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# Efficient synthesis of Idraparinux, the anticoagulant pentasaccharide

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ABSTRACT

An efficient [DEF+GH] route was developed to the synthesis of Idraparinux, which is a fully O-sulfated, O-methylated mimic of the unique Antithrombin III binding domain of heparin.



Heparin, a sulfated polysaccharide belonging to the family of glycosaminoglycans, has been shown to interact with a number of biologically important proteins, thereby playing an essential role in the regulation of various physiological processes.[1] Nevertheless, the most well known is its anticoagulant activity; heparin has been used clinically as an anticoagulant since 1935.[2] Heparin binds with high affinity to the protease inhibitor antithrombin III (AT III), thereby increasing the inhibitory potency of AT III relative to the coagulation factors Xa and thrombin (IIa). However, due to its multiple biological functions, clinical use of heparin also leads to undesirable side effects, such as bleeding complications or heparin-induced thrombocytopenia (HIT). In addition, because of its short half-life of approximately one hour in human body, heparin must be given frequently or as a continuous infusion. Thanks to the legendary works, especially those relatively recently from van Boeckel and Petitou[3] the SAR of the anticoagulant activity of heparin has been clearly deciphered. Remarkably, Fondaparinux (**B** in Fig. 1), a structural analog of the unique antithrombin-binding pentasaccharide domain of heparin (**A** in Fig. 1),[4] was developed as a new antithrombotic drug under the name 'Arixtra' in the USA and Europe in 2001. Compared to unfractionated heparin and low molecular-weight heparin, Fondaparinux has higher anti-Xa activity and longer half-life. Continuous research leads to more potent derivatives; Idraparinux (**1** in Fig. 1), a fully O-sulfated, O-methylated analog, is not only much easier to synthesize than Fondaparinux[5] but also displays higher anti-Xa activity and a longer duration of action.[6] Thus, Idraparinux had been developed into phase III clinical trial for the prevention of thromboembolic events in patients with atrial fibrillation and for the prevention and treatment of venous thromboembolic events (VTE).[7] Herein we report an efficient synthetic route to Idraparinux (**1**).

The retrosynthetic analysis was shown in Figure 2. The glycosidic bond disconnection between the F and G ring was made in the target molecule to provide the trisaccharide donor **3** and disaccharide **4**, of which are close in terms of synthetic complexity. The carboxylic acid function was planned to be elaborated at the disaccharide level to bypass the glycosidic coupling with the usually inactive uronate derivatives.

The preparation of the monosaccharide building blocks **6**, **8** and **10** employed routine transformations starting from D-glucose or the ready available methyl α-D-glucopyranoside as outlined in Scheme 1.

The L-idopyranose building block **7** was synthesized through the epimerization of the 5-OH of a D-glucofuranose derivative via intramolecular epoxide formation (Scheme 2).[13] Thus, methylation of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**14**) followed by selective removal of the 5,6-*O*-isopropylidene group gave vicinal diol **15**. Selective protection of the primary hydroxyl group with the bulky pivaloyl group, followed by mesylation of the remaining secondary hydroxyl group and treatment with *t*-BuOK in *t*-BuOH, furnished the epoxide **17**[14] in high yield (86% for 5 steps). Acidic treatment of epoxide **17** with 0.1 M $H_2SO_4$ at 60 °C resulted in hydrolysis of the 1,2-*O*-isopropylidene group and opening of the 5,6-epoxide, giving 3-*O*-methyl-L-idopyranose, which was directly acetylated to provide a mixture of the anomeric acetates **18**. Treatment of **18** with 4-methoxyphenol and TMSOTf afforded the α-glycoside **19**, which was subjected to removal of the acetyl groups; the resulting 2,4,6-triol was then treated with benzaldehyde and trifluoroacetic acid to provide the 4,6-*O*-benzylidene derivative

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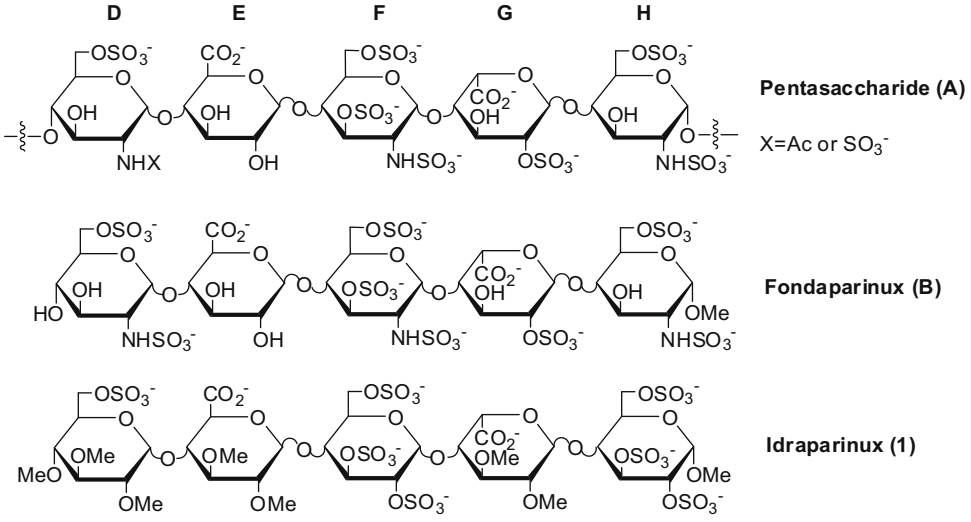



**Fig. 1.** The anticoagulant pentasaccharides Fondaparinux and Idraparinux (**1**).

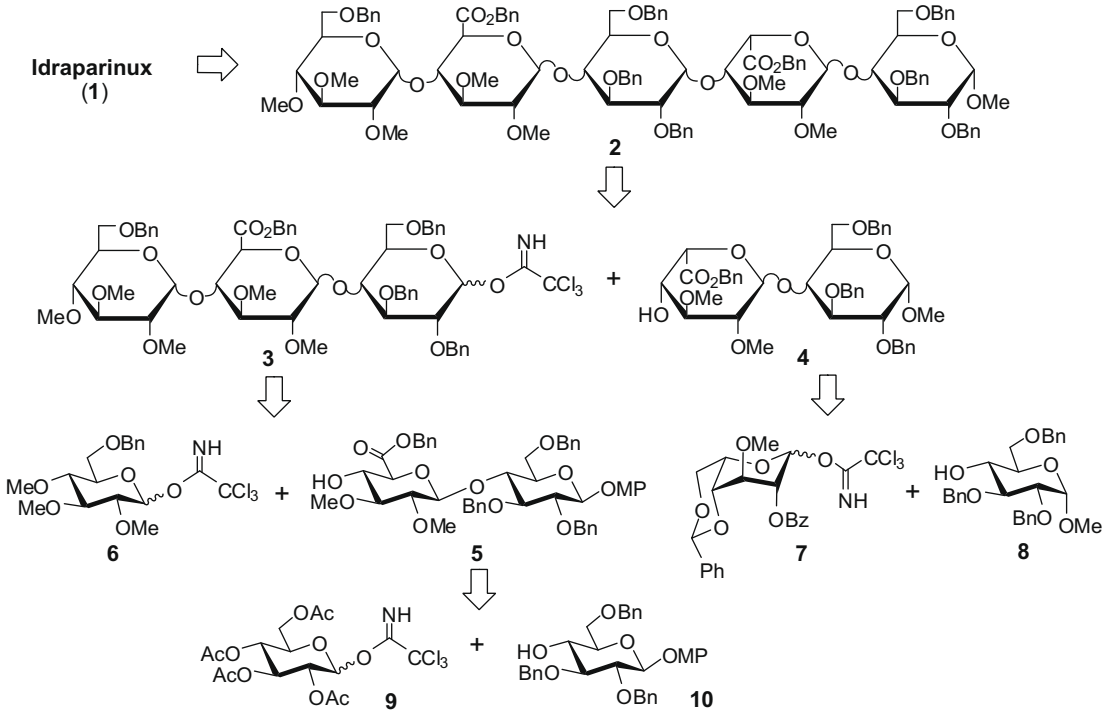
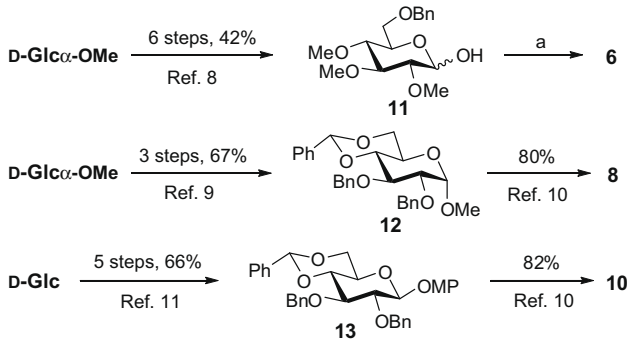


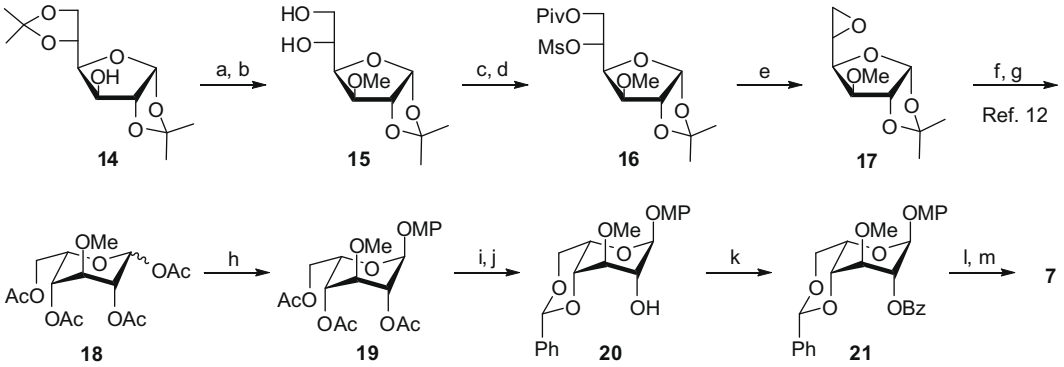

**Fig. 2.** The retrosynthetic analysis of Idraparinux (**1**).



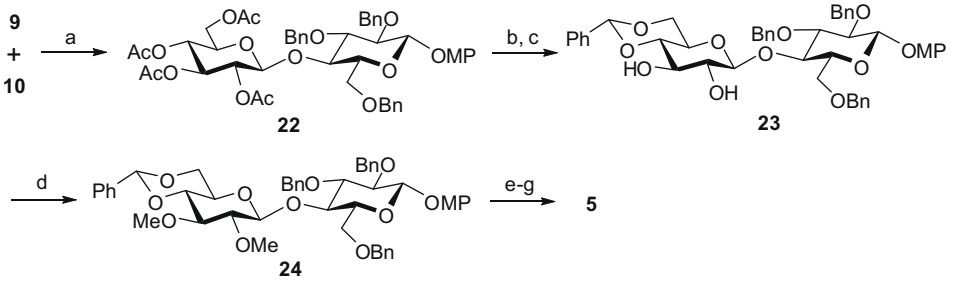

**Scheme 1.** Preparation of the monosaccharide building blocks **6**, **8**, and **10**. Reagents and conditions: (a) $CCl_3CN$, DBU, $CH_2Cl_2$, 0 °C to rt, 88%.[8–11]

**20**. The remaining 2-hydroxyl group was benzoylated to give **21**, which was subjected to the oxidative removal of the 4-methoxyphenyl group; the resulting lactol was treated with $CCl_3CN$ and DBU to provide the desired L-idopyranosyl donor **7**.

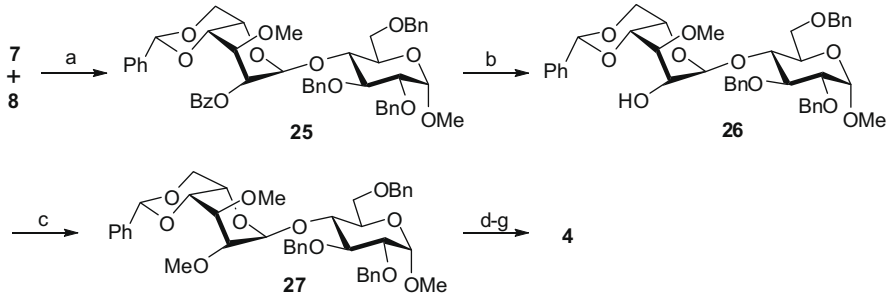
Glycosylation of the 4-OH-glucopyranoside derivative **10** with glucopyranosyl trichloroacetimidate **9**[15] in the presence of trimethylsilyl trifluoromethylsulfonate and 4 Å molecular sieves in dichloromethane at −20 °C gave the desired β-(1→4)-disaccharide **22** in 92% yield (Scheme 3). Saponification of **22** followed by 4′,6′-*O*-benzylidene formation afforded disaccharide **23**. Methylation of the remaining 2- and 3-hydroxyl groups on **23** afforded compound **24**. The 4,6-*O*-benzylidene group was hydrolyzed with 75% AcOH at 75 °C, the resulting diol was subjected to TEMPO mediated selective oxidation of the primary alcohol to the




**Scheme 2.** Preparation of the L-idopyranose building block **7**. Reagents and conditions: (a) $Me_2SO_4$, KOH, DMSO, rt; (b) 60% aq AcOH, rt; (c) PivCl, pyridine, 0 °C; (d) MsCl, pyridine, 0 °C to rt; (e) *t*-BuOK, *t*-BuOH, $CH_2Cl_2$, 0 °C to rt, 86% (5 steps); (f) 0.1 M aq $H_2SO_4$, 60 °C; (g) $Ac_2O$, DMAP, pyridine, 0 °C to rt, 76% (2 steps); (h) *p*-MeOPhOH, TMSOTf, MS 4 Å, $CH_2Cl_2$, 0 °C to rt, 89%; (i) NaOMe, MeOH, rt; (j) PhCHO, TFA, rt, 76% (2 steps); (k) BzCl, $Et_3N$, DMAP, $CH_2Cl_2$, 0 °C to rt, 100%; (l) CAN, $CH_3CN$, toluene, $H_2O$, rt, 91%; (m) $CCl_3CN$, DBU, $CH_2Cl_2$, 0 °C to rt, 100%.[12]




**Scheme 3.** Preparation of the disaccharide **5**. Reagents and conditions: (a) TMSOTf, 4 Å MS, $CH_2Cl_2$, −20 °C to rt, 92%; (b) NaOMe, MeOH, rt; (c) $PhCH(OMe)_2$, *p*-TsOH.$H_2O$, DMF, 50 °C, 95% (2 steps); (d) $Me_2SO_4$, NaH, DMF, 0 °C to rt, 100%; (e) 75% aq. AcOH, 75 °C; (f) TEMPO, KBr, $NaHCO_3$, TBAB, Aliquate 336, $Ca(ClO)_2$, $CH_2Cl_2$, 0 °C; (g) BnBr, $KHCO_3$, DMF, rt, 75% (3 steps).

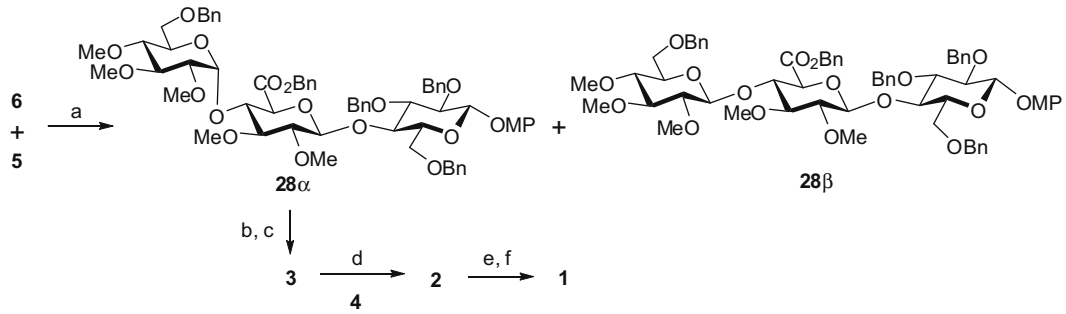



**Scheme 4.** Preparation of the disaccharide **4**. Reagents and conditions: (a) TMSOTf, 4 Å MS, $CH_2Cl_2$, −20 °C to rt, 99%; (b) NaOMe, MeOH, THF, rt, 94%; (c) NaH, $Me_2SO_4$, THF, 0 °C to rt, 97%; (d) *p*-TsOH.$H_2O$, MeOH, $CH_2Cl_2$, rt; (e) TEMPO, KBr, $NaHCO_3$, TBAB, Aliquate 336, $Ca(ClO)_2$, $CH_2Cl_2$, 0 °C; (f) $NaClO_2$, $NaH_2PO_4$, *t*-BuOH, rt; (g) BnBr, $KHCO_3$, DMF, rt, 66% (4 steps).

carboxylic acid,[16] which was then benzylated to yield the benzyl ester **5** in good yield (75% for 3 steps). During these transformations, the sugar moiety ring F could be regarded as a stable anomeric protecting group of ring E.

The synthesis of the G-H unit was started with the glycosylation of the 4-OH-glucopyranoside derivative **8** with the L-idopyranosyl trichloroacetimidate **7** (Scheme 4). The α-(1→4)-linked disaccharide **25** was yielded in nearly quantitative yield and anomeric selectivity. In this case, both the neighboring participation of the 2-*O*-benzoyl group and the anomeric effect of the $^1C_4$ conformation which is locked by the 4,6-*O*-benzylidene group in the L-idopyranosyl donor **7** contributed to the high α-selectivity.[17] The 2′-*O*-benzoyl group in disaccharide **25** was removed and the resulting hydroxyl group was methylated to afford compound **27**. After removal of the 4′,6′-*O*-benzylidene group in **27**, the resulting primary 6′-hydroxyl group was selectively oxidized first to the aldehyde then to the carboxylic acid, which was then esterified to afford the disaccharide benzyl ester **4**.[17b]

The final elaboration of the pentasaccharide **1** was illustrated in Scheme 5. Coupling of the glucopyranosyl trichloroacetimidate **6** with disaccharide acceptor **5** in the presence of trimethylsilyl trifluoromethylsulfonate and powdered 4 Å molecular sieves at room temperature in diethyl ether afforded the desired α-coupled trisaccharide **28α** in a yield of 66%, together with 15% of the separable β-coupled product **28β**. The anomeric 4-methoxyphenyl group in trisaccharide **28α** was removed with CAN, and the resulting lactol was readily converted into the trisaccharide trichloroacetimidate **3**. Coupling of donor **3** with the disaccharide acceptor **4** in the presence of trimethylsilyl trifluoromethylsulfonate and powdered 4 Å molecular sieves at room temperature in




**Scheme 5.** Final elaboration of the pentasaccharide **1**. Reagents and conditions: (a) TMSOTf, $Et_2O$, 4 Å MS, rt, 66% (**28α**), 15% (**28β**); (b) CAN, $CH_3CN$, toluene, $H_2O$, rt, 72%; (c) $CCl_3CN$, DBU, $CH_2Cl_2$, rt, 98%; (d) TMSOTf, 4 Å MS, $CH_2Cl_2$, rt, 51% (73% based on recovery of **4**); (e) Pd/C (10%), $H_2$, *t*-BuOH, $H_2O$, rt; (f) $SO_3$·$Et_3N$, DMF, 50 °C, 93% (2 steps).

dichloromethane afforded the fully protected pentasaccharide **2** in 51% yield (73% based on recovery of **4**). Finally, pentasaccharide **2** was subject to hydrogenolysis of the benzyl protecting groups. The highly polar product without purification was *O*-sulfated directly with triethylamine-sulfur trioxide complex to afford the sulfated pentasaccharide **1**[6a] in an excellent yield of 93% (for two steps).

Summarizing, the potent anti-thromboembolic pentasaccharide Idraparinux (**1**) was synthesized in total 51 steps and in 4% overall yield from D-glucose and methyl α-D-glucopyranoside.[18] The synthetic route is convergent with a linear sequence of 27 steps, and the transformations are scalable. The 4-methoxyphenol glycoside intermediates are easy to be purified by crystallization.

## Acknowledgements

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18. Selected data for the key compounds. Compound **21**: $[\alpha]_D^{23}$ −54.7 (*c* 0.9, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$) δ 3.65 (s, 3H), 3.74 (br s, 1H), 3.77 (s, 3H), 4.08–4.17 (m, 3H), 4.34 (d, *J* = 12.6 Hz, 1H), 5.40 (br s, 1H), 5.63 (s, 1H), 5.71 (s, 1H), 6.82 (d, *J* = 9.0 Hz, 1H), 7.08 (d, *J* = 9.0 Hz, 1H), 7.22–7.39 (m, 6H), 7.48–7.58 (m, 3H), 8.01 (d, *J* = 6.9 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 55.6, 58.2, 60.3, 65.4, 69.7, 72.8, 76.5, 97.2, 100.9, 114.5, 117.7, 126.3, 128.1, 128.2, 128.9, 129.4, 130.1, 133.1, 137.8, 150.5, 154.9, 165.6; MALDI–MS *m/z* 515.7 $[M+Na]^+$; MALDI-HRMS calcd for $C_{28}H_{28}O_8Na$ $[M+Na]^+$ 515.1676, found 515.1668. Compound **22**: $[\alpha]_D^{23}$ −16.2 (*c* 1.0, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$) δ 1.95 (s, 3H), 1.97 (s, 3H), 1.99 (s, 3H), 2.00 (s, 3H), 3.29–3.38 (m, 1H), 3.43–3.48 (m, 1H), 3.60–3.72 (m, 2H), 3.73–3.82 (m, 2H), 3.77 (s, 3H), 3.88 (d, *J* = 12.9 Hz, 1H), 3.95–4.05 (m, 1H), 4.14 (dd, *J* = 12.9, 3.9 Hz, 1H), 4.50 (d, *J* = 12.3 Hz, 1H), 4.65–4.76 (m, 4H), 4.85 (d, *J* = 7.2 Hz, 1H), 4.90–5.08 (m, 5H), 6.81 (d, *J* = 9.0 Hz, 1H), 7.01 (d, *J* = 9.0 Hz, 1H), 7.20–7.43 (m, 15H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 20.46, 20.50, 20.52, 20.6, 55.5, 61.5, 67.7, 67.9, 71.6, 71.9, 73.0, 73.6, 74.7, 74.9, 75.0, 81.4, 82.5, 100.0, 102.7, 114.4, 118.4, 127.2, 127.6, 127.9, 128.0, 128.2, 128.5, 137.8, 138.1, 138.9, 151.4, 155.3, 169.0, 169.3, 170.1, 170.5; MALDI-MS *m/z* 909.5 $[M+Na]^+$; MALDI–HRMS calcd for $C_{48}H_{54}O_{16}Na$, $[M+Na]^+$ 909.3304, found 909.3298. Compound **5**: $[\alpha]_D^{23}$ −16.4 (*c* 1.2, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$) δ 2.81 (d, *J* = 2.4 Hz, 1H), 2.96 (t, *J* = 9.0 Hz, 1H), 3.02 (d, *J* = 8.7 Hz, 1H), 3.49 (s, 3H), 3.53–3.61 (m, 2H), 3.62 (s, 3H), 3.65–3.76 (m, 3H), 3.78 (s, 3H), 3.83–3.90 (m, 2H), 3.97–4.06 (m, 1H), 4.50 (d, *J* = 7.2 Hz, 1H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.76 (d, *J* = 11.4 Hz, 1H), 4.77 (d, *J* = 10.5 Hz, 1H), 4.87 (d, *J* = 7.5 Hz, 1H), 4.98 (d, *J* = 10.5 Hz, 1H), 5.09 (d, *J* = 11.4 Hz, 1H), 6.80 (d, *J* = 9.0 Hz, 1H), 7.02 (d, *J* = 9.0 Hz, 1H), 7.20–7.35 (m, 20H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 55.6, 60.5, 60.9, 67.0, 68.2, 71.5, 73.3, 74.1, 74.9, 75.0, 75.0, 77.2, 81.5, 82.6, 83.4, 85.1, 102.7, 102.7, 114.5, 118.4, 127.1, 127.6, 127.8, 128.0, 128.1, 128.2, 128.3, 128.4, 135.0, 138.1, 138.3, 139.0, 151.5, 155.2, 168.8; ESI-MS *m/z* 873.3 $[M+Na]^+$; MALDI-HRMS calcd for $C_{49}H_{54}O_{13}Na$, $[M+Na]^+$ 873.3457, found 873.3439. Compound **25**: $[\alpha]_D^{23}$ 5.2 (*c* 1.1, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$) δ 3.08 (d, *J* = 12.9 Hz, 1H), 3.37 (s, 3H), 3.54 (s, 3H), 3.55–3.95 (m, 9H), 4.02 (br s, 1H), 4.49 (ABq, 2H), 4.60–4.82 (m, 4H), 5.08–5.15 (m, 3H), 5.35 (s, 1H), 7.10–7.55 (m, 23H), 7.93 (d, *J* = 7.2 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 55.1, 58.1, 59.2, 66.4, 66.4, 68.2, 69.3, 70.1, 72.2, 73.2, 73.3, 73.3, 75.2, 76.7, 80.0, 80.1, 97.1, 97.9, 100.7, 126.3, 127.27, 127.32, 127.4, 127.80, 127.84, 128.0, 128.08, 128.12, 128.14, 128.2, 128.4, 128.7, 129.5, 129.96, 133.00, 137.7, 138.0, 138.2, 139.1, 165.6; ESI-MS *m/z* 855.4 $[M+Na]^+$; MALDI-HRMS calcd for $C_{49}H_{52}O_{12}Na$, $[M+Na]^+$ 855.3351, found 855.3345. Compound **27**: $[\alpha]_D^{23}$ −6.5 (*c* 0.9, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$) δ 3.09 (d, *J* = 13.2 Hz, 1H), 3.17–3.22 (m, 1H), 3.38 (s, 3H), 3.38–3.43 (m, 1H), 3.43 (s, 3H), 3.50 (s, 3H), 3.59 (dd, *J* = 9.3, 3.3 Hz, 1H), 3.68 (br s, 2H), 3.60–3.73 (m, 2H), 3.82–3.87 (m, 2H), 3.93 (t, *J* = 9.3 Hz, 1H), 4.50–4.65 (m, 4H), 4.67 (br s, 1H), 4.78 (d, *J* = 11.7 Hz, 1H), 4.81 (d, *J* = 5.4 Hz, 1H), 5.05 (d, *J* = 8.1 Hz, 1H), 5.28 (s, 1H), 7.22–7.48 (m, 20H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 55.0, 58.3, 59.6, 61.8, 68.2, 68.4, 70.3, 72.7, 73.1, 73.2, 75.4, 77.8, 80.0, 80.3, 82.1, 97.8, 99.6, 100.1, 126.0, 127.3, 127.3, 127.4, 127.7, 127.8, 128.0, 128.11, 128.13, 128.2, 128.5, 137.6, 137.86, 137.91, 138.9; ESI-MS *m/z* 765.3 $[M+Na]^+$; MALDI-HRMS calcd for $C_{43}H_{50}O_{11}Na$, $[M+Na]^+$ 765.3245, found 765.3257. Compound **28α**: $[\alpha]_D^{23}$ 41.4 (*c* 1.0, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$) δ 2.82 (t, *J* = 8.1 Hz, 1H), 2.96–3.04 (m, 2H), 3.13–3.20 (m, 1H), 3.25–3.40 (m, 4H), 3.45 (s, 3H), 3.49 (s, 3H), 3.52 (s, 3H), 3.55 (s, 3H), 3.58 (s, 3H), 3.61 (s, 3H), 3.60–3.74 (m, 6H), 3.77 (s, 3H), 3.75–3.90 (m, 4H), 3.95–4.08 (m, 2H), 4.44–5.03 (m, 12H), 5.53 (d, *J* = 3.6 Hz, 1H), 6.79 (d, *J* = 9.0 Hz, 2H), 7.01 (d, *J* = 9.0 Hz, 2H), 7.20–7.40 (m, 20H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 55.6, 59.3, 60.0, 60.3, 60.5, 60.6, 67.4, 67.85, 67.89, 70.7, 73.3, 73.4, 74.0, 74.3, 75.1, 75.2, 75.4, 77.5, 78.9, 81.5, 81.6, 82.7, 83.2, 83.9, 85.8, 96.3, 102.7, 102.8, 114.5, 118.5, 127.2, 127.5, 127.6, 127.8, 128.07, 128.11, 128.2, 128.3, 128.4, 128.5, 134.9, 138.1, 138.2, 138.3, 138.8, 151.5, 155.2, 168.2; MALDI-MS *m/z* 1167.1 $[M+Na]^+$; MALDI–HRMS calcd for $C_{65}H_{76}O_{18}Na$, $[M+Na]^+$ 1167.4924, found 1167.4955. Compound **28β**: $[\alpha]_D^{23}$ −6.0 (*c* 1.1, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$) δ 2.82 (t,

*J* = 8.4 Hz, 1H), 2.99 (t, *J* = 8.4 Hz, 1H), 3.02 (t, *J* = 8.4 Hz, 1H), 3.06–3.22 (m, 3H), 3.35 (s, 3H), 3.47 (s, 3H), 3.50 (s, 3H), 3.53 (s, 3H), 3.59 (s, 3H), 3.61–3.74 (m, 4H), 3.75 (s, 3H), 3.85–4.05 (m, 3H), 4.22 (d, *J* = 7.8 Hz, 1H), 4.47–5.15 (m, 10H), 4.87(d, *J* = 7.2 Hz, 1H), 6.79 (d, *J* = 8.7 Hz, 2H), 7.02 (d, *J* = 8.7 Hz, 2H), 7.15–7.40 (m, 20H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 55.5, 60.2, 60.5, 60.56, 60.59, 67.2, 68.0, 68.7, 73.1, 73.3, 74.55, 74.57, 75.0, 75.05, 75.12, 77.4, 78.4, 79.1, 81.4, 82.7, 83.0, 83.9, 84.0, 86.3, 102.6, 102.77, 102.83, 114.4, 118.3, 127.1, 127.3, 127.4, 127.5, 127.9, 128.0, 128.15, 128.24, 128.4, 128.5, 134.9, 138.1, 138.3, 138.4, 138.9, 151.4, 155.1, 167.7; ESI-MS *m/z* $[M+Na]^+$; MALDI-HRMS calcd for $C_{65}H_{76}O_{18}Na$, $[M+Na]^+$ 1167.4924, found 1167.4881. Compound **2**: $[\alpha]_D^{23}$ 47.4 (*c* 1.0, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 2.88 (t, *J* = 8.4 Hz, 1H), 2.96 (t, *J* = 7.5 Hz, 1H), 3.17 (t, *J* = 9.7 Hz, 1H), 3.12–3.21 (m, 1H), 3.27 (s, 3H), 3.35–3.52 (m, 6H), 3.37 (s, 3H), 3.44 (s, 6H), 3.47 (s, 3H), 3.52 (s, 3H), 3.55 (s, 6H), 3.69–3.75 (m, 9H), 3.75–3.90 (m, 6H), 3.98 (t, *J* = 9.3 Hz, 1H), 4.30 (d, *J* = 7.5 Hz, 1H), 4.43–4.62 (m, 7H), 4.62–4.69 (m, 5H), 4.73–4.83 (m, 3H), 4.83–5.04 (m, 5H), 5.17 (d, *J* = 3.3 Hz, 1H), 5.24 (d, *J* = 6.9 Hz, 1H), 5.52 (d, *J* = 3.3 Hz, 1H), 7.20–7.37 (m, 45H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 55.3, 59.2, 60.0, 60.2, 60.3, 60.6, 66.6, 67.3, 67.5, 67.9, 68.1, 70.3, 70.8, 71.0, 72.9, 73.3, 73.4, 73.6, 74.1, 74.2, 75.2, 75.4, 77.2, 77.5, 78.8, 78.9, 79.3, 79.5, 80.1, 80.7, 81.6, 83.2, 83.5, 83.8, 85.7, 96.3, 98.3, 98.7, 100.2, 103.0, 127.1, 127.2, 127.4, 127.5, 127.7, 127.8, 128.0, 128.2, 128.4, 128.5, 135.0, 135.3, 137.8, 138.3, 138.5, 139.2, 168.3, 169.1; MALDI–MS *m/z* 1801.8 $[M+Na]^+$; MALDI-HRMS calcd for $C_{101}H_{118}O_{28}Na$, $[M+Na]^+$ 1801.7702, found 1801.7688. Compound **1**: $[\alpha]_D^{23}$ 54.2 (*c* 1.0, $H_2O$); $^1$H NMR (400 MHz, $D_2O$) $\delta$ 3.27 (t, *J* = 8.4 Hz, 1H), 3.30–3.38 (m, 2H), 3.47 (s, 3H), 3.53 (s, 3H), 3.56 (s, 6H), 3.58 (s, 3H), 3.62 (s, 3H), 3.63 (s, 3H), 3.64 (s, 6H), 3.75 (d, *J* = 10.0 Hz, 1H), 3.83–3.97 (m, 4H), 3.98 (t, *J* = 8.8 Hz, 1H), 4.06–4.18 (m, 3H), 4.19–4.45 (m, 8H), 4.56 (br t, *J* = 9.6 Hz, 1H), 4.65 (t, *J* = 9.2 Hz, 1H), 4.66 (d, *J* = 7.6 Hz, 1H), 5.00 (br s, 1H), 5.11 (br s, 1H), 5.17 (d, *J* = 3.6 Hz, 1H), 5.43 (d, *J* = 3.2 Hz, 1H), 5.47 (d, *J* = 4.0 Hz, 1H); ESI-MS *m/z* 774.1 $[M-8Na+6H]^{2-}$, 763.0; $[M-9Na+7H]^{2-}$, 508.5 $[M-9Na+6H]^{3-}$.