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Roxbin B is Cuspinin: Structural Revision and Total Synthesis

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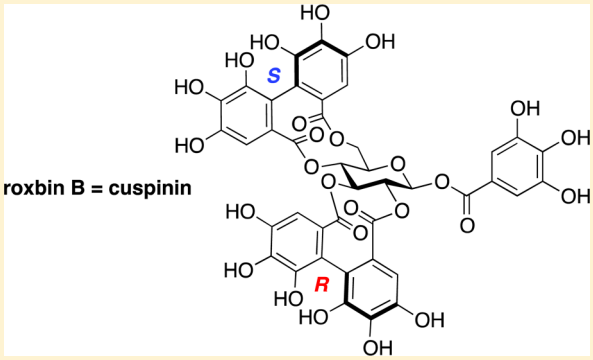
Supporting Information

ABSTRACT: Prompted by the outcome that the synthesized roxbin B was not identical to the natural roxbin B, the structural determination process and spectral data were re-examined, with the finding that roxbin B was very likely to be 1-*O*-galloyl-2,3-(*R*);4,6-(*S*)-bis-*O*-hexahydroxydiphenoyl-*β*-D-glucose (cuspinin). Because the (*R*)-axial chirality is rare in natural products when the hexahydroxydiphenoyl group bridges the 2- and 3-oxygens, the proposed structure of cuspinin was confirmed by the total synthesis, leading to the conclusion that roxbin B is the same as cuspinin.



INTRODUCTION

Ellagitannins are a class of hydrolyzable tannins, hydrolysis of which provides glucose and ellagic acid. The ellagic acid derives from the hexahydroxydiphenoyl (HHDP) group (Figure 1);

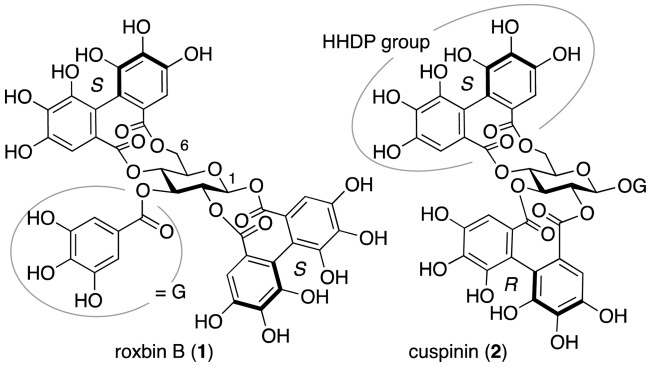


Figure 1. Proposed structures of roxbin B and cuspinin.

therefore, the basic structure of an ellagitannin is that of a glucose-possessing HHDP group(s).[1,2] (−)-Roxbin B is a natural ellagitannin that was isolated from the unripe fruits of *Rosa roxburghii* TRATT in 1987, the structure of which was proposed to be 3-*O*-galloyl-1,2;4,6-bis-*O*-(*S*)-HHDP-*β*-D-glucose (**1**).[3] Recently, we synthesized the proposed structure **1**. However, the synthetically obtained **1** was not identical to the naturally occurring roxbin B.[4]

This discrepancy prompted us to reconsider the structure of roxbin B, and we found that roxbin B was very likely to be 1-*O*-galloyl-2,3-(*R*);4,6-(*S*)-bis-*O*-HHDP-*β*-D-glucose (cuspinin)[5] (**2**). In addition, synthetic works confirmed the proposed structure of cuspinin (**2**), and the synthetic **2** was identified as natural roxbin B; hence, **2** is the correct structure of roxbin B. We describe here all the details of the correction of the structure.

RESULTS AND DISCUSSIONS

Re-examination of the Structural Determination of Roxbin B. The structure **1** reported for roxbin B was proposed based on the evidence summarized as follows.[3] (1) Acid hydrolysis of the natural product demonstrated that the galloyl and HHDP groups and D-glucose configure roxbin B. (2) According to NMR studies, the numbers of the galloyl and HHDP groups are one and two, respectively. The $^4C_1$ conformation and *β*-anomeric stereochemistry of the glucose moiety are based on the coupling constants between the neighboring protons on the pyranose ring (Figure 2). In addition, the large difference in chemical shifts between the protons on C-6 is the decisive factor in determining that one of the HHDP groups bridges the 4,6-position. (3) On the basis of the CD spectrum, which showed a positive Cotton effect at 236 nm, the axial chirality of both HHDP groups was determined to be *S*.[6] These observations support the partial structure **3**, in

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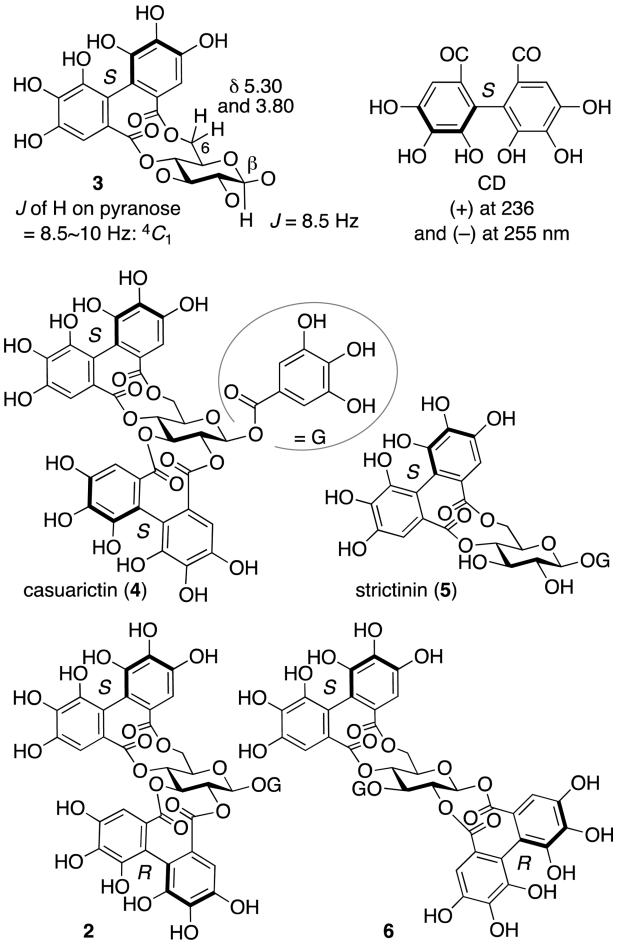

Figure 2. Consideration of the correct structure of roxbin B.

which an (*S*)-HHDP group bridges two of the unassigned three hydroxy oxygens, and a galloyl group is located on the remaining oxygen. Among the three possible bridging positions, namely the 1,2-, 1,3-, or 2,3-positions, roxbin B has the 1,2- or 2,3-HHDP bridge because the 1,3-HHDP bridge should change the $^4C_1$ conformation of the sugar. Of these two possible structures, the 2,3-HHDP-compound is a natural product, casuarictin (**4**),[7] which is not identical to roxbin B. Hence, the structure of roxbin B was concluded to have the 1,2-(*S*)-HHDP bridge.

In the logic of the structural determination, we considered the case when roxbin B might have an (*R*)-HHDP group because its amplitude ($[\theta]$ +2.2 × 10^4) of the Cotton effect at 236 nm in the CD spectrum was smaller than that expected for the presence of two (*S*)-HHDP groups in a molecule.[6] In the present study, the *S*-axial chirality of the 4,6-HHDP bridge was evidenced by remeasurement of the NMR for a sample stored at room temperature for over 20 years, which indicated that roxbin B mostly degraded to strictinin (1-*O*-galloyl-4,6-(*S*)-HHDP-β-D-glucose, **5**)[8] (Figure 2). Thus, the candidates for the correct structure of roxbin B were limited to two, which were **2** and **6** possessing 2,3-(*R*);4,6-(*S*)-HHDP-bridges and 1,2-(*R*);4,6-(*S*)-HHDP-bridges, respectively. Here, **2** corresponds to the structure of cuspinin isolated from *Castanopsis cuspidata* var. *sieboldii* NAKAI (Fagaceae) by Nishioka et al.[5] The literature data of roxbin B were found to be consistent with those of cuspinin within an acceptable error range (see Supporting Information),[3,5] demonstrating that roxbin B is very likely to be cuspinin.

An acyl group at the anomeric center (O-1) on β-D-glucose is generally susceptible to hydrolysis before those at the other positions under mild treatment, such as with hot water or tannase.[9,10] However, in the degradation of roxbin B described above, **5** was detected as the major component in the degraded products, implying that the (*R*)-HHDP residue at O-2/O-3 on the D-glucose core is more labile than the O-1 acyl group, probably due to a stereochemical strain.

Structural Confirmation through Total Synthesis. We then tried to confirm the structure of cuspinin, which is roxbin B, through total synthesis. Synthetically, construction of the 2,3-(*R*)-HHDP bridge is intricate. Intramolecular coupling of fully-*O*-protected galloyl esters on the 2,3-position of glucose provides the (*S*)-HHDP bridge stereoselectively.[11−13] The 2,3-(*R*)-HHDP-bridge was prepared stereoselectively by Ito et al. through the double esterification strategy.[14] The double esterification (Figure 3(1)) is a formation of bislactone **B**

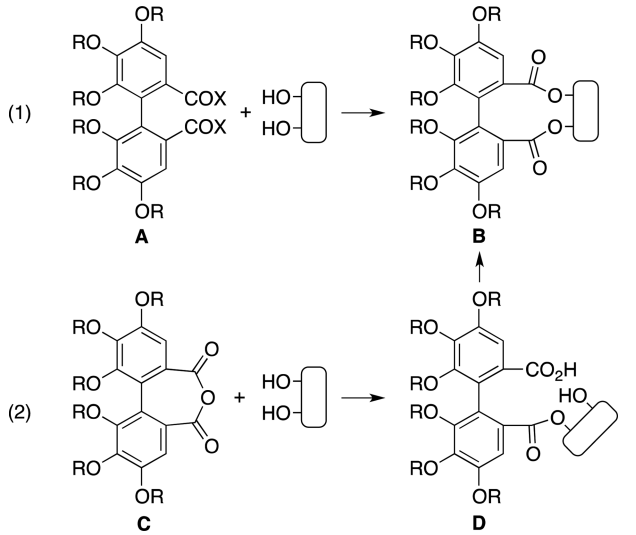

Figure 3. (1) Double esterification and (2) stepwise esterification. R = protecting group, X = leaving group including activated form of carboxylic acid.

starting from HHDP dicarboxylic acid **A** and a diol through successive inter- and intramolecular esterification in one pot.[15] During the double esterification, the kinetic resolution of the rotational isomer of the HHDP group often occurs, which induces the (*R*)-selectivity in Ito's work. However, a fully-*O*-methylated HHDP group is employed in their work. Removal of the methyl protections is quite difficult in ellagitannin synthesis without decomposition of the other parts of the molecule, and thus total synthesis of ellagitannins has never been achieved when the methyl groups protect the phenolic hydroxy groups.[16−20] In addition, the kinetic resolution does not always work as (*R*)-selective. Khanbabaee et al. manipulated racemic hexabenzylated HHDP dicarboxylic acid to provide a 2,3-(*S*)-HHDP compound.[21,22] On the other hand, no diastereoselectivity is observed in Quideau's synthesis.[23] Taken together, the stereoselective procedure for synthesizing the 2,3-(*R*)-HHDP-bridge has been one of the outstanding problems in ellagitannin synthesis.

Under these circumstances, we planned to form the uncertain 2,3-bridge prior to the 4,6-bridge (Scheme 1).

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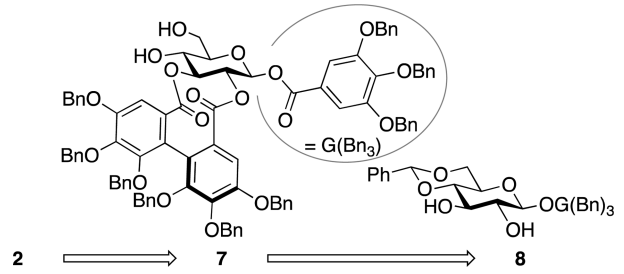
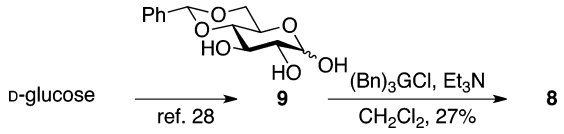
Scheme 1. Retrosynthesis of Cuspinin (2) and the Synthetic Strategy



Thus, the retrosynthetic analysis started with the removal of the 4,6-HHDP bridge of **2**. To form the 2,3-HHDP bridge of **7**, the β-glucosyl gallate **8** would be its precursor.[12] In these formations of the bridges, the key strategy was the two-stage approach to construct the HHDP bridges of **2**, that is, the "double esterification" was applied first using chiral HHDP dicarboxylic acid **A**[25] (Figure 3(1)). Then, the "stepwise esterification" was investigated (Figure 3(2)) if the first approach was not effective. The stepwise esterification utilized anhydride of HHDP dicarboxylic acid **C**[4] to form an ester bond at the more reactive hydroxy group followed by lactonization of the resulting seco acid **D**. For the protecting group of the phenolic hydroxy groups, the benzyl group was chosen because hydrogenolytic debenzylation in the final step of the total synthesis has been verified to be effective.[15,25−27]

The starting material **8** was synthesized by Spring et al. in eight steps from D-glucose.[12] In this work, we prepared **8** in two steps from D-glucose (Scheme 2). Thus, the esterification of

Scheme 2. Two-step Synthesis of 8

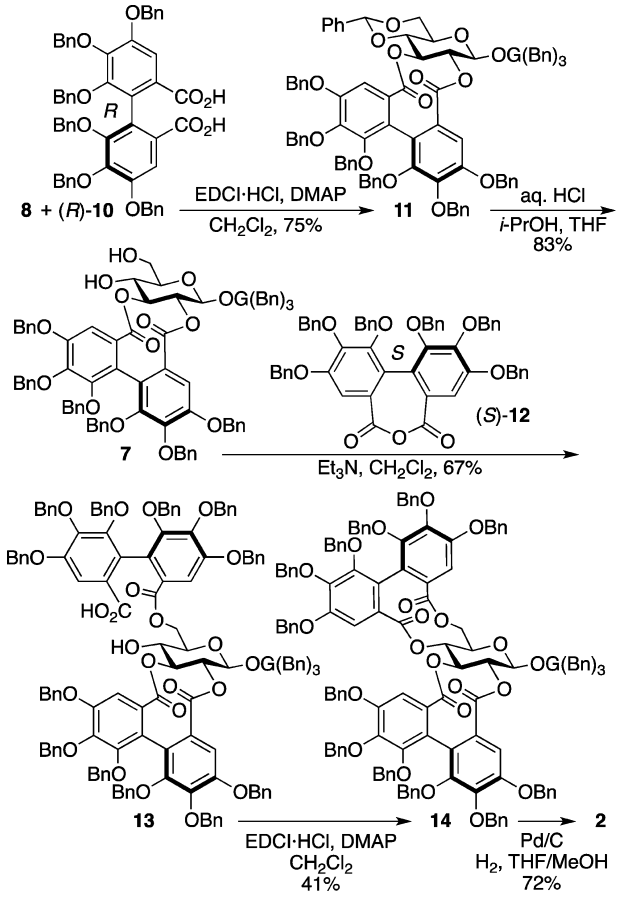


known triol **9**[28] with 3,4,5-tri-*O*-benzylgalloyl chloride [$(Bn)_3GCl$] furnished the anomeric β-gallate to give **8** in 27% yield. For the formation of the β-glycosyl ester, Et_3N was employed to obtain the stereoselectivity.[29]

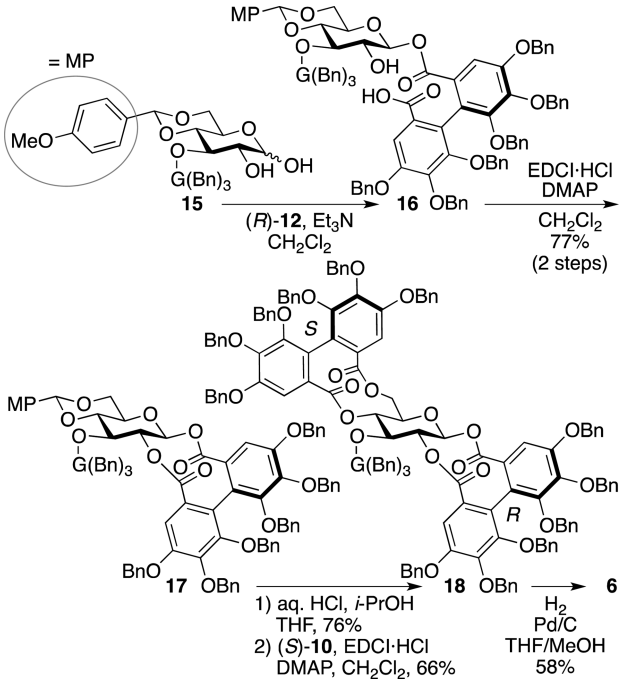
With the two-stage approach as the key strategy of the synthesis, we synthesized cuspinin (**2**) in five steps from diol **8** (Scheme 3). The double esterification at the 2,3-positions of **8** was possible using dicarboxylic acid (*R*)-**10**[25] to furnish 2,3-(*R*)-HHDP-bridged **11**, from which benzylidene acetal was hydrolyzed to give 4,6-diol **7**. Regarding the formation of the 4,6-bridge on **7**, the double esterification of the 4,6-diol with (*S*)-dicarboxylic acid (*S*)-**10**[4] provided the desired **14** but with significant amount of byproducts, in contrast to the 4,6-bridge formation in the synthesis of the proposed structure of roxbin B.[4] We therefore relied on stepwise esterification utilizing acid anhydride (*S*)-**12**.[4] The esterification of diol **7** occurred at the sterically less hindered 6-OH, providing **13**, 4-OH of which was successively esterified intramolecularly to build the 4,6-(*S*)-HHDP-bridge of **14**. Finally, debenzylation of **14** afforded **2**. The ^1H and ^{13}C NMR spectra of synthetic **2** was identical to those of natural cuspinin[5] (and also roxbin B),[3] thereby synthetically confirming their structures.

For more reliability, we synthesized another candidate **6** that possesses the 1,2-(*R*);4,6-(*S*)-HHDP groups (Scheme 4). The

Scheme 3. Synthesis of Cuspinin (2)



Scheme 4. Synthesis of the Second Candidate (6)



synthesis commenced with the formation of the 1,2-HHDP-bridge by stepwise esterification. Thus, treatment of diol **15**[4] with acid anhydride (*R*)-**12** in the presence of Et_3N, followed by lactonization of the obtained β-glycosyl ester **16** provided

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1,2-bridged **17** in 77% yield from **15**. Acid hydrolysis of **17** removed the *p*-methoxybenzylidene acetal, providing the corresponding 4,6-diol (**20**: not shown in Scheme 4) in 76% yield. The double esterification of **20** was possible in this case with (*S*)-**10** to afford 1,2- and 4,6-bridged **18** in 66% yield. Finally, hydrogenolytic cleavage of the benzyl groups gave **6**. The ^{1}H and ^{13}C NMR data of synthesized **6** were obviously different from those of cuspinin.

Resolved NMR Assignment of Cuspinin (= Roxbin B). The reported ^{1}H and ^{13}C NMR assignments of roxbin B and cuspinin include small discrepancies (see Supporting Information).[3,5] We updated the data as summarized in Table 1 to resolve the discrepancies.

The Reason for the Erroneous Structural Assignment for Roxbin B. As we synthesized in the present study a series of ellagitannins possessing the 2,3-(*R*)- and 1,2-(*R* or *S*)-HHDP groups, whose CD spectra have not been available so far, we measured the spectra of the synthetic **1**,[4] **2**, and **6** together with 1-*O*-galloyl-2,3-(*R*)-HHDP-*β*-D-glucose (**19**) (Figure 4) prepared by hydrogenolysis of **7**.

The CD spectrum of **1**, which possessed two (*S*)-HHDP units, showed a strong positive Cotton effect ($[\theta]$ $+9.3 \times 10^4$) at 232 nm and a negative one ($[\theta]$ -3.4×10^4) at 257 nm (Figure 4), while **6** that had the (*R*)- and (*S*)-HHDP groups in the molecule exhibited a weak positive Cotton ($[\theta]$ $+0.7 \times 10^4$) at 214 nm and a negative one ($[\theta]$ -1.2×10^4) at 233 nm. These data indicated that the positive Cotton effect at ca. 230 nm characteristic of the (*S*)-HHDP group was canceled by a slightly stronger Cotton effect with an opposite sign in the same wavelength region due to the (*R*)-congener. The CD spectrum of **19** gave a negative ($[\theta]$ -2.1×10^4) and a positive Cotton effect ($[\theta]$ $+1.4 \times 10^4$) at 215 and 237 nm, respectively. It is noteworthy that the Cotton effects empirically characteristic of a 2,3-(*R*)-HHDP group were found to appear at about 20 nm shorter wavelength than those of the (*S*)-HHDP unit. Cuspinin (**2**) exhibited a negative Cotton effect ($[\theta]$ -2.7×10^4) at 221 nm, and a positive one ($[\theta]$ $+4.0 \times 10^4$) at 235 nm, ascribable to the (*R*)- and (*S*)-HHDP units, respectively. The erroneous structural assignment for natural roxbin B was thus considered to be the result of the missing Cotton effect at the shortest wavelength.

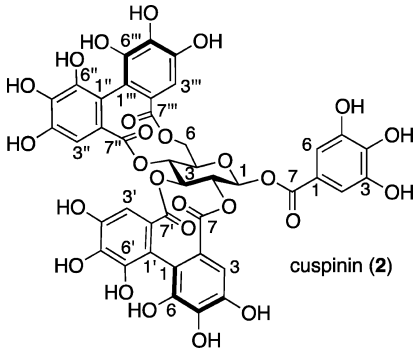
CONCLUSION

We found that roxbin B was cuspinin through the re-examination of spectral data and the synthetic confirmation of the proposed structure of cuspinin. This work thus accomplished the structural revision of roxbin B. In addition, the achieved synthesis of the second candidate when we considered the structural revision of roxbin B strengthened the conclusion. The synthesis of cuspinin is the first stereoselective total synthesis of a 2,3-(*R*)-HHDP-ellagitannin, the axial chirality of which is unusual when the HHDP group bridges the 2- and 3-hydroxy groups of glucose. The synthesis of the second candidate demonstrated that the 1,2-(*R*)-HHDP structure on *β*-D-glucose could be present, the bridge structure of which has not been found in natural ellagitannins. The result expanded the structural diversity of potential ellagitannins.

EXPERIMENTAL SECTION

General Methods. All commercially available reagents were used without further purification. All moisture and air sensitive reactions were performed in glassware equipped with rubber septa (or a septum) under the positive pressure of argon or nitrogen. When

Table 1. Resolved Full Assignments of ^{13}C and ^{1}H NMR of Cuspinin in Acetone-d_6



atom no.	^{13}C[a]	^{1}H[b]		HMBC (H to C)
glucose				
1	92.5	6.08	d (8.2)	galloyl-7
2	77.2	4.89	dd (8.2, 9.8)	1, 3, HHDP-7
3	78.2	5.20	t (9.8)	2, 4, HHDP-7′
4	69.6	4.88	t (9.8)	3, 5, HHDP-7″
5	73.2	4.39	ddd (1.1, 6.7, 9.8)	1, 3, 4
6	63.0	5.30	dd (6.7, 13.5)	HHDP-7‴
		3.79	dd (1.1, 13.5)	4, 5, HHDP-7‴
2,3-HHDP				
1	117.6			
1′	117.4			
2	122.1			
2′	120.2			
3	108.3	6.79	br d	HHDP-1,4,5
3′	111.0	7.11	br d	HHDP-1′,4′,5′
4	144.9			
4′	145.1			
5	137.2			
5′	138.5			
6	145.6[c]			
6′	145.4[d]			
7	168.3			
7′	168.1			
4,6-HHDP				
1″	115.7			
1‴	115.8			
2″	126.4[c]			
2‴	126.1[d]			
3″	107.9	6.70	s	HHDP-1″,4″,5″,6″
3‴	108.3	6.58	s	HHDP-1‴,4‴,5‴,6‴
4″	144.4			
4‴	144.5			
5″	136.4			
5‴	136.4			
6″	145.2			
6‴	145.0			
7″	167.2			
7‴	167.9			
galloyl				
1	120.0			
2,6	110.5	7.25	s	galloyl-1,2,3,4,5,6
3,5	146.2			
4	139.9			
7	164.9			

[a]125 MHz. [b]500 MHz. [c,d]Assignments may be interchanged.

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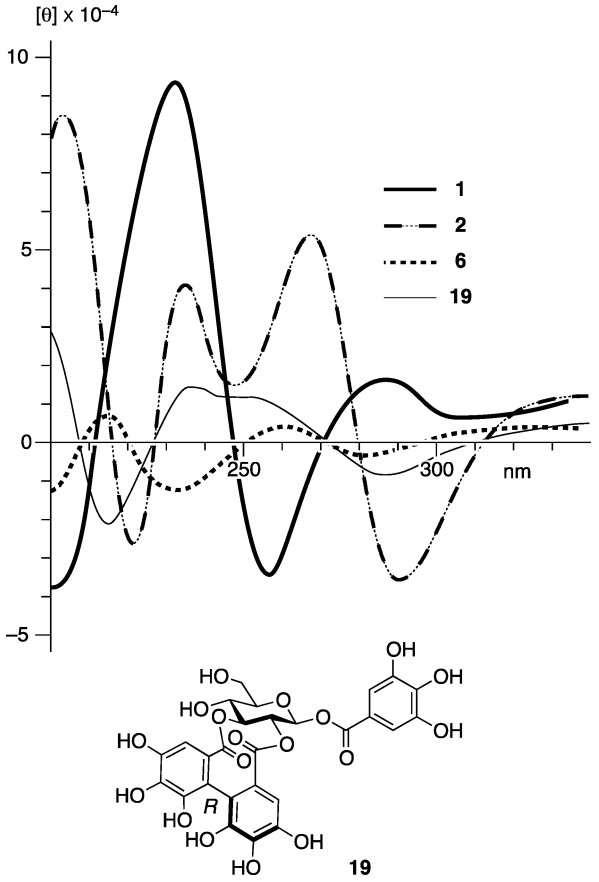

Figure 4. CD spectra of **1**, **2**, **6**, and **19**.

necessary, the glassware was dried under reduced pressure by heating with a heat-gun, and solvents were distilled prior to use. The reaction mixture was magnetically stirred. Concentration was performed under reduced pressure.

The reactions were monitored by TLC and MS. Anhydrous $MgSO_4$ was used to dry organic layers after extraction, and it was removed by filtration through a cotton pad. The filtrate was concentrated and subjected to further purification protocols if necessary. This sequence was represented as "the general drying procedure" in the following experimental methods.

TLC was performed on Merck precoated silica gel 60 F-254 plates or Merck RP-19 F-254 plates. Spots were visualized by exposure to UV light, or by immersion into a solution of 2% anisaldehyde, 5% H_2SO_4 in ethanol or a solution of 10% phosphomolybdic acid in ethanol, followed by heating at ca. 200 °C.

Column chromatography (CC) was performed on Merck silica gel 60 (0.063−0.200 mm or 0.040−0.063 mm), Kanto Chemical silica gel 60 N (Spherical, neutral: 40−50 or 63−210 μm) for the ordinary phase, and Nacalai Tesque Cosmosil 140C18-PREP for the reverse phase. The other carrier materials were noted in each case.

The melting points were uncorrected. Optical rotations were determined with a 100 mm cell at 589 nm. IR spectra were recorded with a spectrophotometer equipped with an ATR sampling unit, and the major absorbance bands are all reported in wavenumbers (cm^{-1}).

NMR spectra (^1H: 400 MHz, ^{13}C: 100 MHz) were observed in acetone-d_6. Either TMS or residual protons of deuterated solvent were used as an internal reference. The ^1H NMR data are indicated by chemical shifts (δ), with the multiplicity, the coupling constants, and the integration in parentheses. The multiplicities are abbreviated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and br, broad. The ^{13}C NMR data are reported as the chemical shifts (δ) with the hydrogen multiplicity obtained from the DEPT spectra. The multiplicities are abbreviated as s, C; d, CH; t, CH_2; and q, CH_3. When the number for carbon was more than one, the number was added in parentheses.

4,6-*O*-Benzylidene-1-*O*-(3,4,5-tri-*O*-benzylgalloyl)-β-D-glucopyranose (8). To a stirred solution of $(Bn)_3GCl$ [prepared from 5.45 mmol of $(Bn)_3GOH$] in CH_2Cl_2 (9.3 mL) were added Et_3N (755 mg, 7.46 mmol) and **9** (1.00 g, 3.73 mmol) in CH_2Cl_2 (28 mL) at rt. After being stirred for 1 h, the mixture was added H_2O (20 mL). The aqueous mixture was extracted with CH_2Cl_2. The combined organic layer was washed with brine. After the general drying procedure, the extract was added silica gel (5 g). The mixture was evaporated to adsorb the reaction products onto the silica gel. The silica gel powder was charged on the top a silica gel column (50 g of SiO_2) and eluted first with CH_2Cl_2 then AcOEt. The roughly separated compound was purified by another CC (30 g of SiO_2, *n*-hexane/AcOEt = 50/50). Finally, crystallization from toluene gave **8** (689 mg, 27% yield) as a white solid. The ^1H NMR spectra was identical to the reported data.[12]

4,6-*O*-Benzylidene-1-*O*-(3,4,5-tri-*O*-benzylgalloyl)-2,3-*O*-(*R*)-[4,4′,5,5′,6,6′-hexabenzyloxy-1,1′-biphenyl-2,2′-dicarboxylate]-β-D-glucopyranose (11). To a stirred solution of **8** (204 mg, 65.9 μmol) and (*R*)-**10**[24] (486 mg, 553 μmol) in CH_2Cl_2 (3.0 mL) were added DMAP (91.1 mg, 746 μmol) and EDCI·HCl (383 mg, 2.00 mmol). After being stirred for 42 h at rt, the mixture was added H_2O (3 mL). The aq mixture was extracted with AcOEt. The combined organic layer was washed with brine. After the general drying procedure, the crude product was purified by CC (20 g of SiO_2, *n*-hexane/AcOEt = 80/20 to 70/30) to afford **11** (334 mg, 75% yield) as a colorless amorphous solid: $[\alpha]_D^{23}$ −31.6 (*c* 0.455, $CHCl_3$); IR 3089, 3064, 3032, 2926, 2875, 1739, 1589, 1497, 1455, 1430, 1408, 1364, 1331, 1214, 1194, 1145, 1093, 1029, 1011, 910, 849, 750, 696; ^1H NMR 7.66−7.17 (m, 46 H), 6.99 (s, 1 H), 6.93−6.76 (m, 7 H), 5.97 (d, *J* = 7.8 Hz, 1 H), 5.83 (s, 1 H), 5.34−5.26 (m, 7 H), 5.16 (s, 2 H), 5.13−5.01 (m, 5 H), 4.94 (d, *J* = 11.0 Hz, 1 H), 4.90 (d, *J* = 9.6 Hz, 1 H), 4.89 (d, *J* = 11.0 Hz, 1 H), 4.85 (d, *J* = 11.2 Hz, 1 H), 4.68 (d, *J* = 11.4 Hz, 1 H), 4.52 (d, *J* = 10.3 Hz, 1 H), 4.36 (dd, *J* = 15.1, 9.8 Hz, 1 H), 4.13 (dd, *J* = 8.7, 8.7 Hz, 1 H), 4.00−3.92 (m, 2 H); ^{13}C NMR 169.1 (s), 167.2 (s), 164.6 (s), 153.7 (s, 2 C), 153.6 (s), 153.4 (s), 153.1 (s), 153.0 (s), 147.6 (s), 144.8 (s), 143.9 (s), 138.7 (s, 2 C), 138.6 (s), 138.3 (s), 138.3 (s), 137.9 (s, 2 C), 137.6 (s), 137.5 (s), 130.0−128.3 (overlapping 48 doublets and 1 singlet: 26 peaks were observed), 127.4 (d, 2 C), 127.0 (s), 126.8 (s), 125.5 (s), 124.7 (s), 123.4 (s), 113.2 (d), 110.2 (d, 2 C), 108.1 (d), 102.2 (d), 93.2 (d), 78.8 (d), 78.1 (d), 77.4 (d), 75.9 (t), 75.8 (t), 75.8 (t), 75.7 (t), 75.5 (t), 71.8 (t, 2 C), 71.6 (t), 71.5 (t), 68.7 (t), 68.2 (d); HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{97}H_{80}O_{18}Na$ 1555.5242, found 1555.5291.

1-*O*-(3,4,5-Tri-*O*-benzylgalloyl)-2,3-*O*-(*R*)-[4,4′,5,5′,6,6′-hexabenzyloxy-1,1′-biphenyl-2,2′-dicarboxylate]-β-D-glucopyranose (7). To a stirred solution of **11** (170 mg, 111 μmol) in THF (0.2 mL) was added a mixture of *i*-PrOH and conc. hydrochloric acid (v/v = 1/1) (0.2 mL) at rt. After being stirred for 37.5 h, the mixture was added saturated aq $NaHCO_3$ (10 mL). The aq mixture was extracted with AcOEt. The combined organic layer was washed with brine. After the general drying procedure, the crude product was purified by CC (2 g of SiO_2, *n*-hexane/AcOEt = 70/30 to 50/50) to afford **7** (132 mg, 83% yield) as a colorless amorphous solid: $[\alpha]_D^{23}$ −27.3 (*c* 1.13, $CHCl_3$); IR 3467, 3064, 3032, 2936, 2880, 1736, 1717, 1589, 1497, 1455, 1429, 1408, 1364, 1331, 1215, 1192, 1095, 1079, 1029, 908, 843, 749, 695; ^1H NMR 7.61−7.57 (m, 9 H), 7.49−7.17 (m, 30 H), 7.20−7.17 (m, 3 H), 6.95−6.75 (m, 7 H), 5.81 (d, *J* = 8.0 Hz, 1 H), 5.36 (d, *J* = 12.3 Hz, 1 H), 5.32 (d, *J* = 12.1 Hz, 1 H), 5.30−5.22 (m, 5 H), 5.16−4.86 (m, 11 H), 4.68 (d, *J* = 11.5 Hz, 1 H), 4.57 (d, *J* = 10.4 Hz, 1 H), 4.02−3.71 (m, 4 H); ^{13}C NMR 169.6 (s), 167.2 (s), 164.6 (s), 153.6 (s, 2 C), 153.5 (s), 153.4 (s), 153.1 (s), 153.0 (s), 147.5 (s), 144.8 (s), 143.7 (s), 138.7 (s, 2 C), 138.5 (s), 138.4 (s), 138.3 (s), 137.9 (s, 2 C), 137.8 (s), 137.5 (s), 129.5−128.3 (overlapping 45 doublets: 24 peaks were observed), 127.3 (s), 127.1 (s), 125.6 (s), 124.9 (s), 123.6 (s), 113.0 (d), 110.1 (d, 2 C), 108.5 (d), 92.7 (d), 82.6 (d), 78.6 (d), 76.8 (d), 75.9 (t), 75.8 (t, 2 C), 75.7 (t), 75.5 (t), 71.8 (t), 71.8 (t, 2 C), 71.5 (t), 68.2 (d), 61.6 (t); HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{90}H_{76}O_{18}Na$ 1467.4929, found 1467.4900.

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1-*O*-(3,4,5-Tri-*O*-benzylgalloyl)-2,3-*O*-(*R*)-[4,4′,5,5′,6,6′-hexabenzyloxy-1,1′-biphenyl-2,2′-dicarboxylate]-6-*O*-(*S*)-[4,4′,5,5′,6,6′-hexabenzyloxy-1,1′-biphenyl-2-carboxylate-2′-carboxylic acid]-β-D-glucopyranose (13). To a stirred solution of (*S*)-**12**[4] (prepared from 226 μmol of **10**) and Et_3N (14.2 mg, 140 μmol) in CH_2Cl_2 (0.8 mL) was added a solution of diol **7** (98.2 mg, 67.9 μmol) in CH_2Cl_2 (1.5 mL) at rt. After being stirred for 6 d at rt, the reaction was quenched by addition of H_2O (1 mL). The aq mixture was extracted with AcOEt. The combined organic layer was washed with brine. After the general drying procedure, the crude product was purified by CC (5 g of SiO_2, *n*-hexane/AcOEt = 75/25 to 65/35) to afford **13** (106 mg, 67%) as a colorless oil: $[\alpha]_D^{23}$ −19.6 (*c* 0.45, $CHCl_3$); IR 3462 3090, 3064, 3032, 2927, 2874, 2859, 1732, 1589, 1497, 1481, 1455, 1430, 1410, 1369, 1334, 1238, 1213, 1192, 1095, 1028, 972, 909, 848, 751, 696; ^{1}H NMR 7.72 (s, 1 H), 7.69 (s, 1 H), 7.65−7.52 (m, 13 H), 7.46−7.13 (m, 54 H), 6.96−6.86 (m, 10 H), 6.75−6.73 (m, 2 H), 5.81 (d, *J* = 7.6 Hz, 1 H), 5.38−5.28 (m, 6 H), 5.24 (d, *J* = 11.7 Hz, 1 H), 5.18−4.81 (m, 22 H), 4.69 (d, *J* = 11.5 Hz, 1 H), 4.60−4.54 (m, 3 H), 4.29 (dd, *J* = 12.1, 5.5 Hz, 1 H), 3.91−3.77 (m, 2 H); ^{13}C NMR 169.7 (s), 168.6 (s), 167.1 (s), 166.7 (s), 164.8 (s), 153.6 (s, 2 C), 153.5 (s), 153.4 (s), 153.1 (s, 2 C), 152.7 (s), 152.4 (s), 151.9 (s), 151.8 (s), 147.7 (s), 146.5 (s), 146.0 (s), 144.7 (s), 143.7 (s), 139.0 (s), 138.9 (s), 138.8 (s), 138.7 (s), 138.6 (s), 138.6 (s), 138.5 (s), 138.4 (s), 138.3 (s), 138.2 (s), 138.2 (s), 137.8 (s, 2 C), 137.8 (s), 137.5 (s), 129.5−128.2 (overlapping 75 doublets and 2 singlets: 20 peaks were observed), 127.9 (s), 127.2 (s), 126.5 (s), 125.6 (s), 124.9 (s), 123.8 (s), 123.3 (s), 112.1 (d), 112.0 (d), 110.1 (d, 4 C), 92.9 (d), 82.3 (d), 76.7 (d), 75.9 (t), 75.9 (t, 2 C), 75.7 (t, 2 C), 75.7 (t), 75.5 (t), 75.2 (t), 75.1 (t), 72.7 (d), 71.8 (t), 71.7 (t), 71.7 (t), 71.6 (t), 71.4 (t), 71.0 (t), 68.4 (d), 64.0 (t); HRMS (ESI-TOF) *m*/*z*: $[M - H]^-$ Calcd for $C_{146}H_{119}O_{27}$ 2303.7939, found 2303.7880.

1-*O*-(3,4,5-Tri-*O*-benzylgalloyl)-2,3-*O*-(*R*)-[4,4′,5,5′,6,6′-hexabenzyloxy-1,1′-biphenyl-2,2′-dicarboxylate]-4,6-*O*-(*S*)-[4,4′,5,5′,6,6′-hexabenzyloxy-1,1′-biphenyl-2,2′-dicarboxylate]-β-D-glucopyranose (14). To a stirred solution of **13** (106 mg, 45.8 μmol) in CH_2Cl_2 (1 mL) were added DMAP (11.3 mg, 92.5 μmol) and EDCI·HCl (27.3 mg, 142 μmol). After being stirred for 1 d at rt, the mixture was added H_2O (2 mL). The aq mixture was extracted with AcOEt. The combined organic layer was washed with brine. After the general drying procedure, the crude product was purified by CC (2 g of SiO_2, *n*-hexane/AcOEt = 80/20) to afford **14** (34.5 mg, 41% yield) as a colorless oil: $[\alpha]_D^{22}$ −44.4 (*c* 1.03, $CHCl_3$); IR 3066, 3031, 3018, 2933, 2877, 1750, 1590, 1497, 1455, 1429, 1413, 1366, 1331, 1216, 1184, 1096, 1073, 1029, 1006, 910, 750; ^{1}H NMR (55 °C) 7.66 (s, 2 H), 7.63 (s, 1 H), 7.54−6.86 (m, 78 H), 6.16 (d, *J* = 8.0 Hz, 1 H), 5.44−4.82 (m, 31 H), 4.64 (d, *J* = 10.8 Hz, 1 H), 4.62 (d, *J* = 10.8 Hz, 1 H), 4.53 (dd, *J* = 9.6, 6.4 Hz, 1 H), 4.46 (d, *J* = 11.2 Hz, 1 H), 4.06 (d, *J* = 13.3 Hz, 1 H); ^{13}C NMR (55 °C) 168.1 (s), 167.9 (s), 167.7 (s), 167.7 (s), 164.8 (s), 154.2 (s), 154.0 (s, 2 C), 153.8 (s, 2 C), 153.7 (s), 153.4 (s), 153.4 (s), 153.1 (s), 152.8 (s), 147.3 (s), 147.1 (s), 145.8 (s), 145.6 (s), 144.9 (s), 138.9 (s), 138.8 (s, 2 C), 138.8 (s, 2 C), 138.7 (s), 138.7 (s), 138.5 (s, 2 C), 138.0 (s, 2 C), 137.9 (s), 137.8 (s, 2 C), 137.5 (s), 130.0 (s), 129.8 (s), 129.5−128.3 (overlapping 75 doublets and 3 singlets: 55 peaks were observed), 127.6 (s), 127.0 (s), 124.9 (s), 124.6 (s), 112.2 (d), 111.9 (d), 111.2 (d, 2 C), 109.6 (d), 109.6 (d), 93.3 (d), 78.8 (d), 77.7 (d), 76.3 (t, 2 C), 76.3 (t), 76.1 (t, 2 C), 75.8 (t, 2 C), 75.5 (t), 73.4 (d), 72.7 (t), 72.5 (t, 2 C), 72.5 (t, 2 C), 72.2 (t), 72.2 (t), 70.5 (d), 64.0 (t); HRMS (FAB) *m*/*z*: $[M + Na]^+$ Calcd for $C_{146}H_{118}O_{26}Na$ 2309.7809, found 2309.7791.

Cuspinin (2). A mixture of **14** (76.5 mg, 33.4 μmol) and Pd on carbon (10 wt %, 28.8 mg) in THF (0.7 mL) and MeOH (0.7 mL) was stirred for 1.5 h at rt under H_2 atmosphere. The mixture was filtered through a cotton-Celite pad to remove Pd/C. The concentrated filtrate was purified by Avicel cellulose (Funakoshi) CC with 2% AcOH, followed by purification on MCI-gel CHP 20P chromatography. Elution with H_2O containing increasing proportions of MeOH gave **2** (22.4 mg, 72% yield) as a gray amorphous powder. The ^{1}H and ^{13}C NMR spectra were identical to those of repurified sample of natural cuspinin; for their comparison, see Supporting Information.

(*R*)-4,4′,5,5′,6,6′-Hexakisbenzyloxy-1,1′-biphenyl-2,2′-dicarboxylic Acid Anhydride ((*R*)-12). To a stirred solution of dicarboxylic acid (*R*)-**10**[25] (163 mg, 186 μmol) in toluene (1.9 mL) and DMF (17 μL) was added $(COCl)_2$ (28 mg, 223 μmol). After being stirred for 40 min at 70 °C, the mixture was concentrated. To the resulting residue was added toluene and the solution was concentrated to azeotropically remove excess $(COCl)_2$. This procedure was repeated three times to provide (*R*)-**12** as a yellow syrup: $[\alpha]_D^{21}$ −14.0 (*c* 1.02, $CHCl_3$). ^{1}H and ^{13}C NMR data for (*R*)-**12** was identical to the literature data.[4] The crude product was used for the next reaction without further purification.

4,6-*O*-Anisylidene-3-*O*-(3,4,5-tri-*O*-benzylgalloyl)-1-*O*-(*R*)-[4,4′,5,5′,6,6′-hexabenzyloxy-1,1′-biphenyl-2-carboxylate-2′-carboxylic acid]-β-D-glucopyranose (16). To a stirred solution of (*R*)-**12** (prepared from 186 μmol of (*R*)-**10** as described above) in CH_2Cl_2 (0.4 mL) was added a mixture of diol **15**[4] (31.5 mg, 43.7 μmol) and Et_3N (12.1 mg, 120 μmol) in CH_2Cl_2 (0.9 mL). After being stirred for 19.5 h at 50 °C, the reaction was quenched by addition of saturated aq NH_4Cl (3 mL). The aq mixture was extracted with AcOEt. The combined organic layer was washed with brine. After the general drying procedure, the crude product was purified by CC (3 g of SiO_2, *n*-hexane/AcOEt = 80/20 to 70/30, followed by SiO_2 1.5 g, *n*-hexane/$CHCl_3$ = 25/75) to afford **16** (48.3 mg, 76% yield) as a colorless oil: $[\alpha]_D^{22}$ −15.5 (*c* 0.925, $CHCl_3$); IR 3734−3088, 3062, 3031, 2957, 2878, 2837, 1738, 1713, 1589, 1519, 1497, 1455, 1250, 1213, 1186, 1077, 1029, 1002, 909, 835, 752, 696; ^{1}H NMR 7.78 (s, 1 H), 7.75 (s, 1 H), 7.61−7.59 (m, 4 H), 7.50−7.17 (m, 41 H), 6.95−6.92 (m, 4 H), 6.85 (d, *J* = 8.7 Hz, 2 H), 5.84 (d, *J* = 7.8 Hz, 1 H), 5.53 (dd, *J* = 9.2, 9.2 Hz, 1 H), 5.51 (s, 1 H), 5.35 (s, 2 H), 5.28 (s, 2 H), 5.16 (d, *J* = 11.7 Hz, 2 H), 5.13−5.05 (m, 7 H), 5.02 (d, *J* = 11.0 Hz, 1 H), 4.97 (d, *J* = 11.0 Hz, 1 H), 4.94 (d, *J* = 10.8 Hz, 1 H), 4.83 (d, *J* = 11.0 Hz, 2 H), 4.21 (dd, *J* = 9.6, 3.9 Hz, 1 H), 3.84−3.60 (m, 7 H); ^{13}C NMR 167.5 (s), 165.7 (s), 165.1 (s), 161.0 (s), 153.5 (s, 2 C), 152.8 (s), 152.6 (s), 152.0 (s), 151.7 (s), 147.1 (s), 146.6 (s), 143.3 (s), 138.9 (s), 138.8 (s, 2 C), 138.8 (s), 138.5 (s), 138.5 (s), 138.2 (s), 138.0 (s, 2 C), 130.9 (s), 130.0 (s), 129.4−128.2 (overlapping 47 doublets and 1 singlet: 26 peaks were observed), 126.9 (s), 126.1 (s), 125.3 (s), 114.1 (d, 2 C), 112.7 (d), 112.5 (d), 109.9 (d, 2 C), 102.2 (d), 95.8 (d), 79.4 (d), 75.9 (t, 2 C), 75.6 (d), 75.5 (t), 75.2 (t), 75.2 (t), 72.9 (d), 72.0 (t), 71.9 (t), 71.8 (t, 2 C), 69.0 (t), 67.5 (d), 55.5 (q); HRMS (ESI-TOF) *m*/*z*: $[M - H]^-$ Calcd for $C_{98}H_{83}O_{20}$ 1579.5478, found 1579.5421.

4,6-*O*-Anisylidene-3-*O*-(3,4,5-tri-*O*-benzylgalloyl)-1,2-*O*-(*R*)-[4,4′,5,5′,6,6′-hexabenzyloxy-1,1′-biphenyl-2,2′-dicarboxylate]-β-D-glucopyranose (17). To a stirred solution of **16** (585 mg, 370 μmol) in CH_2Cl_2 (3.7 mL) were added DMAP (50.4 mg, 413 μmol) and EDCI·HCl (212 mg, 1.11 mmol). After being stirred for 3 h at rt, the mixture was added H_2O (10 mL). The aq mixture was extracted with AcOEt. The combined organic layer was washed with brine. After the general drying procedure, the crude product was purified by CC (20 g of SiO_2, *n*-hexane/AcOEt = 80/20 to 75/25) to afford **17** (398 mg, 73% yield for 2 steps) as a colorless oil: $[\alpha]_D^{24}$ −1.1 (*c* 0.455, $CHCl_3$); IR 3088, 3063, 3032, 2933, 2873, 1760, 1728, 1589, 1519, 1497, 1482, 1455, 1428, 1412, 1368, 1332, 1249, 1214, 1201, 1178, 1150, 1093, 1076, 1003, 970, 909, 832, 750, 696; ^{1}H NMR 7.61−6.87 (m, 53 H), 6.28 (d, *J* = 7.6 Hz, 1 H), 5.91 (dd, *J* = 9.6, 9.6 Hz, 1 H), 5.69 (s, 1 H), 5.34−5.30 (m, 3 H), 5.23−5.10 (m, 8 H), 5.00−4.92 (m, 6 H), 4.71 (d, *J* = 10.5 Hz, 1 H), 4.62 (d, *J* = 10.6 Hz, 1 H), 4.49 (dd, *J* = 10.3, 4.6 Hz, 1 H), 4.22 (dd, *J* = 9.6, 9.6 Hz, 1 H), 4.14 (ddd, *J* = 9.6, 9.6, 4.6 Hz, 1 H), 3.98 (dd, *J* = 10.3, 9.6 Hz, 1 H), 3.75 (s, 3 H); ^{13}C NMR 168.7 (s), 166.7 (s), 165.7 (s), 161.1 (s), 153.8 (s), 153.6 (s), 153.6 (s, 2 C), 153.3 (s), 153.2 (s), 145.2 (s), 145.1 (s), 143.6 (s), 138.7 (s), 138.7 (s), 138.6 (s), 138.5 (s), 138.4 (s), 137.8 (s, 3 C), 137.5 (s), 130.6 (s), 130.0 (s), 129.8 (s), 129.5−128.5 (overlapping 47 doublets and 1 singlet: 26 peaks were observed), 125.6 (s), 122.6 (s), 114.2 (d, 2 C), 109.9 (d, 2 C), 108.1 (d), 107.8 (d), 102.5 (d), 97.4 (d), 79.4 (d), 77.4 (d), 76.1 (t, 2 C), 75.9 (t), 75.9 (t), 75.5 (t), 71.8−71.7 (overlapping 4 triplets and 1

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doublet: 5 peaks were observed), 69.0 (d), 68.8 (t), 55.5 (q); HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{98}H_{82}O_{19}Na$ 1585.5348, found 1585.5355.

3-*O*-(3,4,5-Tri-*O*-benzylgalloyl)-1,2-*O*-(*R*)-[4,4′,5,5′,6,6′-hexabenzyloxy-1,1′-biphenyl-2,2′-dicarboxylate]-β-D-glucopyranose (20). To a stirred solution of **17** (18.9 mg, 12.1 μmol) in THF (0.2 mL) was added a mixture of *i*-PrOH and conc. hydrochloric acid (v/v = 50/1, 0.2 mL) at rt. After being stirred for 2 h, the mixture was added saturated aq $NaHCO_3$ (3 mL). The aq mixture was extracted with AcOEt. The combined organic layer was washed with brine. After the general drying procedure, the crude product was purified by CC (0.6 g of SiO_2, *n*-hexane/AcOEt = 70/30) to afford **20** (13.2 mg, 76% yield) as a white amorphous solid: $[\alpha]_D^{23}$ +40 (*c* 0.66, $CHCl_3$); IR 3475, 3064, 3031, 2928, 2876, 1758, 1723, 1642, 1590, 1498, 1455, 1428, 1413, 1368, 1334, 1215, 1182, 1153, 1100, 1002, 909, 844, 755, 697; ^{1}H NMR 7.62 (s, 2 H), 7.60−6.93 (m, 46 H), 6.91 (s, 1 H), 6.15 (d, J = 7.6 Hz, 1 H), 5.67 (dd, J = 10.1, 9.4 Hz, 1 H), 5.32−5.10 (m, 12 H), 4.99−4.91 (m, 5 H), 4.70 (d, J = 10.8 Hz, 1 H), 4.59 (d, J = 10.5 Hz, 1 H), 4.16−4.05 (m, 2 H), 3.95−3.92 (m, 2 H); ^{13}C NMR 168.7 (s), 166.9 (s), 166.0 (s), 153.8 (s, 2 C), 153.6 (s, 2 C), 153.2 (s, 2 C), 145.0 (s, 2 C), 143.4 (s), 138.7 (s), 138.7 (s), 138.7 (s), 138.5 (s), 138.4 (s), 137.8 (s, 2 C), 137.8 (s), 137.6 (s), 130.2 (s), 130.0 (s), 129.5−128.5 (overlapping 45 doublets: 24 peaks were observed), 126.0 (s), 122.6 (s), 122.4 (s), 110.0 (d, 2 C), 108.1 (d), 107.8 (d), 97.5 (d), 79.8 (d), 77.1 (d), 76.1 (t, 2 C), 75.9 (t), 75.9 (t), 75.9 (t), 75.4 (d), 71.8 (t), 71.8 (t, 2 C), 71.7 (t), 69.0 (d), 61.8 (t); HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{90}H_{76}O_{18}Na$ 1467.4929, found 1467.4905.

3-*O*-(3,4,5-Tri-*O*-benzylgalloyl)-1,2-*O*-(*R*)-[4,4′,5,5′,6,6′-hexabenzyloxy-1,1′-biphenyl-2,2′-dicarboxylate]-4,6-*O*-(*S*)-[4,4′,5,5′,6,6′-hexabenzyloxy-1,1′-biphenyl-2,2′-dicarboxylate]-β-D-glucopyranose (18). To a stirred solution of **20** (14.5 mg, 10.0 μmol) and (*S*)-**10**[4] (22.6 mg, 25.7 μmol) in CH_2Cl_2 (0.2 mL) were added DMAP (8.2 mg, 67.1 μmol) and EDCI·HCl (15.4 mg, 80.3 mmol). After being stirred for 14 h at rt, the mixture was added H_2O (3 mL). The aq mixture was extracted with AcOEt. The combined organic layer was washed with brine. After the general drying procedure, the crude product was purified by CC (0.6 g of SiO_2, *n*-hexane/AcOEt = 70/30) to afford **18** (15.1 mg, 66% yield) as a white amorphous solid: $[\alpha]_D^{22}$ −31.2 (*c* 0.455, $CHCl_3$); IR 3089, 3064, 3032, 2927, 2875, 1758, 1590, 1497, 1481, 1454, 1429, 1413, 1366, 1330, 1236, 1213, 1174, 1144, 1092, 1078, 1027, 1004, 970, 909, 842, 746; ^{1}H NMR 7.63−7.55 (m, 8 H), 7.48−6.86 (m, 73 H), 6.27 (d, J = 7.8 Hz, 1 H), 5.95 (dd, J = 9.8, 9.8 Hz, 1 H), 5.47−5.28 (m, 8 H), 5.25 (d, J = 11.7 Hz, 1 H), 5.22 (d, J = 10.6 Hz, 1 H), 5.15 (d, J = 11.2 Hz, 1 H), 5.07 (s, 4 H), 5.03−4.89 (m, 14 H), 4.80−4.71 (m, 4 H), 4.62 (d, J = 10.8 Hz, 1 H), 4.18 (dd, J = 13.3 Hz, 1 H); ^{13}C NMR 168.5 (s), 168.2 (s), 167.8 (s), 166.8 (s), 166.0 (s), 153.9 (s), 153.8 (s), 153.7 (s), 153.6 (s), 153.5 (s, 2 C), 153.3 (s), 153.3 (s), 153.1 (s, 2 C), 145.5 (s), 145.2 (s, 2 C), 145.0 (s), 143.6 (s), 138.7 (s), 138.7 (s, 2 C), 138.6 (s, 2 C), 138.6 (s), 138.6 (s), 138.5 (s), 138.5 (s), 138.4 (s), 137.8 (s, 2 C), 137.6 (s), 137.6 (s, 2 C), 130.2 (s), 129.9 (s), 129.5−128.3 (overlapping 75 doublets and 2 singlets: 47 peaks were observed), 125.3 (s), 124.5 (s), 124.0 (s), 122.8 (s), 122.7 (s), 110.1 (d, 2 C), 108.9 (d, 2 C), 108.3 (d), 107.9 (d), 97.5 (d), 77.0 (d), 76.1 (t, 2 C), 76.1 (t, 2 C), 76.0 (t), 76.0 (t), 75.9 (t), 75.7 (t), 75.6 (t), 75.4 (t), 74.0 (d), 72.5 (d), 71.9 (t, 3C), 71.7 (t, 2 C), 71.5 (d), 64.0 (t); HRMS (FAB) m/z: $[M + Na]^+$ Calcd for $C_{146}H_{118}O_{26}Na$ 2309.7809, found 2309.7781.

3-*O*-Galloyl-1,2-*O*-(*R*)-hexahydroxydiphenoyl-4,6-*O*-(*S*)-hexahydroxydiphenoyl-β-D-glucopyranose (6). A mixture of **18** (52.3 mg, 22.9 μmol) and Pd on carbon (5 wt %, 9.1 mg) in THF (0.5 mL) and MeOH (0.5 mL) was stirred for 75 min at rt under H_2 atmosphere. To the mixture was added further Pd on carbon (5 wt %, 10.3 mg). The mixture was stirred for additional 1.5 h at rt under H_2 atmosphere. The mixture was filtered through a cotton-Celite pad to remove Pd/C. The concentrated filtrate was purified by CC (0.4 g of Sephadex LH-20, MeOH/H_2O = 70/30 to 100/0) to afford **6** (6.5 mg, 58% yield) as a gray solid: $[\alpha]_D^{21}$ −12.6 (*c* 0.325, MeOH); IR 3363, 2949, 2840, 1733, 1615, 1517, 1446, 1346, 1317, 1177, 1141, 1080, 1012, 741; ^{1}H NMR 7.04 (s, 2 H), 6.65 (s, 1 H), 6.62 (s, 1 H), 6.47 (s, 2 H), 6.04 (d, J = 7.8 Hz, 1 H), 5.78 (dd, J = 10.1, 10.1 Hz, 1 H), 5.38 (dd, J = 13.5, 6.6 Hz 1 H), 5.19 (dd, J = 10.1 Hz, 1 H), 5.13 (dd, J = 10.1, 7.8 Hz, 1 H), 4.54 (dd, J = 10.1, 6.6 Hz, 1 H), 3.95 (d, J = 13.5 Hz, 1 H); ^{13}C NMR 168.9 (s), 168.1 (s), 167.6 (s), 167.2 (s), 166.2 (s), 145.9 (s, 2 C), 145.3 (s), 145.2 (s), 145.2 (s, 2 C), 144.9 (s, 2 C), 144.7 (s), 144.6 (s), 139.2 (s), 136.7 (s, 2 C), 136.6 (s, 2 C), 126.5 (s), 126.1 (s), 126.1 (s), 125.8 (s), 120.6 (s), 115.8 (s), 115.8 (s), 114.8 (s), 114.8 (s), 110.2 (d, 2 C), 108.1 (d), 107.9 (d), 107.4 (d), 107.0 (d), 97.5 (d), 76.6 (d), 74.1 (d), 71.6 (d), 70.7 (d), 63.0 (t); HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{41}H_{27}O_{26}$ 935.0791, found 935.0754.

1-*O*-Galloyl-2,3-*O*-(*R*)-hexahydroxydiphenoyl-β-D-glucopyranose (19). A mixture of **7** (33.8 mg, 23.4 μmol) and Pd on carbon (10 wt %, 9.2 mg) in THF (0.2 mL) and MeOH (0.2 mL) was stirred for 80 min at rt under H_2 atmosphere. The mixture was filtered through a cotton-Celite pad to remove Pd/C. The concentrated filtrate was purified by CC (0.2 g of Sephadex LH-20, MeOH/H_2O = 70/30) to afford **19** (14.0 mg, 96% yield) as a gray solid: $[\alpha]_D^{21}$ −2.25 (*c* 0.80, MeOH); IR 3376, 1716, 1616, 1448, 1351, 1208, 1069, 1037; ^{1}H NMR 7.24 (s, 2 H), 7.07 (s, 1 H), 6.86 (s, 1 H), 5.88 (d, J = 8.2 Hz, 1 H), 4.98 (dd, J = 9.8, 9.8 Hz, 1 H), 4.83 (dd, J = 8.2, 9.8 Hz, 1 H), 3.85 (dd, J = 11.9, 2.0 Hz, 1 H), 3.79−3.73 (m, 2 H), 3.64 (ddd, J = 9.4, 4,2, 2.0 Hz, 1 H); ^{13}C NMR 168.6 (s), 167.5 (s), 164.3 (s), 145.4 (s, 2 C), 144.6 (s), 144.6 (s), 144.2 (s), 144.0 (s), 139.0 (s), 137.3 (s), 136.7 (s), 121.1 (s), 120.2 (s), 119.3 (s), 116.4 (s), 116.3 (s), 109.6 (s), 109.4 (d, 2 C), 108.6 (d), 91.5 (d), 80.9 (d), 77.9 (d), 75.5 (d), 67.5 (d), 60.8 (t); HRMS (ESI-TOF) (m/z) calcd for $C_{27}H_{21}O_{18}$ $[M - H]^-$ 633.0728, found 633.0750.

■ ASSOCIATED CONTENT

Supporting Information

Comparison of literature data (^{1}H and ^{13}C NMR) of natural roxbin B and cuspinin, Comparison of ^{1}H and ^{13}C NMR spectra of natural roxbin B and cuspinin, and synthetic cuspinin, and ^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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