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Tannins and Related Compounds. XXIX.[1] Seven New Methyl Derivatives of Flavan-3-ols and a 1,3-Diarylpropan-2-ol from *Cinnamomum cassia*, *C. obtusifolium* and *Lindera umbellata* var. *membranacea*

SATOSHI MORIMOTO,[a] GEN-ICHIRO NONAKA,[a] ITSUO NISHIOKA,*,[a] NOBUHISA EZAKI,[b] and NOBUO TAKIZAWA[b]

Faculty of Pharmaceutical Sciences, Kyushu University,[a] 3-1-1 Maidashi, Higashi-ku, Fukuoka 812, Japan and Central Research Laboratories, Yomeishu Seizo Co., Ltd.,[b] 2132-37 Nakaminowa, Minowa-machi, Kamiina-gun, Nagano 399-46, Japan

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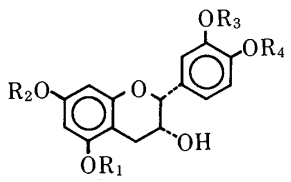
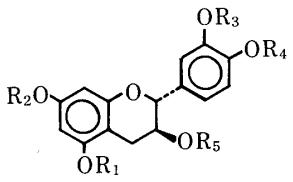
Seven new methyl derivatives of flavan-3-ols (compounds **1**—**7**) and one 1,3-diarylpropan-2-ol (compound **8**) were isolated from three Lauraceous plants (**1**, and **3**—**7** from *Cinnamomum cassia*, **1**, **3** and **4** from *Cinnamomum obtusifolium*, and **1**—**4** and **8** from *Lindera umbellata* var. *membranacea*). Their structures were characterized mainly by proton nuclear magnetic resonance (^{1}H-NMR) examination combined with nuclear Overhauser effect (NOE) experiments as the 3′-*O*-methylate (**1**), 3′,4′-di-*O*-methylate (**2**), 5,3′-di-*O*-methylate (**3**) and 5,7,3′-tri-*O*-methylate (**4**) of (−)-epicatechin, the 4′-*O*-methylate (**5**), 7,4′-di-*O*-methylate (**6**) and 5,7,4′-tri-*O*-methylate (**7**) of (+)-catechin, and 1-(4′,6′-dihydroxy-2′-methoxyphenyl)-3-(4″-hydroxy-3″-methoxyphenyl)-propan-2-ol (**8**).

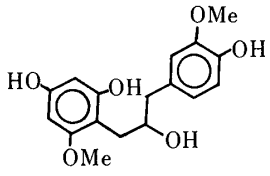
Keywords——*Cinnamomum cassia*; *Cinnamomum obtusifolium*; *Lindera umbellata* var. *membranacea*; Lauraceae; flavan-3-ol methyl ether; 1,3-diarylpropan-2-ol; ^{1}H-NMR; NOE experiment

The methyl derivatives of flavan-3-ols are rarely found in nature, whereas many flav-4-ones substituted with methoxyl groups have been isolated from a variety of plants, although they are presumed to be biosynthetically related to each other.[2-4] Only five flavan-3-ol methyl ethers, namely, 5,7,3′ (or 5,7,4′)-tri-*O*-methyl-(−)-epicatechin,[5] 5,7-di-*O*-methyl-3′,4′-methylenated (±)-epicatechin (from *Cinnamomum cassia*),[5] 3′-*O*-methyl-(−)-epicatechin 7-*O*-β-D-glucopyranoside (from *Symplocos uniflora*),[6] 4′-*O*-methyl-(−)-epigallocatechin (from *Prionostemma aspera* and *Maytenus rigida*)[7] and 5,7,3′-tri-*O*-methyl-(+)-catechin (from *Viguiera quinqueradiata*)[8] have hitherto been isolated. Our chemical studies on phenolic constituents in several Lauraceous plants have led to the isolation of a series of new methyl derivatives of flavan-3-ols [compounds **1** and **3**—**7** from the bark of *Cinnamomum cassia* (東興桂皮), compounds **1**, **3** and **4** from the bark of *Cinnamomum obtusifolium* (ベトナム桂皮), and compounds **1**—**4** from the twig of *Lindera umbellata* var. *membranacea* (烏樟)], together with a 1,3-diarylpropan-2-ol (**8**) (from *L. umbellata* var. *membranacea*). This paper describes the isolation and structure elucidation of these compounds.

Commercial Cassia bark was extracted with H_2O, while the bark of *C. obtusifolium* and the twig of *L. umbellata* var. *membranacea* were each extracted with 60% aqueous acetone. Each extract was subjected to a combination of Sephadex LH-20, MCI-GEL CHP 20P and silica gel chromatographies with various solvent systems to yield the methyl derivatives. (−)-epicatechin (**9**) and (+)-catechin (**10**) were concomitantly isolated from all of the extracts, whereas the previously reported 5,7-di-*O*-methyl-3′,4′-methylenated (±)-epicatechin (**11**)[5] was isolable from only the *Cinnamomum* plants.







8

	R_1	R_2	R_3	R_4
1	H	H	Me	H
2	H	H	Me	Me
3	Me	H	Me	H
4	Me	Me	Me	H
9	H	H	H	H
11	Me	Me	$-CH_2-$	

	R_1	R_2	R_3	R_4	R_5
5	H	H	H	Me	H
5a	Ac	Ac	Ac	Me	Ac
6	H	Me	H	Me	H
6a	Ac	Me	Ac	Me	Ac
7	Me	Me	H	Me	H
7a	Me	Me	Ac	Me	Ac
10	H	H	H	H	H

Compound **1** gave an orange color, characteristic of flavan-3-ols, with the anisaldehyde–sulfuric acid reagent.[9] The proton and carbon-13 nuclear magnetic resonance (^{1}H- and ^{13}C-NMR) spectra of **1** were similar to those of (−)-epicatechin (**9**) except for the presence of a methoxyl group in **1**. Methylation of **1** with diazomethane, yielding 5,7,3′,4′-tetra-*O*-methyl-(−)-epicatechin, established the presence of a falvan skeleton with a (−)-epicatechin stereochemistry. The location of the methoxyl group was comfirmed by nuclear Overhauser effect (NOE) measurement in the ^{1}H-NMR spectrum. Irradiation of the methoxyl signal at δ 3.84 caused 14% enhancement of the integral intensity of the H-2′ signal (δ 7.19, d, J=2 Hz), and this indicated that the methoxy group is present at the C-3′ position. Thus, **1** was established as 3′-*O*-methyl-(−)-epicatechin.

The ^{1}H-NMR spectra (Table I) of compounds **2** and **3** were closely related to each other, showing signals due to an epicatechin skeleton and two methoxyl groups in each case. On methylation, **2** and **3** gave the same product, 5,7,3′,4′-tetra-*O*-methyl-(−)-epicatechin. The electron-impact mass spectrum (EI-MS) of **2** exhibited fragment peaks at *m/z* 180 and 139 formed by a *retro*-Diels–Alder-type fission at the C-ring (Chart 1), indicating that the two methoxyl groups are located at the B-ring (at the C-3′ and C-4′ positions). Accordingly, **2** was characterized as 3′,4′-di-*O*-methyl-(−)-epicatechin. The locations of the methoxyl groups in **3** were concluded to be at the C-5 and C-3′ positions by NOE measurement; irradiation of the methoxyl signal at δ 3.76 caused 11% and 13% enhancements of the integral intensities of the H-4 (δ 2.80) and H-6 (δ 6.07) signals, respectively, while upon irradiation of another methoxyl signal at δ 3.84 the integral intensity of the H-2′ signal (δ 7.17, d, J=2 Hz) was enhanced by 29%. On the basis of these results, **3** was confirmed to be 5,3′-di-*o*-methyl-(−)-epicatechin.

Compound **4** possessed an epicatechin skeleton and three methoxyl groups as revealed by analyses of the ^{1}H-NMR spectrum (Table I) and EI-MS (M^+ at *m/z* 332). Methylation of **4** gave 5,7,3′,4′-tetra-*O*-methyl-(−)-epicatechin. Two of the three methoxyl groups were indicated to be located at the C-7 and C-5 positions by the observation of a *retro*-Diels–Alder fragment peak at *m/z* 167 (Chart 1) in the EI-MS of **4**. The location of the remaining methoxyl group was confirmed to be at the C-3′ position by NOE measurement; when the methoxyl signal at δ 3.84 was irradiated, the integral intensity of the H-2′ signal (δ 7.18, d, J=2 Hz) was enhanced by 26%. Thus, **4** was concluded to be 5,7,3′-tri-*O*-methyl-(−)-epicatechin.

Compound **5** gave a molecular ion peak at *m/z* 304 in the EI-MS. The ^{1}H-NMR spectrum of **5** revealed the presence of a flavan skeleton with a *trans* configuration at the C-2 and C-3 positions (H-2: δ 4.16, d, J=8 Hz), in addition to one methoxyl signal (δ 3.84). Methylation of **5** gave 5,7,3′,4′-tetra-*O*-methyl-(+)-catechin. The methoxyl group was concluded to be located at the C-4′ position from the following evidence. Owing to the

TABLE I. ^{1}H-NMR Spectral Data for Compounds **1**—**7**, (−)-Epicatechin (**9**) and (+)-Catechin (**10**)

	H-2	H-3	H-4	H-6	H-8	H-2′	H-5′	H-6′	OMe
				(δ values, J values in Hz)					
9[a]	4.88	4.20	2.80	6.12	6.22	7.04	6.86	6.78	—
	(s)	(m)	(m)	(d, J=2)	(d, J=2)	(d, J=2)	(d, J=8)	(dd, J=2, 8)	
1[a]	4.92	4.23	2.80	5.93	6.03	7.19	6.73	6.92	3.84 (s)
	(s)	(m)	(m)	(d, J=2)	(d, J=2)	(d, J=2)	(d, J=8)	(dd, J=2, 8)	
2[a]	4.96	4.24	2.83	5.93	6.02	7.19	6.90	7.05	3.84 (s)
	(s)	(m)	(m)	(d, J=2)	(d, J=2)	(d, J=2)	(d, J=8)	(dd, J=2, 8)	
3[a]	4.97	4.20	2.80	6.01	6.07	7.17	6.78	6.96	3.76 (s)
	(s)	(m)	(m)	(d, J=2)	(d, J=2)	(d, J=2)	(d, J=8)	(dd, J=2, 8)	3.84 (s)
4[a]	4.92	4.24	2.79	6.13	6.07	7.18	6.78	6.96	3.76 (s) 3.80 (s)
	(s)	(m)	(m)	(d, J=2)	(d, J=2)	(d, J=2)	(d, J=8)	(dd, J=2, 8)	3.84 (2)
10[a]	4.57	4.00	2.30—3.20	5.92	6.05	6.90	6.80	6.72	—
	(d, J=8)	(m)	(m)	(d, J=2)	(d, J=2)	(d, J=2)	(d, J=8)	(dd, J=2, 8)	
5[a]	4.61	4.00	2.30—3.20	5.89	6.03	6.90	6.95	6.81	3.84 (s)
	(d, J=8)	(m)	(m)	(d, J=2)	(d, J=2)	(d, J=2)	(d, J=8)	(dd, J=2, 8)	
6[b]	4.59	3.88	2.20—2.80	5.87	6.00	6.76	6.89	6.72	3.69 (s)
	(d, J=8)	(m)	(m)	(d, J=2)	(d, J=2)	(d, J=2)	(d, J=8)	(dd, J=2, 8)	3.75 (s)
7[b]	4.64	3.92	2.20—2.80	6.14	6.04	6.80	6.91	6.70	3.72 (s) 3.77 (s)
	(d, J=8)	(m)	(m)	(d, J=2)	(d, J=2)	(d, J=2)	(d, J=8)	(dd, J=2, 8)	3.83 (s)

a) Measured in acetone-d_6. *b*) Measured in DMSO-d_6.

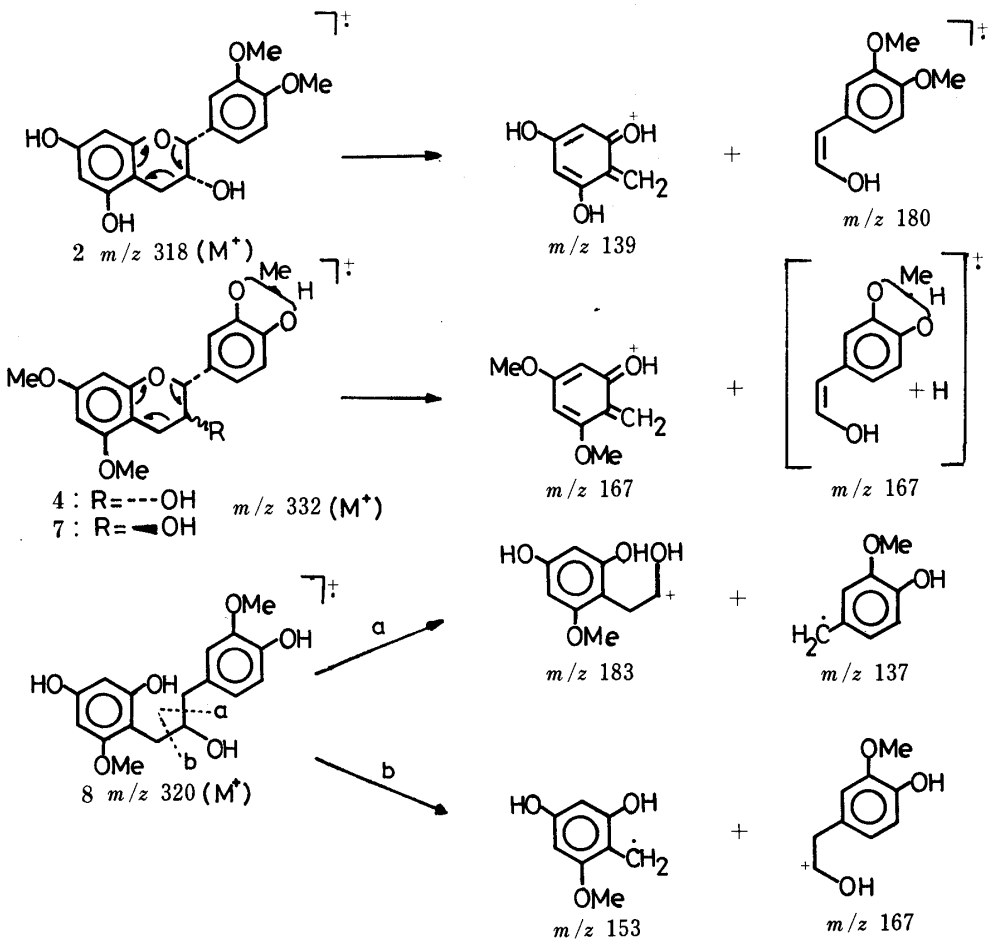


Chart 1

overlapping of the signals due to B-ring protons in the ^{1}H-NMR spectrum of **5**, the tetraacetate (**5a**), prepared by acetylation of **5** with acetic anhydride and pyridine, was used for the NOE experiment; upon irradiation of the methoxyl signal at δ3.79, the integral intensity of the H-5′ signal (δ 6.92, d, J=8 Hz) increased by 29%. From these results, **5** was characterized as 4′-*O*-methyl-(+)-catechin.

Compounds **6** and **7**, on methylation, gave 5,7,3′,4′-tetra-*O*-methyl-(+)-catechin. The ^{1}H-NMR spectra of **6** and **7** showed the presence of two (δ 3.69 and 3.75) and three methoxyl groups (δ 3.72, 3.77 and 3.83), respectively. The methoxyl groups in **6** were concluded to be located at the C-7 and C-4′ positions from an NOE experiment with the triacetate (**6a**). Irradiation of the methoxyl region (δ 3.74—3.78) resulted in 17, 17 and 29% enhancements of the integral intensities of the H-6, H-8 and H-5′ signals, respectively. Thus, **6** was established as 7,4′-di-*O*-methyl-(+)-catechin. The locations of the methoxyl groups in **7** were established to be at the C-5, C-7 and C-4′ positions by NOE measurement in the diacetate (**7a**) and by analysis of the EI-MS of **7**; upon irradiation of the methoxyl region (δ 3.76—3.80), the integral intensity of the H-5′ signal was enhanced by 30%, while the observation of a fragment peak at m/z 167 indicated the remaining two methoxyl groups to be present at the A-ring (Chart 1). Accordingly, **7** was characterized as 5,7,4′-tri-*O*-methyl-(+)-catechin.

The ^{1}H-NMR spectrum of **8** revealed the presence of two benzylic methylenes (δ 2.56—3.00), a hydroxy-bearing methine (δ 4.02) and two methoxyl groups (δ 3.70 and 3.81). Furthermore, in the aromatic region a two-proton singlet signal (δ 6.04) and ABX-type signals [δ 6.64 (dd, J=2, 8 Hz), 6.73 (d, J=8 Hz) and 6.82 (d, J=2 Hz)] were observed, suggesting the presence of phloroglucinol- and catechol-type aromatic rings. These observations indicated **8** to possess a 1,3-diarylpropan-2-ol skeleton. The methoxyl groups were considered to be present at each of the aromatic rings from mass spectral analysis (Chart 1), and one of the methoxyl groups was concluded to be located at the C-2′ position since the ^{13}C-NMR spectrum exhibited an unsymmetrical signal pattern of the phloroglucinol-type ring. Another methoxyl group was confirmed to be located at the C-3′′ position by an NOE experiment; upon irradiation of the methoxyl signal at δ 3.81, the integral intensity of the H-2′′ signal (δ 6.82, d, J=2 Hz) increased by 27%. On the basis of these results, **8** was established as 1-(4′,6′-dihydroxy-2′-methoxyphenyl)-3-(4′′-hydroxy-3′′-methoxyphenyl)propan-2-ol. Compound **8** exists in a racemic form, as confirmed by optical rotatory dispersion (ORD) measurement.

In *Cinnamomum cassia, C. obtusifolium* and *Lindera umbellata* var. *membranacea*, the above-mentioned methyl derivatives are accompanied by several condensed tannins consisting of chains of flavan-3-ol units, and the structures of these compounds will be reported elsewhere.

Experimental

Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-4 digital polarimeter. Infrared (IR) spectra were recorded with a JASCO DS-301 spectrometer, and EI-MS with a JEOL D-300 instrument. ^{1}H- and ^{13}C-NMR spectra were measured with JEOL PS-100 and JEOL FX-100 spectrometers, respectively, with tetramethylsilane as an internal standard, and chemical shifts are given in δ (ppm). Column chromatography was carried out with Sephadex LH-20 (25—100 μ, Pharmacia Fine Chemical Co., Ltd.), MCI-GEL CHP 20P (75—150 μ, Mitsubishi Chemical Industries Ltd.) and Kieselgel 60 (70—230 mesh, Merck). Thin-layer chromatography (TLC) was conducted on precoated Kieselgel 60 F_{254} plates (Merck, 0.2 mm thick) with benzene–acetone (4:1, 3:1, 2:1) and benzene–ethyl formate–formic acid (5:4:1) as solvent systems, and spots were located with anisaldehyde–H_2SO_4 and 10% H_2SO_4 reagents.

Isolation and Extraction

From *Cinnamomum cassia*.——The powdered bark of *C. cassia* (東興桂皮, 59 kg) was extracted with water at room temperature. The extract was concentrated under reduced pressure to give a brown syrup, which was chromatographed over MCI-GEL CHP 20P with water and then with MeOH. The MeOH eluate (365 g) was

subjected to Sephadex LH-20 chromatography. Elution with EtOH afforded fractions 1 (32 g), 2 (11 g), 3 (62 g) and 4 (123 g). Fraction 1 was chromatographed over Sephadex LH-20 (acetone) to give further fractions 1-a and 1-b. Fraction 1-a was subjected to silica gel chromatography using benzene–acetone (4 : 1, 5 : 1 and 6 : 1) to yield compounds **3** (142 mg), **4** (257 mg), **6** (19 mg), **7** (23 mg) and **11** (148 mg), while fraction 1-b was chromatographed over MCI-GEL CHP 20P (40% aqueous MeOH) to afford compounds **1** (72 mg), **5** (18 mg), **9** (518 mg) and **10** (19 mg). Fractions 1—4 contained dimeric, trimeric and higher oligomeric proanthocyanidins.

From *Cinnamomum obtusifolium*——The powdered bark of *C. obtusifolium* (ベトナム桂皮, 5 kg) was extracted with 60% aqueous acetone. The extract was concentrated to dryness to give a dark brown solid (369 g). Chromatography of this solid on Sephadex LH-20 using EtOH gave fractions 1 (25 g), 2 (10 g), 3 (20 g) and 4 (55 g). Fraction 1 was rechromatographed over Sephadex LH-20 with acetone to afford fractions 1-a and 1-b. Fraction 1-a was repeatedly chromatographed over MCI-GEL CHP 20P (60% aqueous MeOH) and silica gel (benzene–acetone; 4 : 1 and 6 : 1) to give compounds **3** (32 mg), **4** (88 mg) and **11** (54 mg). Fraction 1-b was subjected to MCI-GEL CHP 20P chromatography (40% aqueous MeOH) to afford compounds **1** (41 mg), **9** (305 mg) and **10** (12 mg). Other fractions consisted of a mixture of proanthocyanidins.

From *Lindera umbellata* var. *membranacea*——The twig of *L. umbellata* var. *membranacea* (烏樟, 20 kg) was extracted with 60% aqueous acetone. The extract, on concentration, yielded precipitates which were removed by filtration. The filtrate was chromatographed over Sephadex LH-20 with increasing amounts of MeOH in water (1 : 0→0 : 1) to yield fractions 1 (51 g), 2 (67 g), 3 (111 g) and 4 (215 g). Fraction 1 was divided into fractions 1-a and 1-b by Sephadex LH-20 chromatography with EtOH. Chromatography of fraction 1-a on Sephadex LH-20 (acetone) and silica gel (benzene–acetone; 5 : 1 and 6 : 1) afforded compounds **1** (37 mg), **2** (11 mg), **3** (67 mg), **4** (173 mg) and **8** (61 mg). Fraction 1-b was subjected to MCI-GEL CHP 20P chromatography (40% aqueous MeOH) to give compounds **9** (840 mg) and **10** (550 mg).

Compound 1——Colorless prisms (H_2O), mp 237—238 °C, $[\alpha]_D^{28}$ −56.1° ($c=1.05$, acetone). *Anal.* Calcd for $C_{16}H_{16}O_6$: C, 63.15; H, 5.35. Found: C, 63.20; H, 5.30. EI-MS *m/z* (red. int.): 304 [M^+] (54), 166 (95), 139 (100). ^{13}C-NMR (acetone-d_6): 28.9 (C_4), 56.2 (OMe), 66.8 (C_3), 79.3 (C_2), 95.5, 96.1 (C_6, C_8), 99.6 (C_{4a}), 111.9 ($C_{2'}$), 11.50 ($C_{5'}$), 120.4 ($C_{6'}$), 131.8 ($C_{1'}$), 146.6, 147.9 ($C_{3'}$, $C_{4'}$), 156.8, 157.3, 157.5 (C_5, C_7, C_{8a}). ^{1}H-NMR: Table I.

Methylation of **1**: Excess ethereal diazomethane was added to a solution of **1** (10 mg) in EtOH (1 ml), and the mixture was kept standing overnight at room temperature. The solvent was evaporated off *in vacuo*, and the residue was crystallized from EtOH to give colorless needles (8 mg). This compound was identified as 5,7,3′,4′-tetra-*O*-methyl-(−)-epicatechin by direct comparison of the physical data with those of an authentic sample.

Compound 2——Colorless needles (H_2O), mp 199—201 °C, $[\alpha]_D^{28}$ −59.3° ($c=1.13$, acetone). *Anal.* Calcd for $C_{17}H_{18}O_6$: C, 64.14; H, 5.70. Found: C, 64.24; H, 5.55. EI-MS *m/z* (rel. int.): 318 [M^+] (32), 180 (100), 139 (60). ^{1}H-NMR: Table I.

Methylation of **2**: **2** (8 mg) was methylated in the same manner as described for **1** to yield 5,7,3′,4′-tetra-*O*-methyl-(−)-epicatechin (5 mg).

Compound 3——Colorless needles (*n*-hexane–AcOEt), mp 206—208 °C, $[\alpha]_D^{28}$ −66.4° ($c=1.15$, acetone). *Anal.* Calcd for $C_{17}H_{18}O_6$: C, 64.14; H, 5.70. Found: C, 64.32; H, 5.81. EI-MS *m/z* (rel. int.): 318 [M^+] (52), 166 (37), 153 (100). ^{13}C-NMR (acetone-d_6): 29.1 (C_4), 55.6, 56.2 (2×OMe), 66.8 (C_3), 79.4 (C_2), 92.6 (C_6), 96.5 (C_8), 100.6 (C_{4a}), 111.7 ($C_{2'}$), 115.2 ($C_{5'}$), 120.6 ($C_{6'}$), 131.9 ($C_{1'}$), 146.8, 147.8 ($C_{3'}$, $C_{4'}$), 156.7, 157.8, 160.1 (C_5, C_7, C_{8a}). ^{1}H-NMR: Table I.

Methylation of **3**: **3** (10 mg) was treated in the same way as described for **1** to give 5,7,3′,4′-tetra-*O*-methyl-(−)-epicatechin (7 mg).

Compound 4——Colorless needles (benzene), mp 139 °C, $[\alpha]_D^{28}$ −61.2° ($c=1.22$, acetone). *Anal.* Calcd for $C_{18}H_{20}O_6$: C, 66.05; H, 6.07. Found: C, 65.83; H, 6.25. EI-MS *m/z* (rel. int.): 332 [M^+] (31), 167 (100). ^{13}C-NMR (acetone-d_6): 29.1 (C_4), 55.5, 55.7, 56.2 (3×OMe), 66.6 (C_3), 79.6 (C_2), 92.0, 94.2 (C_6, C_8), 101.9 (C_{4a}), 111.7 ($C_{2'}$), 115.2 ($C_{5'}$), 120.5 ($C_{6'}$), 131.7 ($C_{1'}$), 146.8, 147.8 ($C_{3'}$, $C_{4'}$), 156.7, 160.0, 160.4 (C_5, C_7, C_{8a}). ^{1}H-NMR: Table I.

Methylation of **4**: **4** (10 mg) was treated in the same manner as described for **1** to afford 5,7,3′,4′-tetra-*O*-methyl-(−)-epicatechin (5 mg).

Compounds 5——Colorless needles (H_2O), mp 152 °C, $[\alpha]_D^{26}$ +6.7° ($c=0.85$, acetone). *Anal.* Calcd for $C_{16}H_{16}O_6$: C, 63.15; H, 5.35. Found: C, 63.38; H, 5.50. EI-MS *m/z* (rel. int.): 304 [M^+] (35), 166 (78), 139 (100). ^{13}C-NMR (acetone-d_6): 28.1 (C_4), 56.3 (OMe), 68.0 (C_3), 82.1 (C_2), 95.2, 96.1 (C_6, C_8), 100.4 (C_{4a}), 112.0 ($C_{5'}$), 115.0 ($C_{2'}$), 119.6 ($C_{6'}$), 133.0 ($C_{1'}$), 146.9, 148.1 ($C_{3'}$, $C_{4'}$), 156.4, 157.0, 157.4 (C_5, C_7, C_{8a}). ^{1}H-NMR: Table I.

Acetylation of **5**: **5** (7 mg) was acetylated with acetic anhydride (0.5 ml) and pyridine (0.5 ml) at room temperature for 6 h. Excess reagents were removed by blowing N_2 over the solution, and the residue was purified by crystallization from EtOH to yield colorless needles (5 mg) **5a**, mp 136—138 °C, $[\alpha]_D^{26}$ −5.2° ($c=0.53$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$): 1.96, 2.13, 2.24, 2.28 (each 3H, s, OAc), 2.64 (1H, dd, $J=8$, 16 Hz, 4-H), 2.88 (1H, dd, $J=6$, 16 Hz, 4-H), 3.79 (3H, s, OMe), 5.05 (1H, d, $J=7$ Hz, 2-H), 5.25 (1H, m, 3-H), 6.55, 6.65 (each 1H, d, $J=2$ Hz, 6-H, 8-H), 6.92 (1H, d, $J=8$ Hz, 5′-H), 7.00 (1H, d, $J=2$ Hz, 2′-H), 7.18 (1H, dd, $J=2$, 8 Hz, 6′-H).

Methylation of **5**: **5** (5 mg) was methylated as before. Crystallization from EtOH gave colorless needles. This compound was identified as 5,7,3′,4′-tetra-*O*-methyl-(+)-catechin by direct comparison of the physical data with

those of an authentic sample.

Compound 6——Colorless prisms (EtOH), mp 142—144 °C, $[\alpha]_D^{26}$ −3.8° (c=0.87, MeOH). *Anal.* Calcd for $C_{17}H_{18}O_6$: C, 64.14; H, 5.70. Found: C, 63.96; H, 5.54. EI-MS m/z (rel. int.): 318 [M^+] (39), 166 (42), 153 (100). ^{13}C-NMR (DMSO-d_6): 27.6 (C_4), 55.3, 56.0 (2×OMe), 67.8 (C_3), 81.9 (C_2), 93.0, 95.4 (C_6, C_8), 102.8 (C_{4a}), 113.2 ($C_{5'}$), 115.0 ($C_{3'}$), 118.9 ($C_{6'}$), 133.2 ($C_{1'}$), 145.2, 147.7 ($C_{3'}$, $C_{4'}$), 156.9, 157.0, 160.4 (C_5, C_7, C_{8a}). ^{1}H-NMR: Table I.

Acetylation of **6**: **6** (7 mg) was acetylated with acetic anhydride (0.5 ml) and pyridine (0.5 ml). Work-up as described for **5** gave colorless needles (3 mg) **6a**, mp 125—128 °C, $[\alpha]_D^{26}$ −5.8° (c=0.41, $CHCl_3$). ^{1}H-NMR ($CDCl_3$): 1.97, 2.27, 2.28 (each 3H, s, OAc), 2.68 (1H, dd, J=8, 16 Hz, 4-H), 2.92 (1H, dd, J=6, 16 Hz, 4-H), 3.74, 3.78 (each 3H, s, OMe), 5.02 (1H, d, J=7 Hz, 2-H), 5.30 (1H, m, 3-H), 6.22, 6.35 (each 1H, d, J=2 Hz, 6-H, 8-H), 6.90 (1H, d, J=8 Hz, 5′-H), 7.00 (1H, d, J=2 Hz, 2′-H), 7.21 (1H, dd, J=2, 8 Hz, 6′-H).

Methylation of **6**: **6** (10 mg) was methylated in the same manner as described for **5** to afford 5,7,3′,4′-tetra-*O*-methyl-(+)-catechin (9 mg).

Compound 7——Colorless needles (*n*-hexane–AcOEt), mp 125 °C, $[\alpha]_D^{26}$ −8.2° (c=1.03, acetone). *Anal.* Calcd for $C_{18}H_{20}O_6$: C, 66.05; H, 6.07. Found: C, 66.32; H, 5.99. EI-MS m/z (rel. int.): 332 [M^+] (35), 167 (100). ^{13}C-NMR (DMSO-d_6): 28.6 (C_4), 55.5, 55.8, 56.3 (3×OMe), 67.7 (C_3), 82.4 (C_2), 92.3, 94.0 (C_6, C_8), 102.6 (C_{4a}), 112.2 ($C_{5'}$), 114.9 ($C_{2'}$), 119.5 ($C_{6'}$), 133.1 ($C_{1'}$), 147.1, 148.2 ($C_{3'}$, $C_{4'}$), 156.4, 159.5, 160.5 (C_5, C_7, C_{8a}). ^{1}H-NMR: Table I.

Acetylation of **7**: **7** (10 mg) was acetylated with acetic anhydride (0.5 ml) and pyridine (0.5 ml). Work-up as before yielded colorless needles (7 mg) **7a**, mp 120—121 °C, $[\alpha]_D^{26}$ −10.5° (c=0.55, $CHCl_3$). ^{1}H-NMR ($CDCl_3$): 1.96, 2.28 (each 3H, s, OAc), 2.65 (1H, dd, J=8, 16 Hz, 4-H), 2.90 (1H, dd, J=6, 16 Hz, 4-H), 3.76 (6H, s, OMe), 3.80 (3H, s, OMe), 5.02 (1H, d, J=7 Hz, 2-H), 5.30 (1H, m, 3-H), 6.09, 6.16 (each 1H, d, J=2 Hz, 6-H, 8-H), 6.91 (1H, d, J=8 Hz, 5′-H), 7.01 (1H, d, J=2 Hz, 2′-H), 7.21 (1H, dd, J=2, 8 Hz, 6′-H).

Methylation of **7**: **7** (10 mg) was methylated in the same way as before to give 5,7,3′,4′-tetra-*O*-methyl-(+)-catechin (10 mg).

Compound 8——A colorless gum, $[\alpha]_D^{28}$ 0° (c=1.55, acetone). *Anal.* Calcd for $C_{17}H_{18}O_6$: C, 63.73; H, 6.29. Found: C, 63.95; H, 6.39. EI-MS m/z (rel. int.): 320 [M^+] (44), 183 (57), 167 (25), 153 (100), 137 (84). ^{1}H-NMR (acetone-d_6): 2.56—3.00 (4H, m, 1-H, 3-H), 3.70, 3.81 (each 3H, s, OMe), 4.02 (1H, m, 2-H), 6.04 (2H, s, 3′-H, 5′-H), 6.64 (1H, dd, J=2, 8 Hz, 6′-H), 6.73 (1H, d, J=8 Hz, 5′-H), 6.82 (1H, d, J=2 Hz, 2′-H). ^{13}C-NMR (acetone-d_6): 30.9 (C_3), 40.2 (C_1), 55.8, 56.2 (2×OMe), 74.8 (C_2), 92.0 ($C_{3'}$), 97.5 ($C_{5'}$), 106.1 ($C_{1'}$), 113.8 ($C_{2''}$), 115.5 ($C_{5''}$), 122.6 ($C_{6''}$), 131.5 ($C_{1''}$), 145.6, 148.0 ($C_{3''}$, $C_{4''}$), 158.1, 158.4, 160.0 ($C_{2'}$, $C_{4'}$, $C_{6'}$).

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