α-Selective glycosidation of D-tagatofuranose with a 3,4-*O*-isopropylidene protection

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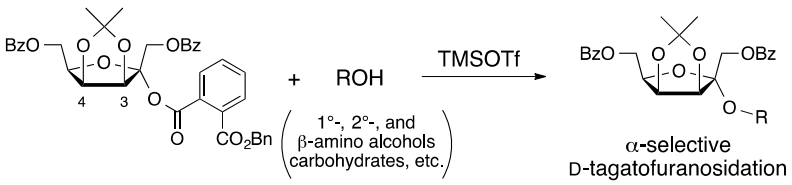
ABSTRACT: An α-selective glycosidation reaction of D-tagatofuranose was successfully achieved using 3,4-*O*-isopropylidene-protected D-tagatofuranose as a glycosyl donor. A variety of glycosyl acceptors, including primary, secondary, and β-amino alcohols, and carbohydrates, can be used for this D-tagatofuranosidation reaction with complete α-selectivities and good yields (57–83%). The stereochemistries at the anomeric positions were determined by nuclear Overhauser effect spectroscopic correlations, as well as comparison of the chemical shifts in the ^{13}C NMR spectra.

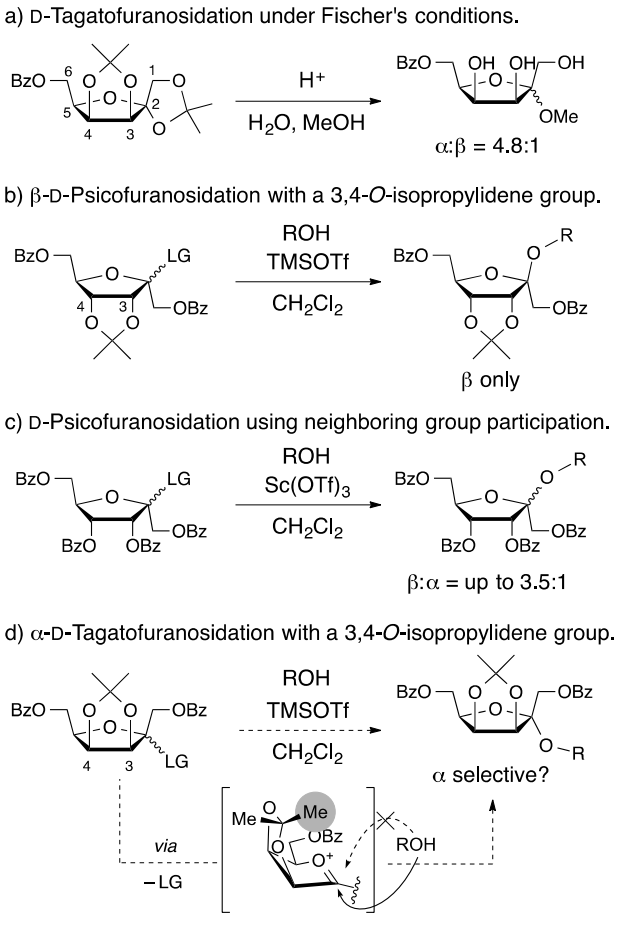


1. Introduction

D-Tagatose, the C4-stereoisomer of D-fructose, is a naturally occurring rare sugar,[1] which due to it being low-calorie in addition to its Generally Recognized As Safe status under the U.S. Food and Drug Administration, it is expected to be used as a low-calorie sweetener in foods and beverages.[2] Furthermore, phase 3 clinical trials for patients with type 2 diabetes mellitus have revealed that oral doses of D-tagatose do not change insulin levels and decrease serum glucose levels after oral glucose intake.[3] Although the natural occurrence of D-tagatose is quite limited, recent advances in the biological mass-production of D-tagatose from D-galactose using L-arabinose isomerase allow access to D-tagatose as a starting material.[4] Kato and co-workers have reported the synthesis of L-deoxygalactonojirimycin (L-DGJ), a non-competitive inhibitor of human lysosome α-galactosidase A, from D-tagatose in four steps.[5] However, there are not many literature studies that detail the synthesis of rare sugar derivatives despite the intensive biological studies that have been carried out on D-tagatose. One of the best ways to derivatize rare sugars is *via* the stereoselective glycosidation reaction of the rare sugar 2-ketohexofuranose. For example, the glycosidation of D-tagatofuranose under the Fischer glycosidation conditions was reported by Baráth et al. during their synthesis of transition state analog inhibitors for N-acetylglycosyltransferases (Scheme 1-a).[6] The glycosidation reaction of 6-*O*-benzoyl 1,2:3,4-di-*O*-isopropylidene-α-D-tagatofuranose was found to produce methyl 6-*O*-benzoyl D-tagatofuranoside, however, the α/β ratio was as low as 4.8:1. In addition, an attempt has been made to achieve direct Fischer glycosidation of D-tagatose that produced a complex mixture of pyranose and furanose sugars, alongside their α- and β-anomers. This results suggested that proper protection of D-tagatose is necessary to avoid the formation of pyranose sugars.[7] On the other hand, we previously reported the β-selective glycosidation of D-psicofuranose, a rare sugar and C3-epimer of D-fructofuranose, with a 3,4-*O*-isopropylidene protecting group (Scheme 1-b).[8] The reactions of 3,4-*O*-isopropylidene protected D-psicofuranose with various glycosyl acceptors proceeded smoothly to give the desired β-D-psicofuranosides as single isomers, while a strategy involving D-psicofuranosylation of the neighboring group with a 3-*O*-benzoyl group resulted in moderate β selectivities (β/α of

up to 3.5:1, Scheme 1-c).[9] Therefore, 3,4-*O*-isopropylidene protection strategies for the glycosidation of D-psicofuranose might be applicable and suitable for stereoselective construction of the α-glycosidic linkage of D-tagatofuranose and this approach would lead to the development of a new method for the synthesis of rare sugar derivatives (Scheme 1-d). In this reaction, glycosylation from the β-face is disfavored due to the interaction between one of the methyl group of 3,4-*O*-isopropylidene group. Herein, we report the α-selective glycosidation of D-tagatofuranose using a 3,4-*O*-isopropylidene-protected D-tagatofuranosyl donor.

Scheme 1. Glycosidation reactions of D-tagatofuranoses and D-psicofuranoses.

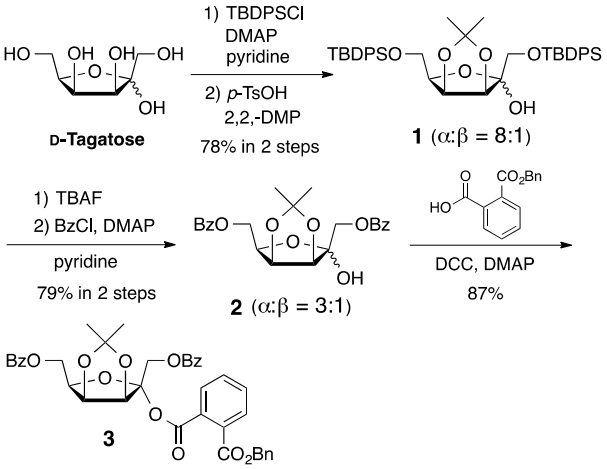


2. Results and discussion

Glycosyl donor **3** was synthesized from commercially available D-tagatose in five steps (Scheme 2). First,

the primary alcohol groups of D-tagatose were *tert*-butyldiphenylsilyl (TBDPS) protected and the secondary alcohol groups at the C3/C4 positions were protected with 3,4-*O*-isopropylidene groups to give furanose **1** in 78% yield in two steps. Replacement of the TBDPS groups with benzoyl groups *via* the treatment of **1** with tetrabutylammonium fluoride (TBAF) followed by benzoyl chloride afforded furanose **2** in 79% yield in two steps. It should be noted that (i) an attempt at the direct benzoylation of the primary alcohol groups of D-tagatose failed because of the predominant formation of 5-*O*-benzoylated pyranose form, which exists as it is the preferred conformation of D-tagatose over the furanose form[10] and (ii) the glycosidation reaction of the phthalate glycosyl donor (structure not shown) prepared from **1** and benzyl hydrogen phthalate did not produce any glycosylated products, possibly because of the steric bulkiness of the TBDPS ethers. Finally, esterification of the anomeric hydroxy group of **2** with Kim's benzyl hydrogen phthalate[11] using *N*,*N*'-dicyclohexylcarbodiimide (DCC) gave the D-tagatofuranosyl donor **3** in 87% yield as a single α-isomer.

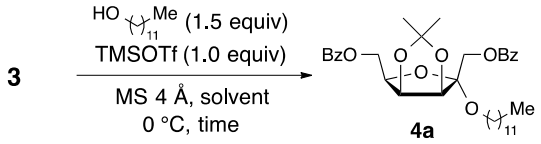
Scheme 2. Synthesis of the glycosyl donor **3**.



Next, the glycosyl donor **3** was subjected to glycosidation with 1-dodecanol in various solvents, as listed in Table 1. Due to the poor solubility of 1-dodecanol below 0 °C, the reaction was conducted at 0 °C in the presence of 4 Å molecular sieves using trimethylsilyl trifluoromethanesulfonate (TMSOTf) as a promoter. The use of less polar

solvents, such as CH_2Cl_2 (81%, entry 1) and toluene (72%, entry 2), resulted in better yields than those obtained from reaction in polar solvents such as MeCN (61%, entry 3), Et_2O (65%, entry 4), and THF (48%, entry 5), although, all of the reactions in any of the solvents afforded glycoside **4a** as a single isomer. The lower yields for the reaction in polar solvents could be caused by solvation of TMSOTf, because no glycosidation reaction occurred in DMF. Finally, CH_2Cl_2 was selected as the optimal solvent and used in the following D-tagatofuranosidation reactions.[12]

Table 1. Solvent screening of the D-tagatofuranosylation of 1-dodecanol.



entry	solvent	time (min)	temp.	yield (%)
1	CH_2Cl_2	30	0 °C	81
2	toluene	30	0 °C	72
3	MeCN	30	0 °C	61
4	Et_2O	30	0 °C	65
5	THF	120	0 °C to rt	48

Stereochemical assignment of the anomeric position of glycoside **4a** was performed using nuclear Overhauser effect spectroscopy (NOESY). Figure 1 shows selected NOESY correlations of **4a**. Since the key NOESY correlations were observed between the methylene protons of the 1-dodecyl group and the H-3/H-5 protons, respectively, the anomeric stereochemistry of **4a** was determined as being α-D-glycoside. Thus, the glycosidation of 3,4-*O*-isopropylidene-protected D-tagatofuranose **3** took place α-selectively.

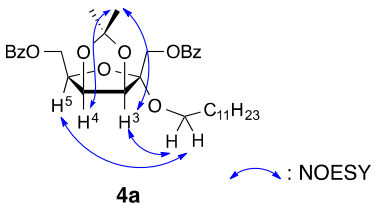
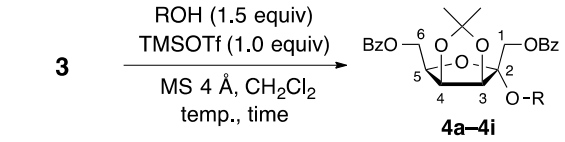
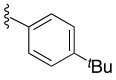
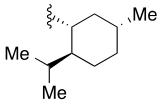
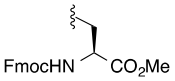
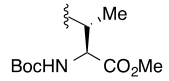


Figure 1. Selected NOESY correlations observed in D-tagatofuranoside **4a**.

Next, the substrate scope of different glycosyl acceptors for the glycosidation of **3** was investigated. The use of primary alcohols such as ethanol, 2,2,2-trifluoroethanol, and phenethyl alcohol gave the corresponding α-D-tagatofuranosides **4b**–**4d** in 73–83% yields (Table 2, entries 2–4). Secondary alcohol (cyclohexanol) and 4-*tert*-butylphenol can also be used as glycosyl acceptors for this D-tagatofuranosidation reaction to give the α-D-glycosides **4e** and **4f** in good yields (entries 5, 6). Glycosylation using alcohols with a stereogenic center such as (–)-menthol produced the desired α-glycoside **4g** selectively in 57% yield (entry 7). To consider future applications of rare sugars in glycopeptide chemistry, L-serine and L-threonine were introduced as glycosyl acceptors to afford the α-D-tagatofuranosylated amino acids **4h** and **4i** in 71 and 73% yields, respectively (entries 8, 9). To avoid the unwanted deprotection of the N-protecting groups of L-α-amino acids during glycosidation, the reaction was conducted at lower temperatures −40 to −30 °C, the results of which can be found in entries 8 and 9.

Table 2. Substrate scope of the glycosyl acceptor for the glycosidation of D-tagatofuranose **3**.



entry	R	product	temp. (°C)	time (h)	yield (%)
1		**4a**	0	0.5	81
2		**4b**	–20	0.5	77
3		**4c**	–20	0.5	73
4		**4d**	–20	1	83
5		**4e**	0	1	76
6		**4f**	–20	1	70
7		**4g**	–20	1	57
8		**4h**	–40	0.5	71
9		**4i**	–40 to –30	2	73

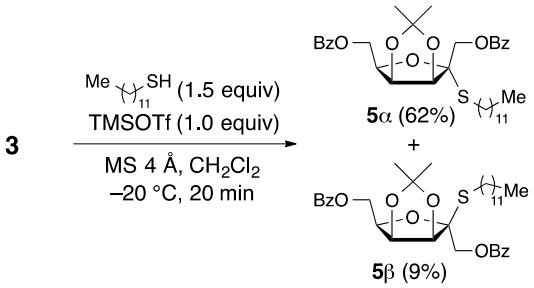
The stereochemistry of the anomeric position was determined by the empirical rule using the chemical shifts observed from ^{13}C NMR spectra, commonly used for hex-2-ulofuranoses.[10,13] Table 3 shows the chemical shifts in the ^{13}C NMR spectra of the sugar parts of the D-tagatofuranoses **1**–**3** as well as those of the D-tagatofuranosides **4a**–**4i**. The chemical shifts in the ^{13}C NMR spectra at the anomeric C2-carbon ($\delta_{C\text{-}2}$) of the α anomers of the D-tagatofuranosides were generally observed between 107–109 ppm, while those of the β anomers of the D-tagatofuranosides were found between 103–105 ppm. Since the C-2 chemical shifts in the ^{13}C NMR spectra of the synthesized D-tagatofuranosides **4a**–**4i** were observed between 106.7–109.5 ppm, the anomeric stereochemistries of **4a**–**4i** were assigned as α-D-glycosides. Although the C-2 chemical shifts in the ^{13}C NMR spectra of hemiacetals **1** and **2** are smaller than the values in empirical rule due to the absence of the aglycone, the $\delta_{C\text{-}2}$ of the α-anomer is lager than the $\delta_{C\text{-}2}$ of the β-anomer.[10,13d,13e]

Table 3. ^{13}C NMR chemical shifts of the D-tagatofuranosyl moieties of compounds **1**–**4**.

	δ_{C-1}	δ_{C-2}	δ_{C-3}	δ_{C-4}	δ_{C-5}	δ_{C-6}
1α	65.4	104.1	85.3	80.4	79.9	61.8
1β	68.0	102.8	80.1	80.5	78.8	62.1
2α	65.5	104.3	84.8	80.4	77.7	63.0
2β	65.4	102.3	79.8	80.3	75.7	63.4
3	63.3	111.2	84.5	80.3	80.8	63.1
4a	59.5	106.8	84.9	80.2	77.6	63.0
4b	59.6	106.9	84.9	80.2	77.7	62.9
4c	59.8	107.7	84.7	79.8	78.5	62.6
4d	59.8	106.7	84.8	80.1	77.5	62.7
4e	60.6	107.7	85.5	80.1	77.7	63.1
4f	60.7	109.5	85.7	79.9	78.3	62.9
4g	60.6	108.4	86.2	80.2	77.8	63.6
4h	61.5	107.1	84.7	80.0	78.2	62.9
4i	60.6	108.4	85.9	79.8	78.2	63.1

The glycosidation reaction of **3** using 1-dodecanethiol as a S-nucleophile was also investigated (Scheme 3). The reaction was observed to take place smoothly to give the desired S-glycoside **5** in 71% yield, albeit in a 7:1 ratio of α- and β-anomers. This moderate α-selectivity could be improved using isopropylidene protection rather than 3-pentylidene protection, in the same way as we previously succeeded in enhancing the β-selectivities of the S-glycosidation reaction of a D-psicofuranosyl donor.[14]

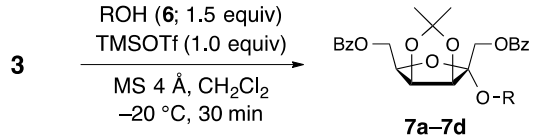
Scheme 3. S-Glycosidation reaction of D-tagatofuranose **3** using 1-dodecanethiol.

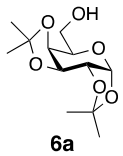
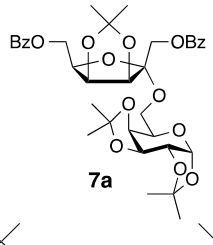
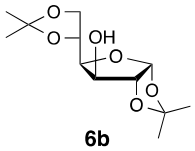
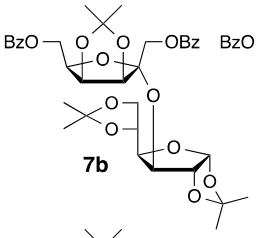
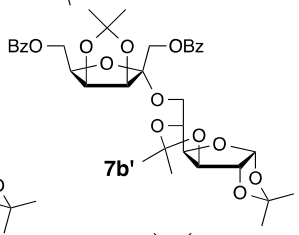
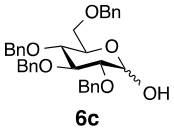
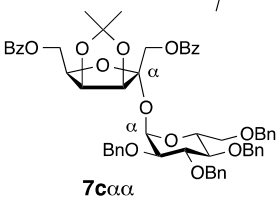
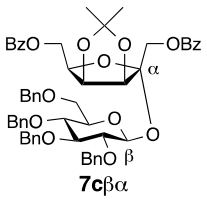
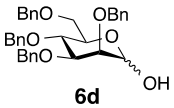
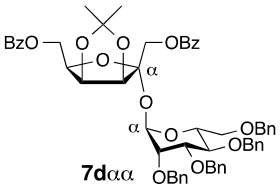
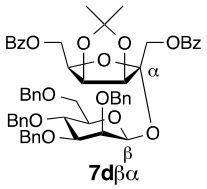


This glycosidation reaction was applied to the synthesis of α-D-tagatofuranosyl disaccharides, the results

of which are shown in Table 4. Glycosidation of **3** with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**6a**) produced the desired disaccharide **7a** as a single isomer in 81% yield (entry 1). On the other hand, the desired product **7b** was obtained in only 30% yield after the D-tagatofuranosylation of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**6b**, entry 2). This low yield was as a result of the formation of the undesired disaccharide **7b'** that has a glycosidic linkage on the O-6 position of the glucofuranose. The byproduct **7b'** was most likely obtained *via* the 5,6-*O*-isopropylidene group isomerization of **6b** to a 3,5-*O*-isopropylidene group prior to the glycosidation reaction. Entries 3 and 4 show the D-tagatofuranosylation of the anomeric hydroxy groups, namely the 2,3,4,6-tetra-*O*-benzyl-D-gluco- and D-mannopyranoses (**6c** and **6d**). Disaccharides **7a** and **7d** were obtained in 76% and 70% yields, respectively, in their selective α-D-furanosyl configurations, while the pyranose-anomeric configurations were a mixture of α and β anomers (9:1 ratio for **7c** and 4:1 ratio for **7d**). The anomeric stereochemistry of the glucopyranoside part of compounds **7cαα** and **7cβα** was determined based on their $J_{1,2}$ coupling constants ($J_{1,2}$ = 3.6 Hz for **7cαα** and $J_{1,2}$ = 8.1 Hz for **7cβα**), while that of the mannopyranoside part of compounds **7dαα** and **7dβα** was determined based on their chemical shifts in the ^{1}H NMR spectra ($\delta_{H\text{-}1}$ = 5.48 ppm for **7dαα** and 4.91 ppm for **7dβα**) by comparison to their D-psicofuranoside analogs ($\delta_{H\text{-}1}$ = 5.77 ppm for α-Man*p*-(1↔2)-β-Psi*f* and 4.94 ppm for β-Man*p*-(1↔2)-β-Psi*f*).[8c]

Table 4. Synthesis of α-D-tagatofuranosyl disaccharides.



entry	ROH	product	yield (%)
1	 **6a**	 **7a**	81
2	 **6b**	 **7b**  **7b'**	30 (**7b**) 41 (**7b'**)
3	 **6c**	 **7c**αα  **7c**βα	76 (αα:βα = 9:1)
4	 **6d**	 **7d**αα  **7d**βα	70 (αα:βα = 4:1)

3. Conclusions

The α-selective glycosidation of D-tagatofuranose was demonstrated for the first time using the 3,4-*O*-isopropylidene-protected D-tagatofuranosyl donor **3**, which was synthesized from commercially available D-tagatose in five steps. A variety of glycosyl acceptors, such as primary, secondary, and β-amino alcohols, and carbohydrates, were used to afford α-D-tagatofuranosides as single isomers, while the D-tagatofuranosylation of 1-dodecanethiol gave a mixture of α- and β-anomers (7:1 ratio). The use of this glycosidation method would lead to the synthesis of new D-tagatose derivatives as candidates for the preparation of fine chemicals, such as medicines and cosmetics. Further studies, including investigations into the functionality of the synthesized α-D-tagatofuranosides are

currently in progress in our group.

4. Experimental

4.1. General methods.

Melting points were taken on an AS ONE melting point apparatus ATM-01 and were uncorrected. Optical rotations were measured on a JASCO DIP-370 polarimeter using $CHCl_3$ as a solvent. ^1H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded on JEOL JNM-AL-400 (400 MHz) or Varian NMR System 500PS SN (500 MHz, 125 MHz, and 470 MHz) spectrometer. Chemical shifts (δ) are reported in parts per million (ppm). Tetramethylsilane and hexafluorobenzene were used as the internal reference (0.00 and –164.90 ppm in $CDCl_3$) for ^1H and ^{19}F NMR spectra, respectively, while the central solvent peak as the reference (77.0 ppm in $CDCl_3$) for ^{13}C NMR spectra. For the assignment of disaccharides NMR spectra, protons of aldose ring are numbered as 1', 2', etc for clarification. IR spectra were recorded on a Shimadzu IRAffinity-1 FT-IR spectrophotometer. High-resolution mass spectra (HRMS) were obtained on a JEOL JMS-T100TD using electrospray ionization (ESI) or direct analysis in real time (DART) ionization in TOF mode. Analytical thin layer chromatography (TLC) was performed with Merck Millipore pre-coated TLC plates, silica gel 60 F_{254}, layer thickness 0.25 mm. Compounds were observed in UV-light at 254 nm and then visualized by staining with iodine, *p*-anisaldehyde, or phosphomolybdic acid stain. Flash column chromatography separations were performed on Kanto Chemical silica gel 60N, spherical neutral, particle size 40-50 □m. All moisture sensitive reactions were conducted under an inert atmosphere. Reagents and solvents were commercial grade and were used as supplied, unless otherwise noted.

4.2. 1,6-Di-*O*-(*tert*-butyldiphenylsilyl)-3,4-*O*-isopropylidene-D-tagatofuranose (1): To a solution of D-tagatose (2.00 g, 11.1 mmol) in pyridine (74 mL) was added *tert*-butyldiphenylchlorosilane (TBDPSCl; 8.66 mL, 33.3 mmol) and 4-(dimethylamino)pyridine (DMAP; 271 mg, 2.22 mmol) at room temperature and the resultant mixture was

stirred at room temperature for 24 h. After quenching the reaction by adding 1 M HCl, the reaction mixture was extracted with EtOAc three times and the combined organic extracts were washed twice with sat. $NaHCO_3$ aq and twice with brine. After drying over anhydrous $MgSO_4$ and concentration under vacuum, the residue was passed through a short plug of silica gel (*n*-hexane, then 20% EtOAc in *n*-hexane) to give crude 1,6-di-*O*-(*tert*-butyldiphenylsilyl) D-tagatofuranose as a yellow oil [R_f = 0.51 (40% EtOAc in *n*-hexane)], which was used for the next step without further purification. A solution of the above triol in 2,2-dimethoxypropane (120 mL) was stirred at room temperature for 1 d and 50 °C for 2 h in the presence of *p*-TsOH·H_2O (2.74 g, 14.4 mmol). After cooling to room temperature, sat. $NaHCO_3$ aq was added to the reaction mixture, which was extracted with EtOAc twice. The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent, the residue was purified by flash column chromatography on silica gel (8% EtOAc in *n*-hexane) to give the desired product **1** (6.04 g, 78% in 2 steps, α/β = 8:1) as yellow oil. R_f = 0.72 (40% EtOAc in *n*-hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ (major isomer): 7.77–7.63 (8H, m, Ar*H*), 7.46–7.28 (12H, m, Ar*H*), 4.81 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.7 Hz, H-4), 4.55 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.31 (1H, ddd, $J_{5,6b}$ = 6.4, $J_{5,6a}$ = 6.2, $J_{4,5}$ = 3.7 Hz, H-5), 3.95 (1H, dd, $J_{6a,6b}$ = 10.3, $J_{5,6a}$ = 6.2 Hz, H-6a), 3.88 (1H, dd, $J_{6a,6b}$ = 10.3, $J_{5,6b}$ = 6.4 Hz, H-6b), 3.88 (1H, d, $J_{1a,1b}$ = 10.6 Hz, H-1a), 3.78 (1H, d, $J_{1a,1b}$ = 10.6 Hz, H-1b), 3.61 (1H, s, O*H*), 1.22 (3H, s, accetonide-CH_3), 1.16 (3H, s, accetonide-CH_3), 1.07 (9H, s, -(CH_3)$_3$), 1.06 (9H, s, -(CH_3)$_3$); δ (minor isomer): 7.77–7.63 (8H, m, Ar*H*), 7.46–7.28 (12H, m, Ar*H*), 4.84 (1H, dd, $J_{3,4}$ = 6.1, $J_{4,5}$ = 3.8 Hz, H-4), 4.70 (1H, d, $J_{3,4}$ = 6.1 Hz, H-3), 4.32 (1H, ddd, $J_{5,6a}$ = 6.9, $J_{5,6b}$ = 5.6, $J_{4,5}$ = 3.8 Hz, H-5), 3.94 (1H, dd, $J_{6a,6b}$ = 10.0, $J_{5,6a}$ = 6.9 Hz, H-6a), 3.85 (1H, dd, $J_{6a,6b}$ = 10.0, $J_{5,6b}$ = 5.6 Hz, H-6b), 3.83 (1H, d, $J_{1a,1b}$ = 10.7 Hz, H-1a), 3.72 (1H, d, $J_{1a,1b}$ = 10.7 Hz, H-1b), 3.31 (1H, s, O*H*), 1.47 (3H, s, accetonide-CH_3), 1.38 (3H, s, accetonide-CH_3), 1.09 (9H, s, -(CH_3)$_3$), 1.04 (9H, s, -(CH_3)$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ (major isomer): 135.73 (2C), 135.70 (2C), 135.69(2C), 135.5 (2C), 133.8, 133.6, 133.1, 132.7, 129.74, 129.73, 129.52, 129.49, 127.7 (2C), 127.64 (2C), 127.57 (2C), 127.48 (2C), 112.4, 104.1 (C-2), 85.3 (C-3), 80.4 (C-4), 79.9 (C-5), 65.4 (C-1), 61.8 (C-6), 26.82 (3C), 26.77 (3C), 25.9, 25.0, 19.29, 19.26; δ (minor isomer): 135.7–135.5

(4C), 135.63 (2C), 135.60 (2C), 133.8–132.7 (2C), 133.6, 132.8, 129.9, 129.80, 129.75 (2C), 127.82 (2C), 127.80 (2C), 127.7–127.5 (4C), 112.8, 102.8 (C-2), 80.5 (C-4), 80.1 (C-3), 78.8 (C-5), 68.0 (C-1), 62.1 (C-6), 26.9 (3C), 26.8 (3C), 26.0, 24.7, 19.24, 19.19. IR (film): 2932, 2859, 1427, 1113 cm^{-1}. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{41}H_{52}O_6Si_2Na$, 719.3200; found, 719.3193.

4.3. 1,6-Di-*O*-benzoyl-3,4-*O*-isopropylidene-D-tagatofuranose (2): To a solution of **1** (688 mg, 0.989 mmol) in THF (10 mL) was added tetrabutylammonium fluoride (TBAF; 1 M in THF, 1.98 mL, 1.98 mmol) solution at room temperature. After stirring for 1 d at room temperature, Dowex 50Wx8 (1.23 g), $CaCO_3$ (412 mg), MeOH (2.9 mL) were added to the reaction mixture, which was further stirred for 1 h at room temperature. The resultant suspension was filtered through a Celite pad and the filter cake was washed with MeOH. After concentration in vacuo, crude 3,4-*O*-isopropylidene-D-tagatofuranose was obtained and used for the next step without further purification. R_f = 0.11 (80% EtOAc in *n*-hexane). To a solution of the above triol and DMAP (60.5 mg, 0.495 mmol) in pyridine (2.6 mL)/CH_2Cl_2 (15 mL) was added benzoyl chloride (BzCl; 1.24 mL, 9.89 mmol) dropwise at 0 °C and the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was quenched by adding MeOH (1.2 mL) and stirred for further 20 min. After removal of solvent, the residue was partitioned into 1 M HCl aq and EtOAc layers. After extraction of aqueous layer by EtOAc twice, combined organic layers were washed with water followed by brine, and dried over anhydrous $MgSO_4$. The crude material was purified by flash column chromatography on silica gel (20% EtOAc in *n*-hexane) to afford dibenzoate **2** (335 mg, 79% in two steps, α/β = 3:1) as a colorless oil. R_f = 0.42 (40% EtOAc in *n*-hexane). ^1H NMR (500 MHz, $CDCl_3$) δ (major isomer): 8.12–8.05 (4H, m, Ar*H*), 7.64–7.53 (2H, m, Ar*H*), 7.50–7.39 (4H, m, Ar*H*), 4.95 (1H, dd, $J_{3,4}$ = 5.8, $J_{4,5}$ = 3.8 Hz, H-4), 4.73 (1H, dd, $J_{6a,6b}$ = 11.6, $J_{5,6a}$ = 4.0 Hz, H-6a), 4.67 (1H, d, $J_{3,4}$ = 5.8 Hz, H-3), 4.67 (1H, d, $J_{1a,1b}$ = 11.9 Hz, H-1a), 4.56 (1H, d, $J_{1a,1b}$ = 11.9 Hz, H-1b), 4.53 (1H, ddd, $J_{5,6b}$ = 7.3, $J_{5,6a}$ = 4.0, $J_{4,5}$ = 3.8 Hz, H-5), 4.47 (1H, dd, $J_{6a,6b}$ = 11.6, $J_{5,6b}$ = 7.3 Hz, H-6b), 3.10 (1H, br s, OH), 1.52 (3H, s, C*H*$_3$), 1.35 (3H, s, C*H*$_3$); δ (minor isomer): 8.12–8.01 (4H, m, Ar*H*), 7.64–7.53 (2H, m, Ar*H*),

7.50–7.39 (4H, m, Ar*H*), 4.94 (1H, dd, $J_{3,4}$ = 6.1, $J_{4,5}$ = 3.8 Hz, H-4), 4.68 (1H, dd, $J_{6a,6b}$ = 11.8, $J_{5,6a}$ = 7.6 Hz, H-6a), 4.64 (1H, d, $J_{3,4}$ = 6.1 Hz, H-3), 4.53 (1H, d, $J_{1a,1b}$ = 11.8 Hz, H-1a), 4.47 (1H, dd, $J_{6a,6b}$ = 11.8, $J_{5,6b}$ = 7.2 Hz, H-6b), 4.39 (1H, d, $J_{1a,1b}$ = 11.8 Hz, H-1b), 4.33 (1H, ddd, *J* = 7.6, 7.2, 3.8 Hz, H-5), 3.49 (1H, br s, OH), 1.60 (3H, s, C*H*$_3$), 1.41 (3H, s, C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ (major isomer): 166.9, 166.4, 133.3, 133.0, 130.1, 129.8 (2C), 129.7 (3C), 128.4 (2C), 128.3 (2C), 113.4, 104.3 (C-2), 84.8 (C-3), 80.4 (C-4), 77.7 (C-5), 65.45 (C-1), 63.0 (C-6), 26.1, 24.8; δ (minor isomer): 166.4, 166.1, 133.6, 133.0, 130.1–129.6 (4C), 129.9, 129.6, 128.5, 128.4–128.3 (2C), 128.4, 113.9, 102.3 (C-2), 80.3 (C-4), 79.8 (C-3), 75.7 (C-5), 65.35 (C-1), 63.4 (C-6), 25.9, 24.6. IR (film): 3437 (br), 2990, 1717, 1277 cm^{-1}. HRMS (DART) *m/z*: $[M + H - H_2O]^+$ calcd for $C_{23}H_{23}O_7$, 411.1444; found, 411.1426.

4.4. Benzyl (1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-D-tagatofuranosyl) phthalate (3): To a solution of furanose **2** (666 mg, 1.56 mmol) in CH_2Cl_2 (16 mL) were added benzyl hydrogen phthalate (1.20 g, 4.68 mmol), *N*,*N*'-dicyclohexylcarbodiimide (DCC; 966 mg, 4.68 mmol), and DMAP (191 mg, 1.56 mmol) at 0 °C, and the reaction mixture was gradually warmed to room temperature. After 1 d, the reaction mixture was filtered through a Celite pad and the filtrate was washed successively with 5% Na_2CO_3 aq, water and brine, and the organic layer was dried over anhydrous $MgSO_4$. The residue was purified by flash column chromatography on silica gel (30% EtOAc in *n*-hexane) to give glycosyl donor **3** (870 mg, 87%) as a colorless oil. R_f = 0.53 (5% Et_2O in $CHCl_3$). $[\alpha]^{29}_D$ = −2.3 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.08–8.01 (4H, m, Ar*H*), 7.83–7.77 (1H, m, Ar*H*), 7.65–7.60 (1H, m, Ar*H*), 7.55–7.47 (4H, m, Ar*H*), 7.41–7.27 (9H, m, Ar*H*), 5.37 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 5.30 (1H, d, *J* = 12.4 Hz, -C*H*HPh), 5.26 (1H, d, *J* = 12.4 Hz, -CH*H*Ph), 5.15 (1H, d, $J_{1a,1b}$ = 12.1 Hz, H-1a), 4.98 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 4.0 Hz, H-4), 4.88 (1H, d, $J_{1a,1b}$ = 12.1 Hz, H-1b), 4.73 (1H, dd, $J_{6a,6b}$ = 12.0, $J_{5,6a}$ = 4.0 Hz, H-6a), 4.62 (1H, ddd, $J_{5,6b}$ = 7.2, $J_{5,6a}$ = 4.0, $J_{4,5}$ = 4.0 Hz, H-5), 4.46 (1H, dd, $J_{6a,6b}$ = 12.0, $J_{5,6b}$ = 7.2 Hz, H-6b), 1.53 (3H, s, C*H*$_3$), 1.37 (3H, s, CC*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.6, 166.5, 166.3, 165.8, 135.4, 132.97, 132.95, 132.92, 131.7, 130.9, 130.5, 129.9, 129.79 (2C), 129.77 (2C), 129.3, 128.9, 128.5 (2C), 128.34, 128.26 (5C), 128.1 (2C), 113.6, 111.2 (C-2), 84.5

(C-3), 80.8 (C-5), 80.3 (C-4), 67.3, 63.3 (C-1), 63.1 (C-6), 26.0, 24.7. IR (film): 2989, 1732, 1717, 1273 cm^{-1}. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{38}H_{34}O_{11}Na$, 689.1999; found, 689.1989.

4.5. General procedure for the glycosidation: A suspension of glycosyl donor **3** (66.6 mg, 0.100 mmol), glycosyl acceptor (1.5 equiv), and powdered molecular sieves 4 Å (100 mg) in CH_2Cl_2 (5 mL) was stirred at room temperature for 30 min, prior to the addition of TMSOTf (0.5–2.0 equiv) at 0 °C. After completion of the reaction under the above-mentioned conditions, the reaction mixture was quenched with Et_3N (0.1 mL). The resultant suspension was filtered through a Celite pad and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (EtOAc in *n*-hexane) to give the desired product.

4.5.1. *n*-Dodecyl 1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranoside (4a): According to the general procedure of glycosidation, compound **4a** was obtained from glycosyl donor **3** and 1-dodecanol in 81% yield. White solid. Eluent for column: 7% EtOAc in *n*-hexane. R_f = 0.62 (5% Et_2O in $CHCl_3$). Mp: 36 °C. $[\alpha]^{19}_D$ = +25.0 (*c* 1.00, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ: 8.11–8.03 (4H, m, Ar*H*), 7.61–7.54 (2H, m, Ar*H*), 7.49–7.42 (4H, m, Ar*H*), 4.92 (1H, dd, $J_{4,5}$ = 5.9, $J_{3,4}$ = 3.9 Hz, H-4), 4.79 (1H, d, $J_{1a,1b}$ = 11.9 Hz, H-1a), 4.71 (1H, dd, $J_{6a,6b}$ = 11.8, $J_{5,6a}$ = 4.3 Hz, H-6a), 4.65 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.47 (1H, dd, $J_{6a,6b}$ = 11.8, $J_{5,6b}$ = 7.4 Hz, H-6b), 4.38 (1H, d, $J_{1a,1b}$ = 11.9 Hz, H-1b), 4.28 (1H, ddd, $J_{5,6b}$ = 7.4, $J_{5,6a}$ = 4.3, $J_{4,5}$ = 3.9 Hz, H-5), 3.58–3.45 (2H, m, -OC*H*$_2$CH$_2$-), 1.49 (3H, s, accetonide-C*H*$_3$), 1.54–1.43 (2H, m, -OCH$_2$C*H*$_2$-), 1.34 (3H, s, accetonide-C*H*$_3$), 1.30–1.12 (m, 18H, -C*H*$_2$-), 0.88 (3H, t, *J* = 7.0 Hz, -CH$_2$C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.3, 165.9, 133.03, 132.98, 130.03, 129.98, 129.8 (2C), 129.7 (2C), 128.34 (2C), 128.31 (2C), 113.2, 106.8 (C-2), 84.9 (C-3), 80.2 (C-4), 77.6 (C-5), 63.0 (C-6), 61.2, 59.5 (C-1), 31.9, 29.7, 29.64, 29.59, 29.55, 29.54, 29.4, 29.3, 26.3, 26.1, 24.8, 22.7, 14.1. IR (film): 2926, 2855, 1718 cm^{-1}. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{35}H_{48}O_8Na$, 619.3247; found, 619.3275.

4.5.2. Ethyl 1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranoside (4b): According to the general procedure of glycosidation, compound **4b** was obtained from glycosyl donor **3** and ethanol in 77% yield. White solids. Eluent for column: 10% EtOAc in *n*-hexane. R_f = 0.66 (40% EtOAc in *n*-hexane). Mp: 35–36 °C. $[\alpha]^{21}_D$ = +24.6 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.13–8.03 (4H, m, Ar*H*), 7.63–7.53 (2H, m, Ar*H*), 7.51–7.39 (4H, m, Ar*H*), 4.92 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.9 Hz, H-4), 4.82 (1H, d, $J_{1a,1b}$ = 11.8 Hz, H-1a), 4.71 (1H, dd, $J_{6a,6b}$ = 11.8, $J_{5,6a}$ = 4.4 Hz, H-6a), 4.64 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.48 (1H, dd, $J_{6a,6b}$ = 11.8, $J_{5,6b}$ = 7.3 Hz, H-6b), 4.38 (1H, d, $J_{1a,1b}$ = 11.8 Hz, H-1b), 4.29 (1H, ddd, $J_{5,6b}$ = 7.3, $J_{5,6a}$ = 4.4, $J_{4,5}$ = 3.9 Hz, H-5), 3.61 (2H, q, *J* = 7.1 Hz, -OC*H*$_2$CH$_3$), 1.50 (3H, s, accetonide-C*H*$_3$), 1.34 (3H, s, accetonide-C*H*$_3$), 1.13 (t, *J* = 7.1 Hz, 3H, -OCH$_2$C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.3, 165.9, 133.04, 133.00, 130.04, 129.98, 129.8 (2C), 129.7 (2C), 128.4 (2C), 128.3 (2C), 113.2, 106.9 (C-2), 84.9 (C-3), 80.2 (C-4), 77.7 (C-5), 62.9 (C-6), 59.6 (C-1), 56.9, 26.1, 24.8, 15.3. IR (KBr): 2982, 1719, 1277 cm^{-1}. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{25}H_{28}O_8Na$, 479.1682; found, 479.1697.

4.5.3. 2,2,2-Trifluoroethyl 1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranoside (4c): According to the general procedure of glycosidation, compound **4c** was obtained from glycosyl donor **3** and 2,2,2-trifluoroethanol in 73% yield. Colorless oil. Eluent for column: 10% EtOAc in *n*-hexane. R_f = 0.66 (40% EtOAc in *n*-hexane). $[\alpha]^{20}_D$ = +39.0 (*c* 1.04, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.10–8.02 (4H, m, Ar*H*), 7.62–7.55 (2H, m, Ar*H*), 7.50–7.42 (4H, m, Ar*H*), 4.96 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.9 Hz, H-4), 4.74 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.71 (1H, d, $J_{1a,1b}$ = 12.3 Hz, H-1a), 4.68 (1H, dd, $J_{6a,6b}$ = 11.9, $J_{5,6a}$ = 4.3 Hz, H-6a), 4.51 (1H, dd, $J_{6a,6b}$ = 11.9, $J_{5,6b}$ = 7.4 Hz, H-6b), 4.44 (1H, d, $J_{1a,1b}$ = 12.3 Hz, H-1b), 4.38 (1H, ddd, $J_{5,6b}$ = 7.4, $J_{5,6a}$ = 4.3, $J_{4,5}$ = 3.9 Hz, H-5), 4.06–3.92 (2H, m, -OC*H*$_2$CF$_3$), 1.51 (3H, s, accetonide-C*H*$_3$), 1.35 (3H, s, accetonide-C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.2, 165.8, 133.2, 133.1, 129.81, 129.78 (2C), 129.65 (2C), 129.69, 128.43 (2C), 128.40 (2C), 123.8 (q, *J* = 277.3 Hz), 113.6, 107.7 (C-2), 84.7 (C-3), 79.8 (C-4), 78.5 (C-5), 62.6 (C-6), 59.8 (C-1), 59.7 (q, *J* = 35.6 Hz), 26.0, 24.7. ^{19}F NMR (470 MHz, $CDCl_3$) δ: –77.1 (t, *J* = 8.7 Hz). IR (KBr): 2991, 2957, 1728, 1275 cm^{-1}. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for

$C_{25}H_{25}F_3O_8Na$, 533.1399; found, 533.1378.

4.5.4. Phenethyl 1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranoside (4d): According to the general procedure of glycosidation, compound **4d** was obtained from glycosyl donor **3** and phenethyl alcohol in 83% yield. White solid. Eluent for column: 15% EtOAc in *n*-hexane. R_f = 0.63 (40% EtOAc in *n*-hexane). Mp: 117 °C. $[\alpha]^{25}_D$ = +31.5 (*c* 1.04, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.10–8.01 (4H, m, Ar*H*), 7.62–7.54 (2H, m, Ar*H*), 7.50–7.42 (4H, m, Ar*H*), 7.18–7.11 (4H, m, Ar*H*), 7.11–7.06 (1H, m, Ar*H*), 4.76 (1H, d, $J_{1a,1b}$ = 11.9 Hz, H-1a), 4.74 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.9 Hz, H-4), 4.61 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.57 (1H, dd, $J_{6a,6b}$ = 11.8, $J_{5,6a}$ = 4.3 Hz, H-6a), 4.36 (1H, d, $J_{1a,1b}$ = 11.9 Hz, H-1b), 4.35 (1H, dd, $J_{6a,6b}$ = 11.8, $J_{5,6b}$ = 7.2 Hz, H-6b), 3.83–3.73 (2H, m, -OC*H*$_2$CH$_2$-), 3.68 (1H, ddd, $J_{5,6b}$ = 7.2, $J_{5,6a}$ = 4.3, $J_{4,5}$ = 3.9 Hz, H-5), 2.85–2.73 (2H, m, -C*H*$_2$Ph), 1.46 (3H, s, C*H*$_3$), 1.31 (3H, s, C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.1, 165.9, 139.1, 133.03, 133.00, 130.02, 129.97, 129.8 (2C), 129.7 (2C), 128.9 (2C), 128.3 (4C), 128.2 (2C), 126.2, 113.1, 106.7 (C-2), 84.8 (C-3), 80.1 (C-4), 77.5 (C-5), 62.7 (C-6), 62.0, 59.8 (C-1), 36.2, 26.1, 24.8. IR (film): 2989, 2360, 1718, 1274 cm^{-1}. HRMS (DART) *m/z*: $[M + Na]^+$ calcd for $C_{31}H_{32}O_8Na$, 555.1995; found, 555.2014.

4.5.5. Cyclohexyl 1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranoside (4e): According to the general procedure of glycosidation, compound **4e** was obtained from glycosyl donor **3** and cyclohexanol in 76% yield. Colorless oil. Eluent for column: 10% EtOAc in *n*-hexane. R_f = 0.59 (5% Et_2O in $CHCl_3$). $[\alpha]^{19}_D$ = −3.3 (*c* 1.02, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.12–8.02 (4H, m, Ar*H*), 7.61–7.54 (2H, m, Ar*H*), 7.50–7.41 (4H, m, Ar*H*), 4.90 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.3 Hz, H-4), 4.75–4.66 (1H, m, H-5), 4.65 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.63 (1H, d, $J_{1a,1b}$ = 12.0 Hz, H-1a), 4.52–4.42 (2H, m, H-6), 4.47 (1H, d, $J_{1a,1b}$ = 12.0 Hz, H-1b), 3.84 (1H, ddd, *J* = 13.6, 9.2, 3.6 Hz, -OC*H*(CH$_2$)$_2$-), 1.94–1.86 (1H, m), 1.74–1.59 (3H, m), 1.55–1.49 (1H, m), 1.47 (3H, s, -C*H*$_3$), 1.31 (3H, s, -C*H*$_3$), 1.36–1.07 (5H, m). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.3, 165.9, 133.02, 132.98, 130.1, 130.0, 129.8 (2C), 129.6

(2C), 128.4 (2C), 128.3 (2C), 113.0, 107.7 (C-2), 85.5 (C-3), 80.1 (C-4), 77.7 (C-5), 70.9, 63.1 (C-6), 60.6 (C-1), 34.3, 33.9, 26.1, 25.4, 24.8, 24.44, 24.37. IR (film): 2935, 1724, 1276 cm^{-1}. HRMS (DART) *m/z*: $[M+NH_4]^+$ calcd for $C_{29}H_{38}NO_8$, 528.2597; found, 528.2581.

4.5.6. 4-*tert*-Butylphenyl 1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranoside (4f): According to the general procedure of glycosidation, compound **4f** was obtained from glycosyl donor **3** and 4-*tert*-butylphenol in 70% yield. White solids. Eluent for column: 13% EtOAc in *n*-hexane. R_f = 0.73 (5% Et_2O in $CHCl_3$). Mp: 110–111 °C. $[\alpha]^{25}_D$ = +5.7 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.15–8.09 (2H, m, Ar*H*), 8.09–8.04 (2H, m, Ar*H*), 7.63–7.55 (2H, m, Ar*H*), 7.51–7.43 (4H, m, Ar*H*), 7.19–7.13 (2H, m, Ar*H*), 7.09–7.03 (2H, m, Ar*H*), 5.03 (1H, dd, $J_{3,4}$ = 5.8, $J_{4,5}$ = 3.7 Hz, H-4), 4.96 (1H, d, $J_{3,4}$ = 5.8 Hz, H-3), 4.79 (1H, dd, $J_{6a,6b}$ = 11.7, $J_{5,6a}$ = 3.6 Hz, H-6a), 4.70 (1H, ddd, $J_{5,6b}$ = 8.1, $J_{4,5}$ = 3.7, $J_{5,6a}$ = 3.6 Hz, H-5), 4.57 (1H, d, $J_{1a,1b}$ = 11.8 Hz, H-1a), 4.56 (1H, dd, $J_{6a,6b}$ = 11.7, $J_{5,6b}$ = 8.1 Hz, H-6b), 4.44 (1H, d, $J_{1a,1b}$ = 11.8 Hz, H-1b), 1.50 (3H, s, accetonide-C*H*$_3$), 1.35 (3H, s, accetonide-C*H*$_3$), 1.24 (9H, s, -(C*H*$_3$)$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.2, 165.6, 150.7, 146.7, 133.1, 133.00, 129.96, 129.7 (5C), 128.4 (4C), 126.1 (2C), 121.0 (2C), 113.5, 109.5 (C-2), 85.7 (C-3), 79.9 (C-4), 78.3 (C-5), 62.9 (C-6), 60.7 (C-1), 34.2, 31.4 (3C), 26.1, 24.9. IR (KBr): 2959, 1730, 1717 cm^{-1}. HRMS (DART) *m/z*: $[M+NH_4]^+$ calcd for $C_{33}H_{40}NO_8$, 578.2754; found, 578.2778.

4.5.7. (–)-Menthyl 1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranoside (4g): According to the general procedure of glycosidation, compound **4g** was obtained from glycosyl donor **3** and (–)-menthol in 57% yield. White solids. Eluent for column: 7% EtOAc in *n*-hexane. R_f = 0.59 (40% EtOAc in *n*-hexane). Mp: 104 °C. $[\alpha]^{24}_D$ = –1.72 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.10–8.04 (4H, m, Ar*H*), 7.60–7.53 (2H, m, Ar*H*), 7.47–7.39 (4H, m, Ar*H*), 4.91 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.9 Hz, H-4), 4.74 (1H, dd, $J_{6a,6b}$ = 12.1, $J_{5,6a}$ = 2.8 Hz, H-6a), 4.73 (1H, d, $J_{1a,1b}$ = 12.1 Hz, H-1a), 4.68 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.54 (1H, ddd, $J_{5,6b}$ = 8.4, $J_{4,5}$ = 3.9, $J_{5,6a}$ = 2.8 Hz, H-5), 4.48 (1H, d,

$J_{1a,1b}$ = 12.1 Hz, H-1b), 4.40 (1H, dd, $J_{6a,6b}$ = 12.1, $J_{5,6b}$ = 8.4 Hz, H-6b), 3.64 (1H, td, J = 10.3, 4.4 Hz), 2.44–2.36 (1H, m), 2.36–2.27 (1H, m), 1.61–1.53 (2H, m), 1.45 (3H, s, accetonide-CH_3), 1.37–1.30 (1H, m), 1.29 (3H, s, accetonide-CH_3), 1.20–1.12 (1H, m), 1.01–0.87 (2H, m), 0.84–0.74 (1H, m), 0.79 (3H, d, J = 7.0 Hz), 0.73 (3H, d, J = 6.5 Hz), 0.42 (3H, d, J = 6.9 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.3, 166.0, 133.02, 139.97, 130.01, 129.97, 129.7 (4C), 128.3 (2C), 128.2 (2C), 112.9, 108.4 (C-2), 86.2 (C-3), 80.2 (C-4), 77.8 (C-5), 73.8, 63.6 (C-6), 60.6 (C-1), 48.5, 42.8, 34.2, 31.4, 26.1, 24.9, 24.8, 23.1, 22.1, 21.3, 16.1. IR (KBr): 2957, 2928, 1724, 1275 cm^{-1}. HRMS (ESI) *m/z*: [M + Na]$^+$ calcd for $C_{33}H_{42}O_8Na$, 589.2777; found, 589.2753.

4.5.8.

***N*-(9-Fluorenylmethoxycarbonyl)-*O*-(1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranosyl)-L-serine methyl ester (4h):** According to the general procedure of glycosidation, compound **4h** was obtained from glycosyl donor **3** and ethanol in 71% yield. Colorless oil. Eluent for column: 30% EtOAc in *n*-hexane. R_f = 0.49 (40% EtOAc in *n*-hexane). $[\alpha]^{20}_D$ = +28.4 (*c* 1.06, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.09–8.03 (2H, m, Ar*H*), 8.03–7.98 (2H, m, Ar*H*), 7.75–7.70 (2H, m, Ar*H*), 7.59–7.53 (1H, m, Ar*H*), 7.53–7.49 (1H, m, Ar*H*), 7.49–7.41 (4H, m, Ar*H*), 7.41–7.34 (4H, m, Ar*H*), 7.29–7.23 (2H, m, Ar*H*), 5.63 (1H, d, J = 7.9 Hz, N*H*), 4.90 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.9 Hz, H-4), 4.79 (1H, d, $J_{1a,1b}$ = 12.0 Hz, H-1a), 4.66 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.57 (1H, dd, $J_{6a,6b}$ = 12.0, $J_{5,6a}$ = 3.7 Hz, H-6a), 4.53 (1H, ddd, J = 7.9, 3.4, 3.2 Hz, -NHC*H*-), 4.44 (1H, dd, $J_{6a,6b}$ = 12.0, $J_{5,6b}$ = 7.7 Hz, H-6b), 4.36 (1H, d, $J_{1a,1b}$ = 12.0 Hz, H-1b), 4.33 (1H, dd, J = 10.4, 7.0 Hz, ArCHC*H*H-), 4.24 (1H, ddd, $J_{5,6b}$ = 7.7, $J_{4,5}$ = 3.9, $J_{5,6a}$ = 3.7 Hz, 1H), 4.17 (1H, dd, J = 10.4, 7.3 Hz, ArCHCH*H*-), 4.12 (1H, dd, J = 7.3, 7.0 Hz, ArC*H*), 3.98 (1H, dd, J = 9.7, 3.4 Hz, -NHCHC*H*H-), 3.95 (1H, dd, J = 9.7, 3.2 Hz, -NHCHCH*H*-), 3.46 (3H, s, -CO_2CH_3), 1.49 (3H, s, accetonide-CH_3), 1.34 (3H, s, accetonide-CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.4, 166.2, 165.7, 155.6, 143.7, 141.2, 133.2, 133.0, 129.8 (3C), 129.74, 129.69 (3C), 128.4 (2C), 128.3 (3C), 127.6 (2C), 127.0, 126.9, 125.0, 124.8, 119.9 (2C), 113.4, 107.1 (C-2), 84.7 (C-3), 80.0 (C-4), 78.2 (C-5), 67.1, 62.9 (C-6), 61.5 (C-1), 59.4, 53.9, 52.4, 46.9, 26.0, 24.7. IR

(KBr): 3368, 2955, 1719, 1275 cm^{-1}. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{42}H_{41}NO_{12}Na$, 774.2526; found, 774.2520.

4.5.9. *N*-(*tert*-Butoxycarbonyl)-*O*-(1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranosyl)-L-threonine methyl ester (4i): According to the general procedure of glycosidation, compound **4i** was obtained from glycosyl donor **3** and ethanol in 73% yield. White solids. Eluent for column: 25% EtOAc in *n*-hexane. R_f = 0.29 (5% Et_2O in $CHCl_3$). Mp: 148 °C. $[\alpha]^{24}_D$ = +30.1 (*c* 1.01, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ: 8.08–8.01 (4H, m, Ar*H*), 7.60–7.54 (2H, m, Ar*H*), 7.49–7.41 (4H, m, Ar*H*), 5.20 (1H, d, *J* = 9.7 Hz, N*H*), 4.89 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.6 Hz, H-4), 4.75–4.66 (1H, m, H-6a), 4.63 (1H, qd, *J* = 6.2, 2.1 Hz, -C*H*CH_3), 4.62 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.57 (1H, d, $J_{1a,1b}$ = 12.1 Hz, H-1a), 4.51 (1H, d, $J_{1a,1b}$ = 12.1 Hz, H-1b), 4.48–4.44 (1H, m, H-5), 4.46–4.42 (1H, m, H-6b), 4.24 (1H, dd, *J* = 9.7, 2.1 Hz, -NHC*H*-), 3.37 (3H, s, -CO_2CH_3), 1.44 (9H, s, -C(C*H*$_3$)$_3$), 1.44 (3H, s, accetonide-C*H*$_3$), 1.35 (3H, d, *J* = 6.2 Hz, -CHC*H*$_3$), 1.26 (3H, s, accetonide-C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.8, 166.3, 165.8, 156.0, 133.10, 133.07, 129.90 (2C), 129.85, 129.83, 129.6 (2C), 128.38 (2C), 128.36 (2C), 113.1, 108.4 (C-2), 85.9 (C-4), 80.1, 79.8 (C-4), 78.2 (C-5), 69.5, 63.1 (C-6), 60.6 (C-1), 58.9, 52.2, 28.3, 26.0, 24.7, 19.2. IR (KBr): 3472, 2968, 1719 cm^{-1}. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{33}H_{41}NO_{12}Na$, 666.2526; found, 666.2546.

4.6. *n*-Dodecyl 1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-2-thio-α- and β-D-tagatofuranoside (5α and 5β): According to the general procedure of glycosidation, compounds **5α** and **5β** was obtained from glycosyl donor **3** and ethanol in 62% and 9% yields, respectively. **5α**: Colorless oil. Eluent for column: 5% EtOAc in *n*-hexane. R_f = 0.68 (20% EtOAc in *n*-hexane). $[\alpha]^{24}_D$ = +47.1 (*c* 1.18, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ: 8.13–8.02 (4H, m, Ar*H*), 7.61–7.52 (2H, m, Ar*H*), 7.50–7.39 (4H, m, Ar*H*), 4.93 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.5 Hz, H-4), 4.79 (1H, d, $J_{1a,1b}$ = 11.5 Hz, H-1a), 4.76 (1H, dd, $J_{6a,6b}$ = 10.6, $J_{5,6a}$ = 2.8 Hz, H-6a), 4.59–4.47 (4H, m, H-1b, 3, 5, 6b), 2.67–2.51 (2H, m, -SC*H*$_2$-), 1.56–1.47 (2H, m), 1.50 (3H, s, accetonide-C*H*$_3$), 1.33 (3H, s, accetonide-C*H*$_3$), 1.31–1.13 (18H, m), 0.88

(3H, t, J = 7.0 Hz, -CH_2CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.2, 165.9, 133.0, 132.9, 130.2, 129.9, 129.8 (2C), 129.7 (2C), 128.33 (2C), 128.30 (2C), 113.3, 94.3 (C-2), 85.9 (C-3), 80.7 (C-4), 78.0 (C-5), 63.1 (C-1), 62.6 (C-6), 31.9, 29.64, 29.62, 29.59, 29.51, 29.50, 29.3, 29.2, 29.1, 27.8, 25.9, 24.8, 22.7, 14.1. IR (neat): 2926, 2855, 1728 cm^{-1}. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{35}H_{48}NO_7SNa$, 635.3018; found, 635.2993. **5β**: Colorless oil. Eluent for column: 10% EtOAc in *n*-hexane. R_f = 0.57 (20% EtOAc in *n*-hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.09–8.00 (4H, m, Ar*H*), 7.61–7.53 (2H, m, Ar*H*), 7.49–7.40 (4H, m, Ar*H*), 5.01 (1H, dd, $J_{3,4}$ = 6.3, $J_{4,5}$ = 4.3 Hz, H-4), 4.92 (1H, d, $J_{3,4}$ = 6.3 Hz, H-3), 4.74–4.67 (1H, m, H-6a), 4.62–4.55 (2H, m, H-5, 6b), 4.55 (1H, d, $J_{1a,1b}$ = 11.8 Hz, H-1a), 4.51 (1H, d, $J_{1a,1b}$ = 11.8 Hz, H-1b), 2.82 (1H, ddd, J = 11.7, 8.3, 6.8 Hz, -SC*H*H-), 2.75 (1H, ddd, J = 11.7, 8.2, 6.9 Hz, -SCH*H*-), 1.63 (3H, s, accetonide-CH_3), 1.63–1.57 (2H, m), 1.37 (3H, s, accetonide-CH_3), 1.35–1.19 (18H, m), 0.88 (3H, t, J = 7.0 Hz, -CH_2CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.4, 165.9, 133.4, 133.0, 130.0, 129.73 (2C), 129.69 (2C), 129.5, 128.6 (2C), 128.3 (2C), 114.5, 93.1 (C-2), 84.6 (C-3), 81.1 (C-4), 79.3 (C-5), 67.1 (C-1), 64.0 (C-6), 31.9, 29.8, 29.65, 29.63, 29.58, 29.52, 29.3, 29.2, 29.1, 28.4, 25.5, 24.6, 22.7, 14.1. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{35}H_{48}NO_7SNa$, 635.3018; found, 635.3023.

4.7.1

6-*O*-(1,6-Di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (7a): According to the general procedure of glycosidation, compound **7a** was obtained from glycosyl donor **3** and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**6a**) in 81% yield. Colorless oil. Eluent for column: 20% EtOAc in *n*-hexane. R_f = 0.38 (5% Et_2O in $CHCl_3$). $[\alpha]^{24}_D$ = +3.62 (*c* 1.04, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.13–8.02 (4H, m, Ar*H*), 7.60–7.51 (2H, m, Ar*H*), 7.47–7.39 (4H, m, Ar*H*), 5.46 (1H, d, $J_{1',2'}$ = 5.0 Hz, H-1'), 4.93 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.8 Hz, H-4), 4.81 (1H, d, $J_{1a,1b}$ = 11.7 Hz, H-1a), 4.71 (1H, dd, $J_{6a,6b}$ = 11.6, $J_{5,6a}$ = 3.4 Hz, H-6a), 4.69 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.50 (1H, ddd, $J_{5,6b}$ = 7.6, $J_{4,5}$ = 3.8, $J_{5,6a}$ = 3.4 Hz, H-5), 4.50 (1H, dd, $J_{3',4'}$ = 7.9, $J_{2',3'}$ = 2.5 Hz, H-3'), 4.45 (1H, dd, $J_{6a,6b}$ = 11.6, $J_{5,6b}$ = 7.6 Hz, H-6b), 4.36 (1H, $J_{1a,1b}$ = 11.7 Hz, H-1b), 4.25 (1H,

dd, $J_{1',2'}$ = 5.0, $J_{2',3'}$ = 2.5 Hz, H-2'), 4.19 (1H, dd, $J_{3',4'}$ = 7.9, $J_{4',5'}$ = 2.0 Hz, H-5'), 3.84 (1H, ddd, $J_{5',6b'}$ = 7.0, $J_{5',6a'}$ = 4.8, $J_{4',5'}$ = 2.0 Hz, H-5'), 3.76 (1H, dd, $J_{6a',6b'}$ = 10.2, $J_{5',6a'}$ = 4.8 Hz, H-6a'), 3.71 (1H, dd, $J_{6a',6b'}$ = 10.2, $J_{5',6b'}$ = 7.0 Hz, H-6b'), 1.48 (3H, s), 1.41 (3H, s), 1.33 (3H, s), 1.29 (3H, s), 1.28 (3H, s), 1.12 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.3, 165.8, 132.9 (2C), 130.2, 130.1, 129.8 (2C), 129.7 (2C), 128.3 (4C), 113.1, 109.2, 108.4, 107.0, 96.3, 84.9, 80.2, 77.9, 71.2, 70.6, 70.4, 67.2, 63.1, 60.9, 60.0, 26.1, 25.9, 25.8, 24.9 (2C), 24.2. IR (film): 2989, 1722 cm^{-1}. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{35}H_{42}O_{13}Na$, 693.2523; found, 693.2525.

4.7.2

4-*O*-(1,6-Di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (7b) and 6-*O*-(1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranosyl)-1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose (7b'): According to the general procedure of glycosidation, compounds **7b** and **7b'** were obtained from glycosyl donor **3** and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**6b**) in 30% and 41% yields, respectively. **7b:** Colorless oil. Eluent for column: 20% EtOAc in *n*-hexane. R_f = 0.15 (5% Et_2O in $CHCl_3$). $[\alpha]^{22}_D$ = +8.9 (*c* 1.01, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.14–8.03 (4H, m, Ar*H*), 7.62–7.52 (2H, m, Ar*H*), 7.48–7.38 (4H, m, Ar*H*), 5.81 (1H, d, $J_{1',2'}$ = 3.6 Hz, H-1'), 4.92 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.6 Hz, H-4), 4.80 (1H, d, $J_{1',2'}$ = 3.6 Hz, H-2'), 4.79 (1H, d, $J_{1a,1b}$ = 12.3 Hz, H-1a), 4.75 (1H, dd, $J_{6a,6b}$ = 11.3, $J_{5,6a}$ = 2.4 Hz, H-6a), 4.71 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.53 (1H, d, $J_{1a,1b}$ = 12.3 Hz, H-1b), 4.48 (1H, d, $J_{3',4'}$ = 3.1 Hz, H-3'), 4.47 (1H, dd, $J_{6a,6b}$ = 11.3, $J_{5,6b}$ = 8.0 Hz, H-6b), 4.43 (1H, ddd, $J_{5,6b}$ = 8.0, $J_{4,5}$ = 3.6, $J_{5,6a}$ = 2.4 Hz, H-5), 4.30 (1H, ddd, $J_{4',5'}$ = 7.6, $J_{5',6b'}$ = 6.2, $J_{5',6a'}$ = 4.7 Hz, H-5'), 4.11 (1H, dd, $J_{4',5'}$ = 7.6, $J_{3',4'}$ = 3.1 Hz, H-4'), 4.01 (1H, dd, $J_{6a',6b'}$ = 8.6, $J_{5',6a'}$ = 4.7 Hz, H-6a'), 3.95 (1H, dd, $J_{6a',6b'}$ = 8.6, $J_{5',6b'}$ = 6.2 Hz, H-6b'), 1.48 (3H, s), 1.43 (3H, s), 1.31 (3H, s), 1.27 (3H, s), 1.07 (3H, s), 1.01 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.3, 165.6, 133.2, 133.0, 130.0, 129.8 (2C), 129.8, 129.7 (2C), 128.4 (2C), 128.3 (2C), 113.5, 111.7, 109.0, 108.9, 104.8, 85.7, 82.9, 80.3, 79.9, 78.6, 76.2, 72.2, 66.6, 63.1, 60.7, 26.8, 26.7, 26.0, 25.9, 24.9, 24.7. IR (KBr): 2988, 2938,

1719 cm^{-1}. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{35}H_{42}O_{13}Na$, 693.2523; found, 693.2527. **7b':** Colorless oil. Eluent for column: 15% EtOAc in *n*-hexane. R_f = 0.24 (5% Et_2O in $CHCl_3$). $[\alpha]^{23}_D$ = +41.8 (*c* 1.01, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ: 8.13–8.03 (4H, m, Ar*H*), 7.62–7.53 (2H, m, Ar*H*), 7.49–7.41 (4H, m, Ar*H*), 5.93 (1H, d, $J_{1',2'}$ = 3.7 Hz, H-1'), 4.88 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.3 Hz, H-4), 4.75–4.70 (1H, m, H-6a), 4.68 (1H, d, $J_{1a,1b}$ = 11.9 Hz, H-1a), 4.68 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.51 (1H, d, $J_{1',2'}$ = 3.7 Hz, H-2'), 4.50–4.43 (2H, m, H-5, 6b), 4.43 (1H, d, $J_{1a,1b}$ = 11.9 Hz, H-1b), 4.21 (1H, dd, $J_{4',5'}$ = 7.2, $J_{3',4'}$ = 3.7 Hz, H-4'), 4.09 (1H, d, $J_{3',4'}$ = 3.7 Hz, H-3'), 3.78 (1H, dd, $J_{6a',6b'}$ = 10.8, $J_{5',6a'}$ = 3.6 Hz, H-6a'), 3.74 (1H, dd, $J_{6a',6b'}$ = 10.8, $J_{5',6b'}$ = 7.0 Hz, H-6b'), 3.65 (1H, ddd, $J_{4',5'}$ = 7.2, $J_{5',6b'}$ = 7.0, $J_{5',6a'}$ = 3.6 Hz, H-5'), 1.48 (3H, s), 1.43 (3H, s), 1.33 (3H, s), 1.29 (3H, s), 1.25 (3H, s), 1.19 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.3, 165.8, 133.01, 132.99, 130.04, 129.98, 129.8 (2C), 129.7 (2C), 128.3 (4C), 113.2, 112.1, 106.9, 106.3, 100.7, 84.8, 83.8, 80.1, 79.5, 77.8, 74.8, 71.3, 62.9, 62.3, 60.4, 27.1, 26.5, 26.1, 24.8, 23.9, 23.9. IR (KBr): 2990, 2938, 1719 cm^{-1}. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{35}H_{42}O_{13}Na$, 693.2523; found, 693.2500.

4.7.3

2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl-(1↔2)-1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranoside (7cαα) and 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl-(1↔2)-1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranoside (7cβα): According to the general procedure of glycosidation, compound **5c** was obtained from glycosyl donor **3** and 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**6c**) in 76% yield (α:β = 9:1) after purification by GPC ($CHCl_3$). Anomers **7cαα** and **7cβα** were separated by HPLC purification (10% EtOAc in *n*-hexane). **7cαα:** Colorless oil. R_f = 0.51 (30% EtOAc in *n*-hexane). $[\alpha]^{24}_D$ = +30.4 (*c* 1.30, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ: 8.06–8.00 (2H, m, Ar*H*), 8.00–7.94 (2H, m, Ar*H*), 7.60–7.51 (2H, m, Ar*H*), 7.46–7.36 (4H, m, Ar*H*), 7.34–7.25 (6H, m, Ar*H*), 7.24–7.17 (5H, m, Ar*H*), 7.17–7.06 (7H, m, Ar*H*), 7.04–6.98 (2H, m, Ar*H*), 5.56 (1H, d, $J_{1',2'}$ = 3.6 Hz, H-1'), 4.95 (1H, d, *J* = 11.0 Hz), 4.91 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.9 Hz, H-4), 4.85 (1H, d, *J* = 11.0 Hz), 4.76 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.72 (1H, d, *J* =

10.8 Hz), 4.69 (1H, d, J = 11.9 Hz), 4.67 (1H, ddd, $J_{5,6b}$ = 7.6, $J_{5,6a}$ = 4.7, $J_{4,5}$ = 3.9 Hz, H-5), 4.66 (1H, d, J = 11.9 Hz), 4.64 (1H, d, J = 11.5 Hz), 4.55 (1H, d, J = 11.5 Hz), 4.54 (1H, dd, $J_{6a,6b}$ = 11.7, $J_{5,6a}$ = 4.7 Hz, H-6a), 4.42 (1H, d, J = 12.1 Hz), 4.39 (1H, dd, $J_{6a,6b}$ = 11.7, $J_{5,6b}$ = 7.6 Hz, H-6b), 4.37 (1H, d, J = 10.8 Hz), 4.14 (1H, d, J = 12.1 Hz), 4.04 (1H, ddd, $J_{4',5'}$ = 9.0, $J_{5',6a'}$ = 2.6, $J_{5',6b'}$ = 1.9 Hz, H-5'), 4.00 (1H, dd, $J_{3',4'}$ = 10.1, $J_{2',3'}$ = 9.8 Hz, H-3'), 3.69 (1H, dd, $J_{3',4'}$ = 10.1, $J_{4',5'}$ = 9.0 Hz, H-4'), 3.58 (1H, $J_{2',3'}$ = 9.8, $J_{1',2'}$ = 3.6 Hz, H-2'), 3.24 (1H, dd, $J_{6a',6b'}$ = 10.8, $J_{5',6a'}$ = 2.6 Hz, H-6a'), 3.03 (1H, dd, $J_{6a',6b'}$ = 10.8, $J_{5',6b'}$ = 1.9 Hz, H-6b'), 1.44 (3H, s), 1.30 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.1, 165.6, 138.7, 138.2, 137.6, 137.5, 133.0, 132.9, 130.0, 129.9, 129.63 (2C), 129.59 (2C), 128.4 (2C), 128.32 (2C), 128.31 (2C), 128.26 (2C), 128.23 (2C), 128.18 (2C), 127.9 (2C), 127.70 (2C), 127.66, 127.62 (2C), 127.56, 127.54, 127.49, 127.47 (2C), 113.2, 107.6, 90.1, 85.0, 81.8, 79.9, 79.0, 77.7, 77.5, 75.4, 74.8, 73.4, 73.3, 71.3, 67.7, 63.2, 62.6, 26.0, 24.8. IR (film): 3030, 2934, 1724 cm^{-1}. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{57}H_{58}O_{13}Na$, 973.3775; found, 973.3754. **7cβα:** Colorless oil. R_f = 0.51 (30% EtOAc in *n*-hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.04–7.99 (2H, m, Ar*H*), 7.96–7.91 (2H, m, Ar*H*), 7.58–7.51 (1H, m, Ar*H*), 7.50–7.45 (1H, m, Ar*H*), 7.44–7.39 (2H, m, Ar*H*), 7.35–7.29 (3H, m, Ar*H*), 7.28–7.24 (4H, m, Ar*H*), 7.23–7.20 (5H, m, Ar*H*), 7.19–7.12 (4H, m, Ar*H*), 7.11–7.05 (6H, m, Ar*H*), 4.93 (1H, d, $J_{1',2'}$ = 8.1 Hz, H-1'), 4.91 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 4.1 Hz, H-4), 4.86 (1H, $J_{5,6b}$ = 7.3, $J_{5,6a}$ = 4.3, $J_{4,5}$ = 4.1 Hz, H-5), 4.84 (1H, d, J = 11.8 Hz), 4.80 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.75 (1H, d, J = 10.8 Hz), 4.74 (1H, d, J = 10.9 Hz), 4.69 (1H, d, J = 10.9 Hz), 4.66 (1H, d, J = 11.8 Hz), 4.62 (1H, dd, $J_{6a,6b}$ = 11.8, $J_{5,6a}$ = 4.3 Hz, H-6a), 4.59 (1H, d, J = 11.9 Hz), 4.55 (1H, d, J = 11.9 Hz), 4.47 (1H, d, J = 10.8 Hz), 4.45 (1H, d, J = 12.0 Hz), 4.43 (1H, dd, $J_{6a,6b}$ = 11.8 Hz, $J_{5,6b}$ = 7.3 Hz, H-6b), 4.31 (1H, d, J = 12.0 Hz), 3.65 (1H, dd, $J_{4',5'}$ = 9.4, $J_{3',4'}$ = 9.0 Hz, H-4'), 3.60 (1H, dd, $J_{3',4'}$ = 9.0, $J_{2',3'}$ = 8.7 Hz, H-3'), 3.52 (2H, d, $J_{5',6'}$ = 2.9 Hz, H-6'), 3.43 (1H, dd, $J_{2',3'}$ = 8.7, $J_{1',2'}$ = 8.1 Hz, H-2'), 3.39 (1H, dt, $J_{4',5'}$ = 9.4, $J_{5',6'}$ = 2.9 Hz, H-5'), 1.43 (3H, s), 1.29 (3H, s). HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{57}H_{58}O_{13}Na$, 973.3775; found, 973.3735.

4.7.4 2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl

-(1↔2)-1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranoside (7dαα) and 2,3,4,6-tetra-*O*-benzyl-β-D-mannpyranosyl-(1↔2)-1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-tagatofuranoside (7dβα): According to the general procedure of glycosidation, compound **7d** was obtained from glycosyl donor **3** and 2,3,4,6-tetra-*O*-benzyl-D-mannopyranose (**6d**) in 70% yield (α:β = 4:1) after purification by GPC ($CHCl_3$). Anomers **7dαα** and **7dβα** were separated by HPLC purification (10% EtOAc in *n*-hexane). **7dαα:** Colorless oil. R_f= 0.49 (30% EtOAc in *n*-hexane). $[\alpha]^{21}_D$ = +29.5 (*c* 1.09, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.10–8.00 (4H, m, Ar*H*), 7.59–7.51 (2H, m, Ar*H*), 7.44–7.36 (4H, m, Ar*H*), 7.36–7.26 (5H, m, Ar*H*), 7.25–7.14 (11H, m, Ar*H*), 7.14–7.04 (4H, m, Ar*H*), 5.48 (1H, d, $J_{1',2'}$ = 2.0 Hz, H-1'), 4.78 (1H, d, *J* = 10.9 Hz), 4.78 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.9 Hz, H-4), 4.69 (1H, dd, $J_{6a,6b}$ = 11.8, $J_{5,6a}$ = 4.5 Hz, H-6a), 4.68 (1H, d, *J* = 11.8 Hz), 4.66 (1H, d, *J* = 11.5 Hz), 4.60 (1H, d, *J* = 12.2 Hz), 4.59 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.56 (1H, d, *J* = 11.8 Hz), 4.54 (1H, d, *J* = 12.2 Hz), 4.52 (1H, d, *J* = 11.5 Hz), 4.48 (1H, d, *J* = 12.1 Hz), 4.43 (1H, d, *J* = 10.8 Hz), 4.40 (1H, dd, $J_{6a,6b}$ = 11.8 Hz, $J_{5,6b}$ = 7.4 Hz, H-6b), 4.20 (1H, d, *J* = 12.1 Hz), 4.04 (1H, dd, $J_{4',5'}$ = 9.8, $J_{3',4'}$ = 9.3 Hz, H-4'), 3.95 (1H, $J_{5,6b}$ = 7.4, $J_{5,6a}$ = 4.5, $J_{4,5}$ = 3.9 Hz, H-5), 3.93 (1H, ddd, $J_{4',5'}$ = 9.8, $J_{5',6a'}$ = 3.7, $J_{5',6b'}$ = 1.8 Hz, H-5'), 3.87 (1H, dd, $J_{3',4'}$ = 9.3, $J_{2',3'}$ = 3.1 Hz, H-3'), 3.45 (1H, dd, $J_{2',3'}$ = 3.1, $J_{1',2'}$ = 2.0 Hz, H-2'), 3.37 (1H, dd, $J_{6a',6b'}$ = 11.0, $J_{5',6a'}$ = 3.7 Hz, H-6a'), 3.18 (1H, dd, $J_{6a',6b'}$ = 11.0, $J_{5',6b'}$ = 1.8 Hz, H-6b'), 1.45 (3H, s), 1.29 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ:166.2, 165.5, 138.54, 138.52, 138.1, 137.9, 133.2, 132.8, 130.0, 129.7, 129.62 (2C), 129.59 (2C), 128.4 (2C), 128.3 (2C), 128.23 (2C), 128.18 (2C), 128.16 (2C), 128.06 (2C), 127.81 (2C), 127.78 (2C), 127.74 (2C), 127.70 (2C), 127.6, 127.5, 127.4, 127.2, 113.4, 107.7, 90.6, 84.7, 79.7, 79.2, 78.3, 75.7, 74.9, 74.5, 73.2, 73.0, 72.5, 72.2, 68.3, 62.7, 62.5, 26.0, 24.8. IR (film): 3030, 2936, 1724 cm^{-1}. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{57}H_{58}O_{13}Na$, 973.3775; found, 973.3797. **7dβα:** Colorless oil. R_f= 0.49 (30% EtOAc in *n*-hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.07–7.99 (4H, m, Ar*H*), 7.60–7.50 (2H, m, Ar*H*), 7.47–7.38 (4H, m, Ar*H*), 7.30–7.28 (1H, m, Ar*H*), 7.25–7.09 (19H, m, Ar*H*), 4.98–4.91 (3H, m, H-4, 5, 1'), 4.82 (1H, d, *J* = 10.9 Hz), 4.75 (1H, d, $J_{3,4}$ = 5.5 Hz, H-3), 4.75 (1H, d, *J* = 12.4 Hz), 4.70 (1H, d, *J* = 12.0 Hz), 4.57 (1H, dd, $J_{6a,6b}$ = 11.7, $J_{5,6a}$ = 4.1 Hz, H-6a), 4.55 (1H, d, *J* = 12.4 Hz), 4.50 (1H, d, *J* = 12.0 Hz), 4.46 (1H, d, *J* = 11.9 Hz), 4.44 (1H, d, *J* = 12.0

Hz), 4.43 (1H, dd, $J_{6a,6b}$ = 11.7 Hz, $J_{5,6b}$ = 7.1 Hz, H-6b), 4.31 (1H, d, J = 12.0 Hz), 4.26 (1H, d, J = 11.8 Hz), 4.23 (1H, d, J = 11.8 Hz), 3.87 (1H, dd, $J_{4',5'}$ = 9.7, $J_{3',4'}$ = 9.4 Hz, H-4'), 3.73 (1H, d, $J_{2',3'}$ = 3.0 Hz, H-2'), 3.58 (1H, dd, $J_{6a',6b'}$ = 10.7, $J_{5',6a'}$ = 3.0 Hz, H-6a'), 3.56 (1H, dd, $J_{6a',6b'}$ = 10.7, $J_{5',6b'}$ = 4.1 Hz, H-6b'), 3.46 (1H, dd, $J_{3',4'}$ = 9.4, $J_{2',3'}$ = 3.0 Hz, H-3'), 3.40 (1H, ddd, $J_{4',5'}$ = 9.7, $J_{5',6b'}$ = 4.1, $J_{5',6a'}$ = 3.0 Hz, H-5'), 1.49 (3H, s), 1.34 (3H, s). HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{57}H_{58}O_{13}Na$, 973.3775; found, 973.3758.

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Electronic Supplementary Information

Electronic Supplementary Information associated with this article can be found in the online version, at xxx.

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12 Other glycosyl donors such as trichloroacetimidate were less effective than the currently used glycosyl phthalate due to the instability of the glycosyl donor during preparation. Thioglycoside donor can be used as an alternative. The glycosidation of thioglycoside **5a** and 1-dodecanol promoted by NIS/TfOH produced **4a** in 70% yield with complete α-selectivity.

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