Tannins and Related Polyphenols of Melastomataceous Plants. V.[1] Three New Complex Tannins from *Melastoma malabathricum* L.

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Malabathrins A (6), E (11) and F (14), new complex tannins consisting of a *C*-glucosidic ellagitannin and a flavan 3-ol, have been isolated from the leaves of *Melastoma malabathricum* L., and their structures were determined by chemical and spectroscopic methods including two-dimensional nuclear magnetic resonance spectroscopy.

Keywords *Melastoma malabathricum*: Melastomataceae; tannin; *C*-glucosidic tannin; complex tannin; malabathrin A; malabathrin E; malabathrin F

The dried leaves of *Melastoma malabathricum* L. are used as a popular crude drug called "daun halendong" in Indonesia, for the treatment of diarrhea, dysentery and leucorrhea.[2] We recently reported the isolation of dimeric hydrolyzable tannins, malabathrins B, C, D, and eleven known tannins (nobotanins B, D, G, H, J, pterocarinin C, casuarictin, strictinin, pedunculagin and two galloylglucoses), from this plant.[1] Further investigation of the leaf extract of this plant led to the isolation of seven *C*-glucosidic ellagitannins including three new complex tannins, named malabathrins A (**6**), E (**11**) and F (**14**), which are composed of a *C*-glucosidic ellagitannin and a flavan-3-ol linked through a C–C bond.[3]

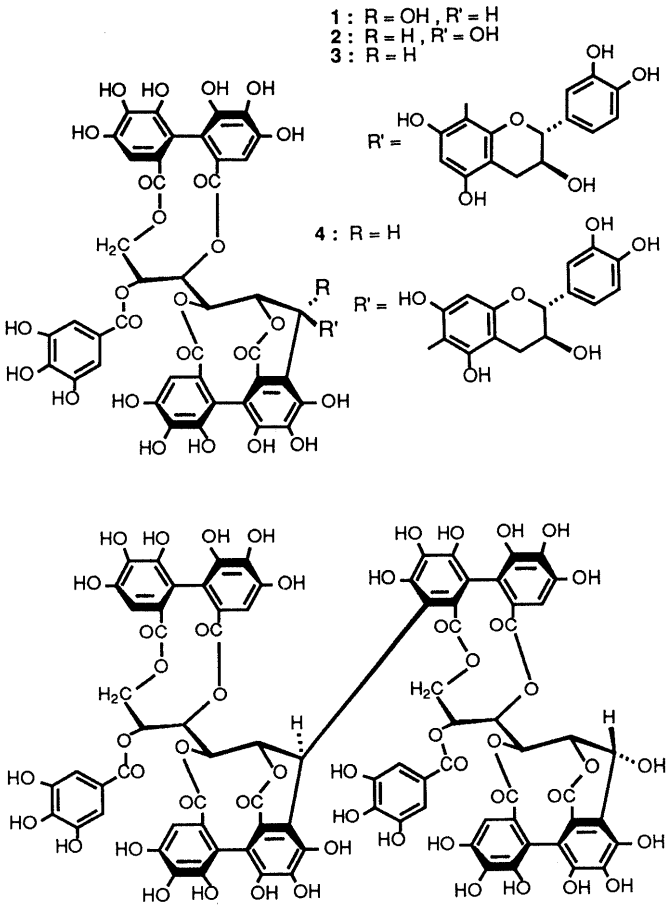

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Chart 1

These tannins were isolated from the 70% aqueous acetone homogenate of the dried leaves of *M. malabathricum* by repeated column chromatography over Diaion HP-20, Toyopearl HW-40 and MCI gel CHP-20P (see Experimental). Among them, three were identified as casuarinin (**1**),[4] and stenophyllanins A (**3**) and B (**4**), based on comparisons of their physico-chemical properties with those of an authentic sample (casuarinin) or with the data reported for stenophyllanins A and B.[5] The fourth tannin (**5**), showed the pseudo-molecular ion peak at *m/z* 1855 $(M+H)^+$ in the fast-atom bombardment mass spectrum (FAB-MS). It was characterized by examination of the proton and carbon-13 nuclear magnetic resonance (^{1}H-NMR and ^{13}C-NMR) spectra as a *C*-glucosidic ellagitannin dimer composed of casuarinin (**1**) and stachyurin (**2**)[4] moieties, connected with each other through a C–C bond, and was found to be identical with alienanin B (**5**) from *Quercus aliena* BL.[6]

The new tannin, malabathrin A (**6**), showed the pseudo-molecular ion peak at *m/z* 1383 $(M+Na)^+$ in the FAB-MS. The ^{1}H-NMR spectrum of **6** exhibited a 1H singlet (δ 6.19), ABX-type signals [δ 6.43 (d, $J=2$ Hz), 6.76 (d, $J=8$ Hz), 6.26 (dd, $J=2$, 8 Hz)], and methylene proton signals [δ 2.80 (d, $J=16$ Hz) and 2.94 (dd, $J=3.5$, 16 Hz)], which are characteristic of a C-6 (or C-8) substituted flavan 3-ol moiety. A pair of protons with a *cis* relationship on the heterocyclic C-ring of the flavan 3-ol moiety, H-2 and H-3, appeared as a broad singlet at δ 5.10 (H-2) and a broad doublet ($J=3.5$ Hz) at δ 5.19 (H-3). A remarkable downfield shift of H-3 from that of (−)-epicatechin (EC) (δ 4.23) and the galloyl proton signal at δ 6.97 (2H, s) imply the presence of an EC 3-*O*-gallate portion in the molecule. The presence of a stachyurin moiety in **6** was indicated by an extra galloyl proton signal [δ 7.09 (2H, s)], three 1H singlets due to hexahydroxydiphenoyl (HHDP) groups [δ 6.91, 6.60, 6.55 (each 1H, s)], and the aliphatic proton signals characteristic of an open-chain glucose core.[4] The upfield shift of the H-1 signal [δ 4.57 (s)] of the glucose core, relative to that (δ 4.91) of **2**, is accounted for by the presence of a C–C bond between C-1 of the glucose core and C-6 (or C-8) of the (−)-epicatechin gallate moiety. The substitution mode at C-6 or C-8 of the EC [or catechin] moiety in the procyanidins (or complex tannins) is generally known to be distinguishable on the basis of the chemical shift of the H-2 signal of the C-ring.[5,7] For example, H-2 in procyanidin B-5 (**7**), which is spatially far from the C-6 substituent, resonates at almost the same position as that of EC, while the corresponding signal in an 8-substituted isomer,

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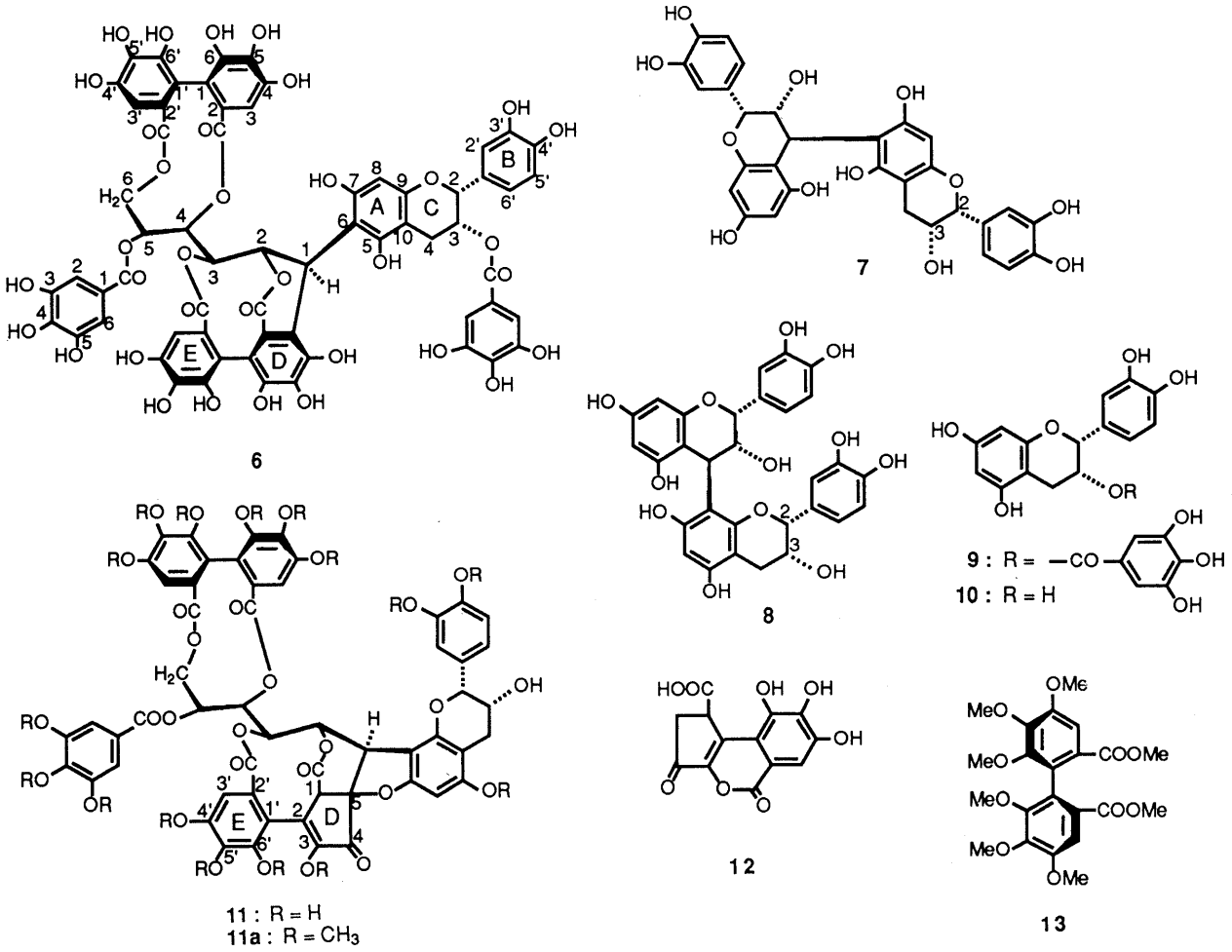

Chart 2

procyanidin B-2 (**8**), shows a significant downfield shift from that of EC. The H-2 signal of **6** appears at δ 5.10, similar to that (δ 5.14) of (−)-epicatechin gallate (**9**), indicating the C-6 substitution on the flavan 3-*O*-gallate moiety in **6**. The configuration at C-1 of the glucose core as illustrated in the formula **6** is evidenced by the small coupling constant ($J<1$) of the H-1 signal, which is analogous to that ($J=2$ Hz) of **2**,[4b] and also by a significant nuclear Overhauser effect (NOE) between the H-1 and H-3 signals in the frame-rotating Overhauser enhancement spectroscopy (ROESY) of **6**.

The circular dichroism (CD) spectrum of **6** exhibited positive ($[\theta]$ $+8.4\times10^4$) and negative ($[\theta]$ -3.3×10^4) Cotton effects at 233 and 262 nm, indicating the *S* chirality for both HHDP groups, though the amplitude at shorter wavelength was about half of that expected for two (*S*)-HHDP groups.[8] This small amplitude is attributable to overlapping of the positive Cotton effect with a strong negative Cotton effect of (−)-epicatechin gallate (**9**) at 207 nm ($[\theta]$ -9.8×10^4).[9]

These structural features of **6**, including the absolute configuration of the HHDP groups, were confirmed by acid-catalyzed condensation of casuarinin (**1**) and (−)-epicatechin gallate (**9**) in boiling dioxane, yielding **6** as the major product.[10] The inversion ($\alpha\rightarrow\beta$) of the configuration at C-1 of the glucose moiety in **1**, upon this condensation, may be due to steric hindrance at the α-site, which is induced by the steric proximity between glucosyl C-1 and the HHDP group at O-4/O-6.[4b] The structure of malabathrin A is represented by the formula **6**, based on these findings.

Malabathrin E (**11**) showed the $(M+Na)^+$ ion peak at *m/z* 1201 in the FAB-MS. Its ^{1}H-NMR spectrum exhibited a 2H singlet (δ 7.00), four 1H singlets (δ 6.92, 6.65, 6.56, 6.01), and three proton signals of ABX-type [δ 7.20 (d, $J=2$ Hz), 6.86 (dd, $J=8$, 2 Hz), 6.89 (d, $J=8$ Hz)], which are similar to those of **6**, except for the absence of a galloyl 2H singlet. The ^{1}H–^{1}H shift correlation spectrum (COSY) revealed that **11** is composed of an open-chain glucose core and an EC moiety (Table I). The C-8 substitution at the EC moiety is evidenced by the downfield shifts of both H-2 and H-3 signals of the EC unit relative to the corresponding signals of (−)-epicatechin (**10**), in an analogous way to procyanidin B-2 (**8**).[7]

Upon comparison of the glucose proton signals of **11** with those of **6**, remarkable differences were observed in the chemical shifts of the H-1 signal (**6**, δ 4.57; **11** δ 3.98), and H-2 signal (**6**, δ 4.67; **11** δ 5.40), showing that the structural difference between **11** and **6** might be in the D-ring. An extra singlet which is absent in the ^{1}H-NMR spectrum of **6** is observed at δ 4.31 in **11**. The ^{13}C-NMR spectrum of **11** exhibited the signals due to a ketone (δ 196.0), a tetrasubstituted double bond (δ 139.3, 149.9), a quaternary carbon (δ 90.3) and a methine carbon (δ 49.6), instead of the D-ring aromatic carbon signals in **6**. The

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TABLE I. ^{1}H-NMR Data for **10**, **11** and **14** [500 MHz, Acetone-d_6–D_2O, J (Hz) in Parentheses]

		10	11	14
Galloyl, HHDP and ring-D, E				
			7.00 s	7.12 s
			6.92 s	6.97 s
			6.65 s	6.74 s
			6.56 s	6.50 s
			4.31 s	4.32 s
EC moiety				
H-2		4.83 s	4.99 s	4.86 br s
H-3		4.16 m	4.32 m	4.17 m
H-4		2.81 dd (16, 4.5)	2.83 dd (16, 3.5)	2.83 dd (16, 3.5)
		2.68 dd (16, 3)	2.69 dd (16, 4.5)	2.67 (16, 3)
H-6		5.88 d (2)	6.01 s	
H-8		5.99 d (2)		6.07 s
H-2′		7.01 d (2)	7.20 d (2)	7.01 d (2)
H-5′		6.75 d (8)	6.89 d (8)	6.76 d (8)
H-6′		6.79 dd (2, 8)	6.86 dd (2, 8)	6.79 dd (2, 8)
Glucose				
H-1			3.98 s	4.14 s
H-2			5.40 m	5.62 s
H-3			5.17 d (4)	5.35 br d (3)
H-4			5.48 dd (4, 9)	5.76 dd (3, 9.5)
H-5			5.23 dd (3, 9)	5.52 dd (3, 9.5)
H-6			4.67 dd (3, 13)	4.80 dd (3, 13)
			4.01 d (13)	4.09 br d (13)

TABLE II. ^{13}C-NMR Data for the Glucose, Epicatechin and Cyclopentenone Moieties of **10**, **11** and **14** (126 MHz, Acetone-d_6–D_2O)

	10	11	14
Glucose			
C-1		46.8	47.8
C-2		81.3	80.5
C-3		75.8	75.2
C-4		72.7	72.2
C-5		71.8	71.8
C-6		64.1	64.5
Epicatechin			
C-2	79.2	79.6	79.7
C-3	66.7	65.8	66.0
C-4	28.8	29.6	28.4
C-5	157.4[a)]	157.5	157.9
C-6	95.3	90.0	104.9
C-7	157.5[a)]	159.6	160.0
C-8	96.0	104.3	97.4
C-9	156.9	152.6	153.1
C-10	99.5	102.1	95.8
C-1′	131.9	131.1	131.6
C-2′	115.3	115.4	115.1
C-3′	145.1	145.0	145.0
C-4′	145.2	145.1	145.2
C-5′	115.1	116.0	115.3
C-6′	119.1	121.0	119.1
Cyclopentenone ring (D-ring)			
C-1		49.6	50.4
C-2		139.3	139.2
C-3		149.9	149.6
C-4		196.0	196.3
C-5		90.3	89.6

a) Assignment is interchangeable.

chemical shifts of the ketone and the tetrasubstituted olefinic carbon signals, are analogous to those of the substituted 1,2-diketone enolate system in brevifolincarboxylic acid (**12**).[11)]

In the ^{1}H–^{13}C long-range COSY (J_{CH} = 7, 9 Hz), the H-1 signal (δ 3.98, s) of the glucose core is correlated, through three-bond coupling, with the signal at δ 159.6 and the ketone carbonyl signal at δ 196.0. The former signal is also correlated with the H-6 signal of the EC moiety, thus being assigned to C-7 of EC. The connectivity between H-1 of the glucose core and C-8 of EC was also indicated by the correlation (two-bond coupling) of the H-1 signal with the C-8 resonance at δ 104.3. Similarly, the H-2 signal of the glucose core is correlated, through three-bond couplings, with the C-8 signal (δ 104.3) of EC, the quaternary carbon (δ 90.3, ring-D C-5), and the ester carbonyl carbon signal at δ 168.8. The other long-range couplings are shown in Fig. 1. These spectral features are analogous to those of mongolicain A, which has a cyclopentenone moiety linked to glucose C-1 through a C–C bond.[12)] The FAB-MS data are also consistent with the proposed structure (**11**) ($C_{55}H_{38}O_{30}$).

Upon methylation with dimethyl sulfate and potassium carbonate, **11** afforded a hexadecamethylate (**11a**). The H-6 signal (δ 6.17) of the EC part in **11a** appeared in the ROESY spectrum, showing an NOE only with the methoxyl signal at δ 3.56,[13)] which supports the presence of an ether linkage at C-7 of the EC moiety. The specific optical rotation ($[\alpha]_D$ −27° (EtOH)) of dimethyl hexamethoxydiphenate (**13**), obtained by methanolysis of **11a**, showed the *S*-configuration of the HHDP group in **11**. The structure **11** of malabathrin E was thus established.

Malabathrin F (**14**) showed the $(M+Na)^+$ ion peak at m/z 1201 in FAB-MS, which is the same as that of **11**. The ^{1}H-NMR spectrum of **14** is similar to that of **11**, except for the chemical shifts of the H-2 and H-3 signals of the EC moiety [δ 4.86 (br s), 4.17 (m)] (Table I). These signals are virtually the same as those [δ 4.83 (s), 4.16 (m)] of (−)-epicatechin (**10**), indicating the presence of the C-6 substituted EC moiety in **14**. Malabathrin F is therefore a regio-isomer of **11** concerning the A-ring substitution in the EC moiety. This conclusion is also supported by the ^{13}C-NMR spectrum, in which only the chemical shifts of the A-ring carbon signals differ from those of **11** (Table II). The C-6 signal of the EC moiety in **14** is shifted downfield (δ 104.9) from that of **10** (δ 95.3), while the C-8 signal (δ 97.4) is almost the same as that of **10** (δ 96.0). On the other hand, the C-10 signal of the EC moiety in **14** showed a remarkable upfield shift ($\Delta\delta$ −3.7 ppm), relative to that of **10**. This upfield shift is comparable to the upfield shift ($\Delta\delta$ −5.3 ppm) of the C-6 signal induced by formation of the ether linkage at C-7 in **11** (Table II), suggesting the presence of an ether bond at C-5 (EC moiety) in **14**. This assignment was substantiated by the ROESY spectrum of the hexadecamethyl derivative (**14a**), which showed an NOE between the H-8 signal (δ 6.04) of the EC moiety and one (δ 3.67) of the methoxyl signals.[14)]

The absolute configuration of the HHDP group in **14** is the same as that of **11**, since their CD spectra are almost superimposable. The structure of malabathrin F was consequently determined as **14**.

Many hydrolyzable tannins, including oligomers, nobotanins A, B, C and E—K, have been found in various plant species (*Tibouchina semidecandra*,[4b)] *Heterocentron roseum*,[15)] *Medinilla magnifica*,[16)] *Schizocentron elegans*,[17)] *Melastoma candidum*[17)] *etc.*) of Melastomataceae, which had been little investigaged chemically, before the in-

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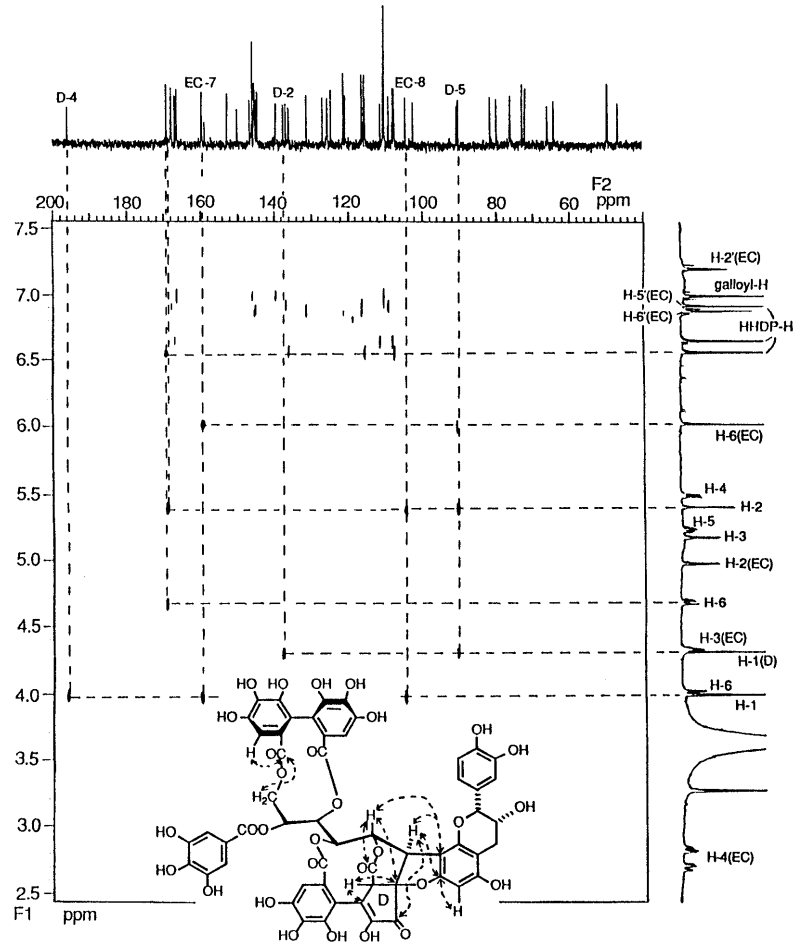
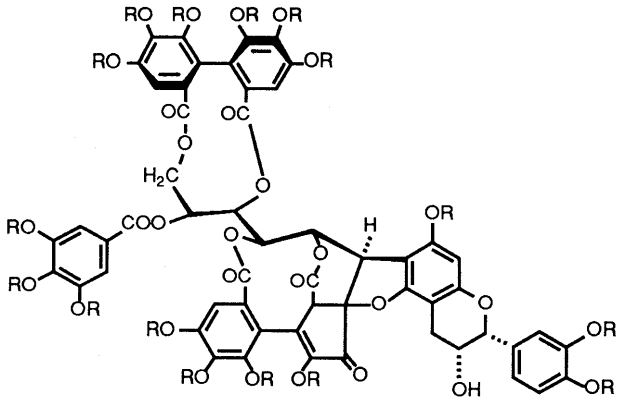


Fig. 1. ^{1}H–^{13}C Long-Range COSY of Malabathrin E (**11**)

Average J_{CH} value = 7 Hz for three- and two-bond coupling. D: D-ring. EC: (−)-epicatechin moiety.



14 : R = H
14a : R = Me

Chart 3

vestigations of this series started. Malabathrins A, E and F, stenophyllanins A and B, and alienanin B, isolated from *M. malabathricum* in the present study, are the first examples of complex tannins and *C*-glucosidic tannin dimers from this family.

Experimental

^{1}H- (500 MHz) and ^{13}C-NMR (126 MHz) spectra were measured on a Varian VXR 500 instrument and chemical shifts are given in δ (ppm) values relative to acetone-d_6 (2.04 ppm for ^{1}H and 29.8 ppm for ^{13}C). FAB-MS were taken on a VG 70-SE high-resolution mass spectrometer using 3-nitrobenzyl alcohol containing NaCl as the matrix agent. High-performance liquid chromatography (HPLC) was conducted on Superspher Si 60 (4 mm × 119 mm) and LiChrospher RP-18 (4 mm × 250 mm) columns, using the following solvent systems: (A) hexane–MeOH–tetrahydrofuran (THF)–HCOOH (60 : 45 : 15 : 1) and oxalic acid (500 mg/1.2 l), (B) 0.05 M phosphate buffer–EtOH–EtOAc (85 : 10 : 5), (C) 0.05 M phosphate buffer–CH_3CN (85 : 15), (D) 0.05 M phosphate buffer–EtOH–EtOAc (87 : 8 : 5), (E) 0.05 M phosphate buffer–CH_3CN (87 : 13), (F) 0.05 M phosphate buffer–EtOH–EtOAc (83 : 12 : 5). Column chromatography was carried out on Toyopearl HW-40 (coarse and fine grades) (Tosoh Corp.), Diaion HP-20 and MCI-gel CHP-20P (Mitsubishi Chemical Industry Co., Ltd.). Thin-layer chromatography (TLC) was conducted on Kieselgel PF_{254} (Merck) with benzene–acetone (10 : 1 or 5 : 1), and visualized under ultraviolet (UV) irradiation.

Plant Materials The crude drug (daun halendong; dried leaves of *Melastoma malabathricum* L.) was purchased at a market in Sukabumi, Cap Lonceng, Indonesia, in August 1988. A voucher specimen (AN-SKJ No. 283) is deposited in the Department of Pharmacognosy, Faculty of Pharmaceutical Sciences, Kyoto University.

Isolation of Tannins The dried leaves and stems (1.4 kg) of *M. malabathricum* were homogenized in 70% aqueous acetone and filtered. The concentrated filtrate was extracted with Et_2O, EtOAc and *n*-BuOH, successively, to give the Et_2O extract (1.9 g), EtOAc extract (20.7 g), *n*-BuOH extract (27.8 g) and H_2O extract (37 g). A part (9.5 g) of the *n*-BuOH extract was chromatographed over Diaion HP-20 with H_2O, and H_2O–MeOH (10% MeOH→20%→30%→40%→50%). The 30% MeOH eluate (1.4 g) was rechromatographed over Toyopearl HW 40 (fine) developing with 70% MeOH→80%→MeOH–acetone–H_2O (7 : 2 : 1) in a stepwise gradient mode. The 80% MeOH eluate gave casuarinin (**1**) (201 mg), and the eluate with MeOH–acetone–H_2O afforded stenophyllanins A (**3**) (99 mg) and B (**4**) (21 mg). The H_2O extract (37 g) was similarly fractionated by column chromatography over Diaion HP-20 with H_2O

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and aqueous MeOH (10% MeOH→20%→30%→50%). The 30% MeOH eluate (3.8 g) was further chromatographed over Toyopearl HW-40 (fine) with 70% MeOH and MeOH. The 70% MeOH eluate (828 mg) was rechromatographed over MCI-gel CHP-20P with 20% MeOH to yield casuarinin (**1**) (116 mg). The MeOH eluate (186 mg) gave alienanin B (**5**) (8.5 mg), after purification by column chromatography over MCI-gel GHP-20P (20% MeOH).

In a separate experiment, the dried leaves (5 kg) were homogenized in 70% aqueous acetone and filtered. The concentrated filtrate was fractionated on a column of Diaion HP-20 developed with H_2O and H_2O–MeOH (10% MeOH→30%→40%→50%→60%) to yield ten fractions (fr.-I—fr.-X) according to the retention time of the main peak in each fraction in normal phase HPLC. Fraction-IV (9.8 g) was purified by a combination of column chromatographies over Toyopearl HW-40 (coarse and fine grades) and MCI-gel CHP-20P with H_2O containing increasing amounts of MeOH to afford casuarinin (**1**) (468 mg). An additional crop of casuarinin (587 mg) was also obtained by rechromatography of fr.-V on Toyopearl HW-40 (coarse) with 70% MeOH. Repeated chromatography of fr.-VI (9 g) over Toyopearl HW-40 (coarse and fine grades) and MCI-gel CHP-20P with a solvent system of H_2O–MeOH in stepwise gradient mode afforded malabathrin A (**6**) (24 mg) and malabathrin E (**11**) (87 mg). Fraction-VIII (5.4 g) was similarly rechromatographed over Toyopearl HW-40 (coarse) with the same solvent system to give malabathrin F (**14**) (33 mg).

Stenophyllanin A (3) A light brown amorphous powder, $[\alpha]_D$ +30° (c=1.0, MeOH), FAB-MS m/z: 1231 $(M+Na)^+$. ^{1}H-NMR (acetone-d_6+D_2O) δ: 2.3—2.9 [m, catechin (Cat) H-4], 4.43 [br s, glucose (Glc) H-1], 5.91 (br s, Cat H-6), 6.5—7.1 (aromatic H). ^{13}C-NMR (acetone-d_6+D_2O) δ: 38.1 (Glc C-1), 69.4 (Glc C-2), 73.0 (Glc C-3), 74.0 (Glc C-4), 81.4 (Glc C-5), 64.8 (Glc C-6), 82.4 [Cat C-2], 67.7 (Cat C-3), 31.6 (Cat C-4), 96.5 (Cat C-6), 101.0 (Cat C-10), 105.6, 107.6, 108.7, 110.1 (HHDP C-3, C-3′), 110.0 (2C) [galloyl (Gal) C-2, C-6), 114.6, 116.4, 116.8 (HHDP C-1, C-1′), 115.6, 115.7 (Cat C-2′, C-5′), 120.5 (Gal C-1), 123.1 (Cat C-6′), 123.4, 125.3, 126.8, 127.7 (HHDP C-2, C-2′), 131.5 (Cat C-1′), 135.0, 136.1, 136.5, 137.5 (HHDP C-5, C-5′), 139.3 (Gal C-4), 142.8, 144.1, 144.2 (2C), 144.4, 145.2, 145.6 (2C), 145.7 (2C) (Cat C-3′, C-5′, HHDP C-4, C-4′, C-6, C-6′), 145.1 (Gal C-3, C-5), 153.9 (Cat C-5), 155.3 (Cat C-7), 156.2 (Cat C-9), 166.2, 167.7, 168.5, 169.1 (2C) (ester carbonyl). These spectral data are in agreement with the reported data.[5]

Stenophyllanin B (4) A light brown amorphous solid, $[\alpha]_D$ +67° (c=1.0, MeOH). FAB-MS m/z: 1209 $(M+H)^+$, 1231 $(M+Na)^+$. ^{1}H-NMR (500 MHz, acetone-d_6+D_2O) δ: 7.09 (2H, Gal), 7.10, 6.88, 6.54 (each 1H, s, HHDP), 6.84 (1H, d, J=2 Hz, Cat H-2′), 6.73 (1H, d, J=8.5 Hz, Cat H-5′), 6.68 (1H, dd, J=2, 8.5 Hz, Cat H-6′), 6.53 (1H, br s, Cat H-8), 2.50 (1H, br m, Cat H-4)), 2.85 (1H, m, Cat H-4), 3.92 (1H, m, Cat H-3), 4.45 (1H, d, J=8.5 Hz, Cat H-2), 4.63 (1H, s, Glc H-1), 4.74 (1H, br s, Glc H-2), 5.16 (1H, t, J=2 Hz, Glc H-3), 5.64 (1H, dd, J=2, 8.5 Hz, Glc H-4), 5.35 (1H, dd, J=3.5, 8.5 Hz, Glc H-5), 4.90 (1H, dd, J=3.5, 13.5 Hz, Glc H-6), 4.03 (1H, d, J=13.5 Hz, Glc H-6). ^{13}C-NMR (acetone-d_6+D_2O) δ: 30.0 (Cat C-4), 38.1 (Glc C-1), 64.4 (Glc C-6), 67.9 (Cat C-3), 71.2, 74.9, 81.3, 82.1 (Glc C-2, C-3, C-4, C-5, Cat C-2), 96.1 (Cat C-8), 103.2 (Cat C-10), 105.7, 107.2 107.3, 108.7 (HHDP C-3, C-3′, Cat C-6), 115.1, 115.5, 115.6, 115.9, 119.1 (HHDP C-1, C-1′, Cat C-2′, C-5′), 119.9, 120.6, 123.6, 125.0, 126.8, 128.8 (HHDP C-2, C-2′, Gal C-1, Cat C-6′), 131.6 (Cat C-1′), 133.1, 135.0, 136.0, 136.6 (HHDP C-5, C-5′), 139.3 (Gal C-4), 142.9, 143.0, 144.2, 144.3 (2C), 145.2 (2C), 145.5, 145.6 (2C), 146.0 (2C) (HHDP C-4, C-4′, C-6, C-6′, Gal C-3, C-5, Cat C-3′, C-4′), 154.9 (2C), 155.3 (Cat C-5, C-7, C-9), 166.1, 167.7, 168.4, 169.0, 169.7 (ester carbonyl). These data were in agreement with those reported for stenophyllanin B.[5]

Alienanin B (5) A light brown amorphous powder, $[\alpha]_D$ +45° (c=1.0, MeOH). FAB-MS: m/z 1855 $(M+H)^+$, 1877 $(M+Na)^+$. ^{1}H-NMR (500 MHz, acetone-d_6+D_2O) δ: 7.07, 7.11 (each 2H, s, Gal), 6.41,6.44, 6.54, 6.71, 6.76 (each 1H, s, HHDP), 5.56 (d, J=5 Hz, Glc H-1), 4.58 (dd, J=2, 5 Hz, Glc H-2), 5.36 (t, J=2 Hz, Glc H-3), 5.28 (dd, J=2, 9 Hz, Glc H-4), 5.25 (dd, J=2, 9 Hz, Glc H-5), 2.97 (d, J=13.5 Hz, Glc H-6), 4.03 (dd, J=2, 13.5 Hz, Glc H-6), 4.73 (d, J=1 Hz, Glc H-1′), 4.89 (dd, J=1, 2 Hz, Glc H-2′), 4.97 (t, J=2 Hz, Glc H-3′), 5.62 (dd, J=2, 8.5 Hz, Glc H-4′), 5.16 (dd, J=3.5, 8.5 Hz, Glc H-5′), 4.03 (dd, J=2, 13.5 Hz, Glc H-6′), 4.78 (dd, J=3.5, 13.5 Hz, Glc H-6′). ^{13}C-NMR (acetone-d_6+D_2O) δ: 67.1 (Glc C-1), 77.1 (Glc C-2), 69.2 (Glc C-3), 74.5 (Glc C-4), 71.4 (Glc C-5), 65.7 (Glc C-6), 40.2 (Glc C-1′), 80.9 (Glc C-2′), 69.5 (Glc C-3′), 74.6 (Glc C-4′), 73.2 (Glc C-5′), 64.3 (Glc C-6′), 105.2, 105.6, 107.2, 107.8, 108.8 (HHDP C-3, C-3′), 113.7, 117.2 [HHDP C-1, C-1′, C-6′ (A-ring)], 165.0, 166.1, 166.4 (2C), 168.2, 168.5, 168.8, 169.1, 169.3, 169.4 (ester carbonyl). These spectral data were consistent with the reported data.[6]

Malabathrin A (6) A light brown amorphous power, $[\alpha]_D$ +7° (c=1.0, MeOH). FAB-MS m/z 1383 $(M+Na)^+$. *Anal.* Calcd for $C_{63}H_{44}O_{35}\cdot 5H_2O$: C, 52.14; H, 3.84. Found: C, 52.14; H, 3.83. CD (MeOH) [θ] (nm): 8.4×10^4 (233), -3.3×10^4 (262), $+6.8\times10^4$ (282), -5.7×10^4 (313). ^{1}H-NMR (500 MHz, acetone-d_6+D_2O) δ: 7.09, 6.97 (each 2H, s, Gal), 6.91, 6.60, 6.55 (each 1H, s, HHDP), 6.19 [1H, s, galloyl epicatechin (GEC) H-8], 6.43 (d, J=2 Hz, GEC H-2′), 6.76 (d, J=8 Hz, GEC H-5′), 6.26 (dd, J=2, 8 Hz, GEC H-6′), 5.10 (br s, GEC H-2), 5.19 (br d, J=3.5 Hz, GEC H-3), 2.80 (d, J=16 Hz, GEC H-4), 2.94 (dd, J=3.5, 16 Hz, GEC H-4), 4.57 (s, Glc H-1), 4.67 (br s, Glc H-2), 5.24 (t, J=2 Hz, Glc H-3), 5.68 (dd, J=2, 8.5 Hz, Glc H-4), 5.37 (dd, J=3.5, 8.5 Hz, Glc H-5), 4.84 (dd, J=3.5, 13.5 Hz, Glc H-6), 4.07 (d, J=13.5 Hz, Glc H-6).

Condensation of Casuarinin (1) and (−)-Epicatechin Gallate (9) A mixture of **1** (250 mg), **9** (120 mg) and camphorsulfonic acid (25 mg) in dry dioxane (60 ml) was refluxed with monitoring of the reaction process by HPLC (normal phase), and after 12 h, the solvent was evaporated off. The residue was suspended in water and extracted successively with Et_2O and EtOAc to remove unreacted **1** and **9**. The residue obtained after evaporation of the aqueous layer was chromatographed over Sephadex LH-20 (2.2×20 cm), developing with EtOH–MeOH (8:2→7:3→5:5) and MeOH. The product (5 mg) from the MeOH eluate was identical with malabathrin A (**6**) by HPLC (normal and reversed phases) and ^{1}H-NMR spectral comparisons. Gallic acid (2.8 mg). **1** (32 mg) and **9** (1.4 mg) were also isolated from the eluates with EtOH–MeOH (8:2) and EtOH–MeOH (7:3).

Malabathrin E (11) A light brown amorphous powder, $[\alpha]_D$ +13° (c=0.7, MeOH). FAB-MS: m/z 1179 $(M+H)^+$, 1201 $(M+Na)^+$. *Anal.* Calcd for $C_{55}H_{38}O_{30}\cdot 5H_2O$: C, 52.06; H, 3.81. Found: C, 51.62; H, 3.80. CD (MeOH) [θ] (nm): $+6.5\times10^4$ (237), -1.8×10^4 (260), $+1.2\times10^4$ (278), -3.3×10^3 (300), $+6.3\times10^3$ (345). ^{13}C-NMR (126 MHz, acetone-d_6+D_2O) δ: 125.1 (Gal C-1), 110.1 (2C) (Gal C-2, C-6), 138.1 (Gal C-4), 116.1, 115.2, 111.4 (HHDP C-1, C-1′), 126.8, 124.0, 120.8 (HHDP C-2, C-2′), 108.8, 108.2, 106.9 (HHDP C-3, C-3′), 137.3, 136.6, 135.8 (HHDP C-5, C-5′), 146.5, 145.9 (2C), 145.3, 145.2, 144.4 (2C), 144.3 (Gal C-3, C-5, HHDP C-4, C-4′, C-6, C-6′), 166.0, 166.7, 167.7, 168.8, 169.1 (ester carbonyl); glucose, epicatechin and cyclopentenone moieties, see Table II.

Methylation of Malabathrin E (11) A mixture of **11** (10 mg), Me_2SO_4 (0.1 ml) and K_2CO_3 (110 mg) in dry acetone (10 ml) was stirred overnight at room temperature, and then refluxed for 2 h. After removal of inorganic materials by filtration, the filtrate was concentrated and purified by preparative TLC (Kieselgel PF_{254}) with benzene–acetone (5:1) (triple development) to yield a hexadecamethylate (**11a**) (1.0 mg) [FAB-MS m/z: 1403 $(M+H)^+$, ^{1}H-NMR (acetone-d_6) δ: 7.16 (2H, s, Gal), 6.87, 7.07, 7.21 (1H, s, HHDP), 7.21 (1H, d, J=2 Hz, EC H-2′), 7.15 (1H, dd, J=2, 8 Hz, EC H-6′), 6.89 (1H, d, J=8 Hz, EC H-5′), 6.17 (1H, s, EC H-6), 5.02 (1H, br s, EC H-2), 4.41 (1H, m, EC H-3), 4.38 (1H, s, Glc H-1), 5.57 (1H, br s, Glc H-2), 5.58 (1H, d, J=4 Hz, Glc H-3), 5.68 (1H, dd, J=4, 8 Hz, Glc H-4), 5.46 (1H, dd, J=3, 8 Hz, Glc H-5), 4.70 (1H, dd, J=3, 13.5 Hz, Glc H-6), 4.24 (1H, d, J=13.5 Hz, Glc H-6), 4.36 (1H, s, ring-D H-1), 3.56—4.00 (16×OMe)]. Methanolysis of **11a** with 1% NaOMe at room temperature for 10 h followed by preparative TLC (benzene–acetone, 10:1) afforded methyl tri-*O*-methylgallate and dimethyl hexamethoxydiphenate (**13**), $[\alpha]_D$ −27° (c=0.4, EtOH).

Malabathrin F (14) A light brown amorphous powder, $[\alpha]_D$ −13° (c=1.0, MeOH). FAB-MS: m/z 1201 $(M+Na)^+$. CD (MeOH) [θ] (nm): $+7.3\times10^4$ (235), -4.8×10^4 (260), $+1.0\times10^4$ (282), -4.5×10^3 (305), $+5.0\times10^3$ (345). ^{13}C-NMR (126 MHz, acetone-d_6+D_2O) δ: 125.3 (Gal C-1), 110.0 (2C) (Gal C-2, C-6), 137.3 (Gal C-4), 116.0, 115.2, 111.1 (HHDP C-1, C-1′), 126.6, 124.3, 120.9 (HHDP C-2, C-2′), 108.8, 107.7, 107.2 (HHDP C-3, C-3′), 137.1, 136.6, 135.8 (HHDP C-5, C-5′), 146.4, 145.7 (2C), 145.1, 144.8, 144.6, 144.3, 144.2 (Gal C-3, C-5, HHDP C-4, C-4′, C-6, C-6′), 166.2, 166.7, 167.7, 168.9, 169.0 (ester carbonyl), glucose, epicatechin and cyclopentenone moieties, see Table II.

Methylation of Malabathrin F (14) Malabathrin F (**14**) (9 mg) was methylated with Me_2SO_4 (0.1 ml) and K_2CO_3 (90 mg) in acetone (10 ml), and worked up in a way similar to that described under methylation of **11** to give a hexadecamethyl derivative (**14a**) (2.7 mg) as a white solid. FAB-MS m/z: 1403 $(M+H)^+$, 1425 $(M+Na)^+$. ^{1}H-NMR (acetone-d_6) δ: 7.36 (2H, s, Gal), 6.85, 7.08, 7.18 (each 1H, s, HHDP), 6.92 (1H, d, J=8.5 Hz, EC H-5′), 7.03 (1H, dd, J=2, 8.5 Hz, EC H-6′), 7.18 (1H, d, J=2 Hz, EC H-2′), 6.04 (1H, s, EC H-6), 5.00 (1H, br s, EC H-2), 4.26 (1H, m, EC H-3), 4.33 (1H, s, Glc H-1), 5.44 (1H, br s, Glc H-2), 5.57 (1H, d, J=3.5 Hz, Glc H-3), 5.73 (1H, dd, J=3.5, 8 Hz, Glc H-4), 5.79

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(1H, diffused dd, $J=3$, 8 Hz, Glc H-5), 4.86 (1H, dd, $J=3$, 13 Hz, Glc H-6), 4.30 (1H, d, $J=13$ Hz, Glc H-6), 4.36 (1H, s, ring-D H-1), 3.59, 3.60, 3.63, 3.67, 3.71, 3.78, 3.79, 3.80, 3.82, 3.84, 3.85, 3.87, 3.93, 4.00 (each 3H, s, OMe × 14), 3.86 (6H, s, OMe × 2).

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