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# Synthetic studies of proanthocyanidins. Part 2: Stereoselective gram-scale synthesis of procyanidin-B3☆

Akiko Saito,[a] Noriyuki Nakajima,[b] Akira Tanaka[c] and Makoto Ubukata[b,*]

[a]*Japan Society for the Promotion of Science, Toyama Prefectural University, Kosugi, Toyama 939-0398, Japan*
[b]*Biotechnology Research Center, Toyama Prefectural University, Kosugi, Toyama 939-0398, Japan*
[c]*College of Technology, Toyama Prefectural University, Kosugi, Toyama 939-0398, Japan*

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**Abstract**—A stereoselective synthesis of procyanidin-B3, a condensed catechin dimer, is described. Condensation of benzylated catechin with various 4-*O*-alkylated flavan-3,4-diol derivatives as an electrophile in the presence of a Lewis acid led to protected procyanidin-B3 and its diastereomer. In particular, the reaction using (2*R*,3*S*,4*S*)-3-acetoxy-5,7,3′,4′-tetrabenzyloxy-4-(2″-ethoxyethoxy)flavan as an electrophile in the presence of TMSOTf at −78°C afforded octa-*O*-benzylated procyanidin-B3 with high levels of stereoselectivity and in excellent isolation yields. Furthermore, we succeeded in a stereoselective gram-scale synthesis of protected procyanidin-B3. 

## 1. Introduction

Proanthocyanidins are a ubiquitous family of polyphenolic natural products and are characterized by the oligomeric structures including an interflavanyl bond between the $C_4-C_8$ or $C_4-C_6$ position of the flavan-3-ol units.[2,3] The biological activities of proanthocyanidins are very interesting in that they have powerful free-radical scavenging activity,[4] antioxidant activity[5] and anti-tumor-promoting effect.[6] For this reason, a number of synthetic efforts have been made to access oligomeric proanthocyanidins. Recent investigations concerning the synthesis of isotopically labeled proanthocyanidins to get direct proof of their gut resorption and their metabolism in humans have appeared in the literature.[7,8] In a previous paper,[1] we described a highly stereoselective synthesis of benzylated (−)-procyanidin-B3, (+)-catechin-(48)-(+)-catechin dimer, in which (2*R*,3*S*,4*S*)-3-acetoxy-5,7,3′,4′-tetrabenzyloxy-4-methoxyflavan **10** was employed as an electrophile in the presence of $TiCl_4$. In this paper, we report further investigations of the condensation reaction with various 4-*O*-alkylated flavan-3,4-diol derivatives as electrophiles and describe the details of the synthesis of authentic samples and a diastereoselectivity determination method. In addition, the reaction succeeded in the stereoselective gram-scale synthesis of benzylated procyanidin-B3.

## 2. Results and discussion

### 2.1. Synthesis of 4-substituted catechin derivatives

DDQ oxidation at the C-4 carbon of a catechin derivative in $CHCl_3$/MeOH was first studied by Roux et al. to give 4-methoxy catechin.[9] Tückmantel et al.[10] reported DDQ oxidation of an epicathechin derivative. DDQ oxidation of the epicathechin derivative in $CHCl_3$/MeOH gave generally low yield, and improved result was obtained by the use of ethylene glycol instead of MeOH to give flavan 3,4-diol hydroxy ethyl ether derivatives in 52% yield. They also described the formation of 2,4-bis-oxidized products in the reaction using methanol or isopropyl alcohol as a nucleophile. We re-examined the benzylic DDQ oxidation of a catechin derivative, 5,7,3′,4′-tetrabenzylcatechin **6**, using five alcohols as nucleophiles. The results are summarized in Table 1. Although the DDQ oxidation using MeOH or isopropyl alcohol as a nucleophile resulted in the formation of many by-products including bis-oxidized products, the desired 4-*O*-methyl derivative **9** and 4-*O*-isopropyl derivative **11** were isolated in 52 and 58%, respectively, as indicated by Tückmantel et al.[10] (entries 1 and 2). When *tert*-butyl alcohol was used, 2,4-bis-oxidation occurred in preference to mono-oxidation. In the presence of ethylene glycol in $CH_2Cl_2$, DDQ oxidation proceeded smoothly to give a 74% yield of 4-*O*-hydroxyethyl derivative **13** (entry 3). DDQ oxidation of 3-acetylated catechin derivative **7** was slower than that of 3-hydroxy catechin derivatives. However, the isolation yield was relatively good, 70% yield (entry 4). DDQ oxidation in the presence of 2-ethoxyethanol (ethyl cellosolve) led to smooth disappearance of **6** and the desired 4-*O*-ethoxyethyl derivative **15** was

☆ For Part 1, see Ref. 1.

*Keywords*: proanthocyanidin; stereoselective synthesis; procyanidin-B3.

* Corresponding author. Tel.: +81-766-56-7500; fax: +81-766-56-2498; e-mail: ubukata@pu-toyama.ac.jp

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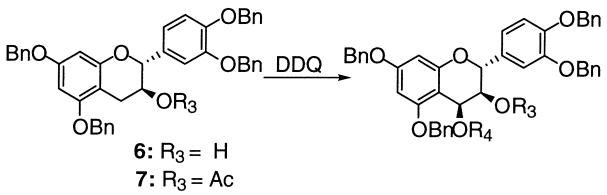
**Table 1**. DDQ oxidation




| Entry | Nucleophile | Catechin | Time (h) | Products | | Isolation yield (%) |
|---|---|---|---|---|---|---|
| | | $R_3$ | | $R_4$ | No. | |
| 1 | Methanol[a] | **6** | 4 | $CH_3$ | **9** | 52 |
| 2 | Isopropyl alcohol | **6** | 8 | $CH(CH_3)_2$ | **11** | 58 |
| 3 | Ethylene glycol | **6** | 6 | $CH_2CH_2OH$ | **13** | 74 |
| 4 | Ethylene glycol | **7** | 12 | $CH_2CH_2OH$ | **14** | 70 |
| 5 | 2-Ethoxyethanol | **6** | 2 | $CH_2CH_2OCH_2CH_3$ | **15** | 98 |
| 6 | Benzyl alcohol | **6** | 12 | $CH_2Ph$ | **17** | 86 |

[a] Ref. 9.

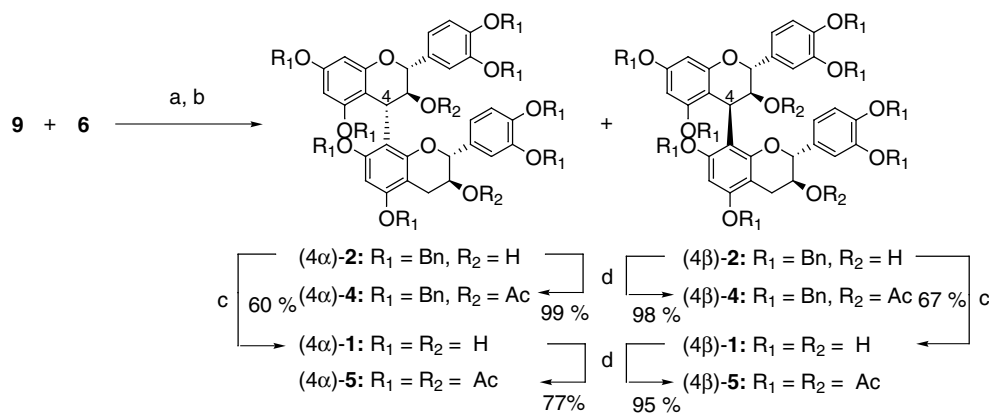
obtained in excellent 98% yield (entry 5). Fortunately, this 4-*O*-ethoxyethyl derivative **15** crystallized from the hexane/EtOAc and, therefore, purification was very easy. 4-*O*-Benzyl derivative **17** was also isolated in 86% yield in the presence of benzyl alcohol even though long reaction time was required at 0°C (entry 6).[11]

## 2.2. Diastereoselectivity determination

Lewis acid catalysts have been employed in the literature to synthesize proanthocyanidins, e.g. $TiCl_4$ for epicatechin[10] and catechin dimer,[8] $SnCl_4$ and $BF_3{\cdot}OEt_2$ for catechin oligomer.[12,13] The derivatives of catechin and epicathechin containing a hydroxyl group at the C-4 position were used as the electrophile in these condensation studies and few reports employed the 4-*O*-alkyl derivatives. Further, the stereoselectivity at the condensation is not sufficient. In this paper, we describe further improvement in the stereoselectivity of the condensation reaction over that attained in our previous studies.[1]

We first synthesized octa-*O*-benzyl procyanidin-B3 (4α)-**2** and its diastereomer (4β)-**2** as the authentic samples by Vercauteren's method[8] (Scheme 1). Condensation of tetra-*O*-benzylated catechin **6** and (2*R*,3*S*,4*S*)-5,7,3′,4′-tetra-benzyloxy-4-methoxyflavan **9** proceeded in the presence of 1 equiv. $TiCl_4$ at 0°C to afford a mixture of (4α)-**2** and (4β)-**2** in 84% coupling yield in a 2.1:1 ratio. The ratio of (4α)-**2** and (4β)-**2** was determined by the isolation yields of each compound from silica gel preparative TLC separation (Merck 1.0 mm, $CHCl_3$/AcOEt, 1/3, 3 times development). (4α)-**2** and (4β)-**2** were separately acetylated with $Ac_2O$, pyridine in the presence of DMAP to give 3,3′-*O*-diacetyl-octa-*O*-benzyl procyanidin-B3 (4α)-**4** and (4β)-**4** in 99 and 98% yield, respectively. Eight benzyl protecting groups were submitted to hydrogenolysis with $Pd(OH)_2$ in THF/MeOH/$H_2O$,[7] and procyanidin-B3 (4α)-**1** and its diastereomer (4β)-**1** were obtained in 60 and 67% yield, respectively (Fig. 1). Full acetylation of ten hydroxy groups of (4α)-**1** afforded decaacetyl derivative (4α)-**5** in 77% yield and also (4β)-**5** was obtained from (4β)-**1** in 95% yield.

In NMR studies of (4α)-**2** and (4β)-**2** in $CDCl_3$ two rotational isomers were observed with 2:1 ratio for (4α)-**2** and 2.5:1 ratio for (4β)-**2**. Rotamers were also observed for (4α)-**4** (1:1), (4β)-**4** (2:1) in $CDCl_3$, (4α)-**1**[14] in acetone-$d_6$ (1:1) and in $CD_3OD$ (2.5:1) solvent. Since all the NMR peaks of (4β)-**1** broadened, it was not possible to confirm the existence of the rotamer. Interestingly, no rotational isomer was observed in decaacetyl derivatives (4α)-**5**[12,15,16] and (4β)-**5**.[12,17] All peaks containing the rotamers for 4α and 4β of **2** and **4** except for the benzyl protecting group were assigned by 2D NMR measurement on the basis of literature values. We were pleased to find that a significant




**Scheme 1.** Synthesis of authentic samples. *Reagents and conditions*: (a) $TiCl_4$, 0°C, 83%; (b) silica gel TLC separation; (c) $H_2$, $Pd(OH)_2$, THF–MeOH–$H_2O$; (d) $Ac_2O$, DMAP, Py.

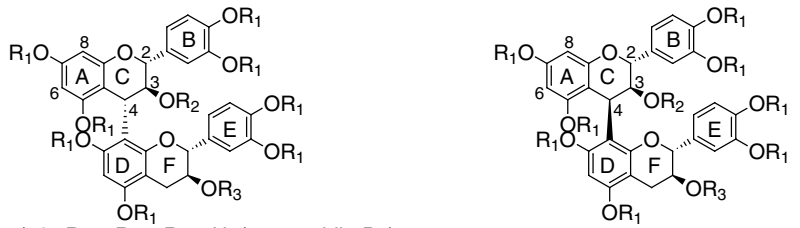
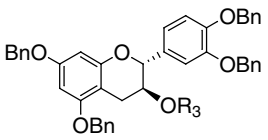



**Figure 1.** Structure of procyanidin and its diastereomer derivatives.

difference is observed in the chemical shift of the C3-proton. The C3-proton $\delta$ 5.83 and $\delta$ 5.80 in (4α)-**4** with 3,4-*trans* configuration appear at about 0.25 ppm lower than the C3-proton $\delta$ 5.53 and $\delta$ 5.58 in (4β)-**4** with 3,4-*cis* configuration. These peaks appear in isolated regions without interference from other peaks even if the sample exists as a mixture. Thus, the diastereomeric ratio of (4α)-**2** to (4β)-**2** could be directly determined by $^1$H NMR measurement of (4α)-**4** and (4β)-**4**. The 2.1:1 ratio on comparison of the peaks at the C3-protons perfectly agreed with the TLC separation rate.



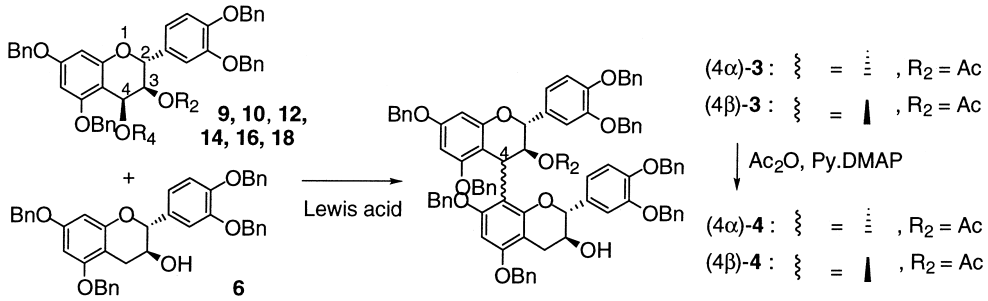
**6**: $R_3$ = H
**7**: $R_3$ = Ac

**Figure 2.** Structure of protected catechins.

## 2.3. Condensation studies

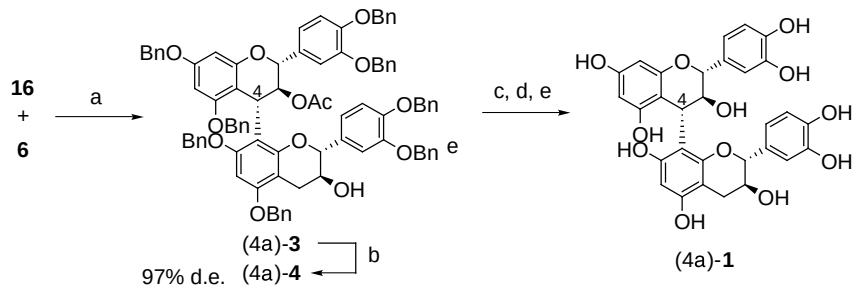
With the simple diastereoselectivity determination method in hand, we re-examined the condensation reaction of 4-*O*-alkyl derivatives with tetra-*O*-benzylated catechin derivative **6** (Fig. 2) under various conditions as summarized in Table 2. The neighboring group participation of the 3-*O*-acetyl moiety was effective in attaining significant improvement in the selectivity as shown in entries 1 and 2. Reaction conditions were first checked using 4-*O*-methyl substituent **10**. The used nucleophilic tetra-*O*-benzylated catechin **6** was in 4.5-fold excess to avoid higher oligomer

**Table 2**. Condensation studies of 4-*O*-alkyl derivatives and tetra-*O*-benzylated catechin derivative **6** in the presence of Lewis acid

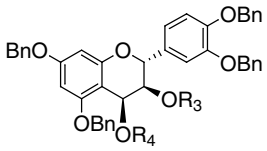



| Entry | Electrophile | | | Solvent | Lewis acid | Temperature (°C) | Coupling[a] yield (%) | Selectivity[b] (4α)-**4**/(4β)-**4** |
|---|---|---|---|---|---|---|---|---|
| | No. | $R_2$ | $R_4$ | | | | | |
| 1 | **9** | H | Me | $CH_2Cl_2$ | $TiCl_4$ | 0 | 84 | 2.1:1 |
| 2 | **10** | Ac | Me | $CH_2Cl_2$ | $TiCl_4$ | 0 | 81 | 7.4:1 |
| 3 | **10** | Ac | Me | $CH_2Cl_2$ | $TiCl_4$ | −40 | 35 | 55:1 |
| 4 | **10** | Ac | Me | $CH_2Cl_2$ | $BF_3{\cdot}OEt_2$ | −78 | 55 | 10:1 |
| 5 | **10** | Ac | Me | $CH_2Cl_2$ | $SnCl_4$ | −78 | 87 | 11:1 |
| 6 | **10** | Ac | Me | $CH_2Cl_2$ | TMSOTf | −78 | quant. | 32:1 |
| 7 | **10** | Ac | Me | Toluene | $BF_3{\cdot}OEt_2$ | 0 | 85 | 4.0:1 |
| 8 | **10** | Ac | Me | Toluene | $SnCl_4$ | 0 | Quant. | 4.4:1 |
| 9 | **10** | Ac | Me | Toluene | TMSOTf | 0 | 89 | 7.0:1 |
| 10 | **12** | Ac | *i*Pr | $CH_2Cl_2$ | TMSOTf | −78 | Quant. | 40:1 |
| 11 | **14** | Ac | $(CH_2)_2OH$ | $CH_2Cl_2$ | TMSOTf | −78 | Quant. | 46:1 |
| 12 | **16** | Ac | EE[c] | $CH_2Cl_2$ | TMSOTf | −78 | Quant. | >48:1 |
| 13 | **18** | Ac | Bn | $CH_2Cl_2$ | TMSOTf | −78 | 88 | 25:1 |

[a] Isolation yield of the dimer mixture.
[b] Selectivities were determined by the $^1$H NMR of the acetylated dimer mixture.
[c] EE represents ethoxyethyl group.




**Scheme 2.** Gram-scale stereoselective synthesis of procyanidin-B3. *Reagents and conditions*: (a) TMSOTf, $CH_2Cl_2$, −78°C, 97%; (b) $Ac_2O$, DMAP, Py; (c) KCN 95%–EtOH, 98%; (d) silica gel column separation >99% de; (e) $H_2$, $Pd(OH)_2$, THF–MeOH–$H_2O$, 67%.




**8** : $R_3 = R_4 = H$
**9** : $R_3 = H$, $R_4 = Me$
**10** : $R_3 = Ac$, $R_4 = Me$
**11** : $R_3 = H$, $R_4 = i$Pr
**12** : $R_3 = Ac$, $R_4 = i$Pr
**13** : $R_3 = H$, $R_4 = (CH_2)_2OH$
**14** : $R_3 = Ac$, $R_4 = (CH_2)_2OH$
**15** : $R_3 = H$, $R_4 = EE$
**16** : $R_3 = Ac$, $R_4 = EE$
**17** : $R_3 = H$, $R_4 = Bn$
**18** : $R_3 = Ac$, $R_4 = Bn$

**Figure 3.** Structure of 4-substituted catechin derivatives.

formation. One equivalent of Lewis acid, $TiCl_4$, $BF_3{\cdot}OEt_2$, $SnCl_4$ and TMSOTf, was added dropwise to a solution of 4-*O*-alkyl derivatives (Fig. 3) and **6** in $CH_2Cl_2$ at each temperature, and the mixture was allowed to react for 5 min. $TiCl_4$-catalyzed reaction of **6** and **9** at 0°C provided 84% yield of products with 2.1:1 ratio (entry 1 and Scheme 1). The ratio of the reaction at −40°C condensation dramatically increased to 55:1; however, the isolation yield decreased to only 35% (entry 3). When $BF_3{\cdot}OEt_2$ and $SnCl_2$ were used as catalyst at −78°C, isolation yield increased up to 55 and 87% with moderate 10:1 ratio (entries 4 and 5). The best results were obtained by using TMSOTf as catalyst; 100% yield with 32:1 selectivity was achieved at −78°C (entry 6). No dimerization product was detected in the reaction with $Et_2AlCl$ and $Ti(Oi\text{-}Pr)_4$ at any temperature. In all reactions in toluene, the benzyl catechin **6** was precipitated below 0°C; therefore, the selectivities obtained at 0°C were maximum 7:1 ratio (entries 7–9) because TMSOTf-catalyzed reaction achieved quantitative yield with excellent selectivity, the differentiation of the 4-*O*-alkyl substituent, Me into *i*Pr, $(CH_2)_2OH$, EE and Bn, was next investigated using TMSOTf as catalyst (entries 10–13). All reactions were accomplished within 5 min. As shown in entry 12, the best result was obtained from the reaction of (2*R*,3*S*,4*S*)-3-acetoxy-5,7,3′,4′-tetrabenzyloxy-4-(2″-ethoxyethoxy)flavan **16** with **6** at −78°C; quantitative yield of product in more than 48:1 selectivity was obtained.

### 2.4. Gram-scale stereoselective synthesis of (4α)-3 and its deprotection

The condensation conditions were applied to a gram-scale synthesis of procyanidin-B3. Gram order of electrophile **16** was synthesized from tetra-*O*-benzyl catechin **6**, and the reaction was carried out under the optimized conditions. The condensation between **16** (0.68 g, 0.87 mmol) and **6** (2.55 g, 3.92 mmol) in the presence of 1.0 equiv. TMSOTf at −78°C was carried out to afford dimerization product (4α)-**3** (1.11 g, 0.83 mmol) in 95% yield in a 66:1 ratio.

The acetyl group of (4α)-**3** thus obtained was hydrolyzed with 10 equiv. KCN in 95% EtOH[18] ($R_f$ value of benzylated B3 is 0.11, and its diastereomer is 0.27 in $CH_2Cl_2$ containing 1.6% AcOEt), in which no epimerization product was detected. The eight remaining benzyl protecting groups were then submitted to hydrogenolysis with $Pd(OH)_2$ and purification in the usual way to give procyanidin-B3 **1**. $[\alpha]_D^{24}=-221$ (*c* 0.38, EtOH) {lit.[7] $[\alpha]_D^{25}=-202$ (*c* 1.0, EtOH), lit.[19] $[\alpha]_{578}^{20}=-244.7$ (*c* 2.0, EtOH)}.

## 3. Conclusion

In conclusion, we were able to synthesize octa-*O*-benzylated procyanidin-B3 (4α)-**3** in high diastereomeric excess. Condensation of benzylated catechin with various 4-*O*-alkylated flavan-3,4-diol derivatives as an electrophile in the presence of a Lewis acid led to protected procyanidin-B3 and its diastereomer. The use of (2*R*,3*S*,4*S*)-3-acetoxy-5,7,3′,4′-tetrabenzyloxy-4-(2″-ethoxyethoxy)flavan as an electrophile in the presence of TMSOTf afforded octa-*O*-benzylated procyanidin-B3 with high levels of stereoselectivity. Furthermore, we succeeded in the stereoselective gram-scale synthesis of procyanidin-B3.

## 4. Experimental

All melting points (mp) are uncorrected. Optical rotation was measured with a HORIBA SEPA-300 spectrometer. $^1H$ NMR spectra were measured with a JEOL JNM-LA400 spectrometer, and mass spectra were recorded with a JEOL JMS-AX500 instrument.

### 4.1. A typical procedure for DDQ oxidation

**4.1.1. (2*S*,3*S*,4*S*)-5,7,3′,4′-Tetrabenzyloxy-4-isopropoxyflavan-3-ol 11.** To a solution of tetra-*O*-benzylated catechin **6** (200 mg, 0.31 mmol) and isopropyl alcohol (2 mL) in $CH_2Cl_2$ (6 mL) was added slowly DDQ (2 equiv., 140 mg, 0.61 mmol) at 0°C. After stirring for 8 h at rt, excess of 4-(dimethylamino)pyridine was added to the solution at 0°C and the mixture was stirred for 10 min. The resulting purple solid was removed by filtration and the filtrate was washed with water and brine, and dried ($Na_2SO_4$). Filtration,

concentration and short silica gel column chromatography ($CHCl_3$) gave **11** (128 mg, 0.18 mmol, 58%) as white foam: $[\alpha]_D^{24}$=+55.1 (*c* 1.20, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) 7.51–7.24 (20H, m), 7.09 (1H, d, *J*=1.7 Hz), 7.01 (1H, dd, *J*=1.7, 8.3 Hz), 6.96 (1H, d, *J*=8.3 Hz), 6.25 (1H, d, *J*=2.3 Hz), 6.17 (1H, d, *J*=2.3 Hz), 5.17 (4H, s), 5.04 (1H, d, *J*=11.2 Hz), 5.01 (1H, d, *J*=11.2 Hz), 4.98 (2H, s), 4.95 (1H, d, *J*=10.2 Hz), 4.87 (1H, d, *J*=3.4 Hz), 4.07 (1H, heptet, 6.1 Hz), 3.81 (1H, ddd, *J*=3.4, 10.0, 10.2 Hz), 2.96 (1H, d, *J*=10.0 Hz, OH), 1.04 (6H, d, *J*=6.1 Hz). FAB-MS (*m/z*) 731 ($[M+Na]^+$, 7), 710 (6), 709 ($[M+H]^+$, 12), 708 (18); FAB-HRMS calcd for $C_{46}H_{45}O_7$ $[M+H]^+$, 709.3165; found: 709.3186.

**4.1.2. (2*R*,3*S*,4*S*)-5,7,3′,4′-Tetrabenzyloxy-4-(2″-hydroxyethyloxy)flavan-3-ol 13.** DDQ oxidation according to the general procedure using **6** (300 mg, 0.46 mmol), DDQ (209 mg, 0.92 mmol) and ethylene glycol (1 mL) in $CH_2Cl_2$ (8 mL) for 6 h afforded 260 mg (75%) of **11** as a white foam: $[\alpha]_D^{24}$=+28.3 (*c* 0.38, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) 7.45–7.26 (20H, m), 7.08 (1H, d, *J*=1.7 Hz), 7.00 (1H, dd, *J*=1.7, 8.3 Hz), 6.93 (1H, d, *J*=8.3 Hz), 6.26 (1H, d, *J*=2.2 Hz), 6.15 (1H, d, *J*=2.2 Hz), 5.17 (1H, d, *J*=12.2 Hz), 5.14 (2H, s), 5.13 (1H, d, *J*=12.2 Hz), 5.07 (1H, d, *J*=11.5 Hz), 5.02 (1H, d, *J*=11.5 Hz), 4.97 (2H, s), 4.95 (1H, d, *J*=12.0 Hz), 4.80 (1H, d, *J*=3.4 Hz), 3.90–3.86 (2H, m), 3.76 (1H, ddd, *J*=3.7, 6.6, 15.1 Hz), 3.65–3.60 (2H, m), 2.96 (1H, br, OH), 2.74 (1H, br, OH); FABMS (*m/z*) 733 ($[M+Na]^+$, 31), 712 (5), 711 ($[M+Na]^+$, 12), 710 (21), FAB-HRMS calcd for $C_{45}H_{43}O_8$ $[M+H]^+$, 711.2958; found, 711.2943.

**4.1.3. (2*S*,3*S*,4*S*)-3-Acetoxy-5,7,3′,4′-tetrabenzyloxy-4-(2″-hydroxyethyloxy)flavan 14.** DDQ oxidation according to the general procedure using **7** (339 mg, 0.49 mmol), DDQ (222 mg, 0.98 mmol) and ethylene glycol (1 mL) in $CH_2Cl_2$ (10 mL) for 12 h afforded 258 mg (70%) of **14** as a white foam: $[\alpha]_D^{24}$=+45.4 (*c* 0.56, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) 7.47–7.28 (20H, m), 7.05 (1H, d, *J*=2.0 Hz), 6.97 (1H, dd, *J*=2.0, 8.3 Hz), 6.92 (1H, d, *J*=8.3 Hz), 6.26 (1H, d, *J*=2.2 Hz), 6.15 (1H, d, *J*=2.2 Hz), 5.27 (1H, dd, *J*=3.2, 10.7 Hz), 5.20 (1H, d, *J*=10.7 Hz), 5.16 (2H, s), 5.15 (2H, s), 5.07 (1H, d, *J*=11.5 Hz), 5.02 (1H, d, *J*=11.5 Hz), 4.99 (1H, d, *J*=11.7 Hz), 4.96 (1H, d, *J*=11.7 Hz), 4.83 (1H, d, *J*=3.2 Hz), 3.79–3.71 (2H, m), 3.60 (2H, br), 2.33 (1H, br, OH), 1.79 (3H, s); FAB-MS (*m/z*) 775 ($[M+Na]^+$, 8), 754 (4), 753 ($[M+H]^+$, 8), 752 (12); FAB-HRMS calcd for $C_{47}H_{45}O_9$ $[M+H]^+$, 753.3064; found, 753.3062.

**4.1.4. (2*R*,3*S*,4*S*)-5,7,3′,4′-Tetrabenzyloxy-4-(2″-ethoxyethoxy)flavan-3-ol 15.** DDQ oxidation according to the general procedure using **6** (500 mg, 0.78 mmol), DDQ (350 mg, 1.54 mmol) and 2-ethoxyethanol (1.5 mL) in $CH_2Cl_2$ (15 mL) for 2 h afforded **15** as a pale yellow solid, which was crystallized from hexane/EtOAc to give 560 mg (98%) of **15** as colorless needles: mp 144.5–145.0°C; $[\alpha]_D^{23}$=+29.5 (*c* 1.60, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) 7.47–7.27 (20H, m), 7.11 (1H, d, *J*=2.0 Hz), 7.00 (1H, dd, *J*=2.0, 8.3 Hz), 6.96 (1H, d, *J*=8.3 Hz), 6.26 (1H, d, *J*=2.2 Hz), 6.15 (1H, d, *J*=2.2 Hz), 5.16 (4H, s), 5.08 (1H, d, *J*=11.4 Hz), 5.03 (1H, d, *J*=11.4 Hz), 4.98 (2H, s), 4.89 (1H, d, *J*=10.5 Hz), 4.77 (1H, d, *J*=3.4 Hz), 4.13 (1H, brs, OH), 3.96–3.83 (3H, m), 3.56–3.45 (4H, m), 1.18 (3H, t, *J*=7.1 Hz). FAB-MS (*m/z*) 761 ($[M+Na]^+$, 11), 740 (4), 739 ($[M+H]^+$, 10), 738 (11); FAB-HRMS calcd for $C_{47}H_{46}O_8$ $[M+H]^+$, 739.3271; found, 739.3268.

**4.1.5. (2*R*,3*S*,4*S*)-4,5,7,3′,4′-Pentabenzyloxyflavan-3-ol 17.** DDQ oxidation according to the general procedure using **6** (500 mg, 0.78 mmol), DDQ (350 mg, 1.54 mmol) and benzyl alcohol (0.8 mL) in $CH_2Cl_2$ (20 mL) for 12 h afforded 568 mg (86%) of **17** as a colorless prism: mp 124.0–125.5°C; $[\alpha]_D^{24}$=+56.4 (*c* 0.48, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) 7.45–7.18 (25H, m), 7.07 (1H, d, *J*=2.0 Hz), 6.99 (1H, dd, *J*=2.0, 8.3 Hz), 6.94 (1H, d, *J*=8.3 Hz), 6.28 (1H, d, *J*=2.2 Hz), 6.18 (1H, d, *J*=2.2 Hz), 5.13 (4H, s), 5.05 (1H, d, *J*=11.2 Hz), 5.01 (1H, d, *J*=11.2 Hz), 5.00 (1H, d, *J*=9.7 Hz), 4.98 (2H, s), 4.96 (1H, d, *J*=3.4 Hz), 4.78 (1H, d, *J*=11.5 Hz), 4.66 (1H, d, *J*=11.5 Hz), 3.90 (1H, dt, *J*=3.4, 9.7 Hz), 2.35 (1H, d, *J*=9.7 Hz); FAB-MS (*m/z*) 780 (11), 779 ($[M+Na]^+$, 16), 758 (10), 757 ($[M+H]^+$, 26), 756 (38); FAB-HRMS calcd for $C_{50}H_{45}O_7$ $[M+H]^+$, 757.3165; found: 757.3151.

### 4.2. Condensation reaction and diastereoselectivity determination

**4.2.1. (2*R*,3*S*,4*S*)-3-Acetoxy-5,7,3′,4′-tetrabenzyloxy-4-isopropoxyflavan 12.** To a solution of **11** (45 mg, 0.063 mmol) in dry pyridine (1 mL) was added $Ac_2O$ (45 mL, 0.126 mmol) and 4-(dimethylamino)pyridine (1 mg) at 0°C. After stirring for 12 h at rt, the reaction mixture was quenched with water, and extracted with ethyl acetate. The organic phase was washed with water and brine, and dried ($Na_2SO_4$). Filtration, concentration and short silica gel column chromatography (hexane/EtOAc) gave each 3-acetyl-tetra-benzyl catechin **12** (45 mg, 0.061 mmol, 97%) as a white foam: $[\alpha]_D^{21}$=+57.1 (*c* 0.44, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) 7.46–7.23 (20H, m), 7.05 (1H, d, *J*=1.7 Hz), 6.97 (1H, dd, *J*=1.7, 8.3 Hz), 6.91 (1H, d, *J*=8.3 Hz), 6.21 (1H, d, *J*=2.2 Hz), 6.13 (1H, d, *J*=2.2 Hz), 5.30 (1H, *J*=10.7 Hz), 5.19 (1H, dd, *J*=2.9, 10.7 Hz), 5.15 (2H, s), 5.14 (2H, s), 5.04 (1H, d, *J*=11.9 Hz), 5.00 (1H, d, *J*=11.9 Hz), 4.98 (1H, d, *J*=11.7 Hz), 4.94 (1H, d, *J*=11.7 Hz), 4.90 (1H, d, *J*=2.9 Hz), 3.84 (1H, heptet, *J*=6.3 Hz), 1.75 (3H, s), 1.10 (3H, d, *J*=6.3 Hz), 1.03 (3H, d, *J*=6.3 Hz); FAB-MS (*m/z*) 774 (12), 773 ($[M+Na]^+$, 24), 752 (13), 751 ($[M+H]^+$, 31), 750 (35); FAB-HRMS calcd for $C_{48}H_{47}O_8$ $[M+H]^+$, 751.3271; found: 751.3267.

**4.2.2. (2*S*,3*S*,4*S*)-3-Acetoxy-5,7,3′,4′-tetrabenzyloxy-4-(2″-ethoxyethoxy)flavan 16.** Acetylation using **15** (300 mg, 0.41 mmol), $Ac_2O$ (45 mL, 0.126 mmol) and 4-(dimethylamino)pyridine (1 mg) in $CH_2Cl_2$ (15 mL) afforded 310 mg (98%) of **16** as a white foam: $[\alpha]_D^{20}$=+64.1 (*c* 0.22, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) 7.46–7.27 (20H, m), 7.06 (1H, d, *J*=1.7 Hz), 6.96 (1H, dd, *J*=1.7, 8.3 Hz), 6.92 (1H, d, *J*=8.3 Hz), 6.24 (1H, d, *J*=2.2 Hz), 6.14 (1H, d, *J*=2.2 Hz), 5.26 (1H, d, *J*=10.7 Hz), 5.21 (1H, dd, *J*=2.9, 10.7 Hz), 5.16 (2H, s), 5.14 (2H, s), 5.05 (1H, d, *J*=11.5 Hz), 5.01 (1H, d, *J*=11.5 Hz), 4.99 (1H, d, *J*=11.7 Hz), 4.96 (1H, d, *J*=11.7 Hz), 4.87 (1H, d, *J*=2.9 Hz), 3.82–3.71 (2H, m), 3.48–3.36 (4H, m), 1.97 (3H, s), 1.14 (3H, t, *J*=7.0 Hz); FAB-MS (*m/z*) 804 (10), 803 ($[M+Na]^+$,

19), 782 (5), 781 ([M+H]$^+$, 11), 780 (14); FAB-HRMS calcd for $C_{49}H_{49}O_9$ [M+H]$^+$, 781.3377; found: 781.3391.

**4.2.3. (2*S*,3*S*,4*S*)-3-Acetoxy-4,5,7,3′,4′-pentabenzyloxyflavan 18.** Acetylation using **17** (22 mg, 0.029 mmol), $Ac_2O$ (14 μL, 0.126 mmol) and 4-(dimethylamino)pyridine (1 mg) in $CH_2Cl_2$ (1 mL) afforded 23 mg (100%) of **18** as a colorless foam: $[\alpha]_D^{24}$=+74.1 (*c* 0.28, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) 7.46–7.20 (25H, m), 7.07 (1H, d, *J*=2.0 Hz), 6.98 (1H, dd, *J*=2.0, 8.3 Hz), 6.92 (1H, d, *J*=8.3 Hz), 6.26 (1H, d, *J*=2.2 Hz), 6.15 (1H, d, *J*=2.2 Hz), 5.32 (1H, d, *J*=10.7 Hz), 5.24 (1H, dd, *J*=3.2, 10.7 Hz), 5.16 (2H, s), 5.15 (2H, s), 5.05 (1H, d, *J*=11.2 Hz), 5.01 (1H, d, *J*=11.2 Hz), 5.02–5.00 (1H, m), 5.00 (1H, d, *J*=11.7 Hz), 4.97 (1H, d, *J*=11.7 Hz), 4.66 (2H, s), 1.72 (3H, s). FAB-MS (*m*/*z*) 822 (15), 821 ([M+Na]$^+$, 25), 800 (14), 799 ([M+H]$^+$, 37), 798 (42); FAB-HRMS calcd for $C_{52}H_{47}O_8$ [M+H]$^+$, 799.3271; found: 799.3286.

**4.2.4. [4,8]-2,3-*trans*-3,4-*cis*:2,3-*trans*-Octa-*O*-benzyl-bi-(+)-catechin and [4,8]-2,3-*trans*-3,4-*trans*:2,3-*trans*-octa-*O*-benzyl-bi-(+)-catechin (Scheme 1). (4α)-2 and its diastereomer (4β)-2.** To a solution of tetra-*O*-benzylated catechin **6** (323 mg, 0.50 mmol, 4.5 equiv.) and (2*R*,3*S*,4*S*)-5,7,3′,4′-tetrabenzyloxy-4-methoxyflavan-3-ol **9** (75 mg, 0.11 mmol) in $CH_2Cl_2$ (20 mL) was added dropwise $TiCl_4$ at 0°C. After stirring for 5 min, the reaction mixture was quenched with sat. sodium hydrogen carbonate. The aqueous solution was extracted with $CHCl_3$ and the organic phase was washed with water and brine, and dried ($Na_2SO_4$). Filtration, concentration and silica gel column chromatography (hexane/ethyl acetate, 6/1–1.5/1) afforded a mixture of octabenzylated procyanidin-B3 (4α)-**2** and its diastereomer (4β)-**2** (120 mg, 84%). Sixty-nine milligrams (0.053 mmol) of the dimer mixture was separated on preparative silica gel thin-layer chromatography (Merck 1.0 mm, $CHCl_3$/AcOEt, 60/1, 3 times development) to give pure 40 mg of (4α)-**2** as a white foam and 20 mg of its diastereomer (4β)-**2** as a white foam. Data for (4α)-**2**: $R_f$ 0.11 ($CH_2Cl_2$ containing 1.6% AcOEt); $[\alpha]_D^{26}$=−106 (*c* 0.80, $CHCl_3$) {lit.[12] $[\alpha]_D^{30}$=−102.9 (*c* 1.9, $CHCl_3$)}; $^1$H NMR (400 MHz, $CDCl_3$, 2:1 mixture of rotational isomers) major isomer: 7.46–7.48 (22.44, m, Bn), 7.15–7.11 (1.32H, m, Bn), 7.01–6.97 (1.32H, m, 2′×2), 6.93–6.81 (4.62H, m, 4Bn, 5′, 5′, 6′), 6.78 (0.66H, dd, *J*=2.0, 8.3 Hz, 6′), 6.23 (0.66H, s, 6D), 6.17 (0.66H, d, *J*=2.4 Hz, 8A), 6.09 (0.66H, d, *J*=2.4 Hz, 6A), 5.20–4.86 (7.92H, m, Bn), 4.83–4.79 (1.32H, m, Bn), 4.72–4.63 (0.66H, m, Bn), 4.66 (0.66H, d, *J*=8.8 Hz, 2C), 4.53 (0.66H, d, *J*=10.7 Hz, Bn), 4.49 (0.66H, d, *J*=9.8 Hz, 4C), 4.28 (0.66H, dd, *J*=8.8, 9.8 Hz, 3C), 3.67–3.61 (0.66H, m, 3F), 3.58 (0.66H, d, *J*=8.8 Hz, 2F), 3.04 (0.66H, dd, *J*=5.8, 16.3 Hz, 4Fα), 2.37 (0.66H, dd, *J*=9.2, 16.3 Hz, 4Fβ), 1.70–1.30 (1.32H, m, br, OH); minor isomer: 7.46–7.48 (11.9H, m, Bn), 7.15–7.11 (0.68H, m, Bn), 6.93–6.81 (2.04H, m, 3Bn, 2′, 5′, 6′), 6.70 (0.34H, d, *J*=8.3 Hz, 5′), 6.59 (0.34H, d, *J*=2.0 Hz, 2′), 6.43 (0.34H, dd, *J*=2.0, 8.3 Hz, 6′), 6.19 (0.34H, d, *J*=2.4 Hz, 8A), 6.08 (0.34H, s, 6D), 6.00 (0.34H, d, *J*=2.4 Hz, 6A), 5.20–4.86 (4.08H, m, Bn), 4.83–4.79 (0.68H, m, Bn), 4.77 (0.34H, d, *J*=8.2 Hz, 2C), 4.72–4.63 (0.68H, m, Bn), 4.49 (0.34H, d, *J*=9.8 Hz, 4C), 4.45 (0.34H, d, *J*=8.2 Hz, 2F), 4.14 (0.34H, dd, *J*=8.2, 9.8 Hz, 3C), 3.67–3.61 (0.34H, m, 3F), 3.16 (0.34H, dd, *J*=5.8, 16.3 Hz, 4Fα), 2.64 (0.34H, dd, *J*=9.5, 16.3 Hz, 4Fβ), 1.70–1.30 (0.68H, m, br, OH); $^{13}$C NMR (100 MHz, $CDCl_3$, 2:1 mixture of rotational isomers) major isomer: 157.9, 157.7, 156.9, 155.50, 155.46, 153.8, 149.2, 149.0, 148.9, 148.5, 137.3, 137.2 (×2), 137.14, 137.09 (×2), 137.0, 136.6, 131.8, 130.6, 128.6, 128.51, 128.47, 128.40 (×4), 128.37 (×2), 128.34, 128.26, 128.1, 127.9, 127.8, 127.70, 127.60, 127.5, 127.45 (×2), 127.43, 127.2 (×2), 127.1 (×2), 121.2, 120.0, 114.8, 114.7, 113.6, 113.5, 111.9, 108.6, 102.4, 94.8, 94.1, 91.7, 82.0, 80.6, 76.6, 73.2, 71.2 (×2), 71.1 (×2), 70.3, 70.0, 69.9, 68.5, 37.2, 28.0; minor isomer: 157.9, 157.5, 156.8, 155.4 (×2), 152.8, 149.2, 149.0, 148.9, 148.7, 137.6, 137.3, 137.2, 137.14, 137.09 (×2), 137.0, 136.9, 131.9, 130.5, 128.50, 128.40 (×2), 128.37, 128.35, 128.27, 128.0, 127.9, 127.8, 127.75 (×2), 127.70, 127.66, 127.60, 127.5 (×2), 127.22, 127.18 (×2), 127.1 (×3), 127.0, 126.9, 120.7, 120.6, 115.0, 114.4, 114.0, 113.7, 112.0, 108.4, 103.2, 94.8, 94.1, 91.7, 81.7, 81.2, 77.2, 73.3, 71.2, 71.1, 71.0, 70.9, 69.83, 69.79, 69.78, 68.3, 372, 28.1. Data for (4β)-**2**: $R_f$ 0.27 ($CH_2Cl_2$ containing 1.6% AcOEt); $[\alpha]_D^{24}$=+96.5 (*c* 0.20, $CHCl_3$) {lit.[12] $[\alpha]_D^{30}$=+106.8 (*c* 1.4, $CHCl_3$)}; $^1$H NMR (400 MHz, $CDCl_3$, 2.5:1 mixture of rotational isomers) major isomer: 7.49–7.15 (25.56H, m, Bn),7.25 (0.71H, d, *J*=1.7 Hz, 2′), 7.10–7.05 (1.42H, m, Bn), 7.03 (0.71H, dd, *J*=1.7, 8.3 Hz, 6′), 6.98–6.97 (1.42H, m, Bn), 6.92 (0.71H, d, *J*=8.3 Hz, 5′), 6.86 (0.71H, d, *J*=1.7 Hz, 2′), 6.82 (0.71H, d, *J*=8.3 Hz, 5′), 6.57 (0.71H, dd, *J*=1.7, 8.3 Hz, 6′), 6.36 (0.71H, s, 6D), 6.05 (0.71H, d, *J*=2.2 Hz, 8A), 5.44 (0.71H, d, *J*=2.2 Hz, 6A), 5.13 (0.71H, d, *J*=9.5 Hz, 2C), 5.12–4.79 (9.94H, m, Bn), 5.07 (0.71H, d, *J*=6.1 Hz, 4C), 4.61 (0.71H, d, *J*=11.4 Hz, Bn), 4.50 (0.71H, d, *J*=11.4 Hz, Bn), 4.21 (0.71H, dd, *J*=6.1, 9.5 Hz, 3C), 3.86 (0.71H, ddd, *J*=6.6, 9.0, 9.6 Hz, 3F), 3.72 (0.71H, d, *J*=9.0 Hz, 2F), 3.28 (0.71H, dd, *J*=6.6, 16.8 Hz, 4Fα), 2.74 (0.71H, brs, OH), 2.65 (0.71H, dd, *J*=9.6, 16.8 Hz, 4Fβ), 1.55 (0.71H, br, OH); minor isomer: 7.49–7.15 (10.73H, m, Bn), 7.10–7.05 (0.87H, m, Bn), 6.97 (0.29H, d, *J*=1.7 Hz, 2′), 6.94 (0.29H, d, *J*=8.0 Hz, 5′), 6.90 (0.29H, dd, *J*=1.7, 8.0 Hz, 6′), 6.85 (0.29H, d, *J*=1.7 Hz, 2′), 6.80 (0.29H, d, *J*=8.0 Hz, 5′), 6.76 (0.29H, dd, *J*=1.7, 8.0 Hz, 6′), 6.23 (0.29H, d, *J*=2.1 Hz, 8A), 6.24 (0.29H, s, 6D), 6.03 (0.29H, d, *J*=2.1 Hz, 6A), 5.12–4.79 (4.06H, m, Bn), 5.07 (0.29H, d, *J*=8.7 Hz, 2C), 4.94 (0.29H, d, *J*=6.9 Hz, 4C), 4.75 (0.29H, d, *J*=12.2 Hz, Bn), 4.55 (0.29H, d, *J*=8.5 Hz, 2F), 4.46 (0.29H, d, *J*=12.2 Hz, Bn), 4.16 (0.29H, dd, *J*=6.9, 8.7 Hz, 3C), 3.54 (0.29H, ddd, *J*=5.6, 8.5, 9.6 Hz, 3F), 3.17 (0.29H, dd, *J*=5.6, 16.4 Hz, 4Fα), 2.66 (0.29H, dd, *J*=9.6, 16.4 Hz, 4Fβ), 2.48 (0.29H, brs, OH), 1.55 (0.29H, br, OH); $^{13}$C NMR (100 MHz, $CDCl_3$, 2.5:1 mixture of rotational isomers) major isomer: 158.4, 156.7, 156.2 (×2), 155.9, 153.5, 149.3, 149.22, 149.16, 148.9, 135.5, 137.3, 137.2 (×2), 137.0 (×3), 136.7, 132.9, 130.4, 128.6 (×2), 128.41 (×2), 128.38, 128.35 (×2), 128.33, 128.1, 128.0 (×2), 127.74, 127.71, 127.65, 127.5 (×4), 127.4, 127.3, 127.22, 127.19, 127.15, 127.05, 121.0, 120.4, 114.6, 114.2, 114.0, 112.4, 109.2, 105.4, 105.2, 93.3, 92.5, 91.7, 82.0 (×2), 77.7, 77.2, 72.0, 71.3, 71.2, 70.4, 69.9, 69.6, 69.4, 68.7, 33.4, 29.1; minor isomer: 158.5, 157.21, 157.16, 156.0, 155.6, 153.5, 149.4, 149.3, 149.1, 148.9, 137.4, 137.3 (×2), 137.2, 137.1 (×3), 136.8, 132.6, 120.7, 128.6 (×2), 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.93, 127.90, 127.8, 127.69 (×3), 127.53, 127.47 (×2), 127.4, 127.3, 127.22, 127.19 (×2), 127.15, 127.1, 120.7, 120.5, 114.9, 114.5, 114.1, 113.0, 109.0, 105.8, 102.7, 94.3, 93.0 (×2),

82.1, 81.5, 77.8, 76.8, 71.3 (×2), 71.2, 71.1, 70.8, 69.9, 69.8, 68.2, 32.5, 28.0.

**4.2.5. [4,8]-2,3-*trans*-3,4-*cis*:2,3-*trans*-Octa-*O*-benzyl-3-*O*-acetyl-bi-(+)-catechin and [4,8]-2,3-*trans*-3,4-*trans*:2,3-*trans*-octa-*O*-benzyl-3-*O*-acetyl-bi-(+)-catechin (Scheme 2). (4α)-3 and its diastereomer (4β)-3.** To a solution of tetra-*O*-benzylated catechin **6** (2.55 g, 3.92 mmol, 4.5 equiv.) and (2*S*,3*S*,4*S*)-3-acetoxy-5,7,3′,4′-tetrabenzyloxy-4-(2″-ethoxy-ethoxy)flavan **16** (0.68 g, 0.87 mmol) in $CH_2Cl_2$ (160 mL) was added dropwise TMSOTf (1.74 mL, 0.87 mmol, 0.5 M solution in $CH_2Cl_2$) at −78°C. After stirring for 5 min, the pale yellow reaction mixture was quenched with sat. sodium hydrogen carbonate. The aq. solution was extracted with $CHCl_3$ and the organic phase was washed with water and brine, and dried ($Na_2SO_4$). Filtration, concentration and silica gel column chromatography (hexane/EtOAc, 6/1–1.5/1) afforded a 1.11 g (95%) of a mixture of (4α)-**3** and its diastereomer (4β)-**3**. A part of the reaction mixture (10 mg) was acetylated in pyridine (1 mL), acetic anhydride (4 μL, 0.043 mmol), 4-(dimethylamino)pyridine (0.5 mg) to afford a 10 mg (97%) of (4α)-**4** and (4β)-**4** mixture. The stereoselectivity of the condensation reaction was determined by $^1$H NMR as 66:1 ratio. Data for (4α)-**3**: $^1$H NMR (400 MHz, $CDCl_3$, 1:1 mixture of rotational isomers) 7.49–6.37 (46H, m), 6.22 (0.5H, s), 6.19 (0.5H, d, *J*=2.2 Hz), 6.16 (0.5H, d, *J*=2.4 Hz), 6.10 (0.5H, d, *J*=2.2 Hz), 6.07 (0.5H, d, *J*=2.4 Hz), 5.95 (0.5H, t, *J*=9.8 Hz), 5.94 (0.5H, s), 5.82 (0.5H, t, *J*=9.5 Hz), 4.91 (0.5H, d, *J*=9.8 Hz), 4.78 (0.5H, d, *J*=9.5 Hz), 4.70 (0.5H, d, *J*=9.8 Hz), 4.62 (0.5H, d, *J*=9.5 Hz), 5.35–4.52 (16.5H, m), 3.90 (0.5H, m), 3.53 (0.5H, dd, *J*=5.1, 9.0 Hz), 3.29 (0.5H, d, *J*=9.0 Hz), 3.01 (0.5H, dd, *J*=5.9, 16.1 Hz), 2.82 (0.5H, dd, *J*=5.1, 16.3 Hz), 2.69 (0.5H, dd, *J*=7.1, 16.3 Hz), 2.31 (0.5H, dd, *J*=9.8, 16.1 Hz), 2.16 (0.5H, br), 1.59 (1.5H, s), 1.50 (1.5H, s), 1.30 (0.5H, br); FAB-MS (*m/z*): 1365 (7), 1364 ([M+Na]$^+$, 9), 1344 (6), 1343 ([M+H]$^+$, 10), 1342 (11).

**4.2.6. [4,8]-2,3-*trans*-3,4-*trans*:2,3-*trans*-Octa-*O*-benzyl-3,3′-di-*O*-acetyl-bi-(+)-catechin. (4α)-4.** To a solution of (4α)-**2** (43 mg, 0.033 mmol) in dry pyridine (2 mL) was added $Ac_2O$ (7.3 μL, 0.066 mmol) and 4-(dimethylamino)-pyridine (1 mg) at 0°C. After stirring for 12 h at rt, the reaction mixture was quenched with water, and extracted with ethyl acetate. The organic phase was washed with water and brine, and dried ($Na_2SO_4$). Filtration, concentration and short silica gel column chromatography (hexane/EtOAc, 5/1) gave (4α)-**4** (45 mg, 99%) as a colorless amorphous; $[\alpha]_D^{27}=-99.6$ (*c* 0.46, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, 1(a):1(b) mixture of rotational isomers) 7.54–7.18 (37H, m, Bn), 7.15–7.12 (1.5H, m, Bn), 6.94–6.92 (1.5H, m, Bn), 6.90 (0.5H, d, *J*=1.9 Hz, 2′a), 6.89 (0.5H, d, *J*=1.9 Hz, 2′b), 6.88 (0.5H, d, *J*=8.5 Hz, 5′b), 6.83 (0.5H, d, *J*=8.5 Hz, 5′a), 6.82 (0.5H, d, *J*=1.8 Hz, 2′b), 6.79 (0.5H, d, *J*=9.1 Hz, 5′b), 6.77–6.73 (1.5H, m, 6′b, 6′a, 6′b), 6.71 (0.5H, d, *J*=2.0 Hz, 2′a), 6.59 (0.5H, d, *J*=8.5 Hz, 5′a), 6.38 (0.5H, dd, *J*=2.0, 8.5 Hz, 6′a), 6.22 (0.5H, s, 6D), 6.19 (0.5H, d, *J*=2.2 Hz, 8A), 6.15 (0.5H, d, *J*=2.4 Hz, 8A), 6.10 (0.5H, d, *J*=2.4 Hz, 6A), 6.01 (0.5H, d, *J*=2.2 Hz, 6A), 5.97 (0.5H, s, 6D), 5.83 (0.5H, dd, *J*=9.1, 10.0 Hz, 3Ca), 5.80 (0.5H, dd, *J*=9.1, 10.0 Hz, 3Cb), 5.83 (0.5H, dd, *J*=9.1, 10.0 Hz, 3Ca), 5.16–5.07 (3.5H, m, Bn), 5.10 (0.5H, ddd, *J*=5.6, 7.8, 9.1, 10.0 Hz, 3Fb), 5.09–4.91 (8.5H, m, Bn), 4.98 (0.5H, d, *J*=9.1 Hz, 3Fb), 4.91 (0.5H, d, *J*=9.1 Hz, 2b), 4.83–4.77 (1H, m, Bn), 4.82 (0.5H, ddd, *J*=3.7, 8.8, 9.0 Hz, 3Fa), 4.74–4.68 (1H, m, Bn), 4.67–4.61 (1H, m, Bn), 4.644 (0.5H, d, *J*=10.0 Hz, 4Ca), 4.638 (0.5H, d, *J*=10.0 Hz, 4Cb), 4.57–4.51 (1H, m, Bn), 3.63 (0.5H, d, *J*=8.8 Hz, 2Fa), 3.01 (0.5H, dd, *J*=3.7, 16.4 Hz, 4Faα), 2.98 (0.5H, dd, *J*=5.6, 16.6 Hz, 4Fbα), 2.70 (0.5H, dd, *J*=7.8, 16.6 Hz, 4Fbβ), 2.38 (0.5H, dd, *J*=9.0, 16.4 Hz, 4Faβ),1.83 (1.5H, s, $CH_3$), 1.75 (1.5H, s, $CH_3$), 1.57 (1.5H, s, $CH_3$), 1.53 (1.5H, s, $CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$, 1(a):1(b) mixture of rotational isomers) 170.2, 169.6, 169.1, 169.0, 158.2, 158.1, 157.7, 157.6, 156.9, 156.7, 156.6, 156.0, 155.5, 155.4, 153.6, 152.8, 149.0, 148.93, 148.90, 148.87, 148.78 (×2), 148.6, 148.5, 138.0, 137.4, 137.30 (×2), 137.27 (×3), 137.25 (×3), 137.19, 137.17, 137.03, 136.96, 136.90, 136.76, 131.7, 131.10, 131.05, 130.8, 128.60, 128.56 (×2), 128.54, 128.50, 128.43 (×4), 128.38 (×7), 128.33, 128.29, 128.15, 128.12 (×2), 127.96, 127.91 (×3), 127.80, 127.77 (×2), 127.73, 127.71, 127.69, 127.63 (×3), 127.5 (×3), 127.44, 127.41 (×2), 127.30 (×4), 127.26 (×2), 127.0, 126.8, 121.2, 120.9, 120.3, 120.2, 114.72, 114.69, 114.60, 114.2 (×2), 114.0, 113.9, 113.6, 110.9, 110.7, 108.3, 108.1, 102.1, 101.5, 94.8 (×2), 94.5, 94.3, 91.3, 90.9, 80.1, 79.9, 77.9, 77.6, 77.2 (×2), 73.0, 72.8, 71.5, 71.4, 71.3, 71.2 (×3), 71.1, 71.0, 70.3, 70.0 (×3), 69.9, 69.8 (×2), 69.6, 35.1, 29.7, 26.4, 25.1, 20.9, 20.8, 20.7, 20.5.

**4.2.7. [4,8]-2,3-*trans*-3,4-*cis*:2,3-*trans*-Octa-*O*-benzyl-3,3′-di-*O*-acetyl-bi-(+)-catechin. (4β)-4.** Acetylation according to the above procedure using 22 mg of (4β)-**2** (0.017 mmol) in pyridine (4 mL), acetic anhydride (16 μL, 0.17 mmol), 4-(dimethylamino)pyridine (0.5 mg) afforded 23 mg (98%) of the (4β)-**4** as a colorless amorphous; $[\alpha]_D^{27}=+110$ (*c* 0.36, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$, 2:1 mixture of rotational isomers) major isomer: 7.46–7.19 (22.44H, m, Bn), 7.18–7.01 (3.96H, m, Bn), 6.94 (0.66H, dd, *J*=1.9, 8.3 Hz, 6′), 6.92 (0.66H, d, *J*=1.9 Hz, 2′), 6.84 (0.66H, d, *J*=8.3 Hz, 5′), 6.83 (0.66H, dd, *J*=1.7 Hz, 2′), 6.78 (0.66H, d, *J*=8.3 Hz, 5′), 6.56 (0.66H, dd, *J*=1.7, 8.3 Hz, 6′), 6.28 (0.66H, s, 6D), 6.03 (0.66H, dd, *J*=2.2 Hz, 8A), 5.58 (0.66H, dd, *J*=6.4, 10.0 Hz, 3C), 5.46 (0.66H, d, *J*=2.2 Hz, 6A), 5.39 (0.66H, d, *J*=10.0 Hz, 2C), 5.16 (0.66H, d, *J*=6.4 Hz, 4C), 5.14 (0.66H, ddd, *J*=6.6, 8.6, 8.8 Hz, 3F), 5.12–4.82 (6.60H, m, Bn), 4.81 (0.66H, d, *J*=11.9 Hz, Bn), 4.80 (1.32H, s, Bn), 4.74 (0.66H, d, *J*=11.9 Hz, Bn), 4.62 (0.66H, d, *J*=11.2 Hz, Bn), 4.54 (0.66H, d, *J*=11.2 Hz, Bn), 3.47 (0.66H, d, *J*=8.8 Hz, 2F), 3.23 (0.66H, dd, *J*=6.6, 16.9 Hz, 4Fα), 2.96 (0.66H, dd, *J*=8.6, 16.9 Hz, 4Fβ), 1.74 (1.98H, s, $CH_3$), 1.59 (1.98H, s, $CH_3$); minor isomer: 7.46–7.19 (11.56H, m, Bn), 7.18–7.01 (2.04H, m, Bn), 6.91 (0.34H, d, *J*=1.9 Hz, 2′), 6.91 (0.34H, d, *J*=8.1 Hz, 5′), 6.90 (0.34H, dd, *J*=1.9, 8.1 Hz, 6′), 6.81 (0.34H, d, *J*=1.7 Hz, 2′), 6.76 (0.34H, dd, *J*=1.7, 8.5 Hz, 6′), 6.58 (0.34H, d, *J*=8.5 Hz, 5′), 6.22 (0.34H, s, 6D), 6.12 (0.34H, d, *J*=2.2 Hz, 8A), 5.96 (0.34H, d, *J*=2.2 Hz, 6A), 5.53 (0.34H, dd, *J*=6.3, 10.0 Hz, 3C), 5.34 (0.34H, d, *J*=10.0 Hz, 2B), 5.12 (0.34H, d, *J*=6.3 Hz, 4C), 5.12–4.82 (4.76H, m, Bn), 5.03 (0.34H, ddd, *J*=5.3, 6.6, 10.0 Hz, 3F), 4.88 (0.34H, d, *J*=10.0 Hz, 2F), 4.71 (0.34H, d, *J*=12.2 Hz, Bn), 4.36 (0.34H, d, *J*=12.2 Hz, Bn), 2.93 (0.34H, dd, *J*=5.3, 16.8 Hz, 4Fα), 2.76 (0.34H, dd, *J*=6.6, 16.8 Hz, 4Fβ), 1.92 (1.02H, s, $CH_3$), 1.67 (1.02H, s, $CH_3$);

$^{13}$C NMR (100 MHz, $CDCl_3$, 2:1 mixture of rotational isomers) major isomer: 169.9, 169.4, 158.4, 157.5, 156.2, 155.9, 155.8, 154.5, 149.0, 148.9 (×2), 148.5, 137.4, 137.3, 137.2 (×2), 137.1, 137.0 (×3), 131.9, 130.8, 128.7, 128.43 (×4), 128.38 (×3), 128.2, 128.1, 127.7 (×2), 127.6, 127.51 (×2), 127.47 (×2), 127.31 (×3), 127.29 (×3), 127.0, 121.2, 120.1, 114.8, 114.2, 114.0, 112.6, 110.0, 105.3, 103.8, 93.5, 92.8, 91.9, 79.3, 77.4, 77.3, 75.8, 71.6, 71.3, 71.2, 70.5, 70.0, 69.9, 69.7, 69.4, 31.1, 26.8, 20.8 (×2); minor isomer: 170.1, 169.2, 158.5, 157.6, 156.9, 156.0, 155.9, 153.4, 149.2, 148.9, 148.8, 148.6, 137.5, 137.4, 137.3 (×2), 137.2 (×2), 137.1, 137.0, 131.8, 131.1, 128.6, 128.5, 128.42 (×2), 128.38 (×2), 128.35, 128.3, 128.05, 128.00, 127.9, 127.8, 127.7, 127.6, 127.51 (×2), 127.47, 127.31, 127.29 (×2), 127.25, 127.19, 127.0, 126.6, 121.1, 119.5, 114.8 (×2), 114.2, 113.3, 109.4, 105.8, 101.2, 94.2, 93.2, 92.1, 78.5, 77.6, 76.9, 75.9, 71.6, 71.2, 71.0, 70.3, 69.9, 69.8, 69.5, 69.3, 29.7, 24.1, 21.1, 20.7.

### 4.3. Synthesis of procyanidin-B3

**4.3.1. [4,8]-2,3-*trans*-3,4-*trans*:2,3-*trans*-Octa-*O*-benzyl-bi-(+)-catechin. (4α)-2.** A solution of (4α)-**3** and (4β)-**3** (0.99 g, 0.74 mmol, 97% de) and KCN (0.97 g, 14.8 mmol, 20 equiv.) in 95% EtOH (30 mL) was refluxed for 24 h. The cooled reaction mixture was concentrated, and the residue was dissolved in EtOAc. The organic phase was washed successively with water, sat. $NH_4Cl$, water and brine, dried over $Na_2SO_4$. After filtration and concentration of the eluent, (4β)-**2** was removed by silica gel column chromatography ($CH_2Cl_2$/EtOAc, 60/1–30/1) as the first fraction and 0.95 g of (4α)-**2** (98%) was obtained from the second fraction: $[\alpha]_D^{24}=-119$ (*c* 1.32, $CHCl_3$) {lit.[12] $[\alpha]_D^{30}=-102.9$ (*c* 1.9, $CHCl_3$)}.

**4.3.2. [4,8]-2,3-*trans*-3,4-*trans*:2,3-*trans*-Bi-(+)-catechin, procyanidin-B3. (4α)-1.** A solution of (4α)-**2** (0.23 g, 0.18 mmol) in THF/MeOH/$H_2O$, 20/1/1 was hydrogenated over 20% $Pd(OH)_2$/C (10 mg) for 12 h at rt. Filtration and concentration afforded a pale brown oil, which was purified by Sephadex® LH-20 column chromatography (MeOH) and normal phase HPLC (KANTO CHEMICAL CO., Mightysil Si 60, AcOEt) to give 65 mg of pure procyanidin-B3 (4α)-**1** (63%) as an amorphous solid. $[\alpha]_D^{24}=-221$ (*c* 0.38, EtOH) {lit.[19] $[\alpha]_{578}^{20}=-244.7$ (*c* 2.0, EtOH)}: $^1$H NMR (400 MHz, $CD_3OD$, 2:1 mixture of rotational isomers) major isomer: 6.73 (0.71H, d, *J*=2.0 Hz), 6.67 (0.71H, d, *J*=8.3 Hz), 6.66 (0.71H, d, *J*=8.0 Hz), 6.58 (0.71H, d, *J*=2.0 Hz), 6.46 (0.71H, dd, *J*=2.0, 8.0 Hz), 6.25 (0.71H, dd, *J*=2.0, 8.3 Hz), 6.06 (0.71H, s), 5.88 (0.71H, d, *J*=2.2 Hz), 5.78 (0.71H, d, *J*=2.2 Hz), 4.57 (0.71H, d, *J*=7.6 Hz), 4.40 (0.71H, d, *J*=7.8 Hz), 4.34 (0.71H, dd, *J*=7.8, 9.8 Hz), 4.25 (0.71H, d, *J*=9.8 Hz), 3.78 (0.71H, ddd, *J*=5.6, 7.6, 8.0 Hz), 2.75 (0.71H, dd, *J*=5.6, 16.3 Hz), 2.48 (0.71H, dd, *J*=8.1, 16.3 Hz); minor isomer δ: 6.95 (0.58H, d, *J*=2.0 Hz), 6.83 (0.29H, dd, *J*=2.0, 8.0 Hz), 6.82 (0.29H, dd, *J*=2.0, 8.0 Hz), 6.75 (0.58H, dd, *J*=2.0, 8.0 Hz), 5.93 (0.29H, s), 5.83 (0.29H, d, *J*=2.5 Hz), 5.80 (0.29H, d, *J*=2.5 Hz), 4.74 (0.29H, d, *J*=7.1 Hz), 4.40 (0.29H, d, *J*=7.8 Hz), 4.34 (0.29H, dd, *J*=7.8, 9.8 Hz), 4.25 (0.29H, d, *J*=9.8 Hz), 4.06 (0.29H, ddd, *J*=5.4, 7.1, 7.8 Hz), 2.81 (0.29H, dd, *J*=5.4, 16.3 Hz), 2.57 (0.29H, dd, *J*=7.8, 16.3 Hz); $^1$H NMR (400 MHz, acetone-$d_6$, 1:1 mixture of rotational isomers) 8.50–7.49 (3H, br, OH), 8.08 (2H, br, OH), 7.91 (2H, brs, OH), 7.49 (1H, brs, OH), 6.95 (0.5H, d, *J*=1.7 Hz), 6.94 (0.5H, d, *J*=1.7 Hz), 6.83 (0.5H, dd, *J*=1.7, 8.3 Hz), 6.79 (0.5H, dd, *J*=1.7, 8.3 Hz), 6.74 (0.5H, d, *J*=8.3 Hz), 6.72 (0.5H, d, *J*=8.3 Hz), 6.72 (0.5H, d, *J*=2.0 Hz), 6.64 (0.5H, d, *J*=8.0 Hz), 6.62 (0.5H, d, *J*=8.0 Hz), 6.59 (0.5H, d, *J*=2.0 Hz), 6.45 (0.5H, dd, *J*=2.0, 8.0 Hz), 6.23 (0.5H, dd, *J*=2.0, 8.0 Hz), 6.13 (0.5H, s), 5.99 (0.5H, s), 5.88 (0.5H, d, *J*=2.2 Hz), 5.81 (0.5H, d, *J*=2.4 Hz), 5.79 (0.5H, d, *J*=2.2 Hz), 5.77 (0.5H, d, *J*=2.4 Hz), 4.67 (0.5H, d, *J*=7.6 Hz), 4.52–4.47 (1.5H, m), 4.41 (0.5H, d, *J*=7.6 Hz), 4.27–4.24 (1H, m), 4.23 (0.5H, d, *J*=9.5 Hz), 4.05–3.99 (0.5H, m), 3.93 (0.5H, brs, OH), 3.87 (0.5H, brs, OH), 3.79 (1H, m), 3.61 (0.5H, brs, OH), 2.84 (0.5H, dd, *J*=5.4, 16.3 Hz), 2.76 (0.5H, dd, *J*=5.6, 16.3 Hz), 2.56 (0.5H, dd, *J*=8.0, 16.3 Hz), 2.47 (0.5H, dd, *J*=8.0, 16.3 Hz); $^{13}$C NMR (100 MHz, $CD_3OD$, 2:1 mixture of rotational isomers) major isomer: 158.62, 157.1 (×2), 155.9, 155.7, 154.9, 146.11, 146.05, 145.8, 145.46, 132.6, 131.9, 120.6, 119.9, 116.4, 116.21, 116.05, 115.5, 108.1, 107.2, 102.2, 97.3, 96.8, 96.0, 84.0, 82.5, 73.70, 68.9, 38.6, 28.8; minor isomer 159.94, 157.4, 157.3, 155.9, 155.8, 155.0, 146.4, 146.11, 145.6, 145.46, 132.4, 132.2, 121.0, 120.2, 120.2, 116.15 (×2), 115.9, 115.2, 108.3, 107.1, 100.5, 97.5, 97.5, 96.2, 84.1, 83.0, 73.70, 68.6, 38.6, 28.7; $^{13}$C NMR (100 MHz, acetone-$d_6$, 1:1 mixture of rotational isomers) 158.7, 158.5, 157.4, 157.2, 157.1, 157.0, 155.5, 155.5, 155.3, 155.0, 154.9, 154.69, 145.71 (×2), 145.6, 145.5, 145.4, 145.2, 145.0, 144.9, 132.6, 132.5, 131.8, 131.5, 120.8, 120.5, 120.1, 119.6, 116.1, 115.9, 115.7, 115.7, 115.6, 115.5, 115.3, 115.1, 107.7 (×2), 106.5, 106.1, 102.4, 100.7, 97.5, 97.2, 97.0, 96.7, 96.14, 96.09, 83.8, 83.6, 83.1, 82.3, 73.3, 73.1, 68.4, 68.1, 38.2, 38.0, 29.0, 28.8.

**4.3.3. [4,8]-2,3-*trans*-3,4-*cis*:2,3-*trans*-Bi-(+)-catechin, (4β)-1.** Hydrogenation according to the above procedure using 19 mg of (4β)-**2** (0.015 mmol) in THF/MeOH/$H_2O$, 20/1/1 (1.0 mL) afforded 6 mg (67%) of the (4β)-**1** as a colorless amorphous solid: $[\alpha]_D^{27}=+31.7$ (*c* 0.10, EtOH); $^1$H NMR (400 MHz, acetone-$d_6$) 8.13 (2H, brs, OH), 8.10–7.50 (6H, br, OH), 7.09 (1H, brs), 6.83 (2H, brs), 6.72 (2H, brs), 6.61 (2H, brs), 6.02 (1H, brs), 5.88 (1H, brs), 5.05 (1H, d, *J*=7.1 Hz), 4.82 (1H, d, *J*=4.9 Hz), 4.20 (1H, brs), 4.07 (1H, brs), 4.01 (1H, brs), 2.86–2.83 (1H, m), 2.57 (1H, dd, *J*=7.1, 13.9 Hz); $^{13}$C NMR (100 MHz, acetone-$d_6$) 157.9, 157.0, 156.8, 155.7 (×2), 155.2, 145.5, 145.4 (×2), 145.3, 132.5, 131.8, 119.8, 119.5, 115.72, 115.65, 115.0, 114.9, 108.1, 105.4, 101.0, 97.5, 96.1, 95.8, 82.7, 79.2, 72.2, 67.9, 39.4, 28.5.

**4.3.4. [4,8]-2,3-*trans*-3,4-*trans*:2,3-*trans*-Deca-*O*-acetyl-bi-(+)-catechin. (4α)-5.** A pyridine solution (3 mL) of (4α)-**1** (10 mg, 0.017 mmol), acetic anhydride (49 μL, 0.52 mmol), was stirred at room temperature for 2 h, and the reaction mixture was quenched by adding sat. aqueous $NH_4Cl$ solution (5 mL). The mixture was extracted with EtOAc (20 mL×3), and the combined organic layers were washed with brine, dried ($Na_2SO_4$), filtered, then concentrated under reduced pressure. The residue was purified by preparative TLC (hexane/EtOAc, 1/1) to give 13 mg of (4α)-**5** (77%) as a colorless oil; $[\alpha]_D^{28}=-117$ (*c* 0.12, $CHCl_3$) {lit.[12] $[\alpha]_D^{30}=-102$ (*c* 0.51, $CHCl_3$)}; $^1$H NMR (400 MHz $CDCl_3$) 7.14 (1H, d, *J*=8.3 Hz), 7.12 (1H, d,

$J$=8.5 Hz), 7.02 (1H, d, $J$=1.9 Hz), 6.95 (1H, dd, $J$=1.9, 8.3 Hz), 6.92 (1H, d, $J$=2.0 Hz), 6.72 (1H, dd, $J$=2.0, 8.5 Hz), 6.64 (1H, s), 6.50 (1H, d, $J$=2.4 Hz), 6.48 (1H, d, $J$=2.4 Hz), 5.63 (1H, dd, $J$=9.3, 10.0 Hz), 5.03 (1H, dt, $J$=5.6, 7.8 Hz), 4.96 (1H, d, $J$=7.8 Hz), 4.76 (1H, d, $J$=10.0 Hz), 4.48 (1H, d, $J$=9.3 Hz), 2.93 (1H, dd, $J$=5.6, 16.5 Hz), 2.66 (1H, dd, $J$=7.8, 16.5 Hz), 2.34 (3H, s), 2.28 (3H, s), 2.27 (3H, s), 2.259 (3H, s), 2.257 (3H, s), 2.255 (3H, s), 2.24 (3H, s), 1.97 (3H, s), 1.93 (3H, s), 1.64 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$) 170.0, 169.1, 168.7, 168.51, 168.48, 168.1, 168.0, 167.9, 167.8 (×2), 155.9, 152.7, 149.5, 149.0, 147.9, 147.5, 142.1, 142.0, 141.50, 141.45, 135.2, 135.2, 125.0, 124.5, 123.5, 123.4, 122.7, 121.9, 116.9, 115.1, 111.5, 110.1, 109.5, 108.2, 78.9, 78.0, 70.4, 68.4, 36.6, 25.7, 21.1, 20.89, 20.86, 20.8, 20.7, 20.62, 20.58 (×2), 20.5, 20.3; FAB-MS ($m/z$) 1022 (6), 1021 ([M+Na]$^+$, 9), 100 (0.8), 999 ([M+H]$^+$, 1.3), 738 (11).

**4.3.5. [4,8]-2,3-*trans*-3,4-*cis*:2,3-*trans*-Deca-*O*-acetyl-bi-(+)-catechin. (4β)-5.** Acetylation according to the above procedure using 5 mg of (4β)-**2** (0.0086 mmol) in pyridine (2 mL), acetic anhydride (24 μL, 0.26 mmol), 4-(dimethylamino)pyridine (0.5 mg) afforded 8.2 mg (95%) of the (4β)-**5** as a colorless oil; $[\alpha]_D^{28}$=+154 ($c$ 0.14, $CHCl_3$) {lit.[12] $[\alpha]_D^{30}$=+131.3 ($c$ 1.4, $CHCl_3$)}; $^1$H NMR (400 MHz, $CDCl_3$) 7.29 (1H, dd, $J$=2.0, 8.3 Hz), 7.193 (1H, d, $J$=2.0 Hz), 7.192 (1H, d, $J$=8.3 Hz), 7.08 (1H, d, $J$=8.3 Hz), 6.98 (1H, dd, $J$=2.0, 8.3 Hz), 6.67 (1H, s), 6.29 (1H, d, $J$=2.4 Hz), 5.95 (1H, d, $J$=2.4 Hz), 5.33 (1H, dd, $J$=6.6, 10.2 Hz), 5.27 (1H, d, $J$=10.2 Hz), 5.12 (1H, ddd, $J$=6.6, 9.0, 9.5 Hz), 4.71 (1H, d, $J$=6.6 Hz), 4.38 (1H, d, $J$=9.5 Hz), 3.19 (1H, dd, $J$=6.6, 16.6 Hz), 2.59 (1H, dd, $J$=9.0, 16.6 Hz), 2.29 (3H, s), 2.28 (3H, s), 2.27 (3H, s), 2.25 (3H, s), 2.24 (3H, s), 2.20 (3H, s), 2.11 (3H, s), 1.89 (3H, s), 1.85 (3H, s), 1.78 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$) 170.0, 169.9, 169.2, 168.8, 168.4, 168.3, 168.1, 168.0, 167.8, 167.8, 155.4, 153.9, 149.6, 148.3, 148.2, 147.8, 142.3, 142.2, 141.8, 141.7, 136.3, 134.6, 125.4, 125.3, 123.4, 123.2, 123.1, 122.3, 115.6, 113.3, 112.8, 110.0, 109.0, 107.2, 78.2, 74.7, 71.1, 68.4, 32.4, 27.1, 21.0, 20.8 (×2), 20.7 (×2), 20.64 (×2), 20.56, 20.3, 20.1.

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