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The Structural Revision and Total Synthesis of Carambolaflavone A

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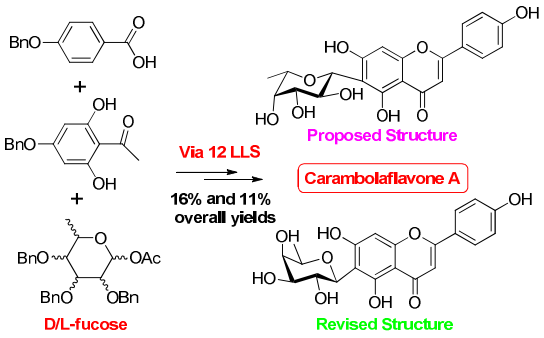
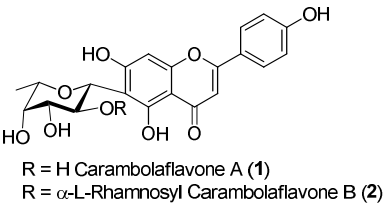


Abstract:

The synthesis of both enantiomers of carambolaflavone A, the antidiabetic and flavonoid *C*-glycoside, was achieved for the first time via a 12-longest-linear-step with 16% (L-fucose) and 11% (D-fucose) overall yields. Through the synthetic investigation the adverse effect of 4A MS in Suzuki *C*-glycosylation was disclosed, the mechanism of hydrogen-bonded-phenol involved Suzuki *C*-glycosylation was clarified, and the authentic structure of carambolaflavone A was also determined.

Diabetes mellitus (DM) is a progressive metabolic disease featured by chronic hyperglycemia due to the decreased insulin secretion from pancreas and increased insulin resistance. According to the statistics of the World Health Organization, more than 346 million people worldwide suffer from diabetes, and about 3.4 million people died from the serious complications of the high blood sugar in 2004, with this number estimated to be doubled by 2030 and type 2 diabetes accounting for 90% of all diabetes cases.[1] Currently available antidiabetic agents are known to cause undesirable side effects such as gastric symptoms, hypoglycemia, body weight gain and so on.[2] Thus, there is an urgent medical need for the development of novel potent hypoglycemic agents, ideally with plant origins.[3] Flavonoid glycosides, widely spread in plant kingdom and acting as common ingredients of human diets,[4] have been proven to possess outstanding antidiabetic effect, thus qualifying them to be promising lead compounds to new hypoglycemic drugs.[5] Carambolaflavone A (**1**) and carambolaflavone B (**2**), the two representative members of flavonoid glycosides, were isolated from the leaves of *Averrhoa carambola* in 2005 (Figure 1).[6] Preliminary bioactivity investigations revealed that both compounds showed acute blood glucose lowering effect via both promotion of glucose-induced insulin secretion and stimulation of glycogen synthesis.[7] Intrigued by the impressive bioactivity as well as the synthetically challenging *C*-glycosidic linkage,[8] we launched a program to study the synthesis of carambolaflavone A, which culminated in the first total synthesis of both enantiomers of **1** as well as the final authentic structure determination of

carambolaflavone A.[8]



R = H Carambolaflavone A (**1**)
R = α-L-Rhamnosyl Carambolaflavone B (**2**)

Figure 1. The proposed chemical structures of carambolaflavone A and B.

To ensure high efficiency of the synthesis, a strategy of fashioning *C*-glycosidic linkage first with a flavone subunit, that is appropriately protected 2,4,6-trihydroxyacetophenone, then elaboration of the flavone scaffold was envisioned (Figure 2).[9] Regarding the key *C*-glycosidic linkage construction, available choices include conventional Suzuki *O*→*C* glycoside rearrangement,[10] Friedel-Crafts glycosylation,[11] and new-emerging metal-mediated cross-coupling approaches.[12] Given that the β-*C*-glycosidic linkage contained in **1** is thermodynamically favored, thus the Suzuki *O*→*C* glycoside rearrangement is preferred with armed perbenzylated L-fucopyranosyl acetate **5** as donor. Accordingly, the monobenzylated 2,4,6-trihydroxyacetophenone **4** was selected as the precursor of the flavone unite, from which the flavone scaffold could be elaborated via a sequence of esterification with acid **3**, Baker-Venkataraman rearrangement under basic condition, and acid-catalyzed cyclization.

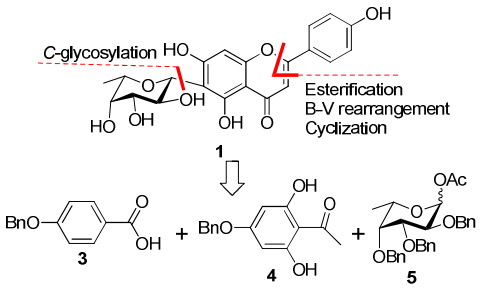
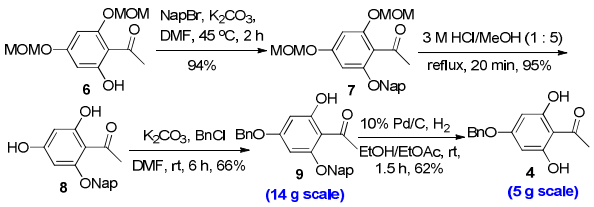


Figure 2. Retrosynthetic analysis of the proposed structure of carambolaflavone A.

The endeavor commenced with the synthesis of **4**.[13] As shown in scheme 1, the intramolecular H-bond fixed 6-OH of dimethoxymethylated 2,4,6-trihydroxyacetophenone **6**[14] was protected with 2-napthylmethyl group (Nap) to produce **7** (94%). The methoxymethyl groups (MOM) in **7** were selectively removed by HCl, delivering the diol intermediate **8** in 95% yield. Intermediate **8** was then subjected to regioselective benzylation under mild conditions (BnCl, K_2CO_3, and room temperature), and the desired monobenzylated acetophenone **9** was isolated in a good 66% yield, which was further treated with controlled hydrogenolysis conditions (H_2, Pd/C, 1.5 h) to realize the selective removal of the Nap group at the presence of Bn (62%), with the main byproduct being over-deprotected product.[15] It is worth mentioning that the route for the synthesis of **4** is reproducible and easily scalable, and more than 5 grams of **4** can be obtained through one pass. Existing approach to generate **4** was also tried,[13] unfortunately, in our hands the practicality was proved to be unsatisfactory not only due to the application of aluminium salt in big amounts but also because of the low benzylation efficiency.

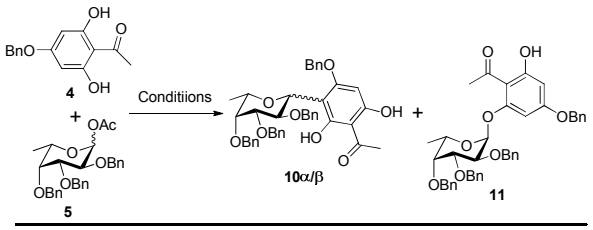


Scheme 1. Synthesis of monobenzylated trihydroxyacetophenone **4**.

With acceptor **4** in hand, now the stage was set for the pivotal *C*-glycosidic linkage construction between **4** and **5** (Table 1). Following the similar conditions devised by Suzuki,[10] that is 0.2 equivalents of $Sc(OTf)_3$ in dry CH_2Cl_2 at the presence of activated 4A molecular sieves at the temperature ranging from -30 °C to rt, the coupling between **4** and perbenzylated L-fucosyl acetate **5**[16] only yielded 25% yield of the desired β-*C*-glycoside **10β**, with the remaining mass balance being α-*C*-glycoside **10α** (30%, for the anomeric proton: 5.70 ppm, d, J = 1.6 Hz) and α-*O*-glycoside **11** (22%, for the anomeric proton: 5.50 ppm, d, J = 3.2 Hz, entry 1). Changing the solvent from CH_2Cl_2 to toluene did not bring about any improvement in the condensation efficiency (8% **10β**, 19% **10α**, and 26% **11**), but the higher boiling point of toluene compared to CH_2Cl_2 rendered the coupling reaction enjoying a broad tunable temperature scope. Thus, toluene was selected as the reaction medium for the following optimization. Increasing the reaction temperature was proved to be an efficient means to suppress the formation of *O*-glycoside **11**, as evidenced by the reaction results obtained at 50 °C and 70 °C, in which only trace amounts of **11** was detected (entries 3 and 4). However, the high percentage of **10α** still compromised the overall efficiency. Increasing the $Sc(OTf)_3$ amounts from 0.2 to 0.5 equivalents led to the desired yield rise for **10β** (78%) and yield drop for **10α** (7%). However, the high

catalyst loading as well as the difficulty associated with purification of **10β** from **10α** still restricts the application. Further optimization revealed that upon treatment of the crude product obtained by conditions 4 with $Sc(OTf)_3$ (0.2 eq) at the absence of 4A MS under otherwise identical conditions, the reaction afforded a clean conversion to the desired **10β** in a high 85% yield (entry 6). The yield could be further improved to 94% via a modification of conditions 4 simply by omitting the 4A MS. Thus, the optimal conditions were fixed as 0.2 equivalents of $Sc(OTf)_3$ in the absence of 4A MS in dry toluene at 70 °C.

Table 1. Optimization of the key *C*-glycosidic linkage formation conditions

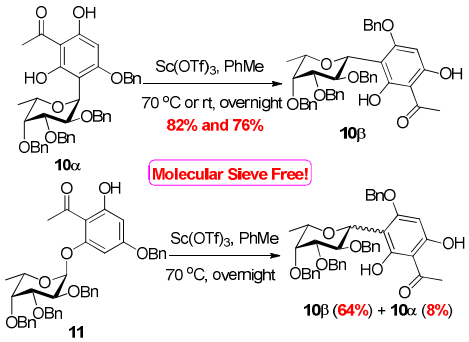


Entry	Conditions	Result[a]
1	$Sc(OTf)_3$ (0.2 eq), 4A MS CH_2Cl_2, -30 °C to rt	**10**α (30%), **10**β (25%), **11** (22%)
2	$Sc(OTf)_3$ (0.2 eq), 4A MS PhMe, rt	**10**α (19%), **10**β (8%), **11** (26%)
3	$Sc(OTf)_3$ (0.2 eq), 4A MS PhMe, 50 °C	**10**α (32%), **10**β (62%), **11** (trace)
4	$Sc(OTf)_3$ (0.2 eq), 4A MS PhMe, 70 °C	**10**α (20%), **10**β (64%), **11** (trace)
5	$Sc(OTf)_3$ (0.5 eq), 4A MS PhMe, 70 °C	**10**α (7%), **10**β (78%)
6	**Conditions 4**,[b] then $Sc(OTf)_3$ (0.2 eq) PhMe, 70 °C	**10**β (85%)
7	$Sc(OTf)_3$ (0.2 eq), PhMe, 70 °C	**10**β (94%)

[a]Isolated yield; [b]Conditions applied in entry 4.

Based on the results obtained during the optimization of the *C*-glycosidic linkage formation, a hypothesis that molecular sieves might have a deleterious effect on the key *O*→*C* rearrangement and α-*C*-glycosidic linkage epimerization processes in Suzuki *C*-glycosylation was put forward. To verify the assumption, the α-*C*-glycoside **10α** and *O*-glycoside **11** were tried to retreated with $Sc(OTf)_3$ under the optimized

conditions (Scheme 2). Indeed, upon treated with $Sc(OTf)_3$, **10α** was efficiently transformed to the desired β-isomer (82%). Surprisingly, the epimerization could even be promoted efficiently by $Sc(OTf)_3$ at room temperature, and **10β** was obtained with a slightly decreased yield (76%). The optimal conditions were then transplanted to *O*-glycoside **11**, again, the desired **10β** was isolated as the predominating product (64%) accompanied by a small amount of **10α** (8%). These results clearly indicate that without 4A MS the epimerization and glycosyl residue *O*→*C* shift can be catalyzed efficiently by $Sc(OTf)_3$ (0.2 eq), and 4A MS is not the ideal desiccant for Suzuki *C*-glycosylation. This presumably can be attributed to the basic property of 4A MS.[17]



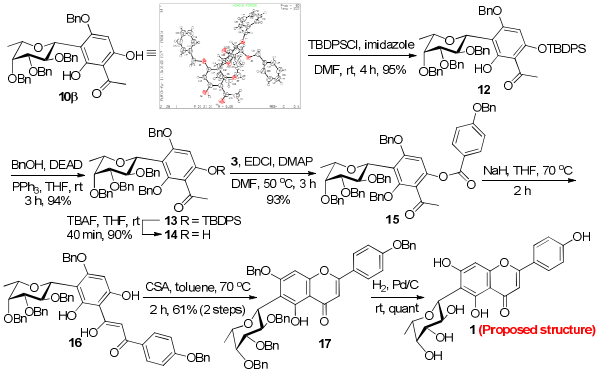
Scheme 2. $Sc(OTf)_3$-catalyzed epimerization and *O*→*C* migration of **10α** and **11** at the absence of 4A MS.

For normal phenol acceptors, it has been widely accepted that the Suzuki *C*-glycosylation proceeded via the corresponding *O*-glycoside intermediates. However, for hydrogen-bonded phenol substrates, a direct *C*-glycosylation mechanism rather than a *O*→*C* migration pathway was proposed by Suzuki and co-workers.[18] Regarding acceptor **4**, also a hydrogen-bonded substrate, the isolation of *O*-glycoside **11** as well as its successful conversion to *C*-glycoside **10β** demonstrates that even for H-bonded

phenol acceptors, the *C*-glycosylation still proceed via the *O*-glycosylation, glycosyl *O*→*C* migration, and epimerization process.

With the optimal conditions for the construction of the challenging *C*-glycosidic linkage settled, our attention was then shifted to the completion of the synthesis of the originally proposed structure of **1** (Scheme 3). With **10β**, whose structure was confirmed both by NMR spectra (for the anomeric proton: 4.99 ppm, d, J = 9.6 Hz) and by X-ray diffraction,[19] as the starting point, the intermediate **12** was obtained with high efficacy via regioselective silylation of the less-hindered OH of **10β**. Interestingly, once the bulky *tert*-butyldiphenylsilyl group (TBDPS) is introduced, the intermediate **12** exists as a pair of atropisomers at room temperature, as evidenced by the NMR spectra that appears in two sets of signals.[20] The appearance of the rotational isomers is attributed to the slow/hindered rotation around the *C*-glycosidic linkage on the NMR time scale. The reactivity of the remaining OH of **12** was low due to the intramolecular bonding with the neighboring carbonyl group as well as the steric hindrance exerted by both flanked *ortho*-substituents, and the protection of it was finally realized by Mitsunobu conditions to generate **13** (94%). Tetrabutylammonium fluoride (TBAF) mediated TBDPS removal generated **14** (90%), which was primed for the fabrication of the flavone skeleton. Dehydrative esterification with acid **3**[21] afforded ester **15** (93%), which was then converted to **16** via Baker-Venkataraman rearrangement under basic conditions. The flavone scaffold was finally furnished by acid-mediated cyclization to give **17** (61%, 2 steps), with the benzyl group at 5-OH was concomitantly removed. Finally, the global deprotection

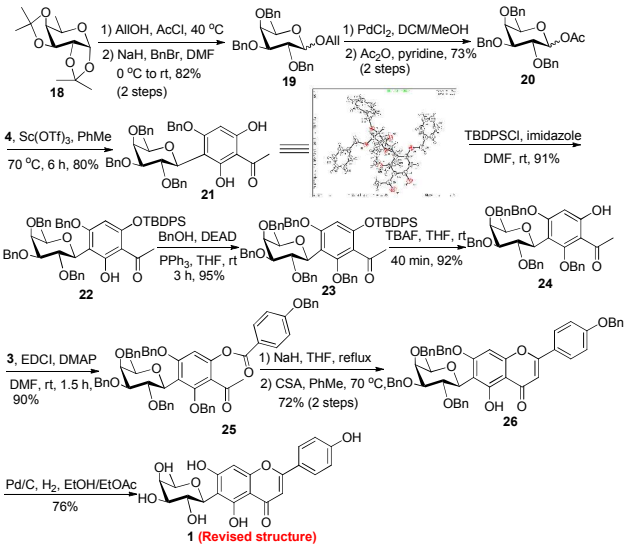
was effected by the conventional hydrogenolysis to produce the proposed **1** quantitatively. Till now, with the cleavage of all bulky protecting groups, the atropisomeric phenomenon disappeared for the proposed **1**, as evidenced by the NMR spectra.[20] Spectrascopic data comparison between those obtained from the synthetic sample and those reported in literature revealed that identical spectroscopic spectra were obtained. However, when the optical property was checked for the synthetic compound, an optical data with a signal opposite to that reported in literature was obtained (-42.3 vs +41.4[*lit.6*]).[20]



Scheme 3. The synthesis of the original proposed structure of **1**

The opposite signal of the optical value as well as the identical NMR spectra to the reported data indicates that the enantiomer of authentic **1** was obtained and the originally proposed structure of **1** was misassigned. In fact, in 2012 Silva et al. have claimed the isolation and characterization of the enantiomer of the proposed **1**. Surprisingly, no spectroscopic comparison with literature[6] was made and no optical value was provided.[22] The promising antihyperglycemic effect as well as the confusing structural information in literature calls on a conclusive structure assignment of **1**. To this end, the synthesis of the enantiomer of the proposed **1** was

launched. As shown in scheme 4, the synthesis of enantiomeric **1** entailed the use of perbenzylated D-fucosyl acetate **20** as donor, which was obtained from **18**[23] through a sequence of 4-step protecting group manipulations, including anomeric allylation, benzylation, deallylation, and acetylation (60%, 4 steps). Under the optimized *C*-glycosylation conditions, the coupling of **20** and **4** proceeded without any event, affording *C*-glycoside **21** in a good 80% yield. Following the procedure established in the synthesis of proposed **1**, compound **21** was finally transformed to the enantiomer of the proposed **1** via intermediates **22**-**25**. It should be pointed out that the efficiency of Baker-Venkataraman rearrangement could be improved considerably by applying 17.0 equivalents of NaH (76% yield for the conversion of **25** to **26**). Pleasantly, besides the identical spectroscopic data, the optical data of the synthetic **1** containing D-fucosyl residue was also proved to be in good accordance with the reported data (+58.8 vs + 41.4[*lit.6*].). Accordingly, the true structure of **1** was unequivocally revised to apigenin-6-*C*-β-D-fucopyranoside. ^{1}H NMR comparison of all two synthetic samples with that reported by Silva et al.[22] led to the recognition of evident discrepancies, especially for the sugar part.[20] Thus, the sugar residue has presumably been incorrectly determined in Silva's literature.



Scheme 4. Synthesis of the enantiomer of the originally proposed **1**

In summary, a highly efficient approach toward carambolaflavone A, a plant-derived and hypoglycemic flavonoid *C*-glycoside, was established, which is featured by the scalable synthesis of appropriately protected 2,4,6-trihydroxyacetophenone and the modified Suzuki *C*-glycosylation. Through the synthetic investigation the adverse effect of 4A MS in Suzuki *C*-glycosylation was disclosed and the mechanism of hydrogen-bonded-phenol involved Suzuki *C*-glycosylation was clarified. Moreover, the authentic structure of carambolaflavone A was revised by synthesizing both enantiomers, which would lay firm foundation for further structure-bioactivity relationship investigation.

Experimental section:

2-Naphthylmethoxy-4,6-dimethoxymethyloxy-acetophenone (7)

To a solution of **6** (72.2 mg, 0.28 mmol) in dry DMF (2.0 mL) was added K_2CO_3 (116.8 mg, 0.85 mmol) at 0 °C. The suspension was stirred at the same temperature for 30 minutes, to which NapBr (74.7 mg, 0.34 mmol) was added at the same temperature under N_2 atmosphere. The reaction mixture was then heated to 45 °C, and the stirring was continued for another 2 h. After cooled to room temperature, the

reaction mixture was diluted with ethyl acetate. The resulting mixture was washed successively with 1N HCl, water, saturated aqueous $NaHCO_3$, and brine, and then dried over Na_2SO_4. Filtration was followed by concentration under reduced pressure afforded a residue, which was further purified by silica gel column chromatography (petroleum ether/ethyl acetate = 4 : 1) to afford **7** (105.1 mg, 94%) as a light yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.83 (m, 4 H), 7.51-7.48 (m, 3 H), 6.48 (d, *J* = 2.0 Hz, 1 H), 6.44 (d, *J* = 2.0 Hz, 1 H), 5.22 (s, 2 H), 5.15 (s, 2 H), 5.13 (s, 2 H), 3.47 (s, 3 H), 3.44 (s, 3 H), 2.50 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.3, 167.7, 165.2, 162.1, 136.0, 133.3, 133.2, 128.8 (2 C), 128.5, 128.1, 127.9, 127.8, 127.2, 126.6 (2 C), 125.7, 106.5, 94.9, 92.5, 71.4, 70.4, 33.5 (2 C); HRMS (ESI) m/z calcd for $C_{23}H_{25}O_6$ $(M+H)^+$ 397.1646, found 397.1638.

2-Naphthylmethoxy-4,6-dihydroxy-acetophenone (8)

To a solution of **7** (860.7 mg, 2.2 mmol) in MeOH (50 mL) was added 3N HCl (10 mL). The resulting mixture was heated to reflux, and the stirring was continued for 20 minutes. After cooled to room temperature, the reaction mixture was poured to cooled water (120 mL, with ice), and white precipitate appeared gradually. The white solid was collected and dried to give **8** (603.9 mg, 96%), which was pure enough for characterization: ^{1}H NMR (400 MHz, DMSO-d6) δ 13.88 (s, 1 H), 10.69 (s, 1 H), 8.04 (d, *J* = 1.6 Hz, 1 H), 7.98-7.93 (m, 3 H), 7.67 (dd, *J* = 1.6, 8.4 Hz, 1 H), 7.56-7.54 (m, 2 H), 6.16 (d, *J* = 2.0 Hz, 1 H), 5.94 (d, *J* = 2.0 Hz, 1 H), 5.32 (s, 2 H), 3.41 (s, 1 H), 2.50 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-d6) δ 202.3, 166.4, 165.0, 162.3, 133.7, 132.8, 132.7, 128.2, 127.9, 127.6, 127.0, 126.4, 126.3, 126.0, 104.8, 95.8 (2 C), 92.5, 70.6, 32.9 (2 C); HRMS (ESI) m/z calcd for $C_{19}H_{17}O_4$ $(M+H)^+$ 309.1121, found 309.1119.

2-Naphthylmethoxy-4-benzyloxy-6-hydroxyl-acetophenone (9)

To a solution of **8** (72.8 mg, 0.24 mmol) in dry DMF (0.5 mL) was added K_2CO_3 (65.3 mg, 0.47 mmol) at 0 ^{o}C under N_2 atmosphere, to which BnCl (54 μL, 0.47 mmol) was added dropwise at the same temperature. After the addition was completed, the reaction mixture was warmed to room temperature and the stirring was continued at the same temperature for another 6 h. Ethyl acetate was added to dilute the reaction,

and the resulting mixture was washed successively with 1N HCl, saturated aqueous $NaHCO_3$, and brine, and then dried over Na_2SO_4. Filtration was followed by concentration under the reduced pressure afforded a residue, which was further purified by silica gel column chromatography (petroleum ether/ethyl acetate = 20 : 1) to afford **9** (62.4 mg, 66%) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.06 (s, 1 H), 7.91-7.86 (m, 4 H), 7.55-7.52 (m, 3 H), 7.43-7.34 (m, 5 H), 6.19 (d, J = 2.4 Hz, 1 H), 6.16 (d, J = 2.4 Hz, 1 H), 5.22 (s, 2 H), 5.06 (s, 2 H), 2.57 (s, 3 H); 13C NMR (100 MHz, CDCl3) δ 201.7, 159.7, 157.0, 155.5, 133.9, 133.3, 133.2, 128.5, 128.1, 127.8, 126.4 (2 C), 126.2, 125.2, 116.5, 96.5, 95.5, 94.9, 94.6, 70.8, 56.5, 56.4, 56.3, 56.2, 32.7 (2 C); HRMS (ESI) m/z calcd for $C_{26}H_{23}O_4$ $(M+H)^+$ 399.1591, found 399.1591.

2,6-Dihydroxy-4-Benzyloxy-acetophenone (4)

To a solution of **9** (2.0 g, 5.1 mmol) in a mixed solvent of ethyl acetate and ethanol (60 mL, v/v = 1 : 1) was added 10% Pd/C (1.4 g). After cooled to -78 ^{o}C, the flask was evacuated and then refilled with H_2. The process was repeated for three times, and the black suspension was warmed up to room temperature. After stirring for another 1.5 h, the Pd/C was removed by filtration through a pad of Celite/silica gel. The filtrate was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 15 : 1) to afford **4** (813.3 mg, 62%) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4) δ 7.37-7.25 (m, 5 H), 5.94 (s, 2 H), 5.00 (s, 2 H), 2.57 (s, 3 H).

***C*-Glycosylation following Suzuki's conditions**

To a solution of **4** (67 mg, 0.26 mmol) and **5** (183 mg, 0.38 mmol) in dry CH_2Cl_2 (6.5 mL) was added $Sc(OTf)_3$ (32 mg, 0.065 mmol) in the presence of 4A MS at -30 ^{o}C under N_2 atmosphere. The reaction mixture was then gradually warmed up to room temperature, and the stirring was continued overnight at the same temperature. After quenched with Et_3N, the reaction mixture was filtered and the filtrate was evaporated under reduced pressure. The resultant residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 20 : 1) to afford α-*C*-glycoside **10α** (52.3 mg, 30%), β-*C*-glycoside **10β** (43.2 mg, 25%), and α-*O*-glycoside **11** (38.4 mg,

22%). For **10α**: $[\alpha]_D^{25}$ = 33.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.96 (s, 1 H), 9.99 (s, 1 H), 7.38-7.30 (m, 8 H), 7.27-7.19 (m, 8 H), 7.16-7.14 (m, 2 H), 6.97 (dd, *J* = 1.2, 8.0 Hz, 2 H), 6.03 (s, 1 H), 5.70 (d, *J* = 1.6 Hz, 1 H), 5.00 (AB, 2 H), 4.53 (s, 2 H), 4.50 (t, *J* = 6.4 Hz, 1 H), 4.44 (AB, 2 H), 4.31 (d, *J* = 12.0 Hz, 1 H), 4.15 (d, *J* = 12.0 Hz, 1 H), 4.05 (dd, *J* = 3.2, 6.4 Hz, 1 H), 3.88 (t, *J* = 3.2 Hz, 1 H), 3.68 (dd, *J* = 1.6, 4.0 Hz, 1 H), 2.66 (s, 3 H), 1.59 (d, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.4, 166.3, 162.2, 161.1, 138.4, 137.5, 136.0, 128.7, 128.6, 128.4 (2 C), 128.3, 128.1, 128.0, 127.8, 127.6, 127.5, 127.3, 106.3, 101.6, 92.4, 73.6, 73.4 (2 C), 72.4, 72.1, 71.5, 70.4, 66.7, 33.3, 13.1; HRMS (ESI) m/z calcd for $C_{42}H_{43}O_8$ $(M+H)^+$ 675.2952, found 675.2943.

For **10β**: $[\alpha]_D^{25}$ = 16.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.88 (d, *J* = 2.0 Hz, 1 H), 7.42-7.29 (m, 15 H), 7.18-7.16 (m, 3 H), 7.03-7.01 (m, 2 H), 6.04 (d, *J* = 3.2 Hz, 1 H), 5.20 (dd, *J* = 2.8, 11.6 Hz, 1 H), 4.99-4.95 (m, 2 H), 4.92 (dd, *J* = 2.0, 12.0 Hz, 1 H), 4.82 (d, *J* = 2.4 Hz, 2 H), 4.74 (dd, *J* = 2.8, 11.6 Hz, 1 H), 4.66 (dd, *J* = 3.2, 11.2 Hz, 1 H), 4.27-4.22 (m, 2 H), 3.77 (t, *J* = 2.8 Hz, 1 H), 3.73 (dt, *J* = 2.8, 9.2 Hz, 1 H), 3.68-3.63 (m, 1 H), 2.62 (d, *J* = 3.6 Hz, 3 H), 1.27 (dd, *J* = 2.4, 6.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.3, 166.6, 162.4, 160.8, 138.6 (2 C), 138.2, 136.4, 128.6, 128.4 (2 C), 128.2, 128.1, 127.8, 127.7, 127.6, 127.5, 106.4, 104.3, 93.1, 84.5, 75.2, 74.6, 73.9, 72.6, 70.5, 33.2, 17.5; HRMS (ESI) m/z calcd for $C_{42}H_{43}O_8$ $(M+H)^+$ 675.2952, found 675.2956.

For **11**: $[\alpha]_D^{25}$ = -40.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.94 (d, *J* = 3.2 Hz, 1 H), 7.40-7.21 (m, 20 H), 6.33 (d, *J* = 2.4 Hz, 1 H), 6.17 (d, *J* = 2.4 Hz, 1 H), 5.50 (d, *J* = 3.2 Hz, 1 H), 5.06 (dd, *J* = 1.6, 11.6 Hz, 1 H), 5.01 (s, 2 H), 4.84-4.76 (m, 3 H), 4.72 (dd, *J* = 2.0, 11.6 Hz, 1 H), 4.64 (dd, *J* = 1.6, 12.0 Hz, 1 H), 4.23-4.19 (m, 1 H), 3.99 (dt, *J* = 2.4, 10.4 Hz, 1 H), 3.88 (q, *J* = 6.4 Hz, 1 H), 3.69 (d, *J* = 2.4 Hz, 1 H), 2.59 (d, *J* = 2.0 Hz, 3 H); 1.17 (dd, *J* = 2.0, 6.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.6, 167.0, 165.1, 161.0, 138.4 (2 C), 138.2, 136.0, 128.8, 128.6, 128.5 (2 C), 128.4, 128.3, 127.9 (2 C), 127.8 (2 C), 127.7, 127.5, 106.5, 97.7, 96.3, 94.0, 78.2, 76.2, 75.2, 73.6, 72.8, 70.1, 68.1, 33.7, 16.7; HRMS (ESI) m/z calcd for $C_{42}H_{43}O_8$ $(M+H)^+$ 675.2952, found 675.2946.

***C*-Glycosylation under the optimized conditions**

To a solution of **4** (172.1 mg, 0.67 mmol) and **5** (379.7 mg, 0.8 mmol) in dry toluene (16 mL) was added $Sc(OTf)_3$ (65.6 mg, 0.13 mmol) at room temperature under N_2 atmosphere. The resulting reaction mixture was heated to 70 ^oC and the stirring was continued overnight at the same temperature. After cooled to room temperature, Et_3N was added to quench the reaction. The volatile solvent was removed *in vacuo* and the obtained residue was purified by silica gel chromatography (petroleum ether/ethyl acetate = 20 : 1 to 10 : 1) to afford **10β** (420.8 mg, 94%) as a white solid.

Conversion of 10α to 10β under the optimized conditions

The optimized conditions to synthesize **10β** were applied to convert **10α** (208.3 mg, 0.31 mmol) to **10β** (170.1 mg, 82%).

Conversion of α-*O*-glycoside 11 to 10β and 10α

The optimized conditions to synthesize **10β** were applied to convert **11** (72.6 mg, 0.11 mmol) to **10β** (46.7 mg, 64%) and **10α** (6.1 mg, 8%).

2-Hydroxy-3-*C*-(2,3,4-tri-*O*-benzyl-β-L-fucopyranosyl)-4-benzyloxy-6-*tert*-butyldiphenylsilyloxy-acetophenone (12)

To a solution of **10β** (900.8 mg, 1.3 mmol) and imidazole (272.6 mg, 4.0 mmol) in dry DMF (5.0 mL) was added TBDPSCl (1.0 mL, 4.0 mmol) under N_2 atmosphere, and the reaction mixture was stirred at room temperature for 4 h. Then, the mixture was quenched with saturated aqueous NH_4Cl, and extracted with EtOAc. The organic layer was washed with brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to give a residue containing **12**. The residue was purified by silica gel column chromatography (PhMe/EtOAc = 100 : 1) to afford **12** (1.2 g, 95%) as a colorless oil: $[\alpha]_D^{25}$ = 22.0 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 14.24 (d, *J* = 4.0 Hz, 1 H), 12.40 (d, *J* = 2.4 Hz, 0.7 H), 7.70-7.64 (m, 10 × 0.7 H), 7.47-7.26 (m, 21 H), 7.24-7.05 (m, 20 × 0.7 H), 7.02-6.84 (m, 9 H), 5.67 (d, *J* = 2.8 Hz, 1 H), 5.61 (d, *J* = 2.4 Hz, 0.7 H), 5.12 (dd, *J* = 2.4, 12.0 Hz, 0.7 H), 4.97 (dd, *J* = 3.2, 10.0 Hz, 1 H), 4.92 (dd, *J* = 2.8, 12.4 Hz, 1 H), 4.81-4.62 (m, 4 H + 5 × 0.7 H), 4.52 (td, *J* = 9.2, 2.8 Hz, 1 H), 4.40 (dd, *J* = 2.8, 11.2 Hz, 1 H), 4.25 (dd, *J* = 2.8, 10.8 Hz, 0.7 H), 4.16-4.12 (m, 3 × 0.7 H), 4.04 (dd, *J* = 2.8, 12.8 Hz, 1 H), 3.96 (dd, *J* = 2.8, 11.2 Hz, 1

H), 3.67-3.57 (m, 3 + 2 × 0.7 H), 3.52 (dd, *J* = 2.0, 6.8 Hz, 0.7 H), 2.91 (d, *J* = 2.4 Hz, 3 H), 2.78 (d, *J* = 2.4 Hz, 3 × 0.7 H), 1.21-1.20 (m, 3 + 3 × 0.7 H), 1.10 (d, *J* = 2.4 Hz, 9 H), 1.07 (d, *J* = 2.4 Hz, 9 × 0.7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.2, 202.7, 164.9, 163.5, 162.4, 161.0, 159.6, 157.6, 139.5, 139.2, 139.1, 139.0 (2 C), 136.2, 135.8, 135.4, 135.3 (2 C), 135.2, 134.9, 132.1, 132.0, 131.9, 131.8, 130.5, 130.4, 130.3 (2 C), 128.4 (2 C), 128.3, 128.2 (3 C), 128.1, 128.0 (3 C), 127.8, 127.6 (2 C), 127.5, 127.4 (2 C), 127.3, 127.2 (2 C), 126.7, 110.9, 107.7, 107.1, 98.0, 97.2, 85.6, 85.3, 78.0, 76.7, 75.0, 74.9, 74.7, 74.4, 74.3, 74.2, 73.5, 73.0, 72.8, 72.7, 69.9, 69.4, 33.7, 33.6, 26.7, 26.6, 19.4, 19.3, 17.7; HRMS (ESI) m/z calcd for $C_{58}H_{61}O_8Si$ $(M+H)^+$ 913.4130, found 913.4106.

3-*C*-(2,3,4-Tri-*O*-benzyl-β-L-fucopyranosyl)-2,4-dibenzyloxy-6-*tert*-butyldiphenyl silyloxy-acetophenone (13)

To a solution of **12** (1.1 g, 1.2 mmol) and PPh_3 (1.3 g, 5.0 mmol) in THF (20 mL) was added benzyl alcohol (0.5 mL, 5.0 mmol) and DEAD (0.79 mL, 5.0 mmol) at 0 °C, the reaction mixture was stirred at room temperature for 4 h. Then, the reaction mixture was concentrated under reduced pressure. The resultant residue was purified by silica gel column chromatography (petroleum/EtOAc = 20/1) to afford **13** (1.2 g, 94%) as a colorless oil. $[\alpha]_D^{25}$ = 35.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.66 (m, 3 + 4 × 0.5 H), 7.63 (dd, *J* = 2.4, 8.0 Hz, 1 H), 7.53 (dd, *J* = 2.4, 8.4 Hz, 1 H), 7.47-7.02 (m, 24 + 31 × 0.5 H), 6.98-6.91 (m, 4 H), 6.88-6.86 (m, 2 H), 5.90 (s, 1 H), 5.85 (s, 0.5 H), 5.60 (d, *J* = 10.0 Hz, 0.5 H), 4.94-4.78 (m, 2 + 2 × 0.5 H), 4.86 (d, *J* = 10.0 Hz, 0.5 H), 4.79 (d, *J* = 12.0 Hz, 1 H), 4.73-4.60 (m, 5 + 5 × 0.5 H), 4.43-4.34 (m, 1 + 3 × 0.5 H), 4.29 (d, *J* = 12.0 Hz, 1 H), 4.21 (d, *J* = 12.8 Hz, 1 H), 3.94 (d, *J* = 11.6 Hz, 1 H), 3.69 (d, *J* = 2.8 Hz, 0.5 H), 3.62-3.58 (m, 1 + 2 × 0.5 H), 3.50 (dd, *J* = 2.4, 8.8 Hz, 1 H), 3.44 (dd, *J* = 6.0, 12.8 Hz, 1 H), 2.57 (s, 3 H), 2.36 (s, 3 × 0.5 H), 1.21 (dd, *J* = 3.2, 6.4 Hz, 3 + 3 × 0.5 H), 1.06 (s, 9 H), 1.02 (s, 9 × 0.5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 202.3, 159.5, 158.9, 157.7, 156.9, 153.1, 152.9, 139.5, 139.3, 139.2, 139.1, 138.8, 137.8, 137.4, 136.6, 136.4, 135.7, 135.6 (2 C), 135.4, 132.6, 132.4, 132.2, 132.1, 130.4, 130.3 (2 C), 130.2, 129.4, 128.6, 128.5, 128.4 (2 C), 128.3, 128.2 (2 C), 128.1 (2 C), 128.0 (2 C), 127.9, 127.7, 127.6 (3 C),

127.5, 127.4, 127.3, 127.2, 127.1, 126.8, 123.2, 121.7, 114.9, 114.3, 102.3, 101.5, 85.8, 85.5, 80.1, 79.0, 78.1, 77.8, 76.4, 75.5, 75.2, 75.0, 74.8, 74.6, 74.5, 73.5, 73.0, 72.7, 70.6, 70.1, 33.0 (2 C), 26.5, 26.4, 19.5, 17.8, 17.7; HRMS (ESI) m/z calcd for $C_{65}H_{67}O_8Si$ $(M+H)^+$ 1003.4600, found 1003.4584.

3-*C*-(2,3,4-Tri-*O*-benzyl-β-L-fucopyranosyl)-2,4-bisbenzyloxy-6-hydroxy-acetophenone (14)

To a solution of **13** (2.1 g, 2.1 mmol) in THF (50.0 mL) was added TBAF (2.9 mL, 10.6 mmol) at 0 ^oC, and the mixture was stirred at room temperature for 40 min. Then, saturated aqueous NH_4Cl was added at 0 ℃, the resulting solution was extracted with Ethyl acetate. The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a residue including **14**. The crude material was further purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10 : 1) to deliver **14** (1.4 g, 90%) as a white foam: $[\alpha]_D^{25}$ = -11.7 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 13.31 (s, 1 H), 13.12 (s, 0.4 H), 7.53 (dd, *J* = 2.0, 8.0 Hz, 2 H), 7.47 (dd, *J* = 1.6, 8.4 Hz, 2 × 0.4 H), 7.43-7.12 (m, 21 + 21 × 0.4 H), 7.00 (d, *J* = 2.4 Hz, 0.4 H), 6.98 (d, *J* = 3.6 Hz, 0.4 H), 6.94 (d, *J* = 1.2 Hz, 1 H), 6.92 (d, *J* = 2.0 Hz, 1 H), 6.35 (s, 0.4 H), 6.33 (s, 1 H), 5.74 (d, *J* = 11.2 Hz, 0.4 H), 5.74 (d, *J* = 11.2 Hz, 0.4 H), 5.16-4.63 (m, 11 + 10 × 0.4 H), 4.49 (d, *J* = 11.2 Hz, 0.4 H), 4.25 (d, *J* = 11.2 Hz, 1 H), 3.67-3.64 (m, 1 + 2 × 0.4 H), 3.63 (q, *J* = 6.4 Hz, 0.4 H), 3.56 (dd, *J* = 3.2, 9.2 Hz, 1 H), 3.46 (q, *J* = 6.4 Hz, 1 H), 2.63 (s, 3 H), 2.33 (s, 3 × 0.4 H), 1.25 (d, *J* = 6.4 Hz, 3 H), 1.12 (d, *J* = 6.4 Hz, 3 × 0.4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.2, 203.7, 165.7, 165.3, 164.7, 163.9, 163.0, 161.9, 139.4, 139.1, 139.0, 138.9 (2 C), 138.7, 137.4, 136.7, 136.2, 136.0, 128.6, 128.5 (2 C), 128.4, 128.3, 128.2 (3 C), 128.1, 128.0 (3 C), 127.9, 127.7 (2 C), 127.6 (2 C), 127.5 (2 C), 127.4 (2 C), 127.2 (2 C), 114.1, 113.3, 111.4, 110.0, 98.5, 97.7, 96.0, 85.8, 81.1, 78.9, 77.4, 77.3, 76.3, 75.2 (2 C), 74.8, 74.7 (2 C), 74.6, 74.4, 73.1, 72.8, 72.7, 70.7, 70.2, 31.7, 31.4, 17.7, 17.6; HRMS (ESI) m/z calcd for $C_{49}H_{49}O_8$ $(M+H)^+$ 765.3422, found 765.3417.

3-*C*-(2,3,4-Tri-*O*-benzyl-β-L-fucopyranosyl)-2,4-dibenzyloxy-6-(4-benzyloxybenzoyloxy)-acetophenone (15)

To a solution of **14** (578.3 mg, 0.76 mmol), **3** (354.2 mg, 1.5 mmol), and DMAP (184.7 mg, 1.5 mmol) in dry DMF (9 mL) was added EDCI (436.1 mg, 2.3 mmol) at room temperature under N_2 atmosphere. The resulting mixture was heated to 50 ^oC, and the solution was stirred at the same temperature for another 3 h. Ethyl acetate was added to dilute the reaction, and the resultant mixture was washed with water, saturated aqueous $NaHCO_3$, brine, and dried over Na_2SO_4. Filtration was followed by concentration under reduced pressure gave a residue, which was further purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10 : 1) to afford **15** (684.2 mg, 93%) as a white foam: $[\alpha]_D^{25}$ = 14.4 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.12-8.07 (m, 2 + 2 × 0.7 H), 7.53 (d, *J* = 6.0 Hz, 2 H), 7.46-7.16 (m, 26 + 27 × 0.7 H), 7.10-7.02 (m, 2 + 3 × 0.7 H), 7.00 (dd, *J* = 2.4, 7.2 Hz, 2 × 0.7 H), 6.94 (d, *J* = 8.4 Hz, 2 H), 6.692 (s, 0.7 H), 6.686 (s, 1 H), 5.64 (d, *J* = 10.0 Hz, 0.7 H), 5.15-5.12 (m, 3 + 2 × 0.7 H), 5.08-4.59 (m, 10 + 10 × 0.7 H), 4.36 (d, *J* = 10.8 Hz, 0.7 H), 4.25 (d, *J* = 11.2 Hz, 1 H), 3.73 (d, *J* = 2.8 Hz, 0.7 H), 3.68-3.64 (m, 1 + 2 × 0.7 H), 3.58 (dd, *J* = 2.4, 9.2 Hz, 1 H), 3.48-3.43 (m, 1 H), 2.50 (d, *J* = 1.6 Hz, 3 H), 2.27 (d, *J* = 1.6 Hz, 3 × 0.7 H), 1.26-1.20 (m, 3 + 3 × 0.7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0, 200.3, 164.4, 163.3, 160.5, 159.8, 158.6, 157.6, 148.9, 148.7, 139.4, 139.1, 139.0 (2 C), 138.9, 138.5, 137.4, 136.8, 136.5, 136.4, 136.3, 132.6 (2 C), 129.1, 128.8, 128.6 (2 C), 128.5 (2 C), 128.4 (2 C), 128.3 (2 C), 128.2 (2 C), 128.1, 128.0, 127.9, 127.7 (2 C), 127.6 (2 C), 127.4 (2 C), 127.3 (2 C), 124.6, 123.0, 121.7 (2 C), 120.3, 119.5, 114.9 (3 C), 105.2, 104.4, 85.9, 85.8, 80.7, 79.0, 78.0, 77.6, 76.2, 75.6, 75.4, 75.2, 75.0 (2 C), 74.5 (2 C), 73.4, 73.0, 72.8, 71.4, 71.0, 70.3, 32.1, 31.9, 17.7; HRMS (ESI) m/z calcd for $C_{63}H_{59}O_{10}$ $(M+H)^+$ 975.4103, found 975.4114.

1-[4-(Benzyloxy)phenyl]-3-[2,6-dishydroxyl-3-(2,3,4-tri-*O*-benzyl-β-L-fucopyranosyl)-4-benzyloxy]phenyl-propane-1,3-dione (16)

To a solution of **15** (959.0 mg, 0.98 mmol) in dry THF (15.0 mL) was added 60% NaH (236 mg, 9.8 mmol) at 0 ^oC. The suspension was stirred at the same temperature for 5 min, then the reaction mixture was heated to reflux and the stirring was continued for another 2 h. After cooled to room temperature, the reaction mixture was diluted with ethyl acetate. The resulting solution was washed with water, saturated

aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and brine, and then dried over Na_2SO_4. Filtration was followed by concentration under reduced pressure gave the crude product **16**, a small aliquot of which was further purified by silica gel column chromatography (petroleum ether/acetone = 10 : 1 to 6 : 1) for detailed characterization: $[\alpha]_D^{25}$ = 53.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.80 (s, 0.6 H), 15.79 (s, 0.6 H), 12.80 (s, 0.6 H), 12.72 (s, 1 H), 7.59 (d, *J* = 9.2 Hz, 2 H), 7.54-7.51 (m, 2 + 2 × 0.6 H), 7.45-7.07 (m, 27 + 28 × 0.6 H), 7.00-6.91 (m, 3 + 2 × 0.6 H), 6.87-6.84 (m, 2 + 2 × 0.6 H), 6.72 (d, *J* = 8.8 Hz, 2 × 0.6 H), 6.35 (s, 0.6 H), 6.34 (s, 1 H), 5.57 (d, *J* = 10.4 Hz, 0.6 H), 5.14-4.89 (m, 7 + 7 × 0.6 H), 4.86-4.76 (m, 4 + 3 × 0.6 H), 4.74-4.67 (m, 2 + 2 × 0.6 H), 4.63-4.58 (m, 1 + 0.6 H), 4.41 (d, *J* = 11.2 Hz, 0.6 H), 4.24 (d, *J* = 11.2 Hz, 1 H), 3.71-3.66 (m, 1 + 2 × 0.6 H), 3.62-3.59 (m, 1 + 0.6 H), 3.55 (q, *J* = 2.4 Hz, 1 H), 1.26 (d, *J* = 6.4 Hz, 3 H), 1.10 (d, *J* = 6.4 Hz, 3 × 0.6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.4, 193.1, 177.4, 177.2, 165.0 (2 C), 163.8, 162.9, 162.1, 161.8 (2 C), 160.4, 139.4, 139.2, 139.0, 138.9, 138.7, 137.6, 136.8, 136.5 (2 C), 136.4, 136.2, 129.0 (2 C), 128.8, 128.7 (2 C), 128.6 (3 C), 128.5 (2 C), 128.4, 128.3 (2 C), 128.2 (2 C), 128.1, 128.0 (3 C), 127.8, 127.7 (2 C), 127.6 (2 C), 127.5, 127.4 (2 C), 127.3 (2 C), 127.2, 126.3, 126.2, 114.9, 114.6, 114.5, 113.8, 109.3, 108.3, 98.9, 98.1, 97.4, 96.6, 86.0, 85.9, 80.6, 78.4, 77.9, 77.4, 76.4, 75.5, 75.2, 74.9, 74.8, 74.7, 74.6, 74.4, 73.5, 73.1, 72.7, 70.8, 70.3, 70.2 (2 C), 17.8, 17.7; HRMS (ESI) m/z calcd for $C_{63}H_{59}O_{10}$ $(M+H)^+$ 975.4103, found 975.4063.

3-*C*-(2,3,4-Tri-*O*-benzyl-β-L-fucopyranosyl)-7,4'-di-*O*-benzyl-apigenin (17)

The remaining crude **16** obtained by the above step was then dissolved in dry toluene (10 mL), to which CSA (297 mg, 1.3 mmol) was added at room temperature. The reaction mixture was heated to 70 °C, and the stirring was continued for another 2 h. After cooled to room temperature, the reaction was diluted with ethyl acetate. The resulting solution was washed successively with water, saturated aqueous $NaHCO_3$, and brine, and then dried over Na_2SO_4. Filtration and concentration gave the crude product, which was further purified by silica gel column chromatography (petroleum ether/acetone = 4 : 1) to afford **17** (523 mg, 61%, for 2 steps) as a yellow solid: $[\alpha]_D^{25}$ = 8.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, acetone-d_6) δ 13.58 (s, 1 H), 13.55 (s, 0.5

H), 7.98 (d, J = 8.8 Hz, 2 + 2 × 0.5 H), 7.66 (dd, J = 1.2, 7.6 Hz, 2 H), 7.51-6.96 (m, 25 + 27 × 0.5 H), 6.80 (s, 0.5 H), 6.76 (s, 1 H), 6.69 (s, 1 H), 6.66 (s, 0.5 H), 5.31-5.18 (m, 4 + 4 × 0.5 H), 5.12 (d, J = 12.0 Hz, 0.5 H), 5.04-4.96 (m, 2 + 2 × 0.5 H), 4.90-4.73 (m, 4 + 4 × 0.5 H), 4.62 (d, J = 11.6 Hz, 1 H), 4.46 (d, J = 11.6 Hz, 0.5 H), 4.28 (d, J = 11.2 Hz, 1 H), 3.94 (t, J = 3.2 Hz, 1 + 0.5 H), 3.80-3.72 (m, 2 + 0.5 H), 3.68 (q, J = 6.4 Hz, 0.5 H), 1.28 (d, J = 6.4 Hz, 3 H), 1.22 (d, J = 6.4 Hz, 3 × 0.5 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 183.4, 183.1, 164.9, 164.5, 164.0, 162.8, 162.4, 161.4, 158.2 (2 C), 140.9, 140.7, 140.4, 140.3, 140.2 (2 C), 137.7, 137.6 (2 C), 129.4 (2 C), 129.1 (2 C), 128.9, 128.8, 128.6, 128.5, 128.4 (2 C), 128.3, 128.2 (2 C), 128.1, 128.0, 127.9, 127.8, 127.7 (2 C), 124.4, 116.2, 111.5, 111.4, 106.2, 105.7, 105.0, 104.9, 92.8, 92.1, 86.8, 86.5, 78.8, 78.5, 77.3, 76.6, 75.7, 75.6, 75.3, 75.2, 74.9, 74.7, 73.7, 73.2, 73.0, 72.7, 71.5, 70.8, 70.7, 17.9, 17.8; HRMS (ESI) m/z calcd for $C_{56}H_{51}O_9$ $(M+H)^+$ 867.3528, found 867.3517.

Carambolaflavone A (1) (proposed structure)

To a solution of **17** (69.6 mg, 0.08 mmol) in a mixed solvent of ethyl acetate and ethanol (10.2 mL, v/v = 1: 5) was added 10% Pd/C (35.7 mg). After the temperature was cooled to -78 ^{o}C, the reaction flask was evacuated and refilled with hydrogen. After this process was repeated for 3 times, the reaction mixture was stirred at room temperature 16 h. Filtration through a pad of Celite and silica gel, and the filtrate was concentrated under reduced pressure to give the crude product, which was further purified by C18 reverse phase chromatography (H_2O/MeOH = 1.5 : 1) to afford the proposed Carambolaflavone A (33.4 mg, 100%) as a light yellow solid: $[\alpha]_D^{25}$ = -42.3 (*c* 1.0, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.47 (s, 1 H), 10.36 (s, 1 H), 7.95 (d, J = 8.4 Hz, 2 H), 6.94 (d, J = 8.8 Hz, 2 H), 6.80 (s, 1 H), 6.54 (s, 1 H), 4.75 (d, J = 5.6 Hz, 1 H), 4.65 (d, J = 10.0 Hz, 2 H), 4.03-3.00 (m, 1 H), 3.69 (q, J = 6.4 Hz, 1 H), 3.57 (t, J = 3.2 Hz, 1 H), 3.42-3.39 (m, 1 H), 1.15 (d, J = 6.4 Hz, 3 H); ^{1}H NMR (400 MHz, DMSO-d_6 + D_2O) δ 7.93 (d, J = 8.4 Hz, 2 H), 6.94 (d, J = 8.8 Hz, 2 H), 6.77 (s, 1 H), 6.55 (s, 1 H), 4.63 (d, J = 9.6 Hz, 1 H), 4.02 (t, J = 9.2 Hz, 1 H), 3.67 (q, J = 6.8 Hz, 1 H), 3.41 (dd, J = 3.2, 9.2 Hz, 1 H), 1.13 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.0, 163.7, 162.8, 161.2, 159.6, 156.3, 128.5, 121.1, 116.0,

109.2, 103.5, 102.8, 94.2, 75.0, 74.0, 73.5, 71.6, 68.6, 17.1; HRMS (ESI) m/z calcd for $C_{21}H_{21}O_9$ $(M+H)^+$ 417.11801, found 417.1191.

Allyl 2,3,4-tri-*O*-benzyl-D-fucopyranoside (19)

To a solution of **18** (1.7 g, 6.8 mmol) in dry Allylic alcohol (15 mL) was added AcCl (1.2 mL) dropwise at 0 ^oC under N_2. After the addition was completed, the reaction mixture was heated to 40 ^oC, and the stirring was continued for another 4 h. After cooled to room temperature, Et_3N was added to quench the reaction, and the volatile solvent was removed under reduced pressure. The residue was roughly purified by short silica gel column chromatography (DCM/MeOH = 15 : 1 to 10 : 1) to give allyl fucoside for the next step without detailed characterization.

To a solution of above obtained allyl fucoside (510.9 mg, 2.5 mmol) in dry DMF (12.5 mL) was added 60% NaH (360.2 mg, 15.0 mmol) at 0 ^oC. After the addition was completed, the stirring was continued at the same temperature for 20 min. Then, the reaction mixture was warmed to room temperature and the stirring was continued for another 2.5 h. Ethyl acetate was added to dilute the reaction and the resultant solution was washed successively with water, 1N HCl, saturated aqueous $NaHCO_3$, and brine, and then dried over Na_2SO_4. Filtration was followed by concentration to yield the crude product, which was further purified by silica gel column chromatography (1.0 g, 87%) as a mixture of α/β isomers as a syrup: $[\alpha]_D^{25}$ = 17.3 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.41-7.24 (m, 15 + 15 × 0.3 H), 6.00-5.87 (m, 1 + 0.3 H), 5.35-5.27 (m, 1 + 0.3 H), 5.21-5.15 (m, 1 + 0.3 H), 5.00-4.64 (m, 6 + 8 × 0.3 H), 4.44-4.39 (m, 1 H), 4.38 (d, *J* = 7.6 Hz, 1 H), 4.15-4.07 (m, 1 + 0.3 H), 4.06-4.02 (m, 0.3 H), 4.01-3.94 (m, 0.3 H), 3.91-3.91 (dd, *J* = 5.6, 6.8 Hz, 0.3 H), 3.86 (dd, *J* = 7.6, 9.6 Hz, 1 H), 3.66 (dd, *J* = 0.8, 2.8 Hz, 0.3 H), 3.56 (d, *J* = 3.2 Hz, 1 H), 3.52 (dd, *J* = 2.8, 9.6 Hz, 1 H), 3.46-3.42 (m, 1 H), 1.19 (d, *J* = 6.4 Hz, 3 H), 1.11 (d, *J* = 6.4 Hz, 3 × 0.3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 139.0, 138.8 (2 C), 134.5, 134.3, 128.6, 128.5, 128.4 (3 C), 128.3, 128.2, 128.1, 127.7 (2 C), 127.6 (3 C), 117.9, 117.0, 103.0, 96.5, 82.7, 79.6 (2 C), 78.1, 76.6, 76.5, 75.3, 75.0, 74.7, 73.5, 73.4 (2 C), 70.5, 70.1, 68.4, 66.5, 17.0, 16.7; HRMS (ESI) m/z calcd for $C_{30}H_{34}O_5Na$ $(M+Na)^+$ 497.2298, found 497.2294.

2,3,4-Tri-*O*-benzyl-D-fucopyranosyl acetate (20)

To a solution of **19** (144.2 mg, 0.3 mmol) in a mixed solvent of DCM/MeOH (8 mL, v/v = 1 : 1) was added $PdCl_2$ (17.0 mg, 0.09 mmol) at room temperature. The reaction was stirred at the same temperature for 6 h, then the black solid was filter off through a pad of Celite/silica gel. The solid was thoroughly washed with DCM, and the resultant solution was washed water and brine, and then dried over Na_2SO_4. Filtration was followed by concentration to yield a residue, which was used for the next step without further purification.

The residue obtained above was dissolved in dry pyridine (2.5 mL), to which Ac_2O (58 μL, 0.6 mmol) was added at 0 ^oC. After the addition was completed, the reaction mixture was warmed to room temperature and the stirring was continued for another 3 h. Ethyl acetate was added to dilute the reaction and the resultant solution was washed successively with water, 1N HCl, saturated $NaHCO_3$, and brine, and then dried over Na_2SO_4. Filtration was followed by concentration to yield a residue, which was further purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10 : 1) to afford **20** (105.1 mg, 73%) as a mixture of α/β isomers. An aliquot of α isomer was isolated for detailed characterization: $[\alpha]_D^{25}$ = 37.9 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.41-7.25 (m, 15 H), 6.38 (d, *J* = 4.0 Hz, 1 H), 5.00 (d, *J* = 11.6 Hz, 1 H), 4.88 (d, *J* = 11.6 Hz, 1 H), 4.76-4.64 (m, 4 H), 4.18 (dd, *J* = 3.6, 10.0 Hz, 1 H), 4.00 (q, *J* = 6.4 Hz, 1 H), 3.91 (dd, *J* = 2.8, 10.0 Hz, 1 H), 3.71 (d, *J* = 3.2 Hz, 1 H), 2.11 (s, 3 H), 1.15 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 138.8, 138.5, 138.2, 128.5 (2 C), 128.4, 128.1, 127.8 (2 C), 127.7, 127.5, 91.0, 79.1, 75.4, 75.1, 73.4, 73.3, 69.2, 21.3, 16.8; HRMS (ESI) m/z calcd for $C_{29}H_{32}O_6NH_4$ $(M+NH_4)^+$ 494.2537, found 494.2534.

2,6-Dihydroxyl-3-*C*-(2,3,4-tri-*O*-benzyl-β-D-fucopyranosyl)-4-benzyloxy-acetophenone (21)

Similar procedure as that used for the synthesis of **10β** was adopted to give **21** (1.55 g, 80%) as a white solid: $[\alpha]_D^{25}$ = -18.9 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 13.88 (s, 1 H), 9.00 (s, 1 H), 7.44-7.30 (m, 15 H), 7.18-7.16 (m, 3 H), 7.04-7.02 (m, 2 H), 6.04 (s, 1 H), 5.20 (d, *J* = 11.2 Hz, 1 H), 4.993 (d, *J* = 9.6 Hz, 1 H), 4.987 (AB, 2

H), 4.82 (s, 2 H), 4.74 (d, *J* = 11.6 Hz, 1 H), 4.66 (d, *J* = 10.8 Hz, 1 H), 4.281 (t, *J* = 9.6 Hz, 1 H), 4.278 (d, *J* = 10.8 Hz, 1 H), 3.77 (d, *J* = 2.4 Hz, 1 H), 3.73 (dd, *J* = 2.4, 9.2 Hz, 1 H), 3.68 (q, *J* = 6.4 Hz, 1 H), 2.62 (s, 3 H), 1.28 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.3, 166.6, 162.3, 160.8, 138.6 (2 C), 138.2, 126.4, 128.6, 128.4 (2 C), 128.1 (2 C), 127.8, 127.7, 127.6, 127.5, 106.4, 104.3, 93.1, 84.5, 75.2, 74.6, 73.9, 72.6, 70.5, 33.2, 17.5; HRMS (ESI) m/z calcd for $C_{42}H_{43}O_8$ $(M+H)^+$ 675.2952, found 675.2946.

2-Hydroxyl-3-*C*-(2,3,4-tri-*O*-benzyl-β-D-fucopyranosyl)-4-benzyloxy-6-*tert*-butyldiphenylsilyloxy-acetophenone (22)

Similar procedure as that used for the synthesis of **12** was adopted to get **22** (1.35 g, 91%) as a white foam: $[\alpha]_D^{25}$ = -28.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.20 (s, 1 H), 12.30 (s, 0.7 H), 7.72-7.64 (m, 10 × 0.7 H), 7.47-7.05 (m, 21 + 20 × 0.7 H), 7.03-6.84 (m, 9 H), 5.66 (s, 1 H), 5.60 (s, 0.7 H), 5.11 (d, *J* = 12.0 Hz, 0.7 H), 4.95 (d, *J* = 9.6 Hz, 1 H), 4.90 (d, *J* = 12.4 Hz, 1 H), 4.81-4.67 (m, 3 + 5 × 0.7 H), 4.64 (d, *J* = 11.6 Hz, 1 H), 4.51 (t, *J* = 9.2 Hz, 1 H), 4.38 (d, *J* = 10.8 Hz, 1 H), 4.23 (d, *J* = 10.8 Hz, 0.7 H), 4.16-4.12 (m, 3 × 0.7 H), 4.04 (d, *J* = 11.6 Hz, 1 H), 3.96 (d, *J* = 10.8 Hz, 1 H), 3.67-3.56 (m, 3 + 2 × 0.7 H), 3.53 (q, *J* = 6.4 Hz, 0.7 H), 2.90 (s, 3 H), 2.77 (s, 3 × 0.7 H), 1.21 (d, *J* = 6.4 Hz, 3 + 3 × 0.7 H), 1.09 (s, 9 H), 1.06 (s, 9 × 0.7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.2, 202.7, 165.0, 163.6, 162.4, 161.1, 159.6, 157.6, 139.5, 139.2 (2 C), 139.1, 139.0, 136.2, 135.9, 135.4 (2 C), 135.3, 135.2, 132.2, 132.0, 131.9, 131.8, 130.5, 130.4 (2 C), 130.3, 128.4 (2 C), 128.3 (2 C), 128.2 (2 C), 128.1, 128.0 (2 C), 127.9, 127.6 (2 C), 127.5 (2 C), 127.4, 127.3 (2 C), 127.2, 126.8, 107.7, 107.1, 98.0, 97.3, 85.6, 85.4, 78.0, 76.7 (2 C), 75.1, 75.0, 74.8, 74.4 (2 C), 74.2, 73.5, 73.0, 72.8, 72.7, 69.9, 69.4, 33.8, 33.6, 26.7, 26.6, 19.4 (2 C), 17.7; HRMS (ESI) m/z calcd for $C_{58}H_{61}O_8Si$ $(M+H)^+$ 913.4130, found 913.4115.

3-*C*-(2,3,4-Tri-*O*-benzyl-β-D-fucopyranosyl)-2,4-dibenzyloxy-6-*tert*-butyldiphenylsilyloxy-acetophenone (23)

Similar procedure as that used for the synthesis of **13** was applied to get **23** (1.28 g, 95%) as a white foam: $[\alpha]_D^{25}$ = -26.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71-7.66 (m, 3 + 4 × 0.5 H), 7.63 (dd, *J* = 1.2, 8.0 Hz, 1 H), 7.53 (dd, *J* = 1.2, 8.0 Hz,

1 H), 7.47-7.01 (m, 24 + 31 × 0.5 H), 6.99-6.92 (m, 4 H), 6.88-6.86 (m, 2 H), 5.90 (s, 1 H), 5.85 (s, 0.5 H), 5.61 (d, J = 10.0 Hz, 0.5 H), 4.95-4.88 (m, 2 + 2 × 0.5 H), 4.86 (d, J = 9.6 Hz, 0.5 H), 4.79 (d, J = 11.6 Hz, 1 H), 4.74-4.61 (m, 5 + 5 × 0.5 H), 4.43-4.35 (m, 1 + 3 × 0.5 H), 2.29 (d, J = 11.6 Hz, 1 H), 4.22 (d, J = 12.4 Hz, 1 H), 3.95 (d, J = 9.4 Hz, 1 H), 3.69 (dd, J = 1.2, 2.8 Hz, 0.5 H), 3.62-3.58 (m, 1 + 2 × 0.5 H), 3.50 (dd, J = 2.8, 9.2 Hz, 1 H), 3.44-3.39 (m, 1 H), 2.58 (s, 3 H), 2.36 (s, 3 × 0.5 H), 1.21 (d, J = 6.4 Hz, 3 × 0.5 H), 1.20 (d, J = 6.4 Hz, 3 H), 1.06 (s, 9 H), 1.03 (s, 9 × 0.5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 202.3, 159.5, 158.9, 157.7, 156.9, 153.1, 152.8, 139.5, 139.3, 139.2, 139.1 (2 C), 138.8, 137.8, 137.4, 136.6, 136.4, 135.7, 135.6 (2 C), 135.4, 132.5, 132.4, 132.2, 132.1, 130.4, 130.3, 130.2 (2 C), 129.3, 128.6, 128.5, 128.4 (2 C), 128.3, 128.2 (2 C), 128.1 (3 C), 128.0 (2 C), 127.8, 127.7, 127.6 (2 C), 127.5 (2 C), 127.3 (2 C), 127.2, 127.1, 126.8, 123.2, 121.7, 114.9, 114.3, 102.2, 101.4, 85.7, 85.5, 80.1, 78.9, 78.1, 77.8, 77.4, 76.4, 75.5, 75.2, 75.0, 74.8, 74.6, 74.5, 74.4, 73.4, 73.0, 72.7, 70.5, 70.1, 33.0 (2 C), 26.5, 26.4, 19.5, 17.8, 17.7; HRMS (ESI) m/z calcd for $C_{65}H_{67}O_8Si$ $(M+H)^+$ 1003.4600, found 1003.4592.

3-*C*-(2,3,4-Tri-*O*-benzyl-β-D-fucopyranosyl)-2,4-dibenzyloxy-6-hydroxyl-acetophenone (24)

Similar procedure as that used for the synthesis of **14** was applied to get **24** (275.8 mg, 92%) as a white solid: $[\alpha]_D^{25}$ = 10.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.30 (d, J = 2.4 Hz, 1 H), 13.10 (d, J = 2.4 Hz, 0.4 H), 7.51 (d, J = 6.8 Hz, 2 H), 7.45 (dd, J = 2.0, 7.6 Hz, 2 × 0.4 H), 7.42-7.11 (m, 21 + 21 × 0.4 H), 6.98 (dd, J = 3.2, 4.8 Hz, 2 × 0.4 H), 6.92 (dd, J = 2.4, 6.0 Hz, 2 H), 6.34 (d, J = 1.6 Hz, 0.4 H), 6.31 (d, J = 1.6 Hz, 1 H), 5.72 (d, J = 11.2 Hz, 0.4 H), 5.15-4.61 (m, 11 + 10 × 0.4 H), 4.48 (d, J = 12.0 Hz, 0.4 H), 4.23 (dd, J = 1.6, 11.2 Hz, 1 H), 3.65 (d, J = 3.6 Hz, 1 + 2 × 0.4 H), 3.61 (q, J = 6.4 Hz, 0.4 H), 3.54 (dd, J = 2.4, 9.6 Hz, 1 H), 3.45 (q, J = 6.4 Hz, 1 H), 2.62 (d, J = 1.6 Hz, 3 H), 2.32 (d, J = 1.6 Hz, 3 × 0.4 H), 1.23 (dd, J = 1.6, 6.4 Hz, 3 H), 1.10 (dd, J = 1.6, 6.4 Hz, 3 × 0.4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.2, 203.7, 165.7, 165.3, 164.7, 163.9, 163.0, 162.0, 139.4, 139.1, 139.0, 138.9 (2 C), 138.7, 137.5, 136.7, 136.2, 136.0, 128.7, 128.5 (2 C), 128.4, 128.3, 128.2 (2 C), 128.1, 128.0 (3 C), 127.9, 127.7 (2 C), 127.6 (2 C), 127.5, 127.4 (2 C), 127.2 (2 C), 114.1, 113.3,

111.4, 110.0, 98.5, 97.7, 86.0, 85.8, 81.1, 78.9, 77.4, 77.3, 76.3, 75.2 (2 C), 74.8, 74.7 (2 C), 74.6, 74.4, 73.1, 72.8, 72.7, 70.7, 70.2, 31.7, 31.4, 17.7, 17.6; HRMS (ESI) m/z calcd for $C_{49}H_{49}O_8$ $(M+H)^+$ 765.3422, found 765.3425.

3-*C*-(2,3,4-Tri-*O*-benzyl-β-D-fucopyranosyl)-2,4-dibenzyloxy-6-(4-benzyloxybenzoyloxy)-acetophenone (25)

Similar procedure as that used for the synthesis of **15** was applied to get **25** (207.9 mg, 90%) as a white foam: $[\alpha]_D^{25}$ = -10.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12-8.07 (m, 2 + 2 × 0.7 H), 7.53 (dd, *J* = 1.6, 8.0 Hz, 2 H), 7.47-7.16 (m, 26 + 27 × 0.7 H), 7.10-7.01 (m, 2 + 3 × 0.7 H), 6.99 (dd, *J* = 1.6, 2.4 Hz, 2 × 0.7 H), 6.94 (dd, *J* = 2.0, 7.6 Hz, 2 H), 6.69 (brs, 1 + 0.7 H), 5.64 (d, *J* = 10.8 Hz, 0.7 H), 5.15-5.12 (m, 3 + 2 × 0.7 H), 5.08-4.60 (m, 10 + 10 × 0.7 H), 4.37 (d, *J* = 10.8 Hz, 0.7 H), 4.26 (d, *J* = 10.8 Hz, 1 H), 3.73 (d, *J* = 2.8 Hz, 0.7 H), 3.68-3.64 (m, 1 + 2 × 0.7 H), 3.58 (dd, *J* = 2.8, 9.2 Hz, 1 H), 3.48 (q, *J* = 6.4 Hz, 1 H), 2.50 (d, *J* = 2.4 Hz, 3 H), 2.27 (d, *J* = 2.4 Hz, 3 × 0.7 H), 1.24 (d, *J* = 6.4 Hz, 3 H), 1.21 (d, *J* = 6.0 Hz, 3 × 0.7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 200.3, 164.3, 163.3, 160.4, 159.8, 158.5, 157.6, 148.8, 148.6, 139.4, 139.1, 139.0 (2 C), 138.9, 138.5, 137.3, 136.8, 136.5, 136.3, 136.2 (2 C), 132.6, 132.5, 129.0, 128.8, 128.6, 128.5 (2 C), 128.4 (2 C), 128.3 (2 C), 128.2 (2 C), 128.1, 128.0 (2 C), 127.8, 127.6 (3 C), 127.5, 127.4 (2 C), 127.3, 127.2, 124.6, 123.0, 121.7 (2 C), 120.3, 119.4, 114.9, 105.1, 104.4, 85.8, 85.7, 80.7, 79.0, 77.9, 77.6, 76.1, 75.6, 75.4, 75.2, 75.0 (2 C), 74.5, 74.4, 73.4, 72.9, 72.7, 71.4, 71.0, 70.3, 32.1, 31.9, 17.7; HRMS (ESI) m/z calcd for $C_{63}H_{59}O_{10}$ $(M+H)^+$ 975.4103, found 975.4110.

4,7-Dibenzyl-6-*C*-(2,3,4-tri-*O*-benzyl-β-D-fucopyranosyl) apigenin (26)

Except for the applied amounts of NaH (17.0 equiv.), identical procedure as that used for the synthesis of **17** was applied to get **26** (96 mg, 72%) as a yellow solid: $[\alpha]_D^{25}$ = -3.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, acetone-d_6) δ 13.47 (s, 1 H), 13.44 (s, 0.5 H), 7.83 (d, *J* = 8.4 Hz, 2 + 2 × 0.5 H), 7.53 (d, *J* = 6.8 Hz, 2 H), 7.38-6.83 (m, 25 + 27 × 0.5 H), 6.67 (s, 0.5 H), 6.64 (s, 1 H), 6.56 (s, 1 H), 6.53 (s, 0.5 H), 5.18-5.12 (m, 2 H), 5.08 (t, *J* = 7.2 Hz, 2 + 2 × 0.5 H), 4.99 (d, *J* = 11.6 Hz, 0.5 H), 4.92-4.83 (m, 2 + 2 × 0.5 H), 4.77-4.60 (m, 4 + 4 × 0.5 H), 4.49 (d, *J* = 11.6 Hz, 1 H), 4.33 (d, *J* = 11.2 Hz, 0.5 H), 4.15 (d, *J* = 11.6 Hz, 1 H), 3.81 (t, *J* = 3.2 Hz, 1 + 0.5 H), 3.67-3.58 (m, 2 +

0.5 H), 3.55 (q, *J* = 6.4 Hz, 0.5 H), 1.15 (d, *J* = 6.0 Hz, 3 H), 1.08 (d, *J* = 6.4 Hz, 3 × 0.5 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 183.4, 183.1, 164.9, 164.7, 164.5, 164.0, 162.8, 162.4, 161.4, 161.1, 158.2 (2 C), 140.8, 140.7, 140.3, 140.2 (2 C), 137.7, 137.6 (2 C), 129.4 (2 C), 129.1 (2 C), 129.0, 128.9, 128.8 (2 C), 128.6, 128.5, 128.4, 128.3 (2 C), 128.2 (2 C), 128.1, 128.0, 127.9, 127.8, 127.7 (2 C), 124.3, 116.2, 111.4 (2 C), 105.7, 104.9 (2 C), 92.8 (2 C), 92.1, 86.8, 86.5, 78.7, 78.5, 77.3, 76.5, 75.7, 75.5, 75.3, 75.2, 74.9, 74.7, 73.7, 73.2, 73.0, 72.7, 71.5, 70.8, 70.7, 17.9, 17.8; HRMS (ESI) m/z calcd for $C_{56}H_{51}O_9$ $(M+H)^+$ 867.3528, found 867.3530.

Carambolaflavone A (1) (revised structure)

Similar procedure as that used for the synthesis of proposed structure of **1** was adopted to get revised structure of **1** (20.8 mg, 76%) as a yellow solid: $[\alpha]_D^{25}$ = 58.8 (*c* 0.8, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.4 Hz, 2 H), 6.97 (d, *J* = 8.0 Hz, 2 H), 6.78 (s, 1 H), 6.58 (s, 1 H), 4.65 (d, *J* = 9.6 Hz, 1 H), 4.06-4.01 (m, 1 H), 3.58 (d, *J* = 2.8 Hz, 1 H), 3.44 (dd, *J* = 3.2, 9.6 Hz, 1 H), 1.16 (d, *J* = 6.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.7, 164.6, 163.5, 161.6, 160.2, 157.0, 129.2, 121.8, 116.7, 109.6, 104.1, 103.3, 94.9, 75.6, 74.8, 74.0, 72.2, 69.0, 17.5; HRMS (ESI) m/z calcd for $C_{21}H_{21}O_9$ $(M+H)^+$ 417.1180, found 417.1180.

Associated content

The Supporting Information is available free of charge on the ACS Publications website at DOI:.

Copies of NMR spectra of all new compounds including 2D NMR for **10α**, **10β**, and **11** (PDF), X-ray crystallographic data for **10β** and **21** (CIF)

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19. CCDC 1544332 (**10β**) and 1585773 (**21**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

20. See supporting information.

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