Indonesian Medicinal Plants. XXII.[1] Chemical Structures of Two New Isopimarane-Type Diterpenes, Orthosiphononones A and B, and a New Benzochromene, Orthochromene A from the Leaves of *Orthosiphon aristatus* (Lamiaceae)

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Two new isopimarane-type diterpenes named orthosiphononones A and B and a new benzochromene named orthochromene A, have been isolated from the water decoction of the leaves of *Orthosiphon aristatus* (Lamiaceae) collected in Java, Indonesia. Their chemical structures have been elucidated on the basis of physicochemical and chemical evidence.

Key words *Orthosiphon aristatus*; Lamiaceae; orthosiphonone; isopimarane-type diterpene; orthochromene; benzochromene

The leaves of *Orthosiphon aristatus* (BL.) Miq. (Lamiaceae, kumis kucing in Javanese) has been prescribed in Javanese traditional medicine (jamu)[2] for the treatment of hypertension and diabetes. We have investigated the chemical constituents of the chloroform-soluble portion from the water decoction of the leaves and isolated one new benzochromene, designated orthochromene A (**3**), and two new isopimarane-type diterpenes, designated orthosiphononones A (**6**) and B (**7**). This paper deals with the elucidation of their chemical structures.

The water decoction was partitioned into a mixture of chloroform and water to give a chloroform-soluble portion (2.3% from the dried leaves) and a water-soluble portion (25%). The chloroform-soluble portion was separated by silica gel column chromatography and normal phase HPLC to afford orthochromene A (**3**, 0.024%), orthosiphononones A (**6**, 0.023%) and B (**7**, 0.003%), together with methylriparіochromene A (**1**, 0.63%),[3] acetovanillo-chromene (**2**, 0.030%),[4] orthosiphol A (**4**, 0.039%)[5] and B (**5**, 0.035%).[5]

Orthochromene A (3) Orthochromene A (**3**), $[\alpha]_D$ ±0°, showed a quasi-molecular ion peak at *m/z* 265 [$C_{15}H_{21}O_4$ $(M+H)^+$] in the FAB-MS. The IR spectrum showed absorption bands due to a hydroxyl (3400 cm^{-1}) group and an aromatic (1595 cm^{-1}) group. The UV spectrum showed absorption bands due to an aromatic (228, 270 nm) chromophore.

The ^{1}H-NMR spectrum of **3** exhibited signals assignable to one *secondary* methyl (δ 1.48, d, J=6.4 Hz, 14-H_3), two *tertiary* methyls (δ 1.46, 1.47, both s, 11- and 12-H_3), two methoxyls (δ 3.88, 3.94, both s, 7- and 8-OCH_3), one hydroxylmethine proton (δ 5.02, q, J=6.4 Hz, 13-H), two olefinic protons (δ 5.55, d, J=9.8 Hz, 3-H; δ 6.22, d, J=9.8 Hz, 4-H) and one aromatic proton (δ 6.74, s, 5-H). The ^{13}C-NMR and the distortionless enhancement by polarization transfer (DEPT) spectra revealed the presence of five methyl carbons, two olefinic carbons, six aromatic carbons, one quaternary carbon, and one hydroxylmethine carbon. From these findings and the heteronuclear multiple bond correlation (HMBC, shown in Fig. 2), it was deduced that orthochromene A (**3**) possesses a benzochromene skeleton. Furthermore, the nuclear Overhauser and exchange spectroscopy (NOESY, Fig. 2) spectrum showed correlation peaks between 2-methyls (11-H, 12-H) and 3-H, 4-H and 5-H, 5-H and 13-H, and 14-H_3 and 7-OCH_3.

Finally, orthochromene A (**3**) was identified with the product (**1a**) prepared from methylriparіochromene A (**1**)[3] by sodium borohydride reduction, and both compounds (**3**, **1a**) were determined to be a 1 : 1 mixture of 13*S* and 13*R* isomers by chiral HPLC analysis.

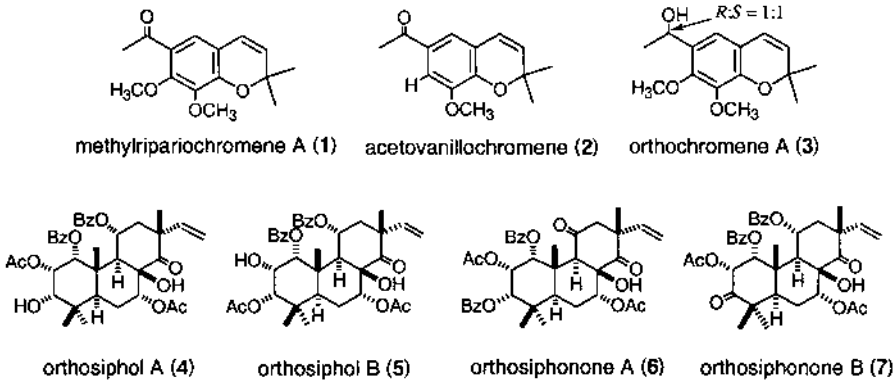

Fig. 1

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Consequently, the chemical structure of orthochromene A was concluded to be **3**.

Orthosiphonone A (6) Orthosiphonone A (**6**) showed quasi-molecular ion peaks at *m/z* 675 [$C_{38}H_{43}O_{11}$ $(M+H)^+$] and 681 [$C_{38}H_{42}LiO_{11}$ $(M+Li)^+$] in the FAB-MS. The IR spectrum showed the presence of a hydroxyl (3450 cm^{-1}) group, a ketonic function (1728 cm^{-1}) in a 6-membered ring and an ester group.

The ^{1}H-NMR spectrum exhibited signals due to four *tertiary* methyls (δ 0.97, 1.14, 1.21, 1.50; 18-H_3, 17-H_3, 19-H_3, 20-H_3), two acetoxymethyls (δ 1.95, 2.12), four methine protons attached to ester groups (δ 5.33, br d, J=3.7 Hz, 3-H; δ 5.45, br s, 7-H; d 5.75, dd, J=3.7, 3.7 Hz, 2-H; δ 6.44, d, J=3.7 Hz, 1-H), three olefinic protons (δ 4.26, d, J=10.4 Hz, 16-Ha; δ 4.72, d, J=17.7 Hz, 16-Hb; δ 5.29, dd, J=10.4, 17.7 Hz, 15-H), and two aromatic rings. The ^{13}C-NMR and DEPT spectra showed the presence of six methyl carbons, three methylene carbons, seventeen methine carbons, two ketonic carbonyl carbons, four ester carbonyl carbons, four *quaternary* carbons, including a carbon attached to a hydroxyl function (δ_C 76.6, 8-C). The above-mentioned findings indicated that orthosiphonone A (**6**) was an isopimarane- or pimarane-type diterpenoid.

The HMBC experiment (Fig. 3) on **6** showed the presence of four characteristic cross-peaks between two hydroxymethine protons (δ 6.44, 5.33; 1- and 3-H) and two benzoyl carbonyl carbons (δ_C 166.4, 164.4; 1- and 3-COPh), and between two hydroxymethine protons (δ 5.75, 5.45; 2- and 7-H) and two acetyl carbonyl carbons (δ_C 170.3, 168.3; 2- and 7-$COCH_3$), respectively. One (δ_C 205.2) of the two ketonic carbonyl carbons was determined to be at the 11-position based on the correlation with 9-H (δ 3.54, s) and 12-H_2 (δ 2.64, 2.76, 1H each, both d, J=18.0 Hz).

The NOESY spectrum (Fig. 3) showed correlation peaks between 19-H_3 and 20-H_3, 2-H and 19-H_3, 2-H and 20-H_3, 6b-H and 20-H_3, and 5-H and 9-H. This evidence revealed that the A and B rings in **6** are oriented to be *trans* and were both in a chair conformation.

Reduction of orthosiphonone A (**6**) with lithium aluminum hydride liberated two heptaols, **8** (9-H: 1H, d, J=2.1 Hz) and **9** (9-H: 1H, d, J=11.0 Hz), in a 3 : 4 ratio. Among them, **9** was also obtained by the same procedure from orthosiphol A (**4**),[5] whose absolute stereochemistry has been determined by the exciton chirality method.[6] Thus, it was clarified that orthosiphonone A (**6**) was an isopimarane-type diterpene and the absolute configuration was as shown.

Orthosiphonone B (7) Orthosiphonone B (**7**) showed quasi-molecular ion peaks at *m/z* 675 [$C_{38}H_{43}O_{11}$ $(M+H)^+$] and 681 [$C_{38}H_{42}LiO_{11}$ $(M+Li)^+$] in the FAB-MS, and the IR and the UV spectra were quite similar to those of orthosiphonone A (**6**).

In the ^{1}H-NMR spectrum, orthosiphonone B (**7**) showed a characteristic AB pattern (δ 5.95, d, J=2.4 Hz, 1-H; d 5.47, d, J=2.4 Hz, 2-H) and the methine proton at C-9 was observed as a doublet (J=7.0 Hz), instead of an ABC pattern (1-H, 2-H, 3-H) and as a singlet (9-H) for **6**. Furthermore, the HMBC experiment (Fig. 4) on **7** showed the presence of cross-peaks between two hydroxymethine protons (1-H, 11-H) and two benzoyl carbonyl carbons (1-COPh and 11-COPh), and between two hydroxymethine protons (2-H and 7-H) and two acetyl carbonyl carbons (2-$COCH_3$ and 7-$COCH_3$), respectively.

Finally, orthosiphonone B (**7**) was prepared from orthosiphol A (**4**)[5] by pyridinium chlorochromate (PCC) oxidation in a satisfactory yield.

From the above-mentioned findings, it was elucidated that the chemical structure of orthosiphonone B was **7**.

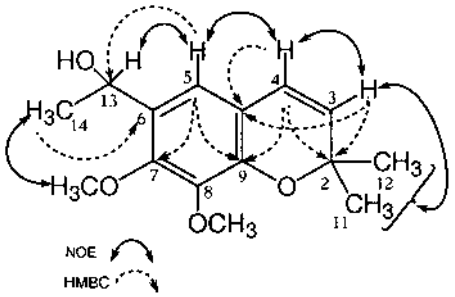


Fig. 2. NOESY and HMBC Correlations for Orthochromene A (**3**)

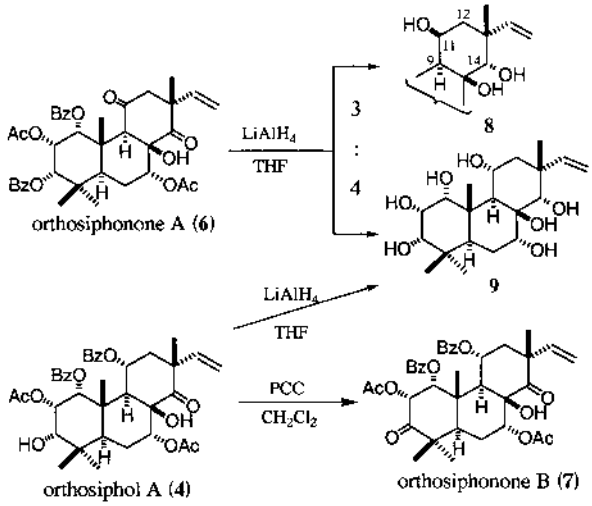
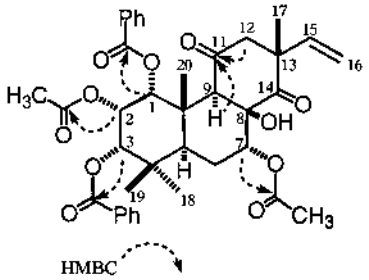


Chart 1



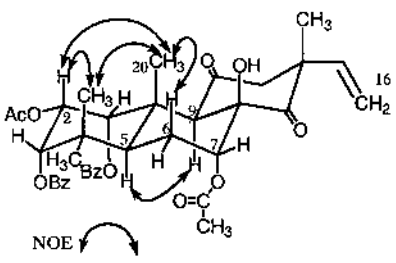


Fig. 3. NOESY and HMBC Correlations for Orthosiphonone A (**6**)

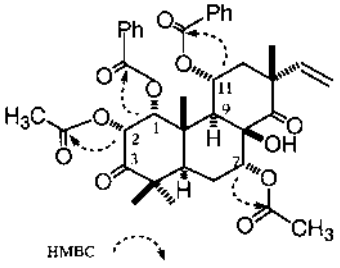


Fig. 4. HMBC Correlations for Orthosiphonone B (**7**)

Experimental

Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-360 digital polarimeter. FAB-MS were recorded on a JEOL SX-102A spectrometer. IR spectra were recorded on a Shimadzu FT-IR 8500 spectrometer. UV spectra were recorded on a Hitachi U-3500 spectrometer. ^{1}H- and ^{13}C-NMR spectra were obtained with a JEOL JNM-Lambda 500 spectrometer operating at 500 and 125 MHz for ^{1}H and ^{13}C nuclei, respectively; chemical shifts are reported in ppm relative to that of tetramethylsilane (δ=0) as an internal standard, and coupling constants are given in hertz. HPLC was carried out with a Shimadzu LC-10A. Column chromatography was carried out on Silica gel 60 (70—230 mesh, Merck). Thin-layer chromatography on Silica gel 60F_{254} (Merck) was used to ascertain the purity of the compounds. The spots were visualized by spraying the plates with 1% $Ce(SO_4)_2$ in 10% aqueous sulfuric acid and then heating.

Plant Materials *Orthosiphon ariatatus* (Bl.) Miq. was collected in Yogjakarta, Java Island, Indonesia, in December 1995, and identified at the Herbarium Bogoriense, Research and Development Centre for Biology-LIPI, Indonesia.

Extraction and Isolation Procedure The leaves (800 g) of *Orthosiphon aristatus* (Bl.) Miq. (Lamiaceae) were extracted four times with boiled water. The combined solution was evaporated under reduced pressure to give the H_2O extract (220 g, 27.5% from the leaves). The H_2O extract (23 g) was partitioned into a chloroform and water mixture (1 : 1). The chloroform phase was concentrated under reduced pressure to give the $CHCl_3$ extract (1.9 g, 2.3%) and the H_2O extract (21.1 g, 25%). The $CHCl_3$ extract (1.5 g) was subjected to silica gel column chromatography (SiO_2 150 g, $CHCl_3$: MeOH=100 : 1→50 : 1→10 : 1→MeOH) to give faction 1 (40 mg, 0.061%), fraction 2 (640 mg, 0.97%), fraction 3 (100 mg, 0.15%), fraction 4 (330 mg, 0.50%), fraction 5 (210 mg, 0.32%), and fraction 6 (200 mg, 0.30%). Fraction 2 (40 mg) was again purified by HPLC (YMC-Pack SIL, 250×10 mm; *n*-hexane : $CHCl_3$=2 : 1) to afford methylripariochromene A (**1**, 26 mg, 0.63%).[3] Separation of fraction 3 (50 mg) by HPLC (YMC-Pack SIL, 250×10 mm, *n*-hexane : EtOAc=2 : 1) afforded acetovanillochromene (**2**, 10 mg, 0.030%)[4] and orthochromene A (**3**, 8 mg, 0.024%). Fraction 4 (330 mg) was chromatographed on silica gel column chromatography (SiO_2 30 g, *n*-hexane : EtOAc=2 : 1→1 : 1→EtOAc) and HPLC (YMC-Pack SIL, 250×10 mm, *n*-hexane : EtOAc=2 : 1) to give orthosiphol A (**4**, 26 mg, 0.039%),[5] B (**5**, 23 mg, 0.035%),[5] and orthosiphonone A (**6**, 15 mg, 0.023%) and B (**7**, 2 mg, 0.003%).

Orthochromene A (**3**): Colorless plates from ether, mp 209—210 °C, $[\alpha]_D$ ±0° (*c*=0.70, in $CHCl_3$ at 23 °C). IR (KBr) cm^{-1}: 3400, 1595. UV (MeOH) nm (ε): 228 (79000), 270 (22000). ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 1.46, 1.47 (3H each, both s, 11-, 12-H_3), 1.48 (3H, d, *J*=6.4 Hz, 14-H_3), 3.88 (3H, s, 8-OCH_3), 3.94 (3H, s, 7-OCH_3), 5.02 (1H, q, *J*=6.4 Hz, 13-H), 5.55 (1H, d, *J*=9.8 Hz, 3-H), 6.24 (1H, d, *J*=9.8 Hz, 4-H), 6.74 (1H, s, 5-H). ^{13}C-NMR (125 MHz, $CDCl_3$, δ_C): 23.6 (14-C), 27.3, 28.0 (11-C, 12-C), 61.0 (8-OMe), 61.4 (7-OMe), 65.8 (13-C), 76.5 (2-C), 117.9 (5-C), 118.0 (10-C), 122.1 (4-C), 129.4 (3-C), 130.2 (6-C), 141.2 (8-C), 145.9 (9-C), 150.8 (7-C). FAB-MS *m/z*: 265 (M+H)$^+$. High-resolution FAB-MS *m/z*: Calcd for $C_{15}H_{21}O_4$: 265.1440. Found: 265.1451 (M+H)$^+$.

Orthosiphonone A (**6**): Colorless needles from ether, mp 127—130 °C, $[\alpha]_D$ −118° (*c*=0.99, in $CHCl_3$ at 22 °C). IR (KBr) cm^{-1}: 3450, 1728, 1285, 1238. UV (MeOH) nm (ε): 228 (11000), 274 (400). ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 0.97 (3H, s, 18-H_3), 1.14 (3H, s, 17-H_3), 1.21 (3H, s, 19-H_3), 1.50 (3H, s, 20-H_3), 1.95 (3H, s, 2-$COCH_3$), 2.01—2.12 (2H, m, 6-H_2), 2.12 (3H, s, 7-$COCH_3$), 2.46 (1H, dd, *J*=2.9, 12.7 Hz, 5-H), 2.64 (1H, d, *J*=18.0 Hz, 12-Ha), 2.76 (1H, d, *J*=18.0 Hz, 12-Hb), 3.54 (1H, s, 9-H), 4.26 (1H, d, *J*=10.4 Hz, 16-Ha), 4.72 (1H, d, *J*=17.7 Hz, 16-Hb), 5.29 (1H, dd, *J*=10.4, 17.7 Hz, 15-H), 5.33 (1H, br d, *J*=3.7 Hz, 3-H), 5.45 (1H, br s, 7-H), 5.75 (1H, dd, *J*=3.7, 3.7 Hz, 2-H), 6.44 (1H, d, *J*=3.7 Hz, 1-H), 7.10 (2H, dd, *J*=7.6, 7.6 Hz), 7.41 (1H, dd, *J*=7.6, 7.6 Hz), 7.86 (2H, d, *J*=7.6 Hz) (3-COPh), 7.30 (2H, dd, *J*=7.6, 7.6 Hz), 7.52 (1H, dd, *J*=7.6, 7.6 Hz), 8.02 (2H, d, *J*=7.6 Hz) (1-COPh). ^{13}C-NMR (125 MHz, $CDCl_3$, δ_C): 16.7 (20-C), 20.8 (2-$\underline{C}H_3CO$), 20.9 (7-$\underline{C}H_3CO$), 21.1 (6-C), 22.3 (19-C), 25.2 (17-C), 28.2 (18-C), 36.2 (5-C), 37.8 (4-C), 43.2 (10-C), 47.6 (12-C), 49.2 (13-C), 51.8 (9-C), 65.7 (2-C), 71.0 (7-C), 73.8 (1-C), 76.3 (3-C), 76.6 (8-C), 116.9 (16-C), 128.1, 130.0, 130.3, 133.5 (1-$\underline{Ph}CO$), 128.1, 129.6, 130.1, 132.8 (3-$\underline{Ph}CO$), 138.5 (15-C), 164.4 (3-Ph$\underline{C}O$), 166.4 (1-Ph$\underline{C}O$), 168.3 (7-$CH_3\underline{C}O$), 170.3 (2-$CH_3\underline{C}O$), 205.2 (11-C), 207.6 (14-C). FAB-MS *m/z*: 675 (M+H)$^+$, 681 (M+Li)$^+$. High-resolution FAB-MS *m/z*: Calcd for $C_{38}H_{42}LiO_{11}$: 681.2887. Found: 681.2893 (M+Li)$^+$.

Orthosiphonone B (**7**): Colorless needles from ether, mp 127—130 °C, $[\alpha]_D$ −51° (*c*=0.49, in $CHCl_3$ at 17 °C). IR (KBr) cm^{-1}: 3400, 1730, 1282, 1236. UV (MeOH) nm (ε): 228 (12,000), 274 (1,000). ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 1.12 (3H, s, 18-H_3), 1.18 (3H, s, 17-H_3), 1.25 (3H, s, 19-H_3), 1.82 (3H, s, 20-H_3), 1.94 (1H, dd, *J*=1.8, 15.6 Hz, 12-Hβ), 2.00 (3H, s, 2-$COCH_3$), 2.04 (1H, br d, *J*=13.3 Hz, 6-Hα), 2.11 (3H, s, 7-$COCH_3$), 2.29 (1H, br t, *J*=13.3 Hz, 6-Hβ), 2.55 (1H, dd, *J*=2.0, 13.3 Hz, 5-H), 2.62 (1H, dd, *J*=5.5, 15.6 Hz, 12-Hα), 3.04 (1H, d, *J*=7.0 Hz, 9-H), 4.71 (1H, d, *J*=11.0 Hz, 16-Ha), 4.78 (1H, d, *J*=17.7 Hz, 16-Hb), 5.47 (1H, d, *J*=2.4 Hz, 2-H), 5.49 (1H, br s, 7-H), 5.68 (1H, dd, *J*=11.0, 17.7 Hz, 15-H), 5.92 (1H, ddd, *J*=1.8, 5.5, 7.0 Hz, 11-H), 5.95 (1H, d, *J*=2.4 Hz, 1-H), 7.10 (2H, dd, *J*=7.6, 7.6 Hz, 3-COPh), 7.30 (2H, dd, *J*=7.6, 7.6 Hz, 1-COPh), 7.41 (1H, dd, *J*=7.6, 7.6 Hz, 3-COPh), 7.52 (1H, dd, *J*=7.6, 7.6 Hz, 1-COPh), 7.86 (2H, d, *J*=7.6 Hz, 3-COPh), 8.02 (2H, d, *J*=7.6 Hz, 1-COPh). ^{13}C-NMR (125 MHz, $CDCl_3$, δ_C): 16.3 (20-C), 20.6 (2-$\underline{C}H_3CO$), 20.9 (7-$\underline{C}H_3CO$), 21.6 (18-C), 22.4 (6-C), 25.2 (19-C), 26.1 (17-C), 39.8 (12-C), 41.9 (5-C), 42.0 (9-C), 43.2 (10-C), 47.6 (4-C), 48.1 (13-C), 68.4 (11-C), 70.5 (7-C), 72.6 (2-C), 75.7 (8-C), 77.0 (1-C), 113.5 (16-C), 128.1, 129.6, 130.0, 133.0 (1-$\underline{Ph}CO$), 128.0, 129.9, 130.7, 132.6 (11-$\underline{Ph}CO$), 141.7 (15-C), 163.6 (1-Ph$\underline{C}O$), 166.2 (11-Ph$\underline{C}O$), 170.3 (7-$CH_3\underline{C}O$), 168.7 (2-$CH_3\underline{C}O$), 205.8 (3-C), 208.3 (14-C). FAB-MS *m/z*: 675 (M+H)$^+$, 681 (M+Li)$^+$. High-resolution FAB-MS *m/z*: Calcd for $C_{38}H_{42}LiO_{11}$: 681.2887. Found: 681.2881 (M+Li)$^+$.

Reduction of Methylripariochromene A (1) with $NaBH_4$ Methylripariochromene A (**4**, 10 mg, 0.038 mmol) in methanol (2.0 ml) was treated with sodium borohydride ($NaBH_4$, 2 mg, 0.053 mmol) and the whole was stirred at room temperature for 1 h. The reaction mixture was quenched with water, and extracted with EtOAc. The EtOAc extract was washed with aqueous saturated NaCl and dried over $MgSO_4$. Removal of the solvent under reduced pressure and separation by silica gel chromatography (SiO_2, 2 g, *n*-hexane : EtOAc=3 : 1) gave the product (9 mg) which was identified with orthochromene A (**3**) by comparison of ^{1}H-NMR, ^{13}C-NMR, IR and UV spectra. Next, the product and orthochromene A (**3**) were analyzed by use of chiral HPLC to determine that both were a 1 : 1 mixture of 13*S* and 13*R* isomers. Chiral HPLC analysis conditions: column, Waters Opti-pack XC (3.9×300 mm); solvent, *n*-hexane : *2*-propanol=98 : 2; flow-rate; 1.0 ml/min; detector; UV (254 nm).

Reduction of Orthosiphonone A (6) with $LiAlH_4$ A solution of orthosiphonone A (**6**, 15 mg) in tetrahydrofuran (THF, 1.5 ml) was added dropwise to a suspension of lithium aluminum hydride (4 mg, 0.11 mmol) in THF (1 ml), and the mixture was stirred at 40 °C for 3 h. The reaction was quenched with aqueous saturated ether and subsequently 4 N aqueous KOH, and the precipitate was removed by filtration. The filtrate was concentrated under reduced pressure to give a product (13 mg) which was purified by reversed-phase HPLC (YMC-Pack ODS-AM, 250×4.6 mm, MeOH : H_2O=1 : 4) to afford **8** (3 mg) and **9** (4 mg).

8: Amorphous solid, $[\alpha]_D$ −11° (*c*=0.18, in MeOH at 20 °C). IR (KBr) cm^{-1}: 3400. ^{1}H-NMR (500 MHz, CD_3OD, δ): 0.94 (3H, s, 19-H_3), 1.00 (3H, s, 18-H_3), 1.35 (3H, s, 20-H_3), 1.42 (3H, s, 17-H_3), 1.44 (1H, 6-Ha), 1.69 (1H, br d, *J*=14.0 Hz, 12-Ha), 2.29 (1H, dd, *J*=3.0, 14.0 Hz, 12-Hb), 2.09 (1H, 6-Hb), 2.11 (1H, br s, 5-H), 2.56 (1H, d, *J*=2.1 Hz, 9-H), 3.46 (1H, br s, 3-H), 3.55 (1H, br s, 14-H), 3.75 (1H, br s, 7-H), 4.00 (1H, br s, 2-H), 4.44 (1H, br s, 11-H), 4.8 (2H, 16-H_2), 5.89 (1H, dd, *J*=10.9, 17.6 Hz, 15-H). ^{13}C-NMR (125 MHz, CD_3OD, δ_C): 18.3 (20-C), 22.9 (19-C), 27.5 (17-C), 27.7 (6-C), 29.5 (18-C), 35.2 (5-C), 39.3 (4-C), 39.4 (12-C), 39.7 (13-C), 42.2 (9-C), 44.9 (10-C), 66.0 (2-C), 69.8 (11-C), 77.1 (8-C), 78.1 (7-C), 79.1 (1-C), 82.7 (3, 14-C), 110.1 (16-C), 150.4 (15-C). FAB-MS *m/z*: 387 (M+H)$^+$, 393 (M+Li)$^+$. High-resolution FAB-MS *m/z*: Calcd for $C_{20}H_{34}LiO_7$: 393.2465. Found: 393.2463 (M+Li)$^+$.

9: Amorphous solid, $[\alpha]_D$ −29° (*c*=0.25, in MeOH at 18 °C). IR (KBr) cm^{-1}: 3450. ^{1}H-NMR (500 MHz, CD_3OD, δ): 0.91 (3H, s, 19-H_3), 1.00 (3H, s, 18-H_3), 1.25 (3H, s, 20-H_3), 1.35 (3H, s, 17-H_3), 1.44 (1H, br d,

J=13.1 Hz, 6-Ha), 1.60 (1H, dd, J=4.3, 11.0 Hz, 12-Ha), 1.95 (1H, dd, J=11.0, 11.0 Hz, 12-Hb), 2.07 (1H, ddd, J=2.1, 13.1, 13.1 Hz, 6-Hb), 2.27 (1H, dd, J=1.8, 13.1 Hz, 5-H), 2.33 (1H, d, J=11.0 Hz, 9-H), 3.27 (1H, br s, 14-H), 3.38 (1H, br s, 3-H), 3.75 (1H, d, J=2.1 Hz, 7-H), 4.00 (1H, br s, 2-H), 4.33 (1H, ddd, J=4.3, 11.0, 11.0 Hz, 11-H), 4.96 (1H, d, J=17.4 Hz, 16-Ha), 4.97 (1H, d, J=11.3 Hz, 16-Hb), 5.89 (1H, dd, J=11.3, 17.4 Hz, 15-H). ^{13}C-NMR(125 MHz, CD_3OD, δ_C): 16.8 (20-C), 22.5 (19-C), 25.2 (17-C), 26.5 (6-C), 29.7 (18-C), 34.3 (5-C), 39.5 (4-C), 42.2 (12-C), 43.3 (13-C), 44.4 (9-C), 45.4 (10-C), 66.1 (2-C), 67.5 (11-C), 76.9 (8-C), 77.7 (7-C), 80.3 (1-C), 82.5 (3-C), 82.9 (14-C), 111.1 (16-C), 149.0 (15-C). FAB-MS m/z: 387 $(M+H)^+$, 393 $(M+Li)^+$. High-resolution FAB-MS m/z: Calcd for $C_{20}H_{34}LiO_7$: 393.2465. Found: 393.2457 $(M+Li)^+$.

Reduction of Orthosiphol A (4) with $LiAlH_4$ A solution of orthosiphol A (**4**, 10 mg) in THF (1 ml) was added dropwise to a suspension of lithium aluminum hydride (3 mg, 0.08 mmol) in THF (1 ml) and the whole was stirred at 40 °C for 3 h. The reaction was quenched with aqueous saturated ether and subsequently 4 N aqueous KOH, and the precipitate was removed by filtration. The filtrate was concentrated under reduced pressure to give a product (13 mg). The product was purified by reversed-phase HPLC (YMC-Pack ODS-AM, 250×4.6 mm, MeOH : H_2O=1 : 4) to afford the product (3 mg), which was identified with **9** by comparison of ^{1}H-NMR, ^{13}C-NMR and IR spectra and $[\alpha]_D$.

Oxidation of Orthosiphol B (5) A solution of orthosiphol B (**5**, 0.0014 mmol, 6 mg) in CH_2Cl_2 (1.0 ml) was treated with a solution of PCC (4 mg) in CH_2Cl_2 at room temperature for 2 h, then the reaction mixture was quenched with dried ether. The precipitate was removed by Florisil column and the filtrate was concentrated under reduced pressure to give a product (7 mg), which was purified by silica gel column chromatography (SiO_2 2 g, n-hexane : EtOAc=2 : 1) to afford orthosiphonone B (**7**, 5 mg, 0.0074 mmol, 83%).

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