Organic & Biomolecular Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: H. He, D. Chen, X. Li, C. Li, J. Zhao and H. Qin, *Org. Biomol. Chem.*, 2019, DOI: 10.1039/C9OB00057G.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/obc

View Article Online
DOI: 10.1039/C9OB00057G

Organic &Biomolecular Chemistry

COMMNICATION

Synthesis of Trisaccharide Repeating Unit of Fucosylated Chondroitin Sulfate

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Haiqing He[a,b], Dong Chen[a,b] , Xiaomei Li[a,b] , , Chengji Li[a,b] Jin-Hua Zhao*, Hong-Bo Qin*[a]

The chemical synthesis of a sulfated trisaccharide repeating unit of fucosylated chondroitin sulfate (FCS), which has significant anticoagulant activity, is described. Well-functionalized monosaccharides were readily prepared and highly efficient glycosylations using a common activator (NIS/TfOH) were also presented. The synthetic trisaccharide 4 could be used to extend the oligosaccharide sequence.

Fucosylated chondroitin sulfate (FCS), a unique glycosaminoglycan (GAG) derivated from sea cucumber, is composed of a chondroitin sulfate (CS)-like backbone and sulfated fucose as side chain, which linked to O-3 of the glucuronic acid (GlcA) (**Figure 1**). [1-5] FCS exhibit various pharmacological effects such as anti-inflammatory, [6, 7]anti-tumor,[6] anti-hyperglycemia actions.,[8, 9] promoting angiogenesis[2], and regulating immune and cell growth. [10] Most importantly, FCS has attracted broad attention for its high anticoagulant and antithrombotic activities because of its selective inhibition of the intrinsic tenase. [1, 11-14] These biological effects are attributed to the sulfated α-fucose and they decrease significantly after selective removal of the sulfated Fuc residues. [15]

It is thought that well-defined oligosaccharides could facilitate the development of more efficacious anticoagulants. In 2015, we reported a series of pure oligosaccharides with precise structure prepared via the deacetylation–deaminative cleavage of FCS.[16] In this paper, nonasaccharide was determined as the minimum structural unit that retained the anticoagulation potency with negligible bleeding risk. Recently, Chen group declared that a depolymerized heptasaccharide was the minimum fragment to obtain similar benefit/risk

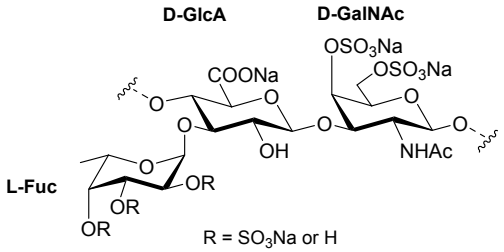


Fig. 1 Repeating unit of FCS

result.[17] This paper also demonstrated that reduction in chain size may dramatically reduce its adverse effect of FXII activation. These results have boosted the discovery of selective inhibitor of intrinsic coagulation pathway.

However, depolymerization of natural FCS is time-consuming and less effective to obtain enough amount of pure compounds for further research. It is necessary to develop an effective synthetic route to investigate the structure and activity relationship between the size and molecular weight. Several groups have published interesting results in this aspect. In 2013 Tamura group reported a synthesis of the trisaccharide β-D-GalNAc(4,6-diS)(1 → 4)[α-L-Fuc(2,4-diS)(1 → 3)]-β-D-GlcA as a repeating unit of FCS.[18] Galactosyl imidate was coupled with glucosyl acceptor in the presence of $BF_3{\cdot}Et_2O$ to afford the 1,2-*trans* disaccharide only in 40% yield due to non-neighbouring group participation. Furthermore, the installation of Fuc branch was not effective considering the way to synthesize donor. Nifantiev's group also published some synthetic works about the β-D-glucuronic acid residue bearing at O-3 α-L-fucosyl or α-L-fucosyl-(1 → 3)-α-L-fucosyl substituents related to structural fragments of FCS, [19] and the Fuc(1 → 6)GalNAc derivatives without sulfated. [20] Additionally, a modular approach to a library of semi-synthetic FCS polysaccharides had been presented by Bedini group via chemical transformation of a microbial sourced unsulfated chondroitin polysaccharide. [21, 22] Recently, significant progress has been reported by Li group for the elegant synthesis of new FCS utilizing their enzyme degradation of chondroitin sulfate

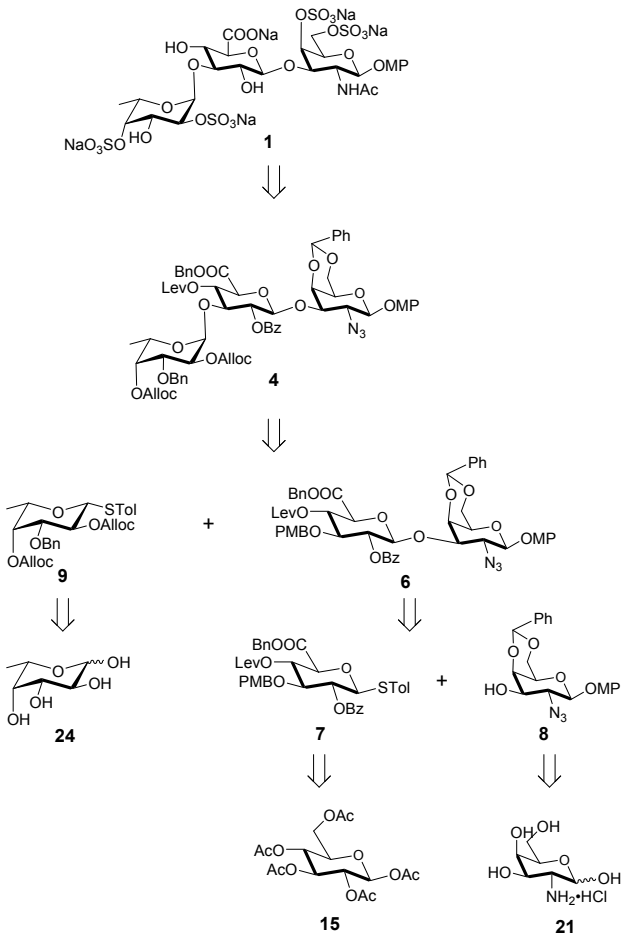
[a] State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, and Yunnan Key Laboratory of Natural Medicinal Chemistry, Kunming 650201, P. R. China. E-mail: qinhongbo@mail.kib.ac.cn; .zhaojinhua@mail.kib.ac.cn;

[b] University of Chinese Academy of Sciences, Beijing 100049, P. R. China.

Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

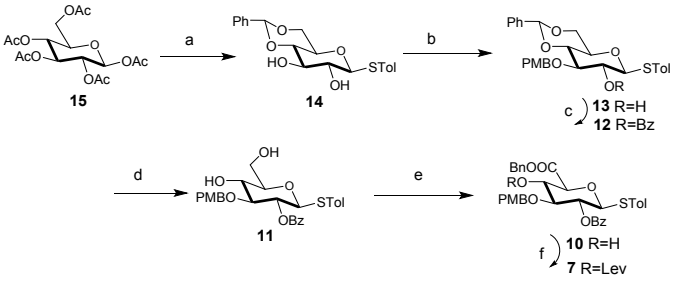
polymers.[23-25] Di-, tetra- and hexasaccharides have been prepared directly and used as backbone, thus improved the synthesis efficacy dramatically.

Herein, we report a synthesis of trisaccharide repeating unit [α-L-Fuc(2,4-diS)(1 → 3)]-β-D-GlcA(1 → 3)-β-D-GalNAc(4,6-diS), *via* a convenient and effective synthetic route, which may provide a different approach to bioactive FCS oligomers.



Scheme 1. A retrosynthetic analysis of trisaccharide **1**. Abbreviations: Ac = acetyl, Ph = Phenyl, MP = 4-methoxyphenyl, Bn = benzyl, Bz = benzoyl, Lev = levulinyl, PMB = p-methoxybenzyl, Alloc = Allyloxycarbonyl, Tol=4-tolyl.

We envisioned a convergent strategy (**Scheme 1**) to access the trisaccharide **1** using a set of functionalized monosaccharide building blocks **7**, **8** and **9**. These were readily accessible from commercially available starting materials **15**, **21** and **24**, respectively. The protecting group strategy was established for selective O-sulfation as well as stereoselectivity of glycosylation. The sulfated 4- and 6-hydroxyls of D-galactosamine were masked with a benzylidene acetal which could selectively be removed with 80% AcOH. The Alloc protecting groups of fucose intended to be O-sulfated and could be more easily removed comparing with the Allyl. [23] The benzoyl protecting C-2 hydroxy of GlcA allowed the stereoselective introduction of 1,2-*trans*-glycosidic linkages by neighbouring group participation. The levulinoyl group was installed at C-4 of GlcA for two reasons: firstly, it could be used as a permanent protection group during the synthesis of **1**, and secondly, it could be selectively removed to extend the main chain if necessary. The carboxylic acid group was blocked with benzyl group due to its higher reactivity than that of methyl ester when it was used as a donor. [26] PMB was used for a temporary protection at C-3 hydroxy of GlcA in order to couple with the Fuc branch. Finally, the Bz and Bn protecting groups were used as permanent protection groups for other free hydroxy groups and would be removed at late stage of synthesis.



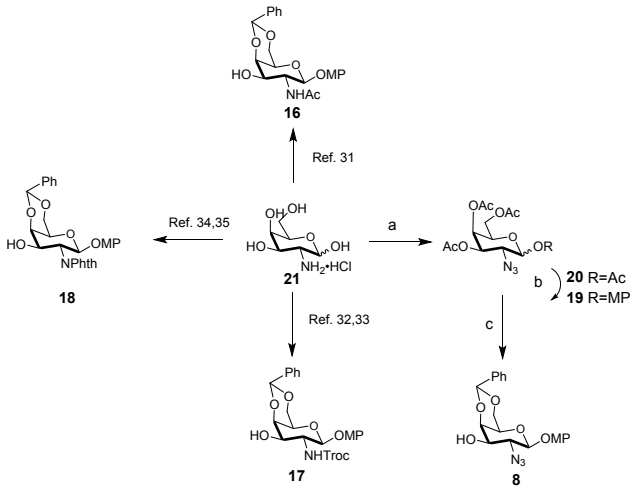
Scheme 2 Synthesis of building block **7**. Reagents and conditions: (a):1) p-toluenethiol, $BF_3{\cdot}Et_2O$, DCM,rt,10h; 2) Na,MeOH,rt,1h; 3) $PhCH(OMe)_2$, MeCN, CSA, 45°C, overnight , 3 steps 91%; (b): 1) Et_3N, TMSCl, DCM, rt, 6h; 2) Et_3SiH, Anisic aldehyde, TMSOTf, DCM, TBAF, overnight, 91%;(c): Bz_2O, DMAP, Et_3N, rt,overnight, 94%; (d): *p*-TsOH·H_2O, MeOH, MeCN,50 °C,3h, 79%; (e): 1) TEMPO, BIAB, DCM, H_2O, rt, 40min; 2) K_2CO_3, BnBr, Acetone, 50 °C, 5h, 68%; (f) LevOH, EDCI, DMAP, DCM, rt, 8h, 93%. $PhCH(OMe)_2$ = benzaldehyde dimethyl acetal, CSA = camphorsulfonic acid, TEMPO = 2,2,6,6-tetramethyl-1-piperidinyloxy, BAIB=2,2,6,6-tetramethyl-1-piperidinyloxy, Et_3N = triethylamine, LevOH = Levulinic acid, EDCI = N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride , DMAP = 4-dimethylaminopyridine

Based on the analysis, monosaccharide building blocks were initially synthesized. The glucouronic acid building block **7** was synthesized starting from commercially available β-D-Glucose pentaacetate **15** in nine steps (**Scheme 2**). Treatment of **15** with *p*-toluenethiol in the presence of $BF_3{\cdot}Et_2O$ provided the β-thioglycoside in almost quantitative yield. [27] Then it was deacetylated under Zemplen conditions, and this was followed by treatment of $PhCH(OMe)_2$ and CSA in acetonitrile to give 4,6-O-benzylidence **14**. The regioselective introduce of Bn was realized with Bu_2SnO, TBAB, PMBCl, but this proved troublesome during chromatographic separation. To avoid the tin reagent, Hung's one-pot protection strategy [28] was used and reaction proceeded smoothly with excellent regioselectivity. Removal of the 4,6-O-benzylidene group of **12** using *p*-TsOH·H_2O gave diol **11** in 79% yield, which was subjected to selective oxidation of the resulting primary hydroxy group with TEMPO in the presence of BAIB as co-oxidant. [29] The resulting carboxylic acid was then esterified in the presence of K_2CO_3, BnBr to give desired **10** in 68% yield over two steps in one-pot. [26, 30] The GlcA thioglycoside donor **7** was obtained by further protection of the remaining C-4 hydroxy group with LevOH and EDCI in the presence of a catalytic amount of DMAP in a yield of 95%.

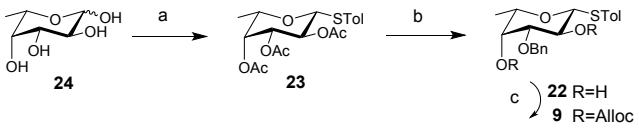
To synthesize the disaccharide efficiently, extensive investigation was made using a number of acceptors with different protecting groups of NH_2, which presumably possess different reactivity in glycosylation. The building blocks **16** [31], **17** [32, 33], **18** [34, 35] could easily be prepared according to the

DOI: 10.1039/C9OB00057C

described synthetic protocols. The building block **8** was synthesized from D-galactosamine hydrochloride **21** in five steps with 37% overall yield (**Scheme 3**). **21** was reacted with imidazole-1-sulfonyl azide, [36] a diazotransfer reagent, to give 2-azido-2-deoxy-d-galactopyranose,[37] followed by global acetylation (Ac_2O, Pyridine, DMAP). Compound **20** was isolated in 75% yield with two steps in one-pot. Then treatment of **20** with 4-methoxyphenol in the presence of TfOH gave **19** as a 1.1: 1 mixture of the corresponding α- and β-isomers. Finally, removal of the three O-acetyl groups by NaOMe, followed by protection of the 4,6- di-OH with $PhCH(OMe)_2$, [31] provided the galactoazide acceptor **8** (β-anomer and α-anomer is not shown).



Scheme 3 Synthesis of disaccharide acceptors **8**,**16**,**17** and **18.** Reagents and conditions: (a): 1) K_2CO_3, imidazole-1-sulfony azide hydrochloride, $CuSO_4{\cdot}5H_2O$, MeOH, rt,4h; 2) Pyridine, Ac_2O, rt, 10h, 2 steps 80% (α/β = 1/7) ; (b): 4-Methoxyphenol, TfOH, DCM, rt, 16h, 96% (α/β = 1.1/1); (c): 1)Na, MeOH, rt, 1h; 2) $PhCH(OMe)_2$, MeCN, p-TsOH, 45°C, overnight , 2 steps, 50% for α, 45% for β (**8**);

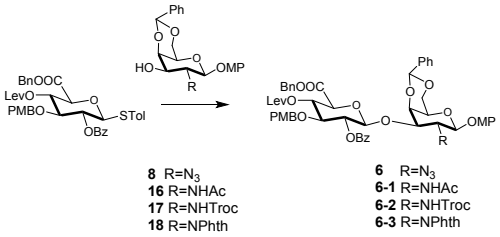


Scheme 4 Synthesis of building block **9**. Reagents and conditions: (a): 1) Pyridine, Ac_2O, rt, 6h; 2) p-Toluenethiol, $BF_3{\cdot}Et_2O$, DCM, rt, 10h, 2 steps 95%; (b): 1) Na, MeOH, rt, 1h; 2) Bu_2SnO, TBAB, BnBr, toluene, reflux, overnight, 68%; (c): Allyl chloroformate, DMAP, DCM, rt, 4h, 86%. Bu_2SnO = dibutyltin oxide, TBAF = tetrabutylammonium fluoride

The synthesis of β-thiofucoside donor **9** is outlined in **Scheme 4**. From L-fucose, the known β-thiofucoside **23**[38] was synthesized with two steps in 95% yield. Deacetylation under Zemplen conditions provided triol, which was regioselectively protected as 3-O-benzylation **22** [39] when treating with Bu_2SnO, BnBr, and TBAF in 75% yield with two steps in one-pot. Then donor **9** was readily obtained with AllocCl and DMAP in 89% yield.

With functionalized donors and acceptors in hand, we initially investigated the synthesis of β $(1\rightarrow3)$ disaccharides. However, the yield was unsatisfactory when thioglycoside was used as a donor for the construction of the disaccharide repeating unit of chondroitin sulphate (CS) according to Zhao's report[31]. Two more steps were needed while transforming the donor into trichloroacetimidate. To avoid it, a direct glycosylation condition of thioglycoside would be explored. Therefore, a series of acceptors had to be tested. As depicted in the **Table 1**. First, N-acetyl acceptor **16** was reacted with glucuronate **7** by activating the thiotolyl group with the NIS/TfOH acid reagent [40] (entry 1). Unfortunately, it failed to afford desired disaccharide.

Table 1 Glycosylation of GlcA and GlaN



entry	acceptor	promoter	Temp/ °C	yield
1	**16**	NIS/TfOH	-45 °C ~ -20 °C	NR[a]
2	**17**	NIS/TfOH	-45 °C ~ -20 °C	NR[a]
3	**18**	NIS/TfOH	-45 °C ~ -20 °C	Trace [b]
4	**8**	NIS/TfOH	-45 °C ~ -20 °C	45% [b,c]
5	**8**	NIS/TfOH	-70 °C ~ -45 °C	75% [c]
6	**8**	NIS/TfOH	-20 °C ~ rt	Trace [b]

[a]: no reaction, and the donor was completely hydrolyzed; [b]: the donor was partially hydrolyzed and incomplete consumption of acceptor; [c]: isolated yield .

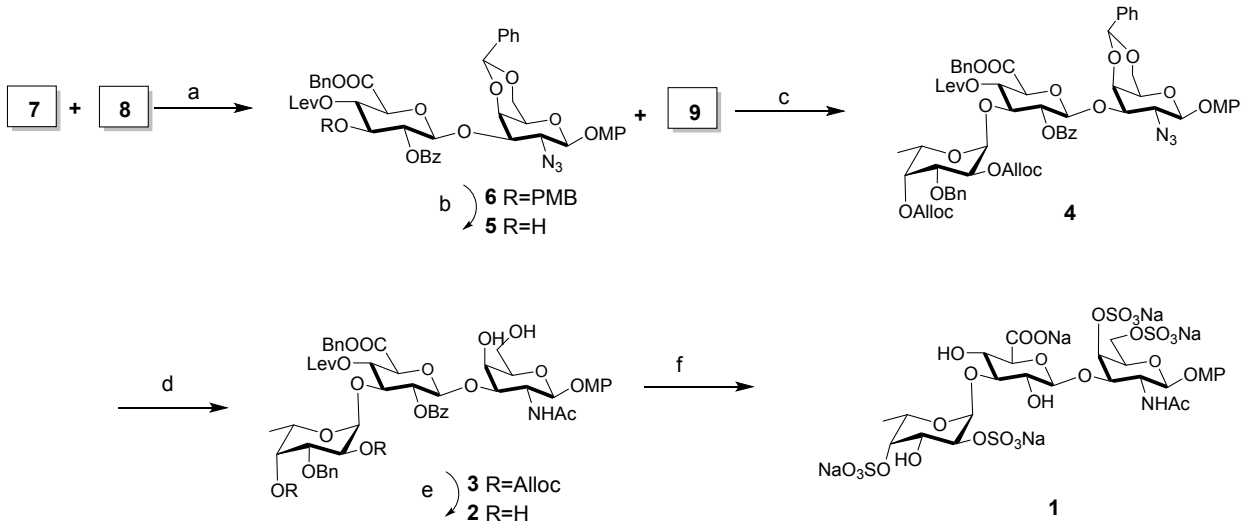
Subsequently, N-trichloroethoxycarbonyl (Troc) group was employed instead of acetyl in the galactosyl building block[41] (entry 2). Surprisingly, no desired product formed, while substantial decomposition of the glycosyl donor was observed, presumably due to the poor solubility of acceptors in organic solvents [41,42] and the low reactivity of donor. After that, the coupling reaction of benzylidene-2-deoxy-2-phthalimido-β--D-galactopyranoside **18** and the donor **7** was studied. However, it only gave trace amount of disaccharide [35] (entry 3) while the donor was partially hydrolyzed. The low yield might be attributed to the steric effect of Phth group. Finally, we tried to couple the 2-azido-2-deoxy-d-galactopyranose **8** with the donor **7** using the same condition as above (entry 4). To our delight, the β-linked disaccharide **6** was isolated in 45% yield while the α-isomer was not detected ($J_{1',2'}$=8.2Hz). The temperature was critical for the reaction. When it was below -70°C, a remarkable increase in the yield to 75% (entry 5) was observed. On the other hand, when the temperature rose to -20°C, the yield decreased heavily because donor hydrolyzation occurred as side reaction (entry 6). We thus concluded that an azido-containing acceptor gave best result for its smaller size and good solubility, when compared with its acetamido, Troc and corresponding Phth acceptor.

To assemble the target trisaccharide **4** (**Scheme 5**), a temporary protection group 3-O-PMB of **6** was removed smoothly by treating with DDQ to obtain disaccharide acceptor **5** in 85% yield. [30] The coupling reaction of **5** with **9** proceeded under similar glycosylation condition to afford exclusively the

View Article Online
DOI: 10.1039/C9OB00057G

α-linked trisaccharide **4** in 83% yield ($J_{1'',2''}$=3.4Hz, see the supporting information). This 1,2-*cis* selectivity, as distinct from typical glycosylation with the assistance of neighbouring group participation, was attributed to reversible *in situ* anomerization and the stabilizing anomeric effect.[42-44]

Next, a series of functional group transformations were carried out (**Scheme 5**). The azido group in **4** was reduced into an amino group with 1,3-propanedithiol [45], then acetylated with Ac_2O in Pyridine, followed by removal of



Scheme 5 Synthesis of trisaccharide **1**. Reagents and conditions: (a): 1) NIS, TfOH, DCM, 1.5h, -70°C -45°C, 40min, 75%; (b): 1) DDQ, DCM, rt, 12h, 85%; (c): NIS,TfOH,-50°C,1h, 83%; (d): 1) 1,3-dimercaptopropane, pyridine, Et_3N,H_2O,1h;2) Ac_2O, Et_3N, DCM,3h; 3) 80% AcOH/H_2O, reflux, 3h, 3 steps 70%; (e): $Pd(PPh_3)_4$, PPh_3, Ammonium formate. THF, 3h, 86%; (f): 1) SO_3·Me_3N, DMF, 60°C, 30h; 2)LiOH, H_2O_2, NaOH, MeOH, THF, rt, 2d; 3) Pd/C, H_2, H_2O, MeOH,1d, 3 steps 69%. NIS = N-iodosuccinimide, TfOH = trifluoromethanesulfonic, DDQ = 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone.

the 4,6-O-benzylidene group using 80% AcOH gave diol **3** in 70% yield with three steps in one-pot. Alloc esters were deprotected to generate **2** with ammonium formate and a catalytic amount of $Pd(PPh_3)_4$ in 85% yield. [46] Per-O-sulfonation of all hydroxyls with sulfur trioxide trimethylamine complex (SO_3·Me_3N) in DMF led to the corresponding sulfated trisaccharide derivative, followed by saponification utilizing sequential LiOOH-NaOH treatment to minimize β-elimination at the C-4 position. [47, 48] The remaining O-Bn group in the fucosyl residue was cleavaged *via* Pd/C-catalyzed hydrogenolysis to yield the target trisaccharide **1** in 69% yield over three steps in one-pot. NMR spectroscopy (DEPT, COSY, HSQC experiments) and mass spectrometry analysis confirmed the structure of **1**.

Conclusions

In summary, we have synthesized a trisaccharide, the repeating unit of FCS, through a convergent synthetic route in 20 collective steps from commercially available starting materials in 1.5% overall yield. The use of one-pot reactions effectively reduced the synthetic and purification steps. The azide group is a crucial and ideal protecting group of the acceptor. And the construction of the fucose-branch with a 1,2-*cis* glycosidic linkages was achieved with exclusive stereoselectivity using Alloc protecting groups. Furthermore, the trisaccharide **4** could be readily transformed into a new donor by oxidative removal of the 4-methoxyphenyl group with ceric ammonium nitrate (CAN). [42,49-51] Meanwhile, it could also act as a new acceptor by selective removal of Lev in the presence of hydrazine hydrate, pyridine and AcOH.[49-52] In addition, the azide group could be easily transformed into other groups in one-pot, such as TFA [31], Troc [53], Phth [54] , which can be used as neighbouring group to control the stereochemistry of further glycosylation. These features make it possible to prepare hexasaccharide and nonasaccharide for further structure–activity relationship research.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This project was funded by the High End Talent Program of Yunnan Province (2015HA028) and the key project of the Natural Science Foundation of Yunnan Province (2016FA004).

References

1. M. Y. Wu, D. D. Wen, N. Gao, C. Xiao, L. Yang, L. Xu, W. Lian, W. L. Peng, J. M. Jiang and J. H. Zhao, *Eur. J. Med. Chem.*, 2015, **92**, 257-269.
2. J. Tapon-Bretaudiere, D. Chabut, M. Zierer, S. Matou, D. Helley, A. Bros, P. A. S. Mourao and A. M. Fischer, *Mol. Cancer. Res.*, 2002, **1**, 96-102.
3. R. P. Vieira and P. A. S. Mourao, *J. Biol. Chem.*, 1988, **263**, 18176-18183.
4. R. P. Vieira, B. Mulloy and P. A. S. Mourao, *J. Biol. Chem.*, 1991, **266**, 13530-13536.
5. V. H. Pomin, *Mar. Drugs*, 2014, **12**, 232-254.
6. L. Borsig, L. C. Wang, M. C. M. Cavalcante, L. Cardilo-Reis, P. L. Ferreira, P. A. S. Mourao, J. D. Esko and M. S. G. Pavao, *J. Biol. Chem.*, 2007, **282**, 14984-14991.
7. C. G. Panagos, D. S. Thomson, C. Moss, A. D. Hughes, M. S. Kelly, Y. Liu, W. G. Chai, R. Venkatasamy, D. Spina, C. P. Page, J. Hogwood, R. J. Woods, B. Mulloy, C. D. Bavington and D. Uhrin, *J. Biol. Chem.*, 2014, **289**, 28284-28298.
8. A. M. F. Tovar and P. A. S. Mourao, *Atherosclerosis*, 1996, **126**, 185-195.
9. A. M. F. Tovar and P. A. S. Mourao, *Atherosclerosis*, 1997, **128**, 255-256.
10. J. Tapon-Bretaudiere, B. Drouet, S. Matou, P. A. S. Mourao, A. Bros, D. Letourneur and A. M. Fischer, *Thromb Haemostasis*, 2000, **84**, 332-+.
11. P. A. S. Mourao, M. S. Pereira, M. S. G. Pavao, B. Mulloy, D. M. Tollefsen, M. C. Mowinckel and U. Abildgaard, *J. Biol. Chem.*, 1996, **271**, 23973-23984.
12. P. A. S. Mourao, M. A. M. Guimaraes, B. Mulloy, S. Thomas and E. Gray, *Brit. J. Haematol.*, 1998, **101**, 647-652.
13. L. B. Ye, L. Xu and J. R. Li, *Carbohyd. Polym.*, 2012, **87**, 2052-2057.
14. M. Y. Wu, R. Huang, D. D. Wen, N. Gao, J. B. He, Z. Li and J. H. Zhao, *Carbohyd. Polym.*, 2012, **87**, 862-868.
15. M. Monteiro-Machado, M. A. Tomaz, R. J. C. Fonseca, M. A. Strauch, B. L. Cons, P. A. Borges, F. C. Patrao-Neto, M. S. Tavares-Henriques, J. M. Teixeira-Cruz, S. Calil-Elias, A. C. O. Cintra, A. M. B. Martinez, P. A. S. Mourao and P. A. Melo, *Toxicon*, 2015, **98**, 20-33.
16. L. Y. Zhao, M. Y. Wu, C. Xiao, L. Yang, L. T. Zhou, N. Gao, Z. Li, J. Chen, J. C. Chen, J. K. Liu, H. B. Qin and J. H. Zhao, *Proc. Natl. Acad. Sci. USA*, 2015, **112**, 8284-8289.
17. X. Zhang, W. Yao, X. Xu, H. Sun, J. Zhao, X. Meng, M. Wu and Z. Li, *Chem.—Eur. J.*, 2018, **24**, 1694-1700.
18. J. Tamura, H. Tanaka, A. Nakamura and N. Takeda, *Tetrahedron Lett.*, 2013, **54**, 3940-3943.
19. N. E. Ustyuzhanina, P. A. Fomitskaya, A. G. Gerbst, A. S. Dmitrenok and N. E. Nifantiev, *Mar. Drugs*, 2015, **13**, 770-787.
20. D. Z. Vinnitskiy, N. E. Ustyuzhanina, A. S. Dmitrenok, A. S. Shashkov and N. E. Nifantiev, *Carbohyd. Res.*, 2017, **438**, 9-17.
21. A. Laezza, A. Iadonisi, C. De Castro, M. De Rosa, C. Schiraldi, M. Parrilli and E. Bedini, *Biomacromolecules*, 2015, **16**, 2237-2245.
22. A. Laezza, A. Iadonisi, A. V. A. Pirozzi, P. Diana, M. De Rosa, C. Schiraldi, M. Parrilli and E. Bedini, *Chem-Eur. J.*, 2016, **22**, 18215-18226.
23. P. Xu, S. Laval, Z. Guo and B. Yu, *Org. Chem. Front.*, 2016, **3**, 103-109.
24. A. A. Joseph, V. P. Verma, X. Y. Liu, C. H. Wu, V. M. Dhurandhare and C. C. Wang, *Eur. J. Org. Chem.*, 2012, 744-753.
25. S. Maza, J. L. de Paz and P. M. Nieto, *Tetrahedron. Lett*, 2011, **52**, 441-443.
26. J. F. Chen, Y. Zhou, C. Chen, W. C. Xu and B. Yu, *Carbohyd. Res.*, 2008, **343**, 2853-2862.
27. S. Arungundram, K. Al-Mafraji, J. Asong, F. E. Leach, I. J. Amster, A. Venot, J. E. Turnbull and G. J. Boons, *J. Am. Chem. Soc.*, 2009, **131**, 17394-17405.
28. C. C. Wang, J. C. Lee, S. Y. Luo, S. S. Kulkarni, Y. W. Huang, C. C. Lee, K. L. Chang and S. C. Hung, *Nature*, 2007, **446**, 896-899.
29. L. J. van den Bos, J. D. C. Codee, J. C. van der Toorn, T. J. Boltje, J. H. van Boom, H. S. Overkleeft and G. A. van der Marel, *Org. Lett.*, 2004, **6**, 2165-2168.
30. X. Dai, W. T. Liu, Q. L. Zhou, C. W. Cheng, C. Yang, S. Q. Wang, M. Zhang, P. Tang, H. Song, D. Zhang and Y. Qin, *J. Org. Chem.*, 2016, **81**, 162-184.
31. S. Yang, A. P. Wang, G. Y. Zhang, X. J. Di, Z. H. Zhao and P. S. Lei, *Tetrahedron*, 2016, **72**, 5659-5670.
32. S. Ghosh, S. Nishat and P. R. Andreana, *J. Org. Chem.*, 2016, **81**, 4475-4484.
33. Z. Wang, L. Y. Zhou, K. El-Boubbou, X. S. Ye and X. F. Huang, *J. Org. Chem.*, 2007, **72**, 6409-6420.
34. R. Panchadhayee and A. K. Misra, *J. Carbohyd. Chem.*, 2008, **27**, 148-155.
35. G. F. Gu, P. J. P. Adabala, M. G. Szczepina, S. Borrelli and B. M. Pinto, *J. Org. Chem.*, 2013, **78**, 8004-8019.
36. G. T. Potter, G. C. Jayson, G. J. Miller and J. M. Gardiner, *J. Org. Chem.*, 2016, **81**, 3443-3446.
37. T. H. Li, H. Ye, X. F. Cao, J. J. Wang, Y. H. Liu, L. F. Zhou, Q. Liu, W. J. Wang, J. Shen, W. Zhao and P. Wang, *Chemmedchem*, 2014, **9**, 1071-1080.
38. C. S. Chao, M. C. Chen, S. C. Lin and K. K. T. Mong, *Carbohyd. Res.*, 2008, **343**, 957-964.
39. M. Giordano and A. Iadonisi, *J. Org. Chem.*, 2014, **79**, 213-222.
40. M. H. S. Marqvorsen, M. J. Pedersen, M. R. Rasmussen, S. K. Kristensen, R. Dahl-Lassen and H. H. Jensen, *J. Org. Chem.*, 2017, **82**, 143-156.
41. E. Danieli, L. Lay, D. Proietti, F. Berti, P. Costantino and R. Adamo, *Org. Lett.*, 2011, **13**, 378-381.
42. H. Satoh, S. Manabe, Y. Ito, H. P. Luthi, T. Laino and J. Hutter, *J. Am. Chem. Soc.*, 2011, **133**, 5610-5619.
43. Y. Tang, J. K. Li, Y. G. Zhu, Y. Li and B. A. Yu, *J. Am. Chem. Soc.*, 2013, **135**, 18396-18405.
44. J. Zhou, L. P. Yang and W. H. Hu, *J. Org. Chem.*, 2014, **79**, 4718-4726.
45. Y. Yang, Y. Li and B. Yu, *J. Am. Chem. Soc.*, 2009, **131**, 12076-+.
46. Y. Hayakawa, H. Kato, M. Uchiyama, H. Kajino and R. Noyori, *J. Org. Chem.*, 1986, **51**, 2400-2402.
47. H. Lucas, J. E. M. Basten, T. G. Vandinther, D. G. Meuleman, S. F. Vanaelst and C. A. A. Vanboeckel, *Tetrahedron*, 1990, **46**, 8207-8228.
48. J. C. Jacquinet, C. Lopin-Bon and A. Vibert, *Chem-Eur. J.*, 2009, **15**, 9579-9595.
49. J. Tamura, K. W. Neumann and T. Ogawa, *Bioorg. Med. Chem. Lett.*, 1995, **5**, 1351-1354.
50. J. Tamura and M. Tokuyoshi, *Biosci. Biotech. Bioch.*, 2004, **68**, 2436-2443.
51. J. I. Tamura, Y. Nakada, K. Taniguchi and M. Yamane, *Carbohydr. Res.*, 2008, **343**, 39-47.
52. C. H. Chang, L. S. Lico, T. Y. Huang, S. Y. Lin, C. L. Chang, S. D. Arco and S. C. Hung, *Angew. Chem. Int. Edit.*, 2014, **53**, 9876-9879.
53. T. K. K. Mong, C. Y. Huang and C. H. Wong, *J. Org. Chem.*, 2003, **68**, 2135-2142.
54. J. Garcia, J. Vilarrasa, X. Bordas and A. Banaszek, *Tetrahedron Lett.*, 1986, **27**, 639-640.

DOI: 10.1039/C9OB00057G