Tannins and Related Compounds. XCI.[1] Isolation and Characterization of Proanthocyanidins with an Intramolecularly Doubly-Linked Unit from the Fern, *Dicranopteris pedata* HOUTT.

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A chemical examination of the polyphenolic constituents of the fern, *Dicranopteris pedata* HOUTT., has led to the isolation of eight new proanthocyanidins possessing a doubly-linked (A-type) unit, together with known flavan-3-ols and proanthocyanidins. On the basis of chemical and spectroscopic evidence, they are characterized as epiafzelechin-(4β→8, 2β→*O*→7)-epiafzelechin-(4α→8)-epiafzelechin (8), epicatechin-(4β→8, 2β→*O*→7)-epiafzelechin-(4α→8)-epiafzelechin (9), epiafzelechin-(4β→8, 2β→*O*→7)-epiafzelechin-(4α→8)-epicatechin (10), epiafzelechin-(4β→8, 2β→*O*→7)-epicatechin-(4α→8)-epicatechin (11), epicatechin-(4β→8, 2β→*O*→7)-epiafzelechin-(4α→8)-epicatechin (12), epicatechin-(4β→8, 2β→*O*→7)-epicatechin-(4α→8)-epiafzelechin (13), epicatechin-(4β→8, 2β→*O*→7)-epicatechin-(4α→8)-epigallocatechin (14) and epiafzelechin-(4β→8)-epicatechin-(4β→8, 2β→*O*→7)-epicatechin-(4α→8)-epicatechin (15).

Keywords *Dicranopteris pedata*; Gleicheniaceae; fern; doubly-linked proanthocyanidin; A-type proanthocyanidin; epiafzelechin; epicatechin; epigallocatechin; condensed tannin; thiolytic degradation

Although the order Filicales comprises about 9000 species and some of them are regarded as rich sources of tannins, there has been almost no work done to identify tannins except for a few cases.[2] In previous papers, we demonstrated the presence of the allosides[3] and carboxymethyl derivatives[4] of flavan-3-ols and proanthocyanidins in the rhizomes of the subtropical fern, *Devallia divaricata* BLUME, growing in Taiwan. In continuing our chemical studies on tannins in ferns, we have examined *Dicranopteris pedata* HOUTT. (Gleicheniaceae) (Japanese name: koshida), which is widely distributed in the southern area of Japan, and this has resulted in the isolation of eight new proanthocyanidins, together with known flavan-3-ols and proanthocyanidins. This paper describes the isolation and characterization of these compounds.

The fresh whole plant of *Dicranopteris pedata* HOUTT. was extracted with 80% aqueous acetone, and the extract was subjected to a combination of chromatographies over Sephadex LH-20, MCI-gel CHP 20P, Bondapak C_{18}/Porasil B, prep-PAK 500/C_{18} and Kusano packed column ODS with various solvent systems to yield compounds **1**—**15**. Among them, compounds **1**—**7** were found to be identical with (−)-epiafzelechin (**1**),[5] (−)-epicatechin (**2**),[6] (−)-epigallocatechin (**3**),[7] epiafzelechin-(4β→8)-epiafzelechin (**4**),[5] epicatechin-(4β→8, 2β→*O*→7)-epicatechin-(4α→8)-epicatechin (**5**),[8] epicatechin-(4β→8)-spicatechin-(4β→8, 2β→*O*→7)-epicatechin-(4α→8)-epicatechin (**6**)[8] and epicatechin-(4β→8)-epicatechin-(4β→8)-epicatechin-(4β→8, 2β→*O*→7)-epicatechin-(4α→8)-catechin (**7**),[8] by comparisons of their physical and spectral data with those of authentic samples.

Compound **8** showed an orange coloration characteristic of proanthocyanidins with the anisaldehyde–sulfuric acid reagent. The ^{13}C-nuclear magnetic resonance (^{13}C-NMR) spectrum of **8** was similar to that of **5** in that it showed signals due to flavan C-2 at δ 79.7 and 78.3, and a ketal carbon at δ 104.4, suggesting that **8** possesses a trimeric constitution with a proanthocyanidin A-type (doubly-linked) unit in the molecule.[9] However, the carbon resonances arising from the flavan B-rings differed from those of **5**, exhibiting the presence of *p*-hydroxyphenyl groups. In addition, the negative fast atom bombardment

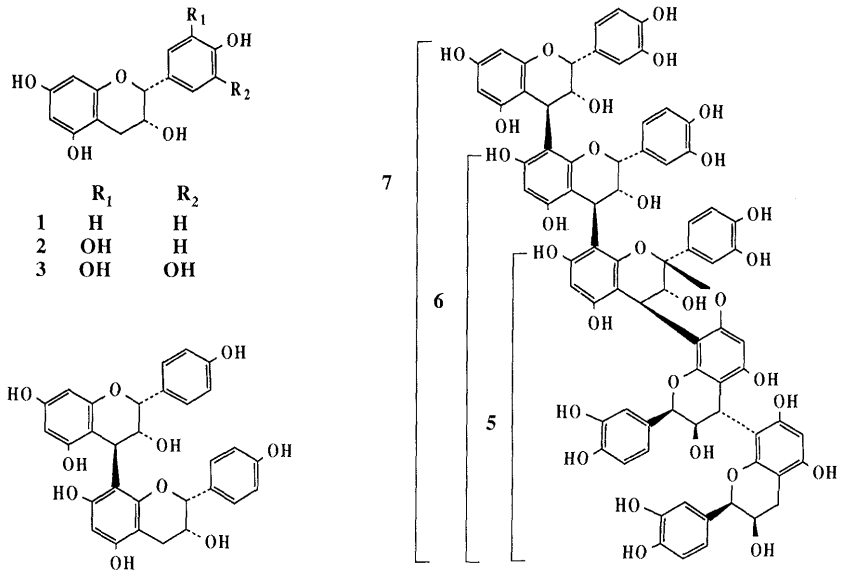
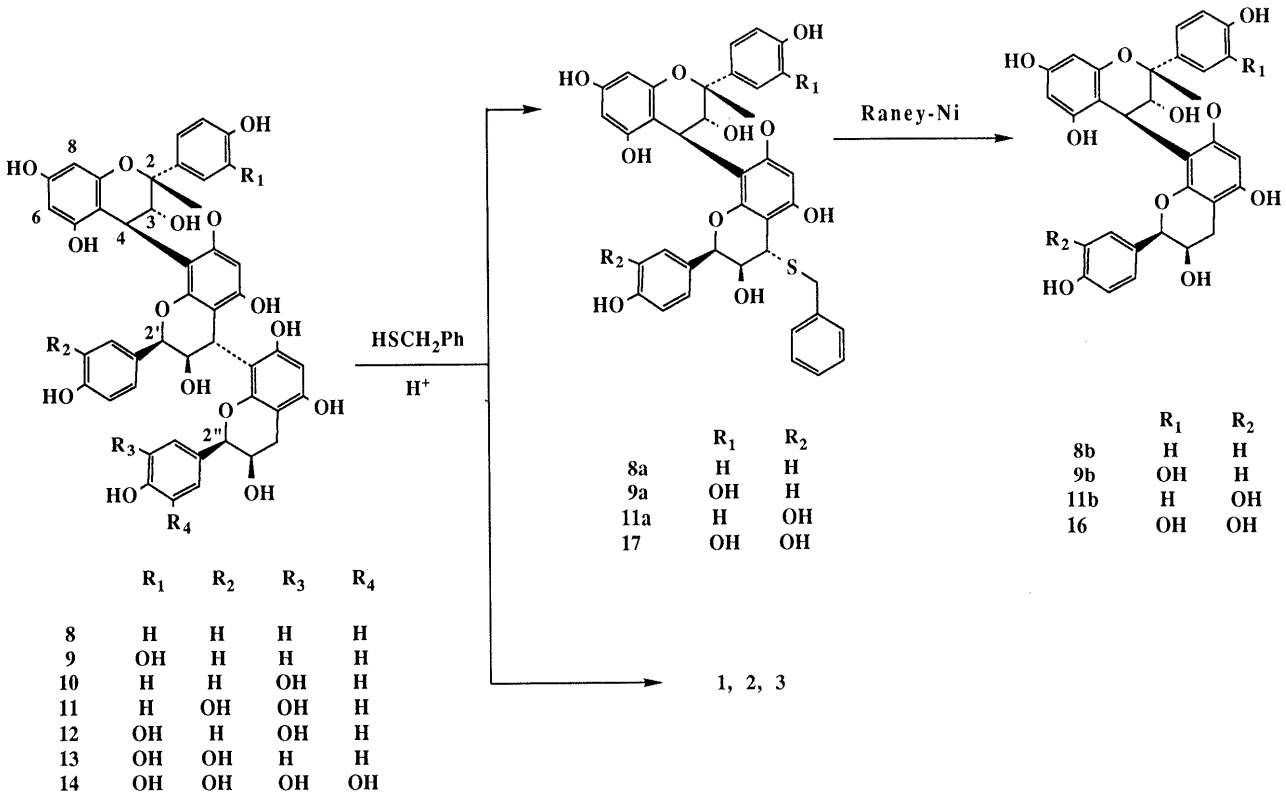


Chart 1



	R_1	R_2	R_3	R_4
8	H	H	H	H
9	OH	H	H	H
10	H	H	OH	H
11	H	OH	OH	H
12	OH	H	OH	H
13	OH	OH	H	H
14	OH	OH	OH	OH

	R_1	R_2
8a	H	H
9a	OH	H
11a	H	OH
17	OH	OH

	R_1	R_2
8b	H	H
9b	OH	H
11b	H	OH
16	OH	OH

Chart 2

mass spectrum (FAB-MS) of **8** showed the $(M-H)^-$ peak at *m/z* 815, which was 48 mass units less than that of **5**, suggesting that **8** consists entirely of epiafzelechin units.

Acid-catalyzed degradation of **8** in the presence of benzylmercaptan yielded a thioether (**8a**) and (−)-epiafzelechin (**1**). When desulfurized with Raney nickel, the thioether (**8a**) afforded a dimeric proanthocyanidin (**8b**). The ^{1}H-NMR spectrum of **8b** was similar to that of proanthocyanidin A-2 (**16**),[8] but differed only in the observation of two sets of A_2B_2-type aromatic signals instead of the ABX-type aromatic signals. Furthermore, the Cotton effects in the circular dichroism (CD) spectrum of **8b** closely resembled those[8,9] of **16**. Therefore, the structure of **8b** was characterized as epiafzelechin-(4β→8, 2β→*O*→7)-epiafzelechin.

The location of the interflavonoid linkage between **8b** and epiafzelechin units was concluded to be at the C-4′ and C-8 positions, since in the ^{1}H-NMR spectra of **8**, the resonances due to flavan C-rings were almost identical with those[8] observed in **5**.[8] Accordingly, the structure of **8** was established as epiafzelechin-(4β→8, 2β→*O*→7)-epiafzelechin-(4α→8)-epiafzelechin (**8**).

Since compounds **9** and **10** possessed similar chromatographic properties, they were initially regarded as homogeneous. However, analysis by high-performance liquid chromatography (HPLC), as well as by ^{1}H- and ^{13}C-NMR spectroscopies, showed the existence of two structural isomers. The mixture was separated successfully by chromatography over Kusano packed column ODS, monitoring by HPLC. The ^{13}C-NMR spectra of **9** and **10** were similar to each other, and were also closely correlated with that of **8**. In particular, the chemical shifts due to the flavan C-ring carbons were almost identical with those observed in **8**. However, resonances attributable to the flavan B-rings indicated the presence of one catechol-type aromatic ring in each case. This was consistent with the negative FAB-MS of **9** and **10**, which showed the same $(M-H)^-$ peak at *m/z* 831, being 16 mass units more than that of **8**.

Treatment of **9** with benzylmercaptan in the presence of acetic acid afforded a thioether (**9a**) and a flavan-3-ol. The latter was found to be identical with (−)-epiafzelechin (**1**).[5] Subsequently, the thioether (**9a**) was desulfurized with Raney nickel to furnish a dimeric proanthocyanidin (**9b**). The ^{1}H-NMR spectrum of **9b** resembled that of the known proanthocyanidin A-2 (**16**), except for the appearance of an A_2B_2-type aromatic signal pattern, suggesting **9b** to be a doubly-linked proanthocyanidin consisting of epiafzelechin and epicatechin units. In addition, in the ^{1}H–^{1}H homonuclear shift correlation (COSY) spectrum of **9b**, a long-range coupling was observed between the lower flavan H-2 (δ 5.05) and one (δ 7.60) of the A_2B_2- type aromatic signals,[10] thus, confirming that the lower flavan unit is epiafzelechin-type. Since the CD spectrum of **9b** was closely correlated with that [$+5\times10^{-4}$ (225), -0.9×10^4 (276)] of **16**, the absolute stereostructure was concluded to be the same as that of **16**. Thus, the structure of **9b** was established as epicatechin-(4β→8, 2β→*O*→7)-epiafzelechin. On the other hand, thiolytic degradation of **10** afforded a thioether and a flavan-3-ol, and these were found to be identical with **8a** and (−)-epicatechin (**2**),[6] respectively. The locations and configurations of the interflavonoid linkages in **9** and **10** were concluded to be the same as those in **5**, based on the fact that the carbon resonances due to the flavan C-rings coincided well with those of **5** in each case. Consequently, the structures of **9** and **10** were characterized as epicatechin-(4β→8, 2β→*O*→7)-epiafzelechin-(4α→8)-epiafzelechin (**9**) and epiafzelechin-(4β→8, 2β→*O*→7)-epiafzelechin-(4α→8)-epicatechin (**10**),

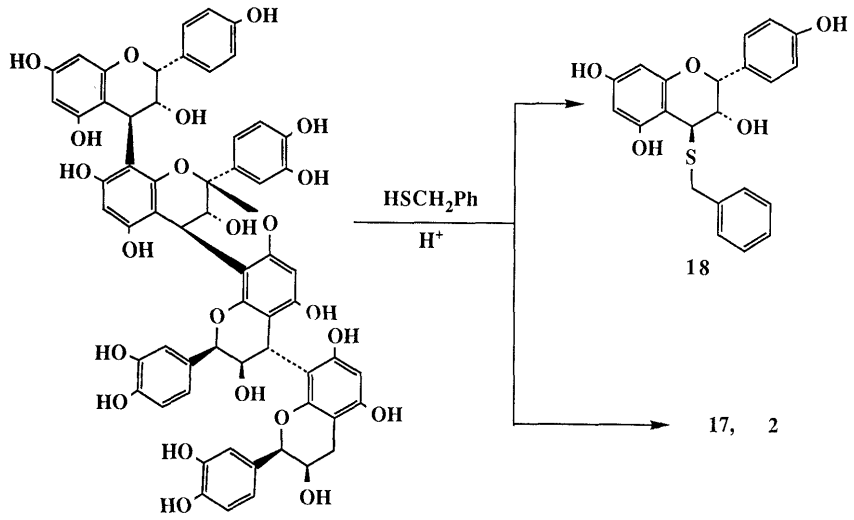


Chart 3

respectively.

Compounds **11**, **12** and **13** were initially obtained as a mixture, which was separated successfully by similar careful reverse-phase chromatography. The negative FAB-MS of **11**, **12** and **13** showed the same $(M-H)^-$ peak at *m/z* 847, which is 16 mass units less than that of **5**. The ^{13}C-NMR spectra of these compounds were similar, and also resembled that of **5**, except for the atomatic carbon signals attributed to the flavan B-rings. Since the ^{13}C-NMR chemical shifts attributed to the flavan C-rings were almost identical with those of **5**, these compounds were considered to have different B-ring substitution systems. Thiolytic degradation of **11** furnished a thioether (**11a**) and (−)-epicatechin (**2**), and subsequent desulfurization of **11a** with Raney nickel afforded a dimeric proanthocyanidin (**11b**). The ^1H-NMR spectrum of **11b** resembled that of **9b**, but differed only in the observation of a long-range coupling between the lower flavan H-2 signal (δ 4.97) and two [δ 7.06 (1H, dd, $J=2$, 8 Hz) and 7.32 (1H, d, $J=2$ Hz)] of the ABX-type aromatic signals in the ^1H–^1H COSY spectrum. Moreover, the CD spectrum of **11b** corresponded to that of **16**, and thus the structure of **11b** was concluded to be epiafzelechin-(4β→8, 2β→*O*→7)-epicatechin. On the other hand, thiolytic degradation of **12** yielded **9a** and **2**, while **13** afforded proanthocyanidin A-2 4′-benzylthioether (**17**)[8] and **1**. Therefore, the structures of compounds **11**, **12** and **13** were represented as shown in Chart 2.

Compound **14** showed, in the negative FAB-MS, the peak at *m/z* 879 due to $(M-H)^-$, which was found to be 16 mass units more than that of **5**. Acid-catalyzed degradation in the presence of benzylmercaptan furnished a thioether and a flavan-3-ol, which were found to be identical with proanthocyanidin A-2 4′-benzylthioether (**17**)[8] and (−)-epigallocatechin (**3**).[7] Based on the fact that the ^{13}C-NMR chemical shifts of the flavan C-ring carbons in **14** agreed well with those observed in **5**, the locations and configurations of interflavonoid linkages were concluded to be the same as those of **5**. Accordingly, **14** was characterized as epicatechin-(4β→8, 2β→*O*→7)-epicatechin-(4α→8)-epigallocatechin (**14**).

Compound **15** showed, in the negative FAB-MS, the $(M-H)^-$ peak at *m/z* 1136 corresponding to a tetrameric constitution. The ^{13}C-NMR spectrum of **15** revealed three flavan C-2 signals at δ 79.6, 78.1 and 75.9, and one ketal carbon signals at δ 104.3, suggesting that **15** is a tetrameric proanthocyanidin possessing a proanthocyanidin A-type unit. Complete thiolytic degradation to afford (−)-epiafzelechin 4-benzylthioether (**18**),[5] **17** and **2** confirmed its constitution. Since the chemical shifts of the carbon resonances attributable to the flavan C-rings were in good agreement with those[8] observed in **6**, the positions and configurations of the interflavonoid linkages were concluded to be the same as those in **6**. Therefore, **15** was characterized as epiafzelechin-(4β→8)-epicatechin-(4β→8, 2β→*O*→7)-epicatechin-(4α→8)-epicatechin (**15**).

In conclusion, the fern, *Dicranopteris pedata*, was found to contain large amounts of proanthocyanidins possessing a proanthocyanidin A-type (doubly-linked) unit, accompanied by B-type (singly-linked) proanthocyanidin dimers. It is of great interest from the biosynthetic point of view that the A-type proanthocyanidin dimer is missing in this plant and that the trimeric proanthocyanidin (**5**) is largely accumulated. Furthermore, the fact that the proanthocyanidin compositions in this fern are quite similar to those of the Angiospermous plants, *Cinnamomum zeylanicum*[8] and *C. sieboldii*,[11] is of great chemotaxonomical interest.

Experimental

The instruments and chromatographic conditions used throughout this work were essentially the same as described in the preceding paper.[12]

Extraction and Isolation The fresh whole plants of *Dicranopteris pedata* (30.5 kg), collected in August 1987 in the Kasuya experimental forest of Kyushu University, were extracted with 80% aqueous acetone at room temperature. The acetone was removed by evaporation under reduced pressure, and the resulting aqueous solution afforded dark green precipitates consisting mainly of chlorophylls, which were removed by filtration. The filtrate was subjected to chromatography over Sephadex LH-20 with H_2O containing increasing amounts of MeOH and then with 50% aqueous acetone to give four fractions (fractions I—IV). Fraction II was subsequently chromatographed over Sephadex LH-20 with acetone to yield four fractions which were individually chromatographed over Sephadex LH-20 (60% aqueous MeOH) and MCI-gel CHP 20P [H_2O–

MeOH (1:0→1:1)] to furnish (−)-epiafzelechin (**1**)[5] (8 mg), epicatechin (**2**)[6] (224 mg), (−)-epigallocatechin (**3**)[7] (13 mg) and epiafzelechin-(4β→8)-epiafzelechin (**4**)[5] (23 mg). Fraction III was fractionated by Sephadex LH-20 column chromatography with EtOH–H_2O (1:0→3:2) into two fractions (fractions III-1 and III-2). Chromatography of fraction III-1 over Sephadex LH-20 [acetone–H_2O (1:0→9:1)] afforded three further fractions (fractions III-1a—III-1c). Repeated chromatography of fraction III-1a over Sephadex LH-20 (60% aqueous MeOH) and prep-PAK 500/C_{18} [H_2O–MeOH (1:0→1:1)] furnished compound **8** (860 mg). Fraction III-1b was chromatographed over Sephadex LH-20 (60% aqueous MeOH) and MCI-gel CHP 20P [H_2O–MeOH (1:0→1:1)] to give a mixture of compounds **9** and **10**, which was separated successfully by chromatography over Kusano packed column ODS (20% aqueous MeOH), monitoring by HPLC, to afford **9** (180 mg) and **10** (374 mg). Repeated chromatography of fraction III-1c over MCI-gel CHP 20P [H_2O–MeOH (1:0→1:1)] and Kusano packed column ODS (20% aqueous MeOH), monitoring by HPLC, furnished compounds **11** (341 mg), **12** (175 mg) and **13** (250 mg). Fraction III-2 was subjected to chromatography over Sephadex LH-20 with 60% aqueous MeOH to give two fractions (fractions III-2a and III-2b). Repeated chromatography of fraction III-2a over MCI-gel CHP 20P and prep-PAK 500/C_{18} with H_2O containing increasing amounts of MeOH afforded compounds **14** (735 mg), **15** (368 mg), epicatechin-(4β→8)-epicatechin-(4β→8, 2β→*O*→7)-epicatechin-(4β→8)-epicatechin (**6**)[8] (3.0 g) and epicatechin-(4β→8)-epicatechin-(4β→8)-epicatechin-(4β→8, 2β→*O*→7)-epicatechin-(4β→8)-epicatechin (**7**)[8] (365 mg). Fraction III-2b consisted mainly of epicatechin-(4β→8, 2β→*O*→7)-epicatechin-(4β→8)-epicatechin (**5**),[8] and was purified by chromatography over Fuji-gel ODS G3 [H_2O–MeOH (1:0→1:1)] to yield **5** (*ca.* 31 g).

Compound 8 A tan amorphous powder, $[\alpha]_D^{24}$ +79.1° (*c*=0.9, acetone). *Anal.* Calcd for $C_{45}H_{36}O_{15}\cdot 3H_2O$: C, 62.06; H, 4.86. Found: C, 62.46; H, 4.89. Negative FAB-MS *m/z*: 815 $(M-H)^-$. The ^{1}H-NMR was complicated by rotational isomerism. ^{13}C-NMR (acetone-d_6+D_2O): 38.1 (C-4′), 78.3 (C-2′), 79.7 (C-2″), 104.4 (C-2).

Compound 9 A tan amorphous powder, $[\alpha]_D^{26}$ +73.3° (*c*=0.7, acetone). *Anal.* Calcd for $C_{45}H_{36}O_{16}\cdot 2H_2O$: C, 62.21; H, 4.64. Found: C, 62.00; H, 4.65. Negative FAB-MS *m/z*: 831 $(M-H)^-$. The ^{1}H-NMR spectrum was complicated by rotational isomerism. ^{13}C-NMR (acetone-d_6+D_2O): 38.0 (C-4′), 66.5 (C-3, 3″), 71.7 (C-3′), 78.2 (C-2′), 79.7 (C-2″), 104.4 (C-2).

Compound 10 A tan amorphous powder, $[\alpha]_D^{26}$ +84.0° (*c*=0.8, acetone). *Anal.* Calcd for $C_{45}H_{36}O_{16}\cdot 3H_2O$: C, 60.94; H, 4.77. Found: C, 60.75; H, 4.73. Negative FAB-MS *m/z*: 831 $(M-H)^-$. The ^{1}H-NMR spectrum was complicated by rotational isomerism. ^{13}C-NMR (acetone-d_6+D_2O): 38.0 (C-4′), 66.5 (C-3, 3″), 71.6 (C-3′), 78.1 (C-2′), 79.7 (C-2″), 104.5 (C-2).

Compound 11 A tan amorphous powder, $[\alpha]_D^{25}$ +72.5° (*c*=0.7, acetone). *Anal.* Calcd for $C_{45}H_{36}O_{17}\cdot 3H_2O$: C, 59.86; H, 4.69. Found: C, 60.38; H, 4.70. Negative FAB-MS *m/z*: 847 $(M-H)^-$. The ^{1}H-NMR spectrum was complicated by rotational isomerism. ^{13}C-NMR (acetone-d_6+D_2O): 38.0 (C-4′), 66.5, 66.7 (C-3, 3″), 71.6 (C-3′), 78.2 (C-2′), 79.7 (C-2″), 104.5 (C-2).

Compound 12 A tan amorphous powder, $[\alpha]_D^{26}$ +103.3° (*c*=0.4, acetone). *Anal.* Calcd for $C_{45}H_{36}O_{17}\cdot 7/2\,H_2O$: C, 59.27; H, 4.75. Found: C, 59.25; H, 4.71. Negative FAB-MS *m/z*: 847 $(M-H)^-$. The ^{1}H-NMR spectrum was complicated by rotational isomerism. ^{13}C-NMR (acetone-d_6+D_2O): 38.1 (C-4′), 66.6 (2C) (C-3, 3″), 71.7 (C-3′), 78.2 (C-2′), 79.9 (C-2″), 104.5 (C-2).

Compound 13 A tan amorphous powder, $[\alpha]_D^{25}$ +80.8° (*c*=0.7, acetone). *Anal.* Calcd for $C_{45}H_{36}O_{17}\cdot 2H_2O$: C, 61.08; H, 4.56. Found: C, 61.38; H, 4.55. Negative FAB-MS *m/z*: 847 $(M-H)^-$. The ^{1}H-NMR spectrum was complicated by rotational isomerism. ^{13}C-NMR (acetone-d_6+D_2O): 38.1 (C-4′), 66.6 (2C) (C-3, 3″), 71.8 (C-3′), 78.3 (C-2′), 79.8 (C-2″), 104.4 (C-2).

Compound 14 A tan amorphous powder, $[\alpha]_D^{24}$ +71.2° (*c*=0.9, acetone). *Anal.* Calcd for $C_{45}H_{36}O_{19}\cdot 3/2H_2O$: C, 59.54; H, 4.33. Found: C, 59.14; H, 4.66. Negative FAB-MS *m/z*: 879 $(M-H)^-$. The ^{1}H-NMR spectrum was complicated by rotational isomerism. ^{13}C-NMR (acetone-d_6+D_2O): 38.1 (C-4′), 66.8 (2C) (C-3, 3″), 71.8 (C-3′), 78.3 (C-2′), 80.1 (C-2″), 104.7 (C-2).

Compound 15 A tan amorphous powder, $[\alpha]_D^{24}$ +53.4° (*c*=0.8, acetone). *Anal.* Calcd for $C_{60}H_{48}O_{23}\cdot 4H_2O$: C, 59.60; H, 4.67. Found: C, 59.70; H, 4.76. Negative FAB-MS *m/z*: 1136 $(M-H)^-$. The ^{1}H-NMR spectrum was complicated by rotational isomerism. ^{13}C-NMR (acetone-d_6+D_2O): 37.2 (C-4″), 38.3 (C-4′), 60.3, 66.6 (C-3′, 3‴), 70.8 (C-3), 71.5 (C-3″), 75.9 (C-2), 78.1 (C-2″), 79.6 (C-2‴), 104.3 (C-2′).

Thiolytic Degradation of 8—15 a) A solution of **8** (151 mg) in EtOH (10 ml) containing AcOH (5 ml) and benzylmercaptan (2 ml) was refluxed for 19 h. After cooling, the reaction mixture was concentrated under reduced pressure to give an oily residue, which was chromatographed over Sephadex LH-20. Elution with acetone afforded (−)-epiafzelechin (**1**)[5] (22 mg) as colorless needles, mp 240—243 °C, $[\alpha]_D^{24}$ −47.2° (*c*=0.4, acetone). Further elution with acetone yielded a fraction containing a thioether, which was subsequently chromatographed over Sephadex LH-20 [H_2O–MeOH (2:3→1:4)] to furnish the thioether (**8a**) (62 mg) as a white amorphous powder, $[\alpha]_D^{24}$ +109.8° (*c*=0.4, acetone). *Anal.* Calcd for $C_{37}H_{30}O_{10}S\cdot 2H_2O$: C, 63.24; H, 4.88. Found: C, 63.01; H, 4.81. Negative FAB-MS *m/z*: 665 $(M-H)^-$, 541 $(M-PhCH_2SH)^-$. ^{1}H-NMR (acetone-d_6): 4.06 (2H, s, $-SCH_2-$), 4.14 (3H, m, 3,3′, 4′-H), 4.34 (1H, d, *J*=4 Hz, 4-H), 5.40 (1H, s, 2′-H), 5.97, 6.08 (each 1H, d, *J*=2 Hz, 8, 6-H), 6.16 (1H, s, 6′-H), 6.87, 6.91, 7.54, 7.63 (each 2H, d, *J*=8 Hz, B-ring H), 7.21—7.48 (5H, m, aromatic H). ^{13}C-NMR (acetone-d_6+D_2O): 28.8 (C-4), 37.4 ($-SCH_2-$), 44.1 (C-4′), 67.3 (C-3′), 70.4 (C-3), 77.4 (C-2′), 96.2, 97.1, 98.0 (C-6, 8, 6′), 100.0, 102.2 (C-4a, 4a′), 103.5 (C-2), 106.8 (C-8′), 115.2, 115.8 (B-ring C-3, 5, 3′, 5′), 129.3, 129.8 (B-ring C-2, 6, 2′, 6′), 127.7, 130.5, 131.4, 139.7 (aromatic C), 151.5, 153.2, 153.8, 156.8, 157.9, 158.4 (C-5, 7, 8a, 5′, 7′, 8a′).

b) A solution of **9** (140 mg) in EtOH (10 ml) containing AcOH (4.5 ml) and benzylmercaptan (2 ml) was refluxed for 10 h. Work-up as described above afforded **1** (10 mg) and **9a** (45 mg) as a white amorphous powder, $[\alpha]_D^{29}$ +102.4° (*c*=0.5, acetone). *Anal.* Calcd for $C_{37}H_{30}O_{11}S\cdot 2H_2O$: C, 61.83; H, 4.77. Found: C, 61.45; H, 4.55. Negative FAB-MS *m/z*: 681 $(M-H)^-$, 557 $(M-PhCH_2SH)^-$. ^{1}H-NMR (acetone-d_6): 4.05 (2H, s, $-SCH_2-$), 4.13 (2H, s, 3′, 4′-H), 4.14 (1H, d, *J*=4Hz, 3-H), 4.33 (1H, d, *J*=4 Hz, 4-H), 5.40 (1H, s, 2′-H), 5.97, 6.07 (each 1H, d, *J*=2 Hz, 6, 8-H), 6.15 (1H, s, 6′-H), 6.83 (1H, d, *J*=8 Hz, B-ring 5-H), 6.91 (2H, d, *J*=8 Hz, B-ring H-3′, 5′), 7.07 (1H, dd, *J*=2, 8 Hz, B-ring 6-H), 7.19 (1H, d, *J*=2 Hz, B-ring 2-H), 7.61 (2H, d, *J*=8 Hz, B-ring 2′, 6′-H), 7.24—7.54 (5H in total, m, aromatic H).

c) A solution of **10** (100 mg) in EtOH (7 ml) containing AcOH (3 ml) and benzylmercaptan (1.5 ml) was refluxed for 12 h. The reaction mixture was worked up as described above to give (−)-epicatechin (**2**)[6] as colorless needles (H_2O), mp 238—240 °C, $[\alpha]_D^{24}$ −49.8° (*c*=0.6, acetone) and **8a** (27 mg).

d) A mixture of **11** (120 mg), AcOH (5 ml) and benzylmercaptan (2 ml) in EtOH (10 ml) was refluxed for 15 h with stirring. The reaction mixture was concentrated under reduced pressure, and an oily residue was chromatographed over Sephadex LH-20 [acetone and MeOH–H_2O (3:2→4:1)] to give **2** (11 mg) and **11a** (58 mg) as a white amorphous powder, $[\alpha]_D^{26}$ +97.5° (*c*=0.4, acetone). *Anal.* Calcd for $C_{37}H_{30}O_{11}S\cdot 2H_2O$: C, 61.83; H, 4.77. Found: C, 62.30; H, 4.67. Negative FAB-MS *m/z*: 681 $(M-H)^-$, 557 $(M-PhCH_2SH)^-$. ^{1}H-NMR (acetone-d_6+D_2O): 4.06 (2H, s, $-SCH_2-$), 4.13 (2H, s, 3′ 4′-H), 5.32 (1H, s, 2′-H), 6.01, 6.10 (each 1H, d, *J*=2Hz, 6, 8-H), 6.19 (1H, s, 6′-H), 6.87 (1H, d, *J*=8 Hz, B-ring 5′-H), 6.89 (2H, d, *J*=8 Hz, B-ring 3, 5-H), 7.05 (1H, dd, *J*=2, 8 Hz, B-ring 6′-H), 7.32 (1H, d, *J*=2 Hz, B-ring 2′-H), 7.35 (2H, d, *J*=8 Hz, B-ring 2, 6-H), 7.21—7.71 (5H in total, m, aromatic H).

e) A mixture of **12** (80 mg), AcOH (3 ml) and benzylmercaptan (1 ml) in EtOH (6 ml) was refluxed for 10 h. Work-up as described above yielded **2** (5 mg) and **9a** (26 mg).

f) Refluxing of a mixture of **13** (100 mg), AcOH (3 ml) and benzylmercaptan (1.5 ml) in EtOH (6 ml) for 16 h, followed by similar chromatographic separation, afforded **1** (8 mg) and proanthocyanidin A-2 4′-benzylthioether (**17**)[8] (26 mg) as a white amorphous powder, $[\alpha]_D^{26}$ +94.9° (*c*=0.9, actone).

g) Refluxing of a mixture of **14** (160 mg), AcOH (5 ml) and benzylmercaptan (2 ml) in EtOH (10 ml) for 10 h, followed by similar chromatographic separation, furnished (−)-epigallocatechin (**3**)[7] (22 mg) as colorless needles (H_2O), mp 219—222 °C, $[\alpha]_D^{24}$ −49.1° (*c*=0.3, acetone), and **17** (55 mg).

h) A solution of **15** (85 mg) in EtOH (8 ml) containing AcOH (5 ml) and benzylmercaptan (3 ml) was refluxed for 9 h with stirring. Work-up as described above gave (−)-epiafzelechin 4-benzylthioether (**18**) (17 mg), **17** (21 mg) and **2** (5 mg).

Desulfurization of 8a, 9a and 11a a) A solution of **8a** (30 mg) in 10% AcOH–EtOH (3 ml) was treated at room temperature with an EtOH slurry of Raney-nickel (W-4) for 1.5 h. After removal of the catalyst by filtration, the filtrate was concentrated under reduced pressure. The residue was purified by Sephadex LH-20 chromatography [H_2O–MeOH (1:0→1:4)] to yield **8b** (16 mg) as a white amorphous powder, $[\alpha]_D^{26}$ +61.9° (*c*=0.6,

acetone). *Anal.* Calcd for $C_{30}H_{24}O_{10}\cdot 2H_2O$: C, 62.06; H, 4.86. Found: C, 61.89; H, 4.82. Negative FAB-MS *m/z*: 543 $(M-H)^-$. CD ($c=1.0\times10^{-2}$, MeOH) $[\theta]^{20}$ (nm)$\times10^{-4}$: +7.06 (220), −1.44 (271). ^{1}H-NMR (acetone-d_6+D_2O): 2.85 (2H, m, 4′-H), 4.16 (1H, d, J=4 Hz, 3-H), 4.32 (1H, br s, 3′-H), 4.39 (1H, d, J=4 Hz, 4-H), 5.05 (1H, s, 2′-H), 6.03, 6.12 (each 1H, d, J=2 Hz, 6, 8-H), 6.19 (1H, s, 6′-H), 6.89, 6.90, 7.54, 7.58 (each 2H, d, J=8 Hz, B-ring H).

b) A solution of **9a** (30 mg) in 10% AcOH–EtOH (3 ml) was treated at room temperature with an EtOH slurry of Raney-nickel (W-4) for 1.5 h. Work-up as described above yielded **9b** (10 mg) as a white amorphous powder, $[\alpha]_D^{26}$ +58.0° (c=0.5, acetone). *Anal.* Calcd for $C_{30}H_{24}O_{11}\cdot 2H_2O$: C, 60.40; H, 4.73. Found: C, 60.48; H, 4.87. Negative FAB-MS *m/z*: 559 $(M-H)^-$. CD ($c=8.6\times10^{-3}$, MeOH) $[\theta]^{20}$ (nm)$\times10^{-4}$: +8.70 (227), −1.79 (272). ^{1}H-NMR (acetone-d_6+D_2O): 2.76—3.02 (2H, m, 4′-H), 4.16 (1H, d, J=4 Hz, 3-H), 4.31—4.35 (2H, m, 3′, 4′-H), 5.05 (1H, s, 2′-H), 5.98, 6.07 (each 1H, d, J=2 Hz, 6, 8-H), 6.15 (1H, s, 6′-H), 6.84 (1H, d, J=8 Hz, B-ring 5-H), 6.88 (2H, d, J=8 Hz, B-ring 3′, 5′-H), 7.08 (1H, dd, J=2, 8 Hz, B-ring 6-H), 7.20 (1H, d, J=2 Hz, B-ring 2-H), 7.60 (2H, d, J=8 Hz, B-ring 2′, 6′-H).

c) **11a** (25 mg) was desulfurized in the same manner to furnish **11b** (4 mg) as a white amorphous powder, $[\alpha]_D^{27}$ +59.9° (c=0.3, acetone). *Anal.* Calcd for $C_{30}H_{24}O_{11}\cdot 9/2H_2O$: C, 56.16; H, 5.18. Found: C, 56.21; H, 5.15. Negative FAB-MS *m/z*: 559 $(M-H)^-$. CD ($c=8.0\times10^{-3}$, MeOH) $[\theta]^{20}$ (nm)$\times10^{-4}$: +6.22 (219), −1.29 (270). ^{1}H-NMR (acetone-d_6): 2.76—3.02 (2H, m, 4′-H), 4.08—4.30 (3H, m, 3, 4, 3′-H), 4.97 (1H, s, 2′-H), 6.00, 6.08 (each 1H, d, J=2 Hz, 6, 8-H), 6.15 (1H, s, 6′-H), 6.85 (1H, d, J=8 Hz, B-ring 5′-H), 6.87 (2H, d, J=8 Hz, B-ring 3, 5-H), 7.06 (1H, dd, J=2, 8 Hz, B-ring 6′-H), 7.32 (1H, d, J=2 Hz, B-ring 2′-H), 7.55 (2H, d, J=8 Hz, B-ring 2′, 6′-H).

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