The Constituents of the Root and Stem of *Aristolochia heterophylla* Hemsl

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Seven new compounds, sodium aristolochate-VII (1), aristolactam-CIV (2), madolin-I (3), -J (4), -K (5), -L (6) and -M (7) together with 71 known compounds were isolated and characterized from the fresh root and stem of *Aristolochia heterophylla* Hemsl. Their structures were determined by spectral methods. Compound 8 was revised as aromadendrane-4 β , 10 β -diol by spectral data and single-crystal X-ray analysis.

Key words *Aristolochia heterophylla*; Aristolochiaceae; madolin-I–M; sesquiterpene; aromadendrane-4 β , 10 β -diol

Aristolochia heterophylla Hemsl (*A. shimada*) is a perennial shrub found in the thickets and forests in Mainland China and Taiwan.¹⁾ The root and fruit of this plant have been used in traditional Chinese medicine as an expectorant, antitussive, analgesic, antiasthmatic and also for the treatment of snakebite and lung inflammation.¹⁾ Aristolochic acids, aristolactams, terpenes and other constituents have been isolated from this species.^{2–10)} We report here the isolation and structural elucidation of seven new compounds, sodium aristolochate-VII (1), aristolactam-CIV (2), madolin-I (3), -J (4), -K (5), -L (6) and -M (7), together with 71 known compounds from a methanol extract of the root and stem of *Aristolochia heterophylla* Hemsl.

Results and Discussion

Sodium aristolochate-VII (1) was isolated as yellowish needles. The UV absorption bands at 222, 264, 310, 367 and 372 nm suggested it is an aristolochic acid derivative.¹¹⁾ The IR spectrum showed the presence of a carboxylic salt and a nitro group at 1544, 1514 and 1392 cm⁻¹.¹²⁾ In the ¹H-NMR spectrum of 1, two methoxyl signals appeared at δ 3.98 and 4.00 (each 3H, s). In the aromatic region, two singlet signals at δ 7.71 and 8.41 were ascribed to H-2 and H-9, respectively. A methylenedioxy group was indicated based on the singlet at δ 6.46. AB type signals at δ 8.80 and 7.74 (each 1H, d, $J=9.5$ Hz) were assigned to H-5 and H-6, respectively. The signal of H-5 appeared at a relatively lower field, at δ 8.80, due to the deshielding effect of the A ring. Compound 1 was dissolved in 5% HCl, applied to a Sephadex LH-20 column and eluted successively with H₂O and MeOH. The residue obtained from the H₂O fraction was confirmed to be a sodium ion by atomic absorption spectroscopy. The MeOH eluted fraction involved methylation with excess CH₂N₂ to afford 1a, which was identified as aristolochic acid-VII methyl ester.¹³⁾ Thus, compound 1 was assigned as sodium aristolochate-VII.

Aristolactam-CIV (2) was obtained as yellowish needles. The mass spectrum showed a molecular ion peak at m/z 325.0956, implying the molecular formula C₁₈H₁₅NO₅. The UV absorption bands at 207, 239, 253, 281, 293, 316 and 399 nm suggested a phenanthrene derivative.¹¹⁾ The IR spectrum revealed a lactamic carbonyl based on the absorption band at 1705 cm⁻¹. In the ¹H-NMR spectrum, two methoxyl and one hydroxymethyl groups appeared at δ 3.98, 4.02 (each 3H, s) and 5.27 (2H, s), respectively. The aromatic region of the spectrum showed an ABX pattern at δ 7.22 (1H,

dd, $J=8.0, 2.0$ Hz), 7.78 (1H, d, $J=8.0$ Hz) and 8.66 (1H, d, $J=2.0$ Hz) attributable to H-7, H-8 and H-5, respectively. One singlet at δ 7.11 (1H, s) was assigned to H-9. The nuclear overhauser and exchange spectroscopy (NOESY) experiment (Fig. 1) showed that both the methoxy groups had correlations with H-5, indicating that the methoxy groups are located at C-4 and C-6. In addition, evidence for the location of the hydroxymethyl group in aristolactam-CIV was mainly inferred from the results of literature which showed that hydroxymethyl or carbonyl groups were substituted at C-2, only.^{14–18)} On the basis of the above results, the structure of aristolactam-CIV was established as 2.

Madolin-I (3) was isolated as an optically active oil, and its molecular formula, C₁₅H₁₈O₃ (M^+ at m/z 246.1258), indicated seven degrees of unsaturation. The presence of α,β -unsaturated γ -lactone was inferred by the IR band at 1751 cm⁻¹, the ¹³C-NMR spectra at δ 174.3 (s), 150.4 (d), 132.5 (s), 82.7 (d) and the ¹H-NMR spectra at δ 6.88 (1H, s), 4.94 (1H, s). The ¹H-NMR and the heteronuclear multiple quantum coherence (HMQC) spectra displayed two terminal methylene groups at δ 5.73 (1H, d, $J=1.4$ Hz), 5.57 (1H, d, $J=2.3$ Hz), 4.84 (1H, s) and 4.75 (1H, s), as well as one olefinic methyl group at δ 1.76 (3H, s). The presence of a bicyclic skeleton in the molecule can be deduced based on the unsaturation values and its evident unsaturated groups (two terminal methylene, an α,β -unsaturated γ -lactone and one carbonyl signal at δ 206.8 in the ¹³C-NMR spectrum). The correlation spectroscopy (COSY) and HMQC spectra readily established the presence of one CH₂=C–CH₂CH₂CH– and one –CH₂CH₂– partial structure. The above fragments could be arranged as shown in formula 3 on the basis of the heteronuclear multiple bond coherence (HMBC) experiment (Fig. 2). On the other hand, the configurations of H-6 and H-7 were determined to be 3 based on the cross peak between H-7 (δ 2.32) with H-6 (δ 4.94) and H-3 α (δ 2.65); and between H-3 β (δ 2.48) with H-13 (δ 1.76) and H-12 (δ 4.75, 4.84) in the NOESY experiment (Fig. 1), together with the comparison of aristolactone 3a.¹⁹⁾ Based on the above analysis, structure 3 was assigned for madolin-I.

Madolin-J (4) was isolated as a colorless oil. The high resolution mass spectrum (HR-MS) showed a $[M]^+$ at m/z 232.1463, corresponding to the molecular formula C₁₅H₂₀O₂ and six degrees of unsaturation. The IR absorption band at 1789 cm⁻¹ and the signal at δ 179.2 (s) in the ¹³C-NMR spectrum suggested the existence of a γ -lactone. The ¹H-NMR and ¹³C-NMR spectra of 4 indicated the presence of

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two sets of trisubstituted double bonds (δ_{H} : 5.20, δ_{C} : 156.0, 109.1; δ_{H} : 5.16, δ_{C} : 131.8, 126.9) and one terminal methylene group (δ_{H} : 4.82, 4.80, δ_{C} : 144.9, 111.4). The presence of these three double bonds and one γ -lactone indicated a bicyclic structure for **4**. The COSY and HMQC spectra established the presence of $-\text{O}-\text{C}=\text{CH}-\text{CH}-\text{CH}_2-\text{CH}_2-\text{CH}=\text{C}-\text{CH}_3$, $\text{CH}_2=\text{C}-\text{CH}_3$ and $-\text{CH}-\text{CH}_2-\text{CH}_2-$ partial structures. The connection of the partial structures was clarified by means of a HMBC experiment, as shown in Fig. 2. Based on the above information, structure **4** was established for madolin-J.

Madolin-K (**5**), a colorless oil with a molecular formula of $\text{C}_{15}\text{H}_{22}\text{O}_2$ (M^+ at m/z 234.1630) indicated five degrees of unsaturation. Compound **5** was revealed by the following spectroscopic evidence to be a bicyclic sesquiterpenoid which contained a formyl group conjugated with a trisubstituted double bond [λ_{max} 260 nm; ν_{max} 1676 cm^{-1} ; δ_{H} : 6.29 (1H, d, $J=9.6$ Hz) and 9.28 (1H, s); δ_{C} : 194.3 (d), 154.2 (d) and 143.7 (s)] as well as another trisubstituted double bond bearing a methyl group [δ_{H} : 1.25 (3H, s) and 5.07 (1H, dd, $J=11.2$, 5.2 Hz); δ_{C} : 134.5 (s) and 124.5 (d)]. In addition, the ^1H - and ^{13}C -NMR signals showed the presence of a partial structure A [δ_{H} : 1.07 (1H, m), 1.28 (3H, s), 1.65 (1H, dd, $J=9.6$, 9.6 Hz), 3.42 (1H, d, $J=11.0$ Hz) and 3.51 (1H, d, $J=$

11.0 Hz); δ_{C} : 72.1 (t), 33.9 (d), 27.3 (s), 26.4 (d), 11.6 (q)], which was also supported by a long range correlation of H-12 and H-13 to C-6 and C-7 in the HMBC spectrum (Fig. 2). In order to confirm the structure of **5**, two-dimensional (2D) shift COSY and long range $^{13}\text{C}-^1\text{H}$ correlation in the HMBC experiment were conducted. The above spectral evidence disclosed the plane structure of madolin-K. The 9.6 Hz coupling constant and nuclear Overhauser effect (NOE) between H-6 and H-7 indicated a *cis* configuration of a cyclopropane moiety.²⁰⁾ On the other hand, the configuration of C-11 was determined to be **5** due to a cross peak between H-6 (δ 1.65) with H-12 (δ 3.42) in the NOESY experiment (Fig. 1). On the basis of above results, structure **5** was assigned for madolin-K.

Madolin-L (**6**) was obtained as an optically active colorless oil, and the molecular formula was determined to be $\text{C}_{16}\text{H}_{24}\text{O}_2$ by HRMS (M^+ , m/z 248.1785). The IR spectrum showed an α,β -unsaturated carbonyl band at 1692 cm^{-1} . The ^1H -NMR spectrum of madolin-L displayed three signals of olefinic protons at δ 6.16 (d, $J=11.0$ Hz), 4.98 (t, $J=7.7$ Hz) and 4.74 (t, $J=7.4$ Hz). The ^{13}C -NMR spectrum of **6** also showed six signals of olefinic carbons. Obviously, two of the double bonds are substituted by a methyl group, which showed a correlation in the COSY spectrum with olefinic

Fig. 1. NOESY Correlations of 2—8

Fig. 2. HMBC Correlations of 3—7

protons at δ 4.98 and 4.74, respectively. In addition, the presence of one methoxyl, two methylene groups and two partial structures, $-\text{CH}_2-\text{CH}(\text{O})-\text{CH}=\text{C}-\text{CHO}$ and $-\text{CH}=\text{C}-\text{CH}_2\text{CH}_2-$ in **6**, were solved by COSY and HMQC spectra. The connections of the partial structures were established by HMBC experiment (Fig. 2). The NOESY experiment of **6** (Fig. 1) showed that all of the $\Delta^{2,3}$, $\Delta^{6,7}$ and $\Delta^{10,11}$ double bonds had *E* configurations, and the optical rotation of **6** indicated that the stereochemistry of the methoxyl group at C-4 is *R*.⁷⁾ Based on the above analyses, madolin-L has structure **6**.

Madolin-M (**7**) was isolated as an optically active oil and was determined to have the molecular formula $\text{C}_{16}\text{H}_{24}\text{O}_2$. It exhibited spectral data similar to madolin-L (**6**). The striking differences included three signals for more deshielded H-1, H-4, H-13 and two signals for shielded H-3 and H-13. The structure was assigned using the COSY, HMQC, HMBC (Fig. 2) and NOESY (Fig. 1) experiments, as shown for **7**. The *Z* configuration of $\Delta^{2,3}$ was supported by a clear correlation between the aldehyde (δ 10.05) and H-4 (δ 4.70) in the NOESY experiment. In addition, the *R* configuration at C-4 was determined by the negative optical rotation.⁷⁾ From the above results, the structure of madolin-M was assigned as **7**.

Aromadendrane-4 β , 10 β -diol (**8**) was isolated as optically active colorless prisms, mp 136—137 °C, with a molecular

Fig. 3. X-Ray Structure of **8**

formula of $\text{C}_{15}\text{H}_{26}\text{O}_2$, which was confirmed by mass spectrometry. The IR absorption band at 3396 cm^{-1} showed the presence of a hydroxyl group in the molecular structure. The NMR spectra (^1H , ^{13}C , COSY, HMQC, HMBC) analyses indicated compound **8** presented four tertiary methyls, four methylenes, four methines and three quaternary carbons (including two bearing oxygen tertiary carbons). According to the above data, the structure of **8** is similar to aromadendrane-4 α , 10 β -diol (**8a**), which was isolated from *Brasilia sickii* by Bohlmann *et al.*²⁰⁾ However, a single-crystal X-ray analysis (Fig. 3) and NOESY experiment (Fig. 1) indicated that the relative stereochemistry of the hydroxyl group at C-4

and C-10 both had β -orientations, respectively. Consequently, the structure of **8** was suggested to be aromaden-drane-4 β , 10 β -diol.

The known compounds aristofolin-B (**9**),²¹ aristolide-A (**10**),⁹ -B (**11**),⁹ borneol (**12**),²² morindaparvin-A (**13**),²¹ *N*-trans-feruloyltyramine (**14**),²³ *N*-cis-feruloyltyramine (**15**),²³ allantoin (**16**),²³ isorhamnetin-3-*O*-robinobioside (**17**),²³ sodium aristolochate-I (**18**),¹² -II (**19**),²⁴ -C (**20**),¹² -IVa (**21**),²⁴ sodium 7-hydroxyaristolochate-A (**22**),¹² aristolochic acid-II (**23**),²³ -C (**24**),²³ -IVa (**25**),²³ methyl aristolochate (**26**),²¹ aristolochic acid II methyl ester (**27**),²³ methyl isovanillate (**28**),²⁵ methyl vanillate (**29**),²³ methyl 22-feruloyloxydocosanoate (**30**),²⁶ vanillin (**31**),¹⁴ vanillic acid (**32**),¹⁴ ferulic acid (**33**),¹⁴ syringic acid (**34**),²⁷ methyl 3,4-dihydroxybenzoate (**35**),²⁸ picrorhizin (**36**),²⁹ methyl paraben (**37**),²³ methyl aristolate (**38**),¹³ cuminyl alcohol (**39**),³⁰ aristolic acid (**40**),¹³ 4,5-dioxodehydroasimilobine (**41**),¹³ cepharadione-A (**42**),²³ aristolactam-BII (**43**),¹³ -AII (**44**),¹³ -AIIa (**45**),¹⁴ -IIIa (**46**),¹⁴ 9-methoxyaristolactam-I (**47**),²³ aristolactam (**48**),²³ piperolactam-A (**49**),³¹ aristolactam-C-*N*- β -D-glucoside (**50**),²³ aristolactam-*N*- β -D-glucoside (**51**),²³ cepharanone-A-*N*- β -D-glucoside (**52**),²³ *trans*-ferulyl esters (**53**),²³ *cis*-ferulyl esters (**54**),²³ β -sitosterol (**55**),¹³ stigmasterol (**56**),²⁴ β -sitosterylglucoside (**57**),¹³ stigmaster-4-en-3,6-dione (**58**),²⁴ aristophyllide-A (**59**),⁸ -B (**60**),⁸ -C (**61**),⁸ -D (**62**),⁸ aristoloterpenate-I (**63**),⁷ -II (**64**),⁷ -III (**65**),⁷ -IV (**66**),⁷ madolin-A (**67**),¹⁹ -B (**68**),¹⁹ -E (**69**),¹⁹ -F (**70**),¹⁰ -G (**71**),¹⁰ -H (**72**),¹⁰ versicolactone-B (**73**),³² aristolactone (**74**),¹⁹ versicolactone-C (**75**),³² manshurolide (**76**),¹⁹ versicolactone-D (**77**),³³ and 1,10-epoxylepidozenal (**78**)³⁴ were also isolated. Their structures were elucidated by comparison of their spectroscopic data (UV, IR, NMR, mass spectrometry) with values in the literature.

Experimental

General Procedures Melting points (Yanagimoto apparatus) are uncorrected. Optical rotations were recorded on a Jasco DIP-370 digital polarimeter. UV spectra of the MeOH solution were obtained on a Hitachi UV-3210 spectrophotometer. The IR spectra of the KBr of discs were recorded on a Shimadzu FT-IR DR-8011 spectrophotometer. Mass and HR mass spectra were measured on a VG-70-250S spectrometer having a direct inlet system. ¹H-NMR and ¹³C-NMR spectra were determined on Bruker AMX-400 and Varian Unity plus 400 spectrometers. Chemical shifts are shown in δ values (ppm) with tetramethylsilane (TMS) as an internal standard.

Plant Material *Aristolochia heterophylla* Hemsl was collected from Tsueg Feng, Nantou Hsien, Taiwan, in May, 1992 and verified by Prof. C.-S. Kuoh. A voucher specimen is deposited in the Herbarium of National Cheng Kung University, Taiwan.

Extraction and Isolation The fresh root and stem (4.5 kg) of *Aristolochia heterophylla* Hemsl were extracted with MeOH ($\times 5$) at room temperature and concentrated under reduced pressure into a brown syrup. To the distilled MeOH was added H₂O, followed by partitioning with Et₂O. The MeOH extract was partitioned successively between H₂O and CHCl₃, then *n*-BuOH. The Et₂O layer was chromatographed directly on silica gel and eluted with *n*-hexane-iso-Pr₂O (9:1) to afford **6** (4 mg), **7** (2 mg), **12** (28 mg), **67** (4 mg), **68** (10 mg) and **78** (1 mg). The CHCl₃ extract was filtered to give **18** (135 mg) and the filtrate was subjected to chromatography on a silica gel column and eluted with gradients of CHCl₃-MeOH (99:1) to afford 7 fractions. Fraction 2 was rechromatographed on silica gel and eluted with *n*-hexane-EtOAc (19:1) to give **4** (12 mg), **8** (24 mg), **26** (22 mg), **38** (6 mg), **53** (5 mg), **54** (3 mg), **58** (180 mg), **59** (9 mg), **60** (3 mg), **61** (7 mg), **62** (1 mg), **63** (15 mg), **64** (2 mg), **65** (4 mg), **66** (1 mg), **69** (8 mg), **72** (16 mg), **76** (230 mg) and **77** (12 mg). Fractions 3 and 4 were combined and underwent chromatography on silica gel using *n*-hexane-EtOAc (19:1) as an eluent to afford **4** (12 mg), **10** (2 mg), **11** (5 mg), **13** (2 mg), **27** (2 mg), **28** (1 mg), **29** (2 mg), **30** (6 mg), **31** (7 mg), **39** (1 mg), **48** (5 mg), **55** (532 mg), **56** (267 mg), **70** (4 mg), **71** (2 mg) and **74** (565 mg), successively. Fractions 5

and 6 were also combined and separated by chromatography on silica gel using CHCl₃-Me₂CO (12:1) as an eluent to give **3** (12 mg), **42** (3 mg), **43** (1 mg), **47** (12 mg), **49** (26 mg) and **73** (375 mg). Fraction 7 underwent chromatography on silica gel and was eluted with a gradient of CHCl₃-MeOH (19:1) to give **2** (1 mg), **14** (7 mg), **15** (9 mg), **40** (220 mg), **41** (31 mg), **44** (26 mg), **57** (12 mg) and **75** (5 mg). The *n*-BuOH layer underwent chromatography on Diaion HP-20 and was eluted with a gradient of H₂O-MeOH to give 9 fractions. Fraction 1 was filtered to give **16** (7 g). Fractions 4 and 5 were combined and chromatographed on Sephadex LH-20 using a gradient of H₂O-MeOH to afford **34** (3 mg), **35** (7 mg) and **37** (2 mg). Fraction 6 also underwent chromatography on Sephadex LH-20 and was eluted with a gradient of H₂O-MeOH to give **17** (510 mg), **36** (5 mg) and **50** (34 mg). Fraction 7 was separated by chromatography on silica gel using CHCl₃-MeOH-H₂O (3:1:0.1) as an eluent to obtain **45** (9 mg) and **52** (36 mg), respectively. Fraction 8 was rechromatographed on silica gel and eluted with CHCl₃-MeOH-H₂O (5:1:0.1) to give **20** (3 mg), **21** (4 mg), **25** (14 mg), **46** (7 mg) and **51** (43 mg). Fraction 9 was also separated by chromatography on silica gel using CHCl₃-MeOH-H₂O (5:1:0.1) to give **1** (2 mg), **9** (5 mg), **19** (12 mg), **22** (2 mg), **23** (2 mg), **24** (4 mg), **32** (4 mg) and **33** (4 mg), successively.

Sodium Aristolochate-VII (1): Yellowish needles. mp: >280°C. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm: 222, 264, 310, 367, 372. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1544 (C=O), 1514, 1392, 1286, 1253, 1087, 1035, 939 (OCH₃). ¹H-NMR (DMSO-*d*₆, 200 MHz) δ : 3.98 (3H, s, OCH₃), 4.00 (3H, s, OCH₃), 6.46 (2H, s, OCH₂O), 7.71 (1H, s, H-2), 7.74 (1H, d, *J*=9.5 Hz, H-6), 8.41 (1H, s, H-9), 8.80 (1H, d, *J*=9.5 Hz, H-5).

Acidification of 1 Compound **1** was dissolved in 1 ml 5% HCl(aq), applied to a Sephadex LH-20 column and eluted successively with H₂O and MeOH. The residue obtained from the H₂O fraction was confirmed to be a sodium ion by atomic absorption spectroscopy. The MeOH eluted fraction was concentrated and the residue was dissolved in 1 ml MeOH, then excess CH₂N₂ ether solution was added to afford **1a**, which was identified as aristolochic acid-VII methyl ester by the ¹H-NMR and IR spectra.

Aristolactam-CIV (2): Yellowish needles. mp: 206–207°C. HR-FAB-MS: Calcd for C₁₈H₁₅O₅, *m/z*: 325.0950 [M⁺]. Found: 325.0956. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 207 (4.54), 239 (4.56), 253 (4.47), 281 (4.33), 293 (4.34), 316 (sh, 4.09), 399 (3.63). IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3202, 1705 (C=O), 1618, 1504, 1421, 1350, 1296. FAB-MS *m/z* (rel. int.): 326 ([M⁺+1, 3], 325 ([M⁺, 4], 307 (17), 289 (12), 176 (24), 15 (24), 154 (100), 152 (13), 139 (15), 138 (30), 137 (52), 136 (77), 120 (13), 107 (28), 105 (11), 91 (10). ¹H-NMR (CD₃OD-*d*₄, 400 MHz) δ : 3.98 (3H, s, OCH₃), 4.02 (3H, s, OCH₃), 5.25 (2H, s, OCH₂O), 7.11 (1H, s, H-9), 7.22 (1H, dd, *J*=8.0, 2.0 Hz, H-7), 7.78 (1H, d, *J*=8.0 Hz, H-8), 8.66 (1H, d, *J*=2.0 Hz, H-5).

Madolin-I (3): Colorless oil. $[\alpha]_D^{25} + 141.3^\circ$ (*c*=0.07, CHCl₃). HR-EI-MS: Calcd for C₁₅H₁₈O₃, *m/z*: 246.1255 [M⁺]. Found: 246.1258. UV $\lambda_{\text{max}}^{\text{MeOH}}$ (log ϵ) nm: 213 (4.05). IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 2925, 2860, 1751, 1679, 1453, 1064, 935. EI-MS *m/z* (rel. int.): 246 ([M⁺, 9], 203 (19), 150 (30), 149 (19), 138 (16), 135 (57), 121 (13), 117 (15), 108 (42), 107 (36), 105 (14), 95 (46), 93 (33), 91 (50), 81 (25), 79 (39), 77 (39), 53 (100). ¹H-NMR (CDCl₃, 400 MHz) δ : 1.49 (1H, ddd, *J*=15.2, 11.1, 9.6 Hz, H-8), 1.76 (3H, s, 13-CH₃), 1.77 (1H, m, H-8), 1.87 (1H, dd, *J*=15.9, 9.6 Hz, H-9), 2.32 (1H, dd, *J*=11.1, 2.1 Hz, H-7), 2.46 (1H, dd, *J*=15.9, 7.2 Hz, H-9), 2.48 (1H, ddd, *J*=12.0, 10.4, 2.6 Hz, H-3), 2.51 (1H, dd, *J*=17.0, 2.6 Hz, H-2), 2.65 (1H, dd, *J*=12.0, 3.1 Hz, H-3), 3.39 (1H, ddd, *J*=17.0, 10.4, 3.1 Hz, H-2), 4.75 (1H, s, H-12), 4.84 (1H, s, H-12), 4.94 (1H, d, *J*=14.0, 5.57 (1H, d, *J*=2.3 Hz, H-14), 5.73 (1H, d, *J*=1.4 Hz, H-14), 6.88 (1H, s, H-5). ¹³C-NMR (CDCl₃, 100 MHz) δ : 21.3 (C-13), 23.3 (C-3), 27.5 (C-8), 28.0 (C-9), 37.6 (C-2), 52.2 (C-7), 82.7 (C-6), 112.2 (C-12), 124.4 (C-14), 132.5 (C-4), 147.7 (C-11), 150.4 (C-5), 152.2 (C-10), 174.4 (C-15), 206.8 (C-1).

Madolin-J (4): Colorless oil. $[\alpha]_D^{25} + 140.3^\circ$ (*c*=0.12, CHCl₃). HR-EI-MS: Calcd for C₁₅H₂₀O₂, *m/z*: 232.1463 [M⁺]. Found: 232.1463. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3089, 2923, 2854, 1789, 1645, 1446, 1120, 977, 927. EI-MS *m/z* (rel. int.): 232 ([M⁺, 48], 217 (7), 204 (11), 189 (10), 177 (14), 162 (11), 149 (14), 138 (26), 120 (27), 107 (57), 93 (48), 79 (49), 67 (100). ¹H-NMR (CDCl₃, 400 MHz) δ : 1.48 (1H, m, H-8), 1.70 (3H, s, H-14), 1.72 (3H, s, H-13), 1.75 (1H, ddd, *J*=14.0, 5.4, 2.0 Hz, H-3), 1.95 (1H, dddd, *J*=14.0, 12.3, 12.3, 2.0 Hz, H-8), 2.06 (1H, m, H-2), 2.13 (1H, dddd, *J*=14.0, 6.9, 6.9, 2.0 Hz, H-3), 2.20 (1H, ddd, *J*=12.3, 12.3, 2.0 Hz, H-9), 2.52 (1H, m, H-9), 2.56 (1H, dddd, *J*=12.2, 12.2, 6.9, 5.4 Hz, H-2), 3.03 (1H, dd, *J*=12.3, 3.6 Hz, H-7), 3.30 (1H, ddd, *J*=6.9, 2.0, 2.0 Hz, H-4), 4.80 (1H, s, H-12), 4.82 (1H, s, H-12), 5.16 (1H, d, *J*=12.2 Hz, H-1), 5.20 (1H, d, *J*=2.0 Hz, H-5). ¹³C-NMR (CDCl₃, 100 MHz) δ : 14.9 (C-14), 21.5 (C-13), 22.7 (C-8), 25.2 (C-2), 26.0 (C-3), 40.5 (C-9), 44.0 (C-4), 48.3 (C-7), 109.1 (C-5), 111.4 (C-12), 126.9 (C-1), 131.8 (C-10), 144.9 (C-11), 156.0 (C-6), 179.2 (C-15).

Madolin-K (5): Colorless oil. $[\alpha]_D^{20} +128.0^\circ$ ($c=0.13$, CHCl_3). HR-EI-MS: Calcd for $\text{C}_{15}\text{H}_{22}\text{O}_2$, m/z : 234.1619 $[\text{M}^+]$. Found: 234.1620. UV $\lambda_{\text{max}}^{\text{MeOH}}$ (log ϵ) nm: 260 (3.92). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 2925, 2858, 1676, 1625, 1515, 1471, 1217. EI-MS m/z (rel. int.): 234 ($[\text{M}^+]$, 14), 216 (47), 201 (11), 187 (30), 175 (21), 161 (23), 146 (71), 134 (40), 119 (34), 107 (92), 91 (100). ^1H -NMR (CDCl_3 , 400 MHz) δ : 0.90 (1H, m, H-8), 1.07 (1H, m, H-7), 1.25 (3H, s, 15- CH_3), 1.28 (3H, s, 13- CH_3), 1.65 (1H, dd, $J=9.6$, 9.6 Hz, H-6), 1.85 (1H, dddd, $J=11.4$, 5.0, 2.4, 2.4 Hz, H-8), 1.99 (1H, dd, $J=12.2$, 4.5 Hz, H-3), 2.07 (1H, ddd, $J=12.5$, 12.5, 2.4 Hz, H-9), 2.12 (1H, m, H-2), 2.15 (1H, m, H-9), 2.20 (1H, m, H-2), 2.77 (1H, ddd, $J=12.2$, 3.4, 3.4 Hz, H-3), 3.42 (1H, d, $J=11.0$ Hz, H-12), 3.51 (1H, d, $J=11.0$ Hz, H-12), 5.07 (1H, dd, $J=11.2$, 5.2 Hz, H-1), 6.29 (1H, d, $J=9.6$ Hz, H-5), 9.28 (1H, d, $J=0.8$ Hz, CHO). ^{13}C -NMR (CDCl_3 , 100 MHz) δ : 11.6 (C-13), 17.3 (C-15), 23.3 (C-8), 23.6 (C-3), 26.4 (C-6), 27.3 (C-11), 27.7 (C-2), 33.9 (C-7), 39.7 (C-9), 72.1 (C-12), 124.5 (C-1), 134.5 (C-10), 143.7 (C-4), 154.2 (C-5), 194.3 (C-14).

Madolin-L (6): Colorless oil. $[\alpha]_D^{20} -88.5^\circ$ ($c=0.05$, CHCl_3). HR-EI-MS: Calcd for $\text{C}_{16}\text{H}_{24}\text{O}_2$, m/z : 248.1776 $[\text{M}^+]$. Found: 248.1785. UV $\lambda_{\text{max}}^{\text{MeOH}}$ (log ϵ) nm: 223 (3.69). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 2924, 2855, 1692, 1462, 1093. EI-MS m/z (rel. int.): 248 ($[\text{M}^+]$, 19), 216 (13), 161 (11), 151 (23), 136 (29), 121 (32), 112 (100), 105 (24), 91 (40). ^1H -NMR (CDCl_3 , 400 MHz) δ : 1.38 (3H, s, H-15), 1.60 (3H, s, H-14), 2.02 (2H, t, $J=5.7$ Hz, H-9), 2.11 (2H, m, H-8), 2.13 (1H, m, H-12), 2.15 (1H, dd, $J=10.0$, 10.0 Hz, H-13), 2.19 (1H, dd, $J=11.0$, 11.0 Hz, H-5), 2.38 (1H, m, H-12), 2.58 (1H, m, H-13), 2.62 (1H, dd, $J=11.0$, 3.8 Hz, H-5), 3.21 (3H, s, OCH_3), 4.04 (1H, ddd, $J=11.0$, 11.0, 3.8 Hz, H-4), 4.74 (1H, t, $J=7.4$ Hz, H-11), 4.98 (1H, t, $J=7.7$ Hz, H-7), 6.16 (1H, d, $J=11.0$ Hz, H-3), 9.47 (1H, s, H-1). ^{13}C -NMR (CDCl_3 , 100 MHz) δ : 15.4 (C-15), 18.6 (C-14), 24.9 (C-8), 25.0 (C-12), 25.4 (C-13), 38.4 (C-9), 44.9 (C-5), 56.1 (OCH_3), 77.0 (C-4), 125.2 (C-11), 128.5 (C-7), 129.8 (C-6), 133.8 (C-10), 145.2 (C-2), 152.8 (C-3), 195.7 (C-1).

Madolin-M (7): Colorless oil. $[\alpha]_D^{20} -23.2^\circ$ ($c=0.03$, CHCl_3). HR-EI-MS: Calcd for $\text{C}_{16}\text{H}_{24}\text{O}_2$, m/z : 248.1776 $[\text{M}^+]$. Found: 248.1781. UV $\lambda_{\text{max}}^{\text{MeOH}}$ (log ϵ) nm: 227 (3.70). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 2924, 2852, 1680, 1454, 1094. EI-MS m/z (rel. int.): 248 ($[\text{M}^+]$, 14), 216 (29), 151 (15), 136 (21), 121 (27), 112 (100), 105 (17), 93 (28). ^1H -NMR (CDCl_3 , 400 MHz) δ : 1.31 (3H, s, H-15), 1.52 (3H, s, H-14), 1.79 (1H, ddd, $J=12.8$, 12.8, 3.6 Hz, H-13), 1.96 (1H, m, H-8), 2.00 (1H, m, H-9), 2.04 (1H, m, H-12), 2.16 (1H, dd, $J=10.8$, 10.8 Hz, H-5), 2.18 (1H, m, H-9), 2.28 (1H, m, H-8), 2.38 (1H, m, H-12), 2.56 (1H, br d, $J=10.8$ Hz, H-5), 2.83 (1H, ddd, $J=12.8$, 3.6, 3.6 Hz, H-13), 3.29 (3H, s, OCH_3), 4.70 (1H, ddd, $J=10.8$, 10.8, 4.4 Hz, H-4), 4.80 (1H, d, $J=11.2$ Hz, H-11), 4.96 (1H, d, $J=10.8$ Hz, H-7), 5.92 (1H, d, $J=10.8$ Hz, H-3), 10.05 (1H, s, H-1). ^{13}C -NMR (CDCl_3 , 100 MHz) δ : 14.9 (C-15), 16.1 (C-14), 25.0 (C-8), 25.8 (C-12), 31.8 (C-13), 39.6 (C-9), 46.2 (C-5), 56.4 (OCH_3), 72.2 (C-4), 125.0 (C-11), 129.0 (C-6), 129.9 (C-7), 135.1 (C-10), 142.3 (C-2), 149.4 (C-3), 190.7 (C-1).

Aromadendrane-4 β ,10 β -diol (8): Colorless prisms. mp: 136–137°C. $[\alpha]_D^{20} -20.2^\circ$ ($c=0.24$, CHCl_3). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3396, 2924, 2862, 1456, 1375, 1109. EI-MS m/z (rel. int.): 238 ($[\text{M}^+]$, 6), 220 (39), 205 (38), 162 (100), 147 (47), 121 (63), 119 (55), 107 (66), 95 (60), 93 (77). ^1H -NMR (CDCl_3 , 400 MHz) δ : 0.40 (1H, ddd, $J=10.7$, 9.6 Hz, H-6), 0.62 (1H, ddd, $J=11.0$, 9.6, 6.0 Hz, H-7), 0.88 (1H, m, H-8), 1.01 (6H, s, H-12, H-13), 1.15 (3H, s, H-15), 1.18 (1H, dd, $J=10.7$, 10.7 Hz, H-5), 1.23 (3H, s, H-14), 1.50–1.90 (8H, m, H-1, 2, 3, 8, 9). ^{13}C -NMR (CDCl_3 , 100 MHz) δ : 16.4 (C-13), 19.5 (C-11), 20.1 (C-8), 20.3 (C-15), 23.8 (C-2), 24.4 (C-14), 26.6 (C-7), 28.3 (C-6), 28.6 (C-12), 41.1 (C-3), 44.4 (C-9), 48.4 (C-5), 56.4 (C-1), 75.0 (C-10), 80.3 (C-4). Crystal data: monoclinic, space group $P2_12_12_1$; $a=10.726$ (5), $b=16.0817$ (18), $c=16.7487$ (19) Å, $U=2888.9$ (15) Å³, $Z=4$, $D_c=0.548$ mg m⁻³, μ (MoK α radiation, $\lambda=0.70930$ Å) crystal dimensions: $0.48\times0.31\times0.34$ mm. Intensity data ($+h$, $+k$, $+l$, $2\theta_{\text{max}}=44.9^\circ$) were recorded on a Nonius diffractometer. The crystal structure was solved by a direct method. Full-Matrix Least-Squares refinement of atomic parameters (anisotropic C, O; isotopic H) converged at $R=0.015$ ($R_w=0.090$) over 1566 reflections with $I>2.5\sigma(I)$.

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