

SYNTHETIC STUDIES OF PROANTHOCYANIDINS. PART 4.¹
THE SYNTHESIS OF PROCYANIDIN B1 AND B4:
TMSOTf-CATALYZED CYCLIZATION OF CATECHIN AND
EPICATECHIN CONDENSATION

Akiko Saito,¹ Noriyuki Nakajima,^{2*} Akira Tanaka,³ and Makoto Ubukata²

¹Biotechnology Center, Toyama Prefecture

²Biotechnology Research Center, Toyama Prefectural University

³Department of Biosources Science, College of Technology, Toyama Prefectural University

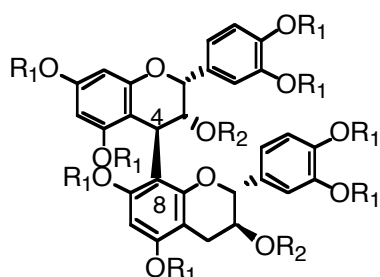
Kosugi, Toyama 939-0398, Japan. e-mail: nori@pu-toyama.ac.jp

Abstract – Highly stereoselective synthesis of 3,4-*trans* series of (+)-catechin and (-)-epicatechin dimers under intramolecular condensation is described. Intramolecular condensation achieved an equimolar amount of coupling with 3,4-*trans* stereoselectivity and we succeeded in the synthesis of two 3,4-*trans* natural procyanidins, procyanidin-B1 and B4.

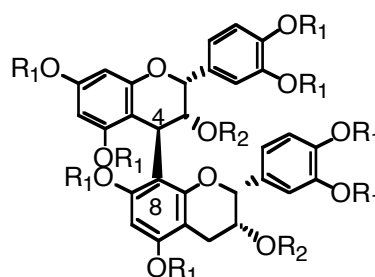
Introduction

Plant proanthocyanidin² and their dimers,^{3,4} (-) procyanidin-B1 (**1**), B2 (**2**), B3 (**3**) and B4 (**4**) consist of (-)-epicatechin (**5**) and (+)-catechin (**6**) components with C(4)-C(8) linkage as shown in Figure 1. They possess various biological activities, powerful free-radical-scavenging activity⁵ and an anti-tumor-promoting effect,⁶ and investigation of these compounds is now increasingly important. In addition, absorption of procyanidin-B1 in rat⁷ and procyanidin-B2 in human⁸ has recently been reported.

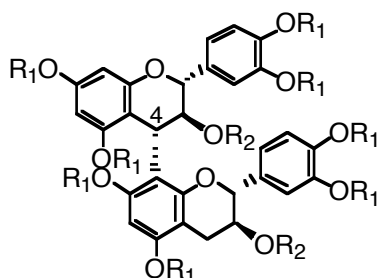
We have studied a synthetic method of proanthocyanidin oligomers. For the synthesis of the 3,4-*trans*-catechin-catechin dimer, procyanidin B3 (**3**),⁹ a potential electrophile and a nucleophile were quantitatively condensed in the presence of TMSOTf at -78°C under intermolecular conditions. However, intermolecular condensation required 4.5 times excess of the nucleophile for the reaction. Therefore, we designed an intramolecular one-to-one coupling method. A potential electrophile and nucleophile units were connected with diester linkers and TMSOTf-catalyzed one-to-one catechin-catechin condensation was carried out.¹ Intramolecular condensation proceeded with reversed 3,4-*cis* selectivity in an excellent yield. The intramolecular condensation method is expected to promote a good oligomerization method. We next examined the intramolecular epicatechin-catechin and catechin-epicatechin condensation with a glutaryl linker.



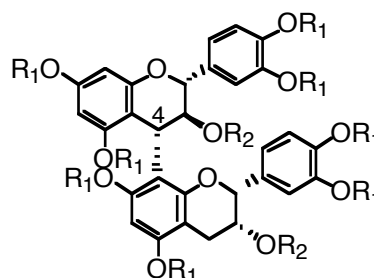
1: $R_1 = R_2 = H$, procyanidin B1
 [(-)-epicatechin-(+)-catechin]
 Bn₈-1: $R_1 = Bn$, $R_2 = H$,
 procyanidin B1 octabenzyl ether
 Ac₁₀-1: $R_1 = R_2 = Ac$,
 procyanidin B1 decaacetyl ester



2: $R_1 = R_2 = H$, procyanidin B2
 [(-)-epicatechin-(-)-epicatechin]
 Bn₈-2: $R_1 = Bn$, $R_2 = H$,
 procyanidin B2 octabenzyl ether



3: $R_1 = R_2 = H$, procyanidin B3
 [(+)-catechin-(+)-catechin]
 Bn₈-3: $R_1 = Bn$, $R_2 = H$,
 procyanidin B3 octabenzyl ether



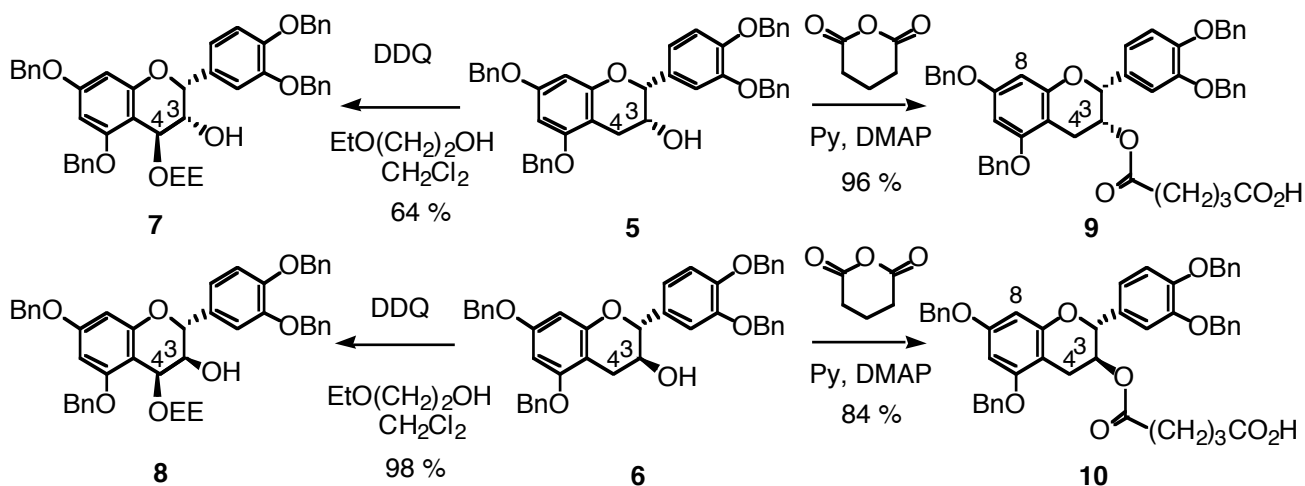
4: $R_1 = R_2 = H$, procyanidin B4
 [(+)-catechin-(-)-epicatechin]
 Bn₈-4: $R_1 = Bn$, $R_2 = H$,
 procyanidin B4 octabenzyl ether
 Ac₁₀-4: $R_1 = R_2 = Ac$,
 procyanidin B4 decaacetyl ester

Figure 1

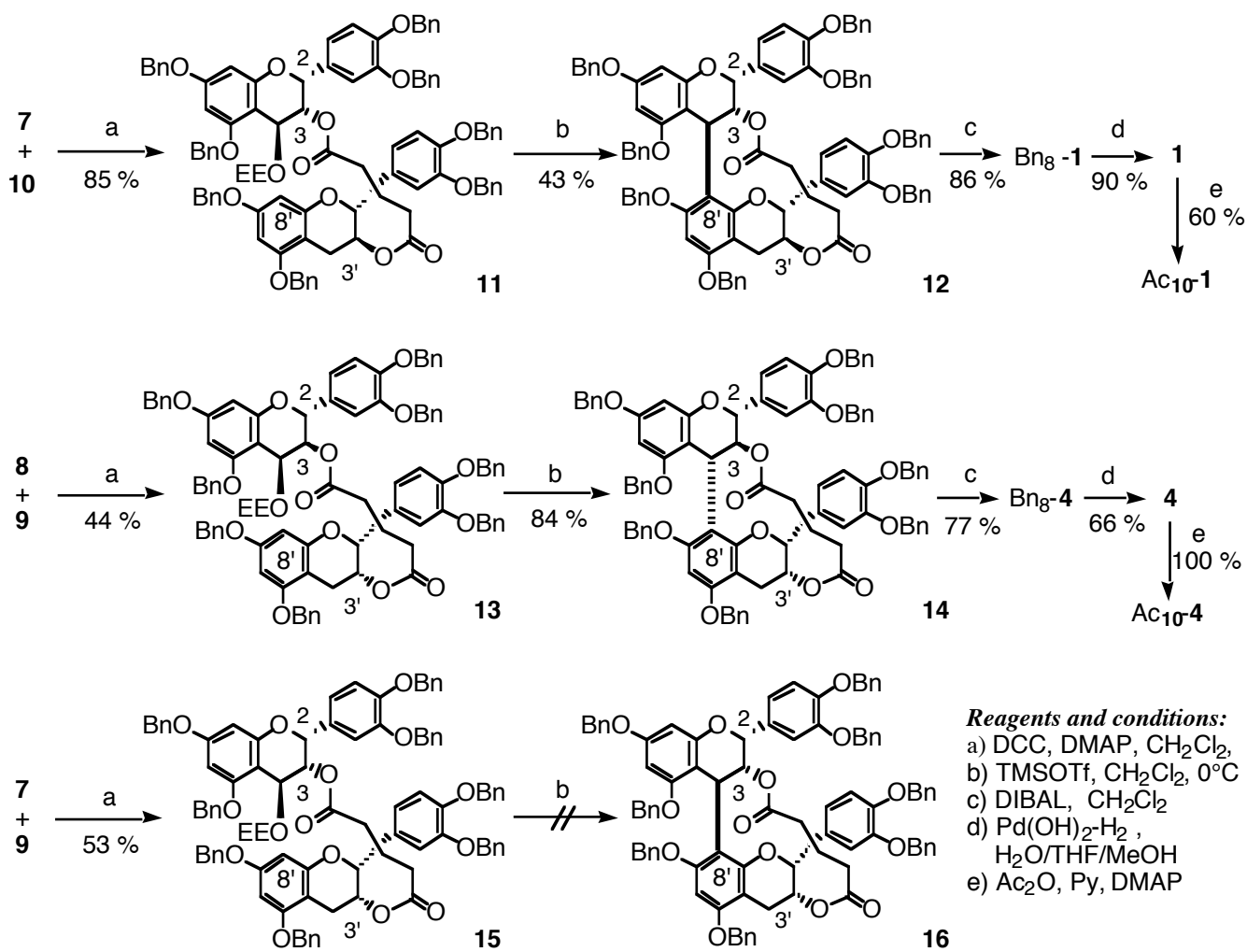
RESULTS AND DISCUSSION

Electrophile units were prepared by the introduction of an oxygen function¹⁰ to the benzylic C-4 position. 4 β -*O*-Ethoxyethyloxytetra-*O*-benzylated (-)-epicatechin (**7**) and 4 β -*O*-ethoxyethyloxytetra-*O*-benzylated (+)-catechin (**8**)⁹ were prepared by DDQ oxidation¹¹ from tetra-*O*-benzylated (-)-epicatechin (**5**) and (+)-catechin (**6**) in the presence of 2-ethoxyethanol in CH₂Cl₂ in 64% and 98% yields, respectively. The 3-hydroxy groups of the C-3 position of **5** and **6** were esterified with glutaric anhydride to give monoesters (**9** and **10**) in 96% and 84% yields, respectively. The resulting carboxylic monoesters were coupled with epicatechin electrophile (**7**) and catechin electrophile (**8**) by the DCC method to give diesters (**11** and **13**) in 85% and 44% yields, respectively. (-)-Epicatechin-(-)-epicatechin glutaryl diester (**15**) was also obtained from **7** and **9** in 53 % yield.

Intramolecular condensation for **11** and **13** was attempted by use of TMSOTf at 0°C for 5 min. The epicatechin electrophile was less reactive and 3,4-*trans*-octa-*O*-benzylated (-)-epicatechin-(4 β →8)-(+)-catechin dimer (**12**) was obtained in 43 % yield. The more reactive catechin electrophile provided 3,4-*trans*-octa-*O*-benzylated (+)-catechin-(4 α →8)-(-)-epicatechin dimer (**14**) in 84 % yield. Interestingly, intramolecular (-)-epicatechin and (-)-epicatechin condensation only provided a messy product. No amount of dimer **16** was detected in the reaction mixture.



Scheme 1



Reagents and conditions:
 a) DCC, DMAP, CH₂Cl₂,
 b) TMSOTf, CH₂Cl₂, 0°C
 c) DIBAL, CH₂Cl₂
 d) Pd(OH)₂-H₂, H₂O/THF/MeOH
 e) Ac₂O, Py, DMAP

Scheme 2

Glutaryl linkers were removed by DIBAL reduction to furnish Bn₈-**1** and Bn₈-**4** in 86% and 77 % yields, respectively. All benzyl groups were finally removed by Pd(OH)₂-catalyzed hydrogenolysis to convert into 3,4-*trans*-(-)-epicatechin-(4β→8)-(+)-catechin dimer, (**1**, procyanidin B1) in 90 % yield and 3,4-*trans*-(+)-catechin-(4α→8)-(-)-epicatechin dimer, (**4**, procyanidin B4) in 66% yield. All the spectral data [NMR, IR, MS] for **1** and **4** were also collected as decaacetates (Ac₁₀-**1**¹² and Ac₁₀-**4**¹³) which were identical with those of authentic samples reported before.

In conclusion, we have synthesized 3,4-*trans*-natural procyanidin dimers, procyanidin-B1, and B4 based on a TMSOTf-catalyzed intramolecular condensation method. Study on the inhibitory activity of the Maillard reaction of the synthesized dimers and their acetates is now underway, and the structure and activity relationship will be reported in due course.

EXPERIMENTAL

All mp are uncorrected. Optical rotation was measured with a HORIBA SEPA-300 polarimeter. IR spectra were measured with a Shimadzu OR-8000 spectrophotometer. ¹H-NMR spectra were measured with a JEOL JNM-LA400 spectrometer, and MS spectra were recorded with a JEOL JMS-AX500 instrument or a JEOL JMS-700V instrument. Synthetic proanthocyanidin dimers (**1** and **4**) were analyzed on a Mightysil® RP-18 GP column (Kanto Chemical Co. Inc, Japan; 250 x 4.6 mm, 5 μm) using the solvents (A) 0.1% CF₃CO₂H in CH₃CN and (B) 0.1% CF₃CO₂H in H₂O. Elution was done with a linear gradient 5 to 100% A in 40 min (flow rate, 0.5 mL/min).

(2R,3R)-5,7,3',4'-tetrabenzoyloxyflavan-3-yl glutarate (9): (2R,3R)-5,7,3',4'-Tetrabenzoyloxyflavan-3-ol (**5**) (710 mg, 1.09 mmol), glutaric anhydride (373 mg, 3.27 mmol) and DMAP (10 mg) in pyridine (30 mL) was stirred at 0°C for 1 h. After stirring for 48 h at rt, the reaction mixture was quenched with water, and extracted with EtOAc. The combined organic phases were washed with brine, and dried (Na₂SO₄). Filtration, concentration and short silica gel column chromatography (hexane/EtOAc, 1/1) gave 797 mg (96 %) of **9** as a white foam: [α]_D²⁵ = -21.5° (c 1.10, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) 7.46-7.21 (20H, m), 7.09 (1H, d, *J* = 1.7 Hz), 6.96 (1H, dd, *J* = 1.7, 8.5 Hz), 6.92 (1H, d, *J* = 8.5 Hz), 6.28 (2H, s), 5.46-5.42 (1H, m), 5.18 (1H, d, *J* = 11.9 Hz), 5.14 (2H, s), 5.13 (1H, d, *J* = 11.9 Hz), 5.01 (4H, s), 5.01-4.97 (1H, m), 3.02 (1H, dd, *J* = 4.4, 17.6 Hz), 2.94 (1H, d, *J* = 17.6 Hz), 2.26-2.05 (4H, m), 1.75-1.64 (2H, m) (The carboxyl proton was not detected.); ¹³C-NMR (100 MHz, CDCl₃) 176.7, 172.1, 158.8, 157.9, 155.4, 149.1, 148.8, 137.2, 136.9, 136.6, 131.0, 128.6, 128.5, 128.45, 128.44, 128.0, 127.9, 127.79, 127.75, 127.6, 127.4, 127.3, 127.2, 123.9, 119.6, 114.7, 113.6, 100.7, 94.7, 93.9, 77.1, 71.5, 71.2, 70.1, 69.9, 67.8, 33.1, 32.5, 25.9, 19.7. IR (neat, cm⁻¹) 3320 (m), 3033 (m), 2930 (m), 1732 (s), 1709 (s), 1620 (s), 1593 (s), 1499 (m), 1454 (m), 1379 (m), 1269 (s), 1145 (s), 1119 (s), 1028 (m), 812 (w), 737 (m), 696 (m); FAB-MS (m/z) 788 (34), 787 ([M+Na]⁺, 62), 767 (14), 766 (41), 765 ([M+H]⁺, 75), 764 (28), 763 (15), 632 (100); FAB-HRMS calcd for C₄₈H₄₅O₉ [M+H]⁺, 765.3064; found, 765.3041.

(2R,3S)-5,7,3',4'-Tetrabenzoyloxyflavan-3-yl glutarate (10): Glutarate formation according to the general procedure using (2R,3S)-5,7,3',4'-tetrabenzoyloxyflavan-3-ol (**6**) (1.00 g, 1.54 mmol), glutaric

anhydride (877 mg, 7.68 mmol) and DMAP (10 mg) in pyridine (20 mL) at 0°C afforded 992 mg (84 %) of **10**: $[\alpha]_D^{24} = +11.9^\circ$ (*c* 1.08, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) 7.42-7.20 (20H, m), 6.97 (1H, d, *J* = 1.2 Hz), 6.89 (1H, d, *J* = 8.3 Hz), 6.86 (1H, dd, *J* = 1.2, 8.3 Hz), 6.26 (1H, d, *J* = 2.2 Hz), 6.23 (1H, d, *J* = 2.2 Hz), 5.32 (1H, ddd, *J* = 5.6, 6.8, 6.8 Hz), 5.13 (2H, s), 5.10 (2H, s), 4.99 (4H, s), 4.95 (1H, d, *J* = 6.8 Hz), 2.90 (1H, dd, *J* = 5.6, 16.6 Hz), 2.70 (1H, dd, *J* = 6.8, 16.6 Hz), 2.29-2.12 (4H, m), 1.80-1.69 (2H, m) (The carboxyl proton was not detected.); ¹³C-NMR (100 MHz, CDCl₃) 178.2, 171.8, 158.9, 157.6, 154.8, 149.0, 148.8, 137.1, 137.0, 136.81, 136.79, 130.8, 128.6, 128.5, 128.44, 128.43, 128.0, 127.9, 127.78, 127.77, 127.5, 127.4, 127.24, 127.23, 120.0, 114.7, 113.4, 101.3, 94.4, 93.8, 78.3, 71.2, 71.1, 70.1, 69.9, 69.1, 33.1, 32.5, 24.1, 19.6; IR (neat, cm⁻¹) 3750 (w), 3065 (w), 3032 (w), 1734 (s), 1700 (s), 1618 (s), 1593 (s), 1508 (s), 1456 (s), 1370 (m), 1261 (m), 1219 (m), 1145 (s), 1093 (w), 1026 (m), 812 (m), 738 (s), 690 (s); FAB-MS (*m/z*) 766 (49), 765 ([M+H]⁺, 92), 632 (100); FAB-HRMS calcd for C₄₈H₄₅O₉ [M+H]⁺, 765.3064; found, 765.3093.

(2R,3R,4R)-5,7,3',4'-Tetrabenzoyloxy-4-ethoxyethoxyflavan-3-yl (2R,3S)-5,7,3',4'-tetrabenzoyloxyflavan-3-yl glutarate (11): A solution of (2R,3R,4S)-5,7,3',4'-tetrabenzoyloxy-4-(2''-ethoxyethoxy)flavan-3-ol (**7**) (75 mg, 0.10 mmol), (2R,3S)-5,7,3',4'-tetrabenzoyloxyflavan-3-yl glutarate (**10**) (153 mg, 0.20 mmol), DCC (41.3 mg, 0.20 mmol) and DMAP (5.00 mg) in CH₂Cl₂ (10 mL) was stirred at 0°C for 1 h. After stirring for 12 h at rt, the reaction mixture was quenched with water, and extracted with CH₂Cl₂. The combined organic phases were washed with brine, and dried (Na₂SO₄). Filtration, concentration and short silica gel column chromatography (hexane/EtOAc, 2/1) gave 126 mg (85 %) of **11** as a colorless amorphous solid: $[\alpha]_D^{24} = +2.57^\circ$ (*c* 0.92, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) 7.48-7.19 (40H, m), 7.11 (1H, d, *J* = 1.7 Hz), 6.99 (1H, dd, *J* = 1.7, 8.3 Hz), 6.92 (1H, d, *J* = 1.7 Hz), 6.91 (1H, d, *J* = 8.3 Hz), 6.79 (1H, d, *J* = 8.3 Hz), 6.74 (1H, dd, *J* = 1.7, 8.3 Hz), 6.24-6.23 (3H, m), 6.21 (1H, d, *J* = 2.2 Hz), 5.27 (1H, s), 5.27-5.22 (1H, m), 5.22 (1H, d, *J* = 2.4 Hz), 5.14 (1H, s), 5.13 (1H, s), 5.10 (2H, s), 5.07 (2H, s), 5.06 (2H, s), 4.96 (4H, s), 4.95 (4H, s), 4.87 (1H, d, *J* = 6.6 Hz), 4.47 (1H, d, *J* = 2.4 Hz), 3.96-3.92 (1H, m), 3.83-3.79 (1H, m), 3.54-3.52 (2H, m), 3.45 (2H, q, *J* = 7.1 Hz), 2.82 (1H, dd, *J* = 5.1, 16.5 Hz), 2.65 (1H, dd, *J* = 6.4, 16.5 Hz), 2.01-1.93 (4H, m), 1.58-1.53 (2H, m), 1.17 (3H, t, *J* = 7.1 Hz); ¹³C-NMR (100 MHz, CDCl₃) 171.9, 171.8, 160.5, 159.4, 158.8, 157.6, 156.1, 154.8, 148.83, 148.76, 137.19, 137.17, 137.1, 137.0, 136.80, 136.76, 136.6, 130.8, 130.6, 128.5-127.2 (Cx28), 119.9, 119.8, 114.8, 114.6, 113.8, 113.2, 101.9, 101.2, 94.3, 94.0, 93.7, 78.0, 77.2, 73.6, 71.4, 71.1, 71.0, 70.2, 70.03, 69.96, 69.85, 69.6, 69.3, 69.2, 68.8, 68.2, 66.3, 32.8, 32.6, 23.8, 19.6, 15.2. IR (neat, cm⁻¹) 3065 (m), 3032 (m), 2932 (m), 2872 (m), 1736 (s), 1618 (s), 1593 (s), 1514 (s), 1454 (s), 1377 (s), 1265 (s), 1147 (s), 1028 (s), 814 (m), 737 (s), 698 (s); FAB-MS (*m/z*) 1486 ([M+H]⁺, 2), 1485 (5), 1484 (7), 631 (100); FAB-HRMS calcd for C₉₅H₈₉O₁₆ [M+H]⁺, 1485.6151; found, 1485.6167.

(2R,3S,4S)-5,7,3',4'-Tetrabenzoyloxy-4-ethoxyethoxyflavan-3-yl (2R,3R)-5,7,3',4'-tetrabenzoyloxyflavan-3-yl glutarate (13): Ester formation according to the general procedure using (2R,3S,4S)-5,7,3',4'-tetrabenzoyloxy-4-(2''-ethoxyethoxy)flavan-3-ol (**8**) (136 mg, 47 μmol), (2R,3R)-5,7,3',4'-tetrabenzoyloxyflavan-3-yl glutarate (**9**) (178 mg, 0.23 μmol), DCC (47 mg, 0.17 μmol) and DMAP (5.00 mg) in CH₂Cl₂

(10 mL) afforded 119 mg (44 %) of **13** as a colorless amorphous solid: $[\alpha]_D^{24} = +21.9^\circ$ (*c* 0.18, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) 7.42-7.24 (40H, m), 7.19-6.79 (6H, m), 6.25 (2H, s), 6.23 (1H, d, *J* = 1.9 Hz), 6.12 (1H, d, *J* = 1.9 Hz), 5.43-5.36 (1H, m), 5.21-5.19 (2H, m), 5.11-4.93 (17H, m), 4.81 (1H, d, *J* = 2.5 Hz), 3.75-3.67 (2H, m), 3.44-3.41 (2H, m), 3.38-3.31 (2H, m), 2.99 (1H, dd, *J* = 4.4, 17.8 Hz), 2.91 (1H, dd, *J* = 2.0, 17.8 Hz), 2.03-1.83 (4H, m), 1.48-1.39 (2H, m), 1.08 (3H, t, *J* = 7.1 Hz); ¹³C-NMR (100 MHz, CDCl₃) 171.9, 171.4, 160.9, 158.8, 158.5, 157.9, 155.8, 155.4, 149.3, 148.83, 148.80, 137.3 (x2), 137.2, 136.9, 136.8, 136.6, 136.5, 131.0, 130.3, 128.6-127.2 (Cx26), 121.4, 119.7, 114.7, 114.42, 114.35, 113.63, 103.59, 100.8, 94.7, 94.2, 93.9, 93.8, 77.2, 74.3, 72.5, 71.4, 71.22, 71.17, 71.0, 70.8, 70.4, 70.10, 70.05, 69.9, 69.8, 68.4, 67.7, 66.3, 32.9, 32.7, 26.0, 19.5, 15.2. IR (neat, cm⁻¹) 3065 (m), 3032 (m), 2932 (m), 2872 (m), 1736 (s), 1616 (s), 1593 (s), 1514 (s), 1499 (s), 1454 (s), 1377 (s), 1267 (s), 1219 (s), 1188 (s), 1147 (s), 1116 (s), 1028 (s), 814 (m), 736 (s), 698 (s); FAB-MS (*m/z*) 1486 ([M+H]⁺, 3), 1485 (5), 1484 (6), 1483 (5), 633 (87), 632 (100), 631 (92); FAB-HRMS calcd for C₉₅H₈₉O₁₆ [M+H]⁺, 1485.6151; found, 1485.6123.

(2R,3R,4S)-5,7,3',4'-Tetrabenzoyloxy-4-ethoxyethoxyflavan-3-yl (2R,3R)-5,7,3',4'-tetrabenzoyloxyflavan-3-yl glutarate (15): Ester formation according to the general procedure using (2R,3R,4S)-5,7,3',4'-tetrabenzoyloxy-4-(2''-ethoxyethoxy)flavan-3-ol (**7**), (121 mg, 0.16 mmol) (2R,3R)-5,7,3',4'-tetrabenzoyloxyflavan-3-yl glutarate (**9**) (125 mg, 0.16 mmol), DCC (33.0 mg, 0.16 mmol) and DMAP (5.00 mg) in CH₂Cl₂ (10 mL) afforded 156 mg (53 %) of **15** as a white foam: $[\alpha]_D^{27} = -7.00^\circ$ (*c* 0.70, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) 7.43-7.23 (40H, m), 7.06 (1H, d, *J* = 1.7 Hz), 7.01 (1H, dd, *J* = 1.7, 8.3 Hz), 7.00 (1H, d, *J* = 1.7 Hz), 6.94 (1H, dd, *J* = 1.7, 8.3 Hz), 6.84 (1H, d, *J* = 8.3 Hz), 6.80 (1H, d, *J* = 8.3 Hz), 6.26-6.23 (4H, m), 5.39 (1H, br s), 5.25 (1H, s), 5.20 (1H, br s), 5.14-5.07 (2H, m), 5.14 (2H, s), 5.03 (4H, s), 4.98-4.95 (1H, m), 4.96-4.94 (1H, m), 4.95 (6H, s), 4.92 (1H, d, *J* = 12.0 Hz), 4.45 (1H, d, *J* = 2.2 Hz), 3.91 (1H, dt, *J* = 4.9, 11.0 Hz), 3.80 (1H, dt, *J* = 4.9, 11.0 Hz), 3.51 (2H, t, *J* = 4.9 Hz), 3.44 (2H, q, *J* = 6.8 Hz), 2.98 (1H, dd, *J* = 4.4, 17.8 Hz), 2.89 (1H, d, *J* = 17.8 Hz), 1.97-1.78 (4H, m), 1.51-1.47 (2H, m), 1.58 (3H, t, *J* = 6.8 Hz); ¹³C-NMR (100 MHz, CDCl₃) 171.93, 171.87, 160.5, 159.4, 158.8, 157.9, 156.2, 155.4, 148.74, 148.67, 137.26, 137.23, 137.1, 136.84, 136.78, 136.67, 136.66, 130.8, 130.5, 128.6-127.16 (Cx27), 119.9, 119.6, 114.7, 114.6, 113.8, 113.5, 102.0, 100.7, 94.8, 94.4, 94.0, 93.9, 73.6, 71.43, 71.38, 70.99, 70.96, 70.2, 70.1, 70.0, 69.9, 69.6, 69.3, 69.2, 68.2, 67.7, 66.4, 60.4, 32.73, 32.70, 25.9, 19.5, 15.2; IR (neat, cm⁻¹) 3032 (m), 2930 (m), 2870 (m), 1736 (s), 1618 (s), 1593 (s), 1510 (s), 1454 (s), 1377 (s), 1267 (s), 1149 (s), 1028 (s), 814 (m), 736 (s), 696 (s); FAB-MS (*m/z*) 1486 ([M+H]⁺, 2), 1485 (3), 1484 (4), 1483 (4), 1482 (3), 633 (85), 632 (100), 631 (87); FAB-HRMS calcd for C₉₅H₈₉O₁₆ [M+H]⁺, 1485.6151; found, 1485.6156.

[4,8]-2,3-cis-3,4-trans:2,3-trans-Octa-O-benzyl-3,3'-O-glutaryl(-)-epicatechin-(+)-catechin (12): To a solution of **11** (219 mg, 0.15 mmol) in CH₂Cl₂ (20 mL) was added dropwise TMSOTf (0.29 mL, 0.15 mmol, 0.5 M solution in CH₂Cl₂) at 0°C. After stirring for 5 min, the pale yellow reaction mixture was quenched with sat. sodium hydrogen carbonate. The aq. solution was extracted with CHCl₃ and the organic phase was washed with water and brine, and dried (Na₂SO₄). Filtration, concentration and

preparative silica gel TLC purification (hexane/EtOAc, 2/1) afforded 90 mg (43 %) of a mixture of **12** as a colorless oil: $[\alpha]_D^{27} = +64.7^\circ$ (*c* 0.22, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) 7.39-7.17 (33H, m), 7.08-6.98 (5H, m), 7.02 (1H, d, *J* = 1.7 Hz), 6.86 (1H, dd, *J* = 1.7, 8.3 Hz), 6.81 (1H, d, *J* = 1.7 Hz), 6.76 (1H, d, *J* = 8.3 Hz), 6.75-6.73 (2H, m), 6.43 (1H, dd, *J* = 1.7, 8.3 Hz), 6.25 (1H, s), 6.21 (1H, d, *J* = 8.3 Hz), 6.05 (1H, d, *J* = 2.2 Hz), 6.03 (1H, d, *J* = 2.2 Hz), 5.84 (1H, dd, *J* = 5.6, 10.0 Hz), 5.38 (1H, br s), 5.35 (1H, d, *J* = 5.6 Hz), 5.26-5.23 (1H, m), 5.07 (2H, s), 5.03 (1H, d, *J* = 11.8 Hz), 4.98 (2H, s), 4.97 (1H, d, *J* = 11.8 Hz), 4.95 (1H, d, *J* = 12.4 Hz), 4.910 (1H, d, *J* = 12.4 Hz), 4.908 (2H, s), 4.88 (1H, d, *J* = 11.5 Hz), 4.87 (1H, d, *J* = 13.2 Hz), 4.82 (1H, d, *J* = 11.5 Hz), 4.77 (1H, d, *J* = 10.0 Hz), 4.76 (1H, d, *J* = 11.7 Hz), 4.69 (1H, d, *J* = 13.2 Hz), 4.62 (1H, d, *J* = 11.7 Hz), 2.89 (1H, dt, *J* = 2.5, 16.8 Hz) 2.49-2.42 (1H, m), 2.32-2.21 (2H, m) 2.22 (1H, dd, *J* = 2.9, 16.8 Hz), 2.16-2.07 (1H, m), 1.86-1.71 (2H, m); ¹³C-NMR (100 MHz, CDCl₃) 172.04, 171.98, 158.2, 157.4, 156.5, 155.5, 154.5, 152.4, 148.5, 148.4, 148.3, 148.2, 137.3, 137.19, 137.17, 137.04, 136.98, 131.9, 130.8, 128.6-126.8 (Cx29), 120.6, 118.4, 114.6, 114.5, 114.3, 114.5, 110.4, 107.7, 100.7, 95.4, 94.2, 91.0, 77.2, 74.9, 72.3, 71.4, 71.0, 70.9, 70.2, 70.1, 69.93, 69.88, 69.3, 33.6, 32.8, 30.3, 19.6; IR (neat, cm⁻¹) 3065 (m), 3032 (m), 2930 (m), 2870 (m), 1732 (s), 1606 (s), 1508 (s), 1456 (s), 1417 (s), 1379 (s), 1265 (s), 1148 (s), 1138 (s), 1028 (s), 910 (w), 848 (w), 810 (m), 736 (s), 698 (s); FAB-MS (*m/z*) 1398 (34), 1397 (68), 1396 ([M+H]⁺, 100), 1395 (79), 1394 (27); FAB-HRMS calcd for C₉₁H₇₉O₁₄ [M+H]⁺, 1396.5504; found, 1395.5490.

[4,8]-2,3-trans-3,4-trans:2,3-cis-Octa-O-benzyl-3,3'-O-glutaryl-(+)-catechin-(-)-epicatechin (14): To a solution of **13** (80 mg, 0.054 mmol) in CH₂Cl₂ (40 mL) was added dropwise TMSOTf (0.11 mL, 0.054 mmol, 0.5 M solution in CH₂Cl₂) at 0°C. After stirring for 5 min, the pale yellow reaction mixture was quenched with sat. sodium hydrogen carbonate. The aq. solution was extracted with CHCl₃ and the organic phase was washed with water and brine, and dried (Na₂SO₄). Filtration, concentration and preparative silica gel TLC purification (hexane/EtOAc, 2/1) afforded 63 mg (84 %) of **14** as a colorless oil: $[\alpha]_D^{24} = -64.1^\circ$ (*c* 1.26, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) 7.45-7.09 (40H, m), 6.94 (1H, d, *J* = 8.3 Hz), 6.94 (1H, d, *J* = 1.7Hz), 6.84-6.77 (2H, m), 6.74 (1H, d, *J* = 8.3Hz), 6.69 (1H, dd, *J* = 1.7, 8.3 Hz), 6.23 (1H, s), 6.23 (1H, d, *J* = 2.2 Hz), 6.21 (1H, d, *J* = 2.2 Hz), 5.79 (1H, dd, *J* = 9.5, 10.3 Hz), 5.34 (1H, br s), 5.21 (1H, d, *J* = 11.9 Hz), 5.15-4.87 (12H, m), 4.96-4.92 (1H, m), 4.84 (1H, d, *J* = 11.9 Hz), 4.73 (1H, d, *J* = 10.3 Hz), 4.65 (1H, d, *J* = 10.2 Hz), 4.54 (1H, d, *J* = 10.2 Hz), 4.05 (1H, br s), 2.91 (1H, d, *J* = 16.9 Hz), 2.61 (1H, dd, *J* = 3.1, 16.9 Hz), 2.41-2.35 (1H, m), 2.23-2.16 (1H, m), 1.89-1.79 (2H, m), 1.44-1.31 (2H, m); ¹³C-NMR (100 MHz, CDCl₃) 171.8, 171.3, 158.2, 157.7, 156.3, 156.1, 156.0, 152.7, 149.1, 149.0, 148.8, 148.0, 137.32, 137.30, 137.28, 137.22, 137.18, 137.09 (x2), 136.5, 131.9, 130.6, 128.60-127.09 (Cx25), 121.5, 118.5, 115.0, 114.6, 113.5, 112.4, 110.6, 108.2, 100.0, 94.9, 94.2, 91.1, 77.2, 76.0, 72.9, 71.4, 71.2, 71.0 (x2), 70.2, 70.1, 70.0 (x2), 68.0, 35.9, 32.9, 32.4, 26.8, 18.3; IR (neat, cm⁻¹) 3065 (w), 3032 (w), 2932 (w), 2870 (w), 1732 (s), 1609 (s), 1514 (m), 1454 (m), 1383 (s), 1265 (s), 1217 (s), 1142 (s), 1118 (s), 1028 (m), 737 (s), 698 (s); FAB-MS (*m/z*) 1397 (30), 1396 ([M+H]⁺, 100); FAB-HRMS calcd for C₉₁H₇₉O₁₄ [M+H]⁺, 1395.5470; found: 1395.5470.

[4,8]-2,3-cis-3,4-trans:2,3-trans-Octa-O-benzyl-(-)-epicatechin-(+)-catechin (Bn₈-1): To a solution

of **12** (48 mg, 0.034 mmol) in CH₂Cl₂ (20 mL) was added 1M solution of DIBAL (0.34 mL, 0.34 mmol) at -78°C. After 30 min at -78°C, the reaction mixture was warmed to rt and then the reaction was quenched with sat. aq. NH₄Cl solution. The reaction mixture was diluted with CHCl₃, and extracted with CHCl₃. The combined organic layers were washed with brine, dried (Na₂SO₄), filtered, and evaporated *in vacuo*. Purification of the residue was accomplished by silica gel preparative TLC (hexane/EtOAc, 2/1) to afford a 38 mg (86%) of Bn₈-**1** as a colorless amorphous solid: $[\alpha]_D^{30} = +53.4^\circ$ (*c* 1.20, CHCl₃); ¹H-NMR (400 MHz, CDCl₃, 0.74: 0.26 mixture of rotational isomers) major isomer: 7.46-6.73 (31.08H, m), 7.00 (0.74H, dd, *J* = 1.7, 8.3 Hz), 6.79 (0.74H, d, *J* = 8.3 Hz), 6.72 (0.74H, d, *J* = 1.7 Hz), 6.50 (0.74H, dd, *J* = 1.7, 8.3 Hz), 6.34 (0.74H, s), 6.02 (0.74H, d, *J* = 2.2 Hz), 5.54 (0.74H, d, *J* = 2.2 Hz), 5.40 (0.74H, br s), 5.12-4.78 (10.36H, m), 4.83 (0.74H, br s), 4.62 (0.74H, d, *J* = 11.2 Hz), 4.52 (0.74H, d, *J* = 11.2 Hz), 4.03 (0.74H, br s), 3.74 (0.74H, ddd, *J* = 6.3, 9.0, 9.3 Hz), 3.65 (0.74H, d, *J* = 9.0 Hz), 3.24 (0.74H, dd, *J* = 6.3, 16.8 Hz), 2.58 (0.74H, dd, *J* = 9.3, 16.8 Hz), 1.60 (0.74H, br s, OH), 1.41 (0.74H, br s, OH); minor isomer: 7.46-6.73 (11.96H, m), 6.21 (0.26H, d, *J* = 2.2 Hz), 6.17 (0.26H, s), 6.06 (0.26H, d, *J* = 2.2 Hz), 5.26 (0.26H, br s), 5.12-4.82 (3.64H, m), 4.68 (0.26H, br s), 4.62 (0.26H, d, *J* = 11.9 Hz), 4.62 (0.26H, br s), 4.40 (0.26H, d, *J* = 11.9 Hz), 3.87 (0.26H, br s), 3.65-3.62 (0.26H, m), 3.17 (0.26H, dd, *J* = 5.1, 16.6 Hz), 2.68 (0.26H, dd, *J* = 8.5, 16.6 Hz), 1.54 (0.26H, br s, OH), 1.68-1.21 (0.26H, m, OH); ¹³C-NMR (100 MHz, CDCl₃, 0.74 : 0.26 mixture of rotational isomers) major isomer: 158.1, 157.0, 155.9, 155.8, 155.1, 154.4, 149.1, 148.9, 148.7, 148.6, 137.3, 137.2 (x2), 137.1, 137.04, 136.98, 132.6, 130.3, 128.6-126.7 (Cx26), 120.5, 119.6, 115.0, 113.9, 113.6, 112.1, 111.2, 104.3, 104.2, 93.5, 93.0, 91.5, 81.6, 75.4, 72.3, 71.4, 71.3, 71.2, 70.5, 70.2, 69.9, 69.5, 69.1, 68.5, 35.6, 29.1; minor isomer: 158.3, 157.7, 156.8, 155.9, 155.8, 155.6, 149.0, 148.9, 148.8, 148.5, 137.7, 137.6, 137.39, 137.38, 137.28, 137.0, 132.5, 131.0, 128.5-126.7 (Cx26), 120.1, 119.9, 114.5, 114.0, 113.0, 112.7, 109.3, 104.6, 102.7, 94.4, 93.2, 92.6, 81.3, 75.5, 71.7, 71.4, 71.2, 71.1, 71.0, 70.7, 69.8, 69.4, 69.2, 68.2, 35.7, 27.7; IR (neat, cm⁻¹) 3550 (m), 3450 (m), 3063 (m), 3032 (m), 2928 (m), 2872 (m), 1605 (s), 1598 (s), 1514 (s), 1454 (s), 1379 (s), 1329 (m), 1265 (s), 1215 (s), 1118 (s), 1072 (s), 1028 (s), 910 (w), 852 (w), 808 (m), 735 (s), 696 (s); FAB-MS (*m/z*) 1324 (12), 1323 (25), 1322 ([M+Na]⁺, 27), 1302 (33), 1301 (74), 1300 ([M+H]⁺, 100), 1299 (67); FAB-HRMS calcd for C₈₆H₇₅O₁₂ [M+H]⁺, 1299.5259; found: 1299.5254.

[4,8]-2,3-trans-3,4-trans:2,3-cis-Octa-O-benzyl-(+)-catechin-(-)-epicatechin (Bn₈-4): To a solution of **14** (21 mg, 0.015 mmol) in CH₂Cl₂ (20 mL) was added 1M solution of DIBAL (0.15 mL, 0.15 mmol) at -78°C. After 30 min at -78°C, the reaction mixture was warmed to rt and then the reaction was quenched with sat. aq. NH₄Cl solution. The reaction mixture was diluted with CHCl₃, and extracted with CHCl₃. The combined organic layers were washed with brine, dried (Na₂SO₄), filtered, and evaporated *in vacuo*. Purification of the residue was accomplished by silica gel preparative TLC (hexane/EtOAc, 2/1) to afford a 15 mg (77 %) of Bn₈-**4** as a colorless amorphous solid: $[\alpha]_D^{30} = -84.7^\circ$ (*c* 0.72, CHCl₃); ¹H-NMR (400 MHz, CDCl₃, 0.67 : 0.33 mixture of rotational isomers) major isomer: 7.45-6.71 (29.48H, m), 6.91 (0.67H, d, *J* = 8.3 Hz), 6.78 (0.67H, d, *J* = 8.3 Hz), 6.22 (0.67H, s), 6.19 (0.67H, d, *J* = 2.2 Hz), 6.12 (0.67H, d, *J* = 2.2 Hz), 5.20-4.46 (10.72H, m), 4.79 (0.67H, d, *J* = 9.0 Hz), 4.50 (0.67H, d, *J* = 9.0 Hz), 4.29 (0.67H, t, *J* = 9.0 Hz), 3.90-3.83 (0.67H, m), 3.78-3.72 (0.67H, m), 2.86 (0.67H, d, *J* = 17.1 Hz),

2.58 (0.67H, dd, $J = 4.4$, 17.1 Hz), 1.67 (0.67H, br s, OH), 1.80-1.20 (0.67H, m, OH); minor isomer: 7.45-6.71 (14.85H, m), 6.47 (0.33H, dd, $J = 1.7$, 8.3 Hz), 6.17 (0.33H, d, $J = 2.2$ Hz), 6.10 (0.33H, d, $J = 2.2$ Hz), 5.99 (0.33H, s), 5.20-4.12 (6.27H, m), 4.49-4.47 (0.33H, m), 4.09-4.07 (0.33H, m), 3.02 (0.33H, d, $J = 17.3$ Hz), 2.89 (0.33H, dd, $J = 4.4$, 17.3 Hz), 1.54 (0.33H, br s, OH), 1.80-1.20 (0.33H, m, OH); ^{13}C -NMR (100 MHz, CDCl_3 , 0.67 : 0.33 mixture of rotational isomers) major isomer: 157.9, 157.8, 156.8, 156.1, 155.4, 153.6, 149.1, 149.0, 148.9, 148.2, 137.4, 137.3, 137.21, 137.17, 137.07, 137.03, 136.6, 132.1, 131.7, 128.5-127.1 (Cx25), 121.2, 118.7, 114.9, 114.4, 113.8, 113.5, 111.6, 108.2, 100.8, 94.8, 94.1, 91.4, 82.1, 77.2, 73.1, 71.4, 71.2, 71.0, 70.9, 70.2, 70.1, 69.93, 69.90, 65.9, 37.0, 28.2; minor isomer: 158.1, 158.0, 156.9, 156.5, 156.0, 152.8, 150.0, 149.1, 148.9, 148.7, 137.6, 137.4, 137.2, 137.1, 137.0, 136.9, 136.8, 131.8, 131.0, 128.56-127.05 (Cx25), 120.9, 119.8, 114.9, 114.4, 113.8, 113.5, 111.6, 108.2, 102.1, 95.3, 94.4, 92.0, 81.8, 78.1, 72.4, 71.7, 71.1, 71.0, 70.9, 70.3, 69.93, 69.86, 69.6, 66.3, 37.3, 28.8; IR (neat, cm^{-1}) 3450 (m), 3065 (w), 3032 (w), 2870 (w), 1736 (m), 1608 (s), 1512 (s), 1454 (s), 1375 (s), 1265 (s), 1136 (s), 1109 (s), 1045 (s), 1028 (s), 910 (s), 735 (s), 698 (s); FAB-MS (m/z) 1324 (23), 1323 (46), 1322 ($[\text{M}+\text{Na}]^+$, 48), 1302 (32), 1301 (64), 1300 ($[\text{M}+\text{H}]^+$, 100), 1299 (71); FAB-HRMS calcd for $\text{C}_{86}\text{H}_{75}\text{O}_{12}$ $[\text{M}+\text{H}]^+$, 1299.5259; found: 1299.5289.

Procyanidin B1 (1): A solution of **14** (35 mg, 0.027 mmol) in THF/MeOH/ H_2O , 20/1/1 (10 mL) was hydrogenated over 20% Pd(OH) $_2$ /C (14 mg) for 12 h in a current of H_2 at rt. Filtration and concentration afforded a pale brown oil, which was purified by Sephadex[®] LH-20 column chromatography (EtOH) to give 14 mg of pure procyanidin-B1 (**1**) (90 %) as a pale brown powder: HPLC ^1R -1, 17.2 min; $[\alpha]_{\text{D}}^{24} = +19.6^\circ$ (c 0.28, EtOH) [lit.,³ $[\alpha]_{578} = +31^\circ$ (c 0.8, EtOH)]; ^1H -NMR (400 MHz, CD_3OD , all the NMR peaks were broadened and discrimination of the rotational isomers were impossible) 6.92-6.88 (1H, m), 6.88-6.70 (1H, m), 6.70-6.65 (4H, m), 6.05-5.90 (3H, m), 5.12-5.08 (1H, m), 4.85-4.80 (1H, m), 4.63-4.57 (1H, m), 4.15-4.00 (1H, m), 3.92 (1H, m), 2.85-2.65 (1H, m), 2.65-2.55 (1H, m); FAB-MS (m/z) 602 (2), 601 ($[\text{M}+\text{Na}]^+$, 4), 176 (100); FAB-HRMS calcd for $\text{C}_{30}\text{H}_{26}\text{O}_{12}\text{Na}$ $[\text{M}+\text{Na}]^+$, 601.1322; found, 601.1309.

Decaacetylprocyanidin-B1 (Ac $_{10}$ -1): Acetylation using **1** (15 mg, 0.026 mmol) with Ac_2O (49 μL , 0.52 mmol) and 4-(dimethylamino)pyridine (1 mg) in pyridine (5 mL) afforded 15 mg (60 %) of Ac $_{10}$ -1 as a colorless amorphous solid: $[\alpha]_{\text{D}}^{21} = +76.3^\circ$ (c 0.16, CHCl_3) [lit.,³ $[\alpha]_{578} = +110^\circ$ (c 1.21, CHCl_3)]; ^1H -NMR (400 MHz, CDCl_3 , 0.86 : 0.14 mixture of rotational isomers) major isomer: 7.29 (0.86H, d, $J = 1.7$ Hz), 7.24 (0.86H, dd, $J = 1.7$, 8.3 Hz), 7.16 (0.86H, d, $J = 8.3$ Hz), 7.09 (0.86H, d, $J = 8.3$ Hz), 6.94 (0.86H, dd, $J = 1.7$, 8.3 Hz), 6.88 (0.86H, d, $J = 1.7$ Hz), 6.68 (0.86H, s), 6.29 (0.86H, d, $J = 2.2$ Hz), 5.99 (0.86H, d, $J = 2.2$ Hz), 5.45 (0.86H, br s), 5.18-5.13 (0.86H, m), 5.05 (0.86H, ddd, $J = 6.6$, 9.3, 9.5 Hz), 4.42 (0.86H, d, $J = 1.7$ Hz), 4.33 (0.86H, d, $J = 9.5$ Hz), 3.21 (0.86H, dd, $J = 6.6$, 16.8 Hz), 2.56 (0.86H, dd, $J = 9.3$, 16.8 Hz), 2.35 (2.58H, s), 2.30 (2.58H, s), 2.28 (7.74H, s), 2.25 (2.58H, s), 2.15 (2.58H, s), 1.89 (2.58H, s), 1.86 (2.58H, s), 1.83 (2.58H, s); minor isomer: 7.29-7.14 (0.56H, m), 7.17 (0.14H, d, $J = 8.5$ Hz), 7.13 (0.14H, d, $J = 8.5$ Hz), 6.74 (0.14H, d, $J = 2.2$ Hz), 6.70 (0.14H, d, $J = 2.2$ Hz), 6.60 (0.14H, s), 5.33 (0.14H, br s), 5.29 (0.14H, br s), 5.21-5.19 (0.28H, m), 4.55 (0.14H, br s), 3.10-3.04 (0.14H, m),

2.78-2.69 (0.14H, m), 2.33-2.25 (1.26H, m), 2.26 (1.26H, s), 1.92 (0.42H, s), 1.95 (0.42H, s), 1.72 (0.42H, s), 1.63 (0.42H, s); ¹³C-NMR (100 MHz, CDCl₃, 0.86 : 0.14 mixture of rotational isomers) major isomer: 169.8 (x2), 169.7, 169.0, 168.9, 168.3, 168.2, 168.1, 167.83, 167.80, 155.5, 154.0, 149.3, 148.7, 147.94, 147.93, 142.3, 141.9, 141.7, 136.4, 134.6, 125.4, 124.5, 123.2, 123.1, 122.3, 122.1, 117.0, 113.6, 111.4, 110.7, 108.6, 107.2, 78.3, 77.2, 73.5, 70.9, 68.4, 34.0, 27.1, 21.2, 21.1, 20.8, 20.7, 20.66 (x3), 20.63, 20.41, 10.0; minor isomer couldn't been identified; IR (neat, cm⁻¹) 2936 (w), 2361 (w), 1770 (s), 1747 (s), 1622 (m), 1597 (m), 1508 (m), 1487 (m), 1425 (m), 1371 (s), 1209 (s), 1126 (m), 1111 (m), 1043 (m), 900 (m), 736 (m); FAB-MS (m/z) 1021 ([M+Na]⁺, 100), 999 ([M+H]⁺, 15); FAB-HRMS calcd for C₅₀H₄₆O₂₂Na [M+Na]⁺, 1021.2378; found, 1021.2358.

Procyanidin B4 (4): Hydrogenation according to the above procedure using 76 mg of **20** (0.058 mmol) in THF/MeOH/H₂O, 20/1/1 (1.0 mL) afforded 22 mg (66 %) of the procyanidin-B4 (**4**) as a colorless amorphous solid: HPLC ^tR-**4**, 19.4 min; [α]_D²⁵ = -222° (c 0.36, EtOH) [lit.,³ [α]₅₇₈ = -193.5° (c 1.0, EtOH)]; ¹H-NMR (400 MHz, CD₃OD, 0.63 : 0.37 mixture of rotational isomers) major isomer: 6.99 (0.63H, d, *J* = 1.9 Hz, B2 or E2), 6.89 (0.63H, d, *J* = 1.9 Hz, B2 or E2), 6.77 (1.26H, dd, *J* = 1.9, 8.1 Hz, B6 and E6), 6.89 (0.63H, d, *J* = 8.1 Hz, B5 or E5), 6.68 (0.63H, d, *J* = 8.1 Hz, B5 or E5), 5.85 (0.63H, s, D6), 5.74 (0.63H, d, *J* = 2.3 Hz, A6 or A8), 5.69 (0.63H, d, *J* = 2.3 Hz, A6 or A8), 4.83 (0.63H, br s, F2), 4.53 (0.63H, d, *J* = 8.0 Hz, C2 or C4), 4.48 (0.63H, dd, *J* = 8.0, 9.5 Hz, C3), 4.32 (0.63H, d, *J* = 9.5 Hz, C2 or C4), 4.18-4.16 (0.63H, m, F3), 2.83 (0.63H, dd, *J* = 4.3, 16.8 Hz, F4), 2.72 (0.63H, dd, *J* = 1.5, 16.8 Hz, F4); minor isomer: 6.62 (0.37H, d, *J* = 8.0 Hz, B5 or E5), 6.59 (0.37H, d, *J* = 1.9 Hz, B2 or E2), 5.58 (0.37H, d, *J* = 1.9 Hz, B2 or E2), 6.51 (0.37H, d, *J* = 8.0 Hz, B5 or E5), 6.35 (0.37H, dd, *J* = 1.9, 8.0 Hz, B6 or E6), 6.31 (0.37H, dd, *J* = 1.9, 8.0 Hz, B6 or E6), 6.00 (0.37H, s, D6), 5.84 (0.37H, d, *J* = 2.5 Hz, A6 or A8), 5.79 (0.37H, d, *J* = 2.5 Hz, A6 or A8), 4.71 (0.37H, br s, F2), 4.36 (0.37H, dd, *J* = 2.2, 6.1 Hz, C3), 4.22 (0.37H, d, *J* = 6.1 Hz, C2 or C4), 4.21 (0.37H, d, *J* = 2.2 Hz, C2 or C4), 3.95-3.85 (0.37H, m, F3), 2.85-2.70 (0.37H, m, F4), 2.60 (0.37H, dd, *J* = 2.2, 17.3 Hz, F4); ¹³C-NMR (100 MHz, CD₃OD, 0.63 : 0.37 mixture of rotational isomers) major isomer: 158.7, 157.5, 157.3, 156.4, 155.9, 155.4, 146.5, 146.1, 145.63, 145.60, 132.6, 132.3, 121.2, 119.1, 116.3, 116.0 (x2), 115.2, 107.4, 107.2, 99.4, 97.6, 97.5, 96.1, 83.8, 80.0, 73.8, 67.4, 38.9, 30.1; minor isomer: 158.5, 157.3, 157.2, 156.3, 155.8, 155.4, 146.0, 145.9, 145.58, 145.55, 132.5, 131.7, 120.5, 120.3, 116.4, 116.0, 115.9, 114.8, 108.7, 108.3, 101.5, 97.7, 97.1, 96.3, 84.0, 79.9, 73.8, 67.8, 38.7, 29.3; FAB-MS (m/z) 602 (1), 601 ([M+Na]⁺, 4), 579 ([M+H]⁺, 3), 176 (100); FAB-HRMS calcd for C₃₀H₂₆O₁₂Na [M+Na]⁺, 601.1322; found, 601.1307.

Decaacetylprocyanidin-B4 (Ac₁₀-4): Acetylation using **4** (10 mg, 0.017 mmol), Ac₂O (32 μL, 0.34 mmol) and 4-(dimethylamino)pyridine (1 mg) in pyridine (2 mL) afforded 17 mg (100 %) of Ac₁₀-**4** as a colorless amorphous solid: [α]_D²⁵ = -120.8° (c 0.24, CHCl₃) [lit.,³ [α]₅₇₈ = -130.8° (c 2.0, CHCl₃)]; ¹H-NMR (400 MHz, CDCl₃, 0.78 : 0.22 mixture of rotational isomers) major isomer: 7.15 (0.78H, d, *J* = 8.3 Hz), 7.10 (0.78H, d, *J* = 8.3 Hz), 6.97 (0.78H, d, *J* = 2.2 Hz), 6.90 (0.78H, dd, *J* = 2.2, 8.3 Hz), 6.90 (0.78H, d, *J* = 2.2 Hz), 6.87 (0.78H, dd, *J* = 2.2, 8.3 Hz), 6.63 (0.78H, s), 6.58 (0.78H, d, *J* = 2.5 Hz), 6.53 (0.78H, d, *J* = 2.5 Hz), 5.72 (0.78H, t, *J* = 9.8 Hz), 5.23-5.21 (0.78H, m), 5.01 (0.78H, br s), 4.82 (0.78H, d, *J* = 9.8 Hz), 4.53 (0.78H, d, *J* = 9.8 Hz), 3.02 (0.78H, dd, *J* = 4.9, 17.8 Hz), 2.76 (0.78H, d, *J* = 17.8

Hz), 2.35 (2.34H, s), 2.30 (2.34H, s), 2.29 (2.34H, s), 2.28 (2.34H, s), 2.26 (2.34H, s), 2.25 (4.68H, s), 1.93 (2.34H, s), 1.86 (2.34H, s), 1.64 (2.34H, s); minor isomer: 7.46 (0.22H, d, $J = 1.9$ Hz), 7.40 (0.22H, dd, $J = 1.9, 8.5$ Hz), 7.35 (0.22H, dd, $J = 1.9, 8.5$ Hz), 7.29 (0.22H, d, $J = 1.9$ Hz), 7.26 (0.22H, d, $J = 8.5$ Hz), 7.24 (0.22H, d, $J = 8.5$ Hz), 6.73 (0.22H, s), 6.68 (0.22H, d, $J = 2.2$ Hz), 6.56 (0.22H, d, $J = 2.2$ Hz), 5.65 (0.22H, t, $J = 9.8$ Hz), 5.56-5.52 (0.22H, m), 5.18 (0.22H, br s), 5.06 (0.22H, d, $J = 9.8$ Hz), 5.02 (0.22H, d, $J = 9.8$ Hz), 2.97 (0.22H, dd, $J = 3.9, 15.9$ Hz), 2.90 (0.22H, d, $J = 15.9$ Hz), 2.32 (0.66H, s), 2.31 (0.66H, s), 2.30 (0.66H, s), 2.29 (0.66H, s), 2.25 (1.32H, s), 1.90 (0.66H, s), 1.83 (0.66H, s), 1.82 (0.66H, s), 1.72 (0.66H, s); ^{13}C -NMR (100 MHz, CDCl_3 , 0.78 : 0.22 mixture of rotational isomers) major isomer: 170.9, 169.4, 168.7, 168.5, 168.4, 168.0, 167.98, 167.93, 167.88, 167.80, 155.7, 153.5, 149.5, 149.2, 148.3, 147.6, 142.1, 142.0, 141.7, 141.4, 135.22, 135.16, 125.0, 124.8, 123.6, 123.5, 123.0, 122.7, 121.8, 116.9, 115.0, 110.4, 110.1, 109.5, 108.1, 78.9, 77.2, 66.1, 36.7, 26.6, 21.1, 20.92, 20.86, 20.7, 20.60, 20.57 (x2), 20.50, 20.4, 20.2; minor isomer: 170.9, 170.3, 168.7, 168.19, 168.17, 168.0, 167.91, 167.88, 167.4, 167.3, 155.6, 152.0, 149.6, 149.1, 147.9, 145.4, 142.4, 142.2, 142.0, 141.8, 135.5, 135.0, 126.1, 125.5, 124.6, 123.9, 123.6, 123.4, 121.6, 117.1, 115.2, 110.2, 109.6, 108.8, 108.4, 67.0 (x2), 66.1, 35.6, 26.1, 21.0, 20.92, 20.86, 20.7, 20.61, 20.57 (x2), 20.49, 20.36, 20.27; IR (neat, cm^{-1}) 3067 (w), 2936 (w), 2361 (w), 1770 (s), 1616 (m), 1506 (m), 1429 (m), 1371 (s), 1240 (s), 1126 (s), 1105 (s), 1049 (s), 1014 (m), 900 (m), 736 (m); FAB-MS (m/z) 1021 ($[\text{M}+\text{Na}]^+$, 100), 999 ($[\text{M}+\text{H}]^+$, 8); FAB-HRMS calcd for $\text{C}_{50}\text{H}_{46}\text{O}_{22}\text{Na}$ $[\text{M}+\text{Na}]^+$, 1021.2378; found, 1021.2384.

ACKNOWLEDGEMENT

We thank the Japan Society for the Promotion of Science (JSPS) for the Young Scientists Research Fellowship (to A. S.) for financial support.

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