[Chem. Pharm. Bull. 33(10)4338—4345(1985)]

# Tannins and Related Compounds. XXXV.[1] Proanthocyanidins with a Doubly Linked Unit from the Root Bark of *Cinnamomum sieboldii* MEISNER

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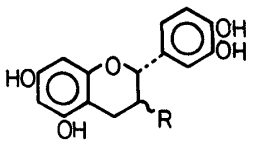
(Received March 13, 1985)

A proanthocyanidin trimer (**1**), two tetramers (**2** and **3**) and a pentamer (**4**) have been isolated from the root bark of *Cinnamomum sieboldii* MEISNER (Lauraceae). The structures of these compounds were established by acid-catalyzed thiolytic degradation, in conjunction with proton and carbon-13 nuclear magnetic resonance analyses. In addition, the presence of (−)-epicatechin (**13**), (+)-catechin (**14**) and known proanthocyanidins B-1 (**5**), B-2 (**6**) and B-5 (**7**), trimers (**8** and **9**), tetramers (**10** and **11**) and a pentamer (**12**) in this plant was demonstrated.

**Keywords**——*Cinnamomum sieboldii*; Lauraceae; proanthocyanidin; tannin; flavan-3-ol; thiolytic degradation

In a previous paper,[2] we demonstrated that cinnamon (the bark of *Cinnamomum zeylanicum* NEES, Lauraceae) contains dimeric, trimeric and higher oligomeric proanthocyanidins which almost exclusively possess a doubly bonded bis-flavan-3-ol unit (a proanthocyanidin A-2 moiety) in the molecule, and that the trimer, among other proanthocyanidins, is extensively accumulated in the secondary metabolic pool. This class of proanthocyanidins is not so frequently encountered in nature in contrast to the singly linked procyanidins which occur widely in unripe fruits and in plants of woody habit. In connection with our study, Otsuka *et al.* recently reported that the aqueous methanolic extract of the root bark of *Cinnamomum sieboldii* MEISNER (日本桂皮) showed a potent anti-inflammatory activity (measured by means of a fertile egg method), and they isolated two trimeric proanthocyanidins as the acetyl and methyl derivatives from the most active fraction.[3] Although they did not determine conclusively the point of linkage between the doubly bonded bisflavanoid part and the remaining flavan-3-ol unit, the proposed structures are closely related to that of our trimeric proanthocyanidin. As part of our chemical studies on tannins and related compounds, we have attempted to determine definitively the structures of these trimers and also to clarify the composition of the higher oligomeric proanthocyanidins in *C. sieboldii*. This paper presents the results of the work.

The fresh root bark of *C. sieboldii* was extracted with 80% aqueous acetone, and the extract was subjected to a combination of Sephadex LH-20 and MCI-gel CHP 20P chromatography with various solvent systems to yield proanthocyanidins **1**—**12**, together with (−)-epicatechin (**13**) and (+)-catechin (**14**). Among the proanthocyanidins, the dimers **5**—**7** and one of the trimers, **8** were identified as procyanidins B-1, B-2 and B-5,[2] and epicatechin-(4$\beta$→8)-epicatechin-(4$\beta$→8)-catechin,[4,5] respectively, by comparisons of their physical and spectral data with those of authentic samples. The oligomers **9**—**12** were shown to consist entirely of (−)-epicatechin units and also to contain a doubly linked bisflavanoid unit in each molecule by examination of the proton and carbon-13 nuclear magnetic resonance ($^1$H- and $^{13}$C-NMR) spectra, and their physical and spectral data coincided with those of the samples obtained from *C. zeylanicum*.[2]



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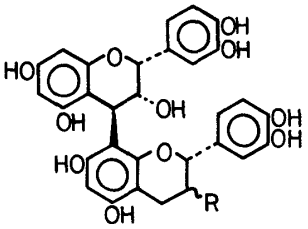

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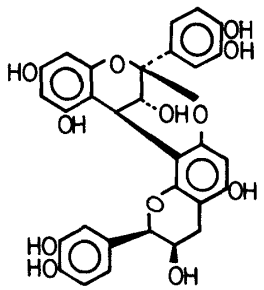

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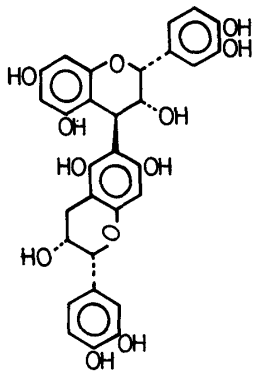

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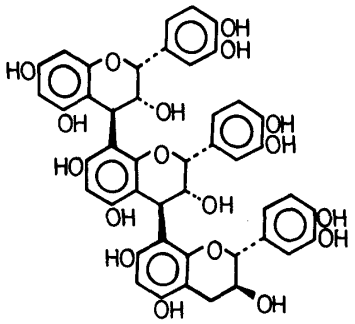

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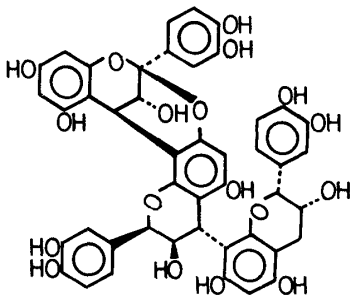

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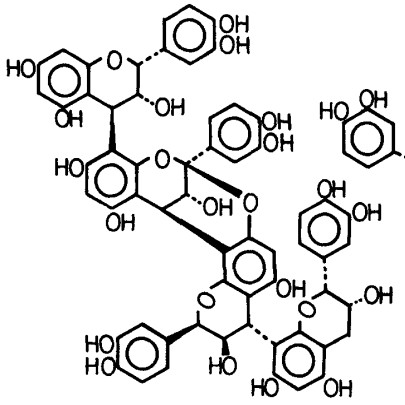
Chart 1



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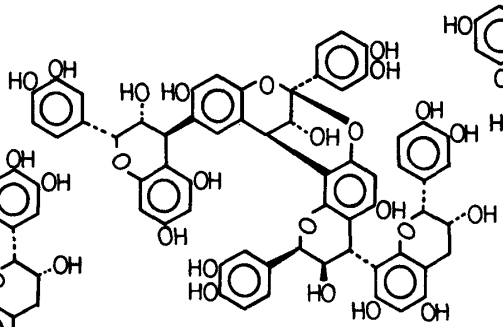

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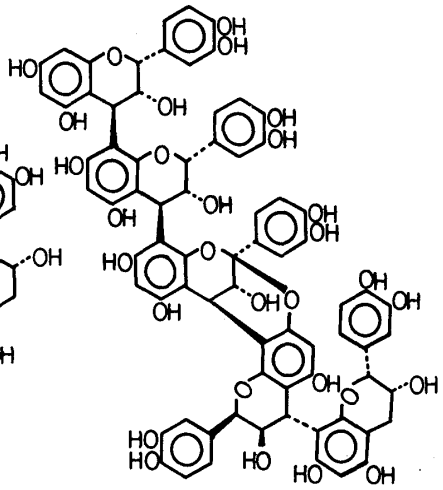

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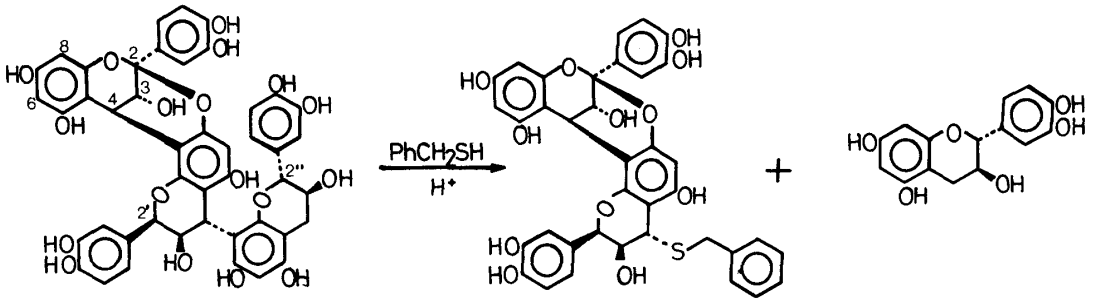
Chart 2

TABLE I. $^{13}$C-NMR Spectral Data for Compounds **1**—**4**, **18** and Proanthocyanidin A-2 (**15**)[a]

| | C-2 | C-3 | C-4 | C-2′ | C-3′ | C-4′ | C-2″ | C-3″ | C-4″ | C-2‴ | C-3‴ | C-4‴ | C-2⁗ | C-3⁗ | C-4⁗ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **15** | 103.6 | 67.1 | 29.9 | 81.1 | 65.7 | 28.5 | | | | | | | | | |
| **1** | 104.3 | 66.5 | 29.5 | 77.8 | 71.4 | 38.0 | 82.7 | 69.2 | 29.1 | | | | | | |
| **18** | 104.9 | 66.6 | 29.6 | 78.0 | 71.3 | 38.1 | 82.7 | 69.4 | 28.7 | | | | | | |
| **2** | 76.6 | 71.9 | 36.8 | 104.4 | 66.5 | 29.7 | 78.8 | 71.9 | 38.0 | 82.9 | 69.3 | 28.5 | | | |
| **3** | 76.6 | 72.4 | 36.9 | 104.7 | 66.6 | 30.0 | 78.9 | 72.4 | 38.0 | 82.7 | 69.4 | 27.3 | | | |
| **4** | 76.9 | 70.6 | 37.0 | 77.0 | 71.8 | 38.2 | 104.6 | 66.8 | 29.0 | 77.5 | 71.8 | 38.2 | 82.7 | 69.5 | 28.1 |

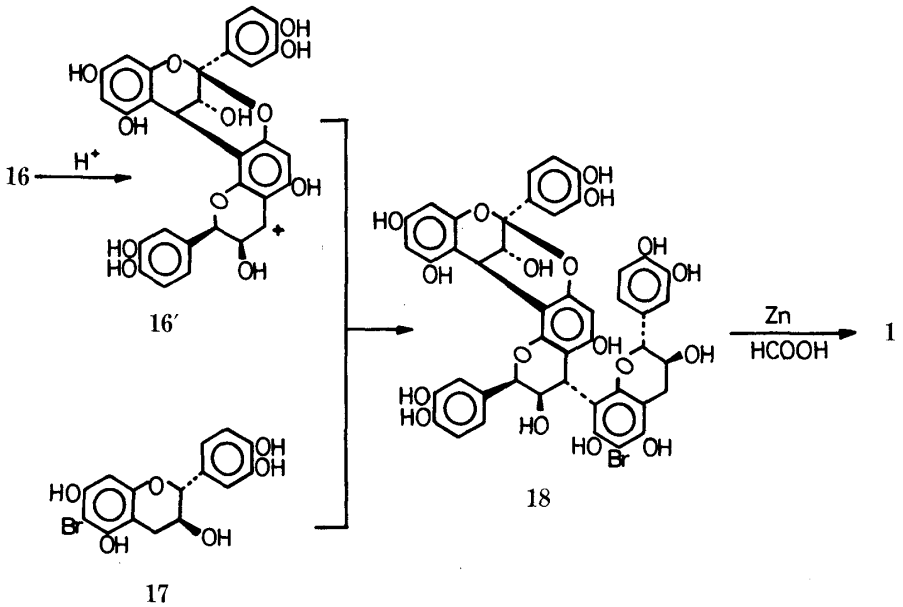
*a*) Spectra were measured at 25.05 MHz in acetone-$d_6$.

Compound **1** was isolated in a crystalline form (mp >300 °C), and gave an orange color with the anisaldehyde–sulfuric acid reagent (characteristic of proanthocyanidins). The triflavanoid constitution of **1** was confirmed by analysis of its fast atom bombardment mass spectrum (FAB-MS) ($[M+H]^+$: *m/z* 865). The $^{13}$C-NMR spectrum (Table I) of **1** showed signals at $\delta$ 77.8 and 82.7 due to epicatechin and catechin C-2 carbons, respectively.[4] In addition, the chemical shift ($\delta$ 104.3) of another C-2 signal was analogous to that ($\delta$ 103.6) of the ketal carbon in proanthocyanidin A-2 (**15**), suggesting that **1** possesses a proanthocyanidin A-type unit in the molecule. Compound **1** was degraded with acid in the presence of benzylmercaptan[6] to give proanthocyanidin A-2 4′-benzylthioether (**16**) and (+)-catechin (**14**), which were identified by comparisons of physical and spectral data with those of authentic samples.[2] The point of the interflavanoid linkage between the A-2 and catechin units was presumed to be C(4′)–C(8), since the $^1$H-NMR spectrum of **1** showed that H-2 signal of the catechin unit at $\delta$ 4.89 (m) which is similar to the chemical shift ($\delta$ 4.91) of the trimer **8**. In order to confirm the position of the interflavanoid linkage unequivocally,




**1** **16** **14**

Chart 3



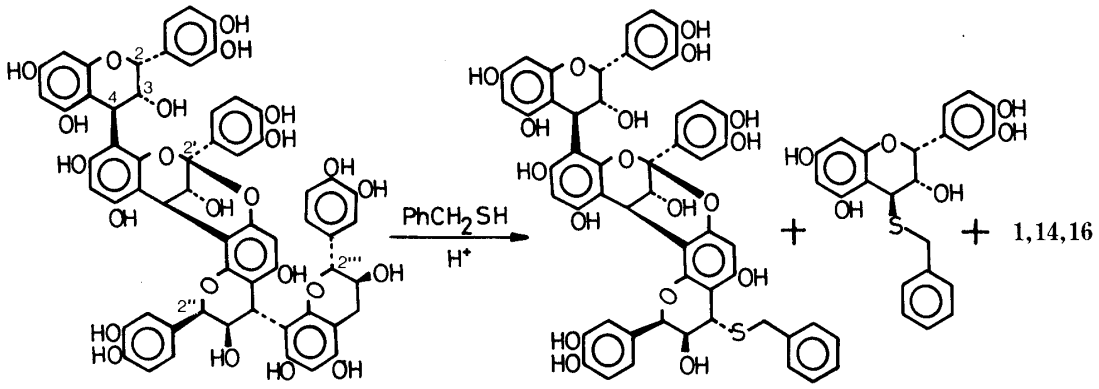

16′ 18 17

Chart 4

condensation[7,8] of the 4′-carbocation (**16′**) formed from the thioether **15** with 6-bromo-(+)-catechin (**17**)[9] was attempted. The 4′-carbocation (**16′**) was easily generated by acid treatment of the thioether **16**. In the presence of 6-bromo-(+)-catechin (**17**), this carbocation attacked the C-8 position of the catechin regio- and stereo-specifically to give a trimeric proanthocyanidin monobromide (**18**), the structure of which was established by analyses of the $^{13}$C-NMR spectrum (Table I) and FAB-MS ($[M+H]^+$: *m/z* 943, 945). Subsequently, this

bromide gave, on debromination with zinc dust and formic acid, a trimeric proanthocyanidin whose spectral data were identical with those of **1**. The configuration of the interflavanoid linkage between the A-2 and catechin units was established as α on the basis of the $^{13}$C-NMR chemical shift of the C-2′ signal.[10] From these chemical and spectral data **1** was characterized as epicatechin-(4β→8, 2β→7)-epicatechin-(4α→8)-catechin.

Compound **2** exhibited an $[M+H]^+$ ion peak at *m/z* 1153 in its FAB-MS, corresponding to a tetrameric constitution. The $^{13}$C-NMR spectrum (Table I) of **2** showed, when compared with that of **1**, additional signals at δ 71.9 and 76.6 due to the C-3 and C-2 carbons, respectively of an epicatechin skeleton in the aliphatic region. The structure of this compound was confirmed as follows. Complete thiolytic degradation of **2** gave (−)-epicatechin 4-benzylthioether (**19**), proanthocyanidin A-2 4′-benzylthioether (**16**) and (+)-catechin (**14**), while on partial thiolytic degradation, **2** afforded, together with the above degradation products, a trimeric proanthocyanidin identical with **1** and a trimeric proanthocyanidin 4″-benzylthioether (**20**): this thioether was previously obtained by similar thiolytic degradation of **10**.[2] Among these degradation products, the formation of **1** and **19** indicated the component units to be connected in the sequence of epicatechin-(4→6 or 4→8)-proanthocyanidin A-2-(4α→8)-catechin. Furthermore, the formation of the thioether **20** limited the mode and the position of the interflavanoid linkage between the epicatechin and A-2 moieties to C(4β)–C(8). Thus, **2** was established as epicatechin-(4β→8)-epicatechin-(4β→8, 2β→7)-epicatechin-(4α→8)-catechin.

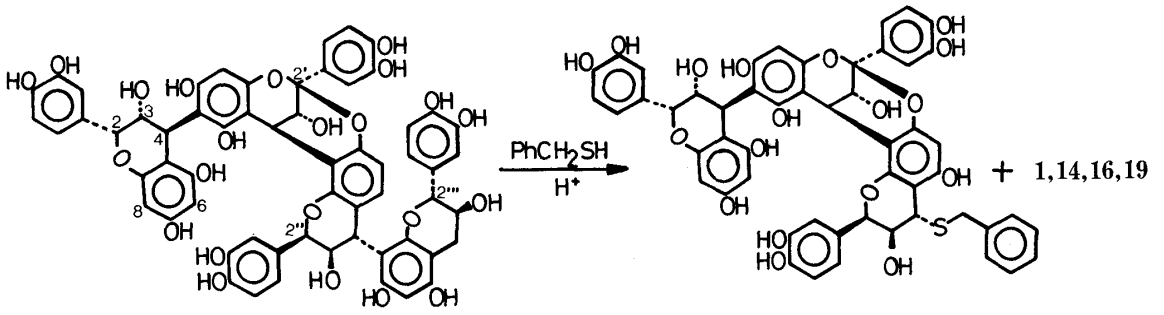



2 20 19

Chart 5

Compound **3** was shown to possess the same constitution as **2** by analyses of the FAB-MS ($[M+H]^+$: *m/z* 1153) and the $^{13}$C-NMR spectrum (Table I), and by complete thiolytic degradation, which gave the thioethers **10** and **19**, and (+)-catechin (**14**). To confirm the points and configurations of the interflavanoid linkages in **3**, partial thiolytic degradation was attempted. On similar treatment, **3** afforded, in addition to the above products, the trimer **1** and a trimeric proanthocyanidin 4″-benzylthioether (**21**), the structure of the latter being confirmed by comparison of physical and spectral data with those of an authentic sample.[2] The formation of compound **1** and the thioether **2** established the structure of **3** to be epicatechin-(4β→6)-epicatechin-(4β→8, 2β→7)-epicatechin-(4α→8)-catechin.

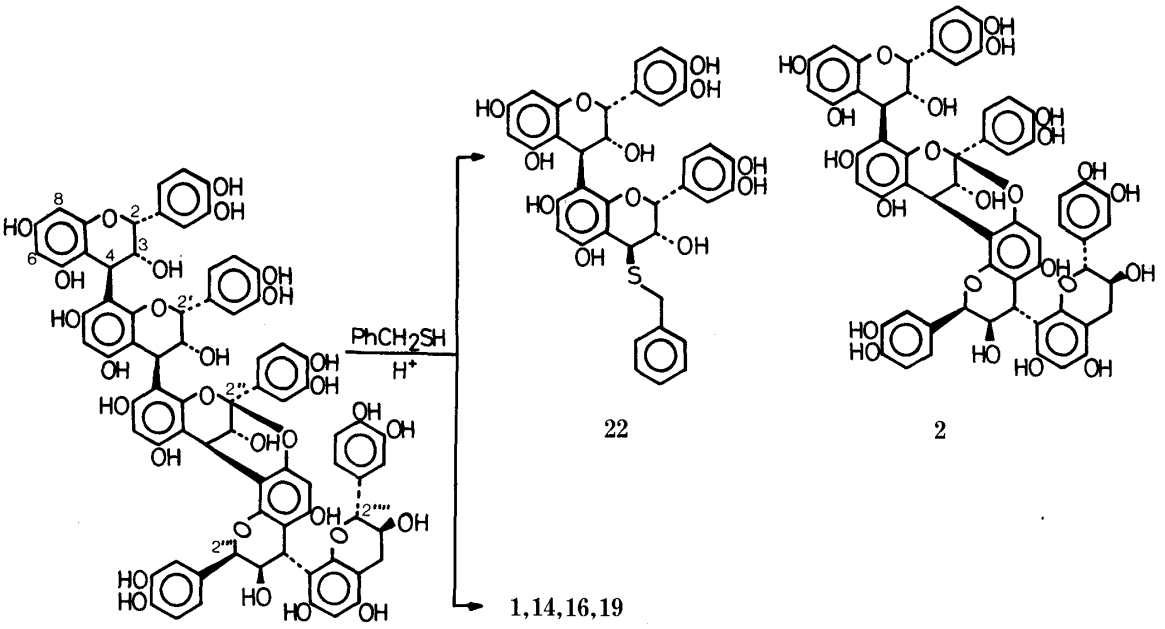
The FAB-MS of compound **4** exhibited an $[M+K]^+$ ion peak at *m/z* 1479, while the field-desorption mass spectrum (FD-MS) of its methyl derivative showed an $M^+$ ion peak at *m/z* 1706. The $^{13}$C-NMR spectrum of **4** exhibited a signal due to a ketal carbon at δ 104.6, together with four C-2 signals at δ 76.9, 77.0, 77.5 and 82.7, the former three being attributed to epicatechin moieties and the remaining one to a catechin unit. These observations suggested that this compound is a pentameric proanthocyanidin possessing epicatechin,




3 21

Chart 6

proanthocyanidin A-2 and catechin units in the molecule. Application of the partial thiolytic degradation method to **4** gave compound **2** and proanthocyanidin B-2 4′-benzylthioether (**22**), and thus enabled the constitution and the mode of the interflavanoid linkage to be established as epicatechin-(4$\beta$→8)-epicatechin-(4$\beta$→8)-epicatechin-(4$\beta$→8, 2$\beta$→7)-epicatechin-(4$\alpha$→8)-catechin.




4 22 2

Chart 7

In conclusion, the root bark of *C. sieboldii* was found to contain large amounts of proanthocyanidins containing a doubly linked bisflavanoid (A-type) unit, accompanied by minor singly linked procyanidins. It is of interest from the chemotaxonomical point of view that the composition of the proanthocyanidins in *C. sieblodii* has much in common with that in the case of *C. zeylanicum*, whereas other *Cinnamomum* plants mainly contain linearly linked procyanidins.[11]

It should be noted that proanthocyanidin trimers **1** and **9** taste sweet, which is in contrast to the astringent taste of other trimeric, tetrameric and pentameric proanthocyanidins.

## Experimental

All melting points were determined on a Yanagimoto micro-melting point apparatus and are uncorrected.

Optical rotations were taken with a JASCO DIP-4 digital polarimeter. FD- and FAB-MS were measured with a JEOL JMS DX-300 instrument. $^1$H- and $^{13}$C-NMR spectra were recorded on JEOL PS-100 and JEOL FX-100 spectrometers, respectively, with tetramethylsilane as an internal standard, and chemical shifts are given in $\delta$ (ppm). The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; dd, double doublet. Column chromatography was carried out with Sephadex LH-20 (25—100 $\mu$, Pharmacia Fine Chemical Co., Ltd.) and MCI-gel CHP 20P (75—150 $\mu$, Mitsubishi Chemical Industries, Ltd.). Thin-layer chromatography (TLC) was conducted on precoated Kieselgel 60 $F_{254}$ plates (0.2 mm, Merck) with benzene–ethyl formate–formic acid (1 : 7 : 1 or 2 : 7 : 1) as solvent systems, and spots were detected by the use of anisaldehyde–sulfuric acid and ferric chloride reagent sprays.

**Extraction and Isolation**——The fresh root bark (12.8 kg) of *Cinnamomum sieboldii*, collected in October at Ibusuki City, Kagoshima Prefecture, was extracted three times with acetone–$H_2O$ (4 : 1). The acetone was removed by evaporation under reduced pressure, and the resulting brown precipitates (negative to the ferric chloride reagent) were removed by filtration. The filtrate was chromatographed over MCI-gel CHP 20P with water and then with MeOH. The MeOH eluate (625 g) was applied to a column of Sephadex LH-20, and elution with increasing amounts of MeOH in water (1 : 0—0 : 1) gave fractions 1 (2.5 g), 2 (6.5 g), 3 (152 g) and 4 (92 g). Fraction 1 was rechromatographed over MCI-gel CHP 20P with 30% aqueous MeOH to yield (−)-epicatechin (**13**) (645 mg) and (+)-catechin (**14**) (135 mg). Repeated chromatography of fraction 2 on Sephadex LH-20 (EtOH) and MCI-gel CHP 20P (30% aqueous MeOH) gave procyanidins B-1 (**5**) (1.8 g) and B-2 (**6**) (2.5 g). Fraction 3 was further divided by Sephadex LH-20 chromatography using EtOH into two fractions, 3-a (3.2 g) and 3-b (104.5 g). Fraction 3-a was chromatographed over Sephadex LH-20 with 60% aqueous MeOH to furnish procyanidin B-5 (**7**) (945 mg) and compound **8** (2.2 g). Fraction 3-b was dissolved in water, and the solution was passed through a column of Sephadex LH-20 with 60% aqueous MeOH to give compound **9** (52.5 g). Further elution with the same solvent, followed by crystallization from $H_2O$, afforded compound **1** (16 g). Sephadex LH-20 chromatography of fraction 4 with 80% aqueous MeOH afforded three fractions 4-a (23 g), 4-b (12 g) and 4-c (3.6 g). Each fraction was repeatedly chromatographed over MCI-gel CHP 20P (30% aqueous MeOH) and Sephadex LH-20 (EtOH) to give compounds **2** (2.2 g), **3** (1.6 g), **4** (452 mg), **10** (15.3 g), **11** (2.3 g) and **12** (596 mg).

**Compound 1**——Colorless needles ($H_2O$), mp >300 °C, $[\alpha]_D^{22}$ +102.3° ($c$=0.9, acetone). *Anal.* Calcd for $C_{45}H_{36}O_{18}\cdot 2H_2O$: C, 60.00; H, 4.48. Found: 59.87; H, 4.53. FAB-MS $m/z$: 865 $(M+H)^+$. $^1$H-NMR (DMSO-$d_6$)[12]: 3.76 (2H, br s, H-3′, H-3″), 3.80 (1H, d, $J$=4 Hz, H-3), 4.25 (1H, d, $J$=4 Hz, H-4), 4.43 (1H, s, H-4′), 4.89 (1H, m, H-2″), 5.13, 5.16 (1H in total, each s, H-2′), 5.60—6.10 (4H in total, H-6, H-6′, H-6″, H-8), 6.50—7.10 (9H in total, B-ring H). $^{13}$C-NMR: Table I.

**Undecamethyl Ether of 1**——A mixture of **1** (150 mg), dimethyl sulfate (1.5 ml) and anhydrous potassium carbonate (2.2 g) in dry acetone (15 ml) was refluxed for 2.5 h with stirring. After the removal of inorganic salts, the filtrate was concentrated to a syrup, which was applied to a column of silica gel. Elution with benzene–acetone (17 : 3) gave the undecamethyl ether (105 mg) as a white amorphous powder, $[\alpha]_D^{22}$ +87.5° ($c$=1.0, acetone). *Anal.* Calcd for $C_{56}H_{58}O_{18}$: C, 66.00; H, 5.74. Found: C, 65.92; H, 5.52. FD-MS $m/z$: 1018 ($M^+$).

**Thiolytic Degradation of 1**——A mixture of **1** (150 mg), benzylmercaptan (2 ml), acetic acid (3 ml) and EtOH (10 ml) was refluxed for 13 h with stirring. The reaction mixture was concentrated under reduced pressure to give an oily residue, which was chromatographed over Sephadex LH-20. Elution with acetone afforded (+)-catechin (**14**). Further elution with the same solvent yielded proanthocyanidin A-2 4′-benzylthioether (**16**) (84 mg) as an off-white amorphous powder, $[\alpha]_D^{24}$ +58.9° ($c$=0.7, acetone). $^1$H-NMR (acetone-$d_6$): 4.04 (2H, s, $-CH_2S-$), 4.12 (2H, s, H-3′, H-4′), 4.14 (1H, d, $J$=4 Hz, H-3), 4.35 (1H, d, $J$=4 Hz, H-4), 5.32 (1H, s, H-2′), 5.96 (1H, d, $J$=2 Hz, H-6), 6.04 (1H, d, $J$=2 Hz, H-8), 6.16 (1H, s, H-6′), 6.80—7.50 (11H in total, aromatic H).

**Preparation of 6-Bromo-(+)-catechin (17)**——A solution of pyridinium hydrobromide perbromide (1.5 g) in acetonitrile (150 ml) was added dropwise to an ice-cooled solution of (+)-catechin (**14**) (2.5 g) in acetonitrile (150 ml). The mixture was kept at 0 °C for 30 min, and then directly chromatographed over Sephadex LH-20 (preswollen in water). Elution with the same solvent removed the excess reagent. The adsorbed catechin bromide was eluted with MeOH. Purification by a column of Sephadex LH-20 with $CHCl_3$–MeOH (2 : 1) afforded 6-bromo-(+)-catechin (**17**)[9] (895 mg) as colorless needles, mp 123 °C (dec.), $[\alpha]_D^{24}$ +9.5° ($c$=1.2, acetone). $^1$H-NMR (acetone-$d_6$): 2.60 (1H, dd, $J$=8, 16 Hz, H-4), 2.96 (1H, dd, $J$=6, 16 Hz, H-4), 4.02 (1H, m, H-3), 4.64 (1H, d, $J$=8 Hz, H-2), 6.12 (1H, s, H-8), 6.70—7.00 (3H in total, B-ring H).

**Condensation of 6-Bromo-(+)-catechin (17) with Proanthocyanidin 4′-Benzylthioether (16)**——A mixture of **16** (1.2 g), **17** (0.6 g), *p*-toluenesulfonic acid (50 mg) in EtOH (30 ml) was kept at room temperature for 48 h with stirring. The reaction mixture was directly chromatographed on Sephadex LH-20. Elution with EtOH yielded a crude product, which was further purified by chromatography over MCI-gel CHP 20P (50% aqueous MeOH) to furnish a trimeric proanthocyanidin monobromide (**18**) (35 mg) as an off-white amorphous powder, $[\alpha]_D^{24}$ +112.0° ($c$=1.2, acetone). *Anal.* Calcd for $C_{45}H_{35}O_{18}Br\cdot 2H_2O$: C, 55.17; H, 4.01. Found: C, 55.48; H, 3.99. FAB-MS $m/z$: 943 $(M+H)^+$. $^{13}$C-NMR: Table I. $^1$H-NMR: see ref. 12.

**Debromination of 18**——A mixture of **18** (30 mg), formic acid (0.3 ml) and zinc dust (54 mg) in EtOH (10 ml) was kept at 60 °C for 6 h. Filtration of the zinc and concentration of the filtrate under reduced pressure gave a solid, which was purified by Sephadex LH-20 chromatography with 80% aqueous MeOH to furnish the product (7.5 mg), which

was shown to be identical with **1** by comparison of the spectral and physical data.

**Compound 2**——A tan amorphous powder, $[\alpha]_D^{24}$ +85.6° ($c$=1.1, acetone). *Anal.* Calcd for $C_{60}H_{48}O_{24}\cdot 3H_2O$: C, 59.70; H, 4.51. Found: C, 59.65; H, 4.44. FAB-MS $m/z$: 1153 $(M+H)^+$. $^{13}$C-NMR: Table I. $^1$H-NMR: see ref. 12.

**Pentadecamethyl Ether of 2**——**2** (150 mg) was methylated in the same way as described for **1**. Purification of the product on a silica gel column [benzene–acetone (4 : 1)] gave the pentadecamethyl ether (87 mg) as a white amorphous powder, $[\alpha]_D^{24}$ +88.3° ($c$=1.1, acetone). *Anal.* Calcd for $C_{75}H_{78}O_{24}$: C, 66.07; H, 5.77. Found: C, 66.25; H, 5.90. FD-MS $m/z$: 1363 $(M+H)^+$.

**Complete Thiolytic Degradation of 2**——A mixture of **2** (90 mg) in EtOH (7 ml) was heated under reflux for 9 h. The products were separated by repeated chromatography over Sephadex LH-20 with EtOH and 80% aqueous MeOH to give **14** (13 mg), **16** (35 mg) and a thioether (**19**) (15 mg). **19**: a white amorphous powder, $[\alpha]_D^{24}$ −35.5° ($c$=1.0, acetone). $^1$H-NMR (acetone-$d_6$): 3.96 (1H, br s, H-3), 4.01 (2H, s, $-CH_2S-$), 4.08 (1H, d, $J$=3 Hz, H-4), 5.24 (1H, s, H-2), 5.90 (1H, d, $J$=2 Hz, H-6), 6.07 (1H, d, $J$=2 Hz, H-8), 6.70—7.60 (8H in total, aromatic H). This compound was identified as (−)-epicatechin 4-benzylthioether by spectral and physical comparisons.[2]

**Partial Thiolytic Degradation of 2**——Treatment of **2** (1.1 g) with benzylmercaptan (4 ml) and acetic acid (3 ml) in EtOH (20 ml), followed by repeated separation on Sephadex LH-20 columns with EtOH and 80% aqueous MeOH as eluants, gave **1** (438 mg), **14** (12 mg), **16** (36 mg), **19** (32 mg) and a trimeric proanthocyanidin 4″-benzylthioether (**20**) (25 mg). **20**: an off-white amorphous powder, $[\alpha]_D^{24}$ +38.9° ($c$=1.4, acetone). $^1$H-NMR (acetone-$d_6$): 4.25 (1H, d, $J$=4 Hz, H-3′), 4.40 (1H, d, $J$=4 Hz, H-4′), 4.76 (1H, s, H-4), 5.11 (1H, s, H-2), 5.27 (1H, s, H-2″).

**Compound 3**——A tan amorphous powder, $[\alpha]_D^{24}$ +110.6° ($c$=1.1, acetone). *Anal.* Calcd for $C_{60}H_{48}O_{24}\cdot 3H_2O$: C, 59.70; H, 4.51. Found: C, 59.90; H, 4.63. FAB-MS $m/z$: 1153 $(M+H)^+$. $^{13}$C-NMR: Table I. $^1$H-NMR: see ref. 12.

**Pentadecamethyl Ether of 3**——**3** (50 mg) was methylated for 3 h with dimethyl sulfate (0.7 ml) and anhydrous potassium carbonate (1.2 g) in dry acetone (10 ml). The mixture was worked up as before, yielding the pentadecamethyl ether (23 mg) as a white amorphous powder, $[\alpha]_D^{24}$ +112.6° ($c$=0.87, acetone). *Anal.* Calcd for $C_{75}H_{78}O_{24}$: C, 66.07; H, 5.77. Found: C, 66.00; H, 5.85. FD-MS $m/z$: 1363 $(M+H)^+$.

**Complete Thiolytic Degradation of 3**——A mixture of **3** (60 mg), benzylmercaptan (2 ml), acetic acid (1 ml) and EtOH (7 ml) was refluxed for 12 h. The reaction mixture was worked up in the same way as described for **2** to give **14** (8 mg), **16** (25 mg) and **19** (10 mg).

**Partial Thiolytic Degradation of 3**——**3** (1.0 g) was degraded in the same manner as described for **2** to give **1** (431 mg), **14** (19 mg), **16** (22 mg), **19** (48 mg) and a trimeric proanthocyanidin 4″-benzylthioether (**21**) (41 mg). **21**: an off-white amorphous powder, $[\alpha]_D^{24}$ +60.0° ($c$=0.7, acetone). $^1$H-NMR (acetone-$d_6$)[12]: 3.95 (2H, s, $-CH_2S-$), 4.59 (1H, s, H-4), 4.88, 5.28, 5.66 (2H in total, each s, H-2, H-2″).

**Compound 4**——A tan amorphous powder, $[\alpha]_D^{24}$ −115.9° ($c$=1.1, acetone). *Anal.* Calcd for $C_{75}H_{60}O_{30}\cdot 3H_2O$: C, 60.24; H, 4.45. Found: C, 60.00; H, 4.81. FAB-MS $m/z$: 1479 $(M+K)^+$. $^{13}$C-NMR: Table I. $^1$H-NMR: see ref. 12.

**Nonadecamethyl Ether of 4**——A mixture of **4** (50 mg), dimethyl sulfate (0.7 ml) and anhydrous potassium carbonate (1.2 g) in dry acetone (10 ml) was refluxed for 3.5 h. Work-up as before furnished the nonadecamethyl ether (22 mg) as a white amorphous powder, $[\alpha]_D^{24}$ +120.8° ($c$=1.1, acetone). *Anal.* Calcd for $C_{94}H_{98}O_{30}\cdot 3H_2O$: C, 65.41; H, 5.84. Found: C, 65.29; H, 5.58. FD-MS $m/z$: 1706 $(M^+)$.

**Partial Thiolytic Degradation of 4**——**4** (300 mg) was heated for 2 h under reflux in EtOH (10 ml) containing acetic acid (2 ml) and benzylmercaptan (3 ml). The reaction mixture was treated as described for **2** to give **1** (15 mg), **2** (120 mg), **14** (8 mg), **16** (12 mg), **19** (21 mg) and a dimeric procyanidin 4′-benzylthioether (**22**) (6 mg). **22**: an off-white amorphous powder, $[\alpha]_D^{24}$ +36.6° ($c$=0.3, acetone). $^1$H-NMR (acetone-$d_6$): 4.08 (2H, s, $-CH_2S-$), 4.13 (1H, s, H-4′), 4.72 (1H, s, H-4), 5.13 (1H, s, H-2), 5.32 (1H, br s, H-2′), 6.00 (3H, s, H-6, H-6′, H-8), 6.70—7.60 (11H in total, aromatic H). This compound was identified as procyanidin B-2 4′-benzylthioether by comparison of the spectral and physical data with those of an authentic sample.[2]

**Acknowledgment** The authors thank Mr. I. Nagaoka, of the Experimental Station of this University for a generous supply of the plant material. They are also indebted to Mr. Y. Tanaka, Miss K. Soeda and Mr. R. Isobe for $^{13}$C-NMR, $^1$H-NMR and MS measurements, respectively. This work was supported by a grant (to G. N., No. 59570897) from the Ministry of Education, Science and Culture, Japan, which is gratefully acknowledged.

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