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Total synthesis of cucurbitoside-like phenolic glycosides by double fluorous and acyl mixture synthesis

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ABSTRACT

The first and simultaneous total syntheses of cucurbitosides A, B, G, and I, seguinosides C and D, and two unnatural analogs were achieved using the technique of fluorous mixture synthesis. The eight precursors of cucurbitoside-like phenolic glycosides were prepared by glycosylation of a mixture of two glucopyranosyl acceptors bearing different fluorous benzyl groups with a mixture of four apiofuranosyl donors bearing benzoyl, 3-methylbutyryl, 4-benzyloxybenzoyl, and 4-nitrobenzoyl groups, followed by a single run of HPLC with serially connected Fluophase® RP and Inertsil® ODS-3 columns. Finally, the individual pure disaccharide precursors were detagged to yield the eight cucurbitoside-like phenolic glycosides.

1. Introduction

New acylated phenolic glycosides, cucurbitosides A–M (Fig. 1), were isolated from the seeds of *Cucurbita moschata* and *Cucurbita pepo*.[1] Cucurbitosides possess a β-D-apiofuranosyl-(1→2)-β-D-glucopyranose sugar chain and an ester linkage with various acyl moieties at C-5′ of apiofuranose. Various pharmacological studies have demonstrated that the water extracted from the seeds of *C. moschata* exhibits hepatoprotective effect.[2] Although this extracted water possesses beneficial biological properties, the biological activity of one family of its water-soluble constituents, the cucurbitosides, has not yet been evaluated. Apiofuranose-containing glycosides, such as saponins, flavinoids, or phenolic glycosides play crucial roles in the biochemistry of plants.[3] Among them, seguinosides A–K and M-leaf movement factor (LMF) and kelampayosides A and B are structurally similar to cucurbitosides, and most of them possess interesting biological activities.[4] Therefore, a chemical synthesis of cucurbitosides is an important step in elucidating the relationship between the structures and biological activities of these natural products.

In the isolation and structure assignment of naturally occurring phenolic glycosides, a reverse-phase HPLC with an ODS column has been often used at the last stage to separate the components of a mixture of structurally similar phenolic glycosides.[4a,b,5] Koike and co-workers have utilized repetitive preparative reverse-phase HPLC for the isolation of cucurbitosides A–M on the basis of the difference in hydrophobicity of phenolic glycosides.[1] These reverse-phase HPLC experiments also demonstrated that the chromatographic behavior of phenolic glycosides on an ODS silica gel is dependent upon the structure of substituents on the sugar chain. These results suggest that these acyl groups are a suitable tool for sorting acyl-tagged molecules. Thus, benzoyl, 3-methylbutyryl, 4-hydroxybenzoyl, and 4-aminobenzoyl groups can be used as sorting tags for a solution-phase mixture synthesis of acylated target compounds.

In 2001, Curran and co-workers reported a fluorous mixture synthesis as the first solution-phase mixture synthetic technique using sorting tags for the simultaneous preparation of individual pure products via intermediate mixtures.[6] In summary, a series of organic substrates are tagged with a series of fluorous tags of different chain lengths. The tagged compounds are mixed and undergo a series of reactions as if they were a single compound. The components of the final mixture of the tagged products are then separated (demixed) depending upon their fluorine atom contents by chromatography over fluorous silica gel, prior to detagging, to give individually pure target products. Fluorous mixture synthesis has been shown to be a powerful technique for preparing small molecule libraries, studying structure–activity relationships, and assigning structures of natural products.[7] The high efficiency and practicality of the methodology have attracted many researchers' interest.

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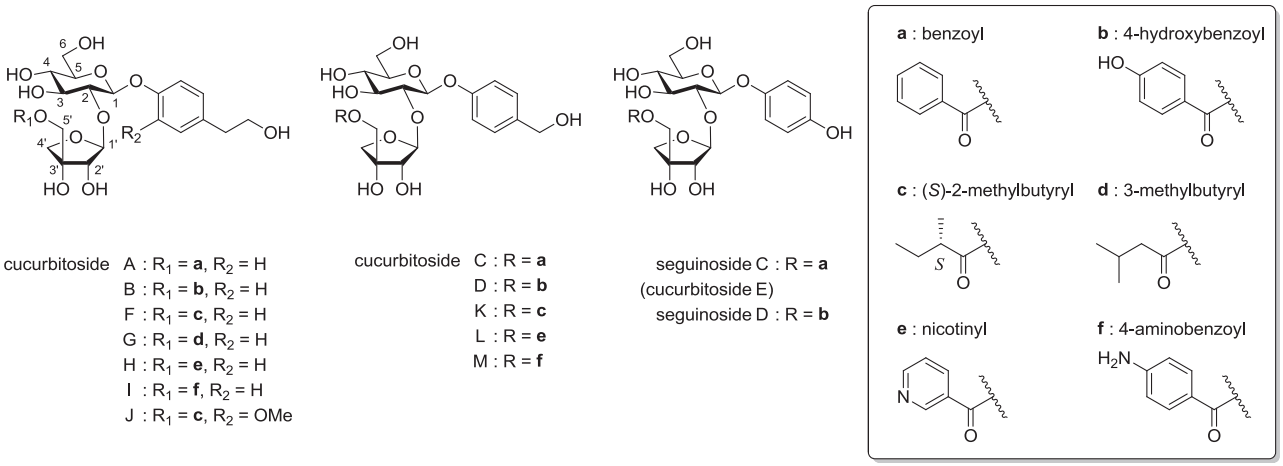


Fig. 1. Structures of cucurbitoside-like phenolic glycosides.

In addition, Curran and Wilcox have recently reported a double mixture synthetic method for preparing 16 stereoisomers of the natural product murisolin via one-pot reactions by the combination of four fluorous tags and four oligoethylene glycol (OEG) tags.[8] First, on the basis of the properties of OEG tags, the 16 components of the mixture were separated into four fractions by flash column chromatography.[9] Each of these four fractions was then further demixed by fluorous HPLC with a Fluoro*Flash*® PF-C8 column. A double mixture synthesis combining fluorous tags and acyl tags is considered to be a good approach for an efficient and expeditious synthesis of cucurbitoside-like phenolic glycosides because of the following reasons. First, these natural products have a high degree of structure similarity. Second, the chemical reactions of acyl-tagged compounds with fluorous-tagged compounds can be conducted with a traditional solution-phase synthetic technique, and the mixture of fluorous- and acyl-tagged compounds can be demixed with fluorous and octadecyl stationary phases.

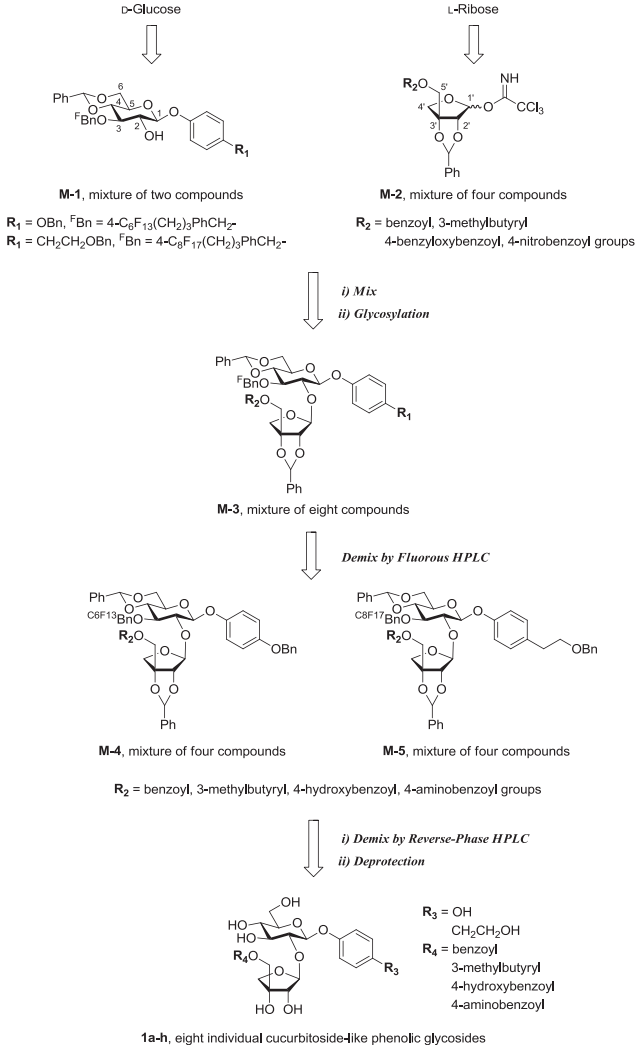
We describe herein the double fluorous and acyl mixture syntheses of eight cucurbitoside-like phenolic glycosides using two fluorous benzyl groups and four acyl groups from D-glucose and L-ribose.

2. Results and discussion

2.1. Synthetic plan of cucurbitoside-like phenolic glycosides

Our synthetic plan of the double mixture synthesis to provide the eight cucurbitoside-like phenolic glycosides **1a**–**h** is shown in Scheme 1. The plan is based on our previous study of the total synthesis of cucurbitoside A.[10]

A mixture (**M-1**) of two fluorous-tagged phenyl β-D-glucopyranosyl acceptors, in which the structure of aglycones differed, is prepared from D-glucose. In the previous study, the fluorous *N*-phenylcarbamoyl (^{F}Car) group was introduced into the C-3 hydroxyl group on glucopyranoside, because this fluorous-protecting group can be removed selectively without damaging other acyl groups. Herein, we replaced the ^{F}Car group with fluorous benzyl (^{F}Bn) group to minimize steps required to remove the protecting groups at the last stage of the synthesis. Another component of the cucurbitoside-like phenolic glycosides, a mixture (**M-2**) of the four acyl-tagged D-apiofuranosyl donors, is prepared from L-ribose. Benzoyl, 3-methylbutyryl, 4-benzyloxybenzoyl, and 4-nitrobenzoyl groups are chosen as the acyl-protecting groups for the C-5′ hydroxyl group on D-apiofuranose and are utilized as sorting tags for demixing the mixture into its individual pure components according to the structure of the acyl groups. To accomplish the total synthesis of the eight target compounds, the mixture of the two acceptors and the mixture of the four donors are mixed and then glycosylated. The resulting mixture of the eight components, **M-3**, is demixed into two fractions by fluorous HPLC depending upon the lengths of the perfluoroalkyl chains. These two fractions, each containing four components, are then demixed by reverse-phase HPLC with an ODS column. The separation depends upon

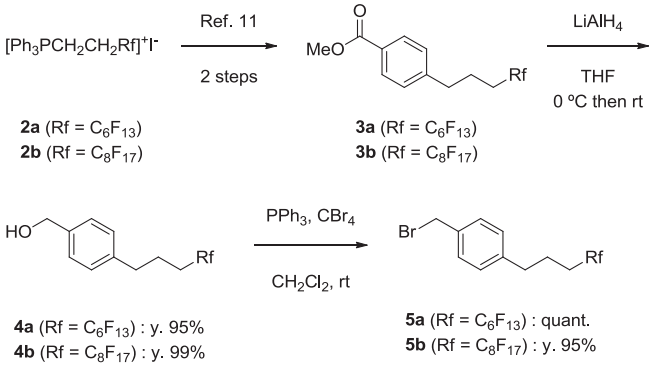


Scheme 1. Strategy for the double mixture synthesis with four fluorous and two acyl tags.

the structure of the acyl groups. The components are finally deprotected to provide the eight cucurbitoside-like phenolic glycosides.

2.2. Preparation of phenyl β-D-glucopyranosyl acceptors 14a and 14b

Fluorous-protecting reagents 4-(3-perfluoroalkyl)propyl benzyl bromides **5a** and **5b** were prepared via fluorous methyl benzoate[11] by the route shown in Scheme 2. Compound **3a**, which was prepared in two steps from fluorous phosphonium salt **2a** and methyl 4-formylbenzoate, was converted into fluorous benzyl alcohol **4a** with $LiAlH_4$. Bromination of **4a** with PPh_3 and CBr_4 in CH_2Cl_2 gave the crystalline and non-lachrymatory fluorous benzyl bromide **5a** in excellent yield. Fluorous benzyl bromide **5b** was also synthesized via a similar route starting from fluorous phosphonium salt **2b**.



Scheme 2. Preparation of fluorous benzyl bromides **5a** and **5b**.

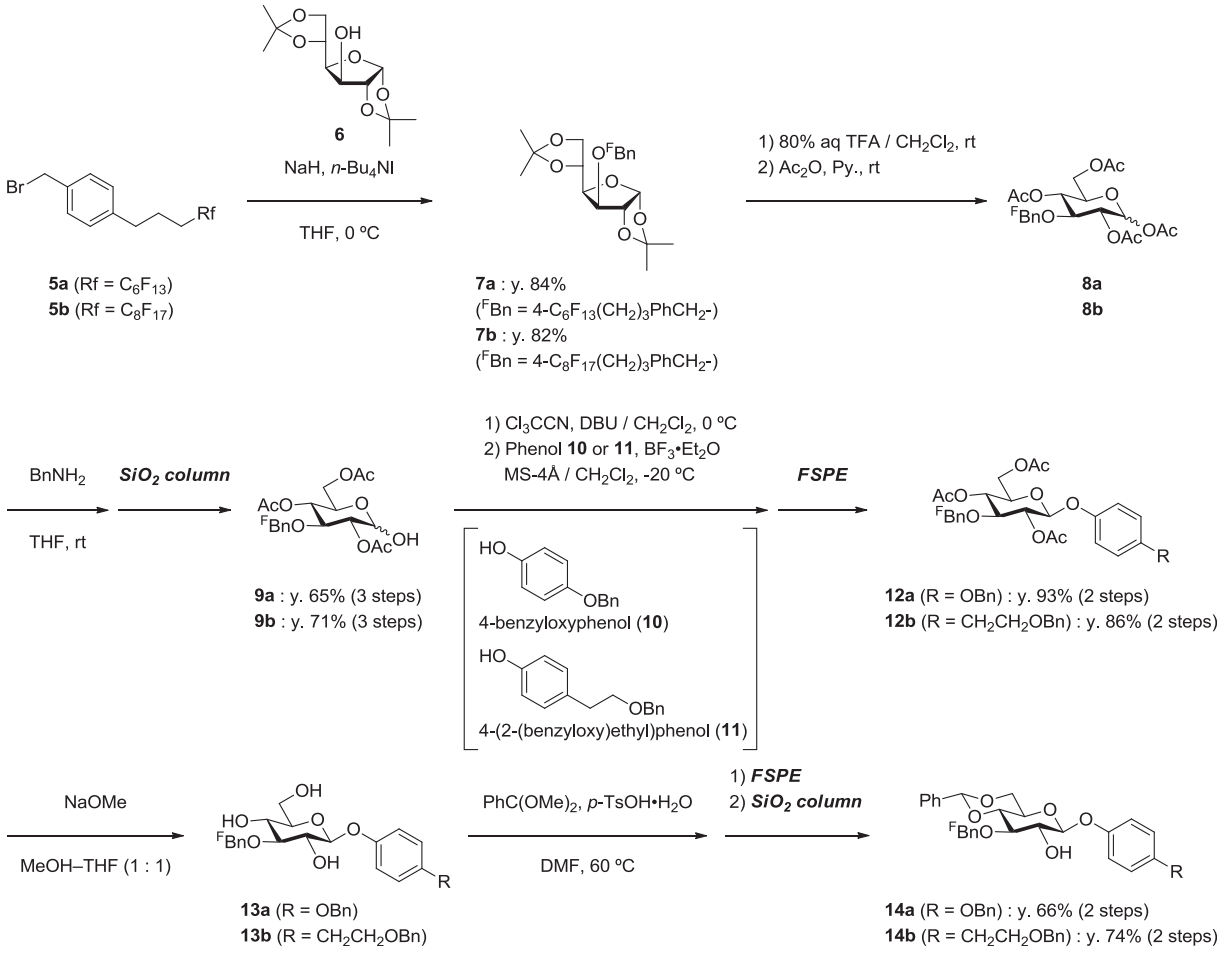
As shown in Scheme 3, the ^{C6F13}Bn-protected phenyl β-D-glucopyranosyl acceptor **14a** was prepared from the fluorous benzyl bromide **5a** and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**6**) in an eight-step synthesis. ^{C6F13}Benzyl bromide **5a** was reacted with **6** to give the 3-*O*-^{C6F13}benzyl derivative **7a** in 84% yield. Acid hydrolysis of **7a** using 80% aq trifluoroacetic acid followed by acetylation with acetic anhydride gave the tetra-*O*-acetylated compound **8a**, which was then reacted with benzylamine. The crude product was purified by silica gel column chromatography to provide 2,3,4-tri-*O*-acetate **9a** in 65% yield. Trichloroacetimidation of **9a** followed by glycosylation with 4-(benzyloxy)phenol (**10**) gave phenyl β-D-glucopyranoside **12a** in 93% yield. Acetyl groups were removed from **12a** with sodium methoxide to give **13a**. Finally, benzylidenation of **13a** with benzaldehyde dimethylacetal in the presence of a catalytic amount of *p*-toluenesulfonic acid monohydrate gave the desired glycosyl acceptor **14a** in 66% yield. Therefore, compound **14a** was successfully prepared from **5a** in 34% overall yield. In these reaction steps, fluorous solid-phase extraction (FSPE) was utilized for the speedy purification of the fluorous intermediates.[12] In FSPE, the reaction mixture was loaded onto a Fluoro*Flash*® column and eluted with 80% aq methanol to remove the non-fluorous compounds.[13] Then, the desired fluorous compound was eluted with a fluorophilic solvent, such as methanol. Next, the glycosyl acceptor **14b**, bearing 4-(benzyloxyethyl)phenol (**11**) as the aglycone, was prepared using a ^{C8F17}benzyl group via a similar route. As a result, the desired compound **14b** was synthesized in 37% overall yield from **5b**.

2.3. Preparation of apiofuranosyl donors 19a–d

Other components of cucurbitoside-like phenolic glycosides, four D-apiofuranosyl donors **19a**–**d**, were prepared from L-ribose in a five-step synthesis, as shown in Scheme 4. Numerous synthetic methods of apiose and its 2,3-*O*-isopropylidene-protected derivative have been published.[14] However, it was reported by Zhu's and Gin's groups that the acetal group on apiofuranose could not be removed without the acid hydrolysis of glycosidic linkages of the oligosaccharide.[15] Therefore, we chose the benzylidene group as the protecting group for the C-2 and C-3 hydroxyl groups on D-apiose because the protecting group can be regioselectively introduced into L-ribose and removed under mild neutral conditions. Acetalization of L-ribose with benzaldehyde in the presence of a catalytic amount of camphorsulfonic acid gave 2,3-*O*-benzylidene-L-ribose **15** as a single stereoisomer. K_2CO_3-catalyzed aldol condensation of **15** with formaldehyde gave the corresponding 2-*C*-hydroxymethyl derivative **16** in 92% yield. Reduction of **16** followed by oxidative cleavage with sodium periodate afforded 2,3-*O*-benzylidene-D-apiofuranose **17** in 87% yield. In the last two steps prior to the double mixture synthesis, the primary hydroxyl group of **17** was selectively acylated with benzoyl chloride, 3-methylbutyryl chloride, 4-benzyloxybenzoyl chloride, and 4-nitrobenzoyl chloride and then the hydroxyl group at C-1 underwent trichloroacetimidation. The results of the selective acylation followed by trichloroacetimidation are shown in Table 1. For example, compound **17** was reacted with benzoyl chloride in the presence of pyridine at −78 °C in CH_2Cl_2 to give the corresponding benzoylated derivative **18a** in 78% yield (entry 1). Likewise, 3-methylbutyrylated, 4-benzyloxybenzoylated and 4-nitrobenzoylated derivatives **18b**–**d** were obtained in 78%, 53%, and 71% yields, respectively (entries 2–4).[16] Since 4-benzyloxybenzoyl chloride was insoluble in CH_2Cl_2 at −78 °C, the yield of product **18c** was lower than those of **18a**, **18b**, and **18d**. Next, these compounds **18a**–**d** were converted into their corresponding imidates **19a**–**d** in high yields by treatment with trichloroacetonitrile and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in CH_2Cl_2 at 0 °C (entries 1–4).

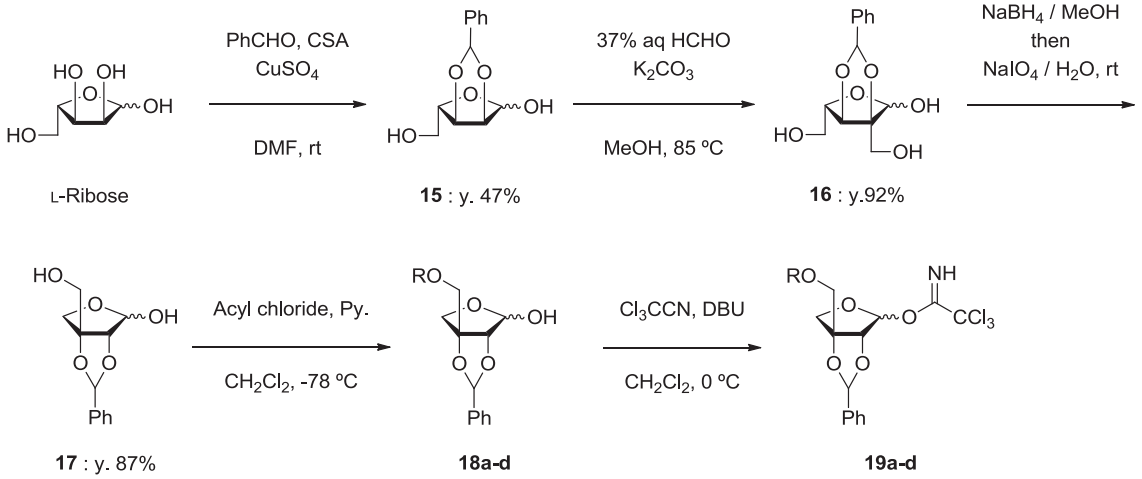
2.4. Double mixture synthesis, analysis, and separation of eight disaccharides 20a–h

Using the fluorous-tagged acceptors and acyl-tagged donors successfully prepared thus far, we attempted a solution-phase mixture synthesis of cucurbitoside-like phenolic glycosides. A mixture of two acceptors **14a** and **14b** were glycosylated with a mixture of four donors **19a**–**d**. The reaction was carried out in anhydrous CH_2Cl_2 at −20 °C in the presence of a catalytic amount of trimethylsilyl trifluoromethane sulfonate and molecular sieves 4 Å (Scheme 5). After purification of the crude product by FSPE, **M-3**, including the eight structural isomers, was analyzed by HPLC with a Fluophase® RP column,[17] Inertsil® ODS-3 column,[18] and standard silica gel TLC to determine the optimal separation conditions. Identification of individual peaks or spots was accomplished by comparing the retention times or R_f values of some components in the mixture with those of the corresponding pure disaccharides that were prepared individually. When a Fluophase® RP column was used, all four ^{C6F13}Bn-tagged disaccharides **20a**–**d** were eluted before all four ^{C8F13}Bn-tagged disaccharides **20e**–**h**, as expected (Fig. 2a). Interestingly, the retention times of the 3-methylbutyrylated disaccharides **20b** and **20f** were largely different from those of the three disaccharides bearing benzoyl, 4-nitrobenzoyl, and 4-benzyloxybenzoyl groups, although the perfluoroalkyl chain length was the same. Besides the interaction between perfluoroalkyl chain and the fluorinated stationary phase, the disaccharides **20b** and **20f** would be strongly retained by the hydrophobic interaction of the 3-methylbutyryl group, which is the only aliphatic substituent in the four acyl-protecting groups, with the fluorinated stationary phase. Next, to demix **M-3** according to the difference of hydrophobicity of the acyl groups, HPLC analysis with an Inertsil® ODS-3 column was carried out. The resulting HPLC trace is shown in Fig. 2b. The eight components of **M-3** were separated into two groups of four peaks. The first four peaks were



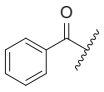
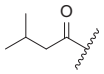
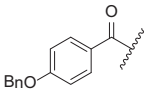
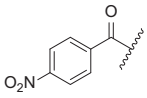
Scheme 3. Preparation of fluorous-tagged phenyl β-D-glucopyranosyl acceptors **14a** and **14b**.

assigned to the four disaccharides **20a**–**d** with ^{C6F13}Bn-tag. The second four peaks were assigned to the four disaccharides **20e**–**h** with ^{C8F17}Bn-tag. The four acyl-tagged disaccharides of the first and second groups were eluted in the same order. The first peaks were due to the 4-nitrobenzoylated disaccharides **20d** and **20h**. The second peaks were due to the benzoylated disaccharides **20a** and **20e**. The third peaks were due to the 3-methylbutyrylated disaccharides **20b** and **20f**, but the peak of impurity was observed and overlapped with the peak of disaccharide **20b**. The fourth peaks were due to the 4-benzyloxybenzoylated disaccharides **20c** and **20g**. However, the retention times of compounds **20c** and **20h** were very close. Finally, TLC analysis of **M-3** on a standard silica gel showed three major spots with R_f values of 0.52, 0.48, and 0.41 and one minor spot with R_f value of 0.34 (Fig. 3).



Scheme 4. Preparation of acyl-tagged apiofuranosyl donors **19a**–**d**.

Table 1
Selective acylation and trichloroacetimidation

Entry	Acyl chloride	R	Yield of selective acylation (%)	Yield of trichloroacetimidation (%)
1	Benzoyl chloride		**18a**: 78	**19a**: 93
2	3-Methylbutyryl chloride		**18b**: 78	**19b**: 86
3	4-Benzyloxybenzoyl chloride		**18c**: 53	**19c**: 83
4	4-Nitrobenzoyl chloride		**18d**: 71	**19d**: 81

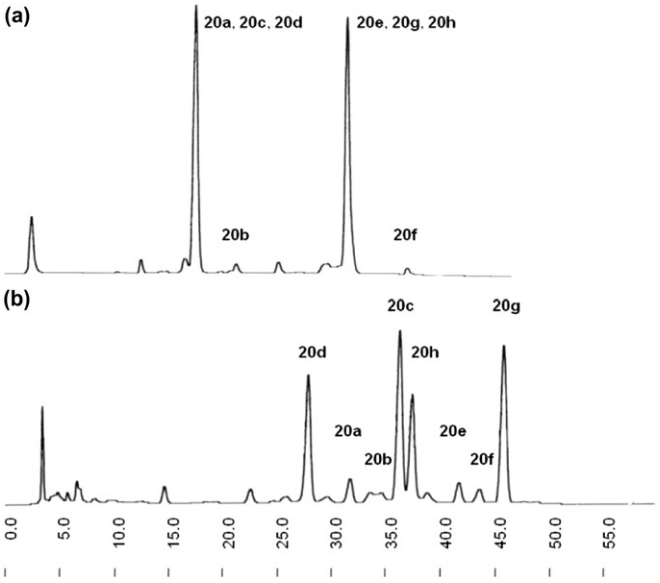


Fig. 2. HPLC analysis of **M-3**. (a) Fluophase® column (4.6 mm×150 mm), CH_3CN/H_2O gradient (80% CH_3CN/H_2O to 100% CH_3CN over 40 min), flow rate 1.0 mL/min, UV detection at 254 nm (b) Inertsil® column (4.6 mm×250 mm), CH_3CN/H_2O gradient (90% CH_3CN/H_2O to 100% CH_3CN over 40 min), flow rate 1.0 mL/min, UV detection at 254 nm.

The high and middle spots (R_f values of 0.52 and 0.48) corresponded to the samples of the 3-methylbutyrylated and benzoylated disaccharides, respectively. However, the low spot (R_f value of 0.41) was a mixture of the 4-nitrobenzoylated and 4-benzyloxybenzoylated disaccharides. Therefore, it was predicted that the four acyl-tagged disaccharides would be difficult to separate on the basis of polarity of acyl groups by standard silica gel chromatography. Considering the results obtained from separations by HPLC and TLC analyses, HPLC purification of **M-3** with a Fluophase® RP column followed by purification with an Inertsil® ODS-3 column would provide the individual compounds. However, this is a time-consuming method. Therefore, we tried to separate the eight components of **M-3** into its individual pure compounds in a single step by using serially connected Fluophase® RP and Inertsil® ODS-3 columns instead of two independent HPLC purification steps (Fig. 4a). For comparison, the separation result obtained using only an Inertsil® ODS-3 column was also listed (Fig. 4b). When the serially connected Fluophase® RP and Inertsil® ODS-3 columns were used, the eight components of **M-3** were cleanly separated with large differences in their retention times. Compared with the separation result obtained using only the ODS column, the difference between the retention times of compounds **20c** and **20h** was particularly improved.

Fig. 3. Using hexane/EtOAc (5:1) as the mobile phase and a normal-phase silica gel TLC, **M-3** was developed four times. The compounds were detected by dipping the plate into Hanessian's (Cerium Molybdate) stain followed by heating. Lane a: **M-3**, Lane b: the samples of synthetic **20a**, Lane c: the samples of synthetic **20b**, Lane d: the samples of synthetic **20c**, Lane e: the samples of synthetic **20d**. When **20e**, **20f**, **20g**, and **20h** were used as the standard samples, a similar separation result was obtained from TLC analysis.

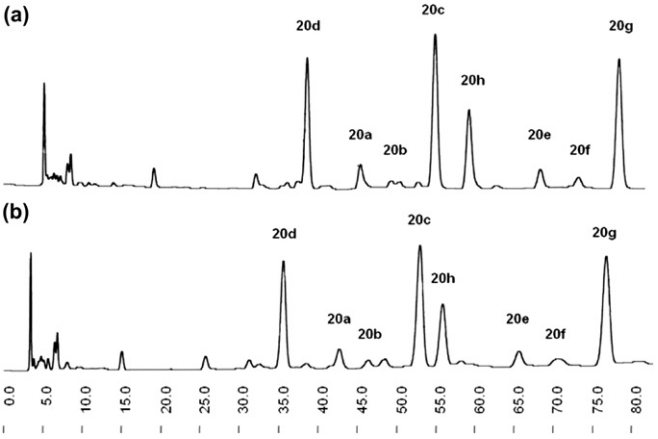
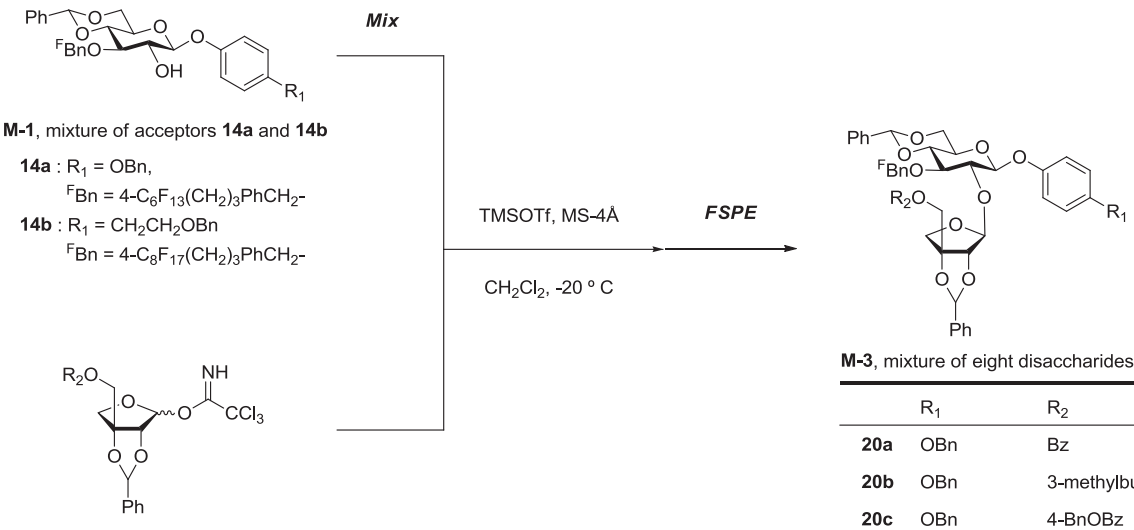


Fig. 4. HPLC analysis of **M-3**. (a) A serially connected Fluophase® column (4.6 mm×150 mm) and Inertsil® ODS-3 column (4.6 mm×250 mm), CH_3CN/H_2O gradient (90% CH_3CN/H_2O to 100% CH_3CN over 120 min), flow rate 1.0 mL/min, UV detection at 254 nm. (b) Inertsil® ODS-3 column (4.6 mm×250 mm), CH_3CN/H_2O gradient (90% CH_3CN/H_2O to 100% CH_3CN over 120 min), flow rate 1.0 mL/min, UV detection at 254 nm.

Usually, Fluophase® RP column easily separates more than four fluorous compounds depending upon their fluorine atom contents. The separation of each component is enhanced with increasing the length of the column. Inertsil® ODS-3 column is suitable for separating the compounds with the acyl groups. The separation of each component is also enhanced with increasing the column length. Therefore, we will be able to control the ability of the serially connected columns to separate more than eight components of the product mixture with changing their length independently. However, it may be impossible for us to separate the components of the product mixture only with the Inertsil® ODS-3 column when the components of the product mixture increase more than 16, for example.

hydrogenolysis (Scheme 6). The crude products were purified by semi-preparative HPLC to provide the six cucurbitoside-like phenolic glycosides **1a**–**c** and **1e**–**f** in high yields (entries 1–3 and 5–7 of Table 2). However, the hydrogenolysis of disaccharides **20d** and **20h** with a catalytic amount of palladium hydroxide on carbon ($Pd(OH)_2/C$) in THF/MeOH was unsuccessful. In this case, an amino group on the aromatic ring that was initially generated by the reduction of the nitro group would have acted as a catalyst poison, inhibiting deprotection of the other protecting groups. Therefore, we examined hydrogenolysis of the compounds **20d** and **20h** under acidic conditions in order to promote the activity of the $Pd(OH)_2/C$ catalyst. When 0.1 M HCl was used as an acid, the yields of these final products **1d** and **1h** were increased to 55% and 33%, re-



	R_1	R_2	^{F}Bn
20a	OBn	Bz	$^{C6F13}Bn$
20b	OBn	3-methylbutyryl	$^{C6F13}Bn$
20c	OBn	4-BnOBz	$^{C6F13}Bn$
20d	OBn	4-NO_2Bz	$^{C6F13}Bn$
20e	CH_2CH_2OBn	Bz	$^{C8F17}Bn$
20f	CH_2CH_2OBn	3-methylbutyryl	$^{C8F17}Bn$
20g	CH_2CH_2OBn	4-BnOBz	$^{C8F17}Bn$
20h	CH_2CH_2OBn	4-NO_2Bz	$^{C8F17}Bn$

Scheme 5. Double mixture synthesis.

The mixture of fluorous- and acyl-tagged compounds was then preparatively demixed to provide its eight components in pure form. **M-3** (80.6 mg) was injected into the serially connected Fluophase® RP and Inertsil® ODS-3 columns, and the columns were eluted over 120 min with a gradient from 90% CH_3CN/H_2O to 100% CH_3CN (Fig. 5). After these eight major fractions were collected and concentrated, the pure compounds **20a**, **20b**, **20c**, **20d**, **20e**, **20f**, **20g**, and **20h** were obtained in 8.4 mg, 8.5 mg, 9.5 mg, 8.8 mg, 10.6 mg, 8.6 mg, 8.0 mg, and 9.1 mg, respectively (Scheme 6). MS analysis and 1D (^1H and ^{13}C) and 2D (^1H–^1H COSY) NMR data of the products demonstrated that compounds **20a**–**h** were the desired disaccharides. In addition, no noticeable peaks due to impurities were observed in the ^1H and ^{13}C NMR spectra of the compounds.

2.5. Total synthesis of eight cucurbitoside-like phenolic glycosides 1a–h

The benzylidene groups and the standard and fluorous benzyl groups of disaccharides **20a**–**c** and **20e**–**g** were removed by

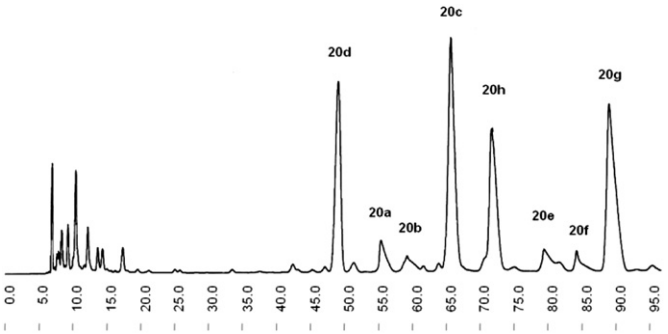
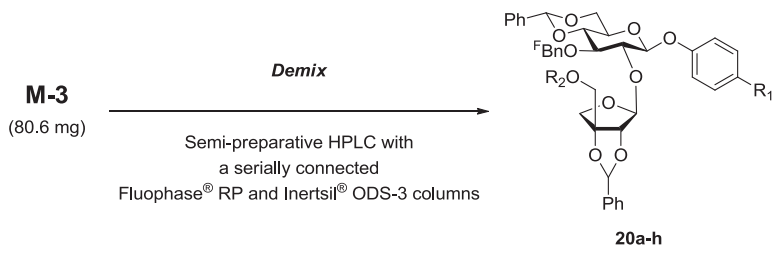


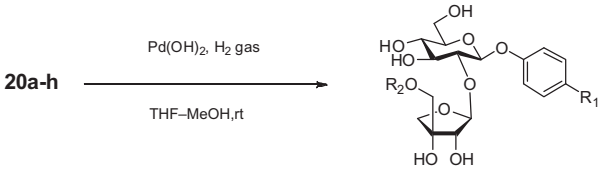
Fig. 5. HPLC chromatogram from the preparative demixing of **M-3**, obtained using serially connected Fluophase® (21.2 mm×250 mm) and Inertsil® ODS-3 (20.0 mm×250 mm) columns, CH_3CN/H_2O gradient (90% CH_3CN/H_2O to 100% CH_3CN over 120 min), flow rate 19.0 mL/min, UV detection at 254 nm.



	R_1	R_2	^{F}Bn
20a (8.4 mg)	OBn	Bz	$^{C6F13}Bn$
20b (8.5 mg)	OBn	3-methylbutyryl	$^{C6F13}Bn$
20c (9.5 mg)	OBn	4-BnOBz	$^{C6F13}Bn$
20d (8.8 mg)	OBn	4-NO_2Bz	$^{C6F13}Bn$
20e (10.6 mg)	CH_2CH_2OBn	Bz	$^{C8F17}Bn$
20f (8.6 mg)	CH_2CH_2OBn	3-methylbutyryl	$^{C8F17}Bn$
20g (8.0 mg)	CH_2CH_2OBn	4-BnOBz	$^{C8F17}Bn$
20h (9.1 mg)	CH_2CH_2OBn	4-NO_2Bz	$^{C8F17}Bn$

Scheme 6. Demix of eight protected disaccharides **20a**–**h**.

Table 2
Hydrogenolysis and optical rotation



Entry	Product			Yield (%)	Optical rotation[c]	
		R_1	R_2		Synthetic sample	Natural product
1	Seguinoside C (**1a**)	OH	Benzoyl	80	−87.8 (*c* 0.59)	−86.3 (*c* 0.58)
2	Analog I (**1b**)	OH	3-Methylbutyryl	Quant.	−88.7 (*c* 1.1)	—
3	Seguinoside D (**1c**)	OH	4-Hydroxybenzoyl	Quant.	−67.4 (*c* 0.43)	−67.1 (*c* 0.39)
4	Analog II (**1d**)	OH	4-Aminobenzoyl	55[a]	−64.7 (*c* 0.62)	—
5	Cucurbitoside A (**1e**)	CH_2CH_2OH	Benzoyl	90	−76.2 (*c* 1.0)	−76.1 (*c* 1.1)
6	Cucurbitoside G (**1f**)	CH_2CH_2OH	3-Methylbutyryl	93	−83.8 (*c* 0.29)	−81.3 (*c* 0.25)
7	Cucurbitoside B (**1g**)	CH_2CH_2OH	4-Hydroxybenzoyl	Quant.	−68.8 (*c* 0.42)	−65.9 (*c* 0.4)
8	Cucurbitoside I (**1h**)	CH_2CH_2OH	4-Aminobenzoyl	33[b]	−63.7 (*c* 0.51)	−57.1 (*c* 0.44)

[a] EtOAc/MeOH was used as solvent instead of THF/MeOH. In addition, aq HCl (0.1 M) was used as an additive.
[b] aq HCl (0.1 M) was used as an additive.
[c] The optical rotation of **1a** was measured in pyridine. The other seven compounds, **1b**–**h**, were measured in methanol.

spectively (entries 4 and 8). An improvement in the yields of the two final products is in progress. The ^{1}H, ^{13}C NMR data, and other physical data obtained from synthetic **1a**, **1c**, **1e**, **1f**, **1g**, and **1h** agreed well with the previously reported values for the corresponding natural products. In addition, the ^{1}H and ^{13}C NMR spectra of synthetic **1a**, **1e**, and **1f** were identical to those of natural seguinoside C, cucurbitosides A and G, samples kindly supplied by Professor K. Koike and Associate Professor W. Li. Two unnatural cucurbitoside-like phenolic glycosides were fully characterized by the usual spectroscopic techniques.

3. Conclusion

We have simultaneously synthesized six natural and two unnatural cucurbitoside-like phenolic glycosides using the technique of double mixture synthesis. Besides fluorous tags, the acyl groups connected to the C-5′ hydroxyl group of these natural products were also utilized as sorting tags for separation. A mixture of protected disaccharides was obtained by a single glycosylation of two fluorous-tagged acceptors with four acyl-tagged donors. It was also demonstrated that the eight precursors of the cucurbitoside-like phenolic glycosides were cleanly separated by a single HPLC purification with serially connected Fluophase® RP and Inertsil® ODS-3 columns depending upon the lengths of their perfluoroalkyl chains and the hydrophobicity of their acyl groups. In comparison with two independent HPLC separations, a single HPLC separation conducted with two serially connected columns was achieved in a shorter time and at a lower cost. This method could also be applied to the synthesis of 16 structural isomers of phenolic glycosides in a single-step reaction of four fluorous benzyl-tagged acceptors with the four acyl-tagged donors. The work is currently underway.

From the realistic point of view, it may be considered to be more practical to synthesize the final products independently from each of the two acceptors and the four donors, because the reaction of the acceptor with the donor is the final step to the precursor of the target product. However, if final precursors are obtained via several steps after mixing the acceptors and donors, the method described here is more practical than that carrying out the steps for each acceptor and donor independently. This report is on a theoretical work to examine an ability of acyl tags as a partner for a fluorous mixture synthesis.

4. Experimental section

4.1. General

Melting points were measured using a Yanaco Model MP-J3 micro-melting point apparatus, and are uncorrected. IR spectra were recorded using a JASCO FT/IR-460 spectrometer on KBr pellets

or liquid film on NaCl. ^{1}H and ^{13}C NMR spectra were measured with Bruker Avance DPX-250 and JEOL JNM-ECA600 spectrometers in $CDCl_3$ or CD_3OD solution with tetramethylsilane as an internal standard. Thin-layer chromatography (TLC) was performed on Merck Silica gel 60 F_{254} plates. Flash column chromatography was performed on silica gel 60 N (spherical, neutral) (40–100 μm, Kanto). Analytical high-performance liquid chromatography (HPLC) was performed with an SHIMADZU LC-10ATvp system, consisting of an LC-10ATvp pump, an FCV-10ALvp low-pressure gradient unit, a DGU-14A degasser, an SPD-10AV UV-VIS detector, and a CTO-10ACvp column oven. Semi-preparative HPLC was performed on an SHIMADZU system equipped with an LC-6AD binary pump, an SCL-10Avp system controller, an SPD-20AV UV/VIS detector, and a DGU-20A_3 degasser. Specific rotations were measured in 1.0 dm tubes using a Perkin–Elmer 241 polarimeter in $CHCl_3$, CH_3OH or pyridine. ESI-TOF mass spectra were recorded with JEOL JMS-T100LC AccuTOF mass spectrometer.

4.2. Preparation of phenyl β-D-glucopyranosyl acceptors 14a and 14b

*4.2.1. 4-(4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluorononyl)benzyl alcohol (**4a**).* To a suspension of lithium aluminum hydride (92 mg, 2.4 mmol) in dry THF (5 mL) was added dropwise a solution of methyl ester **3a** (1.0 g, 2.0 mmol) in dry THF (10 mL) with dropping funnel at 0 °C under argon. After stirring for 1 h at the same temperature, the reaction mixture was warmed to room temperature and stirred for an additional 1 h. The reaction was quenched with saturated aq Na_2SO_4 solution (1 mL). The resulting suspension was then filtered through Celite and the filtrate was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc=3:1 v/v) to give alcohol **4a** (900 mg, 95% yield) as colorless amorphous solids: R_f=0.27 (hexane/EtOAc=3:1 v/v); IR (KBr, disk): ν 3365 cm^{-1} (OH); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.31, 7.18 (4H, each d, J=8.0 Hz, $-C_6H_4-$), 4.67 (2H, d, $J_{1,OH}$=5.8 Hz, CH_2OH), 2.71 (2H, t, J=7.4 Hz, $CH_2CH_2CH_2C_6F_{13}$), 2.19–1.88 (4H, m, $CH_2CH_2CH_2C_6F_{13}$), 1.60 (1H, t, O*H*); ^{13}C NMR (63 MHz, $CDCl_3$): δ 140.1, 139.0, 128.5, 127.4, 65.1, 34.7, 30.3 (t, J_{CF}=22.5 Hz), 21.9; ESI-HRMS calcd for $C_{16}H_{13}F_{13}ONa$ m/z $[M+Na]^+$: 491.0657. Found: 491.0639.

*4.2.2. 4-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-Heptadecafluoroundecyl)benzyl alcohol (**4b**).* To a suspension of lithium aluminum hydride (153 mg, 4.0 mmol) in dry THF (10 mL) was added dropwise a solution of methyl ester **3b** (2.0 g, 3.4 mmol) in dry THF (15 mL) with dropping funnel at 0 °C under argon. After stirring for 1 h at the same temperature, the reaction mixture was warmed to room temperature and stirred for an additional 1 h. The reaction was quenched with saturated aq Na_2SO_4 solution (1 mL). The resulting suspension was then filtered through Celite and the filtrate was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc=3:1 v/v) to give alcohol **4b** (1.9 g, 99% yield) as colorless amorphous solids: R_f=0.27 (hexane/EtOAc=3:1 v/v); IR (KBr, disk): ν 3324 cm^{-1} (OH); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.31, 7.17 (4H, each d, J=8.0 Hz, $-C_6H_4-$), 4.66 (2H, s, CH_2OH), 2.71 (2H, t, J=7.5 Hz, $CH_2CH_2CH_2C_8F_{17}$), 2.19–1.88 (4H, m, $CH_2CH_2CH_2C_8F_{17}$), 1.72 (1H, br s, O*H*); ^{13}C NMR (63 MHz, $CDCl_3$): δ 140.1, 139.0, 128.5, 127.4, 65.1, 34.7, 30.3 (t, J_{CF}=22.5 Hz), 21.9; ESI-HRMS calcd for $C_{18}H_{13}F_{17}ONa$ m/z $[M+Na]^+$: 591.0593. Found: 591.0631.

*4.2.3. 4-(4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluorononyl)benzyl bromide (**5a**).* To a solution of benzyl alcohol **4a** (558 mg, 1.19 mmol) in dry CH_2Cl_2 (12 mL) were added triphenylphosphine (406 mg, 1.55 mmol) and carbon tetrabromide (514 mg, 1.55 mmol). After stirring for 1 h at room temperature, the solvent was evaporated, and the residue was purified by short silica gel column chromatography (hexane) to give benzyl bromide **5a** (620 mg, 98% yield) as colorless solids. The product **5a** was used for the next reaction without further purification.

*4.2.4. 4-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-Heptadecafluoroundecyl)benzyl bromide (**5b**).* To a solution of benzyl alcohol **4b** (1.0 g, 1.76 mmol) in dry CH_2Cl_2 (20 mL) were added triphenylphosphine (600 mg, 2.29 mmol) and carbon tetrabromide (759 mg, 2.29 mmol). After stirring for 1 h at room temperature, the solvent was evaporated, and the residue was purified by short silica gel column chromatography (hexane) to give benzyl bromide **5b** (1.09 g, 98% yield) as colorless solids. The product **5b** was used for the next reaction without further purification.

*4.2.5. 3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluorononyl)benzyl]-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**7a**).* To a solution of 1,2:5,6-di-*O*-isopropyridene-α-D-glucofuranose (**6**) (664 mg, 2.55 mmol) in dry THF (10 mL) was added sodium hydride (55% dispersion in paraffin liquid, 223 mg, 5.11 mmol) at 0 °C under argon. After stirring for 30 min at the same temperature, tetrabutyl ammonium iodide (79 mg, 0.213 mmol) was added, and then a solution of benzyl bromide **5a** (1.13 g, 2.13 mmol) in THF (20 mL) was added dropwise to the solution. After stirring for 16 h at room temperature, the reaction mixture was poured into saturated aq NH_4Cl solution (30 mL), and the aqueous layer was extracted with EtOAc (30 mL×3). The combined organic layer was successively washed with water (10 mL) and brine (10 mL), dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc=6:1 v/v) to give **7a** (1.34 g, 88% yield) as colorless amorphous solids: R_f=0.59 (hexane/EtOAc=2:1 v/v); $[\alpha]_D^{15}$ −11.9 (*c* 0.202, $CHCl_3$); IR (KBr, disk): ν 2989 cm^{-1}, 2938 cm^{-1}, 2879 cm^{-1} (CH_3); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.29, 7.16 (4H, each d, J=8.0 Hz, $-C_6H_4-$), 5.89 (1H, d, $J_{1,2}$=3.7 Hz, H-1), 4.67, 4.61 (2H, each d, J_{AB}=11.8 Hz, $C_6H_4CH_2$), 4.58 (1H, d, $J_{2,1}$=3.7 Hz, H-2), 4.37 (1H, ddd, $J_{5,4}$=7.8 Hz, $J_{5,6}$=6.1 Hz, $J_{5,6'}$=5.9 Hz, H-5), 4.15 (1H, dd, $J_{4,5}$=7.8 Hz, $J_{4,3}$=3.1 Hz, H-4), 4.11 (1H, dd, $J_{6,5}$=6.1 Hz, $J_{6,6'}$=8.6 Hz, H-6), 4.02 (1H, d, $J_{3,2}$=3.1 Hz, H-3), 4.00 (1H, dd, $J_{6',5}$=5.9 Hz, $J_{6',6}$=8.6 Hz, H-6′), 2.71 (2H, t, J=7.5 Hz, $CH_2CH_2CH_2C_6F_{13}$), 2.19–1.88 (4H, m, $CH_2CH_2CH_2C_6F_{13}$), 1.49, 1.43, 1.37, 1.31 (12H, each s, CH_3×4); ^{13}C NMR (63 MHz, $CDCl_3$): δ 140.3, 135.7, 128.4, 128.0, 111.8, 109.0, 105.3, 82.7, 81.7, 81.3, 72.5, 72.2, 67.4, 34.7, 30.3 (t, J_{CF}=22.3 Hz), 26.8, 26.7, 26.2, 25.4, 21.8; ESI-HRMS calcd for $C_{28}H_{31}F_{13}O_6Na$ m/z $[M+Na]^+$: 733.1811. Found: 733.1784.

*4.2.6. 3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-Heptadecafluoroundecyl)benzyl]-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**7b**).* To a solution of 1,2:5,6-di-*O*-isopropyridene-α-D-glucofuranose (**6**) (549 mg, 2.11 mmol) in dry THF (10 mL) was added sodium hydride (55% dispersion in paraffin liquid, 184 mg, 4.22 mmol) at 0 °C under argon. After stirring for 30 min at the same temperature, tetrabutyl ammonium iodide (65 mg, 0.176 mmol) was added, and then a solution of benzyl bromide **5b** (1.11 g, 1.76 mmol) in THF (20 mL) was added dropwise to the solution. After stirring for 16 h at room temperature, the reaction mixture was poured into saturated aq NH_4Cl solution (30 mL), and the aqueous layer was extracted with EtOAc (30 mL×3). The combined organic layer was successively washed with water (10 mL) and brine (10 mL), dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc=6:1) to give **7b** (1.26 g, 88% yield) as colorless needles: mp 67.5–69.9 °C (MeOH); R_f=0.59 (hexane/EtOAc=2:1 v/v); $[\alpha]_D^{11}$ −12.04 (*c* 1.03, $CHCl_3$); IR (KBr, disk): ν 2988, 2937, 2878 cm^{-1} (CH_3); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.29, 7.16 (4H, each d, J=8.0 Hz, $-C_6H_4-$), 5.90 (1H, d, $J_{1,2}$=3.7 Hz, H-1), 4.67, 4.61 (2H, each d, J_{AB}=11.8 Hz, $C_6H_4CH_2$), 4.58 (1H, d, $J_{2,1}$=3.7 Hz, H-2), 4.37

(1H, ddd, $J_{5,4}$=7.7 Hz, $J_{5,6}$=6.0 Hz, $J_{5,6'}$=5.9 Hz, H-5), 4.15 (1H, dd, $J_{4,5}$=7.7 Hz, $J_{4,3}$=3.2 Hz, H-4), 4.12 (1H, dd, $J_{6,5}$=6.0 Hz, $J_{6,6'}$=8.5 Hz, H-6), 4.02 (1H, d, $J_{3,2}$=3.2 Hz, H-3), 4.01 (1H, dd, $J_{6',5}$=5.9 Hz, $J_{6',6}$=8.5 Hz, H-6′), 2.71 (2H, t, J=7.5 Hz, $CH_2CH_2CH_2C_8F_{17}$), 2.19–1.88 (4H, m, $CH_2CH_2CH_2C_8F_{17}$), 1.49, 1.43, 1.38, 1.31 (12H, each s, $CH_3\times4$); ^{13}C NMR (63 MHz, $CDCl_3$): δ 140.3, 135.7, 128.4, 128.0, 111.8, 109.0, 105.3, 82.7, 81.7, 81.3, 72.5, 72.2, 67.4, 34.7, 30.3 (t, J_{CF}=22.3 Hz), 26.8, 26.7, 26.2, 25.4, 21.8; ESI-HRMS calcd for $C_{30}H_{31}F_{17}O_6Na$ m/z $[M+Na]^+$: 833.1747. Found: 833.1720.

*4.2.7. 2,4,6-Tri-O-acetyl-3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyl)benzyl]-α/β-D-glucopyranose (**9a**).* To a solution of **7a** (625 mg, 0.88 mmol) in CH_2Cl_2 (1.5 mL) was added 80% aq TFA solution (1.5 mL). After stirring for 5 h at room temperature, the reaction mixture was carefully poured into saturated aq $NaHCO_3$ solution (10 mL), and the aqueous layer was extracted with EtOAc (10 mL×5). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The residue was then dried in vacuo. The residue was redissolved in pyridine (5 mL), and acetic anhydride (5 mL) was added. After stirring for 11 h at room temperature, the reaction mixture was poured into MeOH at 0 °C and stirred for 10 min. The mixture was evaporated and co-evaporated with toluene. The residue was dried in vacuo. The crude product **8a** was used for the next reaction without further purification. To a solution of the crude product **8a** in dry THF (8 mL) was added benzylamine (144 μL, 1.32 mmol). After stirring for 48 h at room temperature, the solvent was removed by evaporation. The residue was then dissolved in EtOAc (20 mL). The organic layer was successively washed with 1 M aq HCl solution (5 mL), water (5 mL) and brine (5 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc=3:2 v/v) to give hemiacetal **9a** (482 mg, 72% yield, α/β=7:1) as a colorless syrup: R_f=0.18 (hexane/EtOAc=3:2 v/v); $[\alpha]_D^{19}$ +20.8 (*c* 1.0, $CHCl_3$); IR (KBr, disk): ν 3452 cm^{-1} (OH), 1747 cm^{-1} (C=O); ^{1}H NMR (250 MHz, $CDCl_3$) α-anomer: δ 7.20, 7.14 (4H, each d, J=8.3 Hz, $-C_6H_4-$), 5.46 (1H, dd, $J_{1,2}$=3.7 Hz, $J_{1,OH}$=3.8 Hz, H-1), 5.10 (1H, dd, $J_{4,3}$=9.6 Hz, $J_{4,5}$=9.7 Hz, H-4), 4.87 (1H, ddd, $J_{2,1}$=3.7 Hz, $J_{2,3}$=9.9 Hz, $J_{2,OH}$=1.3 Hz, H-2), 4.69, 4.60 (2H, each d, J=11.6 Hz, $C_6H_4CH_2$), 4.22–4.09 (3H, m, H-5, 6, 6′), 4.04 (1H, dd, $J_{3,2}$=9.9 Hz, $J_{3,4}$=9.6 Hz, H-3), 3.24 (1H, dd, $J_{OH,1}$=3.8 Hz, $J_{OH,2}$=1.3 Hz, OH), 2.70 (2H, t, J=7.4 Hz, $CH_2CH_2CH_2C_6F_{13}$), 2.18–1.89 (4H, m, $CH_2CH_2CH_2C_6F_{13}$), 2.08, 2.07, 1.97 (9H, each s, $COCH_3\times3$); β-anomer: δ 5.13–5.05 (1H, m, H-4, overlapped with H-4 signal of α-anomer), 4.91–4.84 (1H, m, H-2, overlapped with H-2 signal of α-anomer), 4.67–4.56 (3H, m, H-1, $C_6H_4CH_2$, overlapped with $C_6H_4CH_2$ signal of α-anomer), 4.24–4.07 (2H, m, H-6, 6′, overlapped with H-5, 6, 6′ signals of α-anomer), 3.73 (1H, t, $J_{3,2}$=9.3 Hz, $J_{3,4}$=9.3 Hz, H-3), 3.64 (1H, ddd, $J_{5,4}$=10.0 Hz, $J_{5,6}$=2.6 Hz, $J_{5,6'}$=5.0 Hz, H-5), 1.98 (3H, s, $COCH_3$); ^{13}C NMR (63 MHz, $CDCl_3$) α-anomer: δ 170.9, 170.1, 169.4, 140.2, 136.2, 128.4, 127.9, 90.4, 76.9, 74.6, 73.4, 69.9, 67.8, 62.3, 34.7, 30.3 (t, J_{CF}=22.3 Hz), 21.8, 20.8, 20.73, 20.69; β-anomer: δ 171.6, 170.8, 169.4, 140.4, 135.8, 128.4, 128.0, 95.9, 79.6, 75.4, 74.2, 72.3, 69.7; ESI-HRMS calcd for $C_{28}H_{29}F_{13}O_9Na$ m/z $[M+Na]^+$: 779.1502. Found: 779.1494.

*4.2.8. 2,4,6-Tri-O-acetyl-3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)benzyl]-α/β-D-glucopyranose (**9b**).* To a solution of **7b** (500 mg, 0.62 mmol) in CH_2Cl_2 (1 mL) was added 80% aq TFA solution (1 mL). After stirring for 5 h at room temperature, the reaction mixture was carefully poured into saturated aq $NaHCO_3$ (10 mL) solution, and the aqueous layer was extracted with EtOAc (10 mL×5). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The residue was then dried in vacuo. The residue was redissolved in pyridine (5 mL), and acetic anhydride (5 mL) was added. After stirring for 11 h at room temperature, the reaction mixture was poured into MeOH at 0 °C and stirred for 10 min. The mixture was evaporated and co-evaporated with toluene. The residue was dried in vacuo. The crude product **8b** was used for the next reaction without further purification. To a solution of the crude product **8a** in dry THF (6 mL) was added benzylamine (101 μL, 0.93 mmol). After stirring for 48 h at room temperature, the solvent was removed by evaporation. The residue was then dissolved in EtOAc (20 mL). The organic layer was successively washed with 1 M aq HCl solution (5 mL), water (5 mL) and brine (5 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc=3:2 v/v) to give hemiacetal **9b** (342 mg, 65% yield, α/β=3:1) as a colorless syrup: R_f=0.18 (hexane/EtOAc=3:2 v/v); $[\alpha]_D^{18}$ +17.1 (*c* 0.21, $CHCl_3$); IR (KBr, disk): ν 3461 cm^{-1} (OH), 1746 cm^{-1} (C=O); ^{1}H NMR (250 MHz, $CDCl_3$) α-anomer: δ 7.20, 7.14 (4H, each d, J=8.3 Hz, $-C_6H_4-$), 5.46 (1H, dd, $J_{1,2}$=3.6 Hz, H-1), 5.10 (1H, dd, $J_{4,3}$=9.6 Hz, $J_{4,5}$=9.1 Hz, H-4), 4.88 (1H, dd, $J_{2,1}$=3.6 Hz, $J_{2,3}$=10.0 Hz, H-2), 4.69, 4.58 (2H, each d, J=11.6 Hz, $C_6H_4CH_2$), 4.22–4.00 (3H, m, H-5, 6, 6′), 4.04 (1H, dd, $J_{3,2}$=10.0 Hz, $J_{3,4}$=9.3 Hz, H-3), 2.69 (2H, t, J=7.4 Hz, $CH_2CH_2CH_2C_8F_{17}$), 2.19–1.86 (4H, m, $CH_2CH_2CH_2C_8F_{17}$), 2.08, 2.07, 1.97 (9H, each s, $COCH_3\times3$); β-anomer: δ 5.14–5.06 (1H, m, H-4, overlapped with H-4 signal of α-anomer), 4.91–4.84 (1H, m, H-2, overlapped with H-2 signal of α-anomer), 4.67–4.56 (3H, m, H-1, $C_6H_4CH_2$, overlapped with $C_6H_4CH_2$ signal of α-anomer), 4.26–4.07 (2H, m, H-6, 6′, overlapped with H-5, 6, 6′ signals of α-anomer), 3.73 (1H, t, $J_{3,2}$=9.3 Hz, $J_{3,4}$=9.3 Hz, H-3), 3.64 (1H, ddd, $J_{5,4}$=10.0 Hz, $J_{5,6}$=2.6 Hz, $J_{5,6'}$=5.0 Hz, H-5), 1.98 (3H, s, $COCH_3$); ^{13}C NMR (63 MHz, $CDCl_3$) α-anomer: δ 171.0, 170.1, 169.5, 140.1, 136.2, 128.4, 127.9, 90.3, 76.9, 74.6, 73.5, 69.9, 67.7, 62.3, 34.7, 30.3 (t, J_{CF}=22.6 Hz), 21.8, 20.8, 20.68, 20.67; β-anomer: δ 171.0, 170.9, 169.4, 140.4, 135.8, 128.4, 128.0, 95.8, 79.7, 75.3, 74.1, 72.3, 69.7; ESI-HRMS calcd for $C_{30}H_{29}F_{17}O_9Na$ m/z $[M+Na]^+$: 879.1438. Found: 879.1438.

*4.2.9. 4-(Benzyloxy)phenyl 2,4,6-tri-O-acetyl-3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyl)benzyl]-β-D-glucopyranoside (**12a**).* To a solution of hemiacetal **9a** (1.90 g, 2.51 mmol) in dry CH_2Cl_2 (20 mL) was added trichloroacetonitrile (3.0 mL, 30.14 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (105 μL, 0.703 mmol) at 0 °C under argon. After stirring for 10 min, the mixture was directly chromatographed on a silica gel column (hexane/EtOAc=4:1 v/v) to give the trichloroacetimidate. A suspension of trichloroacetimidate, phenol **10** (754 mg, 3.77 mmol), and MS-4 Å (2.0 g) in dry CH_2Cl_2 (40 mL) was stirred for 30 min at room temperature under argon. $BF_3\cdot Et_2O$ complex (158 μL, 1.26 mmol) was then added at −20 °C. After stirring for 1 h at the same temperature, the reaction mixture was quenched with an excess amount of triethylamine and filtered through Celite. The filtrate was washed with saturated aq $NaHCO_3$ solution (10 mL) and brine (10 mL), dried over Na_2SO_4, filtered, and concentrated. The residue was loaded onto a fluorous reverse-phase silica gel (Fluoro*Flash*®) column and the column was eluted successively with 80% aq MeOH and EtOAc. The EtOAc fraction was concentrated to give phenyl β-D-glucoside **12a** (2.20 g, 93% yield) as colorless solids: mp 116.9–119.7 °C (MeOH/EtOAc); R_f=0.38 (hexane/EtOAc=3:2 v/v); $[\alpha]_D^{23}$ −8.04 (*c* 1.02, $CHCl_3$); IR (KBr, disk): ν 1745 cm^{-1} (C=O); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.43–7.27 (5H, m, Ph*H*), 7.19, 7.14 (4H, each d, J=8.3 Hz, $-C_6H_4-$), 6.93, 6.87 (4H, each d, J=9.4 Hz, $-C_6H_4-$), 5.29 (1H, dd, $J_{2,1}$=7.8 Hz, $J_{2,3}$=9.3 Hz, H-2), 5.18 (1H, dd, $J_{4,3}$=9.5 Hz, $J_{4,5}$=9.6 Hz, H-4), 5.02, 4.61 (4H, each s, PhCH_2 and $C_6H_4CH_2$), 4.87 (1H, d, $J_{1,2}$=7.8 Hz, H-1), 4.24 (1H, dd, $J_{6,5}$=5.5 Hz, $J_{6,6'}$=12.2 Hz, H-6), 4.15 (1H, dd, $J_{6',5}$=2.8 Hz, $J_{6',6}$=12.2 Hz, H-6′), 3.77 (1H, dd, $J_{3,2}$=9.3 Hz, $J_{3,4}$=9.5 Hz, H-3), 3.70 (1H, ddd, $J_{5,4}$=9.6 Hz, $J_{5,6}$=5.5 Hz, $J_{5,6'}$=2.8 Hz, H-5), 2.70 (2H, t, J=7.4 Hz, $CH_2CH_2CH_2C_6F_{13}$), 2.18–1.86 (4H, m, $CH_2CH_2CH_2C_6F_{13}$), 2.05, 2.03, 2.00 (9H, each s, $COCH_3\times3$); ^{13}C NMR (63 MHz, $CDCl_3$): δ 170.6, 169.3, 169.1, 154.8, 151.3, 140.3, 137.0, 135.8, 128.6, 128.4, 128.1, 128.0, 127.4, 118.5, 115.7, 100.5, 80.00, 73.4, 72.4, 72.3, 70.6, 69.6, 62.4, 34.7, 30.3 (t, J_{CF}=22.3 Hz), 21.8, 20.8, 20.71, 20.69; ESI-HRMS

calcd for $C_{41}H_{39}F_{13}O_{10}Na$ *m/z* $[M+Na]^+$: 961.2233. Found: 961.2250.

*4.2.10. 4-(2-Benzyloxyethyl)phenyl 2,4,6-tri-O-acetyl-3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)benzyl]-β-D-glucopyranoside (**12b**).* To a solution of hemiacetal **9b** (340 mg, 0.397 mmol) in dry CH_2Cl_2 (4 mL) were added trichloroacetonitrile (478 μL, 4.76 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (17 μL, 0.111 mmol) at 0 °C under argon. After stirring for 10 min, the mixture was directly chromatographed on a silica gel column (hexane/EtOAc=5:1 v/v) to give the trichloroacetimidate. A suspension of trichloroacetimidate, phenol **11** (181 mg, 0.79 mmol), and MS-4 Å (400 mg) in dry CH_2Cl_2 (8 mL) was stirred for 30 min at room temperature under argon. $BF_3\cdot Et_2O$ complex (25 μL, 0.20 mmol) was then added at −20 °C. After stirring for 1 h at the same temperature, the reaction mixture was quenched with an excess amount of triethylamine and filtered through Celite. The filtrate was washed with saturated aq $NaHCO_3$ solution (5 mL) and brine (5 mL), dried over Na_2SO_4, filtered, and concentrated. The residue was loaded onto a fluorous reverse-phase silica gel (Fluoro*Flash*®) column and the column was eluted successively with 80% aq MeOH and EtOAc. The EtOAc fraction was concentrated to give phenyl β-D-glucoside **12b** (364 mg, 86% yield) as colorless solids: mp 117.9–119.0 °C (MeOH); R_f=0.41 (hexane/EtOAc=3:2 v/v); $[\alpha]_D^{24}$ −8.29 (*c* 1.05, $CHCl_3$); IR (KBr, disk): *ν* 1744 cm^{-1} (C=O); ^1H NMR (250 MHz, $CDCl_3$): *δ* 7.36–7.25 (5H, m, Ph*H*), 7.19, 7.14 (4H, each d, *J*=8.3 Hz, $-C_6H_4-$), 7.13, 6.90 (4H, each d, *J*=8.6 Hz, $-C_6H_4-$), 5.31 (1H, dd, $J_{2,1}$=7.8 Hz, $J_{2,3}$=9.3 Hz, H-2), 5.19 (1H, dd, $J_{4,3}$=9.4 Hz, $J_{4,5}$=9.6 Hz, H-4), 4.95 (1H, d, $J_{1,2}$=7.8 Hz, H-1), 4.61, 4.51 (4H, each s, PhCH_2 and $C_6H_4CH_2$), 4.23 (1H, dd, $J_{6,5}$=5.5 Hz, $J_{6,6'}$=12.1 Hz, H-6), 4.15 (1H, dd, $J_{6',5}$=2.7 Hz, $J_{6',6}$=12.1 Hz, H-6′), 3.78 (1H, dd, $J_{3,2}$=9.3 Hz, $J_{3,4}$=9.4 Hz, H-3), 3.73 (1H, ddd, $J_{5,4}$=9.6 Hz, $J_{5,6}$=5.5 Hz, $J_{5,6'}$=2.7 Hz, H-5), 3.65 (2H, t, *J*=7.0 Hz, CH_2CH_2OBn), 2.87 (2H, t, *J*=7.0 Hz, CH_2CH_2OBn), 2.69 (2H, t, *J*=7.5 Hz, $CH_2CH_2CH_2C_8F_{17}$), 2.18–1.86 (4H, m, $CH_2CH_2CH_2C_8F_{17}$), 2.05, 2.02, 2.00 (9H, each s, $COCH_3\times3$); ^{13}C NMR (63 MHz, $CDCl_3$): *δ* 170.6, 169.3, 169.1, 155.6, 140.3, 138.4, 135.8, 133.9, 129.9, 128.4, 128.3, 128.1, 127.6, 127.5, 116.9, 99.6, 80.00, 73.0, 72.4, 72.3, 71.2, 69.6, 62.4, 35.5, 34.7, 30.3 (t, J_{CF}=22.3 Hz), 21.8, 20.8, 20.71, 20.68; ESI-HRMS calcd for $C_{45}H_{43}F_{17}O_{10}Na$ *m/z* $[M+Na]^+$: 1089.2483. Found: 1089.2495.

*4.2.11. 4-(Benzyloxy)phenyl 3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyl)benzyl]-β-D-glucopyranoside (**13a**).* To a solution of phenyl-β-D-glucoside **12a** (2.0 g, 2.13 mmol) in THF/MeOH (100 mL, 1:1 v/v) was added sodium methoxide (460 mg, 8.52 mmol). After stirring for 12 h at room temperature, the reaction mixture was neutralized with DOWEX® 50WX8-200 ion-exchange resin and then filtered to remove the resin. The filtrate was concentrated to give **13a**. The product was dried in vacuo at 40 °C for 3 h and used for the next reaction without further purification. Mp 99.5–103.4 °C (colorless solids, H_2O-MeOH); R_f=0.34 (hexane/EtOAc=1:1 v/v); $[\alpha]_D^{21}$ −3.80 (*c* 1.0, $CHCl_3$); IR (KBr, disk): *ν* 3355 cm^{-1} (OH); ^1H NMR (250 MHz, CD_3OD): *δ* 7.42–7.25 (7H, m, Ph*H*), 7.18 (2H, d, *J*=8.1 Hz, $-C_6H_4-$), 7.04, 6.90 (4H, each d, *J*=9.2 Hz, $-C_6H_4-$), 5.02 (2H, s, PhCH_2), 4.92, 4.85 (2H, each d, *J*=11.1 Hz, PhCH_2), 4.79 (1H, d, $J_{1,2}$=7.6 Hz, H-1), 3.88 (1H, dd, $J_{6,5}$=2.3 Hz, $J_{6,6'}$=12.0 Hz, H-6), 3.69 (1H, dd, $J_{6',5}$=5.4 Hz, $J_{6',6}$=12.0 Hz, H-6′), 3.60–3.36 (4H, m, H-2, 3, 4, 5), 2.72 (2H, t, *J*=7.4 Hz, $CH_2CH_2CH_2C_6F_{13}$), 2.22–1.85 (4H, m, $CH_2CH_2CH_2C_6F_{13}$); ^{13}C NMR (63 MHz, $CDCl_3$): *δ* 155.8, 153.5, 141.4, 138.9, 138.4, 129.4, 129.3, 128.8, 128.5, 119.3, 116.9, 103.6, 86.3, 78.1, 75.8, 75.2, 71.7, 71.3, 62.6, 35.5, 31.2 (t, J_{CF}=22.1 Hz), 23.1; ESI-HRMS calcd for $C_{35}H_{33}F_{13}O_7Na$ *m/z* $[M+Na]^+$: 835.1916. Found: 835.1935.

*4.2.12. 4-(2-Benzyloxyethyl)phenyl 3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)benzyl]-β-D-glucopyranoside (**13b**).* To a solution of phenyl-β-D-glucoside **12b** (450 mg, 0.42 mmol) in THF/MeOH (45 mL, 1:2 v/v) was added sodium methoxide (46 mg, 0.84 mmol). After stirring for 12 h at room temperature, the reaction mixture was neutralized with DOWEX® 50WX8-200 ion-exchange resin and then filtered to remove the resin. The filtrate was concentrated to give **13b**. The product was dried in vacuo at 40 °C for 3 h and used for the next reaction without further purification. Mp 85.9–91.3 °C (colorless solids, H_2O-MeOH); R_f=0.44 (hexane/EtOAc=1:2 v/v); $[\alpha]_D^{24}$ −24.30 (*c* 1.07, $CHCl_3$); IR (KBr, disk): *ν* 3368 cm^{-1} (OH); ^1H NMR (250 MHz, $CDCl_3$): *δ* 7.35–7.14 (11H, m, Ph*H*), 6.94 (2H, d, *J*=8.6 Hz, $-C_6H_4-$), 5.01, 4.77 (2H, each d, *J*=11.6 Hz, PhCH_2), 4.91 (1H, d, $J_{1,2}$=7.7 Hz, H-1), 4.51 (2H, s, PhCH_2), 3.92–3.62 (4H, m, H-2, 4, 6, 6′), 3.66 (2H, t, *J*=7.0 Hz, CH_2CH_2OBn), 3.49 (1H, dd, $J_{3,2}$=8.8 Hz, $J_{3,4}$=9.0 Hz, H-3), 3.52–3.45 (1H, m, H-5), 2.88 (2H, t, *J*=7.0 Hz, CH_2CH_2OBn), 2.71 (2H, t, *J*=7.5 Hz, $CH_2CH_2CH_2C_8F_{17}$), 2.51, 2.45 (2H, each br s, O*H*), 2.19–1.88 (5H, m, $CH_2CH_2CH_2C_8F_{17}$ and O*H*); ^{13}C NMR (63 MHz, $CDCl_3$): *δ* 155.4, 140.5, 140.1, 138.9, 138.4, 136.5, 133.8, 130.1, 128.7, 128.5, 128.4, 127.6, 127.5, 127.4, 116.6, 101.0, 83.6, 75.5, 74.6, 74.4, 73.0, 71.2, 70.1, 62.5, 35.5, 34.8, 30.4 (t, J_{CF}=22.1 Hz), 21.8; ESI-HRMS calcd for $C_{39}H_{37}F_{17}O_7Na$ *m/z* $[M+Na]^+$: 963.2166. Found: 963.2187.

*4.2.13. 4-(Benzyloxy)phenyl 4,6-O-benzylidene-3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyl)benzyl]-β-D-glucopyranoside (**14a**).* Phenyl β-D-glucoside **13a** (1.73 g, 2.13 mmol) and benzaldehyde dimethylacetal (623 μL, 4.26 mmol) were dissolved in dry DMF (40 mL) in a 300 mL round-bottomed flask. After *p*-TsOH·H_2O (183 mg, 1.07 mmol) was added, the flask was attached to a rotary evaporator, rotated, evacuated, and lowered into a water bath at approximately 60 °C to removed the MeOH which was formed during the reaction. After 2 h, the reaction mixture was quenched with an excess amount of triethylamine and stirred for 15 min at room temperature. Water (160 mL) was then added to the reaction mixture. The solution was directly loaded onto a Fluoro*Flash*® column and the column was eluted successively with 80% aq MeOH and EtOAc. The EtOAc fraction was concentrated, and the residue was purified by silica gel column chromatography (hexane/EtOAc=5:1 v/v) to give **14a** (1.26 g, 66% yield) as colorless solids: mp 162.3–164.4 °C (MeOH); R_f=0.71 (hexane/EtOAc=1:1 v/v); $[\alpha]_D^{23}$ −7.45 (*c* 1.02, $CHCl_3$); IR (KBr, disk): *ν* 3391 cm^{-1} (OH); ^1H NMR (250 MHz, $CDCl_3$): *δ* 7.52–7.31 (12H, m, Ph*H*), 7.14 (2H, d, *J*=8.0 Hz, $-C_6H_4-$), 7.00, 6.90 (4H, each d, *J*=9.1 Hz, $-C_6H_4-$), 5.59 (1H, s, PhC*H*), 5.02 (2H, s, PhCH_2), 4.96, 4.79 (2H, each d, *J*=11.6 Hz, PhCH_2), 4.90 (1H, d, $J_{1,2}$=7.3 Hz, H-1), 4.36 (1H, dd, $J_{4,3}$=10.4 Hz, $J_{4,5}$=4.9 Hz, H-4), 3.86–3.68 (4H, m, H-2, 3, 6ax, 6eq), 3.57 (1H, ddd, $J_{5,4}$=4.9 Hz, $J_{5,6ax}$=9.8 Hz, $J_{5,6eq}$=8.6 Hz, H-5), 2.69 (2H, t, *J*=7.5 Hz, $CH_2CH_2CH_2C_6F_{13}$), 2.51 (1H, d, $J_{OH,2}$=2.3 Hz, O*H*), 2.19–1.86 (4H, m, $CH_2CH_2CH_2C_6F_{13}$); ^{13}C NMR (63 MHz, $CDCl_3$): *δ* 154.8, 151.1, 140.3, 137.2, 137.0, 136.3, 129.0, 128.6, 128.43, 128.40, 128.3, 127.9, 127.4, 126.0, 118.6, 115.7, 102.4, 101.3, 81.2, 80.2, 74.5, 74.0, 70.5, 68.7, 66.5, 34.7, 30.3 (t, J_{CF}=22.1 Hz), 21.8; ESI-HRMS calcd for $C_{42}H_{37}F_{13}O_7Na$ *m/z* $[M+Na]^+$: 923.2229. Found: 923.2204.

*4.2.14. 4-(2-Benzyloxyethyl)phenyl 4,6-O-benzylidene-3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)benzyl]-β-D-glucopyranoside (**14b**).* Phenyl β-D-glucoside **13a** (397 mg, 0.422 mmol) and benzaldehyde dimethylacetal (246 μL, 1.69 mmol) were dissolved in dry DMF (8 mL) in a 100 mL round-bottomed flask. After *p*-TsOH·H_2O (72 mg, 0.211 mmol) was added, the flask was attached to a rotary evaporator, rotated, evacuated, and lowered into a water bath at approximately 60 °C to removed the MeOH, which was formed during the reaction. After 3 h, the reaction mixture was quenched with an excess amount of triethylamine and stirred for 15 min at room temperature. Water (40 mL) was then added to the reaction mixture. The solution was directly loaded onto a Fluoro*Flash*® column and the column was eluted

successively with 80% aq MeOH and EtOAc. The EtOAc fraction was concentrated, and the residue was purified by silica gel column chromatography (hexane/EtOAc=5:1 v/v) to give **14b** (320 mg, 74% yield) as colorless solids: mp 104.2–108.9 °C (MeOH); R_f=0.74 (hexane/EtOAc=1:1 v/v); $[\alpha]_D^{25}$ −7.21 (*c* 0.97, $CHCl_3$); IR (KBr, disk): ν 3387 cm^{-1} (OH); ^1H NMR (250 MHz, $CDCl_3$): δ 7.52–712 (16H, m, Ph*H*), 6.97 (2H, d, *J*=8.7 Hz, $-C_6H_4-$), 5.59 (1H, s, PhC*H*), 4.97 (1H, d, $J_{1,2}$=7.3 Hz, H-1), 4.97, 4.80 (2H, each d, *J*=11.6 Hz, PhCH_2), 4.51 (2H, s, PhCH_2), 4.37 (1H, dd, $J_{4,3}$=10.4 Hz, $J_{4,5}$=4.9 Hz, H-4), 3.86–3.73 (4H, m, H-2, 3, 6ax, 6eq), 3.66 (2H, t, *J*=7.0 Hz, CH_2CH_2OBn), 3.55 (1H, ddd, $J_{5,4}$=4.9 Hz, $J_{5,6ax}$=10.0 Hz, $J_{5,6eq}$=8.9 Hz, H-5), 2.88 (2H, t, *J*=7.0 Hz, CH_2CH_2OBn), 2.69 (2H, t, *J*=7.5 Hz, $CH_2CH_2CH_2C_8F_{17}$), 2.53 (1H, br s, O*H*), 2.19–1.86 (4H, m, $CH_2CH_2CH_2C_8F_{17}$); ^{13}C NMR (63 MHz, $CDCl_3$): 155.4, 140.3, 138.4, 137.2, 136.3, 134.0, 130.0, 129.0, 128.43, 128.39, 128.35, 128.26, 127.58, 127.53, 126.0, 117.1, 101.7, 101.4, 81.2, 80.3, 74.5, 74.1, 73.0, 71.2, 68.7, 66.6, 35.6, 34.8, 30.4 (t, J_{CF}=22.2 Hz), 21.8; ESI-HRMS calcd for $C_{46}H_{41}F_{17}O_7Na$ *m*/*z* $[M+Na]^+$: 1051.2479. Found: 1051.2429.

4.3. Preparation of apiofuranosyl donors 19a-d

*4.3.1. 2,3-O-Benzylidene-α/β-L-ribofuranose (**15**).* According to the method described by Chan and Just,[19] to a suspension of L-ribose (5.0 g, 33.3 mmol), freshly distilled benzaldehyde (13.5 mL, 133.2 mmol), and $CuSO_4$ (10 g) in dry DMF (15 mL) was added camphorsulfonic acid (3.9 g, 16.7 mmol). After stirring for 48 h at room temperature under argon, the reaction mixture was quenched with triethylamine (15 mL), diluted with CH_2Cl_2 (30 mL), and then Celite (10 g) was added into the mixture. After stirring for 15 min, the suspension was filtered through Celite. The filter cake was washed with CH_2Cl_2 (10 mL×3), and the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane/acetone=5:1 then 3:2 v/v) to give **15** (4.55 g, 57% yield, α/β=1:10) as colorless prisms: mp 124.9–126.5 °C (hexane/EtOAc); R_f=0.26 (hexane/EtOAc=1:1 v/v); $[\alpha]_D^{19}$ +26.2 (*c* 1.01, $CHCl_3$); IR (KBr, disk): ν 3302 cm^{-1} (OH); ^1H NMR (250 MHz, $CDCl_3$) β-anomer: δ 7.52–7.38 (5H, m, Ph*H*), 5.78 (1H, s, PhC*H*), 5.57 (1H, br s, H-1), 4.93 (1H, d, $J_{3,2}$=6.1 Hz, H-3), 4.69 (1H, d, $J_{2,3}$=6.1 Hz, H-2), 4.59 (1H, t, $J_{4,5}$=2.2 Hz, H-4), 4.32, 3.23 (1H, each br s, O*H*×2), 3.80 (1H, dd, $J_{5,4}$=2.2 Hz, H-5); α-anomer: δ 5.99 (1H, s, PhC*H*), 5.51 (1H, dd, $J_{1,2}$=4.2 Hz, $J_{1,OH}$=10.0 Hz, H-1), 4.84 (1H, dd, $J_{3,2}$=6.8 Hz, $J_{3,4}$=1.9 Hz, H-3), 4.75 (1H, dd, $J_{2,1}$=4.2 Hz, $J_{2,3}$=6.1 Hz, H-2), 4.41 (1H, dt, $J_{4,3}$=1.8 Hz, $J_{4,5}$=3.4 Hz, H-4), 3.91 (1H, d, $J_{OH,1}$=10.2 Hz, O*H*), 3.84–3.74 (2H, m, H-5, overlapped with H-5 signal of β-anomer); ^{13}C NMR (63 MHz, $CDCl_3$) β-anomer: δ 135.8, 129.9, 128.4, 126.9, 105.8, 102.7, 87.54, 87.48, 82.6, 63.7; α-anomer: δ 130.2, 128.7, 126.7, 107.4, 97.3, 82.4, 80.7, 80.2, 63.5; ESI-HRMS calcd for $C_{12}H_{14}O_5Na$ *m*/*z* $[M+Na]^+$: 261.0739. Found: 261.0761.

*4.3.2. 2,3-O-Benzylidene-2-C-(hydroxymethyl)-α/β-L-ribofuranose (**16**).* To a solution of **15** (310 mg, 1.30 mmol) and potassium carbonate (252 mg, 1.82 mmol) in MeOH (4.5 mL) was added 37% aq formaldehyde solution (2.7 mL). After stirring for 8 h at 85 °C, the reaction mixture was neutralized with 1 M aq HCl solution and concentrated. The remaining aqueous solution was extracted with CH_2Cl_2 (5 mL×5), and the combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography (hexane/acetone=1:1 v/v) to give **16** (321 mg, 92% yield, α/β=1:4) as colorless prisms: mp 144.1–145.3 °C (EtOH); R_f=0.26 (hexane/acetone=1:1 v/v); $[\alpha]_D^{19}$ +2.5 (*c* 1.1, MeOH); IR (KBr, disk): ν 3367 cm^{-1} (OH); ^1H NMR (250 MHz, CD_3OD) β-anomer: δ 7.52–7.35 (5H, m, Ph*H*), 6.06 (1H, s, PhC*H*), 5.36 (1H, s, H-1), 4.70 (1H, d, $J_{3,4}$=0.7 Hz, H-3), 4.31 (1H, dt, $J_{4,5}$=5.1 Hz, $J_{4,3}$=0.7 Hz, H-4), 3.93 (2H, s, H-6), 3.68 (2H, d, $J_{5,4}$=5.1 Hz, H-5); α-anomer: δ 6.13 (1H, s, PhC*H*), 5.22 (1H, s, H-1), 4.68 (1H, d, $J_{3,4}$=2.0 Hz, H-3), 4.27 (1H, dt, $J_{4,5}$=4.5 Hz, $J_{4,3}$=2.0 Hz, H-4), 3.85 (2H, s, H-6), 3.68 (2H, d, $J_{5,4}$=4.5 Hz, H-5); ^{13}C NMR (63 MHz, CD_3OD) β-anomer: δ 138.7, 130.6, 129.2, 128.2, 107.7, 104.2, 96.3, 88.4, 85.8, 64.1, 62.5; α-anomer: δ 138.0, 130.8, 129.3, 128.4, 109.2, 99.3, 92.5, 85.1, 82.8, 63.4, 63.0; ESI-HRMS calcd for $C_{13}H_{16}O_6Na$ *m*/*z* $[M+Na]^+$: 291.0845. Found: 291.0840.

*4.3.3. 2,3-O-Benzylidene-α/β-D-apiofuranose (**17**).* To a solution of **16** (197 mg, 0.73 mmol) in MeOH (3.7 mL) was cautiously added sodium borohydride (83 mg, 2.19 mmol) in small portions. After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C and then neutralized to pH 7 with 1 M aq HCl solution. To the mixture was then added a solution of sodium periodate (312 mg, 1.46 mmol) in H_2O (3.7 mL), and the reaction mixture was stirred for an additional 1 h at room temperature. After the solvent was evaporated, the remaining aqueous solution was extracted with EtOAc (5 mL×3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc=3:2 v/v) to give **17** (152 mg, 87% yield, α/β=1:10) as a colorless syrup: R_f=0.56 (hexane/acetone=3:2 v/v); $[\alpha]_D^{17}$ −42.2 (*c* 1.0, $CHCl_3$); IR (NaCl, neat): ν 3420 cm^{-1} (OH); ^1H NMR (250 MHz, $CDCl_3$) β-anomer: δ 7.53–7.37 (5H, m, Ph*H*), 5.92 (1H, s, PhC*H*), 5.56 (1H, s, H-1), 4.47 (1H, s, H-2), 4.17, 4.09 (2H, each d, *J*=10.2 Hz, H-4), 3.96, 3.89 (2H, each d, *J*=11.6 Hz, H-5), 3.18 (1H, br s, O*H*), 2.42 (1H, br s, O*H*); α-anomer: δ 6.09 (1H, s, PhC*H*), 5.13 (1H, dd, $J_{1,2}$=3.4 Hz, $J_{1,OH}$=11.5 Hz, H-1), 4.45 (1H, d, $J_{2,1}$=10.7 Hz, H-2), 4.15, 4.09 (2H, each d, *J*=7.3 Hz, H-4), 4.10 (1H, d, $J_{OH,1}$=11.4 Hz, O*H*), 2.42 (1H, br s, O*H*), 3.99–3.87 (2H, m, H-5, overlapped with H-5 signal of β-anomer); ^{13}C NMR (63 MHz, $CDCl_3$) β-anomer: δ 135.9, 129.9, 128.4, 127.0, 106.0, 101.1, 91.9, 87.2, 73.1, 62.8; α-anomer: δ 135.7, 130.2, 128.6, 106.9, 97.8, 91.5, 81.0, 68.7, 62.4; ESI-HRMS calcd for $C_{12}H_{14}O_5Na$ *m*/*z* $[M+Na]^+$: 261.0739. Found: 261.0748.

*4.3.4. 5-O-Benzoyl-2,3-O-benzylidene-α/β-D-apiofuranose (**18a**).* To a solution of **17** (500 mg, 2.10 mmol) and pyridine (864 μL, 10.71 mmol) in dry CH_2Cl_2 (6 mL) was added dropwise benzoyl chloride (267 μL, 2.31 mmol) at −78 °C. After stirring for 1 h at the same temperature, the reaction mixture was quenched with saturated aq $NaHCO_3$ solution (10 mL). The aqueous layer was extracted with CH_2Cl_2 (10 mL×3), and the combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography, using a gradient eluent (hexane/EtOAc=5:1→4:1→3:1→2:1 v/v) to give hemiacetal **18a** (560 mg, 78% yield, α/β=1:7), along with 1,5-di-*O*-benzoylated **18a′** (130 mg, 14% yield, α/β=1:3) and 1-*O*-benzoylated **18a″** (37 mg, 4% yield, α/β=1:4).

Compound **18a**: Colorless syrup; R_f=0.27 (hexane/EtOAc=3:1 v/v); $[\alpha]_D^{19}$ −4.9 (*c* 1.02, $CHCl_3$); IR (KBr, disk): ν 3447 cm^{-1} (OH), 1724 cm^{-1} (C=O); ^1H NMR (250 MHz, $CDCl_3$) β-anomer: δ 8.10–8.07 (2H, m, Ph*H*), 7.58–7.37 (8H, m, Ph*H*), 6.00 (1H, s, PhC*H*), 5.63 (1H, s, H-1), 4.67 (2H, s, H-5), 4.62 (1H, s, H-2), 4.27, 4.22 (2H, each d, *J*=10.4 Hz, H-4); α-anomer: δ 6.16 (1H, s, PhC*H*), 5.19 (1H, d, $J_{1,2}$=3.4 Hz, H-1), 4.64 (2H, s, H-5), 4.55 (1H, d, $J_{2,1}$=3.4 Hz, H-2), 4.30–4.21 (2H, m, H-4, overlapped with H-4 signal of β-anomer); ^{13}C NMR (63 MHz, $CDCl_3$) β-anomer: δ 166.1, 135.8, 133.3, 129.9, 129.7, 128.4, 128.3, 127.0, 106.3, 101.6, 90.2, 87.5, 73.2, 64.7; α-anomer: δ 166.0, 135.4, 133.5, 130.2, 129.6, 129.4, 128.6, 127.0, 107.2, 97.8, 89.6, 81.4, 68.7, 63.9; ESI-HRMS calcd for $C_{19}H_{18}O_6Na$ *m*/*z* $[M+Na]^+$: 365.1001. Found: 365.1010.

*4.3.4.1. 1,5-Di-O-benzoyl-2,3-O-benzylidene-β-D-apiofuranose (**18a′**).* Mp 132.2–134.3 °C (colorless prisms, hexane/EtOAc); $[\alpha]_D^{24}$ −72.9 (*c* 1.01, $CHCl_3$); R_f=0.57 (hexane/EtOAc=3:1 v/v); IR (KBr, disk): ν 1722 cm^{-1} (C=O); ^1H NMR (250 MHz, $CDCl_3$): δ 8.08–7.95

(4H, m, PhH), 7.60–7.35 (11H, m, PhH), 6.63 (1H, s, H-1), 6.09 (1H, s, PhCH), 4.90 (1H, s, H-2), 4.75 (2H, s, H-5), 4.42, 4.28 (2H, each d, J=10.4 Hz, H-4); ^{13}C NMR (63 MHz, $CDCl_3$): δ 166.1, 164.8, 135.5, 133.5, 130.1, 129.8, 129.7, 129.3, 129.2, 128.6, 128.49, 128.6, 127.1, 106.8, 101.8, 90.0, 87.1, 74.8, 63.9; ESI-HRMS calcd for $C_{26}H_{22}O_7Na$ m/z $[M+Na]^+$: 469.1263. Found: 469.1271.

*4.3.4.2. 1-O-Benzoyl-2,3-O-benzylidene-β-D-apiofuranose (**18a**″).* Mp 143.9–145.6 °C (colorless prisms, hexane/EtOAc); $[\alpha]_D^{24}$ −106.5 (c 1.05, $CHCl_3$); R_f=0.16 (hexane/EtOAc=3:1 v/v); IR (KBr, disk): ν 3518 cm^{-1} (OH), 1726 cm^{-1} (C=O); ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.02–7.99 (2H, m, PhH), 7.56–7.38 (8H, m, PhH), 6.60 (1H, s, H-1), 6.00 (1H, s, PhCH), 4.73 (1H, s, H-2), 4.28, 4.11 (2H, each d, J=10.4 Hz, H-4), 4.00 (2H, br s, H-5), 2.35 (1H, br s, OH); ^{13}C NMR (63 MHz, $CDCl_3$): δ 164.8, 135.8, 133.5, 130.0, 129.7, 129.4, 128.5, 128.4, 127.0, 106.8, 101.3, 92.0, 86.5, 75.1, 63.4; ESI-HRMS calcd for $C_{19}H_{18}O_7Na$ m/z $[M+Na]^+$: 365.1001. Found: 365.0993.

*4.3.5. 2,3-O-Benzylidene-5-O-(3-methylbutyryl)-α/β-D-apiofuranose (**18b**).* To a solution of **17** (250 mg, 1.05 mmol) and pyridine (432 μL, 5.35 mmol) in dry CH_2Cl_2 (3 mL) was added dropwise 3-methylbutyryl chloride (142 μL, 1.15 mmol) at −78 °C. After stirring for 2 h at the same temperature, the reaction mixture was quenched with saturated aq $NaHCO_3$ solution (10 mL). The aqueous layer was extracted with CH_2Cl_2 (10 mL×3), and the combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography, using a gradient eluent (hexane/EtOAc=4:1→3:1→2:1 v/v) to give hemiacetal **18b** (262 mg, 78% yield, α/β=1:5), along with 1,5-di-O-acylated **18b**′ (46 mg, 11% yield, α/β=2:3).

Compound **18b**: Mp 106.9–107.7 °C (colorless prisms, hexane/EtOAc); R_f=0.65 (hexane/EtOAc=1:1 v/v); $[\alpha]_D^{19}$ −35.6 (c 0.45, $CHCl_3$); IR (KBr, disk): ν 3475 cm^{-1} (OH), 1739 cm^{-1} (C=O); ^{1}H NMR (250 MHz, $CDCl_3$) β-anomer: δ 7.55–7.37 (5H, m, PhH), 5.92 (1H, s, PhCH), 5.58 (1H, s, H-1), 4.48–4.43 (3H, m, H-2, 5), 4.18, 4.10 (2H, each d, J=10.1 Hz, H-4), 2.86 (1H, br s, OH), 2.28 (2H, d, J=6.6 Hz, $COCH_2CH(CH_3)_2$), 2.19–2.08 (1H, m, $COCH_2CH(CH_3)_2$), 0.98 (6H, d, J=6.6 Hz, CH_3×2); α-anomer: δ 6.08 (1H, s, PhCH), 5.13 (1H, dd, $J_{1,2}$=3.2 Hz, $J_{1,OH}$=11.4 Hz, H-1), 4.48–4.28 (3H, m, H-2, 5, overlapped with H-2, 5 signals of β-anomer), 4.20–4.08 (2H, m, overlapped with H-4 signal of β-anomer), 3.93 (1H, br d, $J_{OH,1}$=12.0 Hz, OH); ^{13}C NMR (63 MHz, $CDCl_3$) β-anomer: δ 172.7, 135.8, 129.9, 128.3, 127.0, 106.2, 101.5, 90.1, 87.4, 73.2, 64.3, 43.1, 25.6, 22.3; α-anomer: δ 172.6, 135.4, 130.2, 128.6, 127.0, 107.1, 97.8, 89.5, 81.3, 68.7, 63.3, 43.1, 25.6; ESI-HRMS calcd for $C_{17}H_{22}O_6Na$ m/z $[M+Na]^+$: 345.1314. Found: 345.1310.

*4.3.5.1. 2,3-O-Benzylidene-1,5-di-O-(3-methylbutyryl)-α/β-D-apiofuranose (**18b**′).* Colorless syrup; R_f=0.88 (hexane/EtOAc=1:1 v/v); IR (KBr, disk): ν 1743 cm^{-1} (C=O); ^{1}H NMR (250 MHz, $CDCl_3$) β-anomer: δ 7.58–7.36 (5H, m, PhH), 6.38 (1H, s, H-1), 5.96 (1H, s, PhCH), 4.55 (1H, s, H-2), 4.46, 4.40 (2H, each d, J=12.0 Hz, H-5), 4.26, 4.00 (2H, each d, J=10.3 Hz, H-4), 2.29, 2.28 (4H, each d, $COCH_2CH(CH_3)_2$×2), 2.18–1.93 (2H, m, $COCH_2CH(CH_3)_2$×2), 0.994, 0.987, 0.979 (12H, each d, J=6.6 Hz, CH_3×4); α-anomer: δ 6.23 (1H, s, PhCH), 6.14 (1H, d, $J_{1,2}$=4.2 Hz, H-1), 4.74 (1H, d, $J_{2,1}$=4.2 Hz, H-2), 4.49, 4.35 (2H, each d, J=11.9 Hz, H-5), 4.24, 3.93 (2H, each d, J=10.2 Hz, H-4), 2.30–2.21 (4H, m, $COCH_2CH(CH_3)_2$×2), 2.18–1.93 (2H, m, $COCH_2CH(CH_3)_2$×2), 1.01–0.81 (12H, each d, J=6.6 Hz, CH_3×4); ^{13}C NMR (63 MHz, $CDCl_3$) β-anomer: δ 172.5, 171.1, 135.6, 130.0, 128.4, 127.0, 106.7, 100.6, 89.8, 86.9, 74.7, 63.6, 43.2, 43.1, 25.62, 25.59, 22.35, 22.29, 22.26; α-anomer: δ 172.5, 171.5, 135.6, 129.7, 128.2, 126.9, 109.5, 96.3, 89.4, 82.4, 72.5, 63.9, 42.9, 25.2, 22.2, 22.1; ESI-HRMS calcd for $C_{22}H_{30}O_7Na$ m/z $[M+Na]^+$: 429.1889. Found: 429.1882.

*4.3.6. 2,3-O-Benzylidene-5-O-(4-benzyloxybenzoyl)-α/β-D-apiofuranose (**18c**).* To a solution of **17** (439 mg, 1.84 mmol) and pyridine (760 μL, 9.38 mmol) in dry CH_2Cl_2 (5.3 mL) was added 4-benzyloxybenzoyl chloride (500 mg, 2.03 mmol) at −78 °C. After stirring for 1 h at the same temperature, the reaction mixture was quenched with saturated aq $NaHCO_3$ solution (10 mL). The aqueous layer was extracted with CH_2Cl_2 (10 mL×3), and the combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography, using a gradient eluent (hexane/Et_2O=3:1→1:1 v/v) to give hemiacetal **18c** (440 mg, 53% yield, α/β=1:6), along with 1,5-di-O-acylated **18c**′ (27 mg, 2% yield, α/β=1:16) and 1-O-acylated **18c**″ (57 mg, 7% yield, β only).

Compound **18c**: Mp 118.1–119.8 °C (colorless prisms, hexane/EtOAc); R_f=0.32 (hexane/Et_2O=1:1 v/v, TLC developed two times); $[\alpha]_D^{24}$ −0.614 (c 1.14, $CHCl_3$); IR (KBr, disk): ν 3475 cm^{-1} (OH), 1709 cm^{-1} (C=O); ^{1}H NMR (250 MHz, $CDCl_3$) β-anomer: δ 8.03, 7.00 (4H, each d, J=8.9 Hz, C_6H_4OBn), 7.55–7.30 (10H, m, PhH), 5.97 (1H, s, PhCH), 5.60 (1H, d, $J_{1,OH}$=1.7 Hz, H-1), 5.10 (2H, s, $PhCH_2$), 4.63 (2H, s, H-5), 4.60 (1H, s, H-2), 4.25, 4.19 (2H, each d, J=10.1 Hz, H-4), 2.94 (1H, br d, $J_{OH,1}$=1.7 Hz,); α-anomer: δ 6.14 (1H, s, PhCH), 5.17 (1H, dd, $J_{1,2}$=3.4 Hz, $J_{1,OH}$=11.8 Hz, H-1), 5.12 (2H, s, $PhCH_2$), 4.60, 4.56 (2H, each d, J=6.4 Hz, H-5), 4.52 (1H, d, $J_{2,1}$=3.4 Hz, H-2), 4.27–4.15 (2H, m, H-4, overlapped with H-4 signal of β-anomer), 3.96 (1H, d, $J_{OH,1}$=11.8 Hz,); ^{13}C NMR (63 MHz, $CDCl_3$) β-anomer: δ 165.8, 162.8, 136.1, 135.9, 131.8, 129.9, 128.6, 128.4, 128.2, 127.4, 127.1, 122.0, 114.6, 106.3, 101.7, 90.3, 87.5, 73.3, 70.1, 64.4; α-anomer: δ 165.7, 163.0, 136.0, 135.5, 131.8, 130.3, 128.6, 128.2, 127.0, 121.7, 114.8, 107.3, 97.9, 89.8, 81.4, 70.2, 68.8, 63.7; ESI-HRMS calcd for $C_{26}H_{24}O_7Na$ m/z $[M+Na]^+$: 471.1420. Found: 471.1407.

*4.3.6.1. 2,3-O-Benzylidene-1,5-di-O-(4-benzyloxybenzoyl)-α/β-D-apiofuranose (**18c**′).* Colorless solids; R_f=0.63 (hexane/Et_2O=1:1 v/v, TLC developed two times); IR (KBr, disk): ν 1716 cm^{-1} (C=O); ^{1}H NMR (250 MHz, $CDCl_3$, selected β-anomer signal): δ 8.00, 7.92, 6.95, 6.94 (8H, each d, J=9.0 Hz, C_6H_4OBn×2), 7.58–7.32 (15H, m, PhH), 6.59 (1H, s, H-1), 6.06 (1H, s, PhCH), 5.09 (4H, s, $PhCH_2$×2), 4.87 (1H, s, H-2), 4.71 (2H, s, H-5), 4.39, 4.24 (2H, each d, J=10.4 Hz, H-4); ^{13}C NMR (63 MHz, $CDCl_3$, selected β-anomer signal): δ 165.7, 164.5, 163.0, 136.02, 136.00, 135.59, 131.94, 131.87, 130.1, 128.7, 128.5, 128.24, 128.23, 127.5, 127.1, 121.9, 121.8, 114.7, 114.6, 106.8, 101.6, 90.1, 87.1, 74.8, 70.2, 63.6; ESI-HRMS calcd for $C_{40}H_{34}O_9Na$ m/z $[M+Na]^+$: 681.2101. Found: 681.2135.

*4.3.6.2. 2,3-O-Benzylidene-1-O-(4-benzyloxybenzoyl)-β-D-apiofuranose (**18c**″).* Mp 153.9–157.1 °C (colorless needles, hexane/EtOAc); R_f=0.21 (hexane/Et_2O=1:1 v/v, TLC developed two times); $[\alpha]_D^{24}$ −85.8 (c 1.02, $CHCl_3$); IR (KBr, disk): ν 3488 cm^{-1} (OH), 1720 cm^{-1} (C=O); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.95, 6.98 (4H, each d, J=8.9 Hz, C_6H_4OBn), 7.55–7.32 (10H, m, PhH), 6.58 (1H, s, H-1), 5.99 (1H, s, PhCH), 5.10 (2H, s, $PhCH_2$), 4.71 (1H, s, H-2), 4.26, 4.09 (2H, each d, J=10.4 Hz), 4.01 (1H, dd, $J_{5,OH}$=6.0 Hz, $J_{5,5'}$=11.9 Hz, H-5), 3.96 (1H, dd, $J_{5',OH}$=5.8 Hz, $J_{5',5}$=11.9 Hz, H-5′), 2.31 (1H, dd, $J_{OH,5}$=6.0 Hz, $J_{OH,5'}$=5.8 Hz, OH); ^{13}C NMR (63 MHz, $CDCl_3$): δ 164.4, 163.0, 136.1, 135.9, 131.9, 130.0, 128.7, 128.4, 128.2, 127.4, 127.0, 121.9, 114.7, 106.8, 101.1, 92.0, 86.5, 75.0, 70.1, 63.5; ESI-HRMS calcd for $C_{26}H_{24}O_7Na$ m/z $[M+Na]^+$: 471.1420. Found: 471.1452.

*4.3.7. 2,3-O-Benzylidene-5-O-(4-nitrobenzoyl)-α/β-D-apiofuranose (**18d**).* To a solution of **17** (500 mg, 2.10 mmol) and pyridine (864 μL, 10.71 mmol) in dry CH_2Cl_2 (6 mL) was added 4-nitrobenzoyl chloride (585 mg, 3.15 mmol) at −78 °C. After stirring for 1 h at the same temperature, the reaction mixture was quenched with saturated aq $NaHCO_3$ solution (10 mL). The aqueous layer was extracted with CH_2Cl_2 (10 mL×3), and the combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, filtered, and

concentrated. The residue was purified by silica gel column chromatography, using a gradient eluent (hexane/EtOAc=4:1→3:1→2:1 v/v) to give hemiacetal **18d** (612 mg, 75% yield, β only), along with 1,5-di-*O*-acylated **18d′** (124 mg, 11% yield, α/β=5:1).

Compound **18d**: Mp 146.3–146.7 °C (light green plates, hexane/EtOAc); R_f=0.55 (hexane/EtOAc=1:1 v/v); $[\alpha]_D^{19}$ −17.2 (*c* 1.02, $CHCl_3$); IR (KBr, disk): *ν* 3399 cm^{-1} (OH), 1727 cm^{-1} (C=O), 1527 cm^{-1} (N=O); ^1H NMR (250 MHz, $CDCl_3$): *δ* 8.32–8.23 (4H, m, $C_6H_4NO_2$), 7.54–7.38 (5H, m, Ph*H*), 5.97 (1H, s, PhC*H*), 5.64 (1H, d, $J_{1,OH}$=2.6 Hz, H-1), 4.76, 4.69 (2H, each d, *J*=11.9 Hz, H-5), 4.61 (1H, s, H-2), 4.29, 4.26 (2H, each d, *J*=10.1 Hz, H-4), 2.82 (1H, d, $J_{OH,1}$=2.6 Hz, O*H*); ^{13}C NMR (63 MHz, $CDCl_3$): *δ* 164.3, 150.8, 135.5, 134.8, 130.9, 130.1, 128.5, 127.0, 123.6, 106.4, 101.6, 90.0, 87.6, 73.3, 65.2; ESI-HRMS calcd for $C_{19}H_{17}NO_8Na$ *m*/*z* $[M+Na]^+$: 410.0852. Found: 410.0866.

*4.3.7.1. 2,3-O-Benzylidene-1,5-di-O-(4-nitrobenzoyl)-α/β-D-apiofuranose (**18d′**).* Colorless syrup; R_f=0.75 (hexane/EtOAc=1:1 v/v); IR (KBr, disk): *ν* 1730 cm^{-1} (C=O), 1529 cm^{-1} (N=O); ^1H NMR (250 MHz, $CDCl_3$) α-anomer: *δ* 8.35–7.90 (8H, m, $C_6H_4NO_2\times2$), 7.57–7.17 (5H, m, Ph*H*), 6.49 (1H, d, $J_{1,2}$=4.3 Hz, H-1), 6.41 (1H, s, PhC*H*), 5.04 (1H, d, $J_{2,1}$=4.3 Hz, H-2), 4.87, 4.75 (2H, each d, *J*=11.9 Hz, H-5), 4.47, 4.23 (2H, each d, *J*=10.3 Hz, H-4); β-anomer: *δ* 6.65 (1H, s, H-1), 6.08 (1H, s, PhC*H*), 4.90, 4.79 (2H, each d, *J*=11.9 Hz, H-5), 4.89 (1H, s, H-2), 4.49, 4.29 (2H, each d, *J*=10.4 Hz, H-4); ^{13}C NMR (63 MHz, $CDCl_3$) α-anomer: *δ* 164.2, 163.1, 150.9, 150.5, 136.0, 134.6, 134.5, 130.9, 130.8, 129.6, 128.2, 126.2, 123.8, 123.3, 109.9, 97.5, 89.5, 82.9, 73.4, 65.5; β-anomer: *δ* 163.0, 135.0, 134.5, 134.4, 130.3, 128.6, 127.0, 123.70, 123.67, 107.1, 102.5, 89.9, 87.0, 75.3, 65.1; ESI-HRMS calcd for $C_{26}H_{20}N_2O_{11}Na$ *m*/*z* $[M+Na]^+$: 559.0965. Found: 559.0935.

*4.3.8. 5-O-Benzoyl-2,3-O-benzylidene-β-D-apiofuranosyl trichloroacetimidate (**19a**).* To a solution of hemiacetal **18a** (1.1 g, 3.21 mmol) in dry CH_2Cl_2 (11 mL) was added trichloroacetonitrile (3.9 mL, 38.56 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (134 μL, 0.90 mmol) at 0 °C under argon. After stirring for 10 min, the mixture was directly chromatographed on a silica gel column (hexane/EtOAc=4:1 v/v) to give trichloroacetimidate **19a** (1.51 g, 96% yield) as colorless needles: mp 110.9–112.9 °C (hexane); R_f=0.62 (hexane/EtOAc=3:2 v/v); $[\alpha]_D^{23}$ −52.70 (*c* 1.11, $CHCl_3$); IR (KBr, disk): *ν* 3331, 1669 cm^{-1} (NH), 1724 cm^{-1} (C=O); ^1H NMR (250 MHz, $CDCl_3$): *δ* 8.68 (1H, s, N*H*), 8.07 (2H, *J*=7.3 Hz, Ph*H*), 7.61–7.39 (8H, m, Ph*H*), 6.53 (1H, s, H-1), 6.08 (1H, s, PhC*H*), 4.89 (1H, s, H-2), 4.71 (2H, s, H-5), 4.43, 4.26 (2H, each d, *J*=10.4 Hz, H-4); ^{13}C NMR (63 MHz, $CDCl_3$): *δ* 166.0, 160.5, 135.5, 133.5, 130.1, 129.8, 129.2, 128.6, 128.4, 127.1, 106.9, 104.8, 90.9, 90.0, 86.6, 75.1, 63.9; ESI-HRMS calcd for $C_{21}H_{13}Cl_3NO_6Na$ *m*/*z* $[M+Na]^+$: 508.0098. Found: 508.0141.

*4.3.9. 2,3-O-Benzylidene-5-O-(3-methylbutyryl)-β-D-apiofuranosyl trichloroacetimidate (**19b**).* To a solution of hemiacetal **18b** (1.1 g, 3.41 mmol) in dry CH_2Cl_2 (11 mL) were added trichloroacetonitrile (4.1 mL, 40.92 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (142 μL, 0.96 mmol) at 0 °C under argon. After stirring for 10 min, the mixture was directly chromatographed on a silica gel column (hexane/EtOAc=10:1 v/v) to give trichloroacetimidate **19b** (1.38 g, 86% yield) as colorless needles: mp 98.5–101.6 °C (hexane/EtOAc); R_f=0.55 (hexane/EtOAc=3:1 v/v); $[\alpha]_D^{23}$ −76.7 (*c* 1.11, $CHCl_3$); IR (KBr, disk): *ν* 3329, 1670 cm^{-1} (NH), 1739 cm^{-1} (C=O); ^1H NMR (250 MHz, $CDCl_3$): *δ* 8.67 (1H, s, N*H*), 7.56–7.35 (5H, m, Ph*H*), 6.49 (1H, s, H-1), 5.99 (1H, s, PhC*H*), 4.74 (1H, s, H-2), 4.45 (2H, s, H-5), 4.33, 4.14 (2H, each d, *J*=10.3 Hz, H-4), 2.29 (2H, d, *J*=6.8 Hz, $COCH_2CH(CH_3)_2$), 2.24–2.04 (1H, m, $COCH_2CH(CH_3)_2$), 0.98 (6H, d, *J*=6.6 Hz, $CH_3\times2$); ^{13}C NMR (63 MHz, $CDCl_3$): *δ* 172.5, 160.4, 135.5, 130.1, 128.4, 127.1, 106.8, 104.6, 91.0, 89.7, 86.5, 75.2, 63.4, 43.1, 25.6, 22.3; ESI-HRMS calcd for $C_{19}H_{22}Cl_3NO_6Na$ *m*/*z* $[M+Na]^+$: 488.0411. Found: 488.0456.

*4.3.10. 2,3-O-Benzylidene-5-O-(4-benzyloxybenzoyl)-β-D-apiofuranosyl trichloroacetimidate (**19c**).* To a solution of hemiacetal **18c** (752 mg, 1.68 mmol) in dry CH_2Cl_2 (7.5 mL) were added trichloroacetonitrile (2.0 mL, 20.12 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (70 μL, 0.47 mmol) at 0 °C under argon. After stirring for 10 min, the mixture was directly chromatographed on a silica gel column (hexane/EtOAc=6:1 v/v) to give trichloroacetimidate **19c** (823 mg, 83% yield) as colorless prisms: mp 131.5–134.0 °C (hexane/EtOAc); R_f=0.57 (hexane/EtOAc=3:2 v/v); $[\alpha]_D^{23}$ −39.9 (*c* 1.05, $CHCl_3$); IR (KBr, disk): *ν* 3351, 1676 cm^{-1} (NH), 1719 cm^{-1} (C=O); ^1H NMR (250 MHz, $CDCl_3$): *δ* 8.67 (1H, s, N*H*), 8.03, 7.01 (4H, each d, *J*=9.0 Hz, C_6H_4OBn), 7.56–7.33 (10H, m, Ph*H*), 6.52 (1H, s, H-1), 6.06 (1H, s, PhC*H*), 5.13 (1H, s, $PhCH_2$), 4.88 (1H, s, H-2), 4.66 (2H, s, H-5), 4.41, 4.25 (2H, each d, *J*=10.4 Hz, H-4); ^{13}C NMR (63 MHz, $CDCl_3$): *δ* 165.7, 162.9, 160.5, 136.1, 135.5, 131.9, 130.1, 128.7, 128.4, 128.2, 127.4, 127.1, 121.8, 106.9, 104.8, 90.9, 90.0, 86.5, 75.0, 70.2, 63.6; ESI-HRMS calcd for $C_{28}H_{24}Cl_3NO_7Na$ *m*/*z* $[M+Na]^+$: 614.0516. Found: 614.0563.

*4.3.11. 2,3-O-Benzylidene-5-O-(4-nitrobenzoyl)-β-D-apiofuranosyl trichloroacetimidate (**19d**).* To a solution of hemiacetal **18d** (570 mg, 1.47 mmol) in dry CH_2Cl_2 (6 mL) were added trichloroacetonitrile (1.8 mL, 17.64 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (61 μL, 0.41 mmol) at 0 °C under argon. After stirring for 10 min, the mixture was directly chromatographed on a silica gel column (hexane/EtOAc=6:1 v/v) to give trichloroacetimidate **19d** (632 mg, 81% yield) as colorless needles: mp 141.8–144.8 °C (hexane/EtOAc); R_f=0.60 (hexane/EtOAc=3:2 v/v); $[\alpha]_D^{23}$ −47.9 (*c* 1.01, $CHCl_3$); IR (KBr, disk): *ν* 3328, 1669 cm^{-1} (NH), 1723 cm^{-1} (C=O), 1529 cm^{-1} (N=O); ^1H NMR (250 MHz, $CDCl_3$): *δ* 8.72 (1H, s, N*H*), 8.31, 8.24 (4H, each d, *J*=9.1 Hz, $C_6H_4NO_2$), 7.56–7.40 (5H, m, Ph*H*), 6.55 (1H, s, H-1), 6.05 (1H, s, PhC*H*), 4.87 (1H, s, H-2), 4.80, 4.72 (2H, each d, *J*=12.0 Hz, H-5), 4.44, 4.27 (2H, each d, *J*=10.4 Hz, H-4); ^{13}C NMR (63 MHz, $CDCl_3$): 164.2, 160.3, 150.9, 135.2, 134.5, 130.9, 130.2, 128.5, 127.1, 123.7, 107.0, 104.6, 90.9, 89.7, 86.6, 75.0, 64.7; ESI-HRMS calcd for $C_{21}H_{17}Cl_3N_2O_8Na$ *m*/*z* $[M+Na]^+$: 552.9948. Found: 552.9919.

4.4. Total synthesis of eight cucurbitoside-like phenolic glycosides 1a–h

*4.4.1. Mixture of 4-(benzyloxy)phenyl 4,6-O-benzylidene-2-O-(5-O-benzoyl-2,3-O-benzylidene-β-D-apiofuranosyl)-3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyl)benzyl]-β-D-glucopyranoside (**20a**), 4-(benzyloxy)phenyl 4,6-O-benzylidene-2-O-[2,3-O-benzylidene-5-O-(3-methylbutyryl)-β-D-apiofuranosyl]-3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyl)benzyl]-β-D-glucopyranoside (**20b**), 4-(benzyloxy)phenyl 4,6-O-benzylidene-2-O-[2,3-O-benzylidene-5-O-(4-benzyloxybenzoyl)-β-D-apiofuranosyl]-3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyl)benzyl]-β-D-glucopyranoside (**20c**), 4-(benzyloxy)phenyl 4,6-O-benzylidene-2-O-[2,3-O-benzylidene-5-O-(4-nitrobenzoyl)-β-D-apiofuranosyl]-3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyl)benzyl]-β-D-glucopyranoside (**20d**), 4-(2-benzyloxyethyl)phenyl 4,6-O-benzylidene-2-O-(5-O-benzoyl-2,3-O-benzylidene-β-D-apiofuranosyl)-3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)benzyl]-β-D-glucopyranoside (**20e**), 4-(2-benzyloxyethyl)phenyl 4,6-O-benzylidene-2-O-[2,3-O-benzylidene-5-O-(3-methylbutyryl)-β-D-apiofuranosyl]-3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)benzyl]-β-D-glucopyranoside (**20f**), 4-(2-benzyloxyethyl)phenyl 4,6-O-benzylidene-2-O-[2,3-O-benzylidene-5-O-(4-benzyloxybenzoyl)-β-D-apiofuranosyl]-3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)benzyl]-*

*β-D-glucopyranoside (**20g**), 4-(2-benzyloxyethyl)phenyl 4,6-O-benzylidene-2-O-[2,3-O-benzylidene-5-O-(4-nitrobenzoyl)-β-D-apiofuranosyl]-3-O-[4-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)benzyl]-β-D-glucopyranoside (**20h**), **M-3**.* A suspension of fluorous acceptors **M-1** (**14a**; 26 mg, 29.2 μmol and **14b**; 30 mg, 29.2 μmol), acylated donors **M-2** (**19a**; 11 mg, 23.3 μmol, **19b**; 11 mg, 23.3 μmol, **19c**; 12 mg, 23.3 μmol, and **19d**; 14 mg, 23.3 μmol), and MS-4 Å (280 mg) in dry CH_2Cl_2 (12 mL) was stirred for 30 min at room temperature under argon. Trimethylsilyl trifluoromethane sulfonate (2 μL, 11.7 μmol) was then added to the suspension at −20 °C. After stirring for 1 h at the same temperature, the reaction mixture was quenched with an excess amount of triethylamine and filtered through Celite and the filtrate was concentrated. The residue was loaded onto a fluorous reverse-phase silica gel (Fluoro*Flash*®) column and the column was eluted successively with 70% aq MeOH and EtOAc. The EtOAc fraction was concentrated to give **M-3** (80.6 mg).

*4.4.2. Semi-preparative HPLC separation of the mixture of eight disaccharides (**M-3**).* **M-3** (80.6 mg) was dissolved in 90% aq CH_3CN solution (3.0 mL). This solution (3.0 mL) was injected into a serially connected Fluophase® RP (21.2×250 mm) and Inertsil® ODS-3 (21.2×250 mm) columns. The column was eluted over 120 min with a liner gradient from 90% CH_3CN/H_2O to 100% CH_3CN. The flow rate was 19 mL/min. The desired eight disaccharides were obtained. Compound **20a**: 8.4 mg (t_R=55.4 min). Compound **20b**: 8.5 mg (t_R=59.2 min). Compound **20c**: 9.5 mg (t_R=65.4 min). Compound **20d**: 8.8 mg (t_R=48.9 min). Compound **20e**: 10.6 mg (t_R=79.4 min). Compound **20f**: 8.6 mg (t_R=84.2 min). **20g**: 8.0 mg (t_R=88.8 min). Compound **20h**: 9.1 mg (t_R=71.5 min).

Compound **20a**: Mp 152.2–156.1 °C (colorless needles, hexane/EtOAc); R_f=0.59 (hexane/EtOAc=2:1 v/v); $[\alpha]_D^{25}$ −28.3 (*c* 1.0, $CHCl_3$); IR (KBr, disk): *ν* 1723 cm^{-1} (C=O); ^1H NMR (250 MHz, $CDCl_3$): *δ* 7.99–7.96 (2H, m, Ph*H*), 7.60–7.27 (20H, m, Ph*H*), 7.07 (2H, d, *J*=8.0 Hz, $-C_6H_4-$), 6.88, 6.80 (4H, each d, *J*=9.2 Hz, $-C_6H_4-$), 6.00, 5.58 (2H each s, PhC*H*×2), 5.78 (1H, s, H-1$_{api}$), 4.95 (2H, s, PhCH_2), 4.92, 4.75 (2H, each d, *J*=11.3 Hz, PhCH_2), 4.82 (1H, d, $J_{1,2}$=7.6 Hz, H-1$_{glc}$), 4.59, 4.49 (2H, each d, *J*=11.9 Hz, H-5$_{api}$), 4.55 (1H, s, H-2$_{api}$), 4.34 (1H, dd, $J_{4,3}$=10.5 Hz, $J_{4,5}$=4.9 Hz, H-4$_{glc}$), 4.24, 4.20 (2H, each d, *J*=10.2 Hz, H-4$_{api}$), 3.95 (1H, dd, $J_{2,1}$=7.6 Hz, $J_{2,3}$=8.6 Hz, H-2$_{glc}$), 3.84–3.74 (3H, m, H-3$_{glc}$, H-6$_{glc}$, H-6′$_{glc}$), 3.45 (1H, ddd, $J_{5,4}$=4.9 Hz, $J_{5,6}$=9.2 Hz, $J_{5,6'}$=9.2 Hz, H-5$_{glc}$), 2.61 (2H, t, *J*=7.6 Hz, CH_2CH$_2$CH$_2$C$_6$F$_{13}$), 2.18–1.86 (4H, m, CH$_2$CH_2CH$_2$C$_6$F$_{13}$); ^{13}C NMR (63 MHz, $CDCl_3$): *δ* 165.9, 154.6, 151.0140.3, 137.2, 137.1, 136.1, 135.9, 133.3, 129.9, 129.7, 129.6, 129.0, 128.8, 128.55, 128.46, 128.37, 128.28, 127.9, 127.4, 127.2, 126.0, 117.8, 115.8, 107.3, 106.5, 101.3, 100.8, 90.2, 87.2, 81.6, 80.9, 76.2, 74.5, 73.3, 70.5, 68.7, 66.2, 34.8, 30.4 (t, J_{CF}=22.2 Hz), 21.8; ESI-HRMS calcd for $C_{61}H_{53}F_{13}O_{12}Na$ *m/z* $[M+Na]^+$: 1247.3227. Found: 1247.3233.

Compound **20b**: Colorless amorphous solids; R_f=0.65 (hexane/EtOAc=2:1 v/v); $[\alpha]_D^{25}$ −41.3 (*c* 1.0, $CHCl_3$); IR (KBr, disk): *ν* 1737 cm^{-1} (C=O); ^1H NMR (250 MHz, $CDCl_3$): *δ* 7.53–7.26 (17H, m, Ph*H*), 7.07 (2H, d, *J*=8.0 Hz, $-C_6H_4-$), 6.94, 6.89 (4H, each d, *J*=8.9 Hz, $-C_6H_4-$), 5.92, 5.58 (2H, each s, PhC*H*×2), 5.76 (1H, s, H-1$_{api}$), 5.02 (2H, s, PhCH_2), 4.92, 4.75 (2H, each d, *J*=11.2 Hz, PhCH_2), 4.89 (1H, d, $J_{1,2}$=7.5 Hz, H-1$_{glc}$), 4.41 (1H, s, H-2$_{api}$), 4.35 (1H, dd, $J_{4,3}$=10.5 Hz, $J_{4,5}$=5.0 Hz, H-4$_{glc}$), 4.33, 4.27 (2H, each d, *J*=11.9 Hz, H-5$_{api}$), 4.12 (2H, s, H-4$_{api}$), 3.95 (1H, dd, $J_{2,1}$=7.5 Hz, $J_{2,3}$=8.4 Hz, H-2$_{glc}$), 3.87–3.74 (3H, m, H-3$_{glc}$, H-6$_{glc}$, H-6′$_{glc}$), 3.48 (1H, ddd, $J_{5,4}$=5.0 Hz, $J_{5,6}$=9.0 Hz, $J_{5,6'}$=9.0 Hz, H-5$_{glc}$), 2.64 (2H, t, *J*=7.6 Hz, CH_2CH$_2$CH$_2$C$_6$F$_{13}$), 2.15 (2H, d, *J*=6.5 Hz, COCH_2CH(CH$_3$)$_2$), 2.17–1.82 (5H, m, CH_2CH$_2$CH$_2$C$_6$F$_{13}$ and COCH$_2$C*H*(CH$_3$)$_2$), 0.92 (6H, d, *J*=6.5 Hz, CH$_3$×2); ^{13}C NMR (63 MHz, $CDCl_3$): *δ* 172.5, 154.7, 151.1, 140.3, 137.2, 137.1, 136.2, 135.9, 129.9, 128.8, 128.6, 128.4, 128.3, 128.0, 127.4, 127.1, 126.0, 118.1, 115.8, 107.2, 106.4, 90.2, 87.2, 81.6, 81.1, 75.9, 74.5, 73.3, 70.6, 68.7, 66.2, 64.3, 43.1, 34.8, 30.4 (t, J_{CF}=22.2 Hz), 25.6, 22.4, 21.8; ESI-HRMS calcd for $C_{59}H_{57}F_{13}O_{12}Na$ *m/z* $[M+Na]^+$: 1227.3540. Found: 1227.3541.

Compound **20c**: Mp 149.8–151.9 °C (colorless needles, hexane/EtOAc); R_f=0.60 (hexane/EtOAc=2:1 v/v); $[\alpha]_D^{12}$ −26.2 (*c* 0.97, $CHCl_3$); IR (KBr, disk): *ν* 1659 cm^{-1} (C=O); ^1H NMR (250 MHz, $CDCl_3$): *δ* 7.92, 6.94 (4H each d, *J*=8.9 Hz, $-C_6H_4-$), 7.55–7.32 (20H, m, Ph*H*), 7.28, 7.07 (4H, each d, *J*=8.0 Hz, $-C_6H_4-$), 6.88, 6.79 (4H, each d, *J*=9.2 Hz, $-C_6H_4-$), 5.98, 5.58 (2H, each s, PhC*H*×2), 5.78 (1H, s, H-1$_{api}$), 5.09, 4.94 (4H, each s, PhCH_2×2), 4.92, 4.75 (2H, each d, *J*=11.3 Hz, PhCH_2), 4.81 (1H, d, $J_{1,2}$=7.6 Hz, H-1$_{glc}$), 4.56, 4.46 (2H, each d, *J*=11.8 Hz, H-5$_{api}$), 4.54 (1H, s, H-2$_{api}$), 4.35 (1H, dd, $J_{4,3}$=10.5 Hz, $J_{4,5}$=4.9 Hz, H-4$_{glc}$), 4.24, 4.19 (2H, each d, *J*=10.2 Hz, H-4$_{api}$), 3.95 (1H, dd, $J_{2,1}$=7.6 Hz, $J_{2,3}$=8.4 Hz, H-2$_{glc}$), 3.84–3.73 (3H, m, H-3$_{glc}$, H-6$_{glc}$, H-6′$_{glc}$), 3.44 (1H, ddd, $J_{5,4}$=4.9 Hz, $J_{5,6}$=9.3 Hz, $J_{5,6'}$=9.0 Hz, H-5$_{glc}$), 2.61 (2H, t, *J*=7.6 Hz, CH_2CH$_2$CH$_2$C$_6$F$_{13}$), 2.14–1.80 (4H, m, CH_2CH$_2$CH$_2$C$_6$F$_{13}$); ^{13}C NMR (63 MHz, $CDCl_3$): *δ* 165.6, 162.8, 154.6, 151.1, 140.3, 137.2, 137.1, 136.1, 135.9, 131.8, 129.9, 129.0, 128.8, 128.7, 128.5, 128.4, 128.3, 127.9, 127.4, 127.2, 126.0, 122.1, 117.8, 115.8, 114.6, 107.3, 106.4, 101.3, 100.9, 90.3, 87.3, 81.6, 81.0, 76.2, 74.6, 73.2, 70.5, 70.2, 68.7, 66.2, 64.4, 34.7, 30.4 (t, J_{CF}=22.6 Hz), 21.8; ESI-HRMS calcd for $C_{68}H_{59}F_{13}O_{12}Na$ *m/z* $[M+Na]^+$: 1353.3646. Found: 1353.3600.

Compound **20d**: Mp 160.5–164.9 °C (light yellow needles, hexane/EtOAc); R_f=0.6 (hexane/EtOAc=2:1 v/v); $[\alpha]_D^{11}$ −29.05 (*c* 1.0, $CHCl_3$); IR (KBr, disk): *ν* 1719 cm^{-1} (C=O), 1529 cm^{-1} (N=O); ^1H NMR (250 MHz, $CDCl_3$): *δ* 8.19, 8.07 (4H each d, *J*=8.9 Hz, $-C_6H_4-$), 7.54–7.32 (15H, m, Ph*H*), 7.28, 7.07 (4H, each d, *J*=8.0 Hz, $-C_6H_4-$), 6.87, 6.78 (4H, each d, *J*=9.3 Hz, $-C_6H_4-$), 5.96, 5.58 (2H, each s, PhC*H*×2), 5.82 (1H, s, H-1$_{api}$), 4.95 (2H, s, PhCH_2), 4.93, 4.75 (2H, each d, *J*=11.2 Hz, PhCH_2), 4.85 (1H, d, $J_{1,2}$=7.6 Hz, H-1$_{glc}$), 4.66, 4.51 (2H, each d, *J*=11.9 Hz, H-5$_{api}$), 4.53 (1H, s, H-2$_{api}$), 4.36 (1H, dd, $J_{4,3}$=10.5 Hz, $J_{4,5}$=4.9 Hz, H-4$_{glc}$), 4.27, 4.21 (2H, each d, *J*=10.2 Hz, H-4$_{api}$), 3.98 (1H, dd, $J_{2,1}$=7.6 Hz, $J_{2,3}$=8.3 Hz, H-2$_{glc}$), 3.88–3.75 (3H, m, H-3$_{glc}$, H-6$_{glc}$, H-6′$_{glc}$), 3.48 (1H, ddd, $J_{5,4}$=4.9 Hz, $J_{5,6}$=9.0 Hz, $J_{5,6'}$=8.8 Hz, H-5$_{glc}$), 2.63 (2H, t, *J*=7.6 Hz, CH_2CH$_2$CH$_2$C$_6$F$_{13}$), 2.15–1.82 (4H, m, CH_2CH$_2$CH$_2$C$_6$F$_{13}$); ^{13}C NMR (63 MHz, $CDCl_3$): *δ* 165.5, 162.7, 154.5, 150.9, 140.1, 137.1, 137.0, 136.0, 135.7, 131.6, 129.7, 128.9, 128.7, 128.5, 128.4, 128.2, 128.12, 128.10,127.8, 127.3, 127.0, 125.9, 122.0, 117.7, 115.6, 114.4, 107.2, 106.3, 101.1, 100.7, 90.1, 87.1, 81.5, 80.9, 76.1, 74.4, 73.1, 70.4, 70.0, 68.6, 66.0, 64.2, 34.6, 30.2 (t, J_{CF}=22.7 Hz), 21.6; ESI-HRMS calcd for $C_{61}H_{52}F_{13}NO_{14}Na$ *m/z* $[M+Na]^+$: 1292.3078. Found: 1292.3067.

Compound **20e**: Colorless amorphous solids; R_f=0.56 (hexane/EtOAc=2:1 v/v); $[\alpha]_D^{18}$ −26.2 (*c* 0.97, $CHCl_3$); IR (KBr, disk): *ν* 1722 cm^{-1} (C=O); ^1H NMR (250 MHz, $CDCl_3$): *δ* 7.98–7.94 (2H, m, Ph*H*), 7.59–7.27 (20H, m, Ph*H*), 7.07 (2H, d, *J*=7.9 Hz, $-C_6H_4-$), 7.05, 6.85 (4H, each d, *J*=8.7 Hz, $-C_6H_4-$), 5.99, 5.58 (2H each s, PhC*H*×2), 5.78 (1H, s, H-1$_{api}$), 4.92, 4.76 (2H, each d, *J*=11.2 Hz, PhCH_2), 4.90 (1H, d, $J_{1,2}$=7.6 Hz, H-1$_{glc}$), 4.55, 4.46 (2H, each d, *J*=11.9 Hz, H-5$_{api}$), 4.54 (1H, s, H-2$_{api}$), 4.50 (2H, s, PhCH_2), 4.35 (1H, dd, $J_{4,3}$=10.5 Hz, $J_{4,5}$=4.9 Hz, H-4$_{glc}$), 4.21 (2H, s, H-4$_{api}$), 3.97 (1H, dd, $J_{2,1}$=7.6 Hz, $J_{2,3}$=8.5 Hz, H-2$_{glc}$), 3.85–3.74 (3H, m, H-3$_{glc}$, H-6$_{glc}$, H-6′$_{glc}$), 3.61 (2H, t, *J*=7.1 Hz, CH$_2$CH_2OBn), 3.49 (1H, ddd, $J_{5,4}$=4.9 Hz, $J_{5,6}$=9.2 Hz, $J_{5,6'}$=8.8 Hz, H-5$_{glc}$), 2.81 (2H, t, *J*=7.1 Hz, CH_2CH$_2$OBn), 2.61 (2H, t, *J*=7.6 Hz, CH_2CH$_2$CH$_2$C$_8$F$_{17}$), 2.14–1.80 (4H, m, CH$_2$CH_2CH_2C$_8$F$_{17}$); ^{13}C NMR (63 MHz, $CDCl_3$): *δ* 165.9, 155.3, 140.3, 138.4, 137.2, 136.1, 135.9, 133.5, 133.3, 130.0, 129.9, 129.7, 129.6, 129.1, 128.8, 128.4, 128.38, 128.36, 128.29, 127.59, 127.54, 127.2, 126.0, 116.3, 107.3, 106.5, 101.3, 100.0, 90.2, 87.2, 81.6, 80.9, 76.1, 74.5, 73.2, 73.0, 71.3, 68.7, 66.2, 64.7, 35.5, 34.8, 30.7 (t, J_{CF}=22.4 Hz), 21.8; ESI-HRMS calcd for $C_{65}H_{57}F_{17}O_{12}Na$ *m/z* $[M+Na]^+$: 1375.3476. Found: 1375.3519.

Compound **20f**: Colorless amorphous solids; R_f=0.62 (hexane/EtOAc=2:1 v/v); $[\alpha]_D^{19}$ −44.51 (*c* 1.02, $CHCl_3$); IR (KBr, disk): *ν* 1739 cm^{-1} (C=O); ^1H NMR (250 MHz, $CDCl_3$): *δ* 7.53–7.26 (17H, m, Ph*H*), 7.15, 6.90 (4H, each d, *J*=8.6 Hz, $-C_6H_4-$), 7.07 (2H, d,

J=8.0 Hz, −C$_6H_4$−), 5.92, 5.58 (2H, each s, PhCH×2), 5.76 (1H, s, H-1$_{api}$), 4.97 (1H, d, $J_{1,2}$=7.6 Hz, H-1$_{glc}$), 4.92, 4.75 (2H, each d, J=11.2 Hz, PhCH_2), 4.52 (2H, s, PhCH_2), 4.40 (1H, s, H-2$_{api}$), 4.36 (1H, dd, $J_{4,3}$=10.5 Hz, $J_{4,5}$=5.0 Hz, H-4$_{glc}$), 4.30, 4.25 (2H, each d, J=12.0 Hz, H-5$_{api}$), 4.12 (2H, s, H-4$_{api}$), 3.98 (1H, dd, $J_{2,1}$=7.6 Hz, $J_{2,3}$=8.2 Hz, H-2$_{glc}$), 3.88−3.75 (3H, m, H-3$_{glc}$, H-6$_{glc}$, H-6′$_{glc}$), 3.66 (2H, t, J=7.1 Hz, CH$_2$CH_2OBn), 3.52 (1H, ddd, $J_{5,4}$=5.0 Hz, $J_{5,6}$=9.4 Hz, $J_{5,6'}$=8.8 Hz, H-5$_{glc}$), 2.88 (2H, t, J=7.1 Hz, CH_2CH$_2$OBn), 2.64 (2H, t, J=7.6 Hz, CH_2CH$_2$CH$_2$C$_8$F$_{17}$), 2.12 (2H, d, J=6.5 Hz, COCH_2CH(CH$_3$)$_2$), 2.16−1.84 (5H, m, CH_2CH$_2$CH$_2$C$_8$F$_{17}$ and COCH$_2$CH(CH$_3$)$_2$), 0.90 (6H, d, J=6.5 Hz, CH$_3$×2); ^{13}C NMR (63 MHz, CDCl$_3$): δ 172.5, 155.4, 140.3, 138.4, 137.2, 136.2, 135.9, 133.6, 130.1, 129.9, 129.0, 128.8, 128.4, 128.3, 127.6, 127.5, 127.1, 126.0, 116.5, 107.2, 106.4, 101.3, 100.1, 90.2, 87.2, 81.6, 81.1, 75.9, 74.6, 73.2, 73.0, 71.3, 68.7, 66.2, 64.2, 43.1, 35.5, 34.8, 30.4 (t, J_{CF}=22.9 Hz), 25.5, 22.4, 21.8; ESI-HRMS calcd for C$_{63}$H$_{61}$F$_{17}$O$_{12}$Na m/z [M+Na]$^+$: 1355.3789. Found: 1355.3788.

Compound **20g**: Mp 129.8−131.9 °C (colorless needles, hexane/EtOAc); R_f=0.53 (hexane/EtOAc=2:1 v/v); $[\alpha]_D^9$ −26.2 (c 0.97, CHCl$_3$); IR (KBr, disk): ν 1717 cm^{-1} (C=O); ^{1}H NMR (250 MHz, CDCl$_3$): δ 7.90, 6.94 (4H each d, J=9.0 Hz, −C$_6H_4$−), 7.54−7.27 (22H, m, PhH), 7.07 (2H, d, J=8.1 Hz, −C$_6H_4$−), 7.05, 6.85 (4H, each d, J=8.6 Hz, −C$_6H_4$−), 5.98, 5.58 (2H, each s, PhCH×2), 5.77 (1H, s, H-1$_{api}$), 5.11, 4.49 (4H, each s, PhCH_2×2), 4.92, 4.75 (2H, each d, J=11.4 Hz, PhCH_2), 4.89 (1H, d, $J_{1,2}$=7.6 Hz, H-1$_{glc}$), 4.54 (1H, s, H-2$_{api}$), 4.52, 4.43 (2H, each d, J=11.9 Hz, H-5$_{api}$), 4.35 (1H, dd, $J_{4,3}$=10.5 Hz, $J_{4,5}$=4.9 Hz, H-4$_{glc}$), 4.20 (2H, s, H-4$_{api}$), 3.97 (1H, dd, $J_{2,1}$=7.6 Hz, $J_{2,3}$=8.5 Hz, H-2$_{glc}$), 3.86−3.72 (3H, m, H-3$_{glc}$, H-6$_{glc}$, H-6′$_{glc}$), 3.61 (2H, t, J=7.1 Hz, CH$_2$CH_2OBn), 3.50 (1H, ddd, $J_{5,4}$=4.9 Hz, $J_{5,6}$=9.2 Hz, $J_{5,6'}$=8.7 Hz, H-5$_{glc}$), 2.82 (2H, t, J=7.1 Hz, CH_2CH$_2$OBn), 2.61 (2H, t, J=7.6 Hz, CH_2CH$_2$CH$_2$C$_8$F$_{17}$), 2.14−1.80 (4H, m, CH_2CH$_2$CH$_2$C$_8$F$_{17}$); ^{13}C NMR (63 MHz, CDCl$_3$): δ 165.6, 162.8, 155.3, 140.3, 138.4, 137.2, 136.3, 136.2, 135.9, 133.5, 131.8, 130.0, 129.9, 129.0, 128.8, 128.7, 128.4, 128.3, 127.58, 127.52, 127.4, 127.2, 126.0, 122.1, 118.7, 116.3, 115.8, 114.6, 107.3, 106.5, 101.3, 100.0, 90.3, 87.2, 81.6, 81.0, 76.2, 74.6, 73.2, 72.9, 71.3, 70.2, 68.7, 66.2, 64.3, 35.5, 34.6, 30.4 (t, J_{CF}=22.2 Hz), 21.8; ESI-HRMS calcd for C$_{72}$H$_{63}$F$_{17}$O$_{13}$Na m/z [M+Na]$^+$: 1481.3895. Found: 1481.3886.

Compound **20h**: Mp 145.1−149.8 °C (colorless needles, hexane/EtOAc); R_f=0.53 (hexane/EtOAc=2:1 v/v); $[\alpha]_D^{11}$ −32.2 (c 0.99, CHCl$_3$); IR (KBr, disk): ν 1730 cm^{-1} (C=O), 1531 cm^{-1} (N=O); ^{1}H NMR (250 MHz, CDCl$_3$): δ 8.19, 8.05 (4H each d, J=8.9 Hz, −C$_6H_4$−), 7.53−7.27 (17H, m, PhH), 7.07 (2H, d, J=8.0 Hz, −C$_6H_4$−), 7.05, 6.85 (4H, each d, J=8.6 Hz, −C$_6H_4$−), 5.96, 5.59 (2H, each s, PhCH×2), 5.82 (1H, s, H-1$_{api}$), 4.92, 4.75 (2H, each d, J=11.2 Hz, PhCH_2), 4.92 (1H, d, $J_{1,2}$=7.6 Hz, H-1$_{glc}$), 4.63, 4.50 (2H, each d, J=11.8 Hz, H-5$_{api}$), 4.53 (1H, s, H-2$_{api}$), 4.49 (2H, s, PhCH_2), 4.36 (1H, dd, $J_{4,3}$=10.4 Hz, $J_{4,5}$=4.9 Hz, H-4$_{glc}$), 4.27, 4.22 (2H, each d, J=10.2 Hz, H-4$_{api}$), 4.01 (1H, dd, $J_{2,1}$=7.6 Hz, $J_{2,3}$=8.2 Hz, H-2$_{glc}$), 3.89−3.76 (3H, m, H-3$_{glc}$, H-6$_{glc}$, H-6′$_{glc}$), 3.61 (2H, t, J=7.0 Hz, CH$_2$CH_2OBn), 3.51 (1H, ddd, $J_{5,4}$=4.9 Hz, $J_{5,6}$=9.3 Hz, $J_{5,6'}$=8.6 Hz, H-5$_{glc}$), 2.80 (2H, t, J=7.0 Hz, CH_2CH$_2$OBn), 2.62 (2H, t, J=7.6 Hz, CH_2CH$_2$CH$_2$C$_8$F$_{17}$), 2.15−1.80 (4H, m, CH_2CH$_2$CH$_2$C$_8$F$_{17}$); ^{13}C NMR (63 MHz, CDCl$_3$): δ 164.0, 155.2, 150.7, 140.3, 138.4, 137.2, 137.0, 135.9, 135.8, 134.7, 133.6, 130.7, 130.0, 129.1, 128.8, 128.42, 128.38, 128.34, 128.29, 127.5, 127.1, 126.0, 123.5, 116.2, 107.1, 106.5, 101.3, 99.9, 90.0, 87.2, 81.6, 81.1, 75.7, 74.6, 73.1, 72.9, 71.1, 68.7, 66.3, 65.2, 35.4, 34.8, 30.4 (t, J_{CF}=22.6 Hz), 21.8; ESI-HRMS calcd for C$_{65}$H$_{56}$F$_{17}$NO$_{14}$Na m/z [M+Na]$^+$: 1420.3327. Found: 1420.3343.

*4.4.3. Seguinoside C (**1a**).* To a solution of disaccharide **20a** (91 mg, 74.3 μmol) in THF/MeOH (60 mL, 1:3 v/v) was added palladium hydroxide (5 mg, 20 wt % on carbon). The suspension was stirred for 12 h at room temperature under hydrogen gas. The mixture was filtered through Celite. The filtrate was concentrated, and the residue was loaded onto a reverse-phase silica gel (Cosmosil® 75C$_{18}$−OPN, 3 g) column and the column was eluted successively with 20%, and 40% aq MeOH. The 40% aq MeOH fraction was concentrated, and the crude product was purified by recrystallization to give **1a** (30.3 mg, 80% yield) as colorless prisms: mp 233.6−237.4 °C (MeOH); R_f=0.19 (CH$_3$Cl/MeOH=4:1 v/v); $[\alpha]_D^{24}$ −87.8 (c 0.59, pyridine); IR (KBr, disk): ν 3444, 3353, 3280 cm^{-1} (OH), 1710 cm^{-1} (C=O); ^{1}H NMR (600 MHz, CD$_3$OD): δ 7.95 (2H, dd, J=1.2 Hz, J=8.4 Hz, H-2‴ and H-6‴), 7.58 (1H, t, J=7.4 Hz, H-4‴), 7.42 (2H, t, J=8.3 Hz, H-3‴ and H-5‴), 6.84 (2H, d, J=8.9 Hz, H-2 and H-6), 6.53 (2H, d, J=8.9 Hz, H-3 and H-5), 5.50 (1H, d, $J_{1,2}$=1.2 Hz, H-1$_{api}$), 4.79 (1H, d, $J_{1,2}$=7.7 Hz, H-1$_{glc}$), 4.39, 4.33 (2H, each d, J=11.3 Hz, H-5$_{api}$), 4.33, 3.91 (2H, each d, J=9.6 Hz, H-4$_{api}$), 4.01 (1H, d, $J_{2,1}$=1.2 Hz, H-2$_{api}$), 3.86 (1H, dd, $J_{6,5}$=2.1 Hz, $J_{6,6'}$=11.9 Hz, H-6′$_{glc}$), 3.66 (1H, dd, $J_{6',5}$=5.2 Hz, $J_{6',6}$=11.9 Hz, H-6′$_{glc}$), 3.62 (1H, dd, $J_{2,1}$=7.7 Hz, $J_{2,3}$=9.3 Hz, H-2$_{glc}$), 3.57 (1H, dd, $J_{3,2}$=9.3 Hz, $J_{3,4}$=8.2 Hz, H-3$_{glc}$), 3.38−3.34 (2H, m, H-4$_{glc}$ and H-5$_{glc}$); ^{13}C NMR (151 MHz, CD$_3$OD): δ 167.7, 153.6, 152.1, 134.3, 131.1, 130.7, 129.5, 118.7, 116.7, 110.5, 101.8, 79.2, 78.8, 78.7, 78.4, 78.0, 75.4, 71.6, 68.4, 62.5; ESI-HRMS calcd for C$_{24}$H$_{28}$O$_{12}$Na m/z [M+Na]$^+$: 531.1478. Found: 531.1449.

*4.4.4. 4-Hydroxyphenyl 2-O-[5-O-(3-methylbutyryl)-β-D-apiofuranosyl]-β-D-glucopyranoside (**1b**).* To a solution of disaccharide **20b** (95 mg, 78.8 μmol) in THF/MeOH (60 mL, 1:3 v/v) was added palladium hydroxide (5 mg, 20 wt % on carbon). The suspension was stirred for 12 h at room temperature under hydrogen gas. The mixture was filtered through Celite. The filtrate was concentrated, and the residue was loaded onto a reverse-phase silica gel (Cosmosil® 75C$_{18}$-OPN, 3 g) column and the column was eluted successively with 20%, and 40% aq MeOH. The 40% aq MeOH fraction was concentrated to give **1b** (38.5 mg, quant.) with sufficient purity. The product **1b** was further purified by semi-preparative HPLC with an Inertsil® ODS-3 column (20×250 mm, isocratic elution; 15% aq CH$_3$CN) to give **1b** (26.5 mg, 69% yield) as a colorless syrup: R_f=0.15 (CH$_3$Cl/MeOH=4:1 v/v); $[\alpha]_D^{24}$ −88.7 (c 1.1, MeOH); IR (KBr, disk): ν 3392 cm^{-1} (OH), 1715 cm^{-1} (C=O); ^{1}H NMR (600 MHz, CD$_3$OD): δ 6.89 (2H, d, J=8.9 Hz, H-3 and H-5), 6.68 (2H, d, J=8.9 Hz, H-2 and H-6), 5.46 (1H, d, $J_{1,2}$=1.4 Hz, H-1$_{api}$), 4.81 (1H, d, $J_{1,2}$=7.4 Hz, H-1$_{glc}$), 4.16, 3.80 (2H, each d, J=9.6 Hz, H-4$_{api}$), 4.14, 4.10 (2H, each d, J=11.3 Hz, H-5$_{api}$), 3.90 (1H, d, $J_{2,1}$=1.4 Hz, H-2$_{api}$), 3.86 (1H, dd, $J_{6,5}$=2.1 Hz, $J_{6,6'}$=12.4 Hz, H-6$_{glc}$), 3.67 (1H, dd, $J_{6',5}$=5.3 Hz, $J_{6',6}$=12.4 Hz, H-6′$_{glc}$), 3.60 (1H, dd, $J_{2,1}$=7.4 Hz, $J_{2,3}$=9.3 Hz, H-2$_{glc}$), 3.56 (1H, dd, $J_{3,2}$=9.3 Hz, $J_{3,4}$=8.2 Hz, H-3$_{glc}$), 3.38−3.35 (2H, m, H-4$_{glc}$ and H-5$_{glc}$), 2.09 (2H, d, J=6.7 Hz, H-2‴), 1.97 (1H, m, H-3‴), 0.88 (6H, d, J=6.7 Hz, H-5‴); ^{13}C NMR (151 MHz, CD$_3$OD): δ 174.5, 153.7, 152.1, 118.9, 116.7, 110.4, 101.8, 79.0, 78.74, 78.67, 78.4, 77.9, 75.3, 71.5, 67.7, 62.5, 43.9, 26.7, 22.70, 22.67; ESI-HRMS calcd for C$_{22}$H$_{32}$O$_{12}$Na m/z [M+Na]$^+$: 511.1791. Found: 511.1793.

*4.4.5. Seguinoside D (**1c**).* To a solution of disaccharide **20c** (111 mg, 83.4 μmol) in THF/MeOH (60 mL, 1:3 v/v) was added palladium hydroxide (7 mg, 20 wt % on carbon). The suspension was stirred for 12 h at room temperature under hydrogen gas. The mixture was filtered through Celite. The filtrate was concentrated, and the residue was loaded onto a reverse-phase silica gel (Cosmosil® 75C$_{18}$−OPN, 3 g) column and the column was eluted successively with 20%, and 40% aq MeOH. The 40% aq MeOH fraction was concentrated to give **1c** (43.6 mg, quant.) with sufficient purity. To compare the optical rotation of the synthetic product with that of the natural product, the product **1b** was further purified by semi-preparative HPLC with an Inertsil® ODS-3 column (20×250 mm, isocratic elution; 25% aq MeOH) to give **1b** (34.5 mg, 79% yield) as colorless amorphous powder: R_f=0.13 (CH$_3$Cl/MeOH=4:1 v/v); $[\alpha]_D^{23}$ −67.4 (c 0.43, MeOH); IR (KBr, disk): ν 3363 cm^{-1} (OH), 1699 cm^{-1} (C=O); ^{1}H NMR (600 MHz, CD$_3$OD): δ 7.82 (2H, d, J=8.8 Hz, H-2‴ and H-6‴), 6.85 (2H, d, J=8.9 Hz, H-2 and H-6), 6.78 (2H, d, J=8.9 Hz, H-3 and H-5), 6.56 (2H, d, J=8.9 Hz, H-3‴ and H-5‴), 5.50

(1H, d, $J_{1,2}$=1.0 Hz, H-1$_{api}$), 4.79 (1H, d, $J_{1,2}$=7.6 Hz, H-1$_{glc}$), 4.34, 4.27 (2H, each d, J=11.3 Hz, H-5$_{api}$), 4.31, 3.90 (2H, each d, J=9.8 Hz, H-4$_{api}$), 4.01 (1H, d, $J_{2,1}$=0.9 Hz, H-2$_{api}$), 3.86 (1H, dd, $J_{6,5}$=1.9 Hz, $J_{6,6'}$=12.4 Hz, H-6′$_{glc}$), 3.67 (1H, dd, $J_{6',5}$=5.2 Hz, $J_{6',6}$=12.2 Hz, H-6′$_{glc}$), 3.62 (1H, dd, $J_{2,1}$=7.6 Hz, $J_{2,3}$=9.1 Hz, H-2$_{glc}$), 3.57 (1H, dd, $J_{3,2}$=9.1 Hz, $J_{3,4}$=8.2 Hz, H-3$_{glc}$), 3.39–3.34 (2H, m, H-4$_{glc}$ and H-5$_{glc}$); ^{13}C NMR (151 MHz, CD_3OD): δ 167.8, 163.6, 153.5, 152.1, 133.0, 121.9, 118.8, 116.7, 116.1, 110.5, 101.8, 79.2, 78.7, 78.6, 78.4, 77.9, 75.4, 71.5, 68.0, 62.5; ESI-HRMS calcd for $C_{24}H_{28}O_{13}Na$ m/z [M+Na]$^+$: 547.1428. Found: 547.1475.

*4.4.6. 4-Hydroxyphenyl 2-O-[5-O-(4-aminobenzoyl)-β-D-apiofuranosyl]-β-D-glucopyranoside (**1d**).* To a solution of disaccharide **20d** (110 mg, 86.6 μmol) in EtOAc/MeOH (27 mL, 1:2 v/v) was added 0.1 M aq HCl solution (0.78 mL) and palladium hydroxide (8 mg, 20 wt % on carbon). The suspension was stirred for 19 h at room temperature under hydrogen gas. The mixture was filtered through Celite, and the filtrate was concentrated. The residue was diluted with H_2O, and then the solution was loaded onto a reverse-phase silica gel (Cosmosil® 75C_{18}–OPN, 3 g) column and the column was eluted successively with 10%, and 20% aq MeOH. The 20% aq MeOH fraction was concentrated to give **1d** (25.0 mg, 55% yield) with sufficient purity. The product was further purified by semi-preparative HPLC with an Inertsil® ODS-3 column (20×250 mm, isocratic elution; 25% aq MeOH) to give **1d** (17.8 mg, 39% yield) as colorless amorphous powder; R_f=0.58 (CH_3Cl/MeOH/H_2O=10:10:3 v/v/v); $[\alpha]_D^{24}$ −64.7 (*c* 0.62, MeOH); IR (KBr, disk): ν 3367 cm^{-1} (OH), 1696 cm^{-1} (C=O), 1603 cm^{-1} (NH); ^{1}H NMR (600 MHz, CD_3OD): δ 7.70 (2H, d, J=8.8 Hz, H-2‴ and H-6‴), 6.86 (2H, d, J=8.9 Hz, H-3 and H-5), 6.58 (2H, d, J=8.8 Hz, H-3‴ and H-5‴), 6.56 (2H, d, J=8.9 Hz, H-2 and H-6), 5.49 (1H, d, $J_{1,2}$=1.1 Hz, H-1$_{api}$), 4.78 (1H, d, $J_{1,2}$=7.6 Hz, H-1$_{glc}$), 4.31, 4.23 (2H, each d, J=11.3 Hz, H-5$_{api}$), 4.30, 3.89 (2H, each d, J=9.8 Hz, H-4$_{api}$), 4.00 (1H, d, $J_{2,1}$=1.0 Hz, H-2$_{api}$), 3.86 (1H, dd, $J_{6,5}$=1.9 Hz, $J_{6,6'}$=11.9 Hz, H-6′$_{glc}$), 3.67 (1H, dd, $J_{6',5}$=5.2 Hz, $J_{6',6}$=12.0 Hz, H-6′$_{glc}$), 3.61 (1H, dd, $J_{2,1}$=7.6 Hz, $J_{2,3}$=9.3 Hz, H-2$_{glc}$), 3.57 (1H, dd, $J_{3,2}$=9.1 Hz, $J_{3,4}$=8.3 Hz, H-3$_{glc}$), 3.38–3.33 (2H, m, H-4$_{glc}$ and H-5$_{glc}$); ^{13}C NMR (151 MHz, CD_3OD): δ 168.4, 154.8, 153.6, 152.2, 132.7, 118.9, 118.2, 116.7, 114.3, 110.5, 101.9, 79.3, 78.8, 78.7, 78.5, 77.9, 75.4, 71.5, 67.7, 62.5; ESI-HRMS calcd for $C_{24}H_{29}NO_{12}Na$ m/z [M+Na]$^+$: 546.1587. Found: 546.1602.

*4.4.7. Cucurbitoside A (**1e**).* To a solution of disaccharide **20e** (79 mg, 58.4 μmol) in THF/MeOH (60 mL, 1:3 v/v) was added palladium hydroxide (5 mg, 20 wt % on carbon). The suspension was stirred for 20 h at room temperature under hydrogen gas. The mixture was filtered through Celite. The filtrate was concentrated, and the residue was loaded onto a reverse-phase silica gel (Cosmosil® 75C_{18}-OPN, 3 g) column and the column was eluted successively with 20%, and 40% aq MeOH. The 40% aq MeOH fraction was concentrated to give **1e** (28.1 mg, 90% yield) with sufficient purity. To compare the optical rotation of the synthetic product with that of the natural product, the product was further purified by semi-preparative HPLC with an Inertsil® ODS-3 column (20×250 mm, isocratic elution; 35% aq MeOH) to give **1e** (15.7 mg, 50% yield) as colorless amorphous powder: R_f=0.22 (CH_3Cl/MeOH=4:1 v/v); $[\alpha]_D^{28}$ −76.2 (*c* 1.0, MeOH); IR (KBr, disk): ν 3379 cm^{-1} (OH), 1716 cm^{-1} (C=O); ^{1}H NMR (600 MHz, CD_3OD): δ 7.93 (2H, dd, J=1.4 Hz, J=8.4 Hz, H-2‴ and H-6‴), 7.58 (1H, tt, J=1.4 Hz, J=7.4 Hz, H-4‴), 7.41 (2H, dd, J=7.5 Hz, J=8.3 Hz, H-3‴, and H-5‴), 6.93 (2H, d, J=8.8 Hz, H-2 and H-6), 6.89 (2H, d, J=8.8 Hz, H-3 and H-5), 5.51 (1H, d, $J_{1,2}$=1.0 Hz, H-1$_{api}$), 4.91 (1H, $J_{1,2}$=7.7 Hz, H-1$_{glc}$), 4.34, 4.28 (2H, each d, J=11.3 Hz, H-5$_{api}$), 4.33, 3.92 (2H, each d, J=9.8 Hz, H-4$_{api}$), 3.98 (1H, d, $J_{2,1}$=1.0 Hz, H-2$_{api}$), 3.87 (1H, dd, $J_{6,5}$=1.9 Hz, $J_{6,6'}$=12.2 Hz, H-6$_{glc}$), 3.66 (1H, dd, $J_{2,1}$=7.7 Hz, $J_{2,3}$=9.3 Hz, H-2$_{glc}$), 3.66 (1H, dd, $J_{6',5}$=5.2 Hz, $J_{6',6}$=12.2 Hz, H-6′$_{glc}$), 3.60 (2H, t, J=7.2 Hz, H-8), 3.60 (1H, t, $J_{3,2}$=9.3 Hz, $J_{3,4}$=9.8 Hz, H-3$_{glc}$), 3.40–3.37 (2H, m, H-4$_{glc}$, H-5$_{glc}$), 2.63 (2H, dt, J=7.2 Hz, J=3.6 Hz, H-7); ^{13}C NMR (151 MHz, CD_3OD): δ 167.7, 157.3, 134.3, 133.9, 131.1, 130.9, 130.7, 129.5, 117.2, 110.4, 100.7, 79.2, 78.8, 78.6, 78.1, 78.0, 75.4, 71.5, 68.5, 64.3, 62.5, 39.4; ESI-HRMS calcd for $C_{26}H_{32}O_{12}Na$ m/z [M+Na]$^+$: 559.1791. Found: 559.1767.

*4.4.8. Cucurbitoside G (**1f**).* To a solution of disaccharide **20f** (87 mg, 65.3 μmol) in THF/MeOH (60 mL, 1:3 v/v) was added palladium hydroxide (6 mg, 20 wt % on carbon). The suspension was stirred for 12 h at room temperature under hydrogen gas. The mixture was filtered through Celite. The filtrate was concentrated, and the residue was loaded onto a reverse-phase silica gel (Cosmosil® 75C_{18}–OPN, 3 g) column and the column was eluted successively with 20%, and 40% aq MeOH. The 40% aq MeOH fraction was concentrated to give **1f** (31.2 mg, 93% yield) with sufficient purity. To compare the optical rotation of the synthetic product with that of the natural product, the product was purified by semi-preparative HPLC with an Inertsil® ODS-3 column (20×250 mm, isocratic elution; 35% aq MeOH) to give **1f** (21.7 mg, 64% yield) as a colorless amorphous powder: R_f=0.27 (CH_3Cl/MeOH=4:1 v/v); $[\alpha]_D^{28}$ −83.8 (*c* 0.29, MeOH); IR (KBr, disk): ν 3378 cm^{-1} (OH), 1732 cm^{-1} (C=O); ^{1}H NMR (600 MHz, CD_3OD): δ 7.13 (2H, d, J=8.6 Hz, H-2 and H-6), 6.96 (2H, d, J=8.7 Hz, H-3 and H-5), 5.46 (1H, d, $J_{1,2}$=1.4 Hz, H-1$_{api}$), 4.94 (1H, d, $J_{1,2}$=7.7 Hz, H-1$_{glc}$), 4.14, 3.81 (2H, each d, J=9.8 Hz, H-4$_{api}$), 4.11, 4.07 (2H, each d, J=11.3 Hz, H-5$_{api}$), 3.88 (1H, d, $J_{2,1}$=1.4 Hz, H-2$_{api}$), 3.86 (1H, dd, $J_{6,5}$=1.9 Hz, $J_{6,6'}$=12.4 Hz, H-6$_{glc}$), 3.69 (2H, t, J=7.2 Hz, H-8), 3.67 (1H, dd, $J_{6',5}$=5.2 Hz, $J_{6',6}$=12.2 Hz, H-6′$_{glc}$), 3.64 (1H, dd, $J_{2,1}$=7.7 Hz, $J_{2,3}$=9.1 Hz, H-2$_{glc}$), 3.58 (1H, dd, $J_{3,2}$=9.1 Hz, $J_{3,4}$=8.6 Hz, H-3$_{glc}$), 3.40–3.35 (2H, m, H-4$_{glc}$ and H-5$_{glc}$), 2.75 (2H, t, J=7.2 Hz, H-7), 2.07 (2H, d, J=7.7 Hz, H-2‴), 1.86 (1H, m, H-3‴), 0.870, 0.867 (6H, each d, J=6.7 Hz, H-5‴); ^{13}C NMR (151 MHz, CD_3OD): δ 174.4, 157.4, 134.1, 130.9, 117.4, 110.4, 100.8, 79.0, 78.8, 78.7, 75.3, 71.5, 67.6, 64.4, 62.5, 43.9, 26.7, 22.71, 22.68; ESI-HRMS calcd for $C_{24}H_{36}O_{12}Na$ m/z [M+Na]$^+$: 539.2104. Found: 539.2071.

*4.4.9. Cucurbitoside B (**1g**).* To a solution of disaccharide **20 g** (135 mg, 92.9 μmol) in THF/MeOH (60 mL, 1:3 v/v) was added palladium hydroxide (10 mg, 20 wt % on carbon). The suspension was stirred for 12 h at room temperature under hydrogen gas. The mixture was filtered through Celite. The filtrate was concentrated, and the residue was loaded onto a reverse-phase silica gel (Cosmosil® 75C_{18}-OPN, 3 g) column and the column was eluted successively with 20%, and 40% aq MeOH. The 40% aq MeOH fraction was concentrated to give **1g** (51.2 mg, quant.) with sufficient purity. To compare the optical rotation of the synthetic product with that of the natural product, the product was further purified by semi-preparative HPLC with an Inertsil® ODS-3 column (20×250 mm, isocratic elution; 30% aq MeOH) to give **1g** (42.9 mg, 84% yield) as a colorless amorphous powder: R_f=0.16 (CH_3Cl/MeOH=4:1 v/v); $[\alpha]_D^{24}$ −68.8 (*c* 0.42, MeOH); IR (KBr, disk): ν 3367 cm^{-1} (OH), 1698 cm^{-1} (C=O); ^{1}H NMR (600 MHz, CD_3OD): δ 7.78 (2H, d, J=8.6 Hz, H-2‴ and H-6‴), 6.94 (2H, d, J=8.2 Hz, H-2 and H-6), 6.89 (2H, d, J=8.3 Hz, H-3 and H-5), 6.74 (2H, d, J=8.6 Hz, H-3‴, and H-5‴), 5.51 (1H, s, H-1$_{api}$), 4.91 (1H, $J_{1,2}$=7.6 Hz, H-1$_{glc}$), 4.33, 3.91 (2H, each d, J=9.8 Hz, H-4$_{api}$), 4.28, 4.22 (2H, each d, J=11.3 Hz, H-5$_{api}$), 3.98 (1H, s, H-2$_{api}$), 3.86 (1H, br d, $J_{6,6'}$=11.7 Hz, H-6$_{glc}$), 3.68–3.65 (2H, m, H-2$_{glc}$, H-6′$_{glc}$), 3.62 (2H, t, J=7.0 Hz, H-8), 3.60 (1H, t, $J_{3,2}$=8.9 Hz, H-3$_{glc}$), 3.41–3.36 (2H, m, H-4$_{glc}$, H-5$_{glc}$), 2.65 (2H, dt, J=7.0 Hz, J=2.4 Hz, H-7); ^{13}C NMR (151 MHz, CD_3OD): δ 167.7, 163.5, 157.3, 133.9, 132.9, 130.9, 121.9, 117.2, 116.1, 110.3, 100.7, 79.2, 78.8, 78.7, 78.1, 78.0, 75.4, 71.4, 67.9, 64.3, 62.5, 39.3; ESI-HRMS calcd for $C_{26}H_{32}O_{13}Na$ m/z [M+Na]$^+$: 575.1741. Found: 575.1770.

*4.4.10. Cucurbitoside I (**1h**).* To a solution of disaccharide **20g** (52 mg, 37.5 μmol) in THF/MeOH (20 mL, 1:3 v/v) were added 0.1 M

aq HCl solution (0.35 mL) and palladium hydroxide (5 mg, 20 wt % on carbon). The suspension was stirred for 4 h at room temperature under hydrogen gas. The mixture was filtered through Celite, and the filtrate was concentrated. The residue was diluted with H_2O, and then the solution was loaded onto a reverse-phase silica gel (Cosmosil® 75C_{18}–OPN, 3 g) column and the column was eluted successively with 15%, and 30% aq MeOH. The 30% aq MeOH fraction was concentrated, and the crude product was further purified by semi-preparative HPLC with an Inertsil® ODS-3 column (20×250 mm, isocratic elution; 30% aq MeOH) to give **1g** (6.8 mg, 33% yield) as colorless amorphous powder: R_f=0.54 (CH_3Cl/MeOH/H_2O=10:10:3 v/v/v); $[\alpha]_D^{24}$ −63.7 (*c* 0.51, MeOH); IR (KBr, disk): ν 3364 cm^{-1} (OH), 1696 cm^{-1} (C=O), 1604 cm^{-1} (NH); ^{1}H NMR (600 MHz, CD_3OD): δ 7.66 (2H, d, J=8.8 Hz, H-2‴ and H-6‴), 6.95 (2H, d, J=8.6 Hz, H-3 and H-5), 6.89 (2H, d, J=8.6 Hz, H-2 and H-6), 6.57 (2H, d, J=8.8 Hz, H-3‴, and H-5‴), 5.50 (1H, s, H-1$_{api}$), 4.90 (1H, $J_{1,2}$=7.7 Hz, H-1$_{glc}$), 4.32, 3.89 (2H, each d, J=9.6 Hz, H-4$_{api}$), 4.26, 4.18 (2H, each d, J=11.2 Hz, H-5$_{api}$), 3.97 (1H, s, H-2$_{api}$), 3.86 (1H, dd, $J_{6,5}$=1.5 Hz, $J_{6,6'}$=12.7 Hz, H-6$_{glc}$), 3.67 (1H, dd, $J_{6',5}$=5.2 Hz, $J_{6',6}$=12.5 Hz, H-6′$_{glc}$), 3.65 (1H, dd, $J_{2,1}$=7.7 Hz, $J_{2,3}$=9.1 Hz, H-2$_{glc}$,), 3.63 (2H, t, J=7.0 Hz, H-8), 3.59 (1H, dd, $J_{3,2}$=8.9 Hz, $J_{3,4}$=8.6 Hz, H-3$_{glc}$), 3.40–3.34 (2H, m, H-4$_{glc}$, H-5$_{glc}$), 2.66 (2H, t, J=7.0 Hz, H-7); ^{13}C NMR (151 MHz, CD_3OD): δ 168.4, 157.3, 154.8, 133.9, 132.7, 130.9, 118.2, 117.3, 114.3, 110.4, 100.9, 79.3, 78.8, 78.7, 78.2, 78.0, 75.5, 71.5, 67.8, 64.3, 62.5, 39.4; ESI-HRMS calcd for $C_{26}H_{32}O_{13}Na$ m/z $[M+Na]^+$: 575.1900. Found: 574.1932.

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16. 1,6-*O*-di-acylated and 1-*O*-acylated derivatives were obtained as a side products. To recycle these compounds,1,6-*O*-di-acylated and 1-*O*-acylated derivatives were removed with NaOMe to give **17** in excellent yields.
17. Fluophase® RP column packed with a perfluorohexylpropylsiloxane-bonded stationary phase is available from Thermo Fisher Scientific Inc.
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