HETEROCYCLES, Vol. 76, No. 2, 2008, pp. 1171 - 1180. © The Japan Institute of Heterocyclic Chemistry
Received, 31st March, 2008, Accepted, 19th May, 2008, Published online, 22nd May, 2008. COM-08-S(N)76

DIMERIC FLAVANS FROM GAMBIR AND THEIR STRUCTURAL CORRELATIONS WITH (+)-CATECHIN

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Abstract – We isolated two new flavan dimers, gambirflavan D3 (**10**) and gambirflavan D4 (**12**), together with gambiriin A3 (**11**), from gambir, a hot-water extract of the leaves and young twigs of *Uncaria gambir*. Because their spectral analyses suggested that they are derived from catechin, we conducted a conversion reaction using (+)-catechin (**1**) to produce these dimers; another new flavan, gambirflavan D5 (**13**), was obtained as a product of this reaction. The structural relationship of these dimeric flavans with (+)-catechin (**1**) is discussed.

INTRODUCTION

Gambir, which is extracted from the leaves and young twigs of *Uncaria gambir* Roxb. (Rubiaceae), is a popular natural medicine for the treatment of diarrhea and sore throats in Asian countries.[1] We previously isolated 12 polyphenolic constituents from gambir and reported a revision of the structures of four of these compounds: gambiriins A1(**3**), A2 (**4**), B1 (**5**), and B2 (**6**).[2] We also elucidated the structure of three new compounds, catechin-(4α→8)-*ent*-epicatechin (**7**) and gamibirflavans D1 (**8**) and D2 (**9**)[3] (Figure 1). In the present study, we isolated two new compounds, gambirflavan D3 (**10**) and gambirflavan D4 (**12**), along with a known compound, gambiriin A3 (**11**). This paper describes the structures of the new compounds and the stereostructure of **11**, which had not been established. To determine the stereostructures of these dimeric compounds unambiguously, (+)-catechin (**1**) in aqueous solution was heated to obtain dimers **10-12**. The product mixture included another new compound, gambirflavan D5

† Dedicated to Prof. Ryoji Noyori on the occasion of his 70th birthday.

(**13**), and thus we also characterized the structure of this compound. The structures of all products suggest a diverse reactivity of catechin and related condensed tannins.

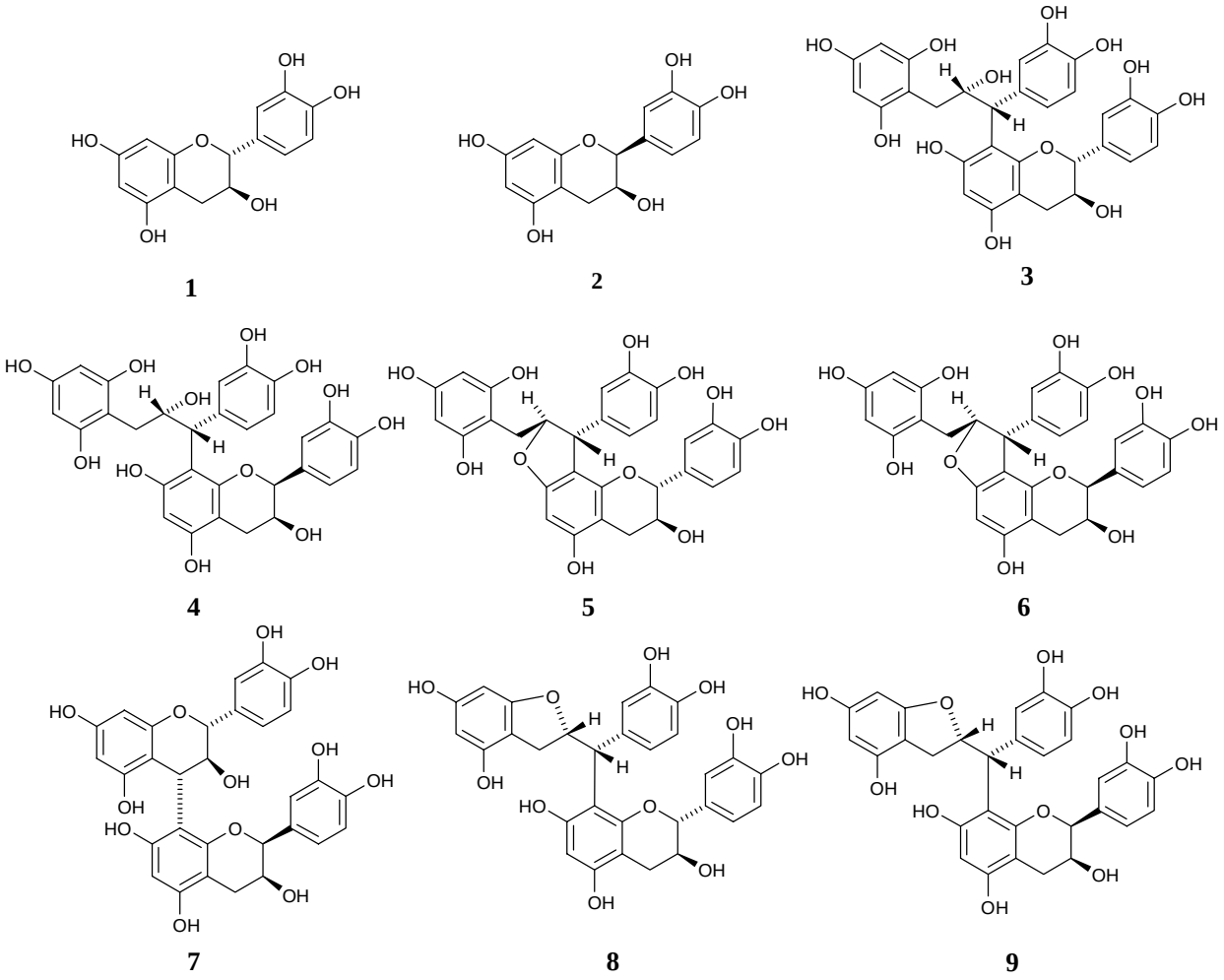

Figure 1. Structures of compounds **1-9** isolated from gambir (*Uncaria gambir* extract)

RESULTS AND DISCUSSION

A methyl alcohol (MeOH) extract of gambir was fractionated by column chromatography on a Diaion HP-20 with increasing concentrations of aqueous MeOH. The eluates from the column were further purified by column chromatography on a Toyopearl HW-40, Sephadex LH-20, Chromatorex ODS-gel, and MCI-gel CHP-20P, and also by preparative HPLC, to give **10, 11,** and **12** along with the compounds reported previously.[2,3] The reaction mixture obtained by heating (+)-catechin (**1**) was also chromatographed in an analogous way to give **10**-**12** and **13** along with the previously reported compounds, **2**-**6**, **8,** and **9**.

Structure of gambirflavan D3 (10)

Gambirflavan D3 (**10**) was obtained as an amorphous powder. The molecular formula was determined to

be $C_{30}H_{26}O_{11}$ by the HR-ESI-MS. The ^{1}H-NMR spectrum showed signals of nine aromatic protons: 2H singlet (δ 5.99, H-3_U and H-5_U), 1H singlet (δ 5.87, H-8_L), and two sets of ABX signals attributable to the protons of B_U and B_L rings. The spectrum also showed two sets of the methine-methine-methylene systems in the aliphatic region, suggesting the presence of the chalcane and catechin structures (see Experimental section). The coupling constant between H-2_L and H-3_L (J = 9.0 Hz) indicated a 2,3-*trans* structure in the catechin residue.

The location of the interflavan linkage between C-α_U and C-6_L was shown by the HMBC correlations H-α_U/C-7_L, H-8_L/C-7_L, H-8_L/C-9_L, and H-2_L/C-9_L, corresponding to the sequence H-α_U – C-7_L – H-8_L – C-9_L – H-2_L. The correlations H-α_U/C-5_L, H-4_L/C-5_L, and H-4_L/C-9_L also supported the assignment of the location [Figure 2(a)]. The molecular formula shown by the ESI-MS indicated that the molecular weight of **10** was 18 mass units smaller than that of gambiriin A1 (**3**). This result, and the downfield shift of an A ring carbon (δ 160.0; C-5_L), suggested that **10** possessed an ether linkage at this carbon (C-5_L). The presence of an ether bond between C-5_L and a hydroxyl group at C-β_U was substantiated by the correlations H-α_U/C-5_L and H-β_U/C-5_L in the HMBC spectrum [Figure 2(a)].

The stereochemistry of **10** was assigned as follows. Compound **10** was obtained from the mixture produced by heating (+)-catechin (**1**). The 2*R*,3*S*-configuration of the lower unit and the *S* configuration of the upper β carbon were thus confirmed based on this conversion. The *trans* relationship between the H-α_U and H-β_U protons on the five-membered ring was indicated by the correlations H-β_U/H-2'$_U$ and H-β_U/H-6'$_U$ in the ROESY spectrum [Figure 2(b)]. The structure of gambirflavan D3 was therefore represented by structure **10**.

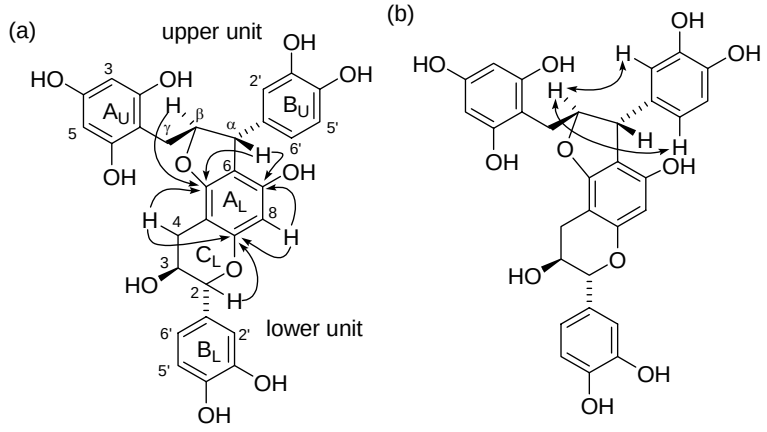

Figure 2. Important 2D-NMR correlations observed for **10**

(a) The HMBC correlations (H → C) indicated the presence of an ether linkage between C-5_L to C-β_U and the location C-α_U → C-6_L of the interflavan linkage. (b) The ROE (H ↔ H) correlations H-β_U/H–2'$_L$ (H-6'$_L$) indicated the *trans* configuration between H-α_U and H-β_U.

Structure of gambiriin A3 (11)

Gambiriin A3 (**11**) was obtained as an amorphous powder whose molecular formula was determined to be $C_{30}H_{28}O_{12}$ by ESI-MS. Although the ^{13}C-NMR spectrum was closely similar to that of gambiriin A1 (**3**), the chemical shift of the C-6_L carbon in **11** (δ 94.9) was different from the corresponding carbon in **3** [δ 97.5 (C-8_L)]. The ^{1}H-NMR spectrum signaling the lower catechin unit and the upper open chain chalcane unit (see Experimental section) indicated the identity of this compound with gambiriin A3, which has a C-α_U – C-6_L linkage in the structure.[4] However, the α and β carbon sterochemistry was not given. The location of the interflavan linkage between C-α_U and C-6_L was shown by the HMBC sequences H-α_U – C-7_L – H-8_L – C-9_L – H-2_L and H-α_U – C-5_L – H-4_L – C-9_L [Figure 3(a)].

Compound **11** was also obtained by heating (+)-catechin (**1**). The 2*R*,3*S*-configurations in the lower unit and the *S* configuration of the upper β carbon were thus confirmed based on this chemical conversion. The small coupling constant between H-α_U and H-β_U (J = 3 Hz) and ROE correlations H-α_U/H-γb_U, H-β_U/H-2'$_U$, and H-β_U/H-6'$_U$ (observed in **3**) coincided with the *R* configuration of C-α_U [Figure 3(b)].

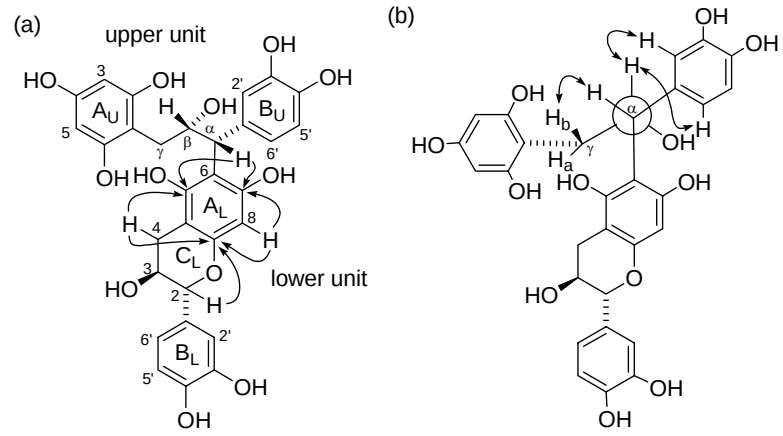

Figure 3. Important 2D-NMR correlations observed for **11**

(a) The HMBC correlations (H → C) indicated the location C-α_U → C-6_L of the interflavan linkage. (b) The ROE (H ↔ H) correlations H-α_U/H-γb_U and H-β_U/H-2'$_U$ (H-6'$_U$) satisfied the *R* configuration at C-α_U based on the conformation indicated.

Structure of gambirflavan D4 (12)

Gambirflavan D4 (**12**) was obtained as an amorphous powder whose molecular formula was determined to be $C_{30}H_{28}O_{12}$ by HR-ESI-MS. Although the ^{1}H-NMR spectrum of **12** was similar to that of gambiriin A3 (**11**), the 2,3-*cis* structure in the lower unit was indicated by the small coupling constant between H-2_L and H-3_L (J < 2 Hz) (see Experimental section). Comparing the ^{13}C-NMR spectra indicated differences in the chemical shifts of C-2_L (δ 79.3 in **12**; 82.7 in **11**) and C-3_L (δ 66.9 in **12**; 68.5 in **11**), corresponding to the presence of epicatechin in **12** instead of catechin in **11**. The HMBC correlations H-α_U/C-5_L,

H-α_U/C-7_L, H-2_L/C-9_L, H-4_L/C-5_L, H-8_L/C-7_L, and H-8_L/C-9_L of **12** showed a linkage between C-α_U and C-6_L [Figure 4(a)].

The 2*S*,3*S*-configuration in the lower unit and the *S* configuration of the upper β-carbon were confirmed based on the chemical conversion from **1** to **12** in a way analogous to that of **11**. The coupling constant between H-α_U and H-β_U (J = 3.5 Hz) and ROE interactions H-α_U/H-γb_U, H-β_U/H-2'$_U$, and H-β_U/H-6'$_U$ indicated the *R* configuration, when the conformation around C-α_U – C-β_U was assigned as shown in Figure 4.

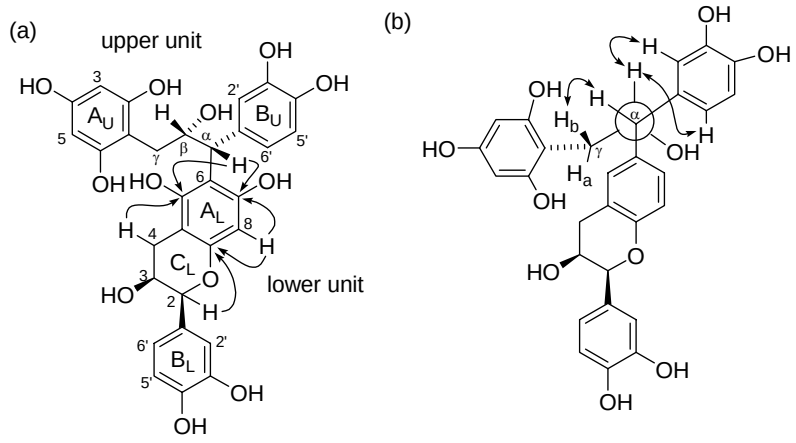

Figure 4. Important 2D-NMR correlations observed for **12**

(a) The HMBC correlations (H → C) indicated the location C-α_U → C-6_L of the interflavan linkage. (b) The ROE (H ↔ H) correlations H-α_U/H-γb_U and H-β_U/H-2'$_U$ (H-6'$_U$) satisfied the *R* configuration at C-α_U based on the conformation indicated.

Structure of gambirflavan D5 (13)

A new compound, gambirflavan D5 (**13**), was obtained as an amorphous powder. Its molecular formula was determined to be $C_{30}H_{28}O_{12}$ by HR-ESI-MS. The chemical shifts of almost all of the carbons were similar to the corresponding carbons for gambiriin A1 (**3**), except for C-α_U (δ 48.7 in **13**, 46.7 in **3**) and C-8_L (δ 110.8 in **13**, 107.2 in **3**).[2] The chemical shift of C-6_L (δ 96.7) was also similar to that of the corresponding carbon of **3** (δ 97.5, C-6_L) rather than that of **11** (δ 94.9, C-8_L), suggesting a C-α_U – C-8_L linkage in **13**. The ROESY spectrum showed the correlations H-α_U/H-2'$_L$, H-α_U/H-6'$_L$, H-β_U/H-2'$_L$, and H-β_U/H-6'$_L$, substantiating the linkage position between C-α_U and C-8_L [Figure 5(a)]. The chemical shifts and the coupling patterns of the protons in the chalcane unit of **13** [δ 4.46 (d, J = 9.0 Hz, H-α_U), 4.77 (d, J = 2.5, 9.0 Hz, H-β_U)] were different from those of **3** [δ 4.86 (d, J = 3.0 Hz, H-α_U), 4.63 (m, H-β_U)].[2] Therefore, the structure of **13** was assigned as the diastereomer of **3** at the C-α_U carbon. The coupling constant between H-α_U and H-β_U (J = 9 Hz) and the ROE interactions H-α_U/H-γa_U, H-α_U/H-γb_U, H-β_U/H-2'$_U$, and H-β_U/H-6'$_U$ also satisfied the conformation in which the configuration of C-α_U is *S* [Figure 5(b)].

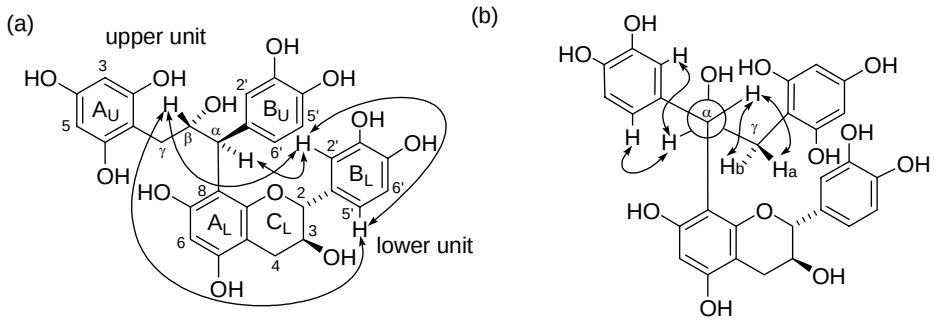

Figure 5. Important 2D-NMR correlations observed for **13**

(a) The ROE (H ↔ H) correlations indicated the location C-α_U→C-8_L of the interflavan linkage. (b) The ROE (H ↔ H) correlations H-α_U/H-γ_U and H-β_U/H-2'$_U$ (H-6'$_U$) satisfied the *S* configuration at C-α_U based on the conformation indicated.

Structural correlations of dimeric flavans with (+)-catechin

Gambiriin A1 (**3**) was the most abundant chalcane-flavan type dimer in gambir[5] and also in the product mixture obtained by heating (+)-catechin (**1**). However, gambirflavan D5 (**13**), the diastereomer at C-α_U of **3**, was only a minor product in the mixture and was not isolated directly from gambir; thus, compounds **3** and **13** may be produced via an intermediate **A** (formed from **1**). The right side of the phenyl–Cα cation–H plane in **A** was less hindered than that of the left side by the attachment of A-ring in **1**, as shown in Figure 6.

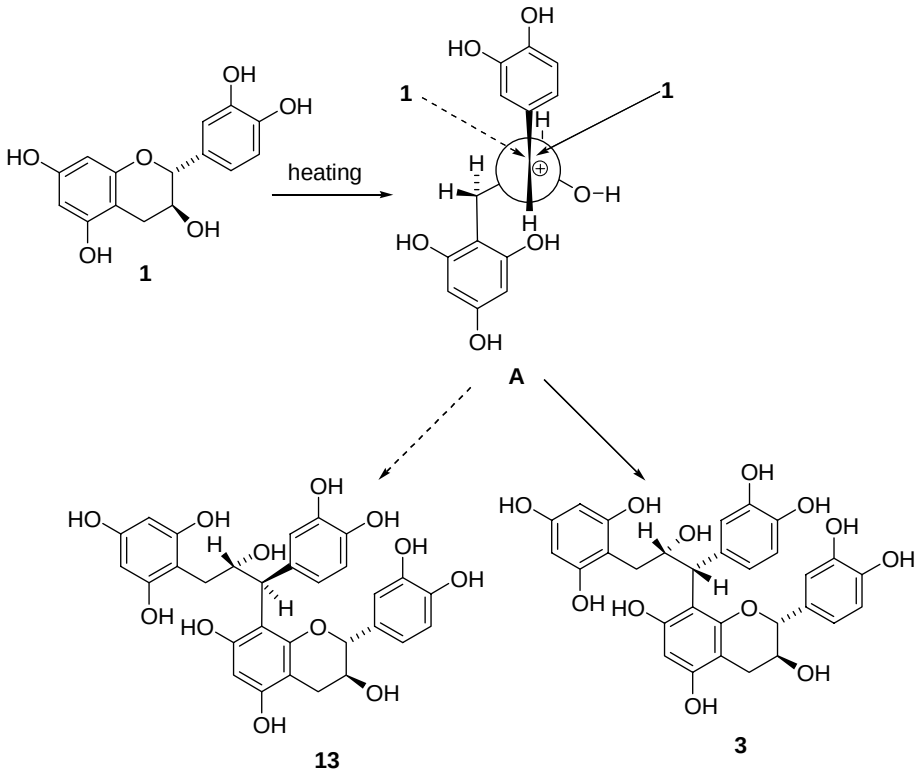

Figure 6. Proposed mechanism for the formation of **3** and **13** from **1**

The attachment of **1** from the right side of the phenyl–Cα cation–H plane of **A** produces **3** (indicated by solid arrow), and that from the left side produces **13** (indicated by dashed arrow).

We obtained four dimeric compounds with structures related to catechin. Figure 7 summarizes the structural correlations of the compounds isolated after heating catechin, as well as previously reported compounds.[2,3] All of these compounds, except for **13**, were also isolated directly from gambir. It can be assumed that these compounds are all produced from (+)-catechin (**1**), not only during biogenetical changes in the leaves of *U. gambir* but also during the preparation of the hot-water extracts of the plant. Our findings will help elucidate the structures and reactivity of condensed tannins that are structurally related to catechin.

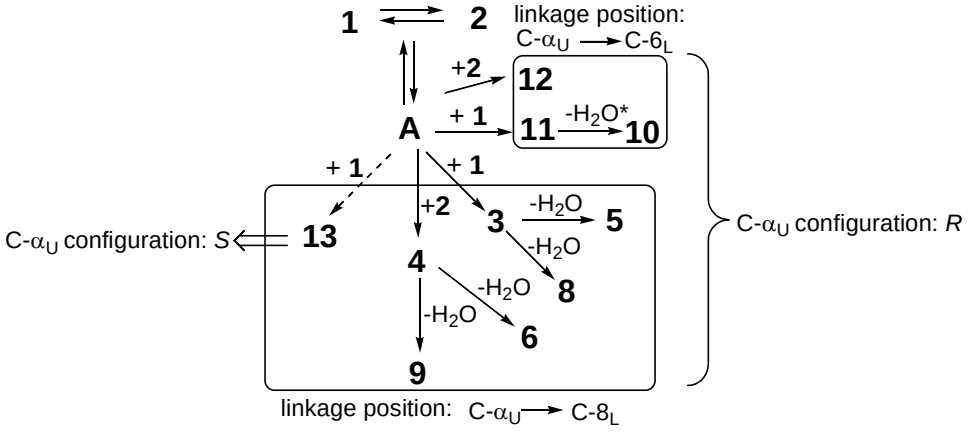

Figure 7. Structural relationship of compounds **2-6** and **8-13**, isolated from the mixture product of heating (+)-catechin (**1**)

*Conversion from **11** to **10** was not evidenced directly.

EXPERIMENTAL

General procedures Optical rotations were measured on a JASCO DIP-1000 digital polarimeter. CD spectra were recorded on a JASCO J-720 spectrophotometer. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR spectra were recorded on a Varian INOVA AS600 spectrometer. ESI-Mass spectra were taken with a Micromass AutoSpec OA-Tof in the positive-ion mode (solvent, 50% MeOH + 0.1% $AcONH_4$; flow rate, 20 μL min^{-1}). Column chromatography (CC) was performed using a Dia-ion HP-20 (Mitsubishi Chemical), Toyopearl HW-40 (Tosho), MCI-gel CHP-20P (Mitsubishi Chemical), Sephadex LH-20 (Amersham Biosciences), and Silica gel-ODS (Chromatorex).

Extraction and isolation Gambir (Lot No. 171203) was purchased from Tochimoto-tenkai-do (Osaka, Japan). The powdered material (2 kg) was homogenized with MeOH (22 L) at room temperature and the filtrate from the homogenate was evaporated to give the extract (1.3 kg). A portion (309 g) of the extract

was subjected to Dia-ion HP-20 CC.[2,3] The 40% MeOH eluate from the Dia-ion HP-20 column was chromatographed using a Toyopearl HW-40, and then MCI-gel CHP-20P columns. Fractions thus obtained were further purified on ODS and Sephadex, and by preparative HPLC, to give gambiriin A3 (**11**) (71.6 mg) and gambirflavan D4 (**12**) (6.4 mg). Fractions obtained from the MCI-gel CHP-20P columns were purified on columns of Toyopearl HW-40 and MCI-gel CHP-20P to give gambirflavan D3 (**10**) (35.6 mg).

Heating an aqueous solution of (+)-catechin (1) Compound **1** (1 g) in H_2O (10 mL) was autoclaved (121 ºC, 2 h) as reported previously.[2,3] The mother liquor after crystallization of un-reacted **1** (660 mg) was chromatographed on a Toyopearl HW-40 column. Fractions containing dimers were chromatographed on an MCI gel CHP-20P column and further purified by preparative HPLC to give gambiriin A3 (**11**) (10.0 mg). Products from **1** (4 g) were separated in a similar way to give gambirflavan D3 (**10**) (11.8 mg), gambirflavan D4 (**12**) (9.5 mg), and gambiflavan D5 (**13**) (12.6 mg).

Gambirflavan D3 (10) A brown amorphous powder, $[\alpha]_D^{24}$ +9.8º (*c* 0.2, acetone). ESI-MS *m/z*: 563 ($[M + H]^+$), 580 ($[M + NH_4]^+$). HR-ESI-MS *m/z*: 580.1832 ($[M + NH_4]^+$) (Calcd for $C_{30}H_{26}O_{11} + NH_4$ 580.1819). CD (MeOH): $[\theta]_{208}$ -2.3 × 10^4, $[\theta]_{222}$ +2.8 × 10^4, $[\theta]_{245}$ -3.7 × 10^4, $[\theta]_{281}$ -2.7 × 10^3. ^{1}H-NMR (600 MHz, acetone-d_6+D_2O, 27 ºC) δ: 2.60 (1H, dd, *J* = 9.0, 15.5 Hz, H-4a_L), 2.90 (1H, dd, *J* = 6.0, 15.5 Hz, H-4a_L), 2.95 (1H, dd, *J* = 6.0, 13.0 Hz, H-γa_U), 3.00 (1H, dd, *J* = 8.5, 13.0 Hz, H-γb_U), 4.02 (1H, dt, *J* = 6.0, 9.0 Hz, H-3_L), 4.36 (1H, d, *J* = 3.5 Hz, H-α_U), 4.54 (1H, d, *J* = 9.0 Hz, H-2_L), 4.80 (1H, ddd, *J* = 3.5, 6.0, 8.5 Hz, H-β_U), 5.87 (1H, s, H-8_L), 5.99 (2H, s, H-3_U, H-5_U), 6.22 (1H, dd, *J* = 2.0, 8.5 Hz, H-6'$_U$), 6.40 (1H, d, *J* = 2.0 Hz, H-2'$_U$), 6.59 (1H, d, *J* = 8.5 Hz, H-5'$_U$), 6.76 (H, dd, *J* = 2.0, 8.5 Hz, H-6'$_L$), 6.78 (1H, d, *J* = 8.5 Hz, H-5'$_L$), 6.91 (1H, d, *J* = 2.0 Hz, H-2'$_L$). ^{13}C-NMR (150 MHz, acetone-d_6+D_2O, 27 ºC): δ 28.9 (C-4_L), 50.0 (C-α_U), 67.9 (C-3_L), 82.9 (C-2_L), 93.1 (C-β_U), 95.3 (2C, C-3_U, C-5_U), 95.9 (C-8_L), 96.4 (C-10_L), 102.3 (C-1_U), 108.6 (C-6_L), 115.0 (C-2'$_U$), 115.3 (C-2'$_L$), 115.5 (C-5'$_L$), 115.6 (C-5'$_U$), 119.3 (C-6'$_U$), 120.0 (C-6'$_L$), 131.8 (C-1'$_L$), 137.2 (C-1'$_U$), 143.8 (C-4'$_U$), 145.4 (C-3'$_U$), 145.5, 145.6, (C-3'$_L$, C-4'$_L$), 153.9 (C-7_L), 156.4 (C-9_L), 157.7 (C-4_U), 158.1 (2C, C-2_U, C-6_U), 160.0 (C-5_L). The C-γ$_U$ signal overlapped with solvent peaks at δ 29-30.

Gambiriin A3 (11) An amorphous brownish powder, $[\alpha]_D^{24}$ -2.4º (*c* 0.5, acetone). ESI-MS *m/z*: 581 ($[M + H]^+$), 603 ($[M + Na]^+$. CD (MeOH): $[\theta]_{209}$ -5.7 × 10^4, $[\theta]_{237}$ -2.1 × 10^4, $[\theta]_{271}$ -3.0 × 10^3, $[\theta]_{279}$ +1.5 × 10^3. ^{1}H-NMR (600 MHz, acetone-d_6+D_2O, 27 ºC): δ 2.55 (1H, dd, *J* = 9.0, 16.0 Hz, H-4a_L), 2.59 (1H, m, H-γa_U), 2.96 (1H, dd *J* = 6.0, 16.0 Hz, H-4b_L), 2.96 (1H, dd, *J* = 6.0, 16.0 Hz, H-γb_U), 3.96 (1H, dt, *J* =

6.0, 8.5 Hz, H-3_L), 4.47 (1H, d, *J* = 9.0 Hz, H-2_L), 4.63 (1H, m, H-β_U), 4.86 (1H, d, *J* = 3.0 Hz, H-α_U), 5.96 (2H, s, H-3_U, H-5_U), 5.99 (1H, s, H-8_L), 6.64 (1H, d, *J* = 8.5 Hz, H-5'$_U$), 6.67 (1H, dd, *J* = 2.0, 8.5 Hz, H-6'$_U$), 6.75 (1H, dd, *J* = 2.0, 8.5 Hz, H-6'$_L$), 6.78 (1H, d, *J* = 8.5 Hz, H-5'$_L$), 6.81 (1H, br s, H-2'$_U$), 6.91, (1H, d, *J* = 2.0 Hz, H-2'$_L$). ^{13}C-NMR (150 MHz, acetone-d_6+D_2O, 27 ºC): δ 46.0 (C-α_U), 68.5 (C-3_L), 77.5 (C-β_U), 82.7 (C-2_L), 94.9 (C-8_L), 95.7 (2C, C-3_U,C-5_U), 101.7 (C-10_L), 105.3 (C-1_U), 107.4 (C-6_L), 115.4 (2C, C-2', C-5'$_L$), 115.5 (C-5'$_U$), 116.3 (C-2'$_U$), 120.2, (C-6'$_L$), 120.2 (C-6'$_U$), 131.9 (C-1'$_L$), 134.9 (C-1'$_U$), 143.6 (C-4'$_U$), 145.2 (C-3'$_U$), 145.5 (C-3'$_L$), 145.7 (C-4'$_L$), 155.0 (C-9_L), 155.8, 156.0 (C-5_L, C-7_L), 157.5 (2C, C-2_U, C-6_U), 157.6 (C-4_U). The C-4_L and C-α_U signals overlapped with solvent peaks at δ 29-30.

Gambirflavan D4 (12) A brown amorphous powder, $[\alpha]_D^{24}$ -16.5º (*c* 0.2, acetone). ESI-MS *m/z* 581 ($[M + H]^+$), 598 ($[M + NH_4]^+$). HR-ESI-MS *m/z* 598.1928 ($[M + NH_4]^+$) (Calcd for $C_{30}H_{28}O_{12}$ +NH_4, 598.1925). CD (MeOH): $[\theta]_{214}$ -3.6 × 10^4, $[\theta]_{239}$ -3.6 × 10^4, $[\theta]_{270}$ -2.9 × 10^3, $[\theta]_{284}$ +2.5 × 10^3. ^{1}H-NMR (600 MHz, acetone-d_6+D_2O, 27 ºC): δ 2.59 (1H, dd, *J* = 9.5, 14.5 Hz, H-γa_U), 2.82 (2H, m, H-4_L), 2.99 (1H, dd, *J* = 1.5, 14.5 Hz, H-γb_U), 4.17 (1H, m, H-3_L), 4.63 (1H, ddd, *J* = 1.5, 3.5, 9.5 Hz, H-β_U), 4.83 (1H, brs, H-2_L), 4.87 (1H, d, *J* = 3.5 Hz, H-α_U), 5.96 (2H, s, H-3_U, H-5_U), 6.06 (1H, s, H-8_L), 6.65 (1H, *d*, *J* = 8.0 Hz, H-5'$_U$), 6.67 (1H, dd, *J* = 2.0, 8.0 Hz, H-6'$_U$), 6.78 (1H, d, *J* = 8.0 Hz, H-5'$_L$), 6.81 (1H, d, *J* = 2.0 Hz, H-2'$_U$), 6.83 (1H, dd, *J* = 2.0, 8.0 Hz, H-6'$_L$), 7.06 (1H, d, *J* = 2.0 Hz, H-2'$_L$). ^{13}C-NMR (150 MHz, acetone-d_6+D_2O, 27 ºC): δ 30.3 (C-γ_U), 46.0 (C-α_U), 66.9 (C-3_L), 77.6 (C-β_U), 79.3 (C-2_L), 95.3 (C-8_L), 95.7 (2C, C-3_U, C-$_U$5), 100.7 (C-10_L), 105.3 (C-1_U), 107.5 (C-6_L), 115.2 (C-2_L), 115.4 (C-5'$_L$), 115.4 (C-5'$_U$), 116.4 (C-2'$_U$), 119.2 (C-6'$_L$), 120.2 (C-6'$_U$), 132.3 (C-1'$_L$), 135.1 (C-1'$_U$), 143.6 (C-4'$_U$), 145.18, 145.21, 145.3 (C-3'$_U$, C-3'$_L$, C-4'$_L$), 155.3 (C-9_L), 155.8 (C-5_L), 156.2 (C-7_L), 157.5 (2C, C-2_U, C-6_U), 157.7 (C-4_U). The C-4_L signal overlapped with solvent peaks at δ 29-30.

Gambirflavan D5 (13) An amorphous brownish powder, $[\alpha]_D^{24}$ -29.2º (*c* 0.5, acetone). ESI-MS *m/z* 581 ($[M + H]^+$). HR-ESI-MS *m/z*: 581.1668 ($[M + H]^+$) (Calcd for $C_{30}H_{28}O_{12}$ +H, 581.1659). CD (MeOH): $[\theta]_{212}$ -9.5 × 10^4, $[\theta]_{247}$ -6.1 × 10^4, $[\theta]_{245}$ +1.2 × 10^3, $[\theta]_{245}$ -3.4 × 10^3. ^{1}H-NMR (600 MHz, acetone-d_6+D_2O, 40 ºC): δ 2.38 (1H, br s, H-γa_U), 2.49 (1H, dd, *J* = 9.0, 16.0 Hz, H-4a_L), 2.93 (1H, dd, *J* = 6.0, 16.0 Hz, H-4b_L), 3.02 (1H, dd, *J* = 2.0, 14.5 Hz, H-γa_U), 3.89 (1H, dt, *J* = 6.0, 9.0 Hz, H-3_L), 4.46 (1H, d, *J* = 8.5 Hz, H-α_U), 4.60 (1H, br d, *J* = 6.0 Hz, H-2_L), 4.77 (1H, d, *J* = 2.0, 8.5 Hz, H-β_U), 5.90 (2H, s, H-3_U, H-5_U), 6.09 (1H, s, H-6_L), 6.59 (1H, d, *J* = 8.5 Hz, H-5'$_U$), 6.73 (1H, dd, *J* = 2.0, 8.5 Hz, H-6'$_L$), 6.76 (1H, d, *J* = 8.5 Hz, H-5'$_L$), 6.79 (1H, d, *J* = 2.5 Hz, 8.5 Hz, H-6'$_U$), 6.92 (1H, d, *J* = 2.0 Hz, H-2'$_L$), 6.99 (1H, d, *J* = 2.5 Hz, H-2'$_U$). ^{13}C-NMR (150 MHz, acetone-d_6+D_2O, 40 ºC): δ 29.7 (C-4_L), 30.2 (C-γ_U),

48.7 (C-α_U), 68.3 (C-3_L), 75.5 (C-β_U), 82.5 (C-2_L), 96.1 (2C, C-3_U, C-5_U), 96.7 (C-6_L), 101.3 (C-10_L), 106.1 (C-1_U), 110.8 (C-8_L), 115.3 (C-5'$_U$), 115.72 (C-2'$_L$), 115.74 (C-5'$_L$), 117.9 (C-2'$_U$), 120.6 (C-6'$_L$), 122.0 (C-6'$_U$), 132.0 (C-1'$_L$), 135.9 (C-1'$_U$), 143.5 (C-3'$_U$), 144.7 (C-4'$_U$), 145.3 (C-3'$_L$), 145.5 (C-4'$_L$), 154.4 (C-9_L), 154.5. (C-7_L), 154.7 (C-5_L), 157.4 (C-4_U), 158.0 (2C, C-2_U, C-6_U).

ACKNOWLEDGEMENTS

The INOVA AS600 NMR instrument used in this study is the property of SC-NMR of Okayama University. This study was partially supported by a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science.

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