Trichloroacetimidate as a Leaving Group in the Ferrier Rearrangement: Highly Stereoselective Synthesis of Pseudogalactal Glycosides

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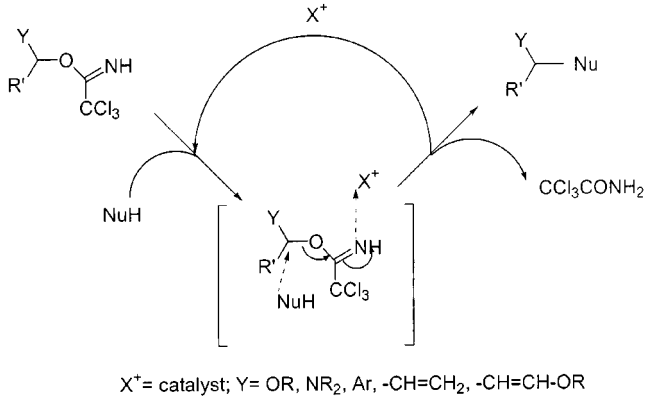
The Ferrier rearrangement of a galactal derivative **2** bearing the trichloroacetimidate functionality as a leaving group at the C-3 position was performed in the presence of trimethylsilyl triflate as catalyst; the corresponding pseudogalactal glycosides were obtained in excellent yield and stereoselectivity with a wide range of acceptors.

Introduction

The acid-catalyzed trichloroacetimidate activation of O,O- and N,O-acetals has proven to be a highly attractive and powerful alternative to the classical glycosidation methods and it is currently one of the most frequently applied strategies for glycoside bond formation (Scheme 1, Y = OR, NR_2).[1−4] Other systems supporting carbenium ion generation such as benzyl and allyl alcohols (Scheme 1, Y = Ar, −CH=CH_2) can be also transformed into the corresponding trichloroacetimidates and then employed in these valuable acid-catalyzed alkylation reactions.[5,6]



Scheme 1. Trichloroacetimidate as leaving group

Of the various possibilities for extension of this reaction principle, the oxyallyl system (Scheme 1, Y = −CH=CH-OR) seemed to be of considerable interest as, due to enhanced resonance stabilization, it should be particularly prone to acid-catalyzed alkylation reactions. The presence of this structural entity in glycals and their potential convenient transformation (by a Ferrier rearrangement) into glycosides of pseudoglycals was reason to investigate this novel conceptual approach, thus also meeting our continued interest in developing new glycosylation methods.[1−4,7−12]

Results and Discussion

Pseudoglycals (hex-2-enoglycopyranosides) have received great attention in recent years in the synthesis of glycopeptide building blocks,[13,14] uronic acids,[15,16] modified carbohydrates,[17] nucleosides,[18,19] oligosaccharides[20−22] and antibiotics[23] and also as chiral building blocks.[24] The Ferrier rearrangement[25−28] is an important acid-catalyzed glycosidation reaction generally involving *O*-acetylated glycals to afford this class of compounds through nucleophilic allylic rearrangement (S_N' reaction); the plethora of reagents or catalysts documented in the literature[29−34] for this transformation is an indication of the importance with which this glycosidation reaction has been addressed. In contrast to other glycals, the Ferrier rearrangement of tri-*O*-acetyl galactal[25−28,35,36] has been reported to be difficult since an unusual behavior is exhibited. Under standard conditions a mixture of pseudogalactal glycosides and 2-deoxy glycosides was produced in low yield, and hence this reaction has been studied less. It is noteworthy to mention that $SnCl_4$ [35] and $LiBF_4$ [36] are the only catalysts known to bring about the rearrangement of tri-*O*-acetyl galactal with simple acceptors. However, these procedures have their limitations in terms of yields, stereoselectivities, uncontrollable formation of by-products, reaction temperatures, compatibility with other functional groups present in the molecule, and the amounts of reagent or catalyst used. We reasoned that if one chooses the trichloroacetimidate moiety as the leaving group at the C-3 position and an efficient catalyst such as trimethylsilyl triflate to cause the desired transformation, the task could become practical.[13] Thus, due to the presence of bulky substituents on the β-side, interme-

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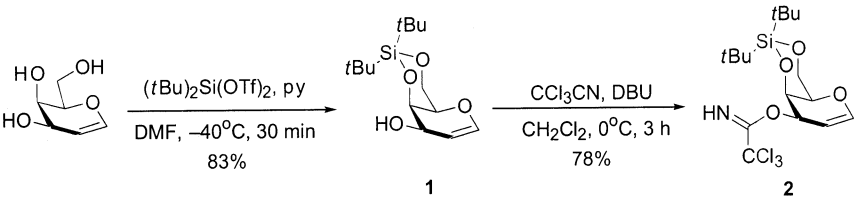
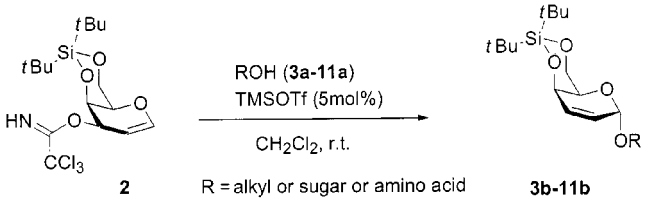


Scheme 2. Synthesis of glycosyl donor **2**



Scheme 3. Reaction of **2** with various alcohols as acceptors

diate tight ion-pair formation, and stereoelectronic effects also favoring the α-attack of nucleophiles, the desired α-glycosides of pseudoglycals should become readily accessible.

The required galactal trichloroacetimidate **2** was synthesized as shown in Scheme 2. 4,6-Di-*tert*-butylsilanediyl-protected galactal **1** was prepared from galactal in 83% yield by the reaction of di-*tert*-butylsilyl ditriflate in the presence of pyridine using DMF as solvent at −40 °C. The treatment of **1** with trichloroacetonitrile in the presence of catalytic amounts of DBU afforded the corresponding trichloroacetimidate donor **2** in 78% yield. Trichloroacetimidate donor **2** was then subjected to a Ferrier rearrangement in the presence of various acceptors with trimethylsilyl triflate as catalyst at room temperature (Scheme 3). In an initial study, trichloroacetimidate donor **2** (1 equiv.) was treated with methanol (**3a**) (1.1 equiv.) as acceptor in the presence of trimethylsilyl triflate (0.05 equiv.) in dichloromethane at ambient temperature for 1 h (entry 1, Table 1). This reaction led regio- and stereoselectively to the desired pseudogalactal methyl α-glycoside **3b** in 94% yield, and no trace of a 2-deoxy glycoside product nor any attack of the nucleophile at C-3 (S_N' reaction) was detected. Thus, to our utmost satisfaction we were successful in proving our hypothesis concerning the reactivity of galactal trichloroacetimidate **2**.

To prove the generality of this protocol, a cross section of acceptors was chosen to react with **2** under the aforementioned conditions (Table 1). Glycosidation of **2** with 2-propanol **4a** (entry 2, Table 1), cyclohexanol **5a** (entry 3, Table 1) and benzyl alcohol **6a** (entry 4, Table 1) proceeded smoothly to furnish the corresponding α-glycosides **4b**, **5b** and **6b** in 94%, 88% and 95% yield, respectively. Similarly, glycosidation of **2** with the Fmoc-protected serine derivative **7a** occurred under similar conditions to produce the corresponding α-glycoside **7b**, which is a potential precursor for our ongoing programme on glycopeptide synthesis (entry 5, Table 1). Sugar residues such as methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**8a**)[37] (entry 6, Table 1) and methyl 2,4,6-tri-*O*-acetyl-β-D-galactopyranoside (**9a**)[38] (entry 7, Table 1) also behaved identically to yield the corresponding α(1−6)- and α(1−3)-linked disaccharides **8b** and **9b** in 95% and 88% yield, respectively. When we used thexyldimethylsilyl 2-deoxy-2-(dimethylmaleoylimido)-3,6-di-*O*-benzyl-β-D-glucopyranoside (**10a**)[39] as acceptor the corresponding glycoside **10b** was obtained as an α/β mixture (10:1) in 88% yield (entry 8, Table 1), this being the only case where some β-anomer could be detected. The versatility of this method was further illustrated by making a disaccharide **11b** with the nucleoside **11a** (entry 9, Table 1). The structural assignments could be further confirmed by treatment of **6b** with tetrabutylammonium fluoride in THF and then with acetic anhydride in pyridine, thus providing the known 4,6-di-*O*-acetyl derivative, which had identical NMR spectroscopic data (^1H, ^{13}C) to those reported previously.[36]

Conclusion

In conclusion, we have developed an efficient and highly regio- and stereoselective protocol for the Ferrier rearrangement of galactal derivatives by using trichloroacetimidate as a leaving group at the C-3 position and trimethylsilyl triflate as catalyst. With various alcohols as acceptors structurally diverse glycosides of pseudogalactals were obtained. Thus, we have demonstrated a novel acid-catalyzed activation of a γ-alkoxyallyl alcohol system providing an α-alkoxyallyl group transfer to nucleophiles in an S_N' reaction. *C*-Glycosylation using the same reaction principle is currently under investigation and the results will be reported shortly.

Experimental Section

General Methods: Solvents were purified according to the standard procedures. TLC was performed on plastic plates coated with Silica Gel 60 F_{254} (E. Merck, layer thickness 0.2 mm). The detection was achieved by treatment with a solution of 20 g ammonium molybdate and 0.4 g cerium(IV) sulfate in 400 mL of 10% aqueous H_2SO_4 or with 15% aqueous H_2SO_4, and heating at 150 °C. Flash chromatography was carried out on silica gel (Baker, 30−60 μm). Optical rotations were determined at room temp. with a Perkin−Elmer 241/MC polarimeter (1 dm cell). NMR spectra were recorded with a Bruker AC 250 and 600 DRX instruments, using tetramethylsilane as internal standard. MALDI mass spectra were recorded on a Kratos Kompact MALDI instrument, using a 2,5-dihydroxybenzoic acid matrix. EI and FAB mass spectra were recorded on a Finnigan MAT 312/AMD 5000 spectrometer, using a 1:1 3-nitrobenzyl alcohol/glycerol matrix.

Table 1. Glycosidation of **2** with various acceptors (**3a**−**11a**)

Entry	Acceptor	Glycoside	Time (h)	Yield (%)[a]
1	MeOH **3a**	**3b**	1	94
2	2-Propanol **4a**	**4b**	0.5	94
3	Cyclohexanol **5a**	**5b**	3	88
4	BnOH **6a**	**6b**	0.5	95
5	**7a**	**7b**	1	98
6	**8a**	**8b**	2	95
7	**9a**	**9b**	0.5	88
8	**10a**	**10b**	1	88[b]
9	**11a**	**11b**	0.5	81

[a] Isolated yields after column chromatography (b) α/β ratio: 10:1.

1,5-Anhydro-4,6-*O*-(di-*tert*-butyl)silanediyl-2-deoxy-D-*lyxo*-hex-1-enitol (1): 4,6-*O*-Protected galactal **1** was prepared in analogy to a protocol for the preparation of 4,6-*O*-(di-*tert*-butyl)silanediyl-D-glucal[40]: Galactal (0.50 g, 3.42 mmol) was dissolved in dry DMF (15 mL) and cooled to −40 °C under an argon atmosphere. Then, under constant stirring, di-*tert*-butylsilyl ditriflate was slowly added to the reaction mixture over a period of 15 min. Stirring was continued for 30 min at −40 °C. Pyridine was added and the reaction allowed to warm to room temperature. Dilution with diethyl ether, washing with water, drying over sodium sulfate and concentration gave a crude product, which was purified on 50 g silica gel (petroleum ether/ethyl acetate 6:1 containing 5% triethylamine) to give **1** (0.68 g, 70%). TLC (petroleum ether/ethyl acetate, 6:1) R_f = 0.32. $[\alpha]_D$ = +31.9 (*c* = 1. 0, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.04 (s, 9 H, C_4H_9), 1.08 (s, 9 H, C_4H_9), 2.74 (d, $^3J_{OH,3}$ = 11.4 Hz, 1 H, OH), 3.88 (s, 1 H, 5-H), 4.23−4.29 (m, 2 H, 6-H_a, 6-H_b), 4.33−4.35 (m, $^3J_{3,2} < 1$, $^3J_{3,4}$ = 5.0, $^3J_{3,OH}$ = 11.4 Hz, 1 H, 3-H), 4.41 (d, $^3J_{4,3}$ = 5.0 Hz, 1 H, 4-H), 4.31 (d, $^3J_{2,1}$ = 6.5 Hz, 1 H, 2-H), 6.31 (dd, $^3J_{1,2}$ = 6.5 Hz, 1 H, 1-H). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 20.9 (*C*Me_3), 23.4 (*C*Me_3), 27.6 (C*Me*$_3$), 27.9 (C*Me*$_3$), 63.7 (C-4), 65.8 (C-6), 68.6 (C-5), 73.3 (C-3), 103.3 (C-2), 143.9 (C-1). MS (MALDI): calcd. 287 + 23 (Na) = 310; found 310 (M + Na)$^+$. $C_{14}H_{26}O_4Si$ (286.44): calcd. C 58.70, H 9.14; found C 58.70, H 9.01.

1,5-Anhydro-2-deoxy-4,6-*O*-(di-*tert*-butyl)silanediyl-3-*O*-trichloroacetimidoyl-D-*lyxo*-hex-1-enitol (2): Selectively protected galactal **1** (0.10 g, 0.35 mmol) was dissolved in dry dichloromethane (3 mL) together with trichloroacetonitrile (0.35 mL, 3.50 mmol). The solution was cooled in an ice-bath and the reaction activated by addition of DBU (5 μL, 0.035 mmol). After 3 h stirring at 0 °C the reaction mixture was directly applied to a silica gel column (30 g, silica gel, toluene/ethyl acetate 98:2 containing 5% triethylamine) to give **2** (0.117 g, 78%). TLC (toluene/ethyl acetate, 10:1) R_f = 0.51. $[\alpha]_D$ = +64.7 (*c* = 2.0, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.00 (s, 9 H, C_4H_9), 1.01 (s, 9 H, C_4H_9), 3.91 (s, 1 H, 5-H), 4.27 (d, $^2J_{6',6}$ = 12.5 Hz, 1 H, 6′-H), 4.31 (d, $^2J_{6,6'}$ = 12.6 Hz, 1 H, 6-H), 4.82 (d, $^3J_{1,2}$ = 6.4 Hz, 1 H, 1-H), 5.08 (d, $^3J_{4,3}$ = 4.9 Hz, 1 H, 4-H), 5.39 (dd, $^3J_{3,2}$ = 2.0, $^3J_{3,4}$ = 4.8 Hz, 1 H, 3-H), 6.48 (dd, $^3J_{2,1}$ = 6.5, $^3J_{2,3}$ = 2.0 Hz, 1 H, 2-H), 8.30 (s, 1 H, NH). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 20.80 (*C*Me_3), 23.41 (*C*Me_3), 26.92 (C*Me*$_3$), 27.60 (C*Me*$_3$), 63.91 (C-4), 67.39 (C-6), 71.45 (C-3), 73.12 (C-5), 91.41 (CCl_3), 98.43 (C-1), 145.90 (C-2), 162.00 (CNH). EI-MS (positive mode): *m*/*z* = 431 [M$^+$]. $C_{16}H_{26}Cl_3NO_4Si$ (430.83): calcd. C 44.60, H 6.08, N 3.25; found C 44.49, H 5.98, N 3.07.

Glycosidation of 2 with Acceptors 3a−11a to Give Glycosides 3b−11b. General Procedure: TMSOTf (0.05 mmol) was added at ambient temperature under an argon atmosphere to a stirred mixture of trichloroacetimidate **2** (1 mmol) and acceptor (1.1 mmol) in dry dichloromethane. The contents were stirred for the required time (Table 1) and monitored by TLC. The reaction was quenched by the addition of solid sodium bicarbonate (90 mg) and diluted with dichloromethane, filtered and concentrated. The crude residue was purified by column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate (10:1) as eluent to furnish the products.

Methyl 4,6-*O*-(Di-*tert*-butyl)silanediyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (3b): TLC (petroleum ether/ethyl acetate, 5:1) R_f = 0.51. $[\alpha]_D$ = +18.5 (*c* = 1.10, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.96 (s, 9 H, C_4H_9), 1.05 (s, 9 H, C_4H_9), 3.34 (s, 3 H, OMe), 3.81 (ddd, $J_{5,6a}$ = 3.0 Hz, $J_{5,6b}$ = 5.3 Hz, $J_{5,4}$ = 8.3 Hz, 1 H, 5-H), 4.15 (dd, $J_{6a,5}$ = 3.0 Hz, $J_{6a,6b}$ = 12.6 Hz, 1 H, 6-H_a),

4.25 (dd, $J_{4,5}$ = 8.5 Hz, $J_{4,3}$ = 5.0 Hz, 1 H, 4-H), 4.35 (dd, $J_{5,6b}$ = 5.3 Hz, $J_{6b,6a}$ = 12.5 Hz, 1 H, 6-H_b), 4.90 (d, $J_{1,2}$ = 3.2 Hz, 1 H, 1-H), 5.85 (dd, $J_{2,1}$ = 3.2 Hz, $J_{2,3}$ = 10.0 Hz, 1 H, 2-H), 6.10 (dd, $J_{3,2}$ = 10.0 Hz, $J_{3,4}$ = 5.5 Hz, 1 H, 3-H). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 20.58 (*C*Me_3), 23.26 (*C*Me_3), 27.25 (C*Me*$_3$), 27.50 (C*Me*$_3$), 55.37 (OMe), 64.69 (C-4), 65.99 (C-6), 67.45 (C-5), 95.49 (C-1), 126.22 (C-2), 129.71 (C-3). EI-MS (positive mode): *m*/*z* = 300 [M^+]. $C_{15}H_{28}O_4Si$ (300.47): calcd. C 59.96, H 9.39; found C 59.81, H 9.14.

Isopropyl 4,6-*O*-(Di-*tert*-butyl)silanediyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (4b): TLC (petroleum ether/ethyl acetate, 5:1) R_f = 0.55. $[\alpha]_D$ = +3.3 (*c* = 1.0, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.97 (s, 9 H, C_4H_9), 1.09 (s, 9 H, C_4H_9), 1.21, 1.30 (2 d, *J* = 6.3 Hz, 6 H, CH*Me*$_2$), 3.40 (sept, *J* = 6.3 Hz, 1 H, *CH*Me_2), 3.81 (ddd, $J_{5,6a}$ = 2.9 Hz, $J_{5,6b}$ = 5.4 Hz, $J_{5,4}$ = 8.1 Hz, 1 H, 5-H), 4.18 (dd, $J_{6a,5}$ = 2.9 Hz, $J_{6a,6b}$ = 12.5 Hz, 1 H, 6-H_a), 4.25 (dd, $J_{4,5}$ = 8.1 Hz, $J_{4,3}$ = 5.2 Hz, 1 H, 4-H), 4.33 (dd, $J_{5,6b}$ = 5.4 Hz, $J_{6b,6a}$ = 12.4 Hz, 1 H, 6-H_b), 4.89 (d, $J_{1,2}$ = 3.0 Hz, 1 H, 1-H), 5.80 (dd, $J_{2,1}$ = 3.0 Hz, $J_{2,3}$ = 10.1 Hz, 1 H, 2-H), 6.13 (dd, $J_{3,2}$ = 10.0 Hz, $J_{3,4}$ = 5.3 Hz, 1 H, 3-H). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 20.68 (*C*Me_3), 20.69 (Me), 23.27 (Me), 23.33 (*C*Me_3), 27.33 (C*Me*$_3$), 27.53 (C*Me*$_3$), 64.71 (C-4), 66.09 (C-6), 67.49 (C-5), 72.08 (*C*HMe_2), 95.53 (C-1), 126.23 (C-2), 129.70 (C-3). EI-MS (positive mode): *m*/*z* = 328 [M^+]. $C_{17}H_{32}O_4Si$ (328.52): calcd. C 62.15, H 9.81; found C 61.93, H 9.65.

Cyclohexyl 4,6-*O*-(Di-*tert*-butyl)silanediyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (5b): TLC (petroleum ether/ethyl acetate, 5:1) R_f = 0.61. $[\alpha]_D$ = +22.6 (*c* = 1.0, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.96 (s, 9 H, C_4H_9), 1.05 (s, 9 H, C_4H_9), 1.51−1.75 (m, 10 H, cyclohexyl), 3.77−3.80 (m, 2 H, 5-H, cyclohexyl), 4.20−4.25 (m, 2 H, 4-H, 6-H_a), 4.31 (m, 1 H, 6-H_b), 4.91 (d, $J_{1,2}$ = 3.1 Hz, 1 H, 1-H), 5.84 (dd, $J_{2,1}$ = 3.2 Hz, $J_{2,3}$ = 10.0 Hz, 1 H, 2-H), 6.13 (dd, $J_{3,2}$ = 10.0 Hz, $J_{3,4}$ = 5.1 Hz, 1 H, 3-H). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 20.66 (*C*Me_3), 23.33 (*C*Me_3), 23.86, 24.17, 25.63 (cyclohexyl), 27.31 (C*Me*$_3$), 27.51 (C*Me*$_3$), 31.47, 33.41 (cyclohexyl), 64.70 (C-4), 66.11 (C-6), 67.48 (C-5), 74.28 (cyclohexyl), 95.50 (C-1), 126.21 (C-2), 129.68 (C-3). EI-MS (positive mode): *m*/*z* = 368 [M^+]. $C_{20}H_{36}O_4Si$ (368.59): calcd. C 65.17, H 9.84; found C 65.01, H 9.69.

Benzyl 4,6-*O*-(Di-*tert*-butyl)silanediyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (6b): TLC (petroleum ether/ethyl acetate, 5:1) R_f = 0.54. $[\alpha]_D$ = +10.8 (*c* = 1.0, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.94 (s, 9 H, C_4H_9), 1.03 (s, 9 H, C_4H_9), 3.86 (ddd, $J_{5,6a}$ = 3.1 Hz, $J_{5,6b}$ = 5.4 Hz, $J_{5,4}$ = 8.4 Hz, 1 H, 5-H), 4.15 (dd, $J_{6a,5}$ = 3.1 Hz, $J_{6a,6b}$ = 12.5 Hz, 1 H, 6-H_a), 4.25 (dd, $J_{4,5}$ = 4.5 Hz, $J_{4,3}$ = 5.0 Hz, 1 H, 4-H), 4.36 (dd, $J_{6b,5}$ = 5.4 Hz, $J_{6b,6a}$ = 12.5 Hz, 1 H, 6-H_b), 4.62 (d, *J* = 11.7 Hz, 1 H, OCH_2Ph), 4.79 (d, *J* = 11.7 Hz, 1 H, OCH_2Ph), 4.88 (d, $J_{1,2}$ = 3.1 Hz, 1 H, 1-H), 5.83 (dd, $J_{2,1}$ = 3.2 Hz, $J_{2,3}$ = 10.0 Hz, 1 H, 2-H), 6.11 (dd, $J_{3,2}$ = 10.0 Hz, $J_{3,4}$ = 5.2 Hz, 1 H, 3-H), 7.24−7.35 (m, 5 H, Ph). EI-MS (positive mode): *m*/*z* = 376 [M^+]. $C_{21}H_{32}O_4Si$ (376.57): calcd. C 66.98, H 8.56; found C 66.71, H 8.44.

***O*-[4,6-*O*-(Di-*tert*-butyl)silanediyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranosyl]-*N*-(fluorenylethoxycarbonyl)-L-serine *tert*-Butyl Ester (7b):** TLC (toluene/ethyl acetate, 10:1) R_f = 0.32. $[\alpha]_D$ = −35.5 (*c* = 2.0, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.97 (s, 9 H, C_4H_9), 1.04 (s, 9 H, C_4H_9), 1.47 (s, 9 H, C_4H_9), 3.83 (s, 1 H, 5-H), 3.96 (dd, $J_{\beta,\alpha}$ = 2.6 Hz, $J_{\beta,\beta}$ = 10.7 Hz, 1 H, β′-H), 4.06 (dd, $J_{\beta,\alpha}$ = 3.4 Hz, $J_{\beta,\beta}$ = 10.7 Hz, 1 H, β-H), 4.24 (m, 2 H, Fmoc-C*H*, 6-H_a), 4.26−4.34 (m, 3 H, Fmoc-CH_2, 6-H_b, 4-H), 4.39−4.43 (m, 2 H, Fmoc-CH_2, α-H), 5.02 (d, $J_{1,2}$ = 3.1 Hz, 1 H, 1-H), 5.80 (dd, $J_{2,1}$ = 3.2 Hz, $J_{2,3}$ = 10.0 Hz, 1 H, 2-H), 5.93 (d, $J_{NH,\alpha}$ = 8.7 Hz, 1 H, NH), 6.11 (dd, $J_{3,2}$ = 10.0 Hz, $J_{3,4}$ = 5.5 Hz, 1 H, 3-H), 7.32 (d, *J* = 7.3 Hz, 2 H, arom. H), 7.40 (t, *J* = 7.3 Hz, 2 H, arom. H), 7.63 (t, *J* = 7.3 Hz, 2 H, arom. H), 7.76 (d, *J* = 7.5 Hz, 2 H, arom. H). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 20.60 (*C*Me_3), 23.11 (*C*Me_3), 27.12 (C*Me*$_3$), 27.50 (C*Me*$_3$), 28.00, 29.71 (C*Me*$_3$), 47.10 (Fmoc-*C*H), 55.00 (α-C), 64.71 (C-4), 66.21 (C-6), 67.20 (Fmoc-*C*H_2) 67.51 (C-5), 69.70, 82.31 (β-C), 95.50 (C-1), 120.00, 125.20 (3 C), 126.22 (C-2), 127.00, 127.10, 127.71 (3 C), 129.71 (C-3), 141.30, 143.81, 143.90, 156.00 (*C*=0), 169.21 (*C*=0). FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 652 [MH^+], 674 [MNa^+].

Methyl *O*-[4,6-*O*-(Di-*tert*-butyl)silanediyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranosyl]-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (8b): TLC (petroleum ether/ethyl acetate, 5:1) R_f = 0.63. $[\alpha]_D$ = +126.5 (*c* = 1.20, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.92 (s, 9 H, C_4H_9), 1.03 (s, 9 H, C_4H_9), 3.29 (s, 3 H, OMe), 3.30 (m, 1 H, 4-H_a), 3.43 (dd, $J_{1a,2a}$ = 3.5 Hz, $J_{2a,3a}$ = 9.6 Hz, 1 H, 2-H_a), 3.59−3.61 (m, 1 H, 6-H_a), 3.69 (m, 1 H, 5-H_a), 3.80 (m, 1 H, 5-H_b), 3.83 (m, 1 H, 6′-H_a), 4.15 (m, 1 H, 6-H_b), 4.26 (m, 1 H, 4-H_b), 4.38 (m, 1 H, 6′-H_b), 4.33 (d, *J* = 3.5 Hz, 1 H, 1-H_a), 4.40−5.00 (m, 6 H, 3 OCH_2Ph) 4.91 (d, $J_{1,2}$ = 3.2 Hz, 1 H, 1-H_b), 5.83 (dd, $J_{2,1}$ = 3.2 Hz, $J_{2,3}$ = 10.0 Hz, 1 H, 2-H_b), 6.12 (dd, $J_{3,2}$ = 10.0 Hz, $J_{3,4}$ = 5.4 Hz, 1 H, 3-H_b), 7.30−7.40 (m, 15 H, 3 Ph). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 20.59 (*C*Me_3), 23.28 (*C*Me_3), 27.27 (C*Me*$_3$), 27.54 (C*Me*$_3$), 55.40 (OMe), 64.59, 67.69, 67.30, 69.54, 69.90, 73.42, 74.85, 75.33, 75.71, 77.21, 79.71, 82.02, 98.10, 127.67, 127.86, 127.93, 128.08, 128.15, 128.40, 128.49, 128.56, 137.91, 138.03, 138.58. FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 733 [MH^+], 755 [MNa^+]. $C_{42}H_{56}O_9Si$ (732.98): calcd. C 68.82, H 7.70; found C 68.63, H 7.53.

Methyl *O*-[4,6-*O*-(Di-*tert*-butyl)silanediyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranosyl]-(1→3)-2,4,6-tri-*O*-acetyl-α-D-galacto-pyranoside (9b): TLC (petroleum ether/ethyl acetate, 5:1) R_f = 0.56. $[\alpha]_D$ = +130.5 (*c* = 0.71, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.94 (s, 9 H, C_4H_9), 1.03 (s, 9 H, C_4H_9), 1.94, 2.06, 2.10 (3 s, 9 H, 3 Ac), 3.37 (m, 1 H, 3-H_a), 3.46 (dd, $J_{2,1}$ = 7.8 Hz, $J_{2,3}$ = 9.5 Hz, 1 H, 2-H_a), 3.54 (s, 3 H, OMe), 3.68 (m, 3 H, 5-H_a, 2 6-H_a), 3.80 (m, 1 H, 5-H_b), 4.00 (dd, $J_{4,5}$= 1.0 Hz, $J_{4,3}$ = 3.5 Hz, 1 H, 4-H_a), 4.15−4.19 (m, 3 H, 4-H_b, 2 6-H_b), 4.21 (d, $J_{1,2}$ = 7.8 Hz, 1 H, 1-H_a), 4.88 (d, $J_{1,2}$ = 3.1 Hz, 1 H, 1-H_b), 5.84 (dd, $J_{2,1}$ = 3.2 Hz, $J_{2,3}$ = 10.0 Hz, 1 H, 2-H_b), 6.13 (dd, $J_{3,2}$ = 10.0 Hz, $J_{3,4}$ = 5.5 Hz, 1 H, 3-H_b). FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 589 [MH^+], 611 [MNa^+]. $C_{27}H_{44}O_{12}Si$ (588.72): calcd. C 55.08, H 7.53; found C 54.89, H 7.41.

Thexyldimethylsilyl *O*-[4,6-*O*-(Di-*tert*-butyl)silanediyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranosyl]-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranoside (10b): TLC (petroleum ether/ethyl acetate, 5:1) R_f = 0.62. $[\alpha]_D$ = +159.0 (*c* = 2.30, chloroform). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.19, 0.22 (2 s, 6 H, 2 SiMe), 0.87, 0.88, 0.89, 0.90 (4 s, 12 H, 4 Me), 0.94 (s, 9 H, C_4H_9), 1.05 (s, 9 H, C_4H_9), 1.59−1.70 (m, 1 H, CH), 1.82 (br. s, 6 H, 2 Me), 3.57 (m, 1 H, 5-H_a), 3.68−3.76 (m, 3 H, 4-H_a, 2 6-H_a), 3.79 (m, 1 H, 5-H_b), 3.85 (m, 1 H, 2-H_a), 4.11 (m, 1 H, 3-H_a), 4.25−4.31 (m, 3 H, 4-H_b, 2 6-H_b), 4.48−4.66 (m, 4 H, 2 CH_2Ph), 4.93 (d, $J_{1,2}$ = 3.1 Hz, 1 H, 1-H_b), 5.37 (d, $J_{1,2}$ = 8.1 Hz, 1-H_a), 5.83 (m, 2-H_b), 6.11 (m, 1 H, 3-H_b), 7.20−7.38 (m, 10 H, 2 Ph). FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 878 [MH^+], 900 [MNa^+].

***O*-[4,6-*O*-(Di-*tert*-butyl)silanediyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranosyl]-(1→5′)-2′3′-*O*-isopropylidineuridine (11b):** TLC (petroleum ether/ethyl acetate, 5:1) R_f = 0.47. $[\alpha]_D$ = −11.9 (*c* = 0.81,

chloroform). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.96 (s, 9 H, C_4H_9), 1.07 (s, 9 H, C_4H_9), 1.35, 1.52 (2 s, 6 H, 2 Me), 3.52 (m, 2 H, 2 5-H_a), 3.78 (m, 1 H, 5-H_b), 4.20−4.27 (m, 3 H, 4-H_b, 2 6-H_b), 4.35 (br. s, 1 H, 4-H_a), 4.82 (m, 2 H, 2-H_a, 3-H_a), 4.88 (d, $J_{1,2}$ = 3.2 Hz, 1 H, 1-H_b), 5.41 (d, $J_{5,6}$ = 5.6 Hz, 1 H, 5-H U), 5.84 (dd, $J_{2,1}$ = 3.2 Hz, $J_{2,3}$ = 10.0 Hz, 1 H, 2-H_b), 5.95 (br. s, 1 H, 1-H_a), 6.14 (dd, $J_{3,2}$ = 10.0 Hz, $J_{3,4}$ = 5.5 Hz, 1 H, 3-H_b), 7.59 (d, $J_{6,5}$ = 5.5 Hz, 1 H, 6-H U), 8.65 (br. s, 1 H, NH). FAB-MS: (positive mode, NBOH/NaI matrix): *m/z* = 553 [MH^+], 575 [MNa^+]. $C_{26}H_{40}N_2O_9Si$ (552.69): calcd. C 56.50, H 7.29, N 5.07; found C 56.37, H 7.08, N 4.89.

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