spectrometers; ^{13}C-NMR spectra, JEOL FX-200 spectrometer; GC-MS, Hitachi M-80 gas chromatograph-

mass spectrometer and Hewlett Packard 5970B mass selective detector combined with a Hewlett Packard 5890A gas chromatograph; HR-MS, Hitachi M-80 gas chromatograph-mass spectrometer; GC, Hewlett Packard 5890A equipped with a Hewlett Packard 3392A integrated recorder; circular dichroism (CD) spectrum, JASCO J-500C spectropolarimeter; optical rotation, Optical Activity AA-10 digital polarimeter. For GC and GC-MS analyses, DB-WAX fused-silica capillary columns (J & W Scientific, INC., i.d. 0.25 mm × 60 m, i.d. 0.33 mm × 60 m) were used and the column temperature was programmed at 3 °C/min from 60 (held for 5 min) to 210 °C and then held. For preparative HPLC, a Waters 6000A solvent delivery system, U6K injector, R-401 differential refractometer, and stainless steel column packed with Chemcosorb 5 Si (Chemco, Inc., i.d. 10 mm × 30 cm) were used. For column chromatography, Wakogel C-100 and C-200 were used.

Extraction and Isolation——The ethereal extract and the neutral fraction of *P. ginseng* collected in Nagano Prefecture (2 kg, dried rootlets) were obtained as described in the previous paper.[1] The neutral fractions (25.6 g) were chromatographed on a silica-gel column using hexane (1000 ml), hexane–ether (9 : 1, v/v, 600 ml), hexane–ether (4 : 1, v/v, 800 ml), ether (800 ml), and acetone (1000 ml) as eluants. The least polar fractions eluted with hexane (2.30 g) were further chromatographed on a silica-gel column impregnated with 10% $AgNO_3$ using hexane as an eluant. Each eluted fraction was further subjected to preparative HPLC (solvent, hexane; column temperature, −45 °C; flow rate, 1.0 ml/min), yielding analytically pure α-panasinsene (**3**) (35.1 mg). β-panasinsene (**4**) (20.4 mg), α-neoclovene (**5**) (32.8 mg), and β-neoclovene (**6**) (11.9 mg). The fractions eluted with hexane–ether (4 : 1, v/v) (1.20 g) were further chromatographed on a silica-gel column using solvents of increasing polarity from benzene to ether. The fractions eluted with benzene–ether (9 : 1, v/v) were further subjected to preparative HPLC (solvent, benzene–ether (97 : 3, v/v); flow rate, 2.5 ml/min), yielding crude panasinsanol A (**1**) and analytically pure panasinsanol B (**2**) (25 mg). Isolation of **1** was carried out by preparative HPLC (solvent, hexane–ether (9 : 1, v/v); column temperature, −45 °C ; flow rate, 1.0 ml/min), yielding analytically pure **1** (4.5 mg).

Panasinsanol A (**1**): Colorless oil. $[\alpha]_D^{25}$ −51.9° (c=0.54, $CHCl_3$). IR (CCl_4): 3630, 1380, 1375 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 200 MHz) δ: 0.91 (6H, s), 1.12, 1.20 (each 3H, s), 2.26 (1H, m). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ: 20.4 (t), 20.7 (q), 23.4 (q), 24.1 (t), 25.0 (q), 28.4 (s), 29.4 (q), 36.5 (t), 37.6 (t), 39.0 (t), 43.4 (t, s), 49.0 (d), 53.8 (s), 72.6 (s). MS m/z (% rel. int.): 222 (M^+, 3), 207 (4), 204 (6), 189 (10), 166 (10), 161 (7), 151 (26), 138 (12), 133 (14), 125 (15), 123 (26), 108 (21), 81 (26), 67 (21), 55 (26), 43 (100), 41 (53), 39 (19). HR-MS m/z: M^+ Calcd for $C_{15}H_{26}O$ 222.1983. Found: m/z 222.1952.

Panasinsanol B (**2**): Colorless oil. $[\alpha]_D^{25}$ −44.3° (c=0.70, $CHCl_3$). IR (CCl_4): 3630, 1370, 1365 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 200 MHz) δ: 0.95 (3H, s, 13-H_3), 1.04 (3H, s, 14-H_3), 1.16 (3H, s, 12-H_3), 1.41 (3H, s, 15-H_3), 1.62 (1H, br d, J=12.9 Hz, 2-H_b), 1.92 (1H, dd, J=2.1, 12.9 Hz, 2-H_a), 2.08 (1H, m, 4-H). ^{13}C-NMR ($CDCl_3$, 50 MHZ) δ: 17.5 (t), 21.4 (q), 24.7 (t), 25.7 (q), 28.4 (s), 29.5 (q), 31.4 (q), 36.4 (t), 37.2 (t), 37.7 (t), 42.9 (t, s), 50.4 (d), 51.9 (s), 73.2 (s). MS m/z (% rel. int.): 222 (M^+, 3), 207 (3), 204 (4), 189 (4), 166 (12), 151 (37), 148 (10), 138 (16), 133 (11), 125 (15), 123 (24), 108 (24), 93 (15), 81 (37), 67 (20), 55 (24), 43 (100), 41 (59), 39 (20). HR-MS m/z: M^+ Calcd for $C_{15}H_{26}O$ 222.1983. Found: m/z 222.1961.

α-Panasinsene (**3**): Colorless oil. $[\alpha]_D^{25}$ −17.0° (c=1.17, $CHCl_3$). The spectral data (^{1}H-NMR, IR, and MS) were identical with those reported for α-panasinsene.[3a]

β-Panasinsene (**4**): Colorless oil. $[\alpha]_D^{25}$ −22.9° (c=0.87, $CHCl_3$). The spectral data (^{1}H-NMR, IR, and MS) were identical with those reported for β-panasinsene.[3a,d]

α-Neoclovene (**5**): Colorless oil. $[\alpha]_D^{25}$ −61.0° (c=1.20, $CHCl_3$). The spectral data (^{1}H-NMR, IR, and MS) were identical with those reported for α-neoclovene.[2a-c]

β-Neoclovene (**6**): Colorless oil. $[\alpha]_D^{25}$ −33.5° (c=0.75, $CHCl_3$). The spectral data (^{1}H-NMR, IR, and MS) were identical with those reported for β-neoclovene.[3a]

Dehydration of 1 with Thionyl Chloride——A solution of **1** (3 mg) in dry pyridine (0.5 ml) at 0 °C was treated with thionyl chloride (0.02 ml). After 2 h, the mixture was poured into ice-water and extracted with ether. The ether solution was washed with saturated brine and dried over anhydrous Na_2SO_4. After removal of the solvent, the residual substance was chromatographed on a silica-gel column. A GC analysis revealed that the least polar fraction (1.2 mg) eluted with hexane consisted of **3** (peak area %, 30%) and **4** (65%), which were directly identified as α-panasinsene and β-panasinsene by comparisons of the MS and retention times on GC with those of authentic samples.[3a]

Dehydration of 2 with Thionyl Chloride——A solution of **2** (15 mg) in dry pyridine (0.7 ml) at 0 °C was treated with thionyl chloride (0.05 ml). After 2 h, the mixture was worked up according to the previously outlined procedure. A GC analysis revealed that the least polar fraction (9 mg) eluted with hexane consisted of **3** (peak area %, 47%) and **4** (53%), which were isolated by preparative HPLC (solvent: hexane column temperature, −45 °C; flow rate, 1.0 ml/min) and identified as α-panasinsene and β-panasinsene by comparisons of the spectral data (^{1}H-NMR, IR, and MS), optical rotations and retention times on GC with those of authentic samples.[3a,d]

Acid-Catalyzed Rearrangement of 1——A solution of **1** (2 mg) in anhydrous ether (1 ml) was added with stirring to a solution (1 ml) prepared from concentrated H_2SO_4 (1 ml) and anhydrous ether (7 ml) at 0 °C.[3b,c] The mixture was stirred for 20 min at 0 °C and then for 30 min at room temperature. The reaction mixture was diluted with ice-water, neutralized with 2 N NaOH solution, and extracted with ether. The ether solution was washed with brine and dried

over anhydrous Na_2SO_4. After removal of the solvent, the residual substance was chromatographed on a silica-gel column. A GC analysis revealed that the least polar fraction (1.3 mg) eluted with hexane consisted of **5** (peak area %, 95%) and **6** (5%), which were directly identified as α-neoclovene and β-neoclovene by comparisons of the MS and retention times on GC with those of authentic samples.[3a]

Acid-Catalyzed Rearrangement of 2——A solution of **2** (7 mg) in anhydrous ether (1 ml) was added with stirring to a solution (1 ml) prepared from concentrated H_2SO_4 (2 ml) and anhydrous ether (7 ml) at 0 °C.[3b,c] The mixture was stirred for 20 min at 0 °C and then for 30 min at room temperature. The reaction mixture was worked up according to the previously outlined procedure. A GC analysis revealed that the least polar fraction (4.2 mg) eluted with hexane consisted of **5** (peak area %, 95%) and **6** (3%). Isolation of **5** was carried out by preparative HPLC (solvent, hexane; column temperature, −45 °C; flow rate, 1.0 ml/min), and **5** was identified as α-neoclovene by comparisons of the spectral data (^{1}H-, ^{13}C-NMR (benzene-d_6), IR, and MS), optical rotations and retention times on GC with those of an authentic sample.[3a-c,5] **6** was directly identified as β-neoclovene by comparisons of the MS and retention times on GC with those of an authentic sample.[3a] Elution with ether gave an unknown alcohol (1.6 mg), but its structure could not be elucidated.

Synthesis of 1 and 2 from (−)-β-Caryophyllene——A solution of commercial grade (−)-β-caryophyllene (Tokyo Kasei) in hexane was washed with diluted 2 N NaOH and then water until the water layer was neutral. The hexane layer was washed with 50% $AgNO_3$ solution and then water. After being dried over anhydrous Na_2SO_4, the hexane extract was concentrated under reduced pressure and the residual oil was carefully chromatographed on a silica-gel column impregnated with 10% $AgNO_3$ and eluted with hexane.[3b,c] Evaporation of the eluate afforded β-caryophyllene, $[\alpha]_D^{25}$ −13.5° (c=3.30, $CHCl_3$).[3g] The GC analysis of β-caryophyllene thus obtained indicated it be 98.5% pure. The synthesis of the tricyclic ketone (**7**) was carried out by the method reported by McKillop *et al.*[3c]

7——Colorless oil. $[\alpha]_D^{25}$ −37.6° (c=1.65, $CHCl_3$). CD ($c=1.21\times10^{-3}$, MeOH) $\Delta\varepsilon_{294}$: +2.7. IR (film): 2950, 1690, 1475, 1425, 1385, 1370, 1325, 1290, 1165, 1140, 935 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 0.86 (6H, s), 0.98 (3H, s). MS m/z (% ref. int.): 206 (M^+, 32), 191 (68), 163 (32), 151 (100), 135 (73), 107 (57).

The spectral data of **7** were in good agreement with those of the known tricyclic ketone.[3a,c] A solution of **7** (50 mg) in anhydrous ether (3 ml) was added to 1.8 N methyl lithium (10 ml) and the mixture was heated to reflux for 1 h under a nitrogen atmosphere.[3f] After this time the solution was cooled and then water was added dropwise. The ether layer was separated, washed with water, and concentrated under reduced pressure, yielding the desired tertiary alcohols (52 mg) (97%), which showed hydroxy but not carbonyl absorption in the IR spectrum, and a GC analysis revealed that the products consisted of two alcohols. Preparative HPLC (solvent, benzene–ether (97 : 3, v/v)) of the mixture gave **1** (44 mg) and **2** (4 mg). The spectral data (^{1}H-NMR, IR) and optical rotation of **1** thus obtained were in good agreement with reported data.[3c,d] Further, the spectral data (^{1}H-, ^{13}C-NMR, IR, and MS), optical rotations, and retention times on GC of these two alcohols thus obtained were in good agreement with those of our naturally occurring **1** and **2**, respectively.

GC and GC-MS Analyses of the Neutral Volatile Oils——The following materials were used: *P. ginseng*, dried rootlets (collected in Nagano and Fukusima Prefectures, each 100 g, and in Korea, 25 g), white ginseng (collected in Nagano Prefecture, cultivated for 5 years, 150 g), red ginseng (collected in Nagano Prefecture, cultivated for 5 years, 75 g); *P. japonicum* (collected in Nagano Prefecture, 150 g); *P. quinquefolium* (obtained from Hong Kong, 30 g); *P. notoginseng* (obtained from China, 100 g). All materials were obtained from Mikuni Co. (Osaka). The neutral volatile oils of these materials were prepared from the neutral fractions of their ethereal extracts by simultaneous steam distillation-extraction using a Nickerson-Likens apparatus.[6] The simultaneous steam distillation-extractions (ether–H_2O (1 : 10, v/v)) were continued for 30 min. The ether solutions were dried over anhydrous Na_2SO_4 and the solvents were removed under reduced pressure at 45 °C, yielding the neutral volatile oils.

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