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ANALYSIS OF BENZYLATION PRODUCTS OF (+)-CATECHIN

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Abstract – Catechin, a flavanol compound from tea leaves, is one of useful starting materials in many synthetic studies toward various flavonoids. For synthesis, benzyl group is frequently chosen for protecting phenolic hydroxyl groups. To clarify the reactivity of each hydroxyl groups of catechin and realize an efficient reaction condition, we analyzed the products of the benzylation reaction of (+)-catechin. Two known and five new compounds were purified from the reaction mixture and their structure was determined. Not only *O*-benzylated products, but also 6 and/or 8-*C*-benzylated compounds were obtained. However, 3-OH group was never benzylated in this reaction.

INTRODUCTION

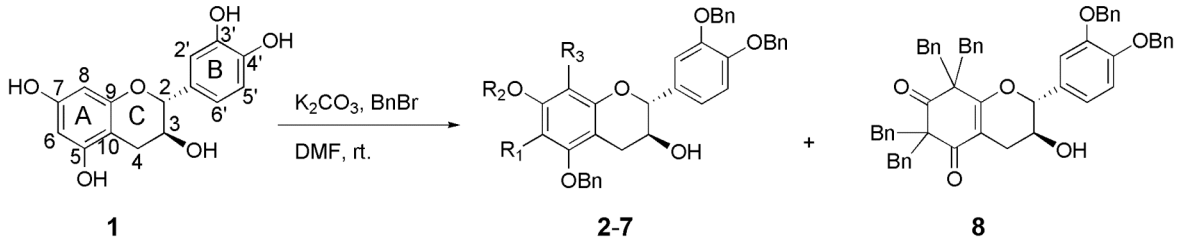
In several synthetic studies on biological active flavonoids, such as procyanidins, glycosylated or acylated flavonoids, and anthocyanins, catechins isolated from tea leaves have been used as a starting material. In such research, phenolic hydroxyl groups have been generally protected by benzyl group. In 1968, Weinges and Seiler already reported benzylated catechins for synthesis of 3-glucosyl and 3-galloyl catechin.[1] They carried out the reaction of (+)-catechin with BnCl and K_2CO_3 in acetone to give 5,7,3',4'-tetra-*O*-benzyl-(+)-catechin (**2**) by low yield coexsisting with 8-benzyl-5,7,3',4'-tetra-*O*-benzyl-(+)-catechin (**3**).[1] In 1991, Kawamoto et al. reported the synthesis of **2** with BnBr and K_2CO_3 in demethylformamide (DMF).[2] Although the reaction yield is not so good, ca. 50%, however, the 3-OH free tetra-*O*-benzylcatechin (**2**) can be obtained in one pot. The authors described that the low yield was caused by side reactions, mainly *C*-benzylation.[2] After this report the same group published an improved prepatation method of **2** via penta-*O*-acetyl-(+)-catechin.[3] Recently, several groups including our group have used **2** for total synthesis of procyanidin,[1-9] anthocyanin[10] and other polyphenols.[11-13] In the preparation of **2**, despite the generation of *C*-benzylated products suppressed the reaction yield,[1,2,4,7,9] no

further study to analyze by-products was carried out except 8-*C*-benzyl product.[1] Here we describe the analysis of benzylation reaction of (+)-catechin by isolation and structure determination of by-products.

RESULTS AND DISCUSSION

Benzylation Reaction of Catechin

According to the reaction condition of Kawamoto et al.[1] **1** (3.0 g) was dissolved in DMF and to the solution K_2CO_3 (4 eq.) and BnBr (4 eq.) were added at 0 °C. The mixture was warmed to rt and stirred for 16 h (Scheme 1). The reaction mixture was then extracted with EtOAc and further purification was carried out. The major product **2** was obtained by SiO_2 chromatography followed by recrystalization to give 53% yield. From the other fraction of SiO_2 chromatography and the mother liquor of recrystalization, **3**-**8** were obtained by repeated SiO_2 chromatography, thin-layer chromatography and ODS-HPLC.



1 **2-7** **8**

	R_1	R_2	R_3	yield (%)
2	H	Bn	H	53
3	H	Bn	Bn	7
4	Bn	Bn	H	4
5	Bn	Bn	Bn	5
6	H	H	H	6
7	H	H	Bn	4
8	-	-	-	1

Scheme 1. Benzylation reaction of (+)-catechin (**1**) and the obtained protucts (**2**-**8**).

Structure of benzylated products

All the products **2**-**8** were analyzed by HR-MS to give the molecular formula as shown in Table 1. These results indicated the total number of Bn groups. The number of *O*-Bn and *C*-Bn residues were determined by ^{1}H NMR spectra, while the signals of methylene protons of *O*-Bn residues were observed around 4.8-5.2 ppm and those of *C*-Bn residues were detected at higher field than that of *O*-Bn residues around 3.8-4.0 ppm. Therefore, it was clarified that many *C*-benzylated products were obtained in this reaction.

Table 1. Molecular formula of **2**-**8** and the estimated number of *O*-Bn and *C*-Bn residues.

	m/z (found) $[M+H]^+$	*m/z* (calcd.) $[M+H]^+$	molecular formula	*O*-Bn	*C*-Bn
2	651.2737	651.2747	$C_{43}H_{38}O_6$	4	0
3	741.3217	741.3216	$C_{50}H_{44}O_6$	4	1
4	741.3210	741.3216	$C_{50}H_{44}O_6$	4	1
5	831.3685	831.3686	$C_{57}H_{50}O_6$	4	2
6	561.2276	561.2277	$C_{36}H_{32}O_6$	3	0
7	651.2760	651.2747	$C_{43}H_{38}O_6$	3	1
8	831.3680	831.3686	$C_{57}H_{50}O_6$	2	4

Structure of each product was determined by further instrumental analysis. ^{1}H NMR spectra indicated that all compounds possessed the same signal patterns corresponding to -CH-CH-CH_2- attributable to C2-C3-C4 of C-ring, and 1,3,4-substituted benzene attributable to B-ring. These results led to the conclusion that the benzylation pattern of B- and C-ring of catechin was the same in all products.

Compound **3** and **4** showed the same molecular formula and numbers of *C*-Bn and *O*-Bn residues. Both ^{1}H NMR spectra were similar each other with one proton signal around 6.2-6.4 ppm, which might be corresponding to H-6 or H-8. Compound **3** showed the HMBC correlations between the methylene signals of *C*-Bn at 3.82 and 3.93 ppm, and C-7 (155.9 ppm) and C-9 (153.0 ppm), and aromatic proton signal at 6.17 ppm and C-5 (155.6 ppm) and C-7. In contrast to those results, **4** showed the HMBC correlations between the methylene signals (4.04 ppm) and C-5 (156.4 ppm) and C-7 (156.9 ppm) and aromatic proton signal at 6.38 ppm and C-7 and C-9 (153.8 ppm). Summarizing the results, **3** was determined to be 8-*C*-Bn compound and **4** to be 6-*C*-Bn compound, respectively. The structure of **4** was also identified by the comparison with the previously reported data.[1] Compound **5** had two *C*-Bn residues, therefore, it was concluded that both the C-6 and C-8 position were benzylated. Thus the structure of **5** was determined to be 6,8-di-*C*-Bn-5,7,3',4'-tetra-*O*-Bn compound.

In ^{1}H NMR of **6** in DMSO-d_6 a singlet signal being corresponding to phenolic hydroxyl proton was observed at 9.24 ppm. However, further NMR analysis could not be carried out because of the overlapping of signals. Therefore, **6** was acetylated by Ac_2O/pyridine and the obtained diacetylated compound **9** was analyzed. All the proton and carbon signals were assigned by various 2D NMR experiments, and the chemical shift of C-5 and C-7 in **9** were deduced to be 157.3 ppm and 150.3 ppm, respectively, although, in **6** the chemical shift of C-5 and C-7 were 157.1 ppm and 157.3 ppm and could not be differentiated. This higher field shift of C-7 should be occurred due to the acetylation of 7-OH,

therefore, the structure of **6** was determined to be 5,3',4'-tri-*O*-Bn compound. ^{1}H NMR of **7** in DMSO-d_6 also showed a signal of phenolic hydroxyl proton at 9.22 ppm with three *O*-Bn and one *C*-Bn residues. Furthermore, **7** lacked one proton signal attributable to H-6 or H-8. The methylene signals of *C*-Bn at 3.69 ppm and 3.79 ppm showed HMBC correlation with C-9 (100.5 ppm). Thus, **7** was determined to be 8-*C*-Bn-5,3',4'-tri-*O*-Bn compound.

MS spectrum of **8** indicated six Bn groups and ^{1}H NMR of **8** showed a spectrum considerably different compared with those of **2**-**7** (Figure 1). In **8**, two sets of methylene signals of *O*-Bn residues were observed around 5.1 ppm. Three protons, to be assigned as H-2', H-5' and H-6', were also observed, however, aromatic signals attributable to H-6 and H-8 were missing. Furthermore, other methylene signals corresponding to *C*-Bn residues were observed at 2-3 ppm, much higher field compared with that of *C*-Bn in **2**-**7**. In ^{13}C NMR two signals corresponding to carbonyl carbons were observed at 194.2 ppm and 207.7 ppm and the existence of C=O groups was also confirmed by IR spectrum (1625 cm^{-1}). HMBC correlations were observed as shown in Figure 2. Two sets of methylene signals at 2.42 ppm and 2.79 ppm (6A), and 2.62 ppm and 3.08 ppm (6B) had a HMBC correlation with C-5 (194.2 ppm). One of 6B signal also had a correlation with C-7 (207.7 ppm). Two sets of methylene signals at 2.11 ppm and 2.65 ppm (8C), and 2.75 ppm and 3.00 ppm (8D) had a HMBC correlation with C-7 (207.7 ppm) and C-9 (171.1 ppm). Furthermore, the signals of C-6 and C-8 were shifted much higher at 66.6 ppm and 59.8 ppm, which was strongly suggested that those two carbons were sp^3, not aromatic carbon. Thus, the structure of **8** was determined to be 2-(*S*)-(3,4-dibenzyloxyphenyl)-6,6,8,8-tetrabenzyl-3-(*S*)-hydroxy-2*H*-3,4,5,6,7,8-hexahydro-chromene-5,7-dione (**8**).

Conclusion

We analyzed the benzylation reaction products of (+)-catechin by BnBr/K_2CO_3 and isolated seven products including five new compound **4**-**8**. In the benzylation reaction of (+)-catechin, even if using 4 eq. of BnBr, various products from tri- to hexa-Bn producnts including *C*-Bn compounds were obtained. In all the isolated products, phenolic hydroxyl groups at 5,3' and 4'-position were completely benzylated and aliphatic 3-OH was not. C-6 and C-8 position may be electron rich, therefore, those carbon might be easily *C*-benzylated. In contrast to these carbon atoms, carbons at B-ring were not benzylated indicating a clear difference in reactivity was observed between A-ring and B-ring. In naringenin, a flavanone, we already observed the difference of *O*-benzylation reactivity that 7-OH was the most reactive to electrophiles in all the other phenols,[14,15] however, in (+)-catechin, a flavanol, 7-OH may be less reactive than 5 and 4'-OH. The quantum calculation of these flavonoids must be done to clarify the reactivity and to develop an efficient reaction.

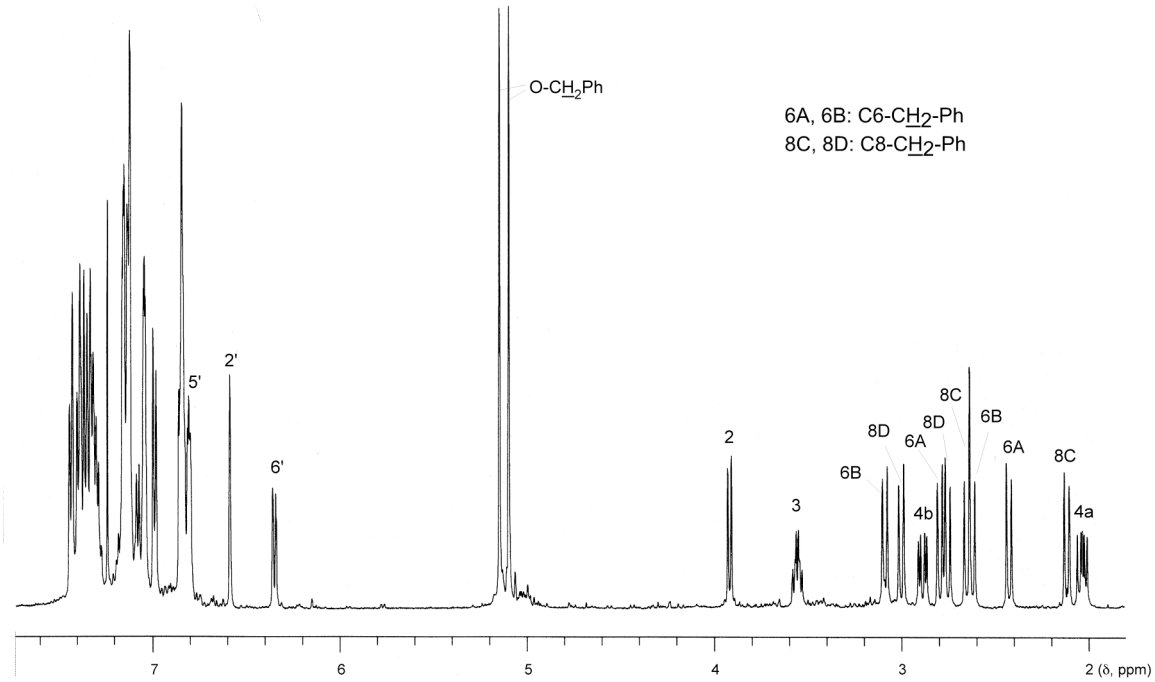


Figure 1. ^{1}H NMR spectrum of **8** ($CDCl_3$, rt, 500 MHz).

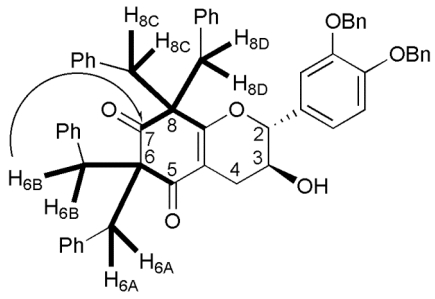


Figure 2. HMBC correlations of **8**. Both thick bonds and an arrow show HBMC correlations.

EXPERIMENTAL

General

Melting points were recorded on a Yanagimoto MP-S3 apparatus and uncorrected. Optical rotations were recorded on a JASCO DIP-140 polarimeter. UV-VIS spectra were recorded on a JASCO V-560 spectrometer. IR spectra were obtained with a JASCO FT/IR-460 plus spectrometer. NMR spectra were obtained with a JEOL ECA-500 (^{1}H: 500 MHz, ^{13}C: 125 MHz), and a JNM-A400 (^{1}H: 400 MHz, ^{13}C: 100 MHz) instrument in a 5-mm ϕ tube at variable temperature using $CDCl_3$ and DMSO-d_6 as a solvent. Chemical shifts were reported as δ (ppm) with the CD_2HCl resonance as a standard and the coupling

constant was expressed in Hz. FABMS (*m*-nitrobenzyl alcohol as a matrix) were recorded on a JEOL JMS-700 spectrometer. Silica gel column chromatography was performed with Fuji Silysia FL60D. Thin layer chromatography was performed on Merck Kieselgel 60 F_{254}. Analytical and preparative HPLC were conducted according to our procedure[16,17] using ODS-columns (Develosil ODS-HG-5, Nomura Chemicals) with aq. MeCN as an eluent.

Benzylation reaction of (+)-catechin (1)

To a flask (200 mL) were added anhydrous DMF (60 mL), K_2CO_3 (8.57 g, 62.0 mmol) and (+)-catechin (**1**, 3.00 g, 10.3 mmol) and cooled at 0 °C under argon atmosphere. To the stirred mixture BnBr (3.09 mL, 26.0 mmol) was added and the mixture was allowed to stand at 0 °C for 30 min, then was warmed to rt and stirred for 15 h. To the reaction mixture was added sat. aq. $NaHCO_3$ (140 mL) and then extraction was performed with EtOAc (100 mL x 3). The EtOAc layer was dried up with $MgSO_4$ and evaporated under reduced pressure to give a crude benzylatedcatechin mixture.

Purification of 2-8

The obtained crude benzylatedcatechin mixture was purified with SiO_2 column (hexane-EtOAc = 4:1 and 1:1) to give a crude **2** fraction and a crude **6** fraction. The crude **2** fraction was recrystalized from hexane-EtOAc = 1:1 to give **2** (2.67 g, 40%). The mother liquor (2.3 g) was purified with SiO_2 column chromatography (hexane-EtOAc = 4:1) to give crude **2**-**5** fraction (2.06 g), and crude **7**, **8** fraction (0.41 g). The crude **2**-**5** fraction was purified with ODS-HPLC (gradient elution from 75% to 85% aq. MeCN) to give **2** (0.86 g, 13%), **5** (0.21 g, 5%), and crude **3**, **4** fraction (0.95 g). The crude **3**, **4** fraction was purified with SiO_2 column chromatography (hexane-EtOAc = 4:1) to give **3** (0.53 g, 7%) and **4** (0.33 g, 4%). From crude **7**, **8** fraction **8** (0.08 g, 1%) was obtained by ODS-HPLC (gradient elution from 70% to 80% aq. MeCN) and **7** (0.13 g, 4%) was purified with ODS-HPLC (gradient elution from 70% to 80% aq. MeCN) followed by TLC ($CHCl_3$). Compound **6** (0.37 g, 6%) was obtained from crude **6** fraction with repeated SiO_2 column (Hexane-EtOAc = 4:1 and 2:1, 1% MeOH-CH_2Cl_2) and ODS-HPLC (gradient elution from 65% to 85% aq. MeCN).

5,7,3',4'-tetra-*O*-Benzyl-(+)-catechin (2)[1,2]

Colorless powder: mp 141-142 °C; $[\alpha]_D^{28.9}$ –0.7 (c 0.5, $CHCl_3$); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 2.47 (1H, dd, J = 16.0, 8.0 Hz, H-4a), 2.77 (1H, dd, J = 16.0, 5.5 Hz, H-4b), 3.97 (1H, m, H-3), 4.64 (1H, d, J = 7.0 Hz, H-2), 5.03 (2H, s, $\underline{CH_2}$-Ph), 5.07 (2H, s, $\underline{CH_2}$-Ph), 5.08 (2H, s, $\underline{CH_2}$-Ph), 5.12 (2H, s, $\underline{CH_2}$-Ph), 6.13 (1H, d, J = 2.0 Hz, H-8), 6.33 (1H, J = 2.0 Hz, H-6), 6.88 (2H, dd, J = 8.5, 1.5 Hz, H-6'), 7.02 (1H, d, J = 8.5 Hz, H-5'), 7.09 (1H, d, J = 1.5 Hz, H-2'), 7.29-7.44 (20H, m, CH_2-$\underline{Ph}$); ^{13}C NMR (DMSO-d_6, 125

MHz) δ 28.1, 65.9, 69.4, 70.3, 70.4, 81.1, 93.5, 94.6, 102.4, 113.9, 114.3, 120.5, 127.4, 127.6, 127.7, 127.8, 127.9, 128.5, 128.6, 132.5, 137.3, 137.4, 137.5, 148.1, 148.2, 155.2, 157.3, 158.2.

8-*C*-Benzyl-5,7,3',4'-tetra-*O*-benzyl-(+)-catechin (3)[1]

Colorless powder: mp 152-153 °C; $[\alpha]_D^{28.4}$ –34.5 (c 0.5, $CHCl_3$); IR (KBr) 3434, 3029, 2892, 1604, 1265, 1119 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.57 (1H, dd, *J* = 16.0, 8.5 Hz, H-4a), 3.00 (1H, dd, *J* = 16.0, 5.5 Hz, H-4b), 3.80 (1H, m, H-3), 3.82 (1H, d, *J* = 14.0 Hz, $\underline{CH_2}$-Ph), 3.93 (1H, d, *J* = 14.0 Hz, $\underline{CH_2}$-Ph), 4.56 (1H, d, *J* = 8.0 Hz, H-2), 4.89-4.97 (6H, m, $\underline{CH_2}$-Ph), 5.07(2H, s, $\underline{CH_2}$-Ph), 6.17 (1H, s, H-6), 6.75 (1H, dd, *J* = 8.5, 1.5 Hz, H-6'), 6.82 (1H, d, *J* = 8.0 Hz, H-5'), 6.85 (1H, d, *J* = 1.5 Hz, H-2'),7.05-7.44 (25H, m, CH_2-$\underline{Ph}$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 27.7, 28.7, 68.4, 70.1, 70.6, 71.1, 71.3, 81.4, 91.3, 102.5, 110.4, 113.4, 114.8, 120.3, 125.3, 127.1, 127.2,127.3, 127.5, 127.8, 127.9, 128.4, 128.5, 128.8, 131.4, 137.0, 137.1, 137.2, 137.3, 142.3, 149.0, 149.1, 153.0, 155.6, 155.9.

6-*C*-Benzyl-5,7,3',4'-tetra-*O*-benzyl-(+)-catechin (4)

Colorless powder: mp 128-129 °C; $[\alpha]_D^{28.5}$ –2.5 (c 0.5, $CHCl_3$); IR (KBr) 3586, 3030, 2862, 1591, 1265, 1121 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.72 (1H, dd, *J* = 16.0, 9.0 Hz, H-4a), 3.00 (1H, dd, *J* = 16.0, 5.5 Hz, H-4b), 3.96 (1H, m, H-3), 4.04 (2H, br., $\underline{CH_2}$-Ph), 4.64 (1H, d, *J* = 8.0 Hz, H-2), 4.65 (1H, d, *J* = 11.0 Hz, $\underline{CH_2}$-Ph), 4.79 (1H, d, *J* = 11.0 Hz, $\underline{CH_2}$-Ph), 4.95 (2H, s, $\underline{CH_2}$-Ph), 5.15 (1H, s, $\underline{CH_2}$-Ph), 5.16 (1H, s, $\underline{CH_2}$-Ph), 5.17 (2H, s, $\underline{CH_2}$-Ph), 6.38 (1H, s, H-8), 6.95 (2H, s, H-2' or 5' or 6'), 7.02 (1H, s, H-2' or 5' or 6'), 7.11-7.44 (25H, m, CH_2-$\underline{Ph}$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.4, 29.6, 68.2, 70.1, 71.3, 74.9, 81.7, 97.0, 106.5, 113.9, 115.0, 116.2, 120.7, 125.5, 127.2, 127.5, 127.7, 127.9, 128.0, 128.1, 128.1, 128.4, 128.5, 130.8, 136.9, 137.0, 137.1, 141.8, 149.2, 149.4, 153.8, 156.4, 156.9.

6,8-Di-*C*-benzyl-5,7,3',4'-tetra-*O*-benzyl-(+)-catechin (5)

Colorless amorphous: $[\alpha]_D^{28.1}$ –19.8 (c 0.5, $CHCl_3$); IR (KBr) 3431, 3029, 1594, 1512, 1453, 1117 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.78 (1H, dd, *J* = 16.0, 9.5 Hz, H-4a), 3.22 (1H, dd, *J* = 16.0, 6.0 Hz, H-4b), 3.86 (1H, m, H-3), 3.99 (1H, d, *J* = 15.0 Hz, $\underline{CH_2}$-Ph), 4.05 (2H, s, $\underline{CH_2}$-Ph), 4.06 (1H, d, *J* = 15.0 Hz, $\underline{CH_2}$-Ph), 4.58(2H, s, $\underline{CH_2}$-Ph), 4.59 (1H, d, *J* = 8.0 Hz, $\underline{CH_2}$-Ph), 4.63 (1H, d, *J* = 8.0 Hz, $\underline{CH_2}$-Ph), 4.78 (1H, d, *J* = 11.0 Hz, H-2), 4.94 (1H, br., $\underline{CH_2}$-Ph), 4.95 (1H, br., $\underline{CH_2}$-Ph), 5.14 (2H, s, $\underline{CH_2}$-Ph), 6.74 (1H, dd, *J* = 8.0, 1.5 Hz, H-6'), 6.86 (1H, d, *J* = 1.5 Hz, H-2'), 6.87 (1H, d, *J* = 8.0 Hz, H-5'), 7.06-7.44 (30H, m, CH_2-$\underline{Ph}$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.8, 30.0, 30.3, 68.3, 71.1, 71.3, 74.5, 75.8, 81.5, 110.9, 113.2, 114.7, 118.4, 120.4, 120.5, 125.5, 125.7, 127.2, 127.4, 127.6, 127.8, 127.9, 128.1, 128.2, 128.3, 128.4, 128.5, 131.0, 137.0, 137.2, 137.3, 141.5, 141.8, 149.1, 141.8, 149.1, 149.2, 152.2, 154.9, 155.6.

5, 3',4'-Tri-*O*-benzyl-(+)-catechin (6)

Colorless amorphous: $[\alpha]_D^{28.8}$ +10.3 (c 0.5, $CHCl_3$); IR (KBr) 3348, 3033, 2909, 1603, 1509, 1454, 1259, 1140, 1116, 1027 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz) δ 2.44 (1H, dd, J = 16.0, 8.0 Hz, H-4a), 2.75 (1H, dd, J = 16.0, 5.5 Hz, H-4b), 3.93 (1H, tt, J = 8.0, 5.5 Hz, H-3), 4.60 (1H, d, J = 8.0 Hz, H-2), 5.02 (2H, s, $\underline{CH_2}$-Ph), 5.09 (2H, s, $\underline{CH_2}$-Ph), 5.11 (2H, s, $\underline{CH_2}$-Ph), 5.87 (1H, d, J = 2.0 Hz, H-6), 6.07 (1H, d, J = 2.0 Hz, H-8), 6.87 (1H, dd, J = 8.5, 2.0 Hz, H-6'), 7.02 (1H, d, J = 8.5 Hz, H-5'), 7.08 (1H, d, J = 2.0 Hz, H-2'), 7.28-7.44 (15H, m, CH_2-$\underline{Ph}$), 9.24 (1H, s, 7-OH); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 28.2, 66.1, 69.2, 70.3, 70.4, 81.0, 93.3, 95.5, 100.5, 113.9, 114.3, 120.5, 127.4, 127.6, 127.8, 127.9, 128.5, 128.6, 132.7, 137.4, 137.6, 148.1, 148.2, 155.1, 157.1, 157.3.

8-*C*-Benzyl-5, 3',4'-tri-*O*-benzyl-(+)-catechin (7)

Colorless powder: mp 157-158 °C; $[\alpha]_D^{28.7}$ -22.0 (c 0.5, $CHCl_3$); IR (KBr) 3426, 3246, 3031, 2919, 1614, 1514, 1251, 1117 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz) δ 2.47 (1H, dd, J = 16.0, 8.0 Hz, H-4a), 2.79 (1H, dd, J = 16.0, 5.5 Hz, H-4b), 3.96 (1H, d, J = 14.0 Hz, $\underline{CH_2}$-Ph), 3.79 (1H, d, J = 14.0 Hz, $\underline{CH_2}$-Ph), 3.84(1H, dt, J = 8.0, 5.5 Hz, H-3), 4.63 (1H, d, J = 8.0 Hz, H-2), 4.95 (1H, d, J = 12.0 Hz, $\underline{CH_2}$-Ph), 4.99 (1H, d, J = 12.0 Hz, $\underline{CH_2}$-Ph), 5.00 (2H, s, $\underline{CH_2}$-Ph), 5.10 (1H, s, $\underline{CH_2}$-Ph), 6.19 (1H, s, H-6), 6.80 (1H, dd, J = 8.5, 2.0 Hz, H-6'), 6.98 (1H, d, J = 8.5 Hz, H-5'), 7.02 (1H, d, J = 2.0 Hz, H-2'), 7.13-7.44 (20H, m, CH_2-$\underline{Ph}$), 9.22 (1H, s, 7-OH); ^{13}C NMR (DMSO-*d6*, 125 MHz) δ 28.3, 28.5, 66.4, 69.2, 70.3, 70.4, 81.0, 93.0, 100.5, 107.1, 113.5, 114.1, 120.4, 125.3, 127.4, 127.8, 127.9, 128.5, 128.6, 132.8, 137.4, 137.6, 142.2, 148.0, 148.1, 152.9, 154.3, 155.0.

2-(*S*)-(3,4-Dibenzyloxyphenyl)-6,6,8,8-tetrabenzyl-3-(*S*)-hydroxy-2*H*-3,4,5,6,7,8-hexahydro-chromene-5,7-dione (8)

Colorless amorphous: $[\alpha]_D^{28.6}$ +10.8 (c 0.5, $CHCl_3$); IR (KBr) 3491, 3030, 2933, 1625, 1265, 1213 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.03 (1H, dd, J = 16.5, 9.5 Hz, H-4a), 2.11 (1H, d, J = 13.5 Hz, $\underline{CH_2}$-Ph), 2.42 (1H, d, J = 13.5 Hz, $\underline{CH_2}$-Ph), 2.62 (1H, d, J = 13.5 Hz, $\underline{CH_2}$-Ph), 2.65 (1H, d, J = 13.5 Hz, $\underline{CH_2}$-Ph), 2.75 (1H, d, J = 13.5 Hz, $\underline{CH_2}$-Ph), 2.79 (1H, d, J = 13.5 Hz, $\underline{CH_2}$-Ph), 2.88 (1H, dd, J = 16.5, 5.5 Hz, H-4b), 3.00 (1H, d, J = 13.5 Hz, $\underline{CH_2}$-Ph), 3.08 (1H, d, J = 13.5 Hz, $\underline{CH_2}$-Ph), 3.55 (1H, dt, J = 9.5, 5.5 Hz, H-3), 3.91 (1H, d, J = 9.5 Hz, H-2), 5.09 (2H, s, $\underline{CH_2}$-Ph), 5.14 (2H, s, $\underline{CH_2}$-Ph), 6.34 (1H, dd, J = 8.0, 2.0 Hz, H-6'), 6.58 (1H, d, J = 2.0 Hz, H-2'), 6.85 (1H, d, J = 8.0 Hz, H-5'), 6.79-7.44 (30H, m, CH_2-$\underline{Ph}$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.4, 40.7, 41.0, 43.6, 44.5, 59.8, 66.6, 67.0, 71.2, 71.7, 82.6, 112.3, 114.7, 115.1, 121.1, 126.7, 126.8, 127.0, 127.3, 127.4, 127.9, 128.0, 128.2, 128.2, 128.5, 130.6, 130.9, 131.2, 136.1, 136.5, 136.9, 137.0, 137.1, 137.2, 148.7, 149.9, 166.8, 194.2, 207.7.

7,3-*O*-Di-*O*-acetyl-5, 3',4'-tri-*O*-benzyl-(+)-catechin (9)

Compound **6** (12.3 mg, 0.022 mmol) was dissolved in Ac_2O (0.5 mL) and pyridine (0.5 mL) and the mixture was stirred at rt for 2 h. To the reaction mixture was added 1 N HCl (5 mL) and extraction was performed with EtOAc (5 mL x 3). The organic layer was dried over $MgSO_4$ and the evaporated under reduced pressure. The residue was purified with TLC (hexane-$CHCl_3$ = 4:5) to give 8.0 mg of **9** (57%). Colorless powder: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.91 (3H, s, Ac), 2.28 (3H, s, Ac), 2.71 (1H, dd, J = 17.0, 6.5 Hz, H-4a), 2.84 (1H, dd, J = 17.0, 6.5 Hz, H-4b), 4.99 (2H, s, $\underline{CH_2}$-Ph), 5.01 (1H, d, J = 6.5 Hz, H-2), 5.09 (2H, s, $\underline{CH_2}$-Ph), 5.12 (2H, s, $\underline{CH_2}$-Ph), 5.29 (1H, q, J = 6.5 Hz, H-3), 6.31 (1H, d, J = 2.0 Hz, H-6), 6.36 (1H, J = 2.0 Hz, H-8), 6.83 (2H, dd, J = 8.5, 2.0 Hz, H-6'), 6.87 (1H, d, J = 8.5 Hz, H-5'), 6.93 (1H, d, J = 2.0 Hz, H-2'), 7.25-7.41 (15H, m, CH_2-$\underline{Ph}$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.0, 21.2, 23.8, 68.6, 70.2, 71.2, 78.0, 98.3, 102.9, 106.3, 113.2, 114.9, 119.6, 127.3, 127.4, 127.8, 128.1, 128.4, 128.5, 128.6, 130.8, 136.4, 137.1, 137.2, 148.8, 148.9, 150.3, 154.5, 157.3, 169.4, 170.1.

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