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The Cyanopivaloyl Ester: A New Protecting Group in the Assembly of Oligorhamnans

Anne Geert Volbeda,[a] Niels R.M. Reintjens,[a] Herman S. Overkleeft,[a] Gijsbert A. van der Marel[a] and Jeroen D. C. Codée*[a]

Abstract: Protecting groups play a vital role in the assembly of oligosaccharides. The pivaloyl (Piv) ester is commonly used to ensure 1,2-*trans* selective glycosylation reactions. A significant drawback of the Piv-ester is its stability, necessitating strong alkaline conditions for its removal. We here present the cyanopivaloyl (CNPiv) group: a modified pivaloyl group, having a cyano group appended to the *tert*-butyl moiety. The CNPiv benefits from the profitable features of the Piv-group (stability and effective neighboring group participation with minimal orthoester formation during glycosylation reactions) but can be removed under mild conditions (reduction of the cyano function followed by mild base treatment). The applicability of the CNPiv group is demonstrated in the assembly of two rhamnose oligosaccharides: a hexarhamnan that represents a fragment of the capsular polysaccharide of *Enterococcus faecium* and a tetrarhamnan that is part of the polyrhamnose backbone of the Lancefield group A carbohydrate (GAC).

Introduction

The success of an oligosaccharide or glycoconjugate synthesis campaign hinges on the protecting group strategy followed.[1,2] Protecting groups are key to discriminate the different hydroxyl and amino groups on the carbohydrate rings and have an important effect on the reactivity of the carbohydrate building block.[3–6] As well, they can be decisive in the stereochemical outcome of a glycosylation. Neighboring group participation by a C-2-*O*-acyl group is an extremely powerful means to ensure the stereoselective formation of 1,2-*trans*-glycosidic linkages. Of all ester-type protecting groups, the pivaloyl (Piv) ester is least prone to provide orthoester side products, formed by attack of the nucleophile at the dioxolenium carbon instead of the anomeric center. The neopentylic nature of the pivaloyl dioxolenium ion makes this intermediate significantly less susceptible to nucleophilic attack. Where this steric protection is beneficial during a glycosylation reaction, the bulk of the Piv group can pose a problem during the removal of this protecting group, necessitating harsh nucleophilic conditions for its removal.

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To enable cleavage of Piv-type esters under less strenuous conditions, various Piv-analogues[7] have been introduced bearing a masked nucleophile four or five atoms away from the Piv-carbonyl group. Liberating this nucleophile sets the stage for intramolecular attack allowing the smooth deprotection of the Piv ester. Figure 1 depicts some members of the relay-cleavage pivaloyl family. 2,2-Dimethylpentenoate **1**[8] can be cleaved by hydroboration of the double bond and ensuing base mediated cleavage. Piv-analogues **2**[9] and **3**[10,11] bear a distal, masked hydroxyl group that can be liberated by either fluoride or methanolate to release the internal nucleophile. We have recently introduced a *para*-methoxyphenyl caged Piv-ester **4**[12] and azido-Piv group **5**[12] that can be removed under oxidative (**4**) and reductive (**5**) conditions, respectively. We exploited the mutual orthogonality of these Piv-groups in the assembly a *Streptococcus mutans* oligosaccharide and also showed the applicability of the azido-Piv group in the solid phase assembly of a β-glucan oligomer.[13] We here introduce a new relay-cleavage pivaloyl family member: the cyanopivaloyl (CNPiv) group (**6**, Figure 1). This group was developed to streamline the global deprotection of oligosaccharides. We reasoned that a pivaloyl group that is removable under hydrogenation conditions, commonly employed to remove benzyl esters in the final stage of an oligosaccharide synthesis, could abridge the endgame. As described here, the reagents to introduce the CNPiv-goup, cyanopivalic acid **8**[14] and the corresponding acid chloride (**9**, CNPivCl) can be readily synthesized on large scale and the protective group can be easily introduced on carbohydrate building blocks. It is stable under commonly used reaction conditions and can be removed through reduction of the cyano-function. We have applied the CNPiv group in the assembly of two bacterial rhamnan structures: a tetrasaccharide, representing part of the backbone structure of the exopolysaccharide of Group A *Streptococcus*[15,16], and an *Enterococcus faecium*[17,18] derived hexarhamnoside.

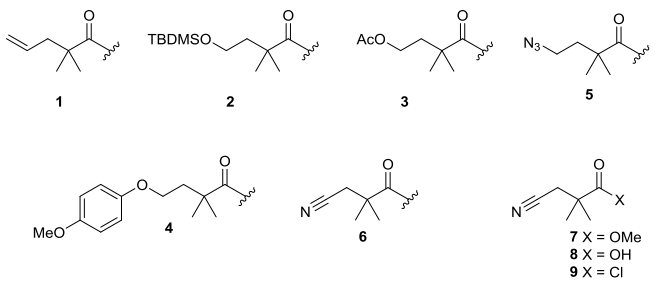
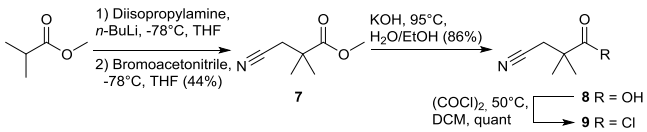


Figure 1. Pivaloyl analogues and new CNPiv **6.**

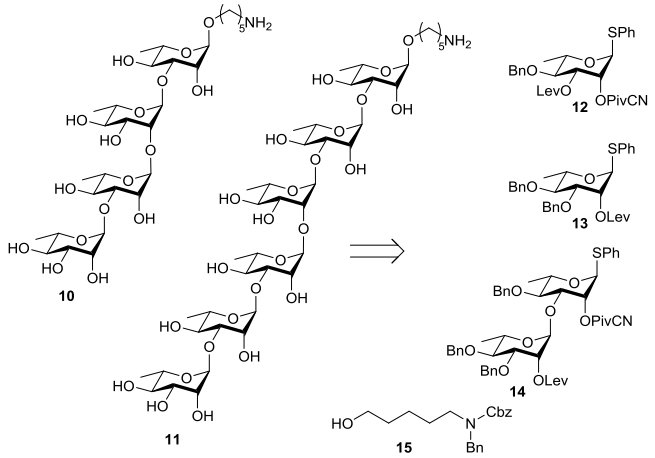
Results and Discussion

The synthesis of required reagents, cyanopivalic acid and the corresponding chloride (CNPiv-Cl) is depicted in Scheme 1. They can be generated through a three or four step reaction sequence in multigram quantities. Reaction of methyl isobutyrate with bromoacetonitrile under the influence of freshly prepared LDA, resulted in cyanide **7**. Saponification of the methyl ester then provided acid **8**, which can be reacted with oxalylchloride to yield acid chloride **9**. Both reagents can be used without further purification.



Scheme 1. Synthesis of CNPiv acid **8** and CNPiv chloride **9**.

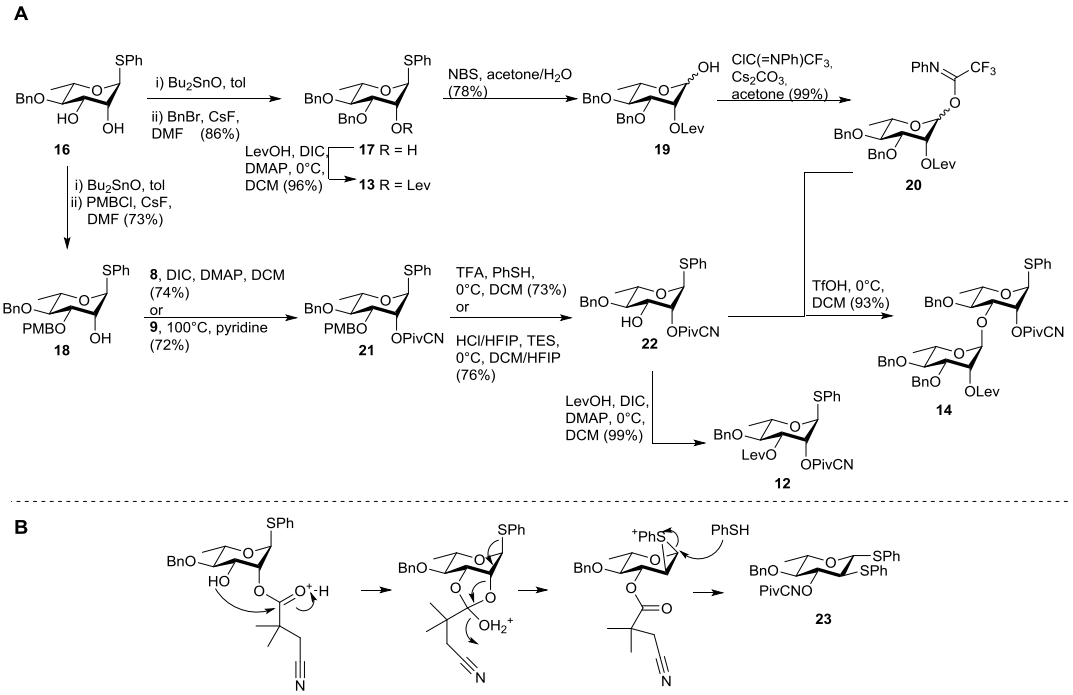
With acid **8** and chloride **9** in hand, the introduction of the CNPiv ester and its use as a protecting group in oligosaccharide synthesis was explored. Two bacterial rhamnan structures, the backbone structure of the exopolysaccharide of Group A *Streptococcus*, and an *Enterococcus faecium* capsular polysaccharide derived hexarhamnoside, were chosen as synthetic targets to validate the performance of the CNPiv group in oligosaccharide assembly.[19–26] The *Enterococcus faecium* capsular polysaccharide is composed of trisaccharide repeating units featuring α-(1,3)- and α-(1,2)-rhamnosyl linkages, whereas the Group A *Streptococcus* repeating unit is a dirhamnoside with α-(1,3) and α-(1,2)-linkages. The target structures for the current study are depicted in Scheme 2. Tetrasaccharide **10** and hexasaccharide **11** each contain two repeating units of the respective capsular polysaccharides. It was envisaged that these two target structures could be assembled from building blocks **12**, **13** and **14**, which are equipped with a levulinoyl group, that serves as a temporary protecting group, to be removed to allow elongation of the rhamnan chains, and/or a CNPiv group, which serves as a permanent participating protecting group. Linker **15**[27] is used to cap the reducing end of the target rhamnans and can serve as a handle for future conjugation chemistries.



Scheme 2. Target compounds and retrosynthetic analysis

The assembly of the building blocks is depicted in Scheme 3. Known diol **16**[28] can be selectively alkylated on the C-3-OH through the intermediacy of the cyclic tin ketal,[29] with either benzylbromide or *para*-methoxybenzylchloride to give rhamnosides **17** and **18** in 86% and 73% yield respectively. Esterification of the C-2-hydoxyl group in **17** with levulinic acid yields donor **13** in excellent yield (96%). Thioglycoside **13** can be converted into the corresponding hemiacetal **19** by *N*-bromosuccinimide driven hydrolysis (78%). Installation of the *N*-phenyltrifluoroacetimidate group[30] on the anomeric alcohol then delivers **20** in high yield (99%). PMB protected rhamnoside **18** is treated with acid chloride **9** and pyridine at elevated temperature to provide fully protected compound **21** in 72% yield. Under standard esterification conditions, applying the CNPiv acid **8** in concert with di-*iso*-propylcarbodiimide (DIC) and dimethylaminopyridine (DMAP), compound **21** was obtained in good yield (74%). To remove the PMB ether, we initially explored deprotection conditions using trifluoroacetic acid and a thiol scavenger.[12] Besides the desired alcohol **22**, these conditions also provided deoxy-L-glucoside **23**, bearing the CNPiv group at its C-3-OH and a C-2-thiophenol group, as a prominent side product. This product is likely the result of the mechanism depicted in Scheme 3B. Under the acidic conditions used, the CNPiv ester can be protonated and subsequently attacked by the neighboring C-3-alcohol. Migration of the CNPiv ester to the C-3 position can be caused by the participating anomeric thiophenol moiety to provide an intermediate episulfonium ion. This is attacked at the anomeric center to provide deoxy-L-glucoside **23**.[31–33]

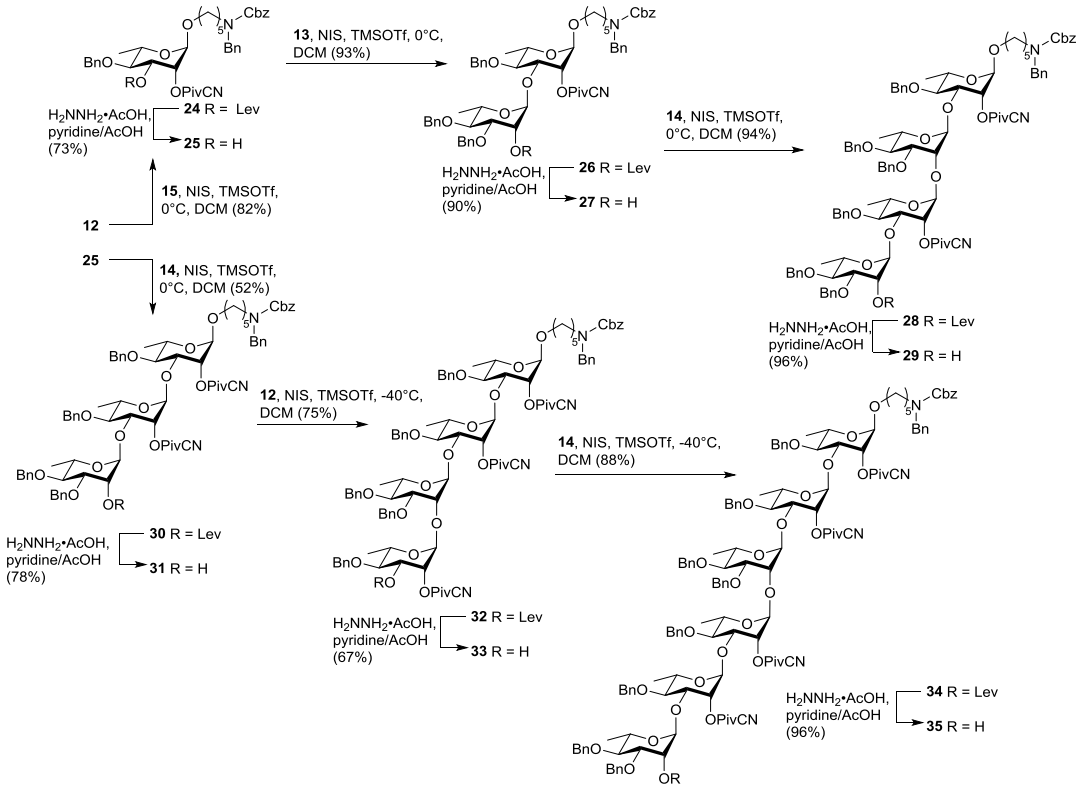
We recently showed that a catalytic amount of HCl in 2,2,2,3,3,3-hexafluoro-*iso*-propanol (HFIP) could be used to cleave electron rich benzyl ethers in a mild and fast manner.[34] Application of these conditions proved effective here to remove the C-3-*O*-PMB from rhamnoside **21**. The reaction time had to be carefully controlled as a prolonged reaction time led to activation of the anomeric thiophenol function. The liberated alcohol in compound **22** was masked with a levulinoyl group to provide building block **12**. Rhamnoside **22** was also used to generate disaccharide building block **14**. To this end, *N*-phenyltrifluoroacetimidate rhamnoside **20** and thiorhamnoside acceptor **22** were combined in a chemoselective glycosylation reaction to provide the dirhamnoside **14** in high yield (93%) and with complete stereoselectivity.



Scheme 3. Building block synthesis.

Having assembled the required building blocks, we turned to the construction of the two target oligosaccharides (Scheme 4). First, the linker-functionalized rhamnoside was generated in a stereoselective, NIS/TMSOTf-mediated glycosylation[35] of donor **12** with protected aminohexanol **15**.

Next the levulinoyl ester was removed to provide the monosaccharide acceptor building block **25**. This monosaccharide was elongated with monorhamnoside **13** to give dimer **26** in 93% yield. Liberation of the C-2"-OH by treatment of **26** with hydrazine set the stage for the next

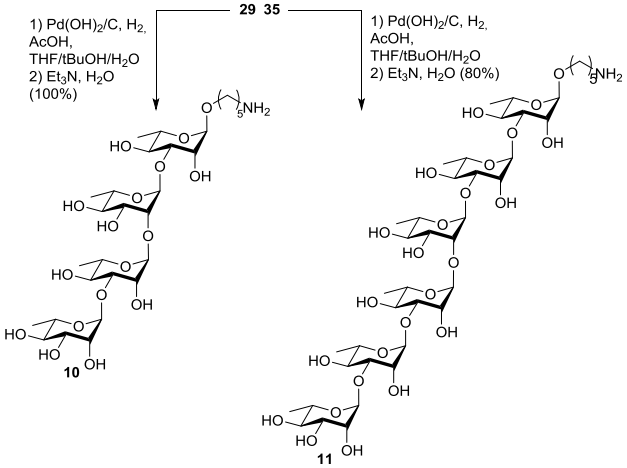


Scheme 4. Synthesis of the fully protected tetra- and hexasaccharide targets.

glycosylation. In this condensation the dimers **14** and **27** were united to provide the fully protected target tetrasaccharide **28** in high yield.

Next the assembly of the protected hexarhamnan **34** was undertaken. To this end linker bearing monorhamnose **25** and dirhamnoside **14** were coupled under the agency of NIS/TMSOTf to provide trisaccharide **30** in 52% yield. Delevulinuylation of **30** was followed by a glycosylation with monorhamnose donor **12** to provide the tetrasaccharide **32** in 75% yield. Removal of the Lev-ester then paved the way for the final glycosylation in which tetramer **33** was elongated with dirhamnoside **14** giving the fully protected hexarhamnan in 88% yield.

With the two fragments in hands, we commenced the deprotection sequence. First the levulinoyl groups were removed. Next all benzyl ethers and cyano groups were reduced by hydrogenolysis using $Pd(OH)_2/C$. The reduction was achieved in two stages, the first of which was executed in a THF/tBuOH/H_2O/AcOH solvent system. After filtration the partially deprotected material was taken up in water and subjected to a second hydrogen event. During the hydrogenation AcOH was added to prevent deactivation of the catalyst. Reduction of the cyano-groups released the primary amines of the Piv-like esters, which under the reaction conditions used are protonated. To affect ring closure, release the 2,2-dimethyl-γ-butyrolactam and complete the removal of the CNPiv esters the crude products were treated with triethylamine in water. The release of the 2,2-dimethyl-γ-butyrolactam could be easily followed by NMR analysis using the characteristic triplets of the liberated lactam. After completion of the reaction, the crude tetra- and hexasaccharide were purified by size exclusion chromatography to provide Group A *Streptococcus* tetrarhamnan **10** and *Entrococcus faecium* hexarhamnan **11** in 100% and 80% respectively.



Scheme 5. Deprotection of the tetra- and hexasaccharide.

Conclusions

Herein we have described the introduction of the cyanopivaloyl ester as a novel hydroxyl protecting group. It features a cyano moiety appended two atoms away from the ester carbonyl to allow for a relay-cleavage of the pivaloyl type ester. This cleavage mechanism alleviated one of the major drawbacks of the pivaloyl ester, that is, its difficult removal.

We have shown the applicability of the novel protecting group in the assembly of two bacterial oligorhamnans. It represents a robust protecting group that tolerates many functional group manipulations and withstands both (Lewis) acidic as well as mild basic conditions. It is a new member of the family of pivaloyl-type protecting groups and may be used in combination with other pivaloyl type esters, such as the recently introduced azidopivaloyl group, as a (semi)-orthogonal pair for the streamlined synthesis of carbohydrates and other complex (bio)molecules.

Experimental Section

General experimental procedures. All chemicals were used as received unless stated otherwise. ^1H and ^{13}C NMR spectra were recorded on a 400/100 MHz, 500/125 MHz, 600/150 MHz or a 850/214 MHz spectrometer. Chemical shifts (δ) are given in ppm relative to tetramethylsilane as internal standard. Coupling constants are given in Hz. All individual signals were assigned using 2D-NMR spectroscopy, HH-COSY, HSQC and HMBC. IR spectra are reported in cm^{-1}. Flash chromatography was performed on silica gel 60 (0.04 – 0.063 mm). TLC-analysis was followed by detection by UV-absorption (254 nm) where applicable and by spraying with 20% sulfuric acid in ethanol followed by charring at ~150 °C or by spraying with a solution of $(NH_4)_6Mo_7O_{24}{\cdot}H_2O$ (25 g/l) and $(NH_4)_4Ce(SO_4)_4{\cdot}2H_2O$ (10 g/l) in 10% sulfuric acid in water followed by charring at 50 °C. LC-MS standard eluents used were A: 100% H_2O, B: 100% acetonitrile, C: 1% TFA in H_2O. The column used was a C18 column (4.6 mmD × 50 mmL, 3µ particle size). All analyses were 13 min, with a flow-rate of 1 ml/min. High-resolution mass spectra were recorded on a LTQ-Orbitrap equipped with an electrospray ion source in positive mode (source voltage 3.5 kV, sheath gas flow 10, capillary temperature 275ºC) with resolution R=60.000 at m/z=400 (mass range = 150-4000) and dioctylphthalate (m/z=391.28428) as "lock mass". High resolution mass measurements were performed on a Synapt G2-Si MALDI-TOF mass spectrometer equipped with a 355-nm laser. 1 uL samples were spotted on the MALDI-plate, followed by applying 1 uL of the the matrix solution (2,5-dihydroxybenzoic acid 100 mg/mL dissolved in H_2O : ACN : dimethylaniline 1 : 1 : 0.02). A laser frequency of 1000 Hz (power set at 60%) was used.

Methyl 3-cyano-2,2-dimethylpropanoate (7) A solution of LDA was prepared by adding *n*-butyllithium in hexanes (1.6 M, 134.8 mL, 215.7 mmol, 1 equiv.) drop wise to a solution of diisopropylamine (33.4 mL, 238 mmol, 1.1 equiv.) in THF (310 mL) at -78°C under argon. After 45 min no more bubbles appeared and methyl isobutyrate (28.2 mL, 246 mmol, 1.13 equiv.) was added. After 1h of stirring at -78°C, bromoacetonitrile (19.5 mL, 280 mmol, 1.26 equiv.) was added. The resulting dark mixture was allowed to warm up gradually to room temperature and stirred overnight. The reaction was neutralized by the addition of 1M HCl (90 mL) and 2M HCl (240 mL) at 0 °C. The mixture was diluted with brine, followed by extraction with Et_2O (3x). The combined organic layers were washed with sat. aq. $NaHCO_3$ (6x), H_2O (6x) and brine (1x), dried over $MgSO_4$, and concentrated *in vacuo*. Purification by column

chromatography (19:1 PE/EtOAc to 4:1 PE/EtOAc) and coevaporation with $CHCl_3$ resulted in the title compound as a light yellow oil (13.45 g, 95.3 mmol). Analytical data are identical to literature precendence.[36]

3-cyano-2,2-dimethylpropanoic acid (8) A suspension was formed by the addition of H_2O (205 mL) and EtOH (35 mL) to compound **7** (13.45 g, 95.3 mmol, 1 equiv.). Lithium hydroxide (98%) (5.85 g, 244 mmol, 2.5 equiv.) was added and the mixture was refluxed at 95°C for 5.5h. The mixture was cooled to 0 °C, quenched with 1M HCl to pH = 1, diluted with H_2O and extracted with EtOAc (2x). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Coevaporation with DCM and $CHCl_3$ resulted in an oil that crystallized out as a light yellow solid (10.41 g, 81.89 mmol, 33% in two steps). IR (neat): 3368, 3192, 2971, 2936, 2884, 2544, 2264, 1699, 1661, 1585, 1474, 1449, 1412, 1398, 1366, 1308, 1240, 1231, 1202, 1184, 1140, 1020, 974, 937, 922, 899, 874, 858, 831, 797, 773, 750, 648 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 11.12 (bs, 1H, OH), 2.63 (s, 2H, CH_2), 1.42 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 181.5 (C=O), 117.4 (CN), 41.0 (C_q), 27.8 (CH_2), 24.7 (CH_3). HRMS calculated for $[C_6H_9NO_2 + H]^+$: 128.07061, found 128.07055.

3-cyano-2,2-dimethylpropanoyl chloride (9) After coevaporation with anhydrous toluene, acid **8** (5.53 g, 43.5 mmol, 1 equiv.) was dissolved in DCM (110 mL). Oxalylchloride (8.4 mL, 97.8 mmol, 2.2 equiv.) was added at room temperature and the solution was refluxed at 40 °C for 40 min allowing the gases produced during the reaction to be stripped by a stream of argon, after which the water cooling was closed and the DCM was allowed to evaporate at 50 °C for 2h. The reaction mixture was cooled and concentrated *in vacuo*. The obtained oil was used directly without further purification. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.70 (s, 2H, CH_2), 1.49 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.6 (C=O), 116.3 (CN), 50.6 (C_q), 27.8 (CH_2), 24.5 (CH_3).

Phenyl 4-O-benzyl-1-thio-α-L-rhamnopyranoside (16) A solution of 80% acetic acid (950 mL) was added to phenyl 4-*O*-benzyl-2,3-di-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside (73.8 g, 191 mmol) and heated to 70 °C and stirred overnight after which TLC analysis showed complete consumption of the starting material. The reaction was cooled down to 0 °C, neutralized with Et_3N, diluted with H_2O and extracted with EtOAc (2x). The combined organic layers were washed with sat. aq. $NaHCO_3$ (5x) and brine (1x), dried over MgSO4 and concentrated in vacuo. Crystallization (EtOH) at -20 °C resulted in the title compound as a white solid (58.3 g, 168.3 mmol, 88%). R_f = 0.51 (2:1 PE/EtOAc). Analytical data are identical to literature precendence.[28]

Phenyl 3,4-di-*O*-benzyl-1-thio-*α*-L-rhamnopyranoside (17) Diol **16** (3.47 g, 10.0 mmol, 1 equiv.) was coevaporated with anhydrous toluene two times under argon and dissolved in anhydrous toluene (100 mL). Dibutyltin oxide (3.00 g, 12.1 mmol, 1.2 equiv.) was added and the white suspension was heated to 105°C. The reaction was stirred overnight after which the clear solution was cooled down and concentrated *in vacuo*. After three times coevaporation with anhydrous toluene under argon, the oil was dissolved in DMF (100 mL). BnBr (1.6 mL, 13.5 mmol, 1.3 equiv.) and CsF (3.05 g, 20.1 mmol, 2 equiv.) were added. After 6h, TLC-MS and TLC analysis showed complete reaction and the reaction mixture was diluted with EtOAc, washed with H_2O (2x), brine (2x), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (PE to 2:1 PE/EtOAc) yielded the title compound as a colorless oil (3.76 g, 8.62 mmol, 86%). R_f = 0.77 (2:1 PE/EtOAc). Analytical data are identical to literature precendence.[29]

Phenyl 3,4-di-*O*-benzyl-2-*O*-levulinoyl-1-thio-*α*-L-rhamnopyranoside (13) After coevaporation with anhydrous toluene (2x) under argon, compound **17** (9.79 g, 22.5 mmol, 1 equiv.) was dissolved in freshly distilled DCM and cooled to 0 °C. Levulinic acid (6.38 mL, 62.9 mmol, 2.8 equiv.), *N,N'*-diisopropylcarbodiimide (4.92 mL, 31.4 mmol, 1.4 equiv.) and 4-dimethylaminopyridine (0.31 g, 2.54 mmol, 0.1 equiv.) were added at 0 °C. After 1.5h the reaction was allowed to warm up to room temperature and stirred overnight. After TLC-MS showed complete consumption of the starting material, the mixture was filtered over Celite and the filtrate was washed with sat. aq. $NaHCO_3$ (2x) and brine (1x). The organic layer was dried over $MgSO_4$, concentrated *in vacuo* and coevaporated with anhydrous toluene. Purification by column chromatography (3:1 PE/EtOAc) and coevaporation with $CHCl_3$ (2x) resulted in the title compound as a yellow oil (11.50 g, 21.51 mmol, 96%). R_f = 0.38 (7:2 PE/EtOAc); IR (neat): 2968, 1728, 1472, 1439, 1358, 1300, 1198, 1132, 1098, 1051, 1022, 903, 835, 783, 733, 689 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.44-7.26 (m, 15H, CH_{arom}), 5.59 (m, 1H, H-2), 5.41 (d, 1H, *J* = 1.2 Hz, H-1), 4.93 (d, 1H, *J* = 10.8 Hz, CH_2 Bn), 4.70 (d, 1H, *J* = 11.2 Hz, CH_2 Bn), 4.63 (d, 1H, *J* = 10.8 Hz, CH_2 Bn), 4.54 (d, 1H, *J* = 11.2 Hz, CH_2 Bn), 4.22 (dq, 1H, *J* = 9.4, 6.2 Hz, H-5), 3.90 (dd, 1H, *J* = 9.3, 3.3 Hz, H-3), 3.48 (t, 1H, *J* = 9.4 Hz, H-4), 2.76-2.69 (m, 4H, 2x CH_2 Lev), 2.16 (s, 3H, CH_3 Lev), 1.33 (d, 3H, *J* = 6.2 Hz, CH_3-6); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 206.3 (C=O Lev ketone), 172.1 (C=O Lev), 138.5, 137.9, 134.0 (C_q C_{arom}), 131.9, 129.2, 128.5, 128.5, 128.3, 128.2, 128.0, 127.9, 127.8 (CH_{arom}), 86.1 (C-1), 80.3 (C-4), 78.4 (C-3), 75.6 (CH_2 Bn), 71.8 (CH_2 Bn), 70.9 (C-2), 69.1 (C-5), 38.1 (CH_2 Lev), 30.0 (CH_3 Lev), 28.3 (CH_2 Lev), 18.0 (CH_3-6); HRMS calculated for $[C_{31}H_{34}O_6S + NH_4]^+$: 552.24144, found 552.24165.

3,4-di-*O*-benzyl-2-*O*-levulinoyl-*α*/*β*-L-rhamnopyranoside (19) Compound **13** (1.07 g, 2.00 mmol, 1 equiv.) was dissolved in acetone/water 3:1 (10 mL) and cooled to 0 °C. *N*-bromosuccinimide (1.08 g, 6.07 mmol, 3 equiv.) was added and the mixture was stirred at 0 °C. The reaction was allowed to warm up to room temperature after 100 min and stirred overnight. The reaction was quenched by addition of sat. aq. $Na_2S_2O_3$, diluted with EtOAc and the organic layer was washed with sat. aq. $NaHCO_3$ (2x), H_2O (1x) and brine (1x). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (3:1 to 1:1 PE/EtOAc) yielded hemiacetal **19** (0.692 g, 1.56 mmol, 78%). R_f = 0.53 (1:1 PE/EtOAc); IR (neat): 1738, 1717, 1362, 1207, 1155, 1063, 1042, 1028, 988, 912, 837, 735, 696 cm^{-1}; NMR assignment for the major isomer: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.33-7.2 (m, 10H, CH_{arom}), 5.25 (m, 1H, H-2), 5.03 (s, 1H, H-1), 4.91-87 (m, 1H, CH_2 Bn), 4.72-4.58 (m, 2H, CH_2 Bn), 4.51-4.45 (m, 1H, CH_2 Bn), 4.00-3.93 (m, 2H, H-3, H-5), 3.40 (t, 1H, *J* = 9.2 Hz, H-4), 2.76-2.60 (m, 4H, 2x CH_2 Lev), 2.11 (s, 3H, CH_3 Lev), 1.27 (d, 3H, *J* = 6.2 Hz, CH_3-6); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 206.9 (C=O Lev ketone), 172.1 (C=O Lev), 138.3, 137.9 (C_q C_{arom}), 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 127.7, 127.6, 127.6 (CH_{arom}), 91.9 (C-1), 80.0 (C-4), 77.4 (C-3), 75.2 (CH_2 Bn), 71.4 (CH_2 Bn), 69.6 (C-2), 67.3 (C-5), 37.9 (CH_2 Lev), 29.7 (CH_3 Lev), 28.0 (CH_2 Lev), 18.0 (CH_3-6). HRMS calculated for $[C_{25}H_{30}O_7 + NH_4]^+$: 460.23298, found 460.23299.

3,4-di-*O*-benzyl-2-*O*-levulinoyl-1-(*N*-[phenyl]-trifluoroacetimidoyl)-*α*/*β*-L-rhamnopyranoside (20) To a solution of compound **19** (0.65 g, 1.47 mmol, 1 equiv.) in acetone (7.4 mL), were added $ClC(=NPh)CF_3$ (0.27 mL, 1.78 mmol, 1.2 equiv.) and Cs_2CO_3 (0.72 g, 2.21 mmol, 1.5 equiv.) at 0 °C. The reaction was allowed to warm up to room temperature after 40 min and stirred for an additional 20 min. TLC analysis showed complete consumption of starting material. The reaction was diluted with EtOAc and the organic layer was washed with H_2O (2x) and brine (1x). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (7:1 PE/EtOAc to EtOAc) yielded the title compound in a 4:1 α/β-ratio (0.894 g, 1.456 mmol, 99%). R_f = 0.54 (4:1 PE/EtOAc); IR (neat): 2922, 1740, 1717, 1454, 1364, 1312, 1207, 1153, 1119, 1072, 1028, 985, 943, 920, 839, 735, 696 cm^{-1}; NMR assignment for the major isomer: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.35-7.23 (m, 12H, CH_{arom}), 7.09-7.06 (m, 1H, CH_{arom}), 6.86-6.80 (m, 2H, CH_{arom}), 6.17 (bs, 1H, H-1), 5.49 (s, 1H, H-2), 4.92 (d, 1H, *J* = 10.8 Hz, CH_2 Bn), 4.71 (d, 1H, *J* = 11.2 Hz, CH_2 Bn), 4.63 (d, 1H,

J = 10.8, CH_2 Bn), 4.55 (d, 1H, *J* = 11.2 Hz, CH_2 Bn), 3.98 (dd, 1H, *J* = 9.2, 2.8 Hz, H-3), 3.90 (m, 1H, H-5), 3.50 (t, 1H, *J* = 9.2 Hz, H-4), 2.75-2.63 (m, 4H, 2x CH_2 Lev), 2.08 (s, 3H, CH_3 Lev), 1.36 (d, 1H, *J* = 6.0 Hz, CH_3-6); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 205.8 (C=O Lev ketone), 171.6 (C=O Lev), 143.2, 138.0, 137.5 (C_q C_{arom}), 128.7, 128.3, 128.3, 128.2, 128.0, 128.0, 127.8, 127.8, 124.4, 199.3 (CH_{arom}), 94.2 (C-1), 79.1 (C-4), 77.2 (C-3), 75.5 (CH_2 Bn), 71.9 (CH_2 Bn), 70.4 (C-5), 67.6 (C-2), 37.7 (CH_2 Lev), 29.6 (CH_3 Lev), 27.9 (CH_2 Lev), 17.9 (CH_3-6). TLC-MS: *m/z* = 636.35 ($M+Na^+$).

Phenyl 4-*O*-benzyl-3-*O*-*p*-methoxybenzyl-1-thio-*α*-L-rhamnopyranoside (18) Diol **16** (6.94 g, 20.0 mmol, 1 equiv.) was coevaporated with anhydrous toluene two times under argon and dissolved in anhydrous toluene (200 mL). Dibutyltin oxide (5.99 g, 24.1 mmol, 1.2 equiv.) was added to the mixture, which was stirred overnight at 105°C. The clear solution was cooled to 0 °C, concentrated *in vacuo* and two times coevaporated with anhydrous toluene under argon. The oil was dissolved in DMF (200 mL), followed by the addition of *p*-methoxybenzyl chloride (3.1 mL, 22.9 mmol, 1.12 equiv.) and CsF (6.08 g, 40.0 mmol, 2 equiv.). After heating the mixture to 80 °C for 5h, TLC analysis showed complete reaction, and the reaction mixture was cooled to 0 °C, diluted with H_2O and extracted two times with EtOAc. The combined organic layers were washed with H_2O (2x) and brine (2x). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo.* Purification by column chromatography (PE to 2:1 PE/EtOAc) and (5:1 PE/EtOAc to 2:1 PE/EtOAc) resulted in the title compound as a clear oil (6.83 g, 14.6 mmol, 73%). R_f = 0.75 (2:1 PE/EtOAc). Analytical data are identical to literature precendence.[29]

Phenyl 4-*O*-benzyl-3-*O*-*p*-methoxybenzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-1-thio-*α*-L-rhamnopyranoside (21)

Method A: Crude chloride **9** (5.53 g, 43.5 mmol, 2 equiv.) was cooled to 0 °C and dissolved in pyridine (20 mL). A solution of compound **18** (10.14 g, 21.7 mmol, 1 equiv.) in pyridine (2x 20 mL) was added to the crude chloride. After an addition of another 50 mL pyridine, the resulting dark mixture was heated to 110 °C. After 1h, TLC and TLC-MS analysis showed complete reaction and the mixture was cooled to 0 °C. The reaction mixture was diluted with EtOAc and washed with H_2O (1x), 1M HCl (2x) and brine (2x). The organic layer was dried over $MgSO_4$, concentrated *in vacuo* and coevaporated with toluene. Purification by flash column chromatography (8:1 PE/EtOAc → 3:1 PE/EtOAc) and (10:1 PE/EtOAc → EtOAc) and coevaporation with $CHCl_3$ resulted in the title compound as an oil (9.04 g, 15.7 mmol, 72%), which contained 5% byproduct.

Method B: Acid **8** (3.49 g, 27.5 mmol, 2 *equiv.*) and compound **18** (6.41 g, 13.75 mmol, 1 *equiv.*) were coevaporated twice with anhydrous toluene after which they were dissolved in dry DCM (35 mL). The solution was cooled to 0 °C and DIC (2.37 mL, 15.13 mmol, 1.1 *equiv.*) and DMAP (0.17 g, 1.37 mmol, 0.1 *equiv.*) were added. The reaction was allowed to stir overnight, after which TLC analysis showed conversion of the starting material in a higher running spot. Filtration over Celite followed by washing with sat. aq. $NaHCO_3$, the organic layer was dried over $MgSO_4$ and concentrated. Purification by flash column chromatography (PE/EtOAc 1:0 → 4:1) yielded the fully protected rhamnopyranoside as a yellow oil (5.86 g, 10.2 mmol, 74%). R_f = 0.68 (3:1 PE/EtOAc); IR (neat): 2974, 2874, 1734, 1612, 1514, 1472, 1454, 1300, 1246, 1136, 1098, 1084, 1030, 820, 739, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.46-7.43 (m, 2H, CH_{arom}), 7.32-7.22 (m, 10H, CH_{arom}), 6.87-6.84 (m, 2H, CH_{Arom}), 5.62 (m, 1H, H-2), 5.37 (d, 1H, *J* = 1.2 Hz, H-1), 4.90 (d, 1H, *J* = 10.8 Hz, CH_2 Bn), 4.64 (d, 1H, *J* = 10.8 Hz, CH_2 Bn), 4.60 (d, 1H, *J* = 10.8 Hz, CH_2 PMB), 4.47 (d, 1H, *J* = 10.4 Hz, CH_2 PMB), 4.24 (dq, 1H, J = 9.4, 6.2 Hz, H-5), 3.90 (dd, 1H, *J* = 9.2, 3.2 Hz, H-3), 3.80 (s, 3H, OCH_3 PMB), 3.42 (t, 1H, *J* = 9.2 Hz, H-4), 2.56 (s, 2H, CH_2 CNPiv), 1.36 (s, 6H, 2x CH_3 CNPiv), 1.32 (d, 3H, *J* = 6.0 Hz, H-6); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 174.1 (C=O CNPiv), 159.5, 138.3, 133.7 (C_q C_{arom}), 132.1, 132.1 130.0, 129.8 (CH_{arom}), 129.3 (C_q C_{arom}), 128.5, 128.3, 128.0, 127.9, 127.8 (CH_{arom}), 117.6 (CN), 114.0, 113.9 (CH_{arom}), 86.0 (C-1), 79.9 (C-4), 78.1 (C-3), 75.5 (CH_2 Bn), 71.6 (CH_2 PMB), 71.4 (C-2), 69.1 (C-5), 55.4 (CH_3 PMB), 41.2 (C_q CNPiv), 28.1 (CH_2 CNPiv), 24.9, 24.8 (CH_3 CNPiv), 18.0 (CH_3-6); HRMS calculated for $[C_{33}H_{37}NO_6S + NH_4]^+$: 593.26798, found 593.26838.

Phenyl 4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-1-thio-*α*-L-rhamnopyranoside (22)

Method A: To a solution of compound **21** (8.47 g, 14.72 mmol, 1 equiv.) in DCM (75 mL), thiophenol (1.65 mL, 16.12 mmol, 1.1 equiv.) was added and the mixture was cooled down to 0 °C, after which trifluoroacetic acid (7.5 mL) was added. The reaction mixture was stirred for 3h, after which TLC-MS analysis showed complete consumption of the starting material. The mixture was diluted with Et_2O, washed with sat. aq. $NaHCO_3$ (4x), H_2O (1x) and brine (1x). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (7:1 PE/EtOAc to 3:1 PE/EtOAc) and coevaporation with DCM and $CHCl_3$ resulted in the title compound as a clear oil (5.38 g, 10.8 mmol, 73%).

Method B: Compound **21** (3.085 g, 5.35 mmol) is dissolved in 27 mL DCM and 27 mL HFIP. The mixture was cooled to 0 °C and TES (2.56 mL, 16.05 mmol, 3 *equiv.*) was added. 26.8 mL of a freshly prepared HCl/HFIP solution (0.2 M, 1 *equiv.*) was added and the reaction was stirred for 7 minutes after which it was quenched with sat. aq. $NaHCO_3$. Purification by column chromatography (PE/EtOAc 1:0 → 8:1) yielded **22** as a colorless oil (0.08 g, 0.175 mmol, 76%). R_f = 0.38 (7:2 PE/EtOAc); IR (neat): 3435, 2974, 2880, 1732, 1471, 1298, 1198, 1136, 1078, 1024, 968, 847, 772, 739, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.48-7.45 (m, 2H, CH_{arom}), 7.36-7.27 (m, 8H, CH_{arom}), 5.40 (m, 1H, H-2), 5.37 (d, 1H, *J* = 1.2 Hz, H-1), 4.79 (d, 2H, *J* = 4.4 Hz, CH_2 Bn), 4.27 (dq, 1H, *J* = 9.4, 6.2 Hz, H-5), 4.09 (dd, 1H, *J* = 9.2, 2.8 Hz, H-3), 3.44 (t, 1H, *J* = 9.2 Hz, H-4), 2.59 (d, 2H, *J* = 4.8 Hz, CH_2 CNPiv), 2.05 (bs, 1H, OH), 1.39 (s, 6H, 2x CH_3 CNPiv), 1.38 (s, 3H, CH_3-6). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 174.3 (C=O CNPiv), 138.0, 133.7 (C_q C_{arom}), 132.1, 129.2, 128.7, 128.3, 128.2, 127.9 (CH_{arom}), 118.0 (CN), 85.8 (C-1), 81.5 (C-4), 75.3 (CH_2 Bn), 74.9 (C-2), 70.8 (C-3), 68.9 (C-5), 41.3 CNPiv), 28.0 (CH_2 CNPiv), 25.0, 25.0 (CH_3 CNPiv), 18.1 (CH_3-6); HRMS calculated for $[C_{25}H_{29}NO_5S + Na]^+$: 478.16586, found 478.16531.

Phenyl 4-*O*-benzyl-3-*O*-(3-cyano-2,2-dimethylpropanoyl)-1-thio-2-thiophenyl-*α*-L-rhamnopyranoside (23) R_f = 0.61 (7:1 PE/EtOAc); IR (neat): 2968, 2847, 1728, 1582, 1472, 1439, 1300, 1198, 1132, 1096, 1051, 1020, 783, 733, 689 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.67-7.61 (m, 2H, CH_{arom}), 7.47-7.42 (m, 2H, CH_{arom}), 7.35-7.23 (m, 11H, CH_{arom}), 5.28 (dd, 1H, *J* = 10.7, 8.2 Hz, H-3), 4.61 (s, 2H, CH_2 Bn), 4.35 (d, 1H, *J* = 10.6 Hz, H-1), 3.35-3.25 (m, 2H, H-4, H-5), 3.03 (t, 1H, *J* = 10.7 Hz, H-2), 2.54 (d, 2H, *J* = 8.7 Hz, CH_2 CNPiv), 1.42 (s, 6H, 2x CH_3 CNPiv), 1.29 (d, 3H, *J* = 5.6 Hz, CH_3-6); ^{13}C NMR (100 MHz, CDCl3) *δ*: 174.2 (C=O CNPiv), 137.5 (C_q C_{arom}), 135.0 (CH_{arom}), 132.7 (C_q C_{arom}), 132.5 (CH_{arom}), 130.1 (C_q C_{arom}), 129.2, 129.0, 128.9, 128.6, 128.1, 127.9, 127.5 (CH_{arom}), 117.6 (CN), 86.5 (C-1), 83.0 (C-4), 75.7 (C-3), 75.3 (C-5), 74.8 (CH_2 Bn), 52.1 (C-2), 41.0 (C_q CNPiv), 28.0 (CH_2 CNPiv), 25.0, 24.8 (CH_3 CNPiv), 18.3 (CH_3-6); HRMS calculated for $[C_{31}H_{33}NO_4S_2 + NH_4]^+$: 565.21893, found 565.21935.

Phenyl 4-*O*-benzyl-3-*O*-levulinoyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-1-thio-*α*-L-rhamnopyranoside (12) After coevaporation of compound **22** (2.47 g, 5.42 mmol, 1 equiv.) with anhydrous toluene (2x) under argon, it was dissolved in distilled DCM (13.5 mL) and cooled to 0 °C. Levulinic acid (1.54 mL, 15.2 mmol, 2.8

equiv.), *N,N'*-diisopropylcarbodiimide (1.2 mL, 7.7 mmol, 1.4 equiv.) and a catalytic amount of 4-dimethylaminopyridine (0.066 g, 0.54 mmol, 0.1 equiv.) were added. After 30 min, TLC-MS analysis showed complete reaction and the mixture was filtered over Celite. The filtrate was washed with sat. aq. $NaHCO_3$ (2x), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (2:1 PE/EtOAc) and coevaporation with DCM and $CHCl_3$ resulted in the title compound as an oil (2.97 g, 5.36 mmol, 99%). R_f = 0.59 (2:1 PE/EtOAc); IR (neat): 2976, 1740, 1717, 1474, 1362, 1300, 1204, 1150, 1132, 1099, 1084, 912, 741, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ*: 7.46-7.43 (m, 2H, CH_{arom}), 7.37-7.24 (m, 8H, CH_{arom}), 5.54 (m, 1H, H-2), 5.36 (d, 1H, *J* = 1.2 Hz, H-1), 5.31 (dd, 1H, *J* = 9.6, 3.2 Hz, H-3), 4.78 (d, 1H, *J* = 11.2 Hz, CH_2 Bn), 4.34 (dq, 1H, *J* = 9.4, 6.0 Hz, H-5), 3.64 (t, 1H, *J* = 9.6 Hz, H-4), 2.77-2.64 (m, 2H, CH_2 Lev), 2.59 (d, 2H, *J* = 1.6 Hz, CH_2 CNPiv), 2.56-2.44 (m, 2H, CH_2 Lev), 2.14 (s, 3H, CH_3 Lev), 1.39 (s, 6H, 2x CH_3 CNPiv), 1.36 (s, 3H, CH_3-6); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 206.0 (C=O Lev ketone), 173.6, 171.7 (C=O CNPiv, Lev), 137.7, 133.1 (C_q C_{arom}), 131.9, 129.0, 128.9, 128.3, 128.0, 127.8 (CH_{arom}), 117.4 (CN), 85.2 (C-1), 78.1 (C-4), 74.8 (CH_2 Bn), 72.2, 72.2 (C-2, C-3), 68.9 (C-5), 41.0 (C_q CNPiv), 27.5 (CH_2 Lev), 29.5 (CH_3 Lev), 27.7, 27.6 (CH_2 Lev, CH_2 CNPiv), 24.7, 24.6 (CH_3 CNPiv), 17.8 (CH_3-6); HRMS calculated for $[C_{30}H_{35}NO_7S + Na]^+$: 576.20264, found 576.20209.

Phenyl 3-*O*-(3,4-di-*O*-benzyl-2-*O*-levulinoyl-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-1-thio-*α*-L-rhamnopyranoside (14) Imidate donor **20** (0.353 g, 0.575 mmol, 1.2 equiv.) and acceptor **22** (0.219 g, 0.481 mmol, 1 equiv.) were coevaporated two times with anhydrous toluene under an argon atmosphere before being dissolved in distilled DCM (4.8 mL) and the mixture was stirred at room temperature for 15 min over activated molecular sieves (3Å). The reaction was cooled to 0 °C and triflic acid (4.5 µL, 0.051 mmol, 0.1 equiv.) was added. After 20 min the reaction was quenched by addition of 0.1 mL Et_3N. The reaction mixture was diluted with Et_2O and washed with H_2O (2x) and brine (2x). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. Purification by size exclusion (1:1 DCM/MeOH) resulted in the title compound as a yellow oil (0.394 g, 0.448 mmol, 93%). R_f = 0.64 (7:2 PE/EtOAc); IR (neat): 2974, 2930, 1740, 1717, 1452, 1364, 1204, 1136, 1117, 1082, 1028, 989, 922, 845, 731, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ*: 7.45-7.20 (m, 20H, CH_{arom}), 5.40 (m, 1H, H-2'), 5.31 (s, 2H, H-1, H-2), 5.07 (s, 1H, H-1'), 4.93 (d, 1H, *J* = 11.2 Hz, CH_2 Bn), 4.79 (d, 1H, *J* = 10.8 Hz, CH_2 Bn), 4.65-4.59 (m, 3H, CH_2 Bn), 4.49 (d, 1H, *J* = 12 Hz, CH_2 Bn), 4.22 (q, 1H, *J* = 6.0 Hz, H-5), 4.12 (dd, 1H, *J* = 9.6, 2.4 Hz, H-3), 3.80 (dd, 1H, *J* = 9.2, 3.2 Hz, H-3'), 3.60 (q, 1H, *J* = 6.0 Hz, H-5'), 3.53 (t, 1H, *J* = 9.6 Hz, H-4), 3.42 (t, 1H, *J* = 9.2 Hz, H-4'), 2.70-2.63 (m, 4H, 2x CH_2 Lev), 2.45 (q, 2H, *J* = 14.0 Hz, CH_2 CNPiv), 2.13 (s, 3H, CH_3 Lev), 1.29 (m, 12H, CH_3-6, CH_3-6', 2x CH_3 CNPiv); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 206.0 (C=O Lev ketone), 173.9, 171.7 (C=O CNPiv, Lev), 138.5, 137.8, 137.6, 133.2 (C_q C_{arom}), 132.1, 131.9, 129.1, 128.8, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5 (CH_{arom}), 117.2 (CN), 99.7 (C-1'), 85.3 (C-1), 80.2 (C-4), 79.4 (C-4'), 77.05 (C-3), 76.8 (C-3'), 75.5 (CH_2 Bn), 74.9 (CH_2 Bn), 74.6 (C-2), 71.1 (CH_2 Bn), 69.2 (C-5), 68.9 (C-2'), 68.5 (C-5'), 40.9 (C_q CNPiv), 37.9 (CH_2 Lev), 29.7 (CH_3 Lev), 28.0 (CH_2 Lev), 27.6 (CH_2 CNPiv), 24.7, 24.6 (CH_3 CNPiv), 17.8, 17.8 (C-6, C-6'); HRMS calculated for $[C_{50}H_{57}NO_{11}S + Na]^+$: 902.35445, found 902.35458.

N-benzyl-N-benzyloxycarbonyl-5-aminopentanyl-4-O-benzyl-3-O-levulinoyl-2-O-(3-cyano-2,2-dimethylpropanoyl)-α-L-rhamnopyranoside (24) Donor **12** (0.843 g, 1.52 mmol, 1 equiv.) and acceptor **15** (1.552 g, 4.74 mmol, 3 equiv.) were coevaporated three times with anhydrous toluene before being dissolved in distilled DCM (17 mL) under an argon atmosphere. Activated molecular sieves (3Å) were added and the mixture was cooled to 0 °C. The mixture was stirred for 15 min, followed by the addition of NIS (0.42 g, 1.9 mmol, 1.2 equiv.) and a solution of TMSOTf in distilled DCM (0.221 M, 0.68 mL, 0.15 mmol, 0.1 equiv.) were added. After 1h, TLC analysis showed fast conversion of the donor and the mixture was allowed to warm to room temperature for 30 min, after which is was quenched with Et_3N. The mixture was diluted with Et_2O and washed with H_2O (2x) and brine (2x). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. Purification by size exclusion (1:1 DCM/MeOH) and coevaporation with $CHCl_3$ resulted in the title compound as a yellow oil (0.957 g, 1.24 mmol, 82%). R_f = 0.35 (2:1 PE/EtOAc); IR (neat): 1738, 1694, 1360, 1300, 1207, 1126, 1063, 1028, 976, 912, 733, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ*: 7.36-7.24 (m, 14H, CH_{arom}), 7.18-7.16 (m, 1H, CH_{arom}), 5.30 (dd, 1H, J = 9.6, 3.2 Hz, H-3), 5.24 (s, 1H, H-2), 5.17 (d, 2H, *J* = 13.2 Hz, CH_2 Cbz), 4.72 (d, 1H, *J* = 11.2 Hz, CH_2 Bn), 4.65-4.63 (m, 2H, CH_2 Bn, H-1), 4.49-4.48 (m, 2H, CH_2 Bn), 3.80 (m, 1H, H-5), 3.60-3.55 (m, 1H, CH_2), 3.50 (t, 1H, *J* = 9.6 Hz, H-4), 3.34 (m, 1H, CH_2), 3.26 (m, 1H, CH_2), 3.20 (m, 1H, CH_2), 2.76-2.64 (m, 2H, CH_2 Lev), 2.61 (d, 2H, *J* = 1.2 Hz, CH_2 CNPiv), 2.53-2.46 (m, 2H, CH_2 Lev) 2.14 (s, 3H, CH_3 Lev), 1.54- 1.48 (m, 4H, 2x CH_2), 1.40 (s, 6H, 2x CH_3 CNPiv), 1.35 (d, 3H, *J* = 12.8 Hz, CH_3-6), 1.26 (m, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 206.3 (C=O Lev ketone), 173.9, 171.8 (C=O CNPiv, Lev), 137.9, 137.8 (C_q), 128.5, 128.4, 128.2, 128.1, 127.9, 127.8, 127.2 (CH_{arom}), 117.5 (CN), 97.0 (C-1), 78.3 (C-4), 75.0 (CH_2 Bn), 72.2 (C-3), 71.0 (C-2), 67.7 (CH_2), 67.5 (C-5), 67.1 (CH_2 Cbz), 50.5, 50.2 (CH_2 Bn), 47.1, 46.1 (CH_2), 41.2 (C_q CNPiv), 37.8 (CH_2 Lev), 29.8 (CH_3 Lev), 29.0 (CH_2), 27.9 (CH_2 CNPiv, Lev), 27.5 (CH_2), 24.9, 24.9 (CH_3 CNPiv), 23.3 (CH_2), 18.1 (CH_3-6). HRMS calculated for $[C_{44}H_{54}N_2O_{10} + Na]^+$: 793.36707, found 793.36653.

N-benzyl-N-benzyloxycarbonyl-5-aminopentanyl-4-O-benzyl- 2-O-(3-cyano-2,2-dimethylpropanoyl)-α-L-rhamnopyranoside (25) Compound **24** (0.212 g, 0.275 mmol, 1 equiv.) was dissolved in pyridine (2.2 mL) and AcOH (0.55 mL). Hydrazine acetate (0.130 g, 1.41 mmol, 5 equiv.) was added and the mixture was stirred for 30 min, after which TLC analysis showed complete reaction. The reaction mixture was quenched with acetone and diluted with EtOAc. The organic layer were washed with H_2O (3x) and brine (1x), dried over $MgSO_4$, concentrated *in vacuo*. Purification by column chromatography (2:1 PE/EtOAc) and coevaporation with $CHCl_3$ resulted in the title compound as an oil (0.135 g, 0.200 mmol, 73%). R_f = 0.52 (2:1 PE/EtOAc); IR (neat): 2934, 1734, 1694, 1472, 1454, 1422, 1368, 1300, 1227, 1128, 1061, 1028, 976, 734, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ*: 7.35-7.24 (m, 14H, CH_{arom}), 7.17-7.16 (m, 1H, CH_{arom}), 5.16 (d, 2H, *J* = 12.4 Hz, CH_2 Cbz), 5.09 (s, 1H, H-2), 4.82 (d, 1H, *J* = 11.2 Hz, CH_2 Bn), 4.69 (d, 1H, *J* = 11.2 Hz, CH_2 Bn), 4.64 (s, 1H, H-1), 4.48 (d, 2H, *J* = 6.8 Hz, CH_2 Bn), 4.07 (bs, 1H, H-3), 3.70 (m, 1H, H-5), 3.57 (m, 1H, CH_2), 3.32 (t, 1H, *J* = 6.4 Hz, H-4), 3,31 (m, 1H, CH_2), 3.30-3.18 (m, 2H, CH_2), 2.58 (d, 2H, *J* = 6.0 Hz, CH_2 CNPiv), 1.54-1.48 (m, 4H, 2x CH_2), 1.39 (s, 6H, 2x CH_3 CNPiv), 1.33 (d, 3H, *J* = 6.0 Hz, CH_3-6), 1.26 (m, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 174.5 (C=O CNPiv), 138.1, 137.9 (C_q C_{arom}), 128.6, 128.6, 128.5, 128.2, 128.1, 128.0, 127.9, 127.3, 127.2 (CH_{arom}), 117.9 (CN), 97.1 (C-1), 81.3 (C-4), 75.2 (CH_2 Bn), 73.5 (C-2), 70.2 (C-3), 67.7 (CH_2), 67.5 (C-5), 67.2 (CH_2 Cbz), 50.5, 50.3 (CH_2 Bn), 47.1, 46.1 (CH_2), 41.2 (C_q CNPiv), 29.7, 29.1 (CH_2), 28.0 (CH_2 CNPiv), 27.5 (CH_2), 25.0, 24.9 (CH_3 CNPiv), 23.4 (CH_2), 18.2 (CH_3-6); HRMS calculated for $[C_{39}H_{48}N_2O_8 + Na]^+$: 695.33358, found 695.32958.

***N*-benzyl-*N*-benzyloxycarbonyl-5-aminopentanyl-3-*O*-(3,4-di-*O*-benzyl-2-*O*-levulinoyl-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranoside (26)** Acceptor **25** (0.358 g, 0.533 mmol, 1 equiv.) and donor **13** (0.352 g, 0.658 mmol, 1.2 equiv.) were coevaporated three times with anhydrous toluene before being dissolved in distilled DCM (7.6 mL) under an argon atmosphere and stirred at room temperature for 20 min over activated molecular sieves (3Å). The reaction was cooled to 0 °C, followed by the addition of NIS (0.178 g, 0.791 mmol, 1.44 equiv.) and a solution of TMSOTf in distilled DCM (0.221 M, 0.24 mL, 0.053 mmol, 0.1 equiv.) were added. After 40 min, TLC and TLC-MS showed complete consumption of the acceptor and the reaction was quenched with 0.1 mL Et_3N. The mixture

was diluted with Et_2O and the organic layer was washed with H_2O (2x) and brine (2x), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by size exclusion (1:1 DCM/MeOH) resulted in the title compound as a yellow oil (0.544 g, 0.496 mmol, 93%). R_f = 0.64 (7:2 PE/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.36-7.20 (m, 24H, CH_{arom}), 7.15 (m, 1H, CH_{arom}), 5.39 (m, 1H, H-2'), 5.15 (d, 2H, *J* = 13.2 Hz, CH_2 Cbz), 5.04 (s, 2H, H-1', H-2), 4.93 (d, 1H, *J* = 11.6 Hz, CH_2 Bn), 4.77 (d, 1H, *J* = 10.8 Hz, CH_2 Bn), 4.64-4.56 (m, 4H, H-1, 2x CH_2 Bn), 4.49-4.46 (m, 3H, CH_2 Bn), 4.11 (d, 1H, *J* = 8.8 Hz, H-3), 3.81 (dd, 1H, *J* = 9.2, 3.2 Hz, H-3'), 3.74 (m, 1H, H-5), 3.68-3.52 (m, 2H, H-5', CH_2), 3.44-3.38 (m, 2H, H-4, H-4'), 3.33-3.18 (m, 3H, CH_2), 2.71-2.63 (m, 4H, 2x CH_2 Lev), 2.48 (q, 2H, *J* = 6.8 Hz, CH_2 CNPiv), 2.11 (s, 3H, CH_3 Lev), 1.53-1.43 (m, 4H, CH_2), 1.31-1.27 (m, 14H, CH_3-6, CH_3-6', 2x CH_3 CNPiv, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 205.9 (C=O Lev ketone), 174.0, 171.6 (C=O CNPiv, Lev), 156.6 (C=O Cbz), 138.5, 137.8, 137.7, 137.6, 136.7 (C_q C_{arom}), 128.9, 128.8, 128.4, 128.4, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.1 (CH_{arom}), 117.2 (CN), 99.6 (C-1'), 96.4 (C-1), 80.1 (C-4), 79.4 (C-4'), 77.4 (C-3), 76.7 (C-3'), 75.5, 74.7 (CH_2 Bn), 73.1 (C-2), 71.0 (CH_2 Bn), 68.9 (C-2'), 68.2 (C-5'), 67.5 (C-5), 67.5 (CH_2), 66.9 (CH_2 Cbz), 50.4, 50.1 (CH_2 Bn), 46.9, 46.0 (CH_2), 40.8 (C_q CNPiv), 37.8 (CH_2 Lev), 29.6 (CH_3 Lev), 28.9 (CH_2), 28.0, 27.8, 27.5, 27.3 (CH_2 CNPiv, CH_2 Lev, CH_2), 24.7, 24.5 (CH_3 CNPiv), 23.2 (CH_2), 17.9, 17.7 (CH_3-6, CH_3-6'). HRMS calculated for $[C_{64}H_{76}N_2O_{14} + NH_4]^+$: 1114.56348, found 1114.56494.

***N*-benzyl-*N*-benzyloxycarbonyl-5-aminopentanyl-3-*O*-(3,4-di-*O*-benzyl-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranoside (27)** Compound **26** (0.526 g, 0.479 mmol, 1 equiv.) was dissolved in pyridine (3.8 mL), cooled to 0 °C and AcOH (0.96 mL) was added, followed by the addition of hydrazine acetate (0.228 g, 2.48 mmol, 5 equiv.). The mixture was allowed to warm up to room temperature and stirred for 1h. The reaction mixture was quenched with acetone and diluted with EtOAc. The organic layer were washed with H_2O (3x) and brine (1x), dried over $MgSO_4$, concentrated *in vacuo*. Purification by column chromatography (2:1 PE/EtOAc) and coevaporation with DCM and $CHCl_3$ resulted in the title compound as an oil (0.433 g, 0.433 mmol, 90%). R_f = 0.64 (7:2 PE/EtOAc); IR (neat): 2972, 2932, 2872, 1734, 1695, 1472, 1452, 1422, 1366, 1300, 1248, 1209, 1126, 1072, 1028, 914, 837, 733, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.36-7.20 (m, 24H, CH_{arom}), 7.15 (m, 1H, CH_{arom}), 5.16 (d, 2H, *J* = 12.8 Hz, CH_2 Cbz), 5.07 (s, 2H, H-1', H-2), 4.88 (d, 1H, *J* = 11.6 Hz, CH_2 Bn), 4.69-4.57 (m, 6H,H-1, 3x CH_2 Bn), 4.48 (d, 2H, *J* = 8.4 Hz, CH_2 Bn), 4.11 (m, 1H, H-3), 3.91 (s, 1H, H-2'), 3.71-3.68 (m, 2H, H-3', H-5), 3.60-3.54 (m, 2H, H-5, CH_2), 3.49-3.38 (m, 2H, H-4, H-4'), 3.37-3.3.13 (m, 3H, CH_2), 2.64 (bs, 1H, OH), 2.49 (q, 2H, *J* = 14.8 Hz, CH_2 CNPiv), 1.53 - 1.22 (m, 16H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 174.0 (C=O CNPiv), 138.6, 137.8, 136.8 (C_q C_{arom}), 128.5, 128.4, 128.2, 128.0, 127.9, 127.9, 127.8, 127.7, 127.5, 127.5, 127.2 (CH_{arom}), 117.3 (CN), 101.6 (C-1'), 96.6 (C-1), 80.3 (C-4), 79.6 (C-4'), 79.0 (C-3'), 77.3 (C-3), 75.5 (CH_2 Bn), 74.8 (CH_2 Bn), 73.3 (C-2), 71.6 (CH_2 Bn), 68.6 (C-2'), 68.0 (C-5'), 67.7 (CH_2), 67.6 (C-5), 67.1 (CH_2 Cbz), 50.5, 50.2 (CH_2 Bn), 47.0, 46.0 (CH_2), 40.9 (C_q CNPiv), 28.9 (CH_2), 27.7 (CH_2 CNPiv), 27.4 (CH_2), 24.8, 24.7 (CH_3 CNPiv), 23.2 (CH_2), 18.0, 17.7 (CH_3-6, CH_3-6'). HRMS calculated for $[C_{59}H_{70}N_2O_{12} + NH_4]^+$: 1016.52670, found 1016.52807.

***N*-benzyl-*N*-benzyloxycarbonyl-5-aminopentanyl-3-*O*-(2-*O*-(3-*O*-(3,4-di-*O*-benzyl-2-*O*-levulinoyl-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranosyl)-3,4-di-*O*-benzyl-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranoside (28)** Acceptor **27** (0.191 g, 0.193 mmol, 0.8 equiv.) and donor **14** (0.220 g, 0.250 mmol, 1 equiv.) were coevaporated three times with anhydrous toluene before being dissolved in distilled DCM (3.6 mL) under an argon atmosphere and stirred at room temperature for 20 min over activated molecular sieves (3Å). The reaction was cooled to 0 °C, followed by the addition of NIS (0.0703 g, 0.312 mmol, 1.2 equiv.) and a solution of TMSOTf in distilled DCM (0.221 M, 0.12 mL, 0.026 mmol, 0.1 equiv.) were added. After 50 min, TLC and TLC-MS showed complete consumption of the acceptor and the reaction was quenched with 0.1 mL Et_3N. The mixture was diluted with Et_2O and the organic layer was washed with H_2O (1x) and brine (2x), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by size exclusion (1:1 DCM/MeOH) and coevaporation with $CHCl_3$ resulted in the title compound as a yellow oil (0.320 g, 0.181 mmol, 94%). R_f = 0.5 (2:1 PE/EtOAc); IR (neat): 2932, 1736, 1697, 1452, 1362, 1206, 1128, 1072, 980, 914, 893, 733, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.34-7.15 (m, 40H, CH_{arom}), 5.41 (s, 1H, H-2'''), 5.23 (s, 1H, H-2''), 5.16 (d, 2H, *J* = 9.6 Hz, CH_2 Cbz), 5.07 (s, 1H, H-1'''), 5.0 (s, 1H, H-2), 4.97 (s, 1H, H-1'), 4.96-4.86 (m, 2H, CH_2 Bn), 4,84 (s, 1H, H-1''), 4.75 (d, 1H, *J* = 10.8 Hz, CH_2 Bn), 4.65-4.56 (m, 8H, H-1, 4x CH_2 Bn), 4.54-4.44 (m, 4H, 2x CH_2 Bn), 4.18 (dd, 1H, *J* = 9.6, 3.2 Hz, H-3''), 4.02 (d, 1H, *J* = 9.2 Hz, H-3), 3.83-3.77 (m, 3H, H-2', H-3''', H-5*), 3.72-3.68 (m, 3H, H-3', H-5*, H-5*), 3.60-3.46 (m, 1H, CH_2), 3.45-3.32 (m, 5H, H-4, H-4', H-4'', H-4''', H-5*), 3.31-3,14 (m, 3H, CH_2), 2.71-2.63 (m, 4H, 2x CH_2 Lev), 2.55-2.35 (m, 4H, 2x CH_2 CNPiv), 2.14 (s, 3H, CH_3 Lev), 1.58 – 1.16 (m, 28H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 206.1 (C=O Lev ketone), 174.2, 173.8, 171.8 (C=O 2x CNPiv, Lev), 138.7, 138.6, 138.2, 138.0, 137.9 (C_q C_{arom}), 128.8, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.1, 127.9, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 127.3 (CH_{arom}), 117.4 (CN), 101.4 (C-1'), 99.4 (C-1'''), 98.5 (C-1''), 96.5 (C-1), 80.3, 80.0, 79.9, 79.6 (C-4, C-4', C-4'', C-4'''), 78.6 (C-3'), 78.2 (C-3), 77.4, 77.1 (C-2', C-3'''), 75.8 (C-3''), 75.6, 75.5, 75.0, 75.0 (CH_2 Bn), 73.4 (C-2), 73.0 (C-2''), 72.0, 71.2 (CH_2 Bn), 69.0 (C-2'''), 68.7, 68.5, 68.4 (C-5*), 67.8 (CH_2), 67.6 (C-5*), 67.1 (CH_2 Cbz), 50.6, 50.3 (CH_2 Bn), 47.1, 46.1 (CH_2), 40.9 (C_q CNPiv), 38.0 (CH_2 Lev), 29.9 (CH_3 Lev), 29.0, 28.1, 27.9, 27.8, 27.7, 27.5 (2x CH_2 CNPiv, CH_2 Lev, 2x CH_2), 24.8, 24.7, 24.7 (CH_3 CNPiv), 23.3 (CH_2), 18.1, 18.0, 17.8, 17.8 (CH_3-6, CH_3-6', CH_3-6'', CH_3-6'''); HRMS calculated for $[C_{103}H_{121}N_3O_{23} + NH_4]^+$: 1786.87623, found 1786.87609. *The difference between 5, 5', 5'', 5''' could not be determined.

***N*-benzyl-*N*-benzyloxycarbonyl-5-aminopentanyl-3-*O*-(2-*O*-(3-*O*-(3,4-di-*O*-benzyl-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranosyl)-3,4-di-*O*-benzyl-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranoside (29)** Compound **28** (0.185 g, 0.104 mmol, 1 equiv.) was dissolved in pyridine (0.82 mL) and AcOH (0.2 mL). Hydrazine acetate (0.050 g, 0.52 mmol, 5 equiv.) was added and the mixture was stirred for 1h. TLC and TLC/MS analysis showed complete consumption of the starting material after which the reaction mixture was quenched with acetone and diluted with EtOAc. The organic layer were washed with H_2O and brine (1x), dried over $MgSO_4$, concentrated *in vacuo*. Purification by column chromatography (PE/EtOAc 4:1 → 2:1) resulted in the title compound as an oil (0.167 g, 0.099 mmol, 96%) R_f = 0.59 (7:2 PE/EtOAc); IR (neat): 2970, 1926, 1736, 1697, 1472, 1454, 1422, 1364, 1298, 1207, 1126, 1072, 1059, 982, 912, 837, 733, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.38-7.15 (m, 40H, CH_{arom}), 5.26 (s, 1H, H-2''), 5.16 (d, 2H, *J* = 10.0 Hz, CH_2 Cbz), 5.11 (s, 1H, H-1'''), 4.99 (s, 1H, H-2), 4.97 (s, 1H, H-1'), 4.91-4.87 (m, 3H, H-1'', CH_2 Bn), 4.69-4.54 (m, 10H, H-1, 5x CH_2 Bn), 4.52-4.47 (m, 3H, 2x CH_2 Bn), 4.17 (dd, 1H, *J* = 9.6, 3.2 Hz, H-3''), 4.02 (d, 1H, *J* = 7.2 Hz, H-3), 3.92 (s, 1H, H-2'''), 3.84 (s, 1H, H-2'), 3.82-3.76 (m, 1H, H-5*), 3.72-3.66 (m, 4H, H-3', H-3''', H-5*, H-5*), 3.58-3.49 (m, 1H, CH_2), 3.47-3.31 (m, 5H, H-4, H-4', H-4'', H-4''', H-5*), 3.28-3,14 (m, 3H, CH_2), 2.56-2.44 (m, 4H, 2x CH_2 CNPiv), 1.57 - 1.16 (m, 28H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 174.2, 173.7 (C=O 2x CNPiv), 138.7, 138.6, 138.3, 137.9, 137.9 (C_q C_{arom}), 128.6, 128.4, 128.4, 128.3, 128.1, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.3 (CH_{arom}), 117.5, 117.4 (CN), 101.4 (C-1'), 101.2 (C-1'''), 98.5 (C-1''), 96.5 (C-1), 80.4, 80.0, 79.9, 79.7 (C-4, C-4', C-4'', C-4'''), 79.2 (C-3'''), 78.7 (C-3'), 78.3 (C-3), 76.2 (C-3''), 75.7 (C-2'), 75.6, 75.5, 75.1, 75.0 (CH_2 Bn), 73.4 (C-2), 73.1 (C-2''), 72.0, 71.8 (CH_2 Bn), 68.7 (C-2''', C-5*), 68.5, 68.1 (C-5*), 67.8 (CH_2), 67.6 (C-5*), 67.2 (CH_2 Cbz), 50.6,

50.3 (CH_2 Bn), 47.1, 46.2 (CH_2), 41.0, 40.9 (C_q CNPiv), 29.8 (CH_2), 29.4, 29.1 (CH_2), 27.8, 27.8 (2x CH_2 CNPiv), 24.9, 24.9, 24.8 (CH_3 CNPiv), 23.3 (CH_2), 18.1, 18.0, 17.8 (CH_3-6, CH_3-6', CH_3-6'', CH_3-6'''). HRMS calculated for $[C_{99}H_{115}N_3O_{21} + NH_4]^+$: 1688.83945, found 1688.84017. *The difference between 5, 5', 5'' 5''' could not be determined.

5-aminopentanyl-3-*O*-(2-*O*-(3-*O*-(α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (10) Tetrasaccharide **29** (0.0345 g, 0.0206 mmol) was dissolved in H_2O/THF/tBuOH (3 mL:1.3 mL:1.3 mL) and several drops of acetic acid were added. The solution was purged with argon for 5 minutes after which $Pd(OH)_2$/C (60 mg, 20% wt loading) was added followed by another purge with argon for 5 minutes. The solution was purged with hydrogen for 5 minutes and kept under a hydrogen atmosphere overnight. The mixture was filtered over a Whatmann filter, which was rinsed 3x with the H_2O/THF/tBuOH mixture. The solution was concentrated and redissolved in 10 mL H_2O. Triethylamine (0.5 mL) was added and the reaction was stirred overnight. Purification using size exclusion chromatography (sephadex LH20 9:1 MeOH/H_2O) followed by two lyophilizations yielded fully deprotected tetrasaccharide **10** in quantitave yield (16.2 mg) as a white powder. ^{1}H NMR (D_2O, 500 MHz): *δ* 5.22 (s, 1H), 5.06 (s, 1H), 4.97 (s, 1H), 4.22 – 4.13 (m, 1H), 4.11 – 4.06 (m, 2H), 4.04 – 3.93 (m, 2H), 3.90 – 3.69 (m, 9H), 3.61 – 3.44 (m, 6H), 3.22 (q, 3H, *J* = 7.3, 7.3, 7.3 Hz), 3.06 – 2.99 (m, 2H), 2.64 (s, 2H), 1.77 – 1.63 (m, 5H), 1.54 – 1.42 (m, 2H), 1.37 – 1.23 (m, 25H); ^{13}C NMR (D_2O, 126 MHz): *δ* 102.4, 102.1, 100.8, 99.7 (4x C-1), 78.1, 77.5, 72.2, 72.0, 71.8, 71.4, 70.2, 70.2, 70.0, 70.0, 69.9, 69.4, 69.3, 69.2, 68.7, 67.5, 46.8, 42.3, 39.4, 28.3, 28.1, 26.6, 25.8, 25.0, 22.5, 16.7, 16.7, 16.7, 16.6, 8.3. HRMS calculated for $[C_{29}H_{53}NO_{17} + H]^+$: 688.33865, found 688.33825.

***N*-benzyl-*N*-benzyloxycarbonyl-5-aminopentanyl-3-*O*-(3-*O*-(3,4-di-*O*-benzyl-2-*O*-levulinoyl-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranoside (30)** Acceptor **25** (0.204 g, 0.303 mmol, 1.1 equiv.) and donor **14** (0.232 g, 0.264 mmol, 1 equiv.) were coevaporated three times with anhydrous toluene before being dissolved in distilled DCM (3.8 mL) under an argon atmosphere and stirred at room temperature for 30 min over activated molecular sieves (3Å). The reaction was cooled to 0 °C, followed by the addition of NIS (0.073 g, 0.32 mmol, 1.2 equiv.) and a solution of TMSOTf in distilled DCM (0.221 M, 0.12 mL, 0.027 mmol, 0.1 equiv.) were added. After 100 min the reaction was quenched with 0.1 mL Et3N, diluted with Et2O and the organic layer was washed with H_2O (2x) and brine (2x). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. Purification by size exclusion (1:1 DCM/MeOH) and coevaporation with $CHCl_3$ resulted in the title compound as a yellow oil (0.199 g, 0.138 mmol, 52%). Rf = 0.31 (2:1 PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.38-7.24 (m, 29H, CH_{arom}), 7.16 (m, 1H, CH_{arom}), 5.36 (m, 1H, H-2''), 5.17-5.13 (m, 3H, H-2', CH_2 Cbz), 5.06 (s, 1H, H-2), 4.98 (s, 2H, H-1', H-1''), 4.89 (d, 1H, *J* = 11.2 Hz, CH_2 Bn), 4.82 (d, 1H, *J* = 10.8 Hz, CH_2 Bn), 4.76 (d, 1H, *J* = 10.8 Hz, CH_2 Bn), 4.62-4.56 (m, 5H, H-1, 2x CH_2 Bn), 4.46-4.43 (m, 3H, 2x CH_2 Bn), 4.11 (d, 1H, *J* = 7.2 Hz, H-3), 4.02 (dd, 1H, *J* = 9.6, 3.2 Hz, H-3'), 3.73 (dd, 1H, *J* = 9.2, 3.2 Hz, H-3''), 3.66-3.54 (m, 4H, H-5, H-5', H-5''', CH_2), 3.46-3.40 (m, 2H, H-4, H-4'), 3.35 (t, 1H, *J* = 9.2 Hz, H-4''), 3.30-3.18 (m, 3H, CH_2), 2.71-2.62 (m, 4H, 2x CH_2 Lev), 2.59 (q, 2H, *J* = 9.6 Hz, CH_2 CNPiv), 2.41 (q, 2H, *J* = 12.4 Hz, CH_2 CNPiv), 2.15 (s, 3H, CH_3 Lev), 1.52 – 1.14 (m, 25H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 206.3 (C=O Lev ketone), 174.4, 173.9, 171.8 (C=O CNPiv, CNPiv, Lev), 138.7, 138.0, 137.9, 137.9, 137.7 (C_q, C_{arom}), 128.6, 128.5, 128.5, 128.4, 128.4, 128.2, 128.0, 128.0, 127.9, 127.8, 127.7, 127.6, 127.4 (CH_{arom}), 117.5, 117.4 (CN), 99.9, 98.9 (C-1', C-1''), 96.7 (C-1), 80.4 (C-4), 79.7 (C-4'), 79.5 (C-4''), 77.4 (C-3''), 77.0 (C-3), 76.7 (C-3'), 75.7, 75.2. 74.9 (CH_2 Bn), 73.2 (C-2), 73.0 (C-2'), 71.2 (CH_2 Bn), 69.0 (C-2''), 68.7, 68.5, 67.8, (C-5, C-5', C-5''), 67.7 (CH_2), 67.2 (CH_2 Cbz), 50.6, 50.2 (CH_2 Bn), 47.1, 46.2 (CH_2), 41.1, 40.9 (C_q CNPiv), 38.1 (CH_2 Lev), 29.9 (CH_3 Lev), 29.8, 29.1 (CH_2), 28.1, 27.9, 27.7, 27.5 (2x CH_2 CNPiv, CH_2 Lev, CH_2), 25.0, 24.9, 24.8, 24.7 (CH_3 CNPiv), 23.4 (CH_2), 18.1, 17.9 (CH_3-6, CH_3-6', CH_3-6''). HRMS calculated for $[C_{83}H_{99}N_3O_{19} + NH_4]$+: 1459.72110, found 1459.72186.

***N*-benzyl-*N*-benzyloxycarbonyl-5-aminopentanyl-3-*O*-(3-*O*-(3,4-di-*O*-benzyl-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranoside (31)** Compound **30** (0.195 g, 0.135 mmol, 1 equiv.) was dissolved in pyridine (1.2 mL) and AcOH (0.3 mL). Hydrazine acetate (0.065 g, 0.69 mmol, 5 equiv.) was added and the mixture was stirred for 45 min, after which TLC-MS analysis showed complete reaction. The reaction mixture was quenched with acetone and diluted with EtOAc. The organic layer were washed with H_2O (3x) and brine (1x), dried over $MgSO_4$, concentrated *in vacuo*. Purification by column chromatography (2:1 PE/EtOAc) and coevaporation with DCM and $CHCl_3$ resulted in the title compound as an oil (0.141 g, 0.105 mmol, 78%). R_f = 0.59 (2:1 PE/EtOAc). IR (neat): 2970, 2930, 1736, 1695, 1454, 1422, 1362, 1298, 1207, 1128, 1072, 1042, 1028, 982, 917, 837, 733, 696 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.39-7.23 (m, 29H, CH_{arom}), 7.15 (m, 1H, CH_{arom}), 5.17-5.15 (m, 3H, H-2', CH_2 Cbz), 5.06 (m, 1H, H-2), 5.03 (s, 1H, H-1''), 4.99 (s, 1H, H-1''), 4.86-4,81 (m, 2H, CH_2 Bn), 4.67 (d, 1H, *J* = 11.2 Hz, CH_2 Bn), 4.61-4.59 (m, 6H, H-1, 3x CH_2 Bn), 4.49-4.47 (m, 2H, CH_2 Bn), 4.13 (dd, 1H, *J* = 9.2, 2.4 Hz, H-3), 4.02 (dd, 1H, *J* = 9.6, 3.2 Hz, H-3'), 3.83 (m, 1H, H-2''), 3.69-3.53 (m, 5H, H-3'', H-5, H-5', H-5''', CH_2), 3.47-3.37 (m, 3H, H-4, H-4', H-4''), 3.27-3.18 (m, 3H, CH_2), 2.58 (q, 2H, *J* = 8.4 Hz, CH_2 CNPiv), 2.44 (q, 2H, *J* = 8.8 Hz, CH_2 CNPiv), 1.52 - 1.14 (m, 25H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 174.4, 173.8, (C=O CNPiv), 138.6, 138.1, 138.0, 137.9, 137.7 (C_q C_{arom}), 128.5, 128.5, 128.1, 128.0, 127.9, 127.9, 127.7, 127.6, 127.3 (CH_{arom}, 117.4, 117.4 (CN), 101.8 (C-1''), 98.8 (C-1'), 96.7 (C-1), 80.4, 80.0, 79.5 (C-4, C-4', C-4''), 79.0 (C-3''), 76.9 (C-3'), 76.6 (C-3), 75.5, 75.2, 74.9 (CH_2 Bn), 73.2 (C-2, C-2'), 71.8 (CH_2 Bn), 68.7 (C-2''), 68.7, 68.1, 67.8 (C-5, C-5', C-5''), 67.7 (CH_2), 67.2 (CH_2 Cbz), 50.6, 50.3 (CH_2 Bn), 47.1, 46.1 (CH_2), 41.2, 40.9 (C_q CNPiv), 29.8, 29.4, 29.1 (CH_2), 27.9, 27.7 (CH_2 CNPiv), 25.0, 24.9, 24.8, 24.7 (CH_3 CNPiv), 23.4 (CH_2), 18.1, 17.9, 17.8 (CH_3-6, CH_3-6', CH_3-6''). HRMS calculated for $[C_{78}H_{93}N_3O_{17} + NH_4]^+$: 1361.68432, found 1361.68484.

***N*-benzyl-*N*-benzyloxycarbonyl-5-aminopentanyl-3-*O*-(3-*O*-(2-*O*-(4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-3-*O*-levulinoyl-*α*-L-rhamnopyranosyl)-3,4-di-*O*-benzyl-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranoside (32)** Acceptor **31** (1.09 g, 0.81 mmol, 1.0 *equiv.*) and donor **12** (0.68 g, 1.22 mmol, 1.5 *equiv.*) were coevaporated three times with anhydrous toluene before being dissolved in dry DCM. The solution was stirred at room temperature on activated molecular sieves after which NIS (0.309 g, 1.377 mmol. 1.7 *equiv.*) was added. The reaction mixture was cooled to -40 °C and treated with 1.4 mL of a freshly prepared solution of TMSOTf in DCM (0.1 M, 1.4 mL, 0.17 *equiv.*). After 65 minutes, TLC analysis showed complete consumption of the acceptor, and the reaction was quenched with 0.5 mL Et3N. The mixture was dilute with EtOAc, washed with sat. aq. $Na_2S_2O_3$, sat. aq. $NaHCO_3$ and sat. aq. NaCl, dried over $MgSO_4$ and concentrated. Column purification (hexanes/acetone 10:1 → 4:1) followed by size exclusion purification (DCM/MeOH 1:1) yielded tetrasaccharide **32** as a yellow oil (1.087 g, 0.608 mmol, 75%). R_f 0.62 (PE/EtOAc, 1/1, v/v); IR (neat, cm^{-1}): 698, 731, 979, 1074, 1128, 1454, 1697, 1737, 2245, 2877, 2935, 2976; ^{1}H NMR ($CDCl_3$ 400 MHz): *δ* 7.37 – 7.13 (m, 35H), 5.44 – 5.36 (m, 1H), 5.33 (dd, 1H, *J* = 9.5, 3.3 Hz), 5.19 – 5.10 (m, 3H), 5.01 – 4.77 (m, 5H), 4.77 – 4.66 (m, 3H), 4.61 (dd, 5H, *J* = 11.0, 5.4 Hz), 4.52 (dd, 3H, *J* = 11.8, 3.7 Hz), 4.48 (s, 1H), 3.91 – 3.76 (m, 2H), 3.70 – 3.64 (m, 2H), 3.64 – 3.54 (m, 2H), 3.47 (dp, 4H, *J* = 14.8, 5.1, 5.1, 4.9, 4.9 Hz), 3.42 – 3.11 (m, 5H), 2.81 – 2.34 (m, 13H), 2.20 – 2.09 (m, 3H), 1.58 – 1.07 (m, 34H) ppm ^{13}C NMR ($CDCl_3$, 101 MHz): *δ* 206.3, 174.3, 173.8, 173.7, 171.7, 138.8, 138.3, 138.0, 137.9, 137.8, 137.6, 128.5, 128.5, 128.4, 128.4, 128.3,

128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.6, 127.6, 127.5, 127.4, 127.3, 117.5, 117.3, 117.3, 101.6, 98.7, 98.6, 96.6, 80.3, 79.7, 79.4, 79.0, 78.3, 77.7, 75.6, 75.3, 75.1, 74.9, 73.2, 73.1, 72.2, 72.0, 70.8, 68.8, 68.6, 68.1, 67.7, 67.6, 67.1, 41.1, 40.8, 37.8, 29.8, 29.1, 27.9, 27.9, 27.8, 27.6, 25.0, 24.9, 24.8, 24.8, 24.8, 24.6, 23.3, 18.0, 17.9, 17.8, 17.7; HRMS (MALDI-TOF): $[M+Na]^+$ calculated for $C_{102}H_{122}N_4O_{24}Na$ 1809,8341, found 1809.8353.

***N*-benzyl-*N*-benzyloxycarbonyl-5-aminopentanyl-3-*O*-(3-*O*-(2-*O*-(4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranosyl)-3,4-di-*O*-benzyl-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranoside (33)** A solution of **32** (0.492 g, 0.275 mmol, 1.0 *equiv.*) in pyridine/AcOH (2.9 mL:0.75 mL) was cooled to 0 °C and treated with H_2NNH_2·AcOH (0.124 g, 1.35 mmol, 5 *equiv.*). After 90 minutes the reaction was quenched with acetone, diluted with EtOAc, washed with H_2O (2x) and sat. aq. NaCl, dried over $MgSO_4$ and concentrated. Purification by column chromatography (hexanes/acetone 9:1 → 4:1) yielded the title compound **33** as a colorless oil (0.306 g, 0.18 mmol, 67%). R_f 0.74 (PE/EtOAc, 1/1, v/v); IR (neat, cm^{-1}): 696, 732, 979, 1028, 1055, 1128, 1454, 1697, 1735, 2245, 2933, 2974, 3030; ^1H NMR (500 MHz, $CDCl_3$) *δ* 7.37 – 7.18 (m, 35H), 5.26 (dd, *J* = 3.1, 1.7 Hz, 1H), 5.19 – 5.13 (m, 3H), 5.13 – 5.02 (m, 3H), 5.00 – 4.93 (m, 3H), 4.90 – 4.79 (m, 4H), 4.78 – 4.62 (m, 5H), 4.62 – 4.59 (m, 2H), 4.59 – 4.42 (m, 8H), 4.11 (dt, *J* = 9.1, 4.6 Hz, 2H), 3.98 (dd, *J* = 9.5, 3.1 Hz, 1H), 3.85 – 3.72 (m, 3H), 3.67 (dd, *J* = 9.0, 2.8 Hz, 2H), 3.65 – 3.48 (m, 4H), 3.48 – 3.12 (m, 11H), 2.66 – 2.38 (m, 9H), 1.64 – 0.94 (m, 34H); ^{13}C NMR (126 MHz, CDCl3) *δ* 174.4, 174.2, 174.0, 138.8, 138.7, 138.3, 138.1, 138.1, 138.0, 137.9, 137.7, 137.0, 132.3, 129.3, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.3, 117.9, 117.4, 117.4, 101.7, 98.8, 96.7, 92.6, 91.9, 81.4, 81.3, 81.1, 80.4, 80.1, 79.8, 79.6, 79.5, 79.1, 78.9, 77.9, 76.8, 75.6, 75.3, 75.2, 75.2, 75.1, 74.9, 74.9, 73.8, 73.3, 73.3, 73.2, 73.0, 72.3, 72.1, 71.8, 70.2, 69.8, 68.7, 68.2, 68.2, 67.8, 67.8, 67.6, 67.2, 50.7, 50.3, 47.2, 46.2, 41.2, 41.2, 40.9, 29.2, 28.1, 28.0, 27.9, 27.8, 27.6, 25.1, 25.0, 24.9, 24.9, 24.8, 24.7, 23.4, 18.3, 18.1, 17.9; HRMS (MALDI-TOF): $[M+Na]^+$ calculated for $C_{97}H_{116}N_4O_{22}Na$ 1711,7973, found 1711.7979.

***N*-benzyl-*N*-benzyloxycarbonyl-5-aminopentanyl-3-*O*-(3-*O*-(3,4-di-*O*-benzyl-2-*O*-(3-*O*-(3-*O*-(3,4-di-*O*-benzyl-2-*O*-levulinoyl-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranosyl)-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranoside (34)** Donor **14** (0.15 g, 0.17 mmol, 1.5 *equiv.*) and acceptor **33** (0.19 g, 0.11 mmol, 1.0 equiv.) were coevaporated three times with anhydrous toluene and kept under argon, after which they were dissolved in anhydrous DCM. Activated molecular sieves were added and the mixture was stirred for 30 minutes at room temperature. After addition of NIS (0.042 g, 0.19 mmol, 1.7 *equiv.*), the solution was cooled to -40 °C, followed by addition of a freshly prepared DCM solution of TMSOTf (0.1 M, 0.18 mL, 0.018 mmol, 0.17 *equiv.*). After TLC and TLC/MS analysis showed complete consumption of the acceptor, the reaction was quenched by addition of 0.3 mL Et_3N and allowed to warm up to room temperature. The mixture was diluted with EtOAc, washed with sat $Na_2S_2O_3$ (aq), dried over $MgSO_4$ and concentrated. Column purification (Hexanes/EtOAc) followed by size exclusion (1:1 DCM/MeOH) yielded fully protected hexasaccharide **34** as yellow glass like solid (0.237 g, 0.096 mmol, 88%). R_f 0.74 (PE/EtOAc, 1/1, v/v); IR (neat, cm^{-1}): 698, 734, 981, 1028, 1043, 1201, 1454, 1697, 1737, 2247, 2875, 2933, 2972; ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.36 – 7.13 (m, 50H), 5.43 – 5.30 (m, 1H), 5.29 – 5.08 (m, 5H), 5.08 – 4.92 (m, 5H), 4.92 – 4.75 (m, 6H), 4.75 – 4.41 (m, 16H), 4.20 – 4.06 (m, 2H), 3.99 (ddd, 2H, *J* = 22.7, 9.5, 3.0 Hz), 3.85 – 3.11 (m, 20H), 2.74 – 2.48 (m, 8H), 2.48 – 2.35 (m, 5H), 2.15 (s, 3H), 1.60 – 1.03 (m, 46H); ^{13}C NMR ($CDCl_3$, 101 MHz): *δ* 206.2, 174.3, 174.0, 173.9, 171.8, 138.7, 138.7, 138.3, 138.0, 137.9, 137.9, 137.7, 137.6, 128.7, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 127.9, 127.9, 127.8, 127.7, 127.7, 127.7, 127.5, 127.3, 117.6, 117.4, 117.3, 100.0, 98.8, 98.5, 96.7, 80.6, 80.4, 79.6, 79.5, 77.0, 76.8, 75.6, 75.2, 74.9, 73.3, 73.2, 73.0, 72.8, 72.0, 71.2, 69.0, 68.8, 68.7, 68.5, 68.5, 67.2, 41.2, 41.1, 40.9, 40.9, 38.1, 29.9, 28.2, 27.9, 27.9, 27.7, 25.0, 24.8, 24.7, 24.7, 23.4, 18.1, 17.9, 17.9; HRMS (MALDI-TOF): $[M+Na]^+$ calculated for $C_{141}H_{167}N_5O_{33}Na$ 2481,1436, found 2481.1436.

***N*-benzyl-*N*-benzyloxycarbonyl-5-aminopentanyl-3-*O*-(3-*O*-(3,4-di-*O*-benzyl-2-*O*-(3-*O*-(3-*O*-(3,4-di-*O*-benzyl-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranosyl)-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranosyl)-4-*O*-benzyl-2-*O*-(3-cyano-2,2-dimethylpropanoyl)-*α*-L-rhamnopyranoside (35)** Compound **34** (0.133 g, 0.054 mmol) was dissolved in 0.8 mL pyridine and 0.2 mL AcOH. The solution was cooled to 0 °C followed by addition of H_2NNH_2·AcOH (0.025 g, 0.27 mmol, 5 *equiv.*) and stirred for 10 minutes at 0 °C. After stirring at rt for 160 minutes, TLC and TLC/MS analysis showed complete conversion of the starting material and the reaction was quenched by addition of acetone. The mixture was diluted with EtOAc, washed with H_2O and sat. aq. NaCl, dried over $MgSO_4$ and concentrated. Column purification (hexanes/acetone) followed by size exclusion purification (DCM:MeOH 1/1) yielded the title hexasaccharide as a yellow glass-like solid (0.124 g, 0.052 mmol, 96%). R_f 0.68 (PE/EtOAc, 1/1, v/v); IR (neat, cm^{-1}): 698, 734, 983, 1028, 1041, 1454, 1697, 1735, 2247, 2875, 2933, 2974; ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.40 – 7.12 (m, 50H), 5.26 – 4.97 (m, 5H), 4.99 – 4.72 (m, 9H), 4.72 – 4.45 (m, 17H), 4.17 (dd, 1H, *J* = 9.5, 3.1 Hz), 4.13 – 4.05 (m, 1H), 3.99 (ddd, 2H, *J* = 21.0, 9.5, 3.1 Hz), 3.85 – 3.53 (m, 10H), 3.49 – 3.29 (m, 8H), 2.61 – 2.32 (m, 10H), 1.49 – 1.03 (m, 46H); ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 174.4, 174.0, 174.0, 173.9, 138.8, 138.7, 138.3, 138.1, 138.1, 138.0, 137.9, 137.8, 137.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.3, 128.1, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.4, 117.5, 117.4, 117.4, 117.4, 101.8, 101.7, 98.8, 98.6, 98.5, 96.7, 80.6, 80.4, 80.1, 79.9, 79.6, 79.1, 78.8, 77.8, 76.9, 75.7, 75.5, 75.4, 75.3, 75.2, 75.0, 74.9, 74.7, 73.3, 73.2, 72.8, 72.0, 71.8, 68.9, 68.7, 68.6, 68.2, 67.8, 67.8, 67.3, 50.7, 46.2, 41.2, 40.9, 40.9, 29.2, 28.0, 27.9, 27.8, 27.8, 25.1, 25.0, 24.9, 24.9, 24.9, 24.8, 24.7, 23.4, 18.1, 17.9; HRMS (MALDI-TOF): $[M+Na]^+$ calculated for $C_{136}H_{161}N_5O_{31}Na$ 2383.1068, found 2383.1064.

5-aminopentanyl-3-*O*-(3-*O*-(2-*O*-(3-*O*-(3-*O*-(α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (11) Compound **35** (0.069 g, 0.029 mmol) was dissolved in a mixture H_2O/THF/tBuOH (3 mL:1.3 mL: 1.3 mL) followed by addition of several drops of acetic acid. The solution was purged for 5 minutes with argon. $Pd(OH)_2$/C (60 mg, 20% wt loading) was added and the solution was purged for another 5 minutes with argon. The solution was then purged with hydrogen for 5 minutes and kept under a hydrogen atmosphere overnight. The mixture was filtered over a Whatmann filter and concentrated. This procedure was repeated two times after which the residue was dissolved in 10 mL H_2O, followed by addition of 0.5 mL Et_3N. The mixture was stirred for 150 minutes and concentrated. Purification using size exclusion chromatography (sephadex LH20 9:1 MeOH/H_2O) followed by three lyophilizations yielded fully deprotected hexasaccharide as a white powder (23.8 mg, 24.4 mmol, 84%). ^1H NMR (D_2O, 600 MHz): *δ* 5.18 (s, 1H, H-1), 5.06 - 4.96 (m, 3H, 3x H-1), 4.92 (d, 1H, *J* = 4.8 Hz, H-1), 4.73 (s, 1H, H-1), 4.15 - 4.08 (m, 2H, 2 x H-2), 4.04 (s, 2H, 2 x H-2), 3.98 (s, 1H, H-2), 3.91 (m, 1H), 3.89 - 3.83 (m, 3H), 3.83 - 3.78 (m, 4H), 3.78 - 3.62 (m, 8H), 3.59 - 3.35 (m, 8H), 3.00 - 2.94 (m, 2H), 1.65 (m, 4H, CH_2), 1.45 (m, 2H, CH_2), 1.41 - 1.31 (m, 2H, CH_2), 1.25 (m, 18H, 6x CH_3-6); ^{13}C NMR (D_2O, 151 MHz): *δ* 121.8, 103.4, 103.4, 103.2, 103.0, 101.8, 100.5 (6x C-1), 79.3, 79.2, 79.1, 79.0, 78.7 (6x C-2), 73.1, 73.0, 72.9,

72.6, 72.3, 72.2, 72.2 , 71.1, 71.0, 71.0, 70.9, 70.8, 70.7, 70.3, 70.2, 70.2, 70.2, 70.1, 70.0, 69.7, 68.4 (6x C-3, 6x C-4, 6x C-5), 67.5, 47.6, 43.2, 40.4, 40.3 (CH_2), 29.2 (CH_2), 29.0, 27.5 (CH_2), 25.9, 23.4 (CH_2), 17.6, 17.6, 17.5 (6x CH_3), 9.2. HRMS (MALDI-TOF): $[M+Na]^+$ calculated for $C_{41}H_{73}NO_{25}Na$ 1002.4364, found 1002.4359.

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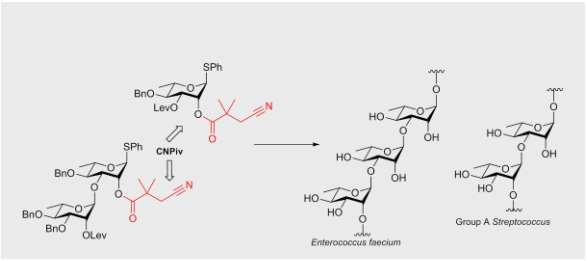

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