Synthesis of Bisflavanol-Type Natural Products and Their Analogues via Self-Coupling of C8-Methylol Catechin Derivatives

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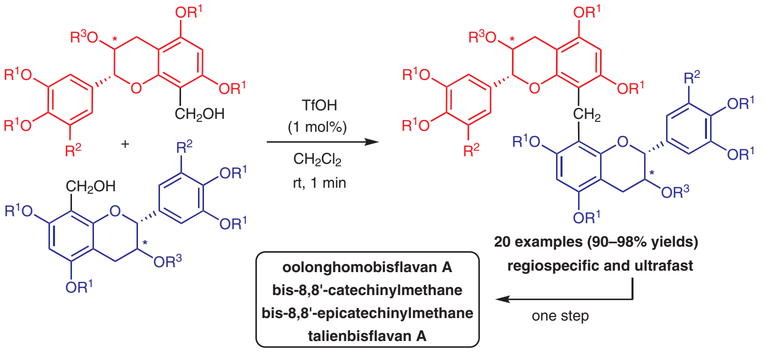


Received: 13.01.2019
Accepted after revision: 25.03.2019

DOI: 10.1055/s-0037-1610707; Art ID: ss-2019-f0023-op

Abstract A highly efficient and regioselective self-coupling of C8-methylol catechin derivatives is developed for the synthesis of dimeric flavanol analogues under metal-free and mild conditions. Its applicability is showcased by the efficient synthesis of bisflavanol-type natural products bis-8,8′-catechinylmethane, bis-8,8′-epicatechinylmethane, talienbisflavan A, and oolonghomobisflavan A. The novel self-coupling mechanism sheds new light on the classical Friedel–Crafts alkylation mechanism in acid-catalyzed catechin–formaldehyde condensation.

Key words bis-flavanol, catechin, self-coupling, metal-free, regioselective

Catechins are a group of flavan-3-ols including (+)-catechin, (–)-epicatechin, (–)-epigallocatechin, (–)-epicatechin gallate, and (–)-epigallocatechin gallate. Catechins are widely distributed throughout the plant kingdom and they are found widely in a number of foods[1] that possess various important biological effects such as antioxidant,[2] antibacterial,[3] antiarteriosclerotic,[4] and anticancer properties.[5] Dimeric flavanols are a class of polyphenols in which catechins are linked through a methylene bridge. Bisflavanol-type natural products, such as bis-8,8′-catechinylmethane (**1**), bis-8,8′-epicatechinylmethane (**2**), talienbisflavan A (**3**), and oolonghomobisflavan A (**4**) were isolated from cacao liquor,[6] *Litchi chinensis*,[7] *Camellia taliensis*[8] and oolong tea,[9] respectively (Figure 1). These flavan-3-ol dimers bear catechol and/or pyrogallol groups, and show stronger radical scavenging activities and lipase inhibition activities than catechin monomers.[8,10] Unfortunately, no comprehensive study of the biological or pharmaceutical activities of these dimeric compounds have been developed because of a lack of efficient synthetic methods and because these compounds are difficult to identify and isolate from natural products. Thus, it is highly desirable to develop a general and efficient strategy for the synthesis of these dimeric flavanol derivatives.

It was reported that bisflavanol-type natural products are synthetically accessible from two catechin derivatives by using an aldehyde or acid as the linchpin. Ducrot reported an elegant synthesis of bis-8,8′-catechinylmethane (**1**) from penta-*O*-benzyl 8-formyl-catechin (**5**) and catechin (**6**) by using an aromatic aldehyde as the linchpin (Scheme 1a).[11] However, bis-8,6′-catechinylmethane (**7**) and bis-8,8′-catechinylmethane (**1**) were obtained in low yields with a poor C8-C8′/C8-C6′ regioselectivity. Selenski developed a trifluoroacetic anhydride catalyzed regioselective synthesis of deca-*O*-benzyl bis-8,8′-catechinylmethane (**10b**) from penta-*O*-benzyl catechin-8-carboxylic acid (**8**) and penta-*O*-benzyl catechin (**9b**) using an aromatic acid as the linchpin (Scheme 1b).[12] Compared with these indirect synthetic protocols, the condensation of catechin with formaldehyde seems to be a more simple and straightforward method for the preparation of methylene-linked flavanol dimers. Indeed, catechin–formaldehyde condensation has been widely studied in the field of wood adhesives[13] and HCHO scavengers,[14] which affords mainly the complex higher oligomer mixtures. The reaction mechanism is widely accepted as an aldol-type reaction via a C8-methylol catechin intermediate.[13,14c] Recently, we reported a $Hf(OTf)_4$-catalyzed catechin–formaldehyde condensation for the synthesis of octa-*O*-benzyl dimeric flavanol (**10a**) from tetra-*O*-benzyl catechin (**9a**) using paraformaldehyde as the linchpin (Scheme 1c).[15] However, the use of expensive and toxic transition-metal limited its application potential in large-scale preparation. Moreover, this synthetic strategy was limited to the tetra-*O*-benzyl substrates. The condensation of less bulky tetra-*O*-methyl catechin derivatives with paraformaldehyde resulted in regioselectivity issues and poly-

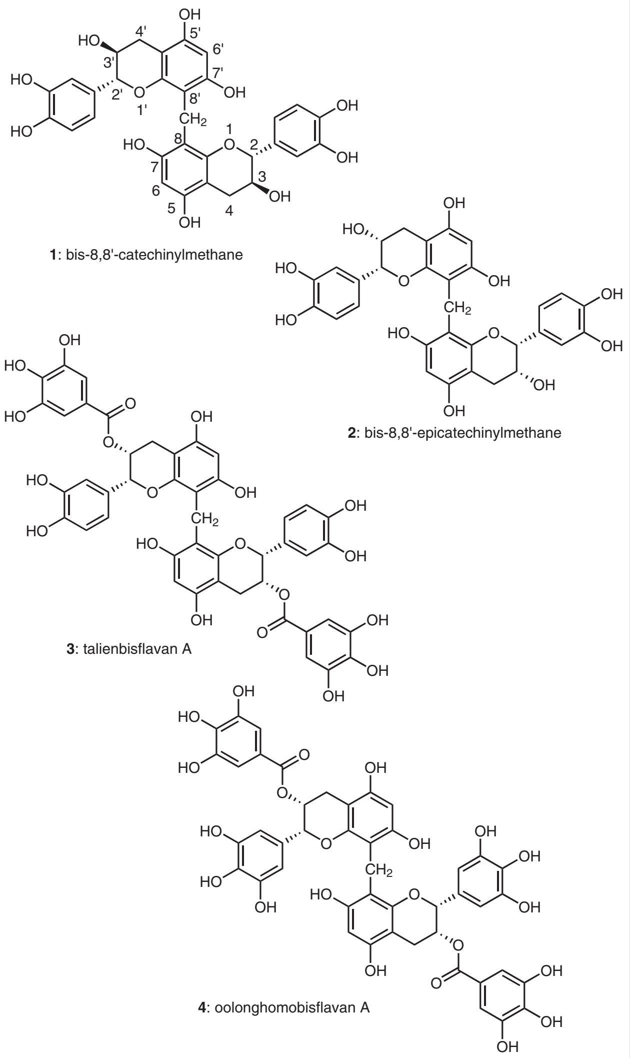
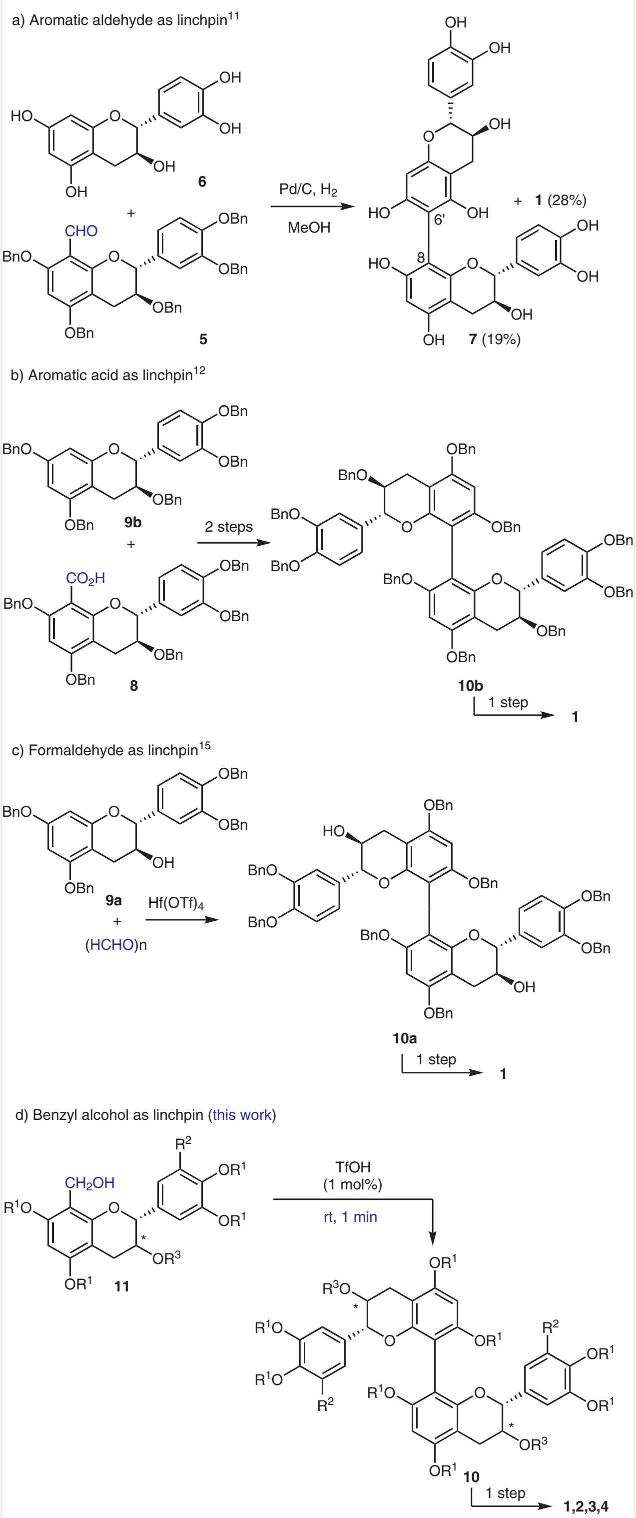


Figure 1 Bisflavanol-type natural products **1**–**4**

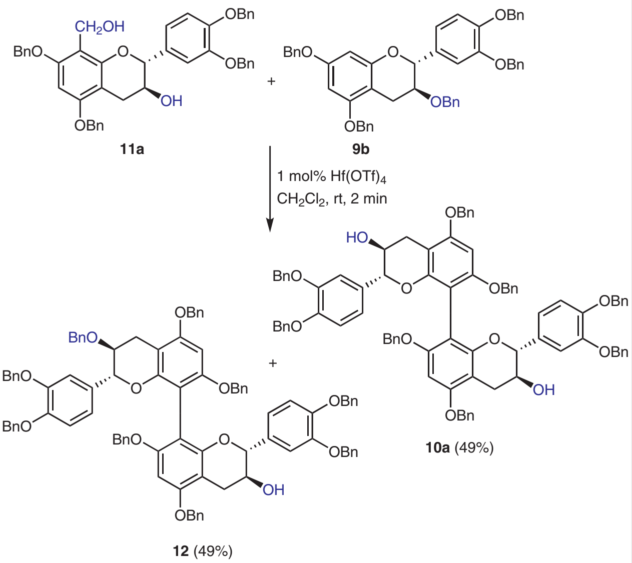


Scheme 1 Synthesis of bisflavanol-type natural products

merization (see Supporting Information for control experiments). In this context, the development of a practical direct C8–C8′ coupling strategy for the regioselective synthesis of bisflavanol-type natural products becomes a high priority. Herein, we would like to report a highly efficient and regioselective synthesis of these dimeric flavanol analogues via a TfOH-catalyzed direct C8–C8′ self-coupling of C8-methylol catechin derivatives **11** using benzyl alcohols as the linchpins (Scheme 1d). The newly developed strategy was then used for the synthesis of bisflavanol-type natural products bis-8,8′-catechinylmethane (**1**), bis-8,8′-epicatechinylmethane (**2**), talienbisflavan A (**3**), and oolonghomobisflavan A (**4**).

Inspired by the previous reports that C8-methylol catechin can undergo Friedel–Crafts alkylation reaction with catechin to provide a symmetrical dimeric flavanol,[13–15] we envisioned that an unsymmetrical dimeric flavanol might be obtained through the use of a C8-methylol catechin and another catechin as the substrates. To probe the feasibility of this hypothesis, the Friedel–Crafts alkylation reaction of

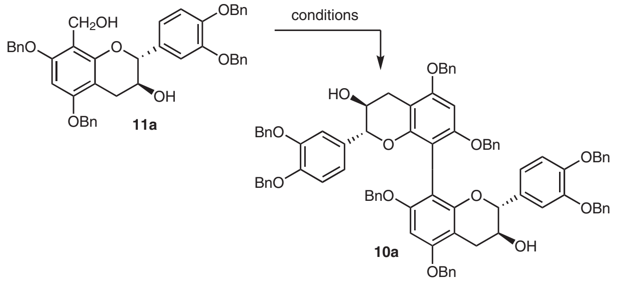
8-methylol tetra-*O*-benzyl catechin (**11a**) with penta-*O*-benzyl catechin (**9b**) was investigated. Surprisingly, an unexpected symmetrical deca-*O*-bis-8,8′-catechinylmethane (**10a**) and the desired unsymmetrical nona-*O*-bis-8,8′-catechinylmethane (**12**) were obtained in 49% and 49% yields, respectively, within 2 minutes in the presence of 1 mol% of $Hf(OTf)_4$ (Scheme 2). Besides the Friedel–Crafts alkylation of 8-methylol tetra-*O*-benzyl catechin (**11a**) with penta-*O*-benzyl catechin (**9b**), a unique direct C8–C8′ self-coupling of 8-methylol tetra-*O*-benzyl catechin (**11a**) took place and thereby resulted in the unexpected deca-*O*-bis-8,8′-catechinylmethane **10a**. Considering the importance of dimeric flavanols in the field of biology and pharmaceutical sciences,[8,10] this unexpected result prompted us to optimize the reaction conditions for the synthesis of dimeric flavanol derivatives.



Scheme 2 Unexpected formation of deca-*O*-bis-8,8′-catechinylmethane (**10a**)

8-Methylol tetra-*O*-benzyl catechin (**11a**) was used as a representative substrate for evaluating the reaction conditions; selected results are shown in Table 1. Treatment of **11a** in the presence of a catalytic amount of acetic acid (CH_3CO_2H, 10 mol%) or aqueous phosphoric acid (H_3PO_4, 10 mol%) in dichloromethane (CH_2Cl_2) at room temperature for 10 min, did not lead to a reaction, and the starting material **11a** was recovered (entries 1 and 2). Gratifyingly, aqueous hydrochloric acid (HCl, 10 mol%), concentrated nitric acid (HNO_3, 10 mol%), concentrated sulfuric acid (H_2SO_4, 10 mol%), and trifluoroacetic acid (CF_3CO_2H, 10 mol%) displayed some efficiency for this reaction. Treatment of **11a** with these Brønsted acids afforded **10a** in 30–65% yields (entries 3–6). The C8–C6′ linked regioisomers were not observed, and the main side products were the dibenzyl ethers derived from the dehydration reaction between two C8-methylol *O*-benzyl catechins. To our delight, methanesulfonic acid ($MeSO_3H$, 2 mol%), *p*-toluenesulfonic acid (*p*-TsOH, 2 mol%), and 10-camphorsulfonic acid (CSA; 2 mol%) were quite effective for this reaction, which afforded **10a** in 80–86% yields (entries 7–9). Compound **10a** was obtained in 92% yield within 1 minute when the reaction was performed in the presence of 1 mol% of trifluoromethanesulfonic acid (TfOH; entry 10). Various Lewis acids were also investigated, which showed excellent efficiency for this reaction to give **10a** in 84–90% yields (entries 11–17). Among them, $FeCl_3$ was an effective promoter for this reaction (entry 13) and might be useful for a large-scale process. However, TfOH was chosen in our investigations because it led to the best yield. Furthermore, the excellent yield was

Table 1 Survey of Conditions for the Self-Coupling of 8-Methylol Tetra-*O*-benzyl catechin (**11a**)[a]



Entry	Promoter	Equiv	Time (min)	Yield (%)[b]
1	CH_3CO_2H	0.1	10	0
2	H_3PO_4 (85%, H_2O)	0.1	10	0
3	HCl (37%, H_2O)	0.1	3	30
4	HNO_3 (98%)	0.1	3	45
5	H_2SO_4	0.1	3	52
6	CF_3CO_2H	0.1	3	65
7	CH_3SO_3H	0.02	2	80
8	*p*-TsOH	0.02	2	82
9	CSA[c]	0.02	1	86
10	TfOH	0.01	1	92
11	$BiCl_3$	0.02	3	84
12	$InCl_3$	0.02	3	84
13	$FeCl_3$	0.02	3	85
14	$BF_3·Et_2O$	0.02	2.5	86
15	$Fe(OTf)_3$	0.01	2.5	87
16	$Hf(OTf)_4$	0.01	2.5	90
17	$Sc(OTf)_3$	0.01	2.5	90
18	TfOH	0.02	2	89

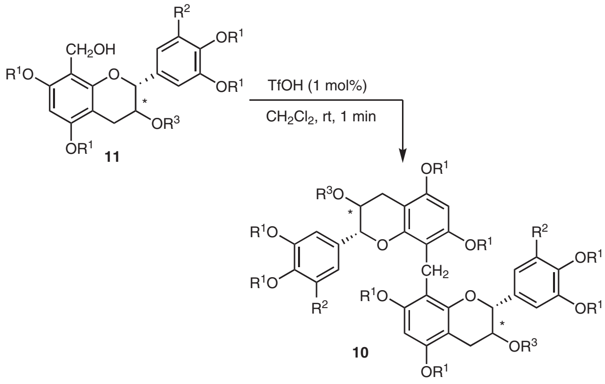
[a] General conditions: **11a** (50 μmol, 1.0 equiv), promoter (0.5–5 μmol, 0.01–0.1 equiv) in CH_2Cl_2 (c = 0.5 M) at room temperature for 1–10 min.
[b] Isolated yield.
[c] CSA = camphorsulfonic acid.
[d] Reaction was carried out at 1 g scale of **11a**.

maintained on scaling up the reaction using 1 gram of **11a** (entry 18).

The optimized reaction conditions proved to be effective for a wide range of C8-methylol catechin derivatives; representative results are listed in Table 2. *O*-Benzyl dimeric flavanols are ideal precursors for the synthesis of dimeric polyphenols because of the easy removal of the *O*-Bn protecting groups under hydrogenolysis conditions.[11,12,15] Thus, C8-methylol tetra-*O*-benzyl catechin derivatives **11a–l** were used as the substrates in this work (entries 1–12). With the 3-position bearing a hydroxyl, *O*-benzyl, *O*-acyl, *O*-MOM, *O*-propyl and *O*-benzoyl, self-coupling reaction of 8-methylol catechins **11a–f** proceeded well in dichloromethane in the presence of TfOH (1 mol%) at room temperature for 1 minute to give dimeric flavanol analogues **10a–f** in 92–98% yields (entries 1–6). Various C8-methylol *O*-benzyl (–)-epicatechin derivatives, such as 8-methylol tetra-*O*-benzyl (–)-epicatechin **11g**, 8-methylol penta-*O*-benzyl (–)-epicatechin **11h**, and 8-methylol hepta-*O*-benzyl (–)-epicatechin gallate **11i** went smoothly in the presence of TfOH to afford the dimers **10g–i** in 90–98% yields (entries 7–9). C8-Methylol *O*-benzyl (–)-epigallocatechin derivatives **11j–l** reacted equally well to give the desired products **10j–l** in 90–98% yields (entries 10–12). *O*-Alkylated catechins exhibit important biological activities,[16] but synthesis of *O*-alkyl dimeric flavanols is challenging. Happily, self-coupling of 8-methylol penta-*O*-alkyl catechin **11m–n** and 8-methylol 3-*O*-acetyl tetra-*O*-alkyl catechin **11o–q** proceeded favorably in the presence of TfOH in dichloromethane at room temperature to generate the dimeric products **10m–q** in 90–93% yields within 1 minute (entries 13–17). 8-Methylol *O*-alkyl epicatechin/epigallocatechin gallate derivatives **11r–t** were also investigated, which reacted equally well under the standard conditions to afford dimeric flavanols **10r–t** in 91–92% yields (entries 18–20). The regioselectivity was very high, and the potential C8–C6′ linked regioisomers were not observed.

The newly developed self-coupling strategy was used for the regioselective synthesis of bis-8,8′-catechinylmethane (**1**; Scheme 3). Tetra-*O*-benzyl catechin (**9a**) was prepared according to our previous report.[15] Treatment of **9a** with $POCl_3$ in *N*,*N*-dimethylformamide (DMF) at room temperature for 8 hours afforded 8-formyl 3-*O*-formyl tetra-*O*-benzyl catechin (**13**) in 87% yield.[17] Reduction of **13** with $LiBH_4$ in tetrahydrofuran (THF) at room temperature for 1 hour took place smoothly to provide 8-methylol tetra-*O*-benzyl catechin (**11a**) in 95% yield. The self-coupling of **11a** went smoothly in the presence of TfOH under mild conditions to afford octa-*O*-bis-8,8′-catechinylmethane (**10a**) in 92% yield. Removal of the eight *O*-Bn functions in **10a** under the hydrogenolysis conditions gave bis-8,8′-catechinylmethane (**1**) in 90% yield.

Table 2 Synthesis of Bisflavanol-Type Natural Product Analogues **10**[a]



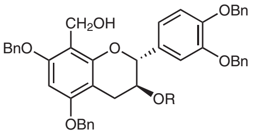
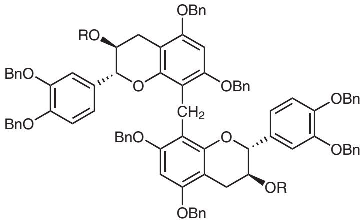
Entry	**11** (R)	Yield of **10** (%)
		
1	**11a** (H)	**10a**: 92
2	**11b** (Bn)	**10b**: 98

Table 2 (continued)

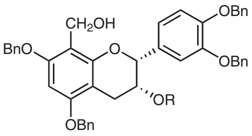
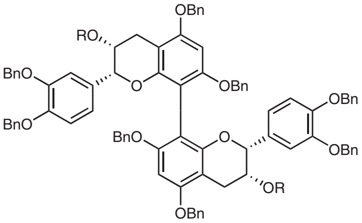
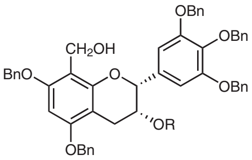
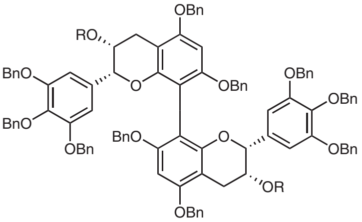
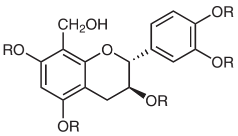
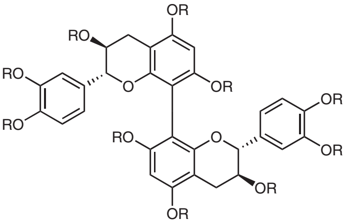
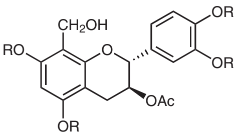
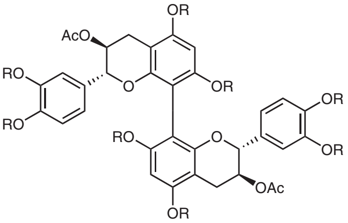
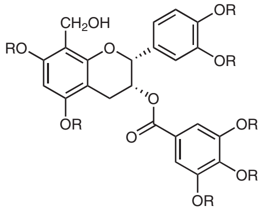
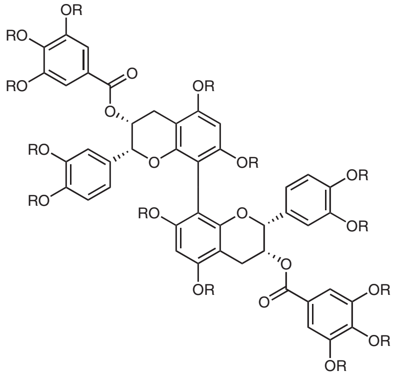
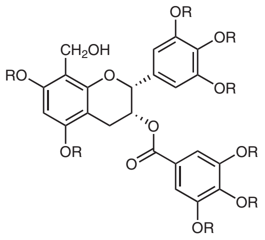
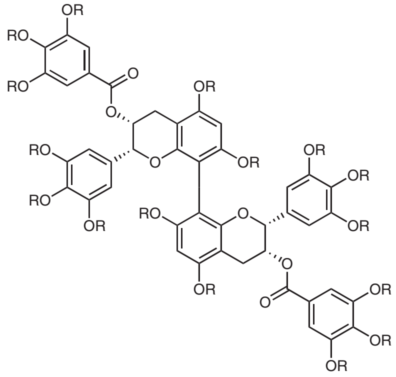
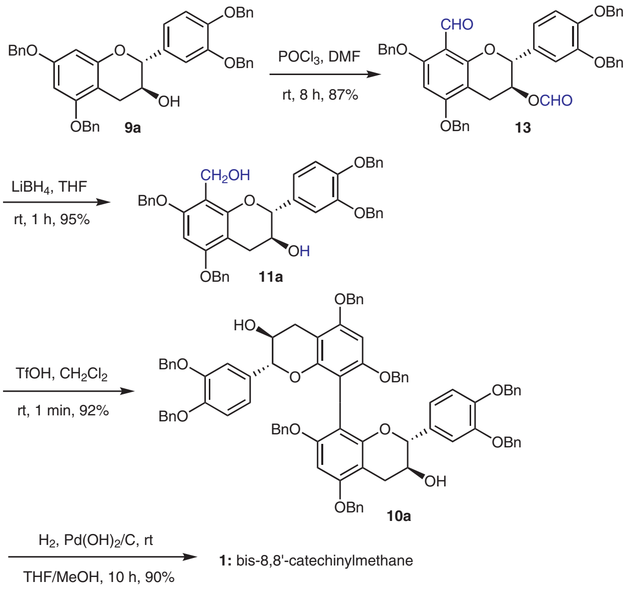
Entry	11 (R)	Yield of 10 (%)
3	**11c** (Ac)	**10c**: 98
4	**11d** (MOM)	**10d**: 98
5	**11e** (propyl)	**10e**: 93
6	**11f** (benzoyl)	**10f**: 98
		
7	**11g** (H)	**10g**: 98
8	**11h** (Bn)	**10h**: 91
9	**11i**(3,4,5-tribenzyloxygallate)	**10i**: 90
		
10	**11j** (H)	**10j**: 98
11	**11k** (Bn)	**10k**: 90
12	**11l**(3,4,5-tribenzyloxygallate)	**10l**: 97
		
13	**11m** (Me)	**10m**: 90
14	**11n** (Et)	**10n**: 91
		
15	**11o** (Me)	**10o**: 90
16	**11p** (Et)	**10p**: 91
17	**11q** (propargyl)	**10q**: 93
Entry	**11** (**R**)	Yield of **10**

Table 2 (continued)

Entry	**11** (R)	Yield of **10** (%)
		
18	**11r** (Me)	**10r**: 91
19	**11s** (propargyl)	**10s**: 92
		
20	**11t** (propargyl)	**10t**: 92

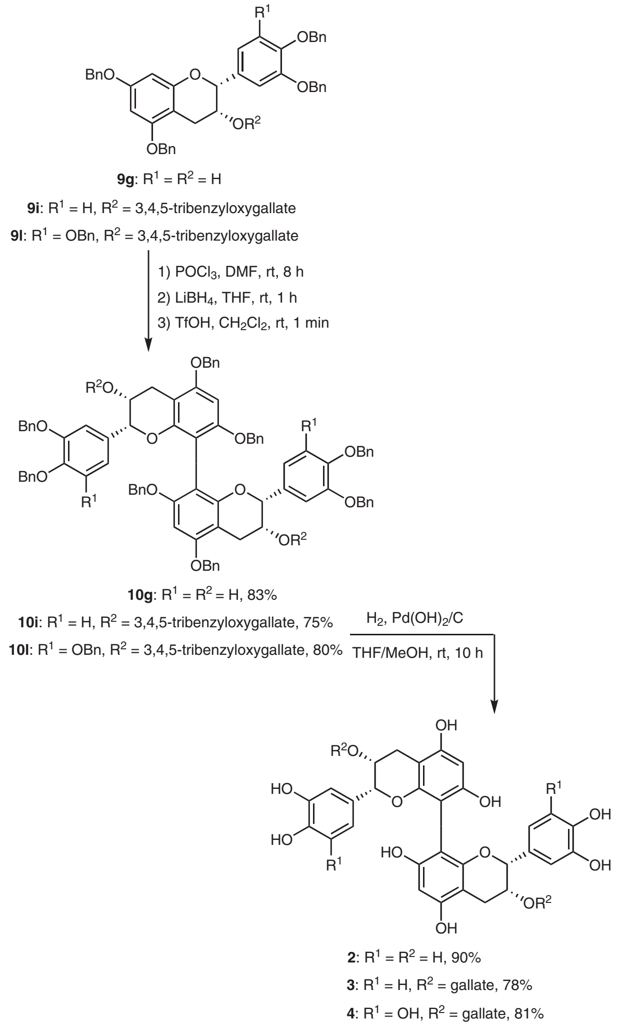
[a] General conditions: **11** (50 μmol, 1.0 equiv), promoter (0.5 μmol, 0.01 equiv) in CH_2Cl_2 (c = 0.5 M) at room temperature for 1 min. Isolated yields given.



Scheme 3 Synthesis of bis-8,8′-catechinylmethane (**1**)

The synthesis of bisflavanol-type natural products **2**–**4** is illustrated in Scheme 4. Tetra-*O*-benzyl epicatechin (**9g**), hepta-*O*-benzyl epicatechin gallate (**9i**), and octa-*O*-benzyl epigallocatechin gallate (**9l**) were prepared according to Chan's reports.[18] By following the procedure summarized in Scheme 3, *O*-benzyl dimeric flavanols **10g**, **10i**, and **10l** were synthesized from the corresponding benzylated catechin monomers **9g**, **9i**, and **9l** in 75–83% overall yields. Subsequent removal of the *O*-Bn functions under hydrogenolysis conditions afforded the desired natural products bis-8,8′-epicatechinylmethane (**2**), talienbisflavan A (**3**), and oolonghomobisflavan A (**4**) in 90, 78, and 81% yields, respectively (Scheme 4).

Acid-catalyzed *ipso*-substitutions on the benzene ring by a dealkylative coupling mechanism are rare,[19] but these could be observed in electron-transfer processes induced by a one-electron oxidant or anodic oxidation.[20] Although we are not able at this time to give the exact mechanism of the acid-catalyzed self-coupling of C8-methylol catechin deriv-



Scheme 4 Synthesis of bis-8,8′-epicatechinylmethane (**2**), talienbisflavan A (**3**), and oolonghomobisflavan A (**4**)

atives, a possible reaction pathway that may lead to dimeric flavanol analogues **10** is illustrated in Scheme 5. The reaction likely takes place through an electrophilic aromatic substitution mechanism rather than the electron-transfer chain mechanism. Acid-catalyzed cleavage of the benzylic C–O bond of C8-methylol catechin derivatives **11** generates the carbocation intermediates **14**,[19c,21] which undergo subsequent addition reaction with another **11** prompted by π–π stacking interactions to form the intermediates **15**. Finally, aromatization reaction of intermediates **15** through the elimination of TfOH and formaldehyde affords the desired dimeric flavanol analogues **10** (Scheme 5).

Catechin–formaldehyde condensation is widely accepted as an aldol condensation-type reaction.[13,14c] One catechin reacted with formaldehyde to form a C8-methylol catechin intermediate, which underwent a subsequent Friedel–Crafts alkylation with another catechin to generate the dimeric flavanol. The present study showed that self-coupling of the C8-methylol catechin intermediate might also be involved in acid-catalyzed catechin–formaldehyde condensation. Indeed, two pathways were involved when treating 8-methylol tetra-*O*-benzyl catechin (**11a**) with penta-*O*-benzyl catechin (**9b**) under acidic conditions, as show in Scheme 2. The result may provide new considerations for C8-methylol catechin derivative-involved organic synthesis.

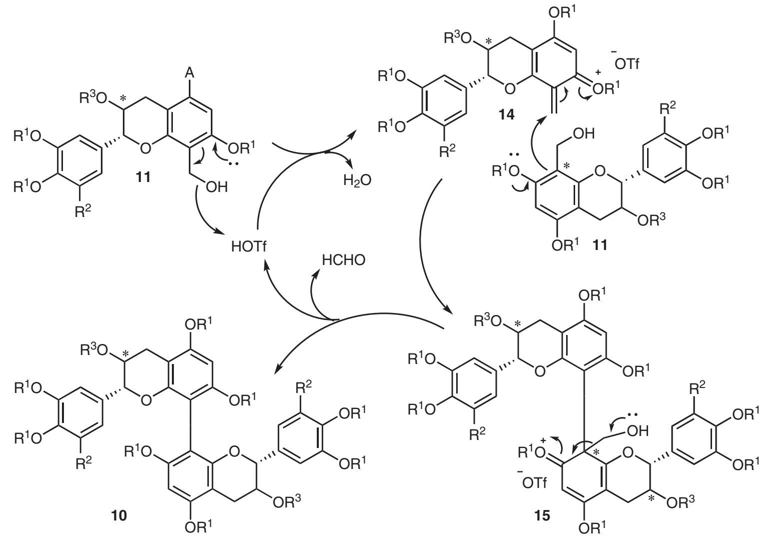
In summary, we have described a TfOH-catalyzed direct C8–C8′ self-coupling of C8-methylol catechin derivatives, which provides a highly efficient, regioselective, and convenient approach for the synthesis of dimeric flavanol analogues under metal-free and mild reaction conditions. This synthetic strategy is employed in the efficient synthesis of bisflavanol-type natural products bis-8,8′-catechinylmethane, bis-8,8′-epicatechinylmethane, talienbisflavan A, and oolonghomobisflavan A. In addition, the self-coupling reaction of C8-methylol catechin derivatives offers a new consideration in catechin–formaldehyde condensation. This industrially applicable reaction could facilitate the preparation of sufficient quantities of these natural products for biological and medical studies. Further applications of this strategy for the synthesis of other bioactive natural products with related skeletons are under investigation, and will be reported in due course.

Common reagents and materials were purchased from commercial sources and were used without further purification. TLC plates were visualized by exposure to ultra violet light (UV). Chemical shifts for protons are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvents [$CHCl_3$: δ = 7.28 ppm, CD_3OD: δ = 3.31 ppm, $(CD_3)_2CO$: δ = 2.05 ppm]. Chemical shifts for carbon resonances are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent [$CDCl_3$: δ = 77.0 ppm, CD_3OD: δ = 49.05 ppm, $(CD_3)_2CO$: δ = 206.26, 29.84 ppm]. Data are represented as: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant in hertz (Hz), and integration.

3-Formyloxy-5,7,3′,4′-tetra-*O*-benzyl-8-formyl-catechin (13); Typical Procedure

To a solution of tetra-*O*-benzyl catechin (**9a**, 97.6 mg, 0.15 mmol) in anhydrous DMF (0.25 mL) was added dropwise $POCl_3$ (69.7 μL, 0.75 mmol) at 0 °C. The resulting solution was stirred at r.t. for 8 h, and then cooled to 0 °C. Subsequently, H_2O (1 mL) was added dropwise to quench the reaction, and the pH was adjusted to 8 with a 2 N NaOH. The mixture was extracted with EtOAc (3 × 5 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (30% EtOAc in petroleum ether) over silica gel to afford aldehyde **13**.

Yield: 92.2 mg (87%); white solid; mp 145–147 °C; $[\alpha]_D^{25}$ –27.0 (*c* = 1.00, $CHCl_3$).



Scheme 5 Plausible reaction mechanism

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.49 (s, 1 H), 7.97 (s, 1 H), 7.49–7.27 (m, 20 H), 6.95 (d, *J* = 1.6 Hz, 1 H), 6.91 (d, *J* = 8.3 Hz, 1 H), 6.87 (dd, *J* = 8.4, 1.6 Hz, 1 H), 6.22 (s, 1 H), 5.50–5.47 (m, 1 H), 5.33 (d, *J* = 4.8 Hz, 1 H), 5.18–5.13 (m, 6 H), 5.05 (s, 2 H), 2.79 (dd, *J* = 17.2, 4.6 Hz, 1 H), 2.71 (dd, *J* = 17.3, 4.9 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.3, 161.9, 161.6, 160.0, 156.6, 149.0, 148.8, 137.1, 137.0, 136.2, 135.7, 130.1, 128.76 (2C), 128.73 (2C), 128.53 (2C), 128.47 (2C), 128.40, 128.1, 127.87, 127.81, 127.4 (2C), 127.29 (2C), 127.27 (2C), 127.0 (2C), 119.0, 114.9, 113.0, 108.7, 101.0, 90.8, 77.5, 71.2, 71.2, 70.8, 70.3, 67.6, 22.3.

IR (film): 3350, 3030, 2930, 2874, 1721, 1670, 1605, 1499, 1373, 1266, 1215, 1145, 1112, 1028, 735, 696 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{45}H_{39}O_8$: 707.2639; found: 707.2646.

8-Methylol Catechins (11); Typical Procedure

To a solution of 8-formyl catechin (0.1 mmol) in THF (0.75 mL) was added $LiBH_4$ (3.3 mg, 0.15 mmol) at 0 °C. The mixture was stirred at r.t. for 1 h, whereupon TLC analysis showed the reaction was complete. Water (5 mL) was added dropwise to quench the reaction. The mixture was extracted with EtOAc (3 × 5 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography over silica gel to afford 8-methylol catechin **11**.

5,7,3′,4′-Tetra-*O*-benzyl-8-methylol-catechin (11a)

Yield: 64.7 mg (95%); white solid; mp 85–87 °C; $[\alpha]_D^{25}$ –13.5 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.31 (m, 20 H), 7.03 (s, 1 H), 6.96 (d, *J* = 2.0 Hz, 2 H), 6.27 (s, 1 H), 5.20 (s, 2 H), 5.19 (s, 2 H), 5.09 (s, 2 H), 5.05 (s, 2 H), 4.75 (s, 2 H), 4.72 (d, *J* = 7.9 Hz, 2 H), 4.02–3.97 (m, 1 H), 3.10 (dd, *J* = 16.5, 5.5 Hz, 1 H), 2.68 (dd, *J* = 16.5, 8.7 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.9, 156.4, 153.3, 149.3, 149.0, 137.2, 137.0, 136.88, 136.87, 131.1, 128.68 (2C), 128.60 (2C), 128.55 (2C), 128.50 (2C), 128.1, 128.0, 127.9 (2C), 127.5 (2C), 127.31 (2C), 127.28 (2C), 127.1 (2C), 120.2, 114.9, 113.7, 109.9, 102.8, 91.4, 81.5, 71.32, 71.31, 70.9, 70.1, 67.9, 54.7, 27.4.

IR (film): 3284, 3030, 1610, 1549, 1522, 1443, 1370, 1254, 1200, 1131, 1110, 759, 680 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{44}H_{41}O_7$: 681.2847; found: 681.2845.

3,5,7,3′,4′-Penta-*O*-benzyl-8-methylol-catechin (11b)

Yield: 72.5 mg (94%); yellow solid; mp 69–70 °C; $[\alpha]_D^{25}$ –17.0 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.25 (m, 23 H), 7.08–7.07 (m, 2 H), 7.00 (s, 1 H), 6.95 (d, *J* = 3.3 Hz, 2 H), 6.24 (s, 1 H), 5.22 (s, 2 H), 5.12 (s, 2 H), 5.07–5.05 (m, 4 H), 4.85 (d, *J* = 7.8 Hz, 1 H), 4.75 (s, 2 H), 4.33 (d, *J* = 11.8 Hz, 1 H), 4.17 (d, *J* = 11.8 Hz, 1 H), 3.75–3.70 (m, 1 H), 3.04 (dd, *J* = 16.6, 5.3 Hz, 1 H), 2.73 (dd, *J* = 16.4, 8.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.7, 156.2, 153.4, 148.8 (2C), 137.9, 137.3, 137.2, 136.95, 136.92, 132.2, 128.67 (2C), 128.63 (2C), 128.55 (2C), 128.48 (2C), 128.3 (2C), 128.04, 127.99, 127.83 (3C), 127.79, 127.6, 127.37 (2C), 127.31 (2C), 127.29 (2C), 127.2 (2C), 120.2, 114.8, 113.6, 109.9, 102.8, 91.3, 80.0, 74.4, 71.6, 71.3, 71.0, 70.8, 70.1, 54.7, 25.9.

IR (film): 3200, 2924, 1610, 1592, 1496, 1350, 1254, 1200, 1120, 735, 699 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{51}H_{47}O_7$: 771.3316; found: 771.3317.

3-Acetoxy-5,7,3′,4′-tetra-*O*-benzyl-8-methylol-catechin (11c)

Yield: 66.5 mg (92%); colorless oil; $[\alpha]_D^{25}$ –10.5 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.30 (m, 20 H), 6.97 (s, 1 H), 6.91–6.85 (m, 2 H), 6.27 (s, 1 H), 5.34–5.30 (m, 1 H), 5.16–5.09 (m, 6 H), 5.03 (s, 2 H), 4.80 (s, 2 H), 2.84 (dd, *J* = 17.1, 5.2 Hz, 1 H), 2.75 (dd, *J* = 17.1, 5.5 Hz, 1 H), 1.97 (s, 3 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 170.2, 156.8, 156.5, 152.7, 148.8 (2C), 137.2, 137.1, 136.8, 136.7, 131.0, 128.69 (2C), 128.62 (2C), 128.51 (2C), 128.46 (2C), 128.1, 128.0, 127.82, 127.78, 127.39 (2C), 127.32 (2C), 127.29 (2C), 127.22 (2C), 119.3, 114.8, 113.1, 109.9, 101.7, 91.2, 77.9, 71.3 (2C), 70.8, 70.1, 68.7, 54.6, 23.4, 21.1.

IR (film): 3259, 2968, 2849, 1742, 1603, 1501, 1297, 1231, 1143, 1019, 733, 679 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C$_{46}$H$_{43}$O$_8$: 723.2952; found: 723.2950.

3-Methoxymethoxy-5,7,3′,4′-tetra-*O*-benzyl-8-methylol-catechin (11d)

Yield: 68.1 mg (94%); colorless oil; [α]$_D^{25}$ –16.7 (*c* = 1.00, CHCl$_3$).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.47–7.30 (m, 20 H), 7.02 (s, 1 H), 6.93 (s, 2 H), 6.25 (s, 1 H), 5.18–5.17 (m, 4 H), 5.07–5.05 (m, 4 H), 4.92 (d, *J* = 7.2 Hz, 1 H), 4.77 (s, 2 H), 4.54 (d, *J* = 6.8 Hz, 1 H), 4.31 (d, *J* = 6.8 Hz, 1 H), 4.03–3.98 (m, 1 H), 3.11 (s, 3 H), 2.97 (dd, *J* = 16.6, 5.3 Hz, 1 H), 2.73 (dd, *J* = 16.5, 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 156.8, 156.3, 153.2, 148.8 (2C), 137.24, 137.18, 136.97, 136.93, 132.2, 128.67 (2C), 128.61 (2C), 128.49 (2C), 128.47 (2C), 128.03, 127.96, 127.82, 127.80, 127.4 (2C), 127.31 (2C), 127.30 (2C), 127.1 (2C), 119.9, 114.9, 113.7, 110.0, 102.6, 95.0, 91.4, 79.6, 72.0, 71.34, 71.28, 70.8, 70.1, 55.3, 54.7, 25.3.

IR (film): 3231, 2931, 1621, 1451, 1261, 1230, 1116, 1028, 742, 702 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C$_{46}$H$_{45}$O$_8$: 725.3109; found: 725.3108.

3-Propoxy-5,7,3′,4′-tetra-*O*-benzyl-8-methylol-catechin (11e)

Yield: 68.7 mg (95%); colorless oil; [α]$_D^{25}$ –16.0 (*c* = 1.00, CHCl$_3$).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.48–7.30 (m, 20 H), 7.04 (s, 1 H), 6.95 (s, 2 H), 6.25 (s, 1 H), 5.20–5.18 (m, 4 H), 5.07–5.06 (m, 4 H), 4.81 (d, *J* = 7.7 Hz, 1 H), 4.76 (s, 2 H), 3.63–3.58 (m, 1 H), 3.33–3.27 (m, 1 H), 3.05–2.96 (m, 2 H), 2.67 (dd, *J* = 16.5, 8.4 Hz, 1 H), 1.38 (q, *J* = 6.9 Hz, 2 H), 0.73 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 156.8, 156.2, 153.5, 148.83, 148.75, 137.32, 137.28, 137.02, 136.98, 132.6, 128.68 (2C), 128.63 (2C), 128.51 (2C), 128.48 (2C), 128.04, 127.98, 127.82, 127.79, 127.42 (2C), 127.35 (2C), 127.32 (2C), 127.2 (2C), 120.2, 114.9, 113.9, 110.0, 103.0, 91.3, 80.0, 75.3, 71.7, 71.39, 71.30, 70.9, 70.1, 54.8, 25.8, 23.0, 10.4.

IR (film): 3265, 2955, 2881, 1625, 1481, 1282, 1232, 1149, 1047, 910, 765, 691 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C$_{47}$H$_{47}$O$_7$: 723.3316; found: 723.3321.

3-Benzoyloxy-5,7,3′,4′-tetra-*O*-benzyl-8-methylol-catechin (11f)

Yield: 73.0 mg (93%); yellow solid; mp 99–100 °C; [α]$_D^{25}$ –20.5 (*c* = 1.00, CHCl$_3$).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.95 (d, *J* = 7.6 Hz, 2 H), 7.55 (t, *J* = 7.4 Hz, 1 H), 7.46–7.31 (m, 22 H), 7.03 (d, *J* = 1.2 Hz, 1 H), 6.95 (dd, *J* = 8.3, 1.5 Hz, 1 H), 6.90 (d, *J* = 8.3 Hz, 1 H), 6.29 (s, 1 H), 5.58–5.54 (m, 1 H), 5.26 (d, *J* = 6.1 Hz, 1 H), 5.14–5.05 (m, 8 H), 4.82 (s, 2 H), 3.02 (dd, *J* = 17.0, 5.3 Hz, 1 H), 2.91 (dd, *J* = 17.0, 6.2 Hz, 1 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 165.6, 156.8, 156.5, 152.9, 148.9 (2C), 137.2, 137.1, 136.9, 136.8, 133.1, 131.1, 129.9, 129.7 (2C), 128.7 (2C), 128.6 (2C), 128.48 (2C), 128.45 (2C), 128.37 (2C), 128.1, 128.0, 127.80, 127.78, 127.4 (2C), 127.34 (2C), 127.28 (2C), 127.2 (2C), 119.5, 115.0, 113.2, 110.0, 101.8, 91.3, 78.2, 71.32, 71.30, 70.8, 70.1, 69.5, 54.7, 23.8.

IR (film): 3262, 2934, 1743, 1622, 1521, 1499, 1269, 1119, 1020, 745, 694 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C$_{51}$H$_{45}$O$_8$: 785.3109; found: 785.3113.

5,7,3′,4′-Tetra-*O*-benzyl-8-methylol-epicatechin (11g)

Yield: 64.7 mg (95%); colorless oil; [α]$_D^{25}$ –35.0 (*c* = 1.00, CHCl$_3$).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.48–7.32 (m, 20 H), 7.14 (s, 1 H), 7.01 (s, 2 H), 6.27 (s, 1 H), 5.22–5.21 (m, 4 H), 5.09 (s, 2 H), 5.05 (s, 2 H), 4.98 (s, 1 H), 4.82 (d, *J* = 5.0 Hz, 2 H), 4.25 (s, 1 H), 3.04 (d, *J* = 17.1 Hz, 1 H), 2.95 (dd, *J* = 17.2, 4.3 Hz, 1 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 157.5, 156.5, 153.2, 149.1, 149.0, 137.3, 137.2, 136.93, 136.90, 131.3, 128.7 (2C), 128.6 (2C), 128.5 (4C), 128.2, 128.03, 127.95, 127.8, 127.4 (2C), 127.3 (4C), 127.1 (2C), 119.2, 115.2, 113.4, 110.2, 101.5, 91.6, 78.4, 71.4 (2C), 70.9, 70.1, 66.0, 54.6, 28.1.

IR (film): 3255, 2944, 1618, 1520, 1459, 1251, 1238, 1111, 1024, 738, 703 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C$_{44}$H$_{41}$O$_7$: 681.2847; found: 681.2849.

3,5,7,3′,4′-Penta-*O*-benzyl-8-methylol-epicatechin (11h)

Yield: 71.7 mg (93%); colorless oil; [α]$_D^{25}$ –37.8 (*c* = 1.00, CHCl$_3$).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.50–7.31 (m, 22 H), 7.20–7.15 (m, 3 H), 7.03–6.94 (m, 4 H), 6.25 (s, 1 H), 5.22 (s, 2 H), 5.10–5.05 (m, 7 H), 4.82 (d, *J* = 3.0 Hz, 2 H), 4.44 (d, *J* = 12.5 Hz, 1 H), 4.32 (d, *J* = 12.4 Hz, 1 H), 3.96 (s, 1 H), 3.00 (d, *J* = 16.9 Hz, 1 H), 2.82 (dd, *J* = 16.9, 3.9 Hz, 1 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 157.1, 156.3, 153.6, 148.7, 148.3, 138.0, 137.4, 137.3, 137.04, 136.99, 132.0, 128.66 (2C), 128.62 (2C), 128.52 (2C), 128.45 (2C), 128.2 (2C), 128.01, 127.98, 127.8, 127.72, 127.67 (2C), 127.5, 127.33 (4C), 127.30 (2C), 127.2 (2C), 119.5, 114.7, 113.6, 110.1, 102.0, 91.3, 78.0, 72.3, 71.4, 71.3, 71.0, 70.8, 70.1, 54.8, 24.5.

IR (film): 3247, 2931, 2870, 1635, 1589, 1281, 1230, 1143, 1021, 720, 674 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C$_{51}$H$_{47}$O$_7$: 771.3316; found: 771.3318.

5,7,3′,4′-Tetra-*O*-benzyl-3-*O*-(3,4,5-tri-*O*-benzylgalloyl)-8-methylol-epicatechin (11i)

Yield: 105.9 mg (96%); colorless oil; [α]$_D^{25}$ –48.7 (*c* = 1.00, CHCl$_3$).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.41–7.25 (m, 37 H), 7.08 (s, 1 H), 6.96 (d, *J* = 8.1 Hz, 1 H), 6.87 (d, *J* = 8.2 Hz, 1 H), 6.31 (s, 1 H), 5.64 (s, 1 H), 5.16–5.05 (m, 13 H), 4.91–4.87 (m, 4 H), 3.12–3.11 (m, 2 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 165.0, 157.1, 156.4, 153.6, 152.4 (2C), 148.9 (2C), 142.5, 137.4, 137.1, 136.9, 136.8, 136.7, 136.6 (2C), 130.9, 128.7 (2C), 128.6 (2C), 128.53 (6C), 128.49 (2C), 128.42 (2C), 128.2 (2C), 128.1, 128.03, 127.98 (2C), 127.94, 127.80, 127.76, 127.6 (4C), 127.3 (2C), 127.24 (4C), 127.19 (2C), 124.9, 119.7, 114.7, 113.4, 110.1, 109.0 (2C), 101.3, 91.2, 77.6, 75.1, 71.26, 71.22, 71.0 (2C), 70.8, 70.1, 68.3, 54.7, 29.7.

IR (film): 3261, 2955, 1740, 1628, 1470, 1275, 1230, 1141, 1012, 760, 685 cm^{-1}.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{72}H_{63}O_{11}$: 1103.4364; found: 1103.4369.

5,7,3′,4′,5′-Penta-*O*-benzyl-8-methylol-epigallocatechin (11j)

Yield: 73.2 mg (93%); colorless oil; $[\alpha]_D^{25}$ –30.2 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.29 (m, 25 H), 6.83 (s, 2 H), 6.29 (s, 1 H), 5.17–4.82 (m, 13 H), 4.25 (s, 1 H), 3.05 (d, *J* = 16.9 Hz, 1 H), 2.95 (dd, *J* = 17.1, 4.1 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.5, 156.5, 153.1, 153.0 (2C), 138.4, 137.8, 137.04 (2C), 136.92 (2C), 133.6, 128.7 (2C), 128.6 (4C), 128.5 (4C), 128.2 (2C), 128.1, 128.0, 127.89 (2C), 127.81, 127.5 (4C), 127.3 (2C), 127.2 (2C), 110.2, 106.0 (2C), 101.5, 91.7, 78.5, 75.2, 71.3 (2C), 70.9, 70.1, 66.1, 54.6, 28.0.

IR (film): 3267, 2960, 1619, 1481, 1277, 1226, 1145, 1029, 759, 698 cm^{-1}.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{51}H_{47}O_8$: 787.3265; found: 787.3272.

3,5,7,3′,4′,5′-Hexa-*O*-benzyl-8-methylol-epigallocatechin (11k)

Yield: 80.7 mg (92%); colorless oil; $[\alpha]_D^{25}$ –33.4 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.30 (m, 25 H), 7.22–7.21 (m, 3 H), 7.04–7.03 (m, 2 H), 6.80 (s, 2 H), 6.27 (s, 1 H), 5.12–5.02 (m, 11 H), 4.83 (s, 2 H), 4.44 (d, *J* = 12.3 Hz, 1 H), 4.29 (d, *J* = 12.5 Hz, 1 H), 3.96 (s, 1 H), 3.01 (d, *J* = 17.0 Hz, 1 H), 2.83 (dd, *J* = 17.3, 3.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.2, 156.4, 153.4, 152.6 (2C), 138.01, 138.00, 137.8, 137.2 (2C), 137.05, 137.0, 134.2, 128.7 (2C), 128.6 (2C), 128.4 (4C), 128.1 (4C), 128.04, 128.01, 127.79 (3C), 127.78 (3C), 127.5, 127.4 (5C), 127.3 (2C), 127.2 (2C), 110.2, 106.3 (2C), 102.0, 91.4, 78.1, 75.2, 72.3, 71.3, 71.1 (2C), 70.8, 70.2, 54.7, 24.7.

IR (film): 3250, 2962, 2853, 1629, 1475, 1263, 1207, 1141, 1026, 755, 693 cm^{-1}.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{58}H_{52}O_8Na$: 899.3554; found: 899.3563.

5,7,3′,4′,5′-Penta-*O*-benzyl-3-*O*-(3,4,5-tri-*O*-benzylgalloyl)-8-methylol-epigallocatechin (11l)

Yield: 114.9 mg (95%); colorless oil; $[\alpha]_D^{25}$ –43.8 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.25 (m, 40 H), 6.78 (s, 2 H), 6.32 (s, 1 H), 5.68 (s, 1 H), 5.14–4.84 (m, 19 H), 3.12–3.11 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.8, 157.1, 156.5, 153.5, 152.9 (2C), 152.5 (2C), 142.8, 138.5, 137.8, 137.5, 136.9 (2C), 136.8, 136.7, 136.5 (2C), 133.2, 128.7 (2C), 128.6 (2C), 128.5 (6C), 128.4 (4C), 128.3 (2C), 128.2 (2C), 128.1 (3C), 128.04, 127.95 (2C), 127.87, 127.80 (2C), 127.7, 127.6 (4C), 127.4 (4C), 127.3 (2C), 127.2 (2C), 125.0, 110.3, 109.2 (2C), 106.6 (2C), 101.4, 91.5, 77.7, 75.18, 75.10, 71.3 (2C), 71.1 (2C), 70.9, 70.2, 68.0, 54.6, 26.0.

IR (film): 3261, 2969, 1715, 1617, 1481, 1292, 1231, 1140, 1029, 758, 701 cm^{-1}.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{79}H_{68}O_{12}Na$: 1231.4603; found: 1231.4610.

3,5,7,3′,4′-Penta-*O*-methyl-8-methylol-catechin (11m)

Yield: 35.1 mg (90%); white foam; $[\alpha]_D^{25}$ +18.0 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.98–6.95 (m, 2 H), 6.88 (d, *J* = 8.0 Hz, 1 H), 6.15 (s, 1 H), 4.94 (d, *J* = 7.1 Hz, 1 H), 4.76 (s, 2 H), 3.91–3.86 (m, 12 H), 3.71–3.66 (m, 1 H), 3.28 (s, 3 H), 2.97 (dd, *J* = 16.5, 5.2 Hz, 1 H), 2.66 (dd, *J* = 16.5, 7.7 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.9, 157.3, 153.1, 148.9, 148.8, 131.6, 119.0, 111.1, 109.9, 109.0, 101.6, 88.0, 79.4, 76.5, 57.2, 56.0, 55.92, 55.91, 55.4, 54.6, 24.2.

IR (film): 3261, 2968, 1620, 1485, 1287, 1231, 1133, 1019, 773, 679 cm^{-1}.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{27}O_7$: 391.1751; found: 391.1750.

3,5,7,3′,4′-Penta-*O*-ethyl-8-methylol-catechin (11n)

Yield: 42.4 mg (92%); colorless oil; $[\alpha]_D^{25}$ +15.5 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.98–6.96 (m, 2 H), 6.89 (d, *J* = 8.8 Hz, 1 H), 6.12 (s, 1 H), 4.81 (d, *J* = 7.9 Hz, 1 H), 4.76–4.75 (m, 2 H), 4.15–4.00 (m, 8 H), 3.69–3.64 (m, 1 H), 3.49–3.41 (m, 1 H), 3.18–3.11 (m, 1 H), 3.03 (dd, *J* = 16.5, 5.5 Hz, 1 H), 2.63 (dd, 1 H, *J* = 16.4, 8.6 Hz, 1 H), 1.49–1.42 (m, 12 H), 1.04 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.1, 156.5, 153.3, 148.51, 148.48, 131.9, 119.3, 113.2, 112.3, 109.3, 102.3, 90.2, 80.1, 75.4, 65.4, 64.6 (2C), 64.5, 63.7, 54.8, 26.0, 15.3, 14.94, 14.85 (2C), 14.7.

IR (film): 3267, 2931, 1641, 1441, 1261, 1236, 1116, 1020, 742, 700 cm^{-1}.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{26}H_{37}O_7$: 461.2534; found: 461.2537.

3-Acetoxy-5,7,3′,4′-tetra-*O*-methyl-8-methylol-catechin (11o)

Yield: 37.7 mg (90%); white foam; $[\alpha]_D^{25}$ +20.5 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.92–6.90 (m, 2 H), 6.84 (d, *J* = 8.8 Hz, 1 H), 6.15 (s, 1 H), 5.40–5.35 (m, 1 H), 5.15 (d, *J* = 6.1 Hz, 1 H), 4.79 (s, 2 H), 3.88–3.84 (m, 12 H), 2.88 (dd, *J* = 16.9, 5.2 Hz, 1 H), 2.72 (dd, *J* = 16.9, 6.2 Hz, 1 H), 2.00 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.1, 157.8, 157.5, 152.6, 149.0, 148.9, 130.4, 118.6, 111.1, 109.5, 109.0, 100.9, 88.1, 78.1, 68.9, 56.0, 55.89, 55.87, 55.4, 54.5, 23.5, 21.0.

IR (film): 3265, 2955, 2881, 2143, 1735, 1615, 1480, 1295, 1222, 1143, 1035, 913, 760, 698 cm^{-1}.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{22}H_{27}O_8$: 419.1700; found: 419.1702.

3-Acetoxy-5,7,3′,4′-tetra-*O*-ethyl-8-methylol-catechin (11p)

Yield: 43.2 mg (91%); colorless oil; $[\alpha]_D^{25}$ +17.5 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.89–6.83 (m, 3 H), 6.12 (s, 1 H), 5.37–5.33 (m, 1 H), 5.11 (d, *J* = 6.3 Hz, 1 H), 4.79 (s, 2 H), 4.12–4.00 (m, 8 H), 2.88 (dd, *J* = 16.9, 5.3 Hz, 1 H, 1 H), 2.72 (dd, *J* = 16.9, 6.4 Hz, 1 H, 1 H), 1.99 (s, 3 H), 1.47–1.39 (m, 12 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.2, 157.1, 156.7, 152.7, 148.5 (2C), 130.4, 118.8, 113.2, 111.6, 109.1, 101.0, 90.0, 78.1, 69.0, 64.6, 64.5, 64.3, 63.7, 54.7, 23.6, 21.1, 14.9, 14.80, 14.79, 14.7.

IR (film): 3262, 2934, 1740, 1632, 1528, 1452, 1254, 1231, 1112, 1021, 745, 704 cm^{-1}.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{26}H_{35}O_8$: 475.2326; found: 475.2324.

3-Acetoxy-5,7,3′,4′-tetra-*O*-propargyl-8-methylol-catechin (11q)

Yield: 46.8 mg (91%); yellow oil; $[\alpha]_D^{25}$ +5.5 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10 (d, *J* = 1.1 Hz, 1 H), 7.05 (d, *J* = 8.3 Hz, 1 H), 6.97 (d, *J* = 8.3 Hz, 1 H), 6.43 (s, 1 H), 5.39–5.35 (m, 1 H), 5.22 (d, *J* = 5.7 Hz, 1 H), 4.81–4.71 (m, 10 H), 2.88 (dd, *J* = 17.1, 5.2 Hz, 1 H), 2.77 (dd, *J* = 17.1, 5.5 Hz, 1 H), 2.60–2.48 (m, 4 H), 2.02 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.2, 155.7, 155.3, 152.8, 147.4, 147.3, 131.5, 119.7, 114.7, 112.8, 110.9, 102.6, 91.5, 78.5, 78.3, 78.1, 77.7, 76.2, 76.0, 75.93, 75.87, 68.6, 56.94, 56.88, 56.82, 56.1, 54.3, 23.1, 21.1.

IR (film): 3307, 3261 2931, 2107, 1628, 1520, 1454, 1255, 1230, 1117, 1019, 778, 715, 640 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{30}H_{27}O_8$: 515.1700; found: 515.1707.

5,7,3′,4′-Tetra-*O*-methyl-3-*O*-(3,4,5-tri-*O*-methylgalloyl)-8-methylol-epicatechin (11r)

Yield: 52.5 mg (92%); white solid; mp 101–102 °C; $[\alpha]_D^{25}$ –20.0 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15 (s, 2 H), 7.07–7.03 (m, 2 H), 6.85 (d, *J* = 8.2 Hz, 1 H), 6.17 (s, 1 H), 5.67 (s, 1 H), 5.21 (s, 1 H), 4.89–4.81 (m, 2 H), 3.90–3.83 (m, 18 H), 3.73 (s, 3 H), 3.11–3.09 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.1, 158.2, 157.4, 153.3, 152.8 (2C), 148.8 (2C), 142.3, 130.3, 124.9, 118.6, 110.9, 109.6, 109.1, 106.9 (2C), 100.2, 88.0, 77.5, 68.5, 60.8, 56.1 (2C), 55.8 (2C), 55.7, 55.4, 54.5, 25.8.

IR (film): 3267, 2960, 2870, 1623, 1481, 1291, 1230, 1141, 1029, 770, 679 cm^{-1}.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{34}O_{11}Na$: 593.1993; found: 593.1999.

5,7,3′,4′-Tetra-*O*-propargyl-3-*O*-(3,4,5-tri-*O*-propargylgalloyl)-8-methylol-epicatechin (11s)

Yield: 67.2 mg (91%); yellow oil; $[\alpha]_D^{25}$ –35.0 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (s, 2 H), 7.34 (s, 1 H), 7.15 (d, *J* = 8.1 Hz, 1 H), 7.06 (d, *J* = 8.2 Hz, 1 H), 6.45 (s, 1 H), 5.66 (s, 1 H), 5.21 (s, 1 H), 4.85–4.63 (m, 16 H), 3.18 (d, *J* = 17.4 Hz, 1 H), 3.11 (dd, *J* = 17.7, 4.0 Hz, 1 H), 2.59–2.45 (m, 7 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.6, 157.4, 156.9, 155.5, 151.2 (2C), 147.6, 147.4, 141.2, 131.6, 125.5, 120.5, 114.6, 114.0, 110.9, 110.2 (2C), 101.5, 91.5, 78.6, 78.5, 78.4, 78.3, 78.3, 77.8, 77.3, 76.4, 76.0, 75.9, 75.7, 75.7, 75.6, 68.6, 60.2, 57.19 (2C), 57.17, 56.8, 56.1, 55.9, 54.1, 25.8.

IR (film): 3310, 3251, 2956, 2100, 1617, 1471, 1275, 1239, 1140, 1020, 761, 685, 625 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{44}H_{35}O_{11}$: 739.2174; found: 739.2178.

5,7,3′,4′,5′-Penta-*O*-propargyl-3-*O*-(3,4,5-tri-*O*-propargylgalloyl)-8-methylol-epigallocatechin (11t)

Yield: 72.9 mg (92%); yellow oil; $[\alpha]_D^{25}$ –42.3 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (s, 2 H), 6.97 (s, 2 H), 6.46 (s, 1 H), 5.70 (s, 1 H), 5.20 (s, 1 H), 4.86–4.59 (m, 18 H), 3.18 (dd, *J* = 17.9, 0.8 Hz, 1 H), 3.11 (dd, *J* = 17.7, 4.1 Hz, 1 H), 2.59–2.43 (m, 8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.5, 156.0, 155.4, 153.3, 151.5 (2C), 151.2 (2C), 141.1, 137.2, 133.6, 125.4, 111.2, 110.0 (2C), 107.3 (2C), 102.0, 91.7, 79.0, 78.6, 78.4, 78.3, 77.8, 77.4, 76.2, 76.0, 75.9, 75.6, 75.3, 68.0, 60.3, 60.2, 57.2 (2C), 57.1 (2C), 56.8, 56.2, 54.2, 25.9.

IR (film): 3302, 3265, 2948, 2105, 1641, 1465, 1634, 1489, 1287, 1236, 1149, 1026, 768, 698, 637 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{47}H_{37}O_{12}$: 793.2280; found: 793.2281.

Dimeric Products (10); Typical Procedure

To a solution of 8-methylol catechins **11** (0.05 mmol) in anhydrous dichloromethane (0.1 mL) was added TfOH (5 μL, 0.1 M dichloromethane, 0.0005 mmol). The mixture was stirred at r.t. for 1 min. Water (2 mL) was poured into the solution, and the mixture was extracted with EtOAc (3 × 3 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography over silica gel to afford dimeric products **10**.

Octa-*O*-benzyl Bis-8,8′-catechinylmethane (10a)

Yield: 30.5 mg (92%); yellow solid; mp 85–87 °C; $[\alpha]_D^{25}$ +6.0 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.17 (m, 40 H), 6.79 (dd, *J* = 9.1, 4.9 Hz, 4 H), 6.59 (dd, *J* = 8.2, 1.5 Hz, 2 H), 6.13 (s, 2 H), 5.16–4.98 (m, 14 H), 4.73 (d, *J* = 11.8 Hz, 2 H), 4.57 (d, *J* = 11.8 Hz, 2 H), 4.14 (d, *J* = 8.5 Hz, 2 H), 4.05 (s, 2 H), 3.14 (dd, *J* = 16.2, 5.7 Hz, 2 H), 2.60 (dd, *J* = 16.2, 9.3 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.1, 154.6, 153.5, 148.9, 148.8, 137.8, 137.39, 137.36, 137.0, 131.7, 128.54, 128.51, 128.4, 128.2, 127.82, 127.80, 127.76, 127.43, 127.39, 127.22, 127.16, 127.1, 120.6, 114.6, 113.8, 111.2, 102.2, 91.1, 80.9, 71.3, 71.0, 70.1, 70.0, 68.5, 28.1, 17.4.

IR (film): 3035, 1624, 1593, 1510, 1495, 1444, 1376, 1254, 1218, 1128, 1113, 742, 695 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{87}H_{77}O_{12}$: 1313.5410; found: 1313.5418.

Deca-*O*-benzyl Bis-8,8′-catechinylmethane (10b)

Yield: 37.0 mg (98%); yellow oil; $[\alpha]_D^{25}$ –6.4 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CHCl_3$): δ = 7.45–7.15 (m, 46 H), 6.93–6.92 (m, 4 H), 6.79 (d, *J* = 8.1 Hz, 2 H), 6.72 (s, 2 H), 6.62 (d, *J* = 8.2 Hz, 2 H), 6.06 (s, 2 H), 5.16 (s, 4 H), 4.97–4.95 (m, 6 H), 4.85 (d, *J* = 12.3 Hz, 2 H), 4.66 (d, *J* = 11.8 Hz, 2 H), 4.46 (d, *J* = 11.8 Hz, 2 H), 4.23 (d, *J* = 8.7 Hz, 2 H), 4.11 (d, *J* = 11.9 Hz, 2 H), 4.00 (s, 2 H), 3.91 (d, *J* = 11.8 Hz, 2 H), 3.47–3.41 (m, 2 H), 3.15 (dd, *J* = 16.2, 5.6 Hz, 2 H), 2.61 (dd, *J* = 16.0, 9.6 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.9, 154.5, 153.6, 148.5, 148.4, 138.3, 137.9, 137.51, 137.49, 137.3, 133.3, 128.51, 128.47, 128.37, 128.10, 128.09, 127.8, 127.6, 127.3, 127.22, 127.19, 127.1, 120.8, 114.6, 113.8, 111.1, 102.3, 90.9, 79.6, 75.3, 71.5, 71.4, 70.6, 70.0, 69.9, 27.2, 17.4.

IR (film): 3065, 3033, 2919, 2873, 1606, 1481, 1292, 1233, 1141, 1020, 758, 700 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{101}H_{89}O_{12}$: 1493.6349; found: 1493.6359.

3,3′-Diacetoxy-octa-*O*-benzyl Bis-8,8´-catechinylmethane (10c)

Yield: 34.6 mg (98%); yellow oil; $[\alpha]_D^{25}$ –10.5 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.20 (m, 40 H), 6.75 (d, *J* = 1.6 Hz, 2 H), 6.70 (d, *J* = 8.3 Hz, 2 H), 6.49 (dd, *J* = 8.3, 1.6 Hz, 2 H), 6.06 (s, 2 H), 5.15–4.92 (m, 14 H), 4.71 (d, *J* = 11.8 Hz, 2 H), 4.54–4.48 (m, 4 H), 4.06 (s, 2 H), 3.00 (dd, *J* = 16.5, 5.7 Hz, 2 H), 2.63 (dd, *J* = 16.5, 8.0 Hz, 2 H), 1.78 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8, 156.2, 154.6, 153.1, 148.7, 148.5, 137.8, 137.4, 137.3, 137.2, 131.6, 128.5, 128.44, 128.39, 128.2, 127.8, 127.73, 127.69, 127.4, 127.3, 127.2, 127.1, 120.2, 114.3, 113.7, 110.9, 101.2, 91.0, 77.9, 71.2, 70.1, 70.0, 69.6, 25.1, 20.9, 17.3.

IR (film): 3061, 2968, 1732, 1660, 1489, 1290, 1231, 1143, 1019, 730, 679 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{91}H_{81}O_{14}$: 1397.5620; found: 1397.5631.

3,3′-Dimethoxymethoxy-octa-*O*-benzyl Bis-8,8′-catechinylmethane (10d)

Yield: 34.7 mg (98%); yellow oil; $[\alpha]_D^{25}$ –4.5 (*c* = 1.00, $CHCl_3$).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.18 (m, 40 H), 6.77–6.74 (m, 4 H), 6.56 (d, *J* = 8.2 Hz, 2 H), 6.06 (s, 2 H), 5.13 (s, 4 H), 5.04–4.93 (m, 8 H), 4.66 (d, *J* = 11.8 Hz, 2 H) 4.46 (d, *J* = 11.8 Hz, 2 H), 4.37 (d, *J* = 6.7 Hz, 2 H), 4.29 (d, *J* = 8.4 Hz, 2 H), 4.03–4.02 (m, 4 H), 3.77–3.72 (m, 2 H), 3.12 (dd, *J* = 16.3, 5.1 Hz, 2 H), 2.92 (s, 6 H), 2.62 (dd, *J* = 16.2, 9.0 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.1, 154.5, 153.5, 148.54, 148.46, 137.9, 137.53, 137.46, 137.3, 133.1, 128.5, 128.43, 128.37, 128.1, 127.71, 127.69, 127.65, 127.31, 127.29, 127.25, 127.1, 120.7, 114.7, 114.1, 111.2, 102.1, 94.9, 91.2, 79.4, 72.9, 71.4, 70.9, 70.0, 55.0, 26.9, 17.4.

IR (film): 3067, 2931, 1611, 1451, 1261, 1232, 1113, 1029, 742, 687 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{91}H_{85}O_{14}$: 1401.5934; found: 1401.5939.

3,3′-Dipropoxy-octa-*O*-benzyl Bis-8,8′-catechinylmethane (10e)

Yield: 32.8 mg (93%); colorless oil; $[\alpha]_D^{25}$ –6.8 (*c* = 1.00, $CHCl_3$).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.15 (m, 40 H), 6.76–6.75 (m, 4 H), 6.59 (d, *J* = 8.1 Hz, 2 H), 6.06 (s, 2 H), 5.14–4.93 (m, 12 H), 4.66 (d, *J* = 11.8 Hz, 2 H), 4.47 (d, *J* = 12.0 Hz, 2 H), 4.19 (d, *J* = 8.9 Hz, 2 H), 4.01 (s, 2 H), 3.31–3.25 (m, 2 H), 3.14–3.07 (m, 4 H), 2.70–2.64 (m, 2 H), 2.54 (dd, *J* = 16.3, 9.5 Hz, 2 H), 1.22 (q, *J* = 7.1 Hz, 4 H), 0.59 (t, *J* = 7.3 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.0, 154.5, 153.7, 148.45, 148.41, 137.9, 137.58, 137.55, 137.45, 133.4, 128.5, 128.43, 128.36, 128.1, 127.7, 127.6, 127.34, 127.29, 127.28, 127.20, 127.1, 120.8, 114.7, 114.2, 111.4, 102.6, 91.1, 79.8, 76.1, 71.7, 71.5, 70.8, 70.10, 70.07, 27.2, 22.9, 17.5, 10.3.

IR (film): 3065, 2955, 2881, 1635, 1481, 1289, 1230, 1141, 1032, 910, 760, 691 cm^{-1}.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{93}H_{88}O_{12}Na$: 1419.6168; found: 1419.6177.

3,3′-Dibenzoyloxy-octa-*O*-benzyl Bis-8,8′-catechinylmethane (10f)

Yield: 37.7 mg (98%); yellow oil; $[\alpha]_D^{25}$ –13.2 (*c* = 1.00, $CHCl_3$).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 7.4 Hz, 4 H), 7.46 (t, *J* = 7.4 Hz, 2 H), 7.35–7.20 (m, 44 H), 6.82 (d, *J* = 1.5 Hz, 2 H), 6.70 (d, *J* = 8.4 Hz, 2 H), 6.58 (dd, *J* = 8.2, 1.4 Hz, 2 H), 6.10 (s, 2 H), 5.37–5.32 (m, 2 H), 5.03 (s, 4 H), 4.93 (s, 4 H), 4.88 (s, 4 H), 4.73 (d, *J* = 11.7 Hz, 2 H), 4.62–4.59 (m, 4 H), 4.12 (s, 2 H), 3.15 (dd, *J* = 16.6, 5.8 Hz, 2 H), 2.78 (dd, *J* = 16.6, 7.8 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.3, 156.3, 154.7, 153.2, 148.8, 148.7, 137.8, 137.31, 137.28, 137.2, 132.8, 131.7, 130.1, 129.5, 128.5, 128.35, 128.34, 128.20, 128.19, 127.7, 127.6, 127.3, 127.22, 127.19, 127.15, 120.2, 114.6, 113.9, 111.1, 101.3, 91.0, 77.9, 71.3, 71.2, 70.3, 70.1, 69.9, 25.2, 17.4.

IR (film): 3062, 2939, 1733, 1652, 1528, 1452, 1255, 1231, 1117, 1029, 742, 695 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{101}H_{85}O_{14}$: 1521.5934; found: 1521.5948.

Octa-*O*-benzyl Bis-8,8′-epicatechinylmethane (10g)

Yield: 32.3 mg (98%); yellow foam; $[\alpha]_D^{25}$ –28.4 (*c* = 1.00, $CHCl_3$).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.11 (m, 40 H), 6.93 (s, 2 H), 6.84 (d, *J* = 8.2 Hz, 2 H), 6.63 (d, *J* = 8.1 Hz, 2 H), 6.21 (s, 2 H), 5.22–5.11 (m, 14 H), 4.77 (s, 2 H), 4.33 (s, 2 H), 4.17 (s, 2 H), 4.00 (s, 2 H), 3.01 (d, *J* = 17.0 Hz, 2 H), 2.82 (dd, *J* = 17.3, 3.9 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.2, 155.3, 153.4, 148.6, 148.4, 137.8, 137.5, 137.4, 137.2, 132.1, 128.56, 128.54, 128.45, 128.3, 127.9, 127.80, 127.77, 127.5, 127.3, 127.2, 119.6, 114.7, 113.6, 111.5, 101.0, 91.8, 77.8, 71.2, 71.1, 70.5, 70.0, 66.1, 28.8, 17.6.

IR (film): 3065, 2931, 1628, 1524, 1453, 1255, 1222, 1114, 1029, 738, 680 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{87}H_{77}O_{12}$: 1313.5410; found: 1313.5418.

Deca-*O*-benzyl Bis-8,8′-epicatechinylmethane (10h)

Yield: 34.4 mg (91%); yellow oil; $[\alpha]_D^{25}$ –40.0 (*c* = 1.00, $CHCl_3$).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.45–6.90 (m, 52 H), 6.75 (d, *J* = 8.3 Hz, 2 H), 6.62 (d, *J* = 8.3 Hz, 2 H), 6.09 (s, 2 H), 5.14 (s, 4 H), 5.02–4.94 (m, 8 H), 4.70 (s, 4 H), 4.43 (s, 2 H), 4.30 (d, *J* = 12.3 Hz, 2 H), 4.19–4.14 (m, 4 H), 3.69 (s, 2 H), 2.94 (d, *J* = 18.6 Hz, 2 H), 2.65 (dd, *J* = 17.1, 4.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.1, 154.9, 153.6, 148.4, 147.9, 138.5, 138.1, 137.7 137.6, 137.4, 133.1, 128.5, 128.4, 128.3, 128.04, 127.96, 127.69, 127.67, 127.5, 127.4, 127.31, 127.26, 127.2, 127.11, 127.05, 119.8, 114.4, 113.8, 111.8, 101.4, 91.6, 72.6, 71.3, 70.8, 70.8, 70.3, 70.0, 24.6, 17.4.

IR (film): 3067, 2960, 2875, 1623, 1489, 1281, 1234, 1140, 1026, 730, 674 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{101}H_{89}O_{12}$: 1493.6349; found: 1493.6355.

Tetradeca-*O*-benzyl Talienbisflavan A (10i)

Yield: 49.1 mg (90%); colorless oil; $[\alpha]_D^{25}$ –105.0 (*c* = 1.00, $CHCl_3$).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.13 (m, 70 H), 7.03 (d, *J* = 7.6 Hz, 4 H), 6.82 (s, 2 H), 6.66 (d, *J* = 8.1 Hz, 2 H), 6.60 (d, *J* = 8.1 Hz, 2 H), 6.17 (s, 2 H), 5.35 (s, 2 H), 5.04–4.92 (m, 20 H), 4.78 (d, *J* = 12.3 Hz, 2 H), 4.70–4.62 (m, 6 H), 4.21–4.17 (m, 4 H), 3.01–2.89 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.2, 156.3, 154.9, 153.7, 152.3, 148.7, 148.5, 142.8, 137.4, 137.3, 137.1, 136.5, 131.8, 128.4, 128.3, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.1, 119.9, 114.5, 113.7, 111.7, 109.5, 101.1, 91.6, 75.0, 71.2, 71.2, 70.6, 70.0, 68.6, 29.4, 17.4.

IR (film): 3065, 3028, 2934, 2870, 1718, 1614, 1590, 1499, 1446, 1428, 1371, 1322, 1269, 1119, 868, 813, 735, 694 cm^{-1}.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{143}H_{120}O_{20}Na$: 2179.8265; found: 2179.8277.

Deca-*O*-benzyl Bis-8,8′-epigallocatechinylmethane (10j)

Yield: 37.8 mg (98%); yellow oil; $[\alpha]_D^{25}$ –25.1 (*c* = 1.00, $CHCl_3$).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.07 (m, 50 H), 6.58 (s, 4 H), 6.18 (s, 2 H), 5.05–4.94 (m, 16 H), 4.77 (d, *J* = 11.9 Hz, 2 H), 4.68 (d, *J* = 12.0 Hz, 2 H), 4.23 (s, 2 H), 4.14 (s, 2 H), 4.01 (d, *J* = 2.8 Hz, 2 H), 3.01 (d, *J* = 17.0 Hz, 2 H), 2.87 (dd, *J* = 17.1, 4.4 Hz, 2 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 156.2, 155.4, 153.5, 152.6, 138.04, 137.99, 137.7, 137.4, 137.0, 134.4, 128.50, 128.49, 128.4, 128.21, 128.16, 127.7, 127.5, 127.3, 127.2, 127.1, 111.4, 106.2, 100.9, 91.7, 78.1, 75.2, 71.0, 70.2, 70.0, 66.1, 28.8, 17.5.

IR (film): 3037, 2960, 1619, 1481, 1277, 1230, 1142, 1021, 738, 692 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C$_{101}$H$_{89}$O$_{14}$: 1525.6247; found: 1525.6254.

Dodeca-*O*-benzyl Bis-8,8′-epigallocatechinylmethane (10k)

Yield: 38.8 mg (90%); yellow oil; $[\alpha]_D^{25}$ –35.6 (*c* = 1.00, CHCl$_3$).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.47–7.03 (m, 52 H), 6.93–6.85 (s, 8 H), 6.69 (s, 4 H), 6.11 (s, 2 H), 5.07 (s, 4 H), 4.97–4.87 (m, 14 H), 4.73 (d, *J* = 6.4 Hz, 2 H), 4.31 (s, 2 H), 4.26 (d, *J* = 12.6 Hz, 2 H), 4.17 (s, 2 H), 4.11 (d, *J* = 12.5 Hz, 2 H), 3.73 (s, 2 H), 3.04 (d, *J* = 17.7 Hz, 2 H), 2.70 (dd, *J* = 17.0, 4.3 Hz, 2 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 156.1, 155.0, 153.7, 152.3, 138.3, 138.1, 138.0, 137.6, 137.4, 137.2, 135.4, 128.54, 128.47, 128.3, 128.1, 128.0, 127.9, 127.7, 127.6, 127.51, 127.46, 127.23, 127.20, 127.15, 127.0, 111.9, 106.4, 101.3, 91.8, 77.7, 75.2, 72.5, 70.86, 70.84, 70.2, 70.1, 24.9, 17.4.

IR (film): 3050, 2962, 2851, 1629, 1471, 1287, 1232, 1131, 1024, 755, 693 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C$_{115}$H$_{101}$O$_{14}$: 1705.7186; found: 1705.7193.

Hexadeca-*O*-benzyl Oolonghomobisflavan A (10l)

Yield: 58.1 mg (97%); colorless oil; $[\alpha]_D^{25}$ –89.0 (*c* = 1.00, CHCl$_3$).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.35–7.05 (m, 84 H), 6.53 (s, 4 H), 6.18 (s, 2 H), 5.45 (s, 2 H), 4.96–4.90 (m, 16 H), 4.84 (s, 4 H), 4.77 (d, *J* = 11.6 Hz, 4 H), 4.68 (s, 4 H), 4.62 (d, *J* = 11.5 Hz, 4 H), 4.20 (d, *J* = 16.5 Hz, 4 H), 3.03 (s, 4 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 165.1, 156.4, 155.0, 153.8, 152.6, 152.4, 143.0, 138.1, 137.9, 137.6, 137.4, 137.2, 136.9, 136.4, 134.0, 128.50, 128.46, 128.4, 128.32, 128.26, 128.16, 128.11, 127.9, 127.77, 127.70, 127.5, 127.3, 127.1, 125.3, 111.9, 109.7, 106.6, 101.2, 91.7, 75.1, 75.0, 71.4, 71.1, 70.5, 70.0, 68.4, 26.4, 17.6.

IR (film): 3061, 2969, 1725, 1627, 1481, 1282, 1230, 1141, 1010, 738, 694 cm^{-1}.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for C$_{157}$H$_{132}$O$_{22}$Na: 2391.9102; found: 2391.9109.

Deca-*O*-methyl Bis-8,8′-catechinylmethane (10m)

Yield: 16.5 mg (90%); white foam; $[\alpha]_D^{25}$ +16.7 (*c* = 1.00, CHCl$_3$).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.81–6.73 (m, 6 H), 5.97 (s, 2 H), 4.32 (d, *J* = 8.4 Hz, 2 H), 3.91–3.81 (m, 18 H), 3.50–3.42 (m, 8 H), 3.13 (s, 6 H), 3.06 (dd, *J* = 16.1, 5.7 Hz, 2 H), 2.47 (dd, *J* = 16.1, 9.7 Hz, 2 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 157.2, 155.4, 153.4, 148.6, 148.5, 132.6, 119.8, 110.7, 110.6, 110.4, 101.3, 88.6, 79.4, 77.2, 57.0, 56.0, 55.9, 55.7, 55.2, 25.8, 16.8.

IR (film): 3061, 2968, 1620, 1485, 1297, 1231, 1143, 1019, 757, 679 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C$_{41}$H$_{49}$O$_{12}$: 733.3219; found: 733.3214.

Deca-*O*-ethyl Bis-8,8′-catechinylmethane (10n)

Yield: 19.9 mg (91%); white foam; $[\alpha]_D^{25}$ +15.2 (*c* = 1.00, CHCl$_3$).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.80 (d, *J* = 8.3 Hz, 2 H), 6.77 (d, *J* = 1.5 Hz, 2 H), 6.70 (dd, *J* = 8.2, 1.5 Hz, 2 H), 5.99 (s, 2 H), 4.18 (s, 6 H), 4.05 (s, 8 H), 3.89 (s, 2 H), 3.80 (s, 4 H), 3.43 (s, 2 H), 3.34 (s, 2 H), 3.07 (dd, *J* = 16.2, 5.9 Hz, 2 H), 2.95 (s, 2 H), 2.46 (dd, *J* = 16.2, 9.7 Hz, 2 H), 1.49 (s, 18 H), 1.17 (t, *J* = 6.9 Hz, 6 H), 0.93 (t, *J* = 7.0 Hz, 6 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 156.4, 154.6, 153.5, 148.2, 148.1, 133.0, 119.8, 113.2, 112.8, 111.2, 102.1, 90.7, 79.7, 76.2, 65.2, 64.7, 64.3, 64.2, 63.6, 27.4, 17.2, 15.4, 15.01, 14.95, 14.88, 14.87.

IR (film): 3067, 2931, 1621, 1450, 1266, 1232, 1110, 1020, 742, 698 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C$_{51}$H$_{69}$O$_{12}$: 873.4784; found: 873.4789.

3,3′-Diacetoxy-octa-*O*-methyl Bis-8,8′-catechinylmethane (10o)

Yield: 17.8 mg (90%); colorless oil; $[\alpha]_D^{25}$ +12.0 (*c* = 1.00, CHCl$_3$).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.74 (d, *J* = 8.2 Hz, 2 H), 6.69 (d, *J* = 1.6 Hz, 2 H), 6.64 (dd, *J* = 8.3, 1.6 Hz, 2 H), 5.98 (s, 2 H), 5.18–5.12 (m, 2 H), 4.53 (s, 2 H), 3.89 (s, 8 H), 3.79 (s, 6 H), 3.78 (s, 6 H), 3.54 (s, 6 H), 2.99 (dd, *J* = 16.3, 5.8 Hz, 2 H), 2.57 (dd, *J* = 16.3, 8.2 Hz, 2 H), 1.88 (s, 6 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 169.8, 157.4, 155.4, 152.9, 148.6, 148.6, 131.0, 119.6, 110.4, 110.0, 100.5, 88.5, 77.9, 69.7, 55.9, 55.8, 55.2, 25.2, 20.9, 16.7.

IR (film): 3065, 2955, 2891, 1713, 1635, 1481, 1292, 1232, 1149, 1035, 913, 760, 698 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C$_{43}$H$_{49}$O$_{14}$: 789.3117; found: 789.3113.

3,3′-Diacetoxy-octa-*O*-ethyl Bis-8,8′-catechinylmethane (10p)

Yield: 20.5 mg (91%); colorless oil; $[\alpha]_D^{25}$ +18.0 (*c* = 1.00, CHCl$_3$).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.73 (d, *J* = 8.3 Hz, 2 H), 6.68 (s, 2 H), 6.58 (d, *J* = 8.1 Hz, 2 H), 5.98 (s, 2 H), 5.14–5.08 (m, 2 H), 4.40 (d, *J* = 8.1 Hz, 2 H), 4.12 (s, 14 H), 3.82–3.67 (m, 4 H), 3.00 (dd, *J* = 16.4, 5.7 Hz, 2 H), 2.55 (dd, *J* = 16.3, 8.5 Hz, 2 H), 1.85 (s, 6 H), 1.47–1.37 (m, 18 H), 1.20 (t, *J* = 6.9 Hz, 6 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 169.8, 156.6, 154.7, 153.0, 148.3, 131.2, 119.7, 113.1, 112.3, 110.9, 100.8, 90.5, 77.9, 70.0, 64.6, 64.4, 64.1, 63.5, 25.4, 20.8, 17.0, 14.9, 14.89, 14.87, 14.79.

IR (film): 3062, 2934, 1735, 1632, 1528, 1452, 1260, 1236, 1117, 1026, 735, 691 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C$_{51}$H$_{65}$O$_{14}$: 901.4369; found: 901.4378.

3,3′-Diacetoxy-octa-*O*-propargyl Bis-8,8′-catechinylmethane (10q)

Yield: 22.8 mg (93%); yellow oil; $[\alpha]_D^{25}$ +19.7 (*c* = 1.00, CHCl$_3$).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.92 (d, *J* = 8.3 Hz, 2 H), 6.87 (s, 2 H), 6.67 (d, *J* = 8.2 Hz, 2 H), 6.27 (s, 2 H), 5.19–5.14 (m, 2 H), 4.77–4.62 (m, 14 H), 4.39 (s, 4 H), 3.95 (s, 2 H), 2.99 (dd, *J* = 16.5, 5.3 Hz, 2 H), 2.61 (dd, *J* = 16.7, 7.6 Hz, 2 H), 2.55–2.46 (m, 8 H), 1.90 (s, 6 H).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 169.8, 155.4, 153.6, 152.9, 147.3, 147.1, 132.1, 120.7, 114.5, 113.8, 112.1, 102.4, 92.1, 79.5, 78.8, 78.6, 78.4, 77.7, 76.0, 75.8, 75.4, 74.9, 69.3, 57.03, 56.94, 56.87, 56.2, 24.7, 20.9, 17.2.

IR (film): 3305, 3054 2931, 2106, 1739, 1628, 1522, 1456, 1255, 1232, 1117, 1026, 738, 680, 627 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for C$_{59}$H$_{49}$O$_{14}$: 981.3117; found: 981.3124.

Tetradeca-*O*-methyl Talienbisflavan A (10r)

Yield: 24.9 mg (91%); yellow solid; mp 85–87 °C; $[\alpha]_D^{25}$ –40.8 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10 (s, 4 H), 6.84–6.80 (m, 4 H), 6.74 (d, *J* = 8.1 Hz, 2 H), 6.09 (s, 2 H), 5.46 (s, 2 H), 4.67 (s, 2 H), 4.07 (s, 2 H), 3.85–3.78 (m, 30 H), 3.61–3.60 (m, 12 H), 3.01–3.00 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.3, 157.5, 155.9, 153.6, 152.7, 148.64, 148.55, 142.3, 131.2, 125.1, 119.1, 111.1, 110.6, 110.5, 107.2, 100.1, 89.0, 76.8, 68.9, 60.7, 56.4, 56.2, 55.8, 55.7, 55.2, 25.8, 16.9.

IR (film): 3067, 2960, 2875, 1623, 1489, 1282, 1230, 1143, 1026, 730, 694 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{59}H_{65}O_{20}$: 1093.4064; found: 1093.4069.

Tetradeca-*O*-propargyl Talienbisflavan A (10s)

Yield: 32.9 mg (92%); yellow oil; $[\alpha]_D^{25}$ –67.4 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (s, 4 H), 6.99–6.97 (m, 4 H), 6.86 (d, *J* = 8.2 Hz, 2 H), 6.39 (s, 2 H), 5.48 (s, 2 H), 4.81–4.41 (m, 30 H), 4.13 (s, 2 H), 3.02–2.98 (m, 4 H), 2.56–2.37 (m, 14 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.7, 155.4, 153.9, 153.4, 151.2, 147.1, 141.3, 132.1, 125.7, 120.5, 114.3, 113.9, 112.6, 110.5, 102.0, 92.8, 79.5, 78.8, 78.7, 78.6, 78.3, 77.9, 76.5, 76.06, 76.05, 75.7, 75.5, 75.0, 68.5, 60.3, 57.39, 57.36, 57.0, 56.8, 56.3, 25.9, 17.4.

IR (film): 3301, 3045, 2955, 2098, 1618, 1467, 1280, 1230, 1145, 1020, 765, 680 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{87}H_{65}O_{20}$: 1429.4064; found: 1429.4069.

Hexadeca-*O*-propargyl Oolonghomobisflavan A (10t)

Yield: 35.4 mg (92%); yellow solid; mp 85–87 °C; $[\alpha]_D^{25}$ –74.9 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (s, 4 H), 6.68 (s, 4 H), 6.40 (s, 2 H), 5.55 (s, 2 H), 4.81–4.48 (m, 34 H), 4.14 (s, 2 H), 3.01–3.00 (m, 4 H), 2.53–2.38 (m, 16 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.5, 155.4, 153.9, 153.32, 151.25, 151.2, 141.5, 137.0, 134.3, 125.7, 112.6, 110.7, 107.7, 101.9, 92.7, 79.5, 79.2, 78.7, 78.6, 78.3, 77.8, 76.5, 76.0, 75.7, 75.5, 75.4, 75.0, 68.1, 60.32, 60.25, 57.5, 57.4, 57.3, 56.3, 25.9, 17.5.

IR (film): 3315, 3067, 2960, 2098, 1619, 1485, 1283, 1234, 1142, 1021, 738, 688 cm^{-1}.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{93}H_{69}O_{22}$: 1537.4275; found: 1537.4280.

Bisflavanol-Type Natural Products; Typical Procedure

To a solution of *O*-benzyl dimeric flavanols **10** (0.01 mmol) in a solvent mixture of THF/MeOH (1:1, v/v, 1 mL) were added $Pd(OH)_2/C$ (5%, 40 mg) in a hydrogen atmosphere. The resulting reaction mixture was stirred at r.t. for 10 h. The reaction mixture was filtered to remove the catalyst. The filtrate was evaporated, and the residue was rapidly purified by flash chromatography (AcOH/MeOH/CH_2Cl_2, 1:5:50) over silica gel to afford bisflavanol-type natural products **1**–**4**.

Bis-8,8′-catechinylmethane (1)

Yield: 5.3 mg (90%); yellow amorphous powder; $[\alpha]_D^{25}$ –104.7 (*c* = 1.50, MeOH).

^{1}H NMR [400 MHz, $(CD_3)_2CO$]: δ = 6.97 (s, 2 H), 6.80 (s, 4 H), 5.99 (s, 2 H), 4.66 (d, *J* = 8.0 Hz, 2 H), 4.10–4.04 (m, 2 H), 3.61 (s, 2 H), 2.94 (dd, *J* = 16.2, 5.3 Hz, 2 H), 2.55 (dd, *J* = 15.7, 8.2 Hz, 2 H).

^{13}C NMR [100 MHz, $(CD_3)_2CO + D_2O$]: δ = 155.3, 155.2, 152.4, 146.0, 145.7, 130.6, 120.1, 115.9, 115.4, 105.2, 100.9, 96.9, 83.6, 69.1, 28.1, 16.4.

IR (film): 3057, 3031, 2932, 2878, 1612, 760 cm^{-1}.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{31}H_{27}O_{12}$: 591.1508; found: 591.1507.

Bis-8,8′-epicatechinylmethane (2)

Yield: 5.3 mg (90%); white amorphous powder; $[\alpha]_D^{25}$ –104.1 (*c* = 0.15, MeOH).

^{1}H NMR (400 MHz, CD_3OD): δ = 6.97 (s, br, 2 H), 6.75 (s, br, 4 H), 5.98 (s, 2 H), 4.78 (s, br, 2 H), 4.12 (s, br, 2 H), 3.90 (s, 2 H), 2.85 (dd, *J* = 16.6, 4.7 Hz, 2 H), 2.70 (d, *J* = 16.8 Hz, 2 H).

^{13}C NMR (100 MHz, CD_3OD): δ = 155.7, 155.1, 153.5, 145.8, 131.6, 119.6, 115.8, 115.3, 106.6, 100.4, 96.7, 80.3, 67.0, 28.8, 16.6.

IR (film): 3065, 3033, 2919, 2873, 1606, 763 cm^{-1}.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{31}H_{27}O_{12}$: 591.1508; found: 591.1507.

Talienbisflavan A (3)

Yield: 7.0 mg (78%); yellow amorphous powder; $[\alpha]_D^{14}$ –105.4 (*c* = 0.10, methanol).

^{1}H NMR (400 MHz, CD_3OD): δ = 6.93 (s, 4 H), 6.86 (s, 2 H), 6.71–6.66 (m, 4 H), 6.03 (s, 2 H), 5.44 (s, br, 2 H), 4.79 (s, br, 2 H), 3.95 (s, 2 H), 2.95 (dd, *J* = 17.5, 3.5 Hz, 2 H), 2.80 (d, *J* = 17.4 Hz, 2 H).

^{13}C NMR (100 MHz, CD_3OD): δ = 167.5, 155.9, 155.2, 153.6, 146.5, 146.2, 145.9, 139.8, 130.3, 121.5, 119.7, 116.0, 115.4, 110.1, 106.7, 100.5, 96.8, 79.1, 69.4, 26.9, 16.8.

IR (film): 3407, 1695, 1615, 1451, 1229, 1038, 766 cm^{-1}.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{45}H_{35}O_{20}$: 895.1727; found: 895.1725.

Oolonghomobisflavan A (4)

Yield: 7.5 mg (81%); white amorphous powder; $[\alpha]_D^{25}$ –271.1 (*c* = 1.00, acetone).

^{1}H NMR [400 MHz, $(CD_3)_2CO$]: δ = 7.08 (s, 4 H), 6.76 (s, 4 H), 6.12 (s, 2 H), 5.64–5.59 (m, 2 H), 5.11 (s, 2 H), 4.00 (s, br, 2 H), 3.14–3.00 (m, 4 H).

^{13}C NMR [100 MHz, $(CD_3)_2CO + D_2O$]: δ = 166.2, 156.0, 155.7, 152.7, 146.4, 145.9, 138.9, 133.5, 129.9, 121.7, 110.3, 106.8, 105.7, 99.2, 97.6, 79.3, 68.9, 26.9, 16.4.

IR (film): 3410, 1695, 1617, 1445, 1224, 1035, 765 cm^{-1}.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{45}H_{35}O_{22}$: 927.1625; found: 927.1629.

Funding Information

This work was supported by the National Natural Science Foundation of China (21672046 and 21372054), the Fundamental Research Funds for the Central Universities (HIT.NSRIF.201701), and the Foundation from Huancui District of Wehai City.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1610707.

References

(1) (a) Ferreira, D.; Bekker, R. *Nat. Prod. Rep.* **1996**, *13*, 411. (b) Ferreira, D.; Slade, D. *Nat. Prod. Rep.* **2002**, *19*, 517.

(2) (a) Xu, Y.; Ho, C. T.; Amin, S. G.; Han, C.; Chuang, F. L. *Cancer Res.* **1992**, *52*, 3875. (b) Von Gadow, A.; Joubert, E.; Hansmann, C. F. *Food Chem.* **1997**, *60*, 73. (c) Hirano, R.; Sasamoto, W.; Matsumoto, A.; Itakura, H.; Igarashi, O.; Kondo, K. *J. Nutr. Sci. Vitaminol.* **2001**, *47*, 357.

(3) (a) Gibbons, S.; Moser, E.; Kaatz, G. W. *Planta Med.* **2004**, *70*, 1240. (b) Gradišar, H.; Pristovšek, P.; Plaper, A.; Jerala, R. *J. Med. Chem.* **2007**, *50*, 264.

(4) (a) Miura, Y.; Chiba, T.; Tomita, I.; Koizumi, H.; Miura, S.; Umegaki, K.; Hara, Y.; Ikeda, M.; Tomita, T. *J. Nutr.* **2001**, *131*, 27. (b) Calixto, J. B.; Campos, M. M.; Otuki, M. F.; Santos, A. R. *Planta Med.* **2004**, *70*, 93.

(5) (a) Kinjo, J.; Nagao, T.; Tanaka, T.; Nonaka, G.; Okawa, M.; Nohara, T.; Okabe, H. *Biol. Pharm. Bull.* **2002**, *25*, 1238. (b) Landis-Piwowar, K. R.; Huo, C.; Chen, D. I.; Milacic, V.; Shi, G.; Chan, T. H.; Dou, Q. P. *Cancer Res.* **2007**, *67*, 4303. (c) Chen, D.; Wan, S. B.; Yang, H.; Yuan, J.; Chan, T. H.; Dou, Q. P. *Adv. Clin. Chem.* **2011**, *53*, 155.

(6) Hatano, T.; Miyatake, H.; Natsume, M.; Osakabe, N.; Takizawa, T.; Ito, H.; Yoshida, T. *Phytochemistry* **2002**, *59*, 749.

(7) Ma, Q.; Xie, H.; Li, S.; Zhang, R.; Zhang, M.; Wei, X. *J. Agric. Food Chem.* **2014**, *62*, 1073.

(8) Zhu, L. F.; Xu, M.; Zhu, H. T.; Wang, D.; Yang, S. X.; Yang, C. R.; Zhang, Y. J. *J. Agric. Food Chem.* **2012**, *60*, 12170.

(9) Hashimoto, F.; Nonaka, G.; Nishioka, I. *Chem. Pharm. Bull.* **1989**, *37*, 3255.

(10) (a) Nakai, M.; Fuki, U.; Asami, S.; Toyoda-Ono, Y.; Iwashita, T.; Shibata, H.; Mitsunaga, T.; Hashimoto, F. *J. Agric. Food Chem.* **2005**, *53*, 4593. (b) Gao, D. F.; Zhang, Y. J.; Yang, C. R.; Chen, K. K.; Jiang, H. J. *J. Agric. Food Chem.* **2008**, *56*, 7517. (c) Liu, Q.; Zhang, Y. J.; Yang, C. R.; Xu, M. *J. Agric. Food Chem.* **2009**, *57*, 586. (d) Gao, D. F.; Xu, M.; Yang, C. R.; Xu, M.; Zhang, Y. J. *J. Agric. Food Chem.* **2010**, *58*, 8820.

(11) Boyer, F. D.; Ducrot, P. H. *Tetrahedron Lett.* **2005**, *46*, 5177.

(12) Pariollaud, M.; Cockrell, J.; Selenski, C. *Tetrahedron Lett.* **2014**, *55*, 2484.

(13) (a) Hillis, W. E.; Gerda, U. *J. Appl. Chem.* **1959**, *9*, 474. (b) Kiatgrajai, P.; Wellons, J. D.; Gollob, L.; White, J. D. *J. Org. Chem.* **1982**, *47*, 2913. (c) Fechtal, M.; Riedl, B.; Calvé, L. *Holzforschung* **1993**, *47*, 419.

(14) (a) Takagaki, A.; Fukai, K.; Nanjo, F.; Hara, Y. *J. Wood Sci.* **2000**, *46*, 334. (b) Takagaki, A.; Fukai, K.; Nanjo, F.; Hara, Y.; Watanabe, M.; Sakuragawa, S. *Mokuzai Gakkaishi* **2000**, *46*, 231. (c) Toshiyuki, T.; Tomomi, M.; Hiroshi, K.; Fumiaki, N. *J. Wood Sci.* **2008**, *54*, 329.

(15) Huang, D.-M.; Li, H.-J.; Wang, J.-H.; Wu, Y.-C. *Org. Biomol. Chem.* **2018**, *16*, 585.

(16) (a) Wan, S. B.; Dou, Q. P.; Chan, T. H. *Tetrahedron* **2006**, *62*, 5897. (b) Sánchez-del-Campo, L.; Otón, F.; Tárraga, A.; Cabezas-Herrera, J.; Chazarra, S.; Rodríguez-López, J. N. *J. Med. Chem.* **2008**, *51*, 2018. (c) Imai, K.; Nakanishi, I.; Ohno, A.; Kurihara, M.; Miyata, N.; Matsumoto, K. I.; Nakamura, A.; Fukuhara, K. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 2582. (d) Sarmiento, V.; Ramirez-Sanchez, I.; Moreno-Ulloa, A.; Romero-Perez, D.; Chávez, D.; Ortiz, M.; Najera, N.; Correa-Basurto, J.; Villarreal, F.; Ceballos, G. *Bioorg. Med. Chem. Lett.* **2018**, *28*, 658.

(17) Srivastava, V.; Negi, A. S.; Kumar, J. K.; Gupta, M. M. *Steroids* **2006**, *71*, 632.

(18) (a) Wan, S. B.; Chen, D.; Dou, Q. P.; Chan, T. H. *Bioorg. Med. Chem.* **2004**, *12*, 3521. (b) Osanai, K.; Huo, C.; Landis-Piwowar, K. R.; Dou, Q. P.; Chan, T. H. *Tetrahedron* **2007**, *63*, 7565. (c) Qin, X. L.; Li, X. M.; Yuan, J.; Chen, D.; Jiang, T.; Dou, Q. P.; Chan, T. H.; Wan, S. B. *Synth. Commun.* **2012**, *42*, 3524.

(19) (a) Lai, Y. Y.; Lin, N. T.; Liu, Y. H.; Wang, Y.; Luh, T. Y. *Tetrahedron* **2007**, *63*, 6051. (b) Cao, D.; Kou, Y.; Liang, J.; Chen, Z.; Wang, L.; Meier, H. *Angew. Chem. Int. Ed.* **2009**, *48*, 9721. (c) Sawama, Y.; Masuda, M.; Asai, S.; Goto, R.; Nagata, S.; Nishimura, S.; Monguchi, Y.; Sajiki, H. *Org. Lett.* **2015**, *17*, 434. (d) Okada, Y.; Wakamatsu, H.; Sugai, M.; Kauppinen, E. I.; Chiba, K. *Org. Lett.* **2015**, *17*, 4264.

(20) (a) Rathore, R.; Kochi, J. K. *J. Org. Chem.* **1995**, *60*, 7479. (b) Branchi, B.; Bietti, M.; Erocolani, G.; Izquierdo, M. A.; Miranda, M. A.; Stella, L. *J. Org. Chem.* **2004**, *69*, 8874.

(21) (a) Wilsdorf, M.; Leichnitz, D.; Reissig, H. U. *Org. Lett.* **2013**, *15*, 2494. (b) Wang, K.; Tan, L. L.; Chen, D. X.; Song, N.; Xi, G.; Zhang, S. X. A.; Li, C. J.; Yang, Y. W. *Org. Biomol. Chem.* **2012**, *10*, 9405.