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FULL PAPER

Short synthesis of idraparinux by applying a 2-*O*-methyl-4,6-*O*-arylmethylene thioidoside as a 1,2-trans α-selective glycosyl donor

Fruzsina Demeter[a], Fanni Veres[a], Mihály Herczeg*[a,b] and Anikó Borbás*[a]

Dedication ((optional))

Abstract: The fully *O*-sulfated, *O*-methylated, heparin-related anticoagulant pentasaccharide idraparinux was prepared by a new synthetic pathway in 38 steps using D-glucose and methyl α-D-glucopyranoside as starting materials, with 23 steps for the longest linear route. The L-idose-containing **GH** fragment was obtained by a short and straightforward synthesis whereby a 4,6-cyclic-acetal-protected L-idosyl thioglycoside bearing a C2-nonparticipating group was used as the α-selective glycosyl donor. The novel L-idose donor was prepared with high chemo- and stereoselectivity by hydroboration–oxidation-based C5 epimerization starting from an orthogonally protected α-thioglucoside. The assembly of the pentasaccharide backbone was achieved by an **F**+**GH** and **DE**+**FGH** coupling sequence with full stereoselectivity in each glycosylation step.

Introduction

Heparin polysaccharide and its smaller fragments are invaluable drugs in the prevention and treatment of thromboembolic diseases owing to their anticoagulant properties.[1] Heparin binds to and activates antithrombin which, in turn, inhibits blood coagulation factors IIa and Xa.[2] Characterization of the shortest heparin sequence able to activate antithrombin, the **DEFGH** pentasaccharide **1**, along with SAR studies led to the synthetic antithrombotic drug fondaparinux (Arixtra, **2**), possessing selective factor Xa inhibitory activity by means of activation of antithrombin[3] (**Figure 1**). The lengthy and demanding synthesis of fondaparinux[4] spurred research to design simplified analogues that are easier to prepare. The replacement of glucosamine by glucose units and the introduction of methyl ethers to hydroxyls on non-crucial positions resulted in the discovery of non-glycosaminoglycan derivatives such as idraparinux (**3**)[3,5] which is an extremely potent heparinoid antithrombotic. Idraparinux binds to antithrombin significantly stronger than fondaparinux through the additional interaction of the extra sulfate group of the **H** glucose unit as well as through hydrophobic interactions. The potency of idraparinux is associated with its long half-life which allows a convenient once-a-week administration in humans. However, in the lack of neutralizing agent, the long elimination half-life proved to be a double-edged sword, and the development of idraparinux was stopped due to major bleeding events during treatment for more than six months.[6]

Recently, new antidotes have emerged in the anticoagulant therapy.[7] Andexanet alfa, a recombinant protein designed as a specific reversal agent against both direct and indirect factor Xa inhibitors, was approved by FDA in 2018.[8] Aripazine (ciraparantag), a synthetic small cationic compound is another, clinically investigated reversal agent with promising activity against heparinoid anticoagulants.[9] These new results might attract renewed interest toward idraparinux.

Despite the simplified structure, the synthesis of idraparinux still poses challenges like the efficient synthesis of the L-idosyl building block as well as the introduction of methyl ethers onto the uronic acid residues which are prone to suffer β-elimination under basic conditions of the etherification.

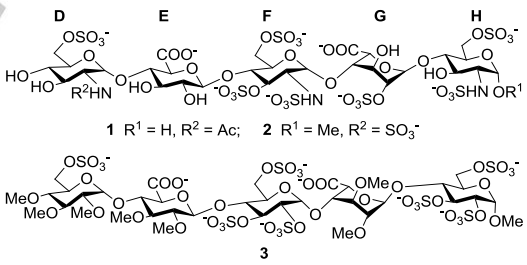

Figure 1. Structure of the AT-binding pentasaccharide domain of heparin (**1**) and the synthetic anticoagulant pentasaccharides fondaparinux (**2**) and idraparinux (**3**).

In most syntheses, orthogonally protected 2-*O*-acyl L-idopyranose or L-iduronic acid building block is prepared from D-glucose *via* various lengthy procedures[10] and used as a C2-participating glycosyl donor (**Scheme 1**, **A**). The 2-*O*-acyl group ensures the required 1,2-trans stereoselectivity upon glycosylation, however, its change into methyl ether further lengthens the synthesis at an oligosaccharide level.[5,11-14] Recently, Lopatkiewicz and co-workers established a nonglycosylating chemical strategy for the synthesis of idraparinux in which the **GH** and **EF** disaccharide units were prepared from the same cellobiose (**Scheme 1**, **B**).[15] They introduced the needed methyl ethers at an early stage of the synthesis and the functionalized cellobiose was transformed to the **GH** unit *via* epimerization of C5' by an elimination-addition

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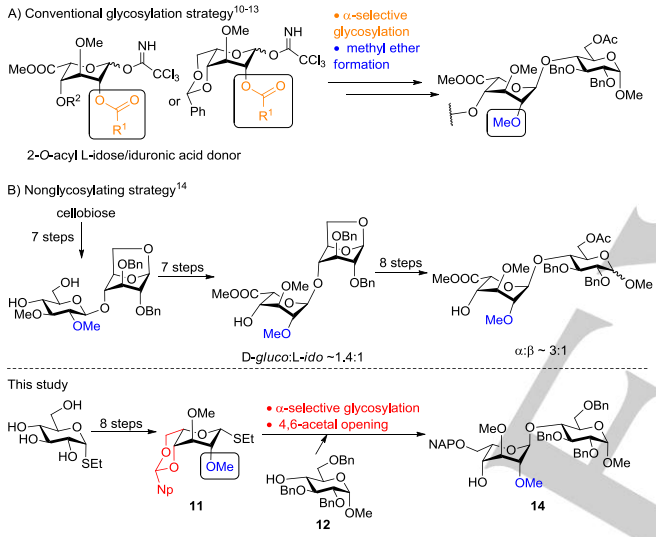
sequence. The synthesis of fully protected idraparinux was significantly shortened and improved by this imaginative approach which still has weaknesses such as the low efficacy of the C5' epimerization step as well as the low stereoselectivity during conversion of the 1,6-anhydro ring of unit **H** into methyl α-glycoside.

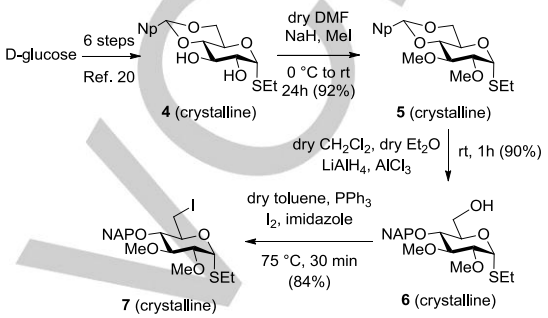
Very recently, we published a straightforward new synthesis of L-idosyl glycosyl donors starting from orthogonally protected α-thioglucosides.[16] The key steps include C5 epimerization by hydroboration/oxidation of the corresponding 5-enopyranosides followed by a 4,6-*O*-acetal formation of the obtained L-idosides. We demonstrated in model glycosylations of a GlcNAc acceptor that the 4,6-arylmethylene acetal ensures full 1,2-trans α-selectivity in the absence of a participating group at C2 position. On the basis of these results we envisioned a significantly shortened route to idraparinux by applying a 2,3-di-*O*-methylated L-idosyl donor for the synthesis of the **GH** fragment.



Scheme 1. Synthetic strategies toward the **GH** fragment of idraparinux.

Results and Discussion

We have developed an efficient synthetic strategy for idraparinux[14] and related pentasaccharides[17,18] which was based on the coupling of an **FGH** acceptor and a **DE** donor, both containing a non-oxidized precursor of the hexuronic acid unit, and formation of the uronic acids was performed in one step at the pentasaccharide level. While keeping this post-glycosylation oxidation strategy,[19] we devised a significantly shortened synthesis for the **GH** building block by utilizing a new, non-participating L-idosyl glycosyl donor which is readily available from a suitably protected α-thioglucoside by our recent method.[16] The synthesis of the starting α-thioglucoside **4**[20] was accomplished by stereoselective introduction of the ethylthio aglycon to 2-acetoxy-D-glucal by photoinduced hydrothiolation[21,22] followed by deacetylation and 4,6-*O*-(2-naphthyl)methylenation. The methyl ether functions of the final product were introduced into positions 2 and 3 at this early stage of synthesis to give **5** in 92% yield. Next, the regioselective ring opening of the 4,6-*O*-(2-naphthyl)methylene acetal using the $LiAlH_4$-$AlCl_3$ reagent combination in a 3:1 ratio[23] resulted in compound **6** in an excellent 90% yield. Subsequent substitution of the 6-OH group with iodine gave **7** in 84% yield. It is worth mentioning that each compound of this reaction sequence was obtained in crystalline form (**Scheme 2**).



Scheme 2. Synthesis of the 6-deoxy-6-iodo-α-thioglucoside derivative **7**.

Conversion of **7** into the L-idoside derivative **8** was carried out by the well-established C5-epimerization method including NaH-mediated elimination, hydroboration using BH_3·THF and oxidation with H_2O_2 under basic conditions.[24,25]

While this reaction sequence had proceeded both in high yield and high stereoselectivity starting from 2,3-di-*O*-benzyl α-thioglucosides,[16] upon dehydrohalogenation of the 2,3-di-*O*-methylated **7** with sodium hydride a number of byproducts were observed by TLC and, after hydroboration/oxidation, the expected L-idose derivative **8** was only formed in low 41% yield (**Scheme 3**, Route A). Thus, we attempted to produce the 5,6-unsaturated **7a** derivative by another method using silver fluoride in dry pyridine (**Scheme 3.**, Route B). To our great satisfaction, the AgF-mediated elimination provided cleanly the 6-deoxy-α-D-*xylo*-hex-5-enopyranoside **7a** which was subjected directly to hydroboration-oxidation to produce the desired L-idose derivative **8** in a good yield of 66% over three steps (87% per step). As we expected, the α-anomeric configuration of **7a** ensured the required high L-*ido* selectivity in the hydroboration step and the D-*gluco* epimer by-product **6** was formed only in a negligible amount. Moreover, the oxidation occurred with high chemoselectivity indicated by the small extent of overoxidized by-product **9**. (The structure of **6** and **9** was identified on the basis of the MS data and NMR spectra of their inseparable mixture.) The observed high stereo- and chemoselectivity of the hydroboration/oxidation of the α-thioglycoside is in line with our previous results.[16] A third by-product, the 6-fluoro derivative (**10**) of the initial glucose compound was also isolated from the reaction mixture in an 11% yield. It must have been formed during the elimination reaction, but could not be distinguished by TLC from the 5,6-unsaturated derivative.

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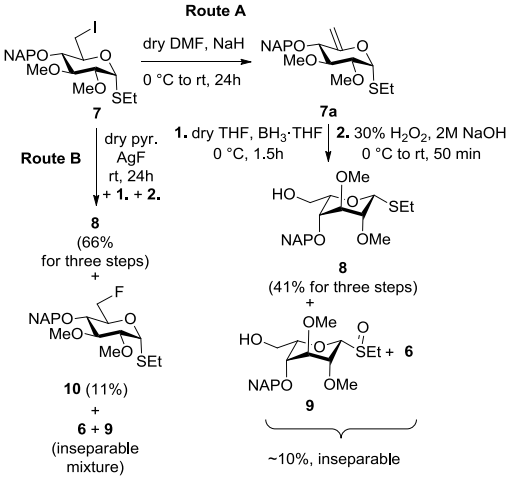
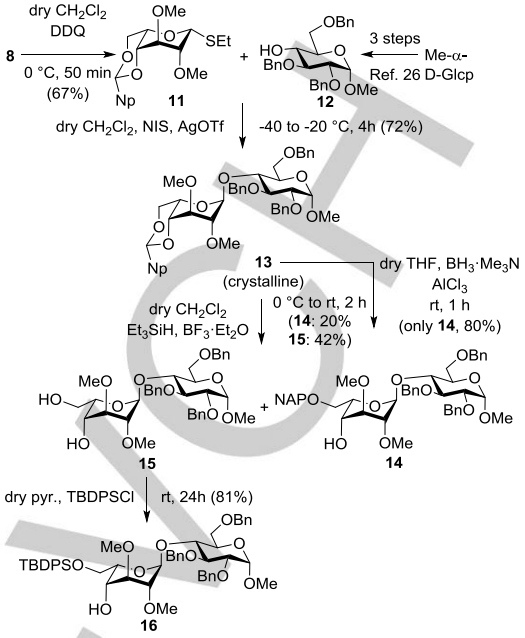


Scheme 3. The elimination and epimerization reactions of compound **7**.

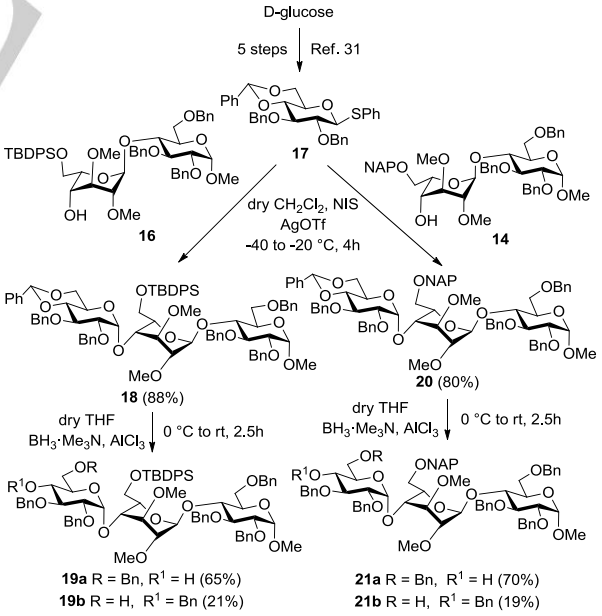
Next, compound **8** was converted to the corresponding 4,6-*O*-(2-napthyl)methylene derivative **11** by oxidative ring closure with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (**Scheme 4**). It was followed by the key step of the synthesis, glycosylation of monosaccharide acceptor **12**[26] with the new, non-participating L-idosyl donor **11**. We demonstrated earlier that glycosylation reaction between the 2,3-di-*O*-benzyl congener of **11** and a GlcNAc acceptor of low reactivity proceeded with full 1,2-trans α-selectivity.[16] However, it was questionable whether donor **11** was able to ensure complete stereoselectivity when reacting with an acceptor of higher reactivity. To our great delight, condensation of acceptor **12** and donor **11** upon iodonium ion activation resulted in the desired α-linked **GH** disaccharide with full stereoselectivity in high yield and in crystalline form. The exclusive α-stereoselectivity can be explained by the steric hinderence of the C2-protecting group to prevent nucleophilic attack from the β-face and by the controlling effect[27,28] of the 4,6-*O*-cyclic protecting group which has been demonstrated to ensure α-selectivity in D-glucosylation and D-galactosylation reactions.

Conversion of the fully protected disaccharide **13** to an acceptor by regioselective ring opening reaction was first attempted with a $BF_3{\cdot}Et_2O$-Et_3SiH[29] reagent combination. Unfortunately, the main product of the reaction was diol **15** and the expected 6'-ether **14** was only formed in a low 20% yield. Hence, we turned to the $Me_3N{\cdot}BH_3$-$AlCl_3$ reagent system which is known to cleave the 4,6-*O*-acetals with a solvent dependent regioselectivity.[26,30] In THF, the required 4'-OH/6'-*O*-ether **14** was isolated as the only product in 80% yield. Diol **15** was also converted to a disaccharide acceptor building block by regioselective silylation of the primary hydroxyl group. Treatment of **15** with *tert*-butyldiphenylsilyl chloride (TBDPSCl) in dry pyridine provided acceptor **16** in excellent yield.



Scheme 4. Preparation of **GH** disaccharide **13** and its transformations to acceptors **14** and **16**.

Glycosylation of disaccharide **16** with thioglycoside donor **17**[31] upon iodonium ion activation resulted in **FGH** trisaccharide **18** with the desired α-interglycosidic linkage in 88% yield (**Scheme 5.**).



Scheme 5. Synthesis of the **FGH** disaccharide acceptors **19a** and **21a**.

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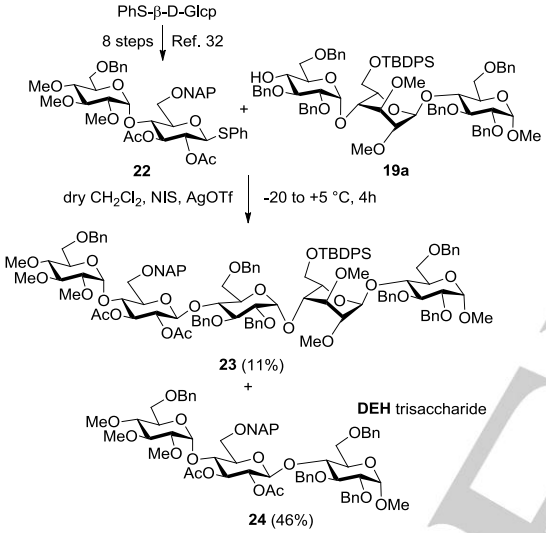
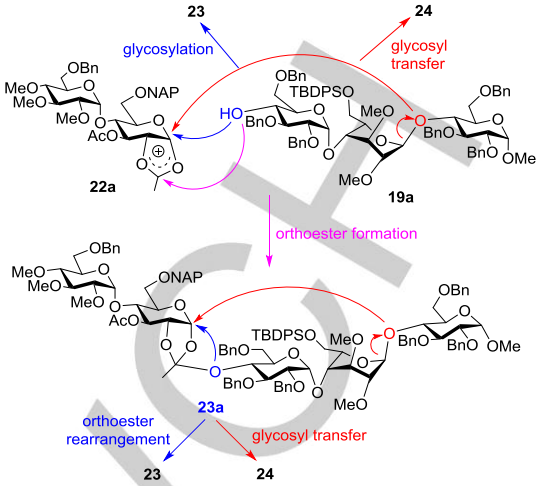
Conversion of **18** to acceptor **19a** was achieved again by a regioselective ring-opening reaction using the $Me_3N{\cdot}BH_3$-$AlCl_3$ reagent system in THF to produce the desired product in 65% yield along with the regioisomeric by-product **19b** isolated in 21%. Following the above reaction path, the 6'-ONAP-containing **14** was converted to another trisaccharide acceptor, compound **21a**, with similar efficacy.

The assembly of the non-oxidized precursor of the final product idraparinux was initially carried out by glycosylation of trisaccharide acceptor **19a** with the non-glucuronide type **DE** disaccharide donor **22**[32] (**Scheme 6**). Surprisingly, condensation of disaccharide **22** and trisaccharide **19a** upon NIS-AgOTf activation provided the **DEH** trisaccharide **24** as the major product in 46% yield, and the needed pentasaccharide **23** was formed in a very low yield of 11%.



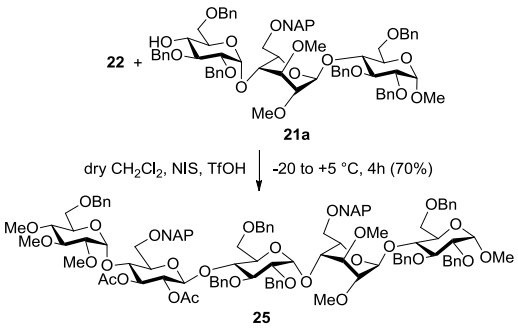
Scheme 6. Synthesis of the protected pentasaccharide **23** by applying the silyl-containing acceptor **19a**.

The formation of trisaccharide **24** can be explained either by direct attack of the α-L-idosyl glycosidic oxygen onto the anomeric carbon of the dioxolenium ion formed from **22** or by an intramolecular glycosyl transfer reaction *via* the orthoester intermediate **23a** (**Scheme 7**). The intermolecular glycosyl transfer to **22a** could only occur if **19a** adopts a conformation in which the free hydroxyl group is extremely shielded thereby the attack of the interglycosidic oxygen, nucleophilicity of which is enhanced by the surrounding electron-donating ether substituents, becomes dominant. Another, more probable mechanism is the formation of orthoester **23a** which then can undergo either a conventional rearrangement to give the expected pentasaccharide **23** or can be transformed to trisaccharide **24** by intramolecular transfer of unit **H** onto the glycosidic center of unit **E**.



Scheme 7. Plausible mechanism of the formation of **DEH** trisaccharide **24**.

In the hope of a more efficient synthesis of the protected pentasaccharide skeleton, disaccharide **22** was reacted with the NAP-group-containing disaccharide acceptor **21a** upon NIS-TfOH activation. This case the [2+3] coupling reaction proceeded with high efficacy to provide the expected protected pentasaccharide **25** with complete β-stereoselectivity, in 70% yield (**Scheme 8**). The significant difference in the **DE**+**FGH** coupling outcome upon changing a remote protecting group in the acceptor **FGH** (**19a** versus **21a**) can be explained by the different steric and electronic properties of the TBDMS and the NAP protecting group. Another possible reason for the different efficacy of the two glycosylations is that different promoter systems were applied in the two coupling reactions. We hypothesize that under the NIS-AgOTf promotion the orthoester formation may be more preferred compared to the NIS-TfOH promotion. As the formation of the needed pentasaccharide proceeded with high efficacy with acceptor **21a**, we did not study further the intriguing behaviour of acceptor **19a**.



Scheme 8. The [2+3] coupling reaction with the NAP-containing trisaccharide acceptor **21a**.

The synthesis was continued with the NAP-containing pentasaccharide **25** of which we had a sufficient amount for the remaining transformations (**Scheme 9**). First, compound **25** was

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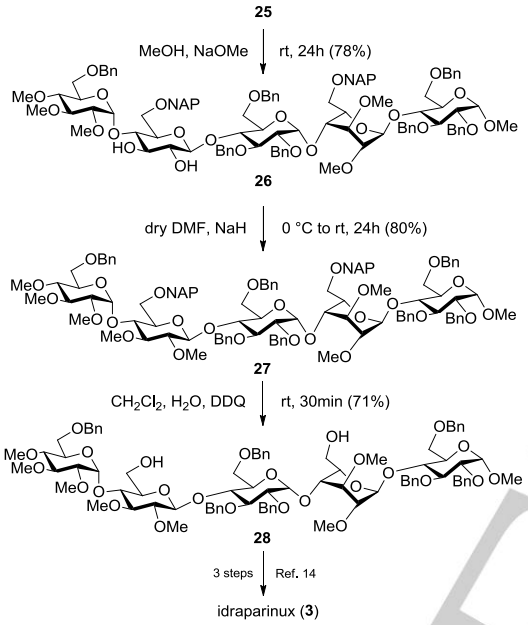
subjected to Zemplén deacetylation to produce diol **26**. Introduction of the methyl ethers to the freed hydroxyls was accomplished by standard alkylation using methyl iodide and sodium hydride to afford the desired compound **27** in 80% yield. Next, the primary hydroxyls that were to be oxidized in units **E** and **G** were liberated in one step by oxidative cleavage of the NAP groups with DDQ[33] to provide diol **28**[14] in 70% yield. The final transformations of **28** into idraparinux, involving TEMPO-BAIB-mediated oxidation, removal of benzyl ethers by catalytic hydrogenation and *O*-sulfation using $SO_3 \cdot Et_3N$, were performed according to our previous method.[14]



Scheme 9. The transformation of the 6-*O*-NAP containing protected pentasaccharide.

Conclusions

We have developed a new approach to the synthesis of idraparinux in which the novel and efficient preparation of a 4,6-*O*-acetal-containing L-idose donor and its utilization for the synthesis of the **GH** disaccharide fragment were the key steps. The synthesis of the new idosyl donor was achieved from a properly protected α-thioglucoside in four steps including AgF-mediated elimination, stereoselective hydroboration using $BH_3 \cdot THF$, chemoselective oxidation with H_2O_2 and DDQ-mediated oxidative acetal ring-closure. By applying this donor, due to the controlling effect of the 4,6-acetal group, the **GH** building block was prepared with full 1,2-trans-α-stereoselectivity in the absence of a participating group at C2 position. Typically, L-idose or L-iduronic acid donors with a C2 participating group have been applied for the construction of the α-L-idosyl glycosidic linkage.[10,34] The demonstrated α-stereodirecting effect of the 4,6-cyclic acetal in the presence of an ether protecting group at C2 position pave the way to designing new, more diverse protecting group strategies for the synthesis of heparin and heparin sulfate oligosaccharides. Another advantage of this new strategy to **GH** unit is that most synthetic intermediates were obtained in crystalline form. The idopyranosyl-containing **GH** unit was successfully incorporated to a late-stage oxidation strategy whereby the non-oxidized pentasaccharide backbone was created by an **F**+**GH** and **DE**+**FGH** coupling sequence, with full stereoselectivity in each glycosylation step, followed by simultaneous formation of two carboxylic functions at the pentasaccharide level.

Applying this new approach the target pentasaccharide **3** could be achieved in a 38-step synthesis starting from D-glucose and methyl α-D-glucopyranoside with 23 steps for the longest linear route. To the best of our knowledge, this is the shortest route to idraparinux yet reported.

Experimental Section

General Information. Optical rotations were measured at room temperature on a Perkin–Elmer 241 automatic polarimeter. TLC analysis was performed on Kieselgel 60 F_{254} (Merck) silica–gel plates with visualization by immersing in a sulfuric-acid solution (5% in EtOH) followed by heating. Column chromatography was performed on silica gel 60 (Merck 0.063–0.200 mm) and Sephadex LH-20 (Sigma–Aldrich, bead size: 25–100 mm). Organic solutions were dried over $MgSO_4$ and concentrated under vacuum. ^1H and ^{13}C NMR spectroscopy (^1H: 400 and 500 MHz; ^{13}C: 100.28 and 125.76 MHz) were performed on Bruker DRX-400 and Bruker Avance II 500 spectrometers at 25 °C. Chemical shifts are referenced to $SiMe_4$ or sodium 3-(trimethylsilyl)-1-propanesulfonate (DSS, δ = 0.00 ppm for ^1H nuclei) and to solvent signals ($CDCl_3$: δ = 77.00 ppm, CD_3OD: δ = 49.15 ppm for ^{13}C nuclei). MALDI-TOF MS analyses of the compounds were carried out in the positive reflektron mode using a BIFLEX III mass spectrometer (Bruker, Germany) equipped with delayed-ion extraction. 2,5-Dihydroxybenzoic acid (DHB) was used as matrix and $F_3CCOONa$ as cationising agent in DMF. HRMS measurements were carried out on a maXis II UHR ESI-QTOF MS instrument (Bruker) in positive ionization mode. The following parameters were applied for the electrospray ion source: capillary voltage: 3.6 kV; end plate offset: 500 V; nebulizer pressure: 0.5 bar; dry gas temperature: 200 °C and dry gas flow rate: 4.0 L/min. Constant background correction was applied for each spectrum, the background was recorded before each sample by injecting the blank sample matrix (solvent). Na-formate calibrant was injected after each sample which enabled internal calibration during data evaluation. Mass spectra were recorded by otofControl version 4.1 (build: 3.5, Bruker) and processed by Compass DataAnalysis version 4.4 (build: 200.55.2969).

Ethyl 2,3-di-*O*-methyl-4,6-*O*-(2-naphthyl)methylene-1-thio-α-D-glucopyranoside (5). Compound **4**[20] (540 mg, 1.766 mmol) was dissolved in dry DMF (8.0 mL) and NaH (60%, 170 mg, 4.238 mmol, 1.2 equiv./OH) was slowly added to the solution at 0 °C. After stirring for 30 min at 0 °C, MeI (275 µL, 4.415 mmol, and 1.25 equiv./OH) was added. When complete conversion of the starting material into a main spot had been observed by TLC analysis (24 h at room temperature), CH_3OH (2.5 mL) was added. The reaction mixture was stirred for 5 min and the solvents were evaporated. The residue was dissolved in CH_2Cl_2 (100 mL), and washed with H_2O (2 x 35 mL), the organic layer was dried, filtered and evaporated. The crude product was purified by column chromatography (7:3 *n*-hexane/acetone) to give **5** (634 mg, 92%) as white crystals. $[\alpha]_D^{25}$ +203.6 (*c* 0.14, $CHCl_3$); M.p.: 145-147 °C (EtOAc/*n*-hexane); R_f 0.43 (7:3 *n*-hexane/acetone); ^1H NMR ($CDCl_3$, 500 MHz) δ 7.97-7.47 (m, 7H, arom), 5.70 (s, 1H, H_{ac}), 5.54 (d, *J* = 4.9 Hz, 1H, H-1), 4.34-4.28 (m, 2H, H-5, H-

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6a), 3.83-3.79 (m, 1H, H-6b), 3.64 (s, 3H, OC*H*$_3$), 3.61-3.56 (m, 3H, H-2, H-3, H-4), 3.52 (s, 3H, OC*H*$_3$), 2.65-2.54 (m, 2H, SC*H*$_2$CH$_3$), 1.31 (t, *J* = 7.4 Hz, 3H, SCH$_2$C*H*$_3$) ppm; ^{13}C NMR (CDCl$_3$, 125 MHz) *δ* 134.8, 133.8, 133.0 (3C, 3 x C$_q$ arom), 128.5-123.9 (7C, arom), 101.8 (1C, C$_{ac}$), 83.8 (1C, C-1), 82.4, 81.4, 80.3 (3C, C-2, C-3, C-4), 69.1 (1C, C-6), 62.9 (1C, C-5), 61.3, 58.6 (2C, 2 x OCH$_3$), 24.0 (1C, SCH$_2$CH$_3$), 14.9 (SCH$_2$CH$_3$) ppm; MS (ESI-TOF): *m/z* calcd for C$_{21}$H$_{26}$NaO$_5$S: 413.1393 [M+Na]$^+$; found: 413.1403.

Ethyl 2,3-di-*O*-methyl-4-*O*-(2-naphthyl)methyl-1-thio-α-D-glucopyranoside (6). To a stirred solution of the 4,6-*O*-acetal derivative **5** (1.53 g, 3.918 mmol) in a mixture of dry CH$_2$Cl$_2$ (44 mL) and dry Et$_2$O (18 mL) were added successively LiAlH$_4$ (669 mg, 17.631 mmol, 4.5 equiv.) and a solution of AlCl$_3$ (784 mg, 5.877 mmol, 1.5 equiv.) in dry Et$_2$O (11 mL) under argon at 0 °C. When the TLC (6:4 *n*-hexane/EtOAc) indicated complete disappearance of the starting material (1 h), the reaction mixture was cooled in an ice-bath, and the excess of reagent was decomposed by careful addition of EtOAc (79 mL) followed by H$_2$O (19 mL), and the stirring was continued for additional 5 min. The mixture obtained, consisting of a grey, non-filterable suspension and a clear organic phase, was poured into a separating funnel and diluted with EtOAc (200 mL). The layers were separated and the organic phase was washed with H$_2$O (3 x 50 mL), dried over MgSO$_4$ and concentrated. The residue was purified by column chromatography (6:4 *n*-hexane/EtOAc) to give **6** (1.38 g, 90%) as white crystals. [α]$_D^{25}$ +230.0 (*c* 0.10, CHCl$_3$); M.p.: 103-105 °C (EtOAc/*n*-hexane); *R*$_f$ 0.43 (7:3 *n*-hexane/acetone); ^{1}H NMR (CDCl$_3$, 400 MHz) *δ* 7.84-7.44 (m, 7H, arom), 5.48 (d, *J* = 5.1 Hz, 1H, H-1), 5.03 (d, *J* = 11.4 Hz, 1H, NAP-C*H*$_{2a}$), 4.83 (d, *J* = 11.4 Hz, 1H, NAP-C*H*$_{2b}$), 4.09 (dt, *J* = 3.3 Hz, *J* = 8.9 Hz, 1H, H-5), 3.83-3.73 (m, 3H), 3.66, 3.50 (2 x s, 6H, 2 x OC*H*$_3$), 3.57-3.47 (m, 2H), 2.61-2.50 (m, 2H, SC*H*$_2$CH$_3$), 1.74 (t, 1H, H-6-O*H*), 1.28 (t, *J* = 7.4 Hz, 3H, SCH$_2$C*H*$_3$) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz) *δ* 135.8, 133.4, 133.1 (3C, 3 x C$_q$ arom), 128.3-126.1 (7C, arom), 84.3 (1C, C-1), 82.8, 82.0, 77.5, 71.1 (4C, skeleton carbons), 75.0 (1C, NAP-*C*H$_2$), 62.1 (1C, C-6), 61.3, 58.3 (2C, 2 x OCH$_3$), 24.0 (1C, SCH$_2$CH$_3$), 14.8 (1C, SCH$_2$*C*H$_3$) ppm; MS (ESI-TOF): *m/z* calcd for C$_{21}$H$_{28}$NaO$_5$S: 415.1550 [M+Na]$^+$; found: 415.1574; C$_{21}$H$_{28}$KO$_5$S: 431.1289 [M+Na]$^+$; found: 431.1286.

Ethyl 6-deoxy-6-iodo-2,3-di-*O*-methyl-4-*O*-(2-naphthyl)methyl-1-thio-α-D-glucopyranoside (7). To the solution of thioglucoside **6** (419 mg, 1.068 mmol) in dry toluene (6.3 mL), triphenylphosphine (420 mmol, 1.602 mmol, 1.5 equiv.), imidazole (218 mg, 3.204 mmol, 3.0 equiv.) and iodine (387 mg, 1.495 mmol, 1.4 equiv.) were added. The reaction mixture was stirred at 75 °C for 30 min then cooled to room temperature. To the stirred mixture NaHCO$_3$ (210 mg) in water (2.6 mL) was added at room temperature. After 5 min 10% aqueous solution of Na$_2$S$_2$O$_3$ (5.0 mL) was added and the mixture was diluted with EtOAc (125 mL) and washed with H$_2$O (2 x 35 mL). The organic layer was separated, dried over MgSO$_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography (8:2 *n*-hexane/EtOAc) to give **7** (450 mg, 84%) as white crystals. [α]$_D^{25}$ +146.0 (*c* 0.40, CHCl$_3$); M.p.: 82-84 °C (EtOAc/*n*-hexane); *R*$_f$ 0.41 (8:2 *n*-hexane/EtOAc); ^{1}H NMR (CDCl$_3$, 400 MHz) *δ* 7.85-7.45 (m, 7H, arom), 5.50 (d, *J* = 4.7 Hz, 1H, H-1), 5.08 (d, *J* = 11.2 Hz, 1H, NAP-C*H*$_{2a}$), 4.88 (d, *J* = 11.2 Hz, 1H, NAP-C*H*$_{2b}$), 3.87-3.83 (m, 1H, H-5), 3.64, 3.50 (2 x s, 6H, 2 x OC*H*$_3$), 3.55-3.53 (m, 2H, H-2, H-3), 3.49-3.47 (m, 1H, H-6a), 3.40 (dd, *J* = 5.5 Hz, *J* = 10.7 Hz, 1H, H-6b), 3.34 (t, *J* = 8.8 Hz, 1H, H-4), 2.69-2.58 (m, 2H, SC*H*$_2$CH$_3$), 1.29 (t, *J* = 7.4 Hz, 3H, SCH$_2$C*H*$_3$) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz) *δ* 135.7, 133.4, 133.1 (3C, 3 x C$_q$ arom), 128.4-126.0 (7C, arom), 84.0 (1C, C-2), 82.6 (1C, C-1), 81.9 (1C, C-3), 81.5 (1C, C-4), 75.3 (1C, NAP-*C*H$_2$), 69.4 (1C, C-5), 61.2, 58.2 (2C, 2 x OCH$_3$), 24.0 (1C, SCH$_2$CH$_3$), 14.8 (1C, SCH$_2$*C*H$_3$), 8.2 (1C, C-6) ppm; MS (ESI-TOF): *m/z* calcd for C$_{21}$H$_{27}$INaO$_4$S: 525.0567 [M+Na]$^+$; found: 525.0567.

Ethyl 2,3-di-*O*-methyl-4-*O*-(2-naphthyl)methyl-1-thio-β-L-idopyranoside (8), ethyl 2,3-di-*O*-methyl-4-*O*-(2-naphthyl)methyl-1-thio-β-L-idopyranoside sulfoxide (9) and ethyl 6-deoxy-6-fluoro-2,3-di-*O*-methyl-4-*O*-(2-naphthyl)methyl-1-thio-α-D-glucopyranoside (10). M**ethod I.**: A vigorously stirred solution of iodide **7** (1.38 g, 2.746 mmol) in dry DMF (23 mL) was cooled to 0 °C, NaH (132 mg, 5.494 mmol, 2.0 equiv.) was added and the reaction mixture was stirred at room temperature for 24 h. After the complete disappearance of the starting material, MeOH (2.0 mL) was added and the mixture was concentrated. The residue was dissolved in CH$_2$Cl$_2$ (250 mL) and washed with H$_2$O (2 x 50 mL). The organic layer was separated, dried over MgSO$_4$ and concentrated under reduced pressure. To a stirred solution of the crude product (954 mg, 2.548 mmol) in anhydrous THF (6.5 mL) a solution of BH$_3$·THF complex in THF (1M, 25.5 mL, 25.487 mmol, 10.0 equiv.) was added at 0 °C. The reaction mixture was kept at this temperature for 1.5 h. Then H$_2$O$_2$ (30%, 6.5 mL) and an aqueous solution of NaOH (2M, 13.5 mL) were added at 0 °C and the reaction mixture was stirred at room temperature for 50 min. Subsequently, the reaction mixture was diluted with EtOAc (150 mL) and washed with saturated aqueous solution of NH$_4$Cl (2 x 25 mL), H$_2$O (25 mL) and brine (25 mL). The organic layer was separated, dried over MgSO$_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (7:3 *n*-hexane/acetone) to give **8** (411 mg, 41% for three steps) as a colourless syrup and **6** and **9** (100 mg, ~10% inseparable mixture, ratio of **6** : **9** ≈ 3 : 1) as a colourless syrup.

M**ethod II.**: A vigorously stirred solution of iodide **7** (440 mg, 0.876 mmol) in dry pyridine (8.8 mL) AgF (556 mg, 4.379 mmol, 5.0 equiv.) was added and the reaction mixture was stirred in the dark at room temperature for 24 h. After the complete disappearance of the starting material the mixture was diluted with EtOAc (15 mL), filtered through a pad of Celite® and concentrated under reduced pressure. To a stirred solution of the crude product (300 mg, 0.801 mmol) in anhydrous THF (2.0 mL) a solution of BH$_3$·THF complex in THF (1M, 8.0 mL, 8.011 mmol, 10.0 equiv.) was added at 0 °C. The reaction mixture was kept at this temperature for 1.5 h. Then H$_2$O$_2$ (30%, 2.0 mL) and an aqueous solution of NaOH (2M, 4.25 mL) were added at 0 °C and the reaction mixture was stirred at room temperature for 50 min. Subsequently, the reaction mixture was diluted with EtOAc (100 mL) and washed with saturated aqueous solution of NH$_4$Cl (2 x 15 mL), H$_2$O (15 mL) and brine (15 mL). The organic layer was separated, dried over MgSO$_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (6:4 *n*-hexane/acetone) to give **8** (204 mg, 66% for three steps) as a colourless syrup and **6** and **9** (34 mg, ~11% inseparable mixture, ratio of **6** : **9** ≈ 2 : 1) as a colourless syrup and **10** (34 mg, 11%).

Data of the mixture of **6** and **9**: Characteristic NMR signals: ^{1}H NMR (CDCl$_3$, 400 MHz) *δ* 5.45 (d, *J* = 5.1 Hz, 1H, H-1 d-*gluco*), 5.12 (d, *J* = 2.2 Hz, 0.5H, H-1 l-*ido*-sulfoxide); MS (MALDI-TOF): *m/z* calcd for C$_{21}$H$_{28}$NaO$_5$S (**6**): 415.155 [M+Na]$^+$; found: 415.292; *m/z* calcd for C$_{21}$H$_{28}$NaO$_6$S (**9**): 431.151 [M+Na]$^+$; found: 431.246.

Data of **8**: [α]$_D^{25}$ +52.0 (*c* 0.55, CHCl$_3$); *R*$_f$ 0.25 (7:3 *n*-hexane/acetone); ^{1}H NMR (CDCl$_3$, 400 MHz) *δ* 7.85-7.47 (m, 7H, arom), 4.81 (d, *J* = 12.4 Hz, 1H, NAP-C*H*$_{2a}$), 4.80 (d, *J* = 1.6 Hz, 1H, H-1), 4.70 (d, *J* = 12.5 Hz, 1H, NAP-C*H*$_{2b}$), 4.02 (dd, *J* = 7.9 Hz, *J* = 11.5 Hz, 1H, H-6a), 3.78 (ddd, *J* = 1.9 Hz, *J* = 4.3 Hz, *J* = 6.6 Hz, 1H, H-5), 3.60-3.57 (m, 2H, H-3, H-6b), 3.51 (s, 3H, OC*H*$_3$), 3.41 (s, 1H, H-4), 3.30 (s, 4H, H-2, OC*H*$_3$), 2.71 (qd, *J* = 2.8 Hz, *J* = 7.4 Hz, 2H, SC*H*$_2$CH$_3$), 1.99 (s, 1H, H-6-O*H*), 1.28 (t, *J* = 7.4 Hz, 3H, SCH$_2$C*H*$_3$) ppm; ^{13}C NMR (CDCl$_3$, 100 MHz) *δ* 135.4, 133.2, 133.1 (3C, 3 x C$_q$ arom), 128.5-126.2 (7C, arom), 83.4 (1C, C-1), 78.5 (1C, C-2), 77.3 (1C, C-5), 73.3 (1C, C-3), 72.4 (1C, NAP-*C*H$_2$), 71.4 (1C, C-4), 62.8 (1C, C-6), 59.2, 58.1 (2C, 2 x OCH$_3$), 25.8 (1C, SCH$_2$CH$_3$), 15.5 (1C,

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SCH_2CH_3) ppm; MS (ESI-TOF): *m/z* calcd for $C_{21}H_{28}NaO_5S$: 415.1550 $[M+Na]^+$; found: 415.1552.

Data of **10**: $[\alpha]_D^{25}$ +184.0 (*c* 0.20, $CHCl_3$); R_f 0.64 (6:4 *n*-hexane/acetone); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.85-7.44 (m, 7H, arom), 5.51 (d, *J* = 4.0 Hz, 1H, H-1), 5.05 (d, *J* = 11.3 Hz, 1H, NAP-CH_{2a}), 4.80 (d, *J* = 11.3 Hz, 1H, NAP-CH_{2b}), 4.67 (ddd, *J* = 3.3 Hz, *J* = 10.3 Hz, Hz, *J* = 47.2 Hz , 1H, H-6a), 4.55 (ddd, *J* = 1.5 Hz, *J* = 10.3 Hz, *J* = 47.3 Hz, 1H, H-6b), 4.24-4.14 (m, H-5), 3.66 (s, 3H, OCH_3), 3.55-3.52 (m, 3H, H-2, H-3, H-4), 3.51 (s, 3H, OCH_3), 2.57 (tdd, *J* = 5.4 Hz, *J* = 7.4 Hz, *J* = 12.8 Hz, 2H, SCH_2CH$_3$), 1.29 (t, *J* = 7.4 Hz, 3H, SCH_2CH_3) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 135.7, 133.4, 133.2 (3C, 3 x C_q arom), 128.4-126.0 (7C, arom), 84.3 (1C, C-1), 82.3 (d, *J* = 172 Hz, 1C, C-6), 83.0, 81.8 (2C, C-2, C-3), 76.7 (d, *J* = 5.9 Hz, 1C, C-4), 75.3 (1C, NAP-CH_2), 70.2 (d, *J* = 18.1 Hz, 1C, C-5), 61.3, 58.3 (2C, 2 x OCH_3), 24.1 (1C, SCH_2CH_3), 14.8 (1C, SCH_2CH_3) ppm; MS (ESI-TOF): *m/z* calcd for $C_{21}H_{27}FNaO_4S$: 417.1506 $[M+Na]^+$; found: 417.1506.

Ethyl 2,3-di-*O*-methyl-4,6-*O*-(2-naphthyl)methylene-1-thio-β-L-idopyranoside (11). To a vigorously stirred solution of **8** (160 mg, 0.407 mmol) in dry CH_2Cl_2 (11 mL) DDQ (139 mg, 0.611 mmol, 1.5 equiv.) and 4 Å MS (115 mg) were added. After 50 min the mixture was diluted with CH_2Cl_2 (100 mL), filtered, extracted with a saturated aqueous solution of $NaHCO_3$ (2 x 25 mL) and H_2O (2 x 25 mL), dried and concentrated. The crude product was purified by silica gel chromatography (7:3 *n*-hexane/acetone) to give **11** (106 mg, 67%) as a colourless syrup. $[\alpha]_D^{25}$ +55.7 (*c* 0.21, $CHCl_3$); R_f 0.35 (7:3 *n*-hexane/acetone); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.96-7.44 (m, 7H, arom), 5.62 (s, 1H, H_{ac}), 4.87 (d, *J* = 1.3 Hz, 1H, H-1), 4.36 (d, *J* = 12.5 Hz, 1H, NAP-CH_{2a}), 4.07 (dd, *J* = 2.0 Hz, *J* = 12.5 Hz, 1H, NAP-CH_{2b}), 3.97 (s, 1H, H-4), 3.70 (t, *J* = 2.2 Hz, 1H, H-3), 3.58 (d, *J* = 1.1 Hz, 1H, H-5), 3.49, 3.47 (2 x s, 6H, 2 x OCH_3), 3.36 (s, 1H, H-2), 2.76 (q, *J* = 7.4 Hz, 2H, SCH_2CH_3), 1.31 (t, *J* = 7.4 Hz, 3H, SCH_2CH_3) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 135.8, 133.8, 133.0 (3C, 3 x C_q arom), 128.4-124.6 (7C, arom), 101.6 (1C, C_{ac}), 82.3 (1C, C-1), 77.2 (1C, C-2), 75.4 (1C, C-3), 71.7 (1C, C-4), 70.1 (1C, C-6), 68.6 (1C, C-5), 58.4, 58.2 (2C, 2 x OCH_3), 25.6 (1C, SCH_2CH_3), 15.1 (1C, SCH_2CH_3) ppm; MS (ESI-TOF): *m/z* calcd for $C_{21}H_{26}NaO_5S$: 413.1393 $[M+Na]^+$; found: 413.1393.

Methyl [2,3-di-*O*-methyl-4,6-*O*-(2-naphthyl)methylene-α-L-idopyranosyl]-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (13). To a solution of compound **11** (200 mg, 0.512 mmol) and compound **12**[26] (357 mg, 0.768 mmol, 1.5 equiv.) in dry CH_2Cl_2 (6.0 mL) 4 Å molecular sieves (0.25 g) were added. After stirring at room temperature for 30 min, the mixture was cooled to −40 °C and solutions of NIS (173 mg, 0.768 mmol, 1.5 equiv.) in dry THF (240 µL) and AgOTf (32 mg, 0.123 mmol, 0.24 equiv.) in dry toluene (240 µL) were added. After stirring at −40 °C to −20 °C for 4 h, TLC analysis (6:4 *n*-hexane/EtOAc) showed complete consumption of the donor. The reaction mixture was neutralized with Et_3N (50 µL), diluted with CH_2Cl_2 (150 mL), and filtered. The filtrate was washed with an aqueous solution of $Na_2S_2O_3$ (10%, 25 mL), a saturated aqueous solution of $NaHCO_3$ (2 x 25 mL), and water (2 x 25 mL), dried, and concentrated. The crude product was purified by column chromatography on silica gel (6:4 *n*-hexane/EtOAc) to give compound **13** (294 mg, 72%) as white crystals. $[\alpha]_D^{25}$ +1.1 (*c* 0.09, $CHCl_3$); R_f 0.36 (6:4 *n*-hexane/EtOAc); M.p.: 162-164 °C (EtOAc/*n*-hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.91-7.22 (m, 22H, arom), 5.43 (s, 1H, H_{ac}), 5.05 (d, *J* = 11.2 Hz, 1H, Bn-CH_{2a}), 4.85 (d, *J* = 4.9 Hz, 1H, H-1'), 4.78-4.56 (m, 6H, Bn-CH_{2b}, 2 x Bn-CH_2, H-1), 3.98-3.77 (m, 5H, H-3, H-4, H-4', H-5', H-6'a), 3.70-3.69 (m, 2H, H-6a,b), 3.59 (dd, *J* = 3.6 Hz, *J* = 9.5 Hz, 1H, H-2), 3.54 (s, 1H, H-5), 3.51 (s, 3H, OCH_3), 3.46-3.43 (m, 1H, H-3'), 3.44, 3.38 (2 x s, 6H, 2 x OCH_3), 3.20 (dd, *J* = 4.9 Hz, *J* = 9.1 Hz, 1H, H-2'), 3.16 (dd, *J* = 2.2 Hz, *J* = 13.2 Hz, 1H, H-6'b) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.2, 138.1, 137.8, 135.5, 133.6, 132.9 (6C, 6 x C_q arom), 128.5-124.0 (22C, arom), 100.4, (1C, C-1'), 100.0 (1C, C_{ac}), 98.1 (1C, C-1), 82.3 (1C, C-3), 80.6 (1C, C-2), 80.3, 80.2 (2C, C-2', C-3'), 78.2 (1C, C-4'), 75.7, 73.5, 73.4 (3C, 3 x Bn-CH_2), 73.0 (1C, C-4), 70.6 (1C, C-5), 68.7 (1C, C-6'), 68.5 (1C, C-6), 62.0 (1C, C-5'), 59.8, 58.6 (2C, 2 x OCH_3), 55.2 (1C, C-1-OCH_3) ppm; MS (ESI-TOF): *m/z* calcd for $C_{47}H_{52}NaO_{11}$: 815.3402 $[M+Na]^+$; found: 815.3399.

Methyl [2,3-di-*O*-methyl-6-*O*-(2-naphthyl)methyl-α-L-idopyranosyl]-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (14) and methyl (2,3-di-*O*-methyl-α-L-idopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (15).

Method I.: To a solution of compound **13** (250 mg, 0.315 mmol) in anhydrous CH_2Cl_2 (3.2 mL) at 0 °C Et_3SiH (604 µL, 3.784 mmol, 12.0 equiv.) and $BF_3{\cdot}Et_2O$ (80 µL, 0.631 mmol, 2.0 equiv.) were added. The reaction mixture was stirred for 2 h at 0 °C. Than the mixture was diluted with CH_2Cl_2 (100 mL), washed with saturated aqueous solution of $NaHCO_3$ (2 x 20 mL), dried over $MgSO_4$ and concentrated. The crude product was purified by column chromatography on silica gel (1:1 *n*-hexane/EtOAc) to give compound **14** (52 mg, 20%) as a colourless syrup and compound **15** (105 mg, 42%) as a colourless syrup.

Method II.: To a solution of compound **13** (126 mg, 0.159 mmol) in anhydrous THF (500 µL) 4 Å MS (121 mg) and $Me_3N{\cdot}BH_3$ (70 mg, 0.953 mmol, 6.0 equiv.) were added and stirred for 30 min at room temperature. After 30 min $AlCl_3$ (127 mg, 0.953 mmol, 6.0 equiv.) was added and the reaction mixture was stirred at room temperature for 30 min. The mixture was diluted with CH_2Cl_2 (100 mL), washed with water (2 x 20 mL), dried over $MgSO_4$ and concentrated. The crude product was purified by column chromatography on silica gel (1:1 *n*-hexane/EtOAc) to give compound **14** (101 mg, 80%) as a colourless syrup.

Data of **14**: $[\alpha]_D^{25}$ +3.3 (*c* 0.12, $CHCl_3$); R_f 0.40 (1:1 *n*-hexane/EtOAc); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.80-7.20 (m, 22H, arom), 5.08 (s, 1H, H-1'), 4.95-4.43 (m, 9H, NAP-CH_2, 3 x Bn-CH_2, H-1), 4.39 (td, *J* = 1.3 Hz, *J* = 5.7 Hz, 1H, H-5'), 3.94-3.86 (m, 2H), 3.79-3.57 (m, 5H), 3.52-3.46 (m, 3H), 3.40, 3.34, 3.27 (3 x s, 9H, 3 x OCH_3), 3.20 (s, 1H), 3.14 (d, *J* = 9.3 Hz, 1H, C-4-O*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.2, 138.2, 138.0, 135.9, 133.3, 132.9 (6C, 6 x C_q arom), 128.4-125.7 (22C, arom), 98.1 (2C, C-1, C-1'), 80.4, 80.3, 77.5, 77.4, 74.6, 70.1, 66.9, 66.8 (8C, skeleton carbons), 75.4, 73.5, 73.3 (4C, NAP-CH_2, 3 x Bn-CH_2), 69.8, 68.9 (2C, C-6, C-6'), 58.5, 58.3 (2C, 2 x OCH_3), 55.2 (1C, C-1-OCH_3) ppm; MS (MALDI-TOF): *m/z* calcd for $C_{47}H_{54}NaO_{11}$: 817.356 $[M+Na]^+$; found: 817.381.

Data of **15**: $[\alpha]_D^{25}$ −5.5 (*c* 0.20, $CHCl_3$); R_f 0.13 (1:1 *n*-hexane/EtOAc); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.27-7.18 (m, 15H, arom), 4.96 (d, *J* = 10.5 Hz, 1H, Bn-CH_{2a}), 4.89 (s, 1H, H-1'), 4.72-4.45 (m, 6H, Bn-CH_{2b}, 2 x Bn-CH_2, H-1), 4.08-4.06 (m, 1H, H-5'), 3.84-3.78 (m, 2H, H-3, H-3'), 3.72-3.70 (m, 1H, H-4), 3.56 (s, 2H, H-6a,b), 3.51 (dd, *J* = 3.3 Hz, *J* = 8.8 Hz, 1H, H-2), 3.45-3.40 (m, 1H, H-5), 3.37 (s, 3H, OCH_3), 3.35-3.31 (m, 1H, H-4'), 3.29, 3.17 (2 x s, 6H, 2 x OCH_3), 3.28-3.12 (m, 2H, H-6'a,b), 3.07-3.05 (m, 1H, H-2'), 1.83 (s, 1H, C-6'-O*H*), 1.24 (s, 1H, C-4'-O*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.5, 138.0, 137.7 (3C, 3 x C_q arom), 128.5-127.7 (15C, arom), 98.0, (1C, C-1), 97.0 (1C, C-1), 80.3 (1C, C-2), 80.1 (1C, C-3), 76.9, 76.8 (2C, C-2', C-4'), 75.8, 73.6 (2C, 2 x Bn-CH_2), 73.5 (1C, C-3'), 73.4 (1C, Bn-CH_2), 70.2 (1C, C-4), 68.9 (1C, C-6), 67.1, 67.0 (2C, C-5, C-5'), 63.0 (1C, C-6'), 58.4, 58.2 (2C, 2 x OCH_3), 55.2 (1C, C-1-OCH_3) ppm; MS (MALDI-TOF): *m/z* calcd for $C_{36}H_{46}NaO_{11}$: 667.293 $[M+Na]^+$; found: 667.344.

Methyl (6-*O*-*tert*-butyldiphenylsilyl-2,3-di-*O*-methyl-α-L-idopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (16). To a solution of **15** (103 mg, 0.157 mmol) in dry pyridine (540 µL), *tert*-butyldiphenylsilyl chloride (81 µL, 0.314 mmol, 2 equiv.) was added. The mixture was stirred for 24 h at room temperature. After the complete

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disappearance of the starting material, the mixture was concentrated. The residue was dissolved in EtOAc (75 mL), washed with 1 M aqueous solution of HCl (2 x 10 mL), water (10 mL), saturated aqueous solution of $NaHCO_3$ (2 x 10 mL), and water (2 x 10 mL), dried, and concentrated. The crude product was purified by column chromatography on silica gel (7:3 *n*-hexane/acetone) to give compound **16** (114 mg, 81%) as a colourless syrup. $[\alpha]_D^{25}$ +5.4 (*c* 0.13, $CHCl_3$); R_f 0.41 (7:3 *n*-hexane/acetone); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.69-7.15 (m, 25H, arom), 5.08 (s, 1H, H-1'), 4.88-4.49 (m, 7H, 3 x Bn-CH_2, H-1), 4.26 (t, *J* = 5.1 Hz, 1H, H-5'), 3.93-3.84 (m, 2H), 3.83-3.75 (m, 4H), 3.69-3.61 (m, 2H), 3.51-3.47 (m, 2H), 3.41, 3.36, 3.24 (3 x s, 9H, 3 x OCH_3), 3.18 (s, 1H), 1.26 (s, 1H, C-4'-O*H*), 1.02 (s, 9H, 3 x *t*-Bu-CH_3) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.0, 138.3, 138.1, 133.4, 133.3 (5C, 5 x C_q arom), 129.6-127.3 (25C, arom), 98.4, 98.3 (2C, C-1, C-1'), 80.8, 80.2, 77.8, 77.6, 74.4, 70.0, 68.1, 66.7 (8C, skeleton carbons), 75.6, 73.6 (2C, 2 x Bn-CH_2), 69.0 (1C, C-6), 63.5 (1C, C-6'), 58.4, 58.3 (2C, 2 x OCH_3), 55.2 (1C, C-1-OCH_3), 26.9 (3C, 3 x *t*-Bu-CH_3), 19.2 (1C, C_q *t*-Bu) ppm; MS (MALDI-TOF): *m/z* calcd for $C_{52}H_{64}NaO_{11}Si$: 915.411 $[M+Na]^+$; found: 915.550.

Methyl (2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-(1→4)-(6-*O*-*tert*-butyldiphenylsilyl-2,3-di-*O*-methyl-α-L-idopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (18). To a solution of compound **16** (54 mg, 0.060 mmol) and compound **17**[31] (52 mg, 0.096 mmol, 1.6 equiv.) in dry CH_2Cl_2 (708 µL) 4 Å molecular sieves (50 mg) were added. After stirring at room temperature for 30 min, the mixture was cooled to −40 °C and solutions of NIS (33 mg, 0.145 mmol, 1.5 equiv.) in dry THF (45 µL) and AgOTf (6.0 mg, 0.023 mmol, 0.24 equiv.) in dry toluene (45 µL) were added. After stirring at −40 °C to −20 °C for 4 h, TLC analysis (7:3 *n*-hexane/EtOAc) showed complete consumption of the donor. The reaction mixture was neutralized with Et_3N (25 µL), diluted with CH_2Cl_2 (75 mL), and filtered. The filtrate was washed with an aqueous solution of $Na_2S_2O_3$ (10%, 10 mL), a saturated aqueous solution of $NaHCO_3$ (2 x 10 mL), and water (2 x 10 mL), dried, and concentrated. The crude product was purified by column chromatography on silica gel (7:3 *n*-hexane/EtOAc) to give compound **18** (70 mg, 88%) as a colourless syrup. $[\alpha]_D^{25}$ −1.8 (*c* 0.11, $CHCl_3$); R_f 0.30 (7:3 *n*-hexane/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.74-7.19 (m, 40H, arom), 5.50 (s, 1H, H_{ac}), 5.28 (d, *J* = 3.9 Hz, 1H, H-1"), 5.01 (d, *J* = 7.2 Hz, 1H, H-1'), 4.99-4.62 (m, 8H, 4 x Bn-CH_2), 4.62 (d, *J* = 3.6 Hz, 1H, H-1), 4.49 (q, *J* = 12.2 Hz, 2H, Bn-CH_2), 4.01 (dd, *J* = 4.5 Hz, *J* = 10.1 Hz, 1H, H-6"a), 3.93-3.84 (m, 7H, H-3, H-3', H-3", H-4', H-5, H-6a, H-6'a), 3.77-3.75 (m, 2H, H-5', H-6'b), 3.65-3.56 (m, 5H, H-2", H-4, H-4", H-6b, H-6"b), 3.55-3.52 (m, 1H, H-5"), 3.51 (s, 3H, C-3'-OCH_3), 3.49-3.48 (m, 1H, H-2), 3.46 (s, 3H, C-2'-OCH_3), 3.42 (s, 3H, C-1-OCH_3), 3.00 (t, *J* = 7.7 Hz, 1H, H-2'), 1.03 (s, 9H, 3 x *t*-Bu-CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 139.5, 139.0, 138.6, 138.5, 138.3, 137.5, 132.9, 132.7 (8C, 8 x C_q arom), 129.9-126.2 (40C, arom), 101.2 (1C, C_{ac}), 101.0 (1C, C-1'), 99.4 (1C, C-1"), 98.1 (1C, C-1), 85.5 (1C, C-2'), 82.5 (1C, C-3'), 82.4 (1C, C-4"), 80.6 (1C, C-3), 79.2 (1C, C-2), 79.1 (1C, C-2"), 78.9 (1C, C-4), 78.7 (1C, C-3"), 75.9 (1C, C-4'), 75.6, 75.2 (2C, 2 x Bn-CH_2), 73.8 (1C, C-5'), 73.7, 73.4 (3C, 3 x Bn-CH_2), 70.8 (1C, C-5), 69.4 (1C, C-6), 68.8 (1C, C-6"), 63.2 (1C, C-5"), 62.8 (1C, C-6'), 60.6, 60.5 (2C, 2 x OCH_3), 55.3 (1C, C-1-OCH_3), 27.1 (3C, 3 x *t*-Bu-CH_3), 19.1 (1C, C_q *t*-Bu) ppm; MS (MALDI-TOF): *m/z* calcd for $C_{79}H_{90}NaO_{16}Si$:1345.589 $[M+Na]^+$; found: 1345.662.

Methyl (2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-(6-*O*-*tert*-butyldiphenylsilyl-2,3-di-*O*-methyl-α-L-idopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (19a) and methyl (2,3,4-tri-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-(6-*O*-*tert*-butyldiphenylsilyl-2,3-di-*O*-methyl-α-L-idopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (19b). To a solution of **18** (63 mg, 0.048 mmol) in dry THF (144 µL) 4 Å MS (36 mg) and $Me_3N{\cdot}BH_3$ (21 mg, 0.286 mmol, 6 equiv.) were added and the reaction mixture was stirred for 30 min at room temperature. After 30 min $AlCl_3$ (38 mg, 0.286 mmol, 6 equiv.) was added and the mixture was stirred at room temperature for 2 h. After 2.5 h the reaction mixture was diluted with CH_2Cl_2 (5.0 mL), and washed with H_2O (2 x 5 mL). The organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified by silica gel chromatography (7:3 *n*-hexane/acetone) to give **19a** (40 mg, 65%) as a colourless syrup and **19b** (13 mg, 21%) as a colourless syrup.

Data of **19a**: $[\alpha]_D^{25}$ +13.0 (*c* 0.13, $CHCl_3$); R_f 0.36 (7:3 *n*-hexane/acetone); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.72-7.12 (m, 40H, arom), 5.27 (d, *J* = 3.5 Hz, 1H, H-1"), 4.99 (d, *J* = 7.2 Hz, 1H, H-1'), 4.97-4.62 (m, 8H, 4 x Bn-CH_2), 4.60 (d, *J* = 3.6 Hz, 1H, H-1), 4.52-4.40 (m, 4H, 2 x Bn-CH_2), 3.93 (dd, *J* = 4.7 Hz, *J* = 11.3 Hz, 1H, H-6'a), 3.89-3.83 (m, 6H, H-3, H-3', H-4, H-4', H-5', H-6a), 3.81-3.79 (m, 1H, H-6'b), 3.67-3.56 (m, 4H, H-3", H-4", H-5, H-6b), 3.54-3.49 (m, 2H, H-2", H-6"a), 3.50 (s, 3H, C-3'-OCH_3), 3.47-3.46 (m, 1H, H-2), 3.45 (s, 3H, C-2'-OCH_3), 3.41 (s, 3H, C-1-OCH_3), 3.42-3.35 (m, 2H, H-5", H-6"b), 3.01 (t, *J* = 7.2 Hz, 1H, H-2'), 2.24 (d, *J* = 2.5 Hz, 1H, C-4"-O*H*), 1.04 (s, 9H, 3 x *t*-Bu-CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 139.6, 139.0, 138.6, 138.5, 138.3, 138.0, 133.2, 132.9 (8C, 8 x C_q arom), 129.9-127.2 (40C, arom), 100.8 (1C, C-1'), 98.6 (1C, C-1"), 98.2 (1C, C-1), 85.1 (1C, C-2'), 82.1 (1C, C-3'), 81.4 (1C, C-3"), 80.6 (1C, C-3), 79.2 (1C, C-2), 79.1 (1C, C-2"), 78.8 (1C, C-4"), 76.0 (1C, C-4'), 75.6, 75.3, 73.8, 73.7 (4C, 4 x Bn-CH_2), 73.6 (1C, C-4), 73.4, 72.5 (2C, 2 x Bn-CH_2), 70.9, 70.8, 70.7 (3C, C-5, C-5', C-5"), 69.3 (1C, C-6), 69.1 (1C, C-6"), 62.8 (1C, C-6'), 60.5, 60.4 (2C, 2 x OCH_3), 55.3 (1C, C-1-OCH_3), 27.1 (3C, 3 x *t*-Bu-CH_3), 19.3 (1C, C_q *t*-Bu) ppm; MS (ESI-TOF): *m/z* calcd for $C_{79}H_{92}NaO_{16}Si$: 1347.6047 $[M+Na]^+$; found: 1347.6037.

Data of **19b**: $[\alpha]_D^{25}$ +17.2 (*c* 0.97, $CHCl_3$); R_f 0.31 (7:3 *n*-hexane/acetone); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.70-7.18 (m, 40H, arom), 5.24 (d, *J* = 3.6 Hz, 1H, H-1"), 4.99 (d, *J* = 10.6 Hz, 1H, Bn-CH_{2a}), 4.96 (d, *J* = 7.0 Hz, 1H, H-1'), 4.91-4.61 (m, 9H, Bn-CH_{2b}, 4 x Bn-CH_2), 4.60 (d, *J* = 3.0 Hz, 1H, H-1), 4.47 (q, *J* = 12.2 Hz, 2H, Bn-CH_2), 3.91 (dd, *J* = 4.9 Hz, *J* = 11.3 Hz, 1H, H-6'a), 3.88-3.76 (m, 8H, H-3, H-3', H-3", H-4', H-5, H-5', H-6a, H-6'b), 3.65 (t, *J* = 9.4 Hz, 1H, H-4), 3.58 (dd, *J* = 7.0 Hz, *J* = 10.8 Hz, 1H, H-6b), 3.53-3.46 (m, 5H, H-2, H-2", H-4", H-6"a,b), 3.50 (s, 3H, C-3'-OCH_3), 3.46 (s, 3H, C-2'-OCH_3), 3.41 (s, 3H, C-1-OCH_3), 3.38-3.36 (m, 1H, H-5"), 3.00 (t, *J* = 7.2 Hz, 1H, H-2'), 1.48-1-45 (m, 1H, C-6"-O*H*), 1.04 (s, 9H, 3 x *t*-Bu-CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 139.6, 138.5, 138.4, 133.2, 132.8, 131.2 (8C, 8 x C_q arom), 128.5-127.2 (40C, arom), 100.7 (1C, C-1'), 98.6 (1C, C-1"), 98.2 (1C, C-1), 85.2 (1C, C-2'), 82.3 (1C, C-3'), 81.8 (1C, C-3"), 80.6 (1C, C-3), 79.7 (1C, C-2"), 79.2 (1C, C-2), 78.8 (1C, C-4), 77.5 (1C, C-4"), 76.2 (1C, C-4'), 75.6, 75.2 (4C, 4 x Bn-CH_2), 74.2 (1C, C-5'), 73.4, 72.8 (2C, 2 x Bn-CH_2), 71.8 (1C, C-5"), 70.8 (1C, C-5), 69.3 (1C, C-6), 62.6 (1C, C-6'), 61.8 (1C, C-6"), 60.5, 60.4 (2C, 2 x OCH_3), 55.3 (1C, C-1-OCH_3), 27.1 (3C, 3 x *t*-Bu-CH_3), 19.2 (1C, C_q *t*-Bu) ppm; MS (MALDI-TOF): *m/z* calcd for $C_{79}H_{92}NaO_{16}Si$: 1347.605 $[M+Na]^+$; found: 1347.877.

Methyl (2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-methyl-6-*O*-(2-naphthyl)methyl-α-L-idopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (20). To a solution of compound **14** (90 mg, 0.113 mmol) and compound **17**[31] (98 mg, 0.181 mmol, 1.6 equiv.) in dry CH_2Cl_2 (1320 µL) 4 Å molecular sieves (80 mg) were added. After stirring at room temperature for 30 min, the mixture was cooled to −40 °C and solutions of NIS (61 mg, 0.272 mmol, 1.5 equiv.) in dry THF (84 µL) and AgOTf (11 mg, 0.043 mmol, 0.24 equiv.) in dry toluene (84 µL) were added. After stirring at −40 °C to −20 °C for 4 h, TLC analysis (7:3 *n*-hexane/EtOAc) showed complete consumption of the donor. The reaction mixture was neutralized with Et_3N (200 µL), diluted with CH_2Cl_2 (100 mL), and filtered. The filtrate was washed with an aqueous solution of $Na_2S_2O_3$ (10%, 20 mL), a saturated aqueous solution of $NaHCO_3$ (2 x 20 mL), and water (2 x 20 mL), dried, and concentrated. The crude product was purified by column chromatography on silica gel (65:35 *n*-hexane/EtOAc) to give compound **20** (111 mg, 80%) as a colourless syrup. $[\alpha]_D^{25}$ +11.0 (*c* 0.10, $CHCl_3$); R_f 0.50 (6:4 *n*-hexane/EtOAc); ^{1}H NMR

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($CDCl_3$, 500 MHz) δ 7.72-7.19 (m, 37H, arom), 5.52 (s, 1H, H_{ac}), 5.25 (d, J = 3.8 Hz, 1H, H-1"), 4.98 (d, J = 6.9 Hz, 1H, H-1'), 4.98-4.60 (m, 8H, 4 x Bn-CH_2), 4.58 (d, J = 4.0 Hz, 1H, H-1), 4.48-4.38 (m, 4H, NAP-CH_2, Bn-CH_2), 4.15 (dd, J = 4.7 Hz, J = 10.1 Hz, 1H, H-6"a), 4.04 (dd, J = 4.6 H, J = 9.5 Hz, 1H, H-5'), 3.93-3.88 (m, 4H, H-3, H-3", H-4, H-4'), 3.79-3.74 (m, 5H, H-3', H-5, H-5", H-6a, H-6'a), 3.71-3.64 (m, 3H, H-6b, H-6'b, H-6"b), 3.60 (t, J = 9.4 Hz, 1H, H-4"), 3.58 (dd, J = 3.8 Hz, J = 9.4 Hz, 1H, H-2"), 3.52 (s, 3H, C-3'-OCH_3), 3.50-3.47 (m, 1H, H-2), 3.49 (s, 3H, C-2'-OCH_3), 3.36 (s, 3H, C-1-OCH_3), 3.05 (t, J = 7.4 Hz, 1H, H-2') ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 139.4, 138.8, 138.5, 138.3, 137.5, 135.8, 133.3, 132.8 (9C, 9 x C_q arom), 129.9-125.6 (37C, arom), 101.2 (1C, C_{ac}), 100.0 (1C, C-1'), 99.1 (1C, C-1"), 98.4 (1C, C-1), 84.8 (1C, C-2'), 82.5 (1C, C-3'), 82.3 (1C, C-4"), 80.2 (1C, C-3), 79.4 (1C, C-2), 79.0 (1C, C-2"), 78.3 (1C, C-4'), 76.6 (1C, C-4), 76.3 (1C, C-3"), 75.3, 75.0, 73.6, 73.2 (6C, NAP-CH_2, 5 x Bn-CH_2), 72.2 (1C, C-5'), 70.4 (1C, C-5), 69.1 (1C, C-6'), 68.9 (1C, C-6"), 68.3 (1C, C-6), 63.3 (1C, C-5"), 60.4, 60.3 (2C, 2 x OCH_3), 55.3 (1C, C-1-OCH_3) ppm; MS (ESI-TOF): *m/z* calcd for $C_{74}H_{80}NaO_{16}$: 1247.5339 $[M+Na]^+$; found: 1247.5331.

Methyl (2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-methyl-6-*O*-(2-naphthyl)methyl-α-L-idopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (21a) and methyl (2,3,4-tri-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-methyl-6-*O*-(2-naphthyl)methyl-α-L-idopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (21b). To a solution of **20** (95 mg, 0.077 mmol) in dry THF (235 µL) 4 Å MS (60 mg) and $Me_3N{\cdot}BH_3$ (34 mg, 0.465 mmol, 6 equiv.) were added and the reaction mixture was stirred for 30 min at room temperature. After 30 min $AlCl_3$ (62 mg, 0.465 mmol, 6 equiv.) was added and the mixture was stirred at room temperature for 2 h. After 2 h the reaction mixture was diluted with CH_2Cl_2 (50 mL), and washed with H_2O (2 x 15 mL). The organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified by silica gel chromatography (6:4 *n*-hexane/EtOAc) to give **21a** (66 mg, 70%) as a colourless syrup and **21b** (18 mg, 19%) as a colourless syrup.

Data of **21a**: $[\alpha]_D^{25}$ +26.7 (*c* 0.12, $CHCl_3$); R_f 0.66 (1:1 *n*-hexane/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.74-7.16 (m, 37H, arom), 5.27 (d, J = 3.5 Hz, 1H, H-1"), 4.98 (d, J = 7.4 Hz, 1H, H-1'), 4.96-4.60 (m, 8H, 4 x Bn-CH_2), 4.58 (d, J = 4.3 Hz, 1H, H-1), 4.49-4.36 (m, 6H, NAP-CH_2, 2 x Bn-CH_2), 4.10 (dd, J = 4.8 Hz, J = 9.8 Hz, 1H, H-5'), 3.94-3.86 (m, 3H, H-3, H-4, H-4'), 3.80 (dd, J = 3.7 Hz, J = 10.7 Hz, 1H, H-6a), 3.77-3.73 (m, 3H, H-3', H-5, H-6'a), 3.69-3.60 (m, 5H, H-3", H-4", H-5", H-6b, H-6'b), 3.55-3.50 (m, 2H, H-2", H-6"a), 3.51 (s, 3H, C-3'-OCH_3), 3.49-3.44 (m, 2H, H-2, H-6"b), 3.47 (s, 3H, C-2'-OCH_3), 3.36 (s, 3H, C-1-OCH_3), 3.06 (t, J = 7.3 Hz, 1H, H-2'), 2.23 (s, 1H, C-4"-O*H*) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 139.4, 138.8, 138.6, 138.4, 138.0, 135.9, 133.4, 132.9 (9C, 9 x C_q arom), 128.6-125.8 (37C, arom), 100.0 (1C, C-1'), 98.4 (1C, C-1), 98.0 (1C, C-1"), 84.5 (1C, C-2'), 82.2 (1C, C-3'), 80.9 (1C, C-3"), 80.3 (1C, C-3), 79.5 (1C, C-2), 79.3 (1C, C-2"), 76.6 (1C, C-4), 76.0 (1C, C-4'), 75.5, 75.2, 73.7, 73.6, 73.3, 72.4 (7C, NAP-CH_2, 6 x Bn-CH_2), 71.9 (1C, C-5'), 70.9, 70.8 (2C, C-4", C-5"), 70.5 (1C, C-5), 69.4 (1C, C-6'), 69.2 (1C, C-6"), 68.4 (1C, C-6), 60.3, 60.2 (2C, 2 x OCH_3), 55.4 (1C, C-1-OCH_3) ppm; MS (ESI-TOF): *m/z* calcd for $C_{74}H_{82}NaO_{16}$: 1249.5495 $[M+Na]^+$; found: 1249.5487.

Data of **21b**: $[\alpha]_D^{25}$ +31.8 (*c* 2.70, $CHCl_3$); R_f 0.46 (1:1 *n*-hexane/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.72-7.19 (m, 37H, arom), 5.24 (d, J = 3.6 Hz, 1H, H-1"), 4.97 (d, J = 10.8 Hz, 1H, Bn-CH_{2a}), 4.98 (d, J = 6.9 Hz, 1H, H-1'), 4.89-4.69 (m, 7H, Bn-CH_{2b}, 3 x Bn-CH_2), 4.60-4.58 (m, 2H, Bn-CH_2), 4.57 (d, J = 4.6 Hz, 1H, H-1), 4.49-4.36 (m, 4H, NAP-CH_2, Bn-CH_2), 4.06 (dd, J = 4.6 Hz, J = 9.6 Hz, 1H, H-5'), 3.93-3.84 (m, 4H, H-3, H-3", H-4, H-4'), 3.79 (dd, J = 3.7 Hz, J = 10.7 Hz, 1H, H-6a), 3.76-3.72 (m, 3H, H-3', H-5, H-6'a), 3.69-3.66 (m, 2H, H-6b, H-6'b), 3.60-3.55 (m, 3H, H-5", H-6"a,b), 3.52-3.46 (m, 3H, H-2, H-2", H-4"), 3.51 (s, 3H, C-3'-OCH_3), 3.48 (s, 3H, C-2'-OCH_3), 3.37 (s, 3H, C-1-OCH_3), 3.05 (t, J = 7.3 Hz, 1H, H-2'), 1.70 (s, 1H, C-6"-O*H*) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 139.4, 138.8, 138.6, 138.4, 138.3, 135.9, 133.4, 132.9 (9C, 9 x C_q arom), 128.6-125.7 (37C, arom), 100.1 (1C, C-1'), 98.5 (1C, C-1), 98.0 (1C, C-1"), 84.7 (1C, C-2'), 82.5 (1C, C-3'), 81.7 (1C, C-3"), 80.3 (1C, C-3), 79.9 (1C, C-2"), 79.5 (1C, C-2), 77.3 (1C, C-4"), 76.7 (1C, C-4), 76.1 (1C, C-4'), 75.5, 75.4, 75.2, 73.7, 73.3, 72.8 (7C, NAP-CH_2, 6 x Bn-CH_2), 72.0 (1C, C-5'), 71.7 (1C, C-5"), 70.5 (1C, C-5), 69.2 (1C, C-6'), 68.4 (1C, C-6), 61.7 (1C, C-6"), 60.4 (2C, 2 x OCH_3), 55.4 (1C, C-1-OCH_3) ppm; MS (ESI-TOF): *m/z* calcd for $C_{74}H_{82}NaO_{16}$: 1249.5495 $[M+Na]^+$; found: 1249.5483.

Methyl (6-*O*-benzyl-2,3,4-tri-*O*-methyl-α-D-glucopyranosyl)-(1→4)-[2,3-di-*O*-acetyl-6-*O*-(2-naphthyl)methyl-β-D-glucopyranosyl]-(1→4)-(2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-(6-*O*-*tert*-butyldiphenylsilyl-2,3-di-*O*-methyl-α-L-idopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (23) and methyl (6-*O*-benzyl-2,3,4-tri-*O*-methyl-α-D-glucopyranosyl)-(1→4)-[2,3-di-*O*-acetyl-6-*O*-(2-naphthyl)methyl-β-D-glucopyranosyl]-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (24). To a solution of trisaccharide acceptor **19a** (32 mg, 0.024 mmol) and disaccharide donor **22**[32] (28.6 mg, 0.036 mmol, 1.5 equiv.) in dry CH_2Cl_2 (1.2 mL) 4 Å MS (150 mg) were added and the reaction mixture was stirred at room temperature. After 30 min the stirred mixture was cooled to −20 °C under argon. After at this temperature, NIS (12 mg, 0.054 mmol, 1.5 equiv. to the donor) was dissolved in dry THF (30 µL) and AgOTf (2 mg, 0.009 mmol, 0.24 equiv. to the donor) dissolved in dry toluene (30 µL) were added. The temperature was allowed to warm up to +5 °C and the reaction mixture was stirred for 4 h. After 4 h the reaction mixture was quenched with Et_3N (150 µL), diluted with CH_2Cl_2 (25 mL), filtered and the mixture was washed with saturated aqueous solution of $Na_2S_2O_3$ (2 x 5 mL), saturated aqueous solution of $NaHCO_3$ (5 mL) and with H_2O (2 x 5 mL) until neutral pH. The organic layer was dried on $MgSO_4$ and concentrated. The crude product was purified by silica gel chromatography (6:4 *n*-hexane/EtOAc to 1:1 *n*-hexane/EtOAc) to give **23** (5 mg, 11%) as a colourless syrup and **24** (22 mg, 46%) as a colourless syrup.

Data of **23**: $[\alpha]_D^{25}$ +27.0 (*c* 0.10, $CHCl_3$); R_f 0.48 (1:1 *n*-hexane/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.80-7.10 (m, 52H, arom), 5.27 (d, J = 3.8 Hz, 1H, H-1"), 5.12-4.25 (m, 22H, 7 x Bn-CH_2, NAP-CH_2, 4 x H-1, H-2-E, H-3-E), 3.96-2.98 (m, 46H, 6 x OCH_3, 28 skeleton hydrogen), 2.02, 1.95 (2 x s, 6H, 2 x Ac-CH_3), 1.03 (s, 9H, *t*-Bu-CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 148.7, 147.5, 144.8, 143.8, 143.5, 139.5, 138.3, 137.6, 133.3, 133.2, 132.9, 132.8 (12C, 12 x C_q arom), 135.7-125.6 (52C, arom), 101.1, 100.0, 98.9, 98.2, 98.0 (5C, 5 x C-1), 85.0, 83.4, 82.0, 80.6, 80.4, 79.4, 79.2, 76.8, 75.6, 75.3, 75.2, 73.0, 71.4, 71.1, 69.0, 68.5, 67.7 (20C, skeleton carbons), 75.1, 73.5, 73.1 (9C, 7 x Bn-CH_2, 2 x NAP-CH_2), 70.9, 70.8, 70.7 (3C, C-5, C-5', C-5"), 67.7, 68.5, 68.7, 69.0 (4C, 4 x C-6), 63.2 (1C, C-6-G), 60.9, 60.5, 59.4 (5C, 5 x OCH_3), 55.4 (1C, C-1-OCH_3), 21.2, 20.9 (2C, 2 x Ac-CH_3), 27.1 (3C, 3 x *t*-Bu-CH_3), 19.2 (1C, C_q *t*-Bu) ppm; MS (MALDI-TOF): *m/z* calcd for $C_{116}H_{136}NaO_{28}Si$: 2027.888 $[M+Na]^+$; found: 2027.809.

Data of **24**: $[\alpha]_D^{25}$ +25.8 (*c* 0.12, $CHCl_3$); R_f 0.35 (1:1 *n*-hexane/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.81-7.13 (m, 27H, arom), 5.11 (t, J = 9.1 Hz, 1H, H-3'), 5.07 (d, J = 3.5 Hz, 1H, H-1"), 5.02 (d, J = 11.6 Hz, 1H, Bn-CH_{2a}), 4.85 (dd, J = 9.4 Hz J = 8.2 Hz, 1H, H-2'), 4.77-4.58 (m, 5H, Bn-CH_{2b}, 2 x Bn-CH_2), 4.56-4.52 (m, 2H, H-1, H-1'), 4.48-4.27 (m, 4H, NAP-CH_2, Bn-CH_2), 3.92 (t, J = 9.2 Hz, 1H, H-4'), 3.90-3.85 (m, 2H, H-3, H-4), 3.75 (dd, J = 10.7 Hz, J = 3.2 Hz, 1H, H-6a), 3.69-3.60 (m, 5H, H-5, H-5", H-6b, H-6'a,b), 3.58 (s, 3H, C-3'-OCH_3), 3.44 (dd, J = 10.1 Hz, J = 3.3 Hz, 1H, H-6"a), 3.42-3.37 (m, 3H, H-2, H-3", H-6"b), 3.41, 3.40 (2 x s, 6H, C-4"-OCH_3, C-2"-OCH_3), 3.34 (s, 3H, C-1-OCH_3), 3.23-3.21 (m, 1H, H-5'), 3.17 (t, J = 9.5 Hz, 1H, H-4"), 3.05 (dd, J = 9.8 Hz, J = 3.5 Hz, 1H, H-2"), 2.01, 1.94 (2 x s, 6H, 2 Ac-CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.1, 169.8 (2C, 2 x C_q Ac), 139.6, 138.4, 138.2, 137.8, 136.2, 133.4, 133.0 (7C, 7 x C_q arom), 128.8-125.8 (27C, arom), 100.0 (1C, C-1'), 98.5 (1C, C-1), 97.9 (1C, C-1"), 83.3 (1C, C-3"), 81.9 (1C, C-2"), 80.3 (1C, C-3), 79.4 (1C, C-4"),

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79.3 (1C, C-2), 77.1 (1C, C-4), 75.3 (1C, C-3'), 75.2 (1C, C-5'), 75.0 (1C, C-4'), 74.0, 73.8, 73.4 (5C, 4 x Bn-*C*H$_2$, NAP-*C*H$_2$), 73.0 (1C, C-2'), 71.3 (1C, C-5"), 70.0 (1C, C-5), 68.8 (1C, C-6'), 68.5 (1C, C-6"), 67.9 (1C, C-6), 60.8 (1C, C-3"-OCH$_3$), 60.5 (1C, C-4"-OCH$_3$), 59.4 (1C, C-2"-OCH$_3$), 55.4 (1C, C-1-OCH$_3$), 21.2, 20.9 (2C, 2 x Ac-CH$_3$) ppm; MS (ESI-TOF): *m/z* calcd for $C_{65}H_{76}NaO_{18}$: 1167.4924 [M+Na]$^+$; found: 1167.4885.

Methyl (6-*O*-benzyl-2,3,4-tri-*O*-methyl-α-D-glucopyranosyl)-(1→4)-[2,3-di-*O*-acetyl-6-*O*-(2-naphthyl)methyl-β-D-glucopyranosyl]-(1→4)-(2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-[2,3-di-*O*-methyl-6-*O*-(2-naphthyl)methyl-α-L-idopyranosyl]-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (25). To a solution of trisaccharide acceptor **21a** (38 mg, 0.031 mmol) and disaccharide donor **22**[32] (37 mg, 0.047 mmol, 1.5 equiv.) in dry CH_2Cl_2 (1.2 mL) 4 Å MS (250 mg) were added and the reaction mixture was stirred at room temperature. After 30 min the stirred mixture was cooled to −20 °C under argon. After at this temperature, NIS (16 mg, 0.070 mmol, 1.5 equiv. to the donor) and TfOH (2.0 µL, 0.020 mmol, 0.3 equiv. to the NIS) dissolved in dry THF (28 µL) were added. The temperature was allowed to warm up to +5 °C and the reaction mixture was stirred for 4 h. Than reaction mixture was quenched with Et_3N (150 µL), diluted with CH_2Cl_2 (25 mL), filtered and the mixture was washed with saturated aqueous solution of $Na_2S_2O_3$ (2 x 5 mL), saturated aqueous solution of $NaHCO_3$ (5 mL) and H_2O (2 x 5 mL) until neutral pH. The organic layer was dried on $MgSO_4$ and concentrated. The crude product was purified by silica gel chromatography (55:45 *n*-hexane/EtOAc to 1:1 *n*-hexane/EtOAc) to give **25** (41 mg, 70%) as a colourless syrup. $[\alpha]_D^{25}$ +60.0 (*c* 0.10, $CHCl_3$); R_f 0.45 (1:1 *n*-hexane/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) *δ* 7.77-7.07 (m, 49H, arom), 5.22 (d, *J* = 3.7 Hz, 1H, H-1-F), 5.09-5.05 (m, 2H, H-1-D, H-3-E), 4.97-4.95 (m, 2H, 2 x Bn-C*H*$_{2a}$), 4.89 (d, *J* = 6.9 Hz, 1H, H-1-G), 4.82 (t, *J* = 8.3 Hz, 1H, H-2-E), 4.80-4.25 (m, 18H, H-1-H, H-1-E, 2 x NAP-C*H*$_2$, 2 x Bn-C*H*$_{2b}$, 5 x Bn-C*H*$_2$), 4.05 (dd, *J* = 5.0 Hz, *J* = 9.7 Hz, 1H, H-5-G), 3.95-3.84 (m, 5H, H-3-H, H-4-E, H-4-F, H-4-G, H-4-H), 3.79-3.68 (m, 7H, H-3-F, H-5-F, H-5-H, H-6a-F, H-6a-G, H-6a,b-H), 3.67-3.61 (m, 4H, H-3-G, H-6b-G, H-6a,b-E), 3.60-3.55 (m, 4H, H-5-D, C-3-D-OC*H*$_3$), 3.50-3.44 (m, 10H, H-2-F, H-2-H, H-6b-F, H-6a-D, C-2-G-OC*H*$_3$, C-3-G-OC*H*$_3$), 3.43-3.39 (m, 8H, H-3-D, H-6b-D, C-2-D-OC*H*$_3$, C-3-D-OC*H*$_3$), 3.34 (s, 3H, C-1-H-OC*H*$_3$), 3.20-3.15 (m, 2H, H-4-D, H-5-E), 3.06-3.00 (m, 2H, C-2-D, H-2-G), 2.00, 1.82 (2 x s, 6H, 2 x Ac-C*H*$_3$) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) *δ* 170.1, 169.7 (2C, 2 x Ac-*C*H$_3$), 139.6, 139.5, 138.6, 138.5, 138.3, 138.2, 137.7, 136.2, 135.9, 133.4, 133.9 (13C, 13 x C_q arom), 128.9-125.8 (49C, arom), 100.0 (1C, C-1-E), 99.8 (1C, C-1-G), 98.6 (1C, C-1-F), 98.4 (1C, C-1-H), 97.9 (1C, C-1-D), 84.5 (1C, C-2-G), 83.3 (1C, C-3-D), 82.2 (1C, C-3-G), 81.9 (1C, C-2-D), 80.3 (1C, C-3-H), 80.0 (1C, C-3-F), 79.5 (1C, C-2-H), 79.4 (1C, C-4-D), 79.0 (1C, C-2-F), 76.8 (1C, C-4-F), 76.6 (1C, C-4-H), 76.5 (1C, C-4-G), 75.5 (1C, NAP-*C*H$_2$), 75.3, (1C, C-3-E), 75.2 (1C, C-5-E), 75.0 (1C, NAP-*C*H$_2$), 74.9 (1C, C-4-E), 73.8, 73.7, 73.4, 73.3, 73.1 (7C, 7 x Bn-*C*H$_2$), 72.9 (1C, C-2-E), 72.2 (1C, C-5-G), 71.3 (1C, C-5-D), 71.0 (1C, C-5-F), 70.5 (1C, C-5-H), 68.9 (1C, C-6-G), 68.8 (1C, C-6-E), 68.5 (1C, C-6-D), 68.3 (1C, C-6-H), 67.6 (1C, C-6-F), 60.8 (1C, C-3-D-OC*H*$_3$), 60.5 (2C, C-3-G-OC*H*$_3$, C-4-D-OC*H*$_3$), 60.3 (1C, C-2-G-OC*H*$_3$), 59.3 (1C, C-2-D-OC*H*$_3$), 55.4 (1C, C-1-H-OC*H*$_3$), 21.1, 20.8 (2C, 2 x Ac-*C*H$_3$) ppm; MS (MALDI-TOF): *m/z* calcd for $C_{111}H_{126}NaO_{28}$: 1931.190 [M+Na]$^+$; found: 1931.124.

Methyl (6-*O*-benzyl-2,3,4-tri-*O*-methyl-α-D-glucopyranosyl)-(1→4)-[6-*O*-(2-naphthyl)methyl-β-D-glucopyranosyl]-(1→4)-(2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-[2,3-di-*O*-methyl-6-*O*-(2-naphthyl)methyl-α-L-idopyranosyl]-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (26). Compound **25** (33 mg, 0.017 mmol) was dissolved in MeOH (1.0 mL) and NaOMe was added (5 mg, 0.092 mmol, pH ≈ 10) and the reaction mixture was stirred at room temperature for 24 h. Than the reaction mixture was neutralized by Amberlite IR-120 (H^+) ion-exchange resin, filtrated, washed with MeOH and concentrated. The crude product was purified by column chromatography (65:35 = *n*-hexane/acetone) to give **26** (25 mg, 78 %) as a colourless syrup. $[\alpha]_D^{25}$ +55.0 (*c* 0.06, $CHCl_3$); R_f 0.29 (7:3 *n*-hexane/acetone); ^{1}H NMR ($CDCl_3$, 500 MHz) *δ* 7.77-7.13 (m, 49H, arom), 5.22 (d, *J* = 3.7 Hz, 1H, H-1-F), 5.03 (d, *J* = 3.5 Hz, 1H, H-1-D), 4.96 (d, *J* = 5.9 Hz, 1H, H-1-G), 4.95-4.28 (m, 20H, H-1-H, H-1-E, 2 x NAP-C*H*$_2$, 7 x Bn-C*H*$_2$), 4.00-3.96 (m, 2H, H-4-F, H-5-G), 3.90-3.82 (m, 3H, H-3-F, H-4-G, H-6a-F), 3.79-3.65 (m, 9H, H-3-H, H-3-G, H-4-H, H-5-H, H-5-F, H-6a,b-H, H-6a,b-G), 3.61 (s, 3H, C-3-D-OC*H*$_3$), 3.59-3.57 (m, 1H, H-5-D), 3.56 (s, 3H, C-2-D-OC*H*$_3$), 3.54-3.50 (m, 2H, H-3-E-O*H*, H-6a-E), 3.48 (s, 4H, H-2-F, C-3-G-OC*H*$_3$), 3.47-3.40 (m, 13H, H-2-H, H-3-D, H-3-E, H-4-E, H-6a-D, H-6b-F, H-6b-E, C-2-G-OC*H*$_3$, C-4-D-OC*H*$_3$), 3.36 (s, 3H, C-1-H-OC*H*$_3$), 3.33-3.29 (m, 2H, H-2-E, H-6b-D), 3.22 (s, 1H, C-2-E-O*H*), 3.19-3.13 (m, 3H, H-2-D, H-4-D, H-5-E), 3.05-3.02 (m, 1H, H-2-G) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) *δ* 139.5, 138.6, 138.4, 138.1, 137.7, 136.4, 136.0, 133.4, 133.0, 132.9 (13C, 13 x C_q arom), 128.6-125.8 (49C, arom), 103.1 (1C, C-1-E), 100.6 (1C, C-1-D), 100.0 (1C, C-1-G), 98.5 (1C, C-1-H), 98.3 (1C, C-1-F), 84.7 (1C, C-2-G), 84.1 (1C, C-3-D), 82.9 (1C, C-2-D), 82.5 (1C, C-3-G), 82.0 (1C, C-4-E), 80.6 (1C, C-3-F), 80.3 (1C, C-3-H), 79.5 (2C, C-2-H, C-4-D), 79.4 (1C, C-2-F), 76.7 (2C, C-4-F, C-4-H), 76.3 (1C, C-4-G), 76.1 (1C, C-3-E), 75.3, 74.8 (2C, 2 x NAP-*C*H$_2$), 74.7, (1C, C-5-E), 74.0 (1C, C-2-E), 73.7, 73.6, 73.4, 73.3, 72.9 (7C, 7 x Bn-*C*H$_2$), 72.0 (1C, C-5-G), 71.4 (1C, C-5-D), 70.8 (1C, C-5-F), 70.5 (1C, C-5-H), 69.3 (1C, C-6-G), 69.0 (1C, C-6-E), 68.5 (2C, C-6-D, C-6-H), 68.3 (1C, C-6-F), 60.9 (1C, C-3-D-OC*H*$_3$), 60.6 (1C, C-4-D-OC*H*$_3$), 60.3 (3C, C-2-G-OC*H*$_3$, C-3-G-OC*H*$_3$, C-2-D-OC*H*$_3$), 55.4 (1C, C-1-H-OC*H*$_3$) ppm; MS (MALDI-TOF): *m/z* calcd for $C_{107}H_{122}NaO_{26}$: 1845.812 [M+Na]$^+$; found: 1845.714.

Methyl (6-*O*-benzyl-2,3,4-tri-*O*-methyl-α-D-glucopyranosyl)-(1→4)-[2,3-di-*O*-methyl-6-*O*-(2-naphthyl)methyl-β-D-glucopyranosyl]-(1→4)-(2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-[2,3-di-*O*-methyl-6-*O*-(2-naphthyl)methyl-α-L-idopyranosyl]-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (27). To a solution of **26** (21 mg, 0.0115 mmol) in dry DMF (250 µL) was added NaH (60%, 10 mg, 0.250 mmol) at 0 °C. After stirring for 30 min at 0 °C, MeI (20 µL, 0.321 mmol) was added and stirred for 24 h at room temperature. When complete conversion of the starting material into a main spot had been observed by TLC analysis, CH_3OH (500 µL) was added. The reaction mixture was stirred for 5 min and the solvents were evaporated. The residue was dissolved in CH_2Cl_2 (25 mL), and washed with H_2O (2 x 5.0 mL), the organic layer was filtered, dried and evaporated. The crude product was purified by silica gel chromatography (6:4 = *n*-hexane/acetone) to give **27** (16 mg, 80%) as a colourless syrup. $[\alpha]_D^{25}$ +45.7 (*c* 0.07, $CHCl_3$); R_f 0.58 (6:4 *n*-hexane/acetone); ^{1}H NMR ($CDCl_3$, 500 MHz) *δ* 7.78-7.08 (m, 49H, arom), 5.58 (d, *J* = 3.7 Hz, 1H), 5.23 (d, *J* = 3.6 Hz, 1H), 5.02-4.06 (m, 21H, 3 x H-1, 7 x Bn-C*H*$_2$, 2 x NAP-C*H*$_2$), 4.06 (dd, *J* = 4.7 Hz, *J* = 9.6 Hz, 1H), 3.98 (t, *J* = 9.4 Hz, 1H), 3.89-3.62 (m, 17H), 3.62-3.32 (m, 4H), 3.60, 3.54, 3.48, 3.45, 3.38, 3.36, 3.33 (7 x s, 24H, 8 x OC*H*$_3$), 3.29-3.21 (m, 4H), 3.15 (dd, *J* = 3.7 Hz, *J* = 9.8 Hz, 1H), 3.04-3.00 (m, 1H), 2.94-2.91 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) *δ* 139.7, 139.4, 138.6, 138.4, 138.2, 138.0, 136.5, 135.9, 133.4, 133.0, 132.9 (13C, 13 x C_q arom), 128.7-125.7 (49C, arom), 102.9, 100.0, 98.5, 96.3 (5C, 5 x C-1), 86.7, 84.7, 84.6, 83.6, 82.4, 81.9, 80.4, 79.9, 79.5, 79.4, 79.0, 77.0, 76.7, 76.2, 74.8, 72.4, 72.2, 71.4, 70.9, 70.5 (20C skeleton carbons), 75.6, 74.9, 73.8, 73.5, 73.4, 73.3, 73.2 (9C, 2 x NAP-*C*H$_2$, 7 x Bn-CH$_2$), 69.4, 68.3, 68.2, 67.8 (5C, 5 x C-6), 60.9, 60.5, 60.3, 59.8, 59.6 (7C, 7 x OCH$_3$), 55.4 (1C, C-1-H-OCH$_3$) ppm; MS (MALDI-TOF): *m/z* calcd for $C_{109}H_{126}NaO_{26}$: 1873.843 [M+Na]$^+$; found: 1873.749.

Methyl (6-*O*-benzyl-2,3,4-tri-*O*-methyl-α-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-methyl-β-D-glucopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-methyl-α-L-idopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (28). To a vigorously stirred solution of **27** (14 mg, 0.007 mmol) in CH_2Cl_2 (2.0 mL) and H_2O (250 µL), DDQ (5.0 mg, 0.021 mmol) was added. After 30 min the mixture was diluted with CH_2Cl_2 (20 mL) and extracted with saturated aqueous $NaHCO_3$ (2 x 5 mL) and H_2O (2 x 5 mL), dried and concentrated. The crude

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product was purified by silica gel chromatography (6:4 *n*-hexane/acetone) to give **28** (8 mg, 71%) as a colourless syrup. $[\alpha]_D^{25}$ +61.4 (*c* 0.08, CH_2Cl_2); R_f 0.52 (6:4 *n*-hexane/acetone); ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.39-7.18 (m, 35H, arom), 5.52 (d, *J* = 3.7 Hz, 1H), 5.15 (d, *J* = 3.4 Hz, 1H), 4.93-4.50 (m, 16H, 7 x Bn-CH_2, 2 x H-1), 4.28 (d, *J* = 7.8 Hz, 1H), 3.93-3.63 (m, 15H), 3.62-3.15 (m, 12H), 3.61, 3.58, 3.54, 3.49, 3.44, 3.42, 3.39, 3.35 (8 x s, 24H, 8 x OCH_3), 3.03-2.94 (m, 3H), 2.36, 2.08 (2 x s, 2H, 2 x OH) ppm; ^{13}C NMR ($CDCl_3$, 90 MHz) δ 138.7, 138.4, 138.0, 137.8, 137.7, 137.5, 137.4 (7C, 7 x C_q arom), 128.2-127.3 (35C, arom), 102.3, 98.6, 97.8, 97.0, 96.3 (5C, 5 x C-1), 86.1, 84.4, 83.1, 82.6, 81.5, 81.4, 80.1, 79.6, 79.2, 78.4, 75.2, 74.1, 73.9, 71.2, 70.8, 70.6, 70.1 (20C, skeleton carbons), 75.5, 74.9, 73.2, 73.1, 72.7 (7C, 7 x Bn-*C*H_2), 68.1, 68.0, 67.4, 61.6 (5C, 5 x C-6), 60.4, 60.1, 60.0, 59.6, 59.4, 59.3, 59.2 (7C, 7 x O*C*H_3), 54.9 (C-1-H-O*C*H_3) ppm; MS (ESI-TOF): *m/z* calcd for $C_{87}H_{110}NaO_{26}$: 1593.7178 $[M+Na]^+$; found: 1593.7163.

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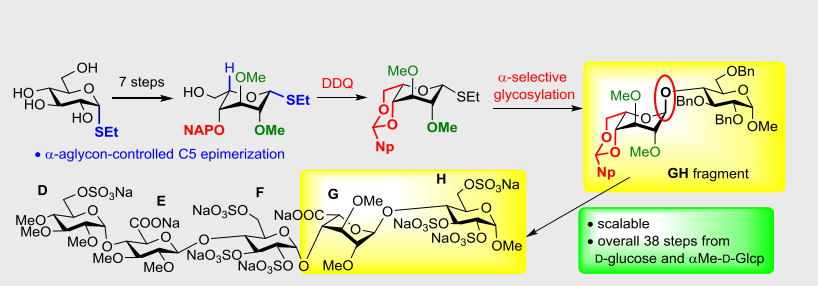
Layout 2:

FULL PAPER



The α-L-iduronic acid is a key component of heparin-related anticoagulants like idraparinux. Hitherto, L-idose or iduronic acid donors with a C2 participating group, obtained via lengthy procedures, have been exclusively applied for the construction of the α-idosidic linkage. Our new route to idraparinux is based on short and straightforward synthesis of a 4,6-cyclic-acetal-protected L-idosyl thioglycoside bearing a C2-nonparticipating group, which can be used directly as an α-selective glycosyl donor building block. The assembly of idraparinux was achieved by an **F**+**GH** and **DE**+**FGH** coupling sequence with full stereoselectivity in each glycosylation step.

Fruzsina Demeter, Fanni Veres, Mihály Herczeg and Anikó Borbás**

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Short synthesis of idraparinux by applying a 2-*O*-methyl-4,6-*O*-arylmethylene thioidoside as a 1,2-trans α-selective glycosyl donor

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