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Efficient one-pot synthesis of glycosyl disulfides

Goreti Ribeiro Morais and Robert A. Falconer*

Institute of Cancer Therapeutics, School of Life Sciences, University of Bradford, Bradford BD7 1DP, UK

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Abstract—Methodology for the efficient and facile synthesis of glycosyl disulfides is reported. A one-pot procedure employing mild conditions using diethyl azodicarboxylate is described to synthesise a series of glycosyl disulfides in excellent yields.

1. Introduction

The surface of the mammalian cell is decorated by many complex carbohydrates, with key roles in communication, migration and disease, particularly cancer.[1] To understand these processes better, there is a need for molecular probes with stability in biological systems. The disulfide bond plays an important role in the formation of higher order structures in peptides and proteins, and recent work has also highlighted the potential of glycosyl disulfides as useful tools in the study of glycobiology.[2–4] Diglycosyl disulfides have been studied as potential O-glycoside mimics, for example, in lectin binding,[3,5,6] and for the study of carbohydrate structure.[7,8] Natural glycosyl disulfides are relatively rare, however, but mixed glycosyl disulfides (and their synthesis) have recently received attention due to their use as donors in oligosaccharide synthesis[9] in addition to their biological application. Compounds with disulfide linkages have also been investigated as anti-cancer agents,[10] including bioreductive prodrugs.[11]

Current methods to synthesise glycosyl disulfides include the use of alkylsulfonate esters,[7–9,12] selenylsulfides,[4,13] benzyltriethylammonium tetrathiomolybdate,[14] sulfenyl bromides[15] and other procedures involving multiple steps under aqueous conditions.[2,3] Our previous work on the synthesis of thioglycosides using the Mitsunobu reaction[16,17] led us to investigate the use of azo compounds in the synthesis of glycosyl disulfides, both symmetrical and non-symmetrical. There is one report of the use of diethyl azodicarboxylate, in a two-stage reaction for the synthesis of aryl disulfides.[18] However, the two-stage procedure (with intermediate isolation and purification) had the disadvantage of prolonged reaction times, extreme conditions and moderate yields. Hummel recently used this two-stage process to produce an ethyl glycosyl disulfide, for use in thioglycoside synthesis.[19]

The first use of a series of azo derivatives in a one-pot synthesis of glycosyl disulfides under mild, neutral conditions and with excellent yields is reported. A series of commercially available azo compounds were initially examined, using the reaction between per-*O*-acetyl-1-thioglucose **1** and benzyl mercaptan as a model reaction (Table 1). The sugar and the reacting thiol were sequentially added to a stirred solution of the azo compound in THF—the yellow solution became colourless as the reaction proceeded. Clearly, DEAD and DIAD produced the highest yields (Table 1) with ADDP being particularly ineffective (the combination of ADDP and trimethylphosphine worked particularly well in the synthesis of thioglycosides, in our previous work).[16] The significant by-product in each reaction was the symmetrical diglucosyl disulfide, meaning that optimisation of these reaction conditions was necessary. DEAD was used for the remainder of this study, although our results indicate that DIAD is an equally effective alternative. Interestingly, the polymer-supported DEAD behaved extremely poorly in these reactions, with no significant formation of the product using either THF or DMF as a solvent. We assume the nature of the resin and/or the reactivity of the immobilised agent to be the cause.

Keywords: Glycosyl disulfide; Glycoside; Thioglycoside.
* Corresponding author. Tel.: +44 1274 235842; fax: +44 1274 233234; e-mail: r.a.falconer1@bradford.ac.uk

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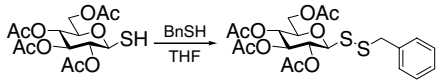
Table 1. Comparison of azo-compounds in the synthesis of benzyl glycosyl disulfide **2a**



1 **2a**

Entry	Reagent (1.2 equiv)	Yield (%)
1	ADDP (azodicarbonyldipiperidine)	16
2	DIAD (diisopropyl azodicarboxylate)	61
3	DTAD (di-*tert*-butyl azodicarboxylate)	44
4	DEAD (diethyl azodicarboxylate)	68
5	DEAD[a]	nd[b]

Conditions: **1** (1 equiv); benzyl mercaptan (1.2 equiv); 3 h; rt.
[a] Polymer-supported DEAD.
[b] Not determined.

The conditions for this type of reaction were subsequently optimised, varying solvent, reaction time, proportions of reactants and the order of their addition. A twofold excess of DEAD over the thiosugar was found to be optimum. Reactions were best in THF, with dichloromethane and dimethylformamide producing lower yields.

The study was then extended to include the synthesis of a series of non-symmetrical disulfides, including aromatic and heterocyclic moieties (Table 2, entries 1–4 and 8–14), and by incorporating per-O-acetylated 1-thiosugars of galactose, mannose and rhamnose, in addition to glucose. Interestingly, using the same order of addition of reagents, non-symmetrical alkyl disulfides

Table 2. Synthesis of glycosyl disulfides

$$R^1\text{–SH} + R^2\text{–SH} \rightarrow R^1\text{–S–S–}R^2$$

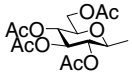
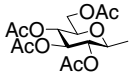
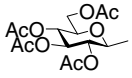
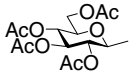
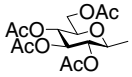
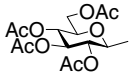
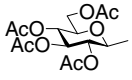
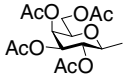
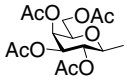
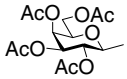
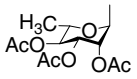
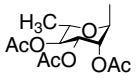
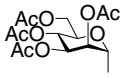
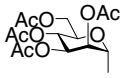
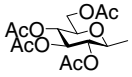
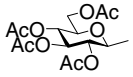
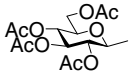
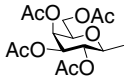
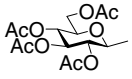
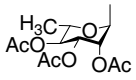
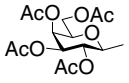
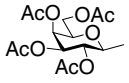
Entry	R^1	R^2	Conditions	Product	Yield (%)	Reference
1			A	**2a**	95	15
2			A	**2b**	94	15
3			A	**2c**	78[a]	20
4			A	**2d**	95	21
5			B	**2e**	46	22
6			B	**2f**	43	5
7			C	**2g**	85	23
8			A	**2h**	88	15
9			A	**2i**	72	15
10			A	**2j**	66	24
11			A	**2k**	87	25
12			A	**2l**	80	26

Table 2 (*continued*)

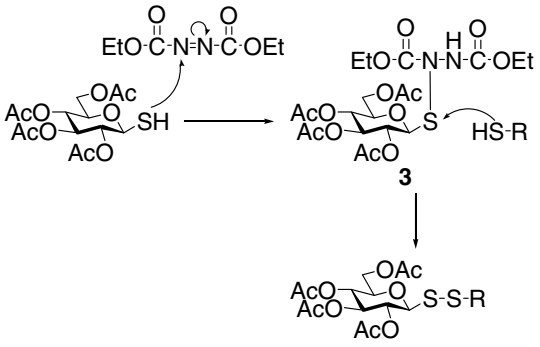
Entry	R^1	R^2	Conditions	Product	Yield (%)	Reference
13			A	**2m**	95	15
14			A	**2n**	93	27
15			D	**2o**	95	7,8
16			E	**2p**	79	7,8
17			E	**2q**	72	28
18			D	**2r**	86	29

Conditions: (A) R^1SH (1 equiv), R^2SH (2 equiv), DEAD (2 equiv), THF, 3 h, rt; (B) R^1SH (1 equiv), R^2SH (6 equiv), DEAD (2 equiv), THF, 24 h, reflux; (C) R^2SH (2 equiv), DEAD (2 equiv), THF, 12 h, rt, followed by R^1SH (1 equiv), 3 h, rt; (D) R^1SH (2 equiv), DEAD (1 equiv), THF, 3 h, rt; (E) R^1SH (1 equiv), R^2SH (1.1 equiv), DEAD (2 equiv), THF, 1 h, rt.

[a] DIAD used in place of DEAD.

(entries 5–7) required longer reaction times, producing products in moderate yields only. However, reversal of the order of addition of the reagents, that is, the sugar thiol being added after complex formation between the alkyl thiol and DEAD, significantly increased the reaction yield from a modest 24% to 85% (entry 7), as compared to ethyl thioglycoside, using the original conditions (entry 6). Symmetrical and non-symmetrical diglycosyl disulfides were also synthesised, all in excellent yields (entries 15–18).

A closer analysis of these reactions revealed that the thiosugar reacts very quickly with DEAD to form intermediate **3**[30] (Scheme 1). The reacting thiol then acts as a nucleophile, forming the disulfide and leaving the saturated DEAD by-product (and conversely the thiosugar reacted with the thiol–DEAD complex in the reverse order of addition). A twofold excess of DEAD was required to prevent the thiosugar reacting with the rapidly formed sugar–DEAD intermediate (which also occurs rapidly) in place of the reacting thiol. In addition, the thiosugar was added to the DEAD solution, as opposed to the reverse, to further minimise this. In the case of symmetrical diglycosyl disulfide synthesis, this was not necessary: a twofold excess of the sugar over DEAD allowed smooth conversion to the product in excellent yields (entries 15 and 18). The high reactivity of thiosugars towards a DEAD–sugar intermediate also means that large excesses were not required for the synthesis of non-symmetrical compounds (entries 16 and 17). Entry 3 confirms that DIAD is of equal effectiveness as DEAD using these conditions—the yield using DEAD was 76%, that is, lower than that of DIAD.



Scheme 1.

In summary we have described a convenient one-pot synthesis of glycosyl disulfides, using mild and neutral conditions, and in excellent yields. We are currently investigating the application of these compounds to biological systems.

2. Typical experimental procedure

2,3,4,6-Tetra-*O*-acetyl-1-thio-β-D-glucopyranose **1** (50 mg, 0.138 mmol, 1.0 equiv) in THF (1 mL) and benzyl mercaptan (0.275 mmol, 33 μL, 2 equiv) were sequentially added to a solution of DEAD (0.275 mmol, 44 μL, 2.0 equiv) in THF (2 mL) under an inert atmosphere. The reaction was stirred at room temperature for 3 h. The reaction mixture was subsequently evaporated and purified by flash chromatography (petroleum ether–ethyl acetate 1:1) to give **2a** (64 mg, 95%).

Acknowledgements

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References and notes

1. Sell, S. *Hum. Pathol.* **1990**, *21*, 1003–1019.
2. Hamachi, I.; Nagase, T.; Shinkai, S. *J. Am. Chem. Soc.* **2000**, *122*, 12065–12066.
3. Andre, S.; Pei, Z.; Siebert, H. C.; Ramstrom, O.; Gabius, H. J. *Bioorg. Med. Chem.* **2006**, *14*, 6314–6326.
4. Gamblin, D. P.; Garnier, P.; van Kasteren, S.; Oldham, N. J.; Fairbanks, A. J.; Davis, B. G. *Angew. Chem., Int. Ed.* **2004**, *43*, 828–833.
5. Pei, Z. C.; Aastrup, T.; Anderson, H.; Ramstrom, O. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2707–2710.
6. Pei, Z. C.; Larsson, R.; Aastrup, T.; Anderson, H.; Lehn, J. M.; Ramstrom, O. *Biosens. Bioelectron.* **2006**, *22*, 42–48.
7. Szilagyi, L.; Illyes, T. Z.; Herczegh, P. *Tetrahedron Lett.* **2001**, *42*, 3901–3903.
8. Brito, I.; Lopez-Rodriguez, M.; Benyei, A.; Szilagyi, L. *Carbohydr. Res.* **2006**, *341*, 2967–2972.
9. Grayson, E. J.; Ward, S. J.; Hall, A. L.; Rendle, P. M.; Gamblin, D. P.; Batsanov, A. S.; Davis, B. G. *J. Org. Chem.* **2005**, *70*, 9740–9754.
10. Bittman, R.; Li, Z.; Samadder, P.; Arthur, G. *Cancer Lett.* **2007**, *251*, 53–58.
11. Vrudhula, V. M.; MacMaster, J. F.; Li, Z.; Kerr, D. E.; Senter, P. D. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 3591–3594.
12. Davis, B. G.; Ward, S. J.; Rendle, P. M. *Chem. Commun.* **2001**, 189–190.
13. Hotchkiss, T.; Kramer, H. B.; Doores, K. J.; Gamblin, D. P.; Oldham, N. J.; Davis, B. G. *Chem. Commun.* **2005**, 4264–4266.
14. Sivapriya, K.; Suguna, P.; Shubashree, S.; Sridhar, P. R.; Chandrasekaran, S. *Carbohydr. Res.* **2007**, *342*, 1151–1158.
15. Bell, R. H.; Horton, D.; Miller, M. J. *Carbohydr. Res.* **1969**, *9*, 201–214.
16. Falconer, R. A.; Jablonkai, I.; Toth, I. *Tetrahedron Lett.* **1999**, *40*, 8663–8666.
17. Malkinson, J. P.; Falconer, R. A. *Tetrahedron Lett.* **2002**, *43*, 9549–9552.
18. Mukaiyama, T.; Takahashi, K. *Tetrahedron Lett.* **1968**, *56*, 5907–5908.
19. Hummel, G.; Hindsgaul, O. *Angew. Chem., Int. Ed.* **1999**, *38*, 1782–1784.
20. Compound **2c**: $[\alpha]_D^{20}$ -134.5 ± 1 (*c* 0.59, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 1.92, 1.95, 1.96, 2.05 (4s, 12H, 4OAc), 3.65 (m, 1H, H-5), 4.04 (m, 2H, H-6 and H-6′), 4.63 (d, 1H, H-1, $J_{1,2} = 9.6$ Hz), 5.04 (dd, 1H, H-4, $J_{4,3} = J_{4,5} = 9.6$ Hz), 5.20 (m, 2H, H-2 and H-3), 7.07 (m, 1H), 8.55 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.62, 20.67, 20.70, 20.83, 61.79, 67.84, 69.50, 73.82, 76.04, 86.58, 118.28, 118.33, 157.77, 157.99, 169.34, 170.29, 170.50, 170.65; ES^+ MS $C_{18}H_{22}O_9N_2S_2$ (474) *m/z* (%) 497 $[M+Na]^+$ (100). HRMS (ESI): $[M+H]^+$ calcd for $C_{18}H_{23}O_9N_2S_2$, 475.0839; found, 475.0835.
21. Compound **2d**: $[\alpha]_D^{20}$ -252.5 ± 1 (*c* 0.64, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 1.75, 1.99, 2.00, 2.09 (4s, 12H, 4OAc), 3.78 (m, 1H, H-5), 4.07 (m, 2H, H-6 and H-6′), 4.74 (d, 1H, H-1, $J_{1,2} = 9.3$ Hz), 5.08 (dd, 1H, H-4, $J_{3,4} = J_{4,5} = 9.3$ Hz), 5.24 (m, 2H, H-2 and H-3), 7.33 (t, 1H, $^3J = 8.1$ Hz), 7.42 (t, 1H, $^3J = 8.1$ Hz), 7.77 (d, 1H, $^3J = 8.1$ Hz), 7.86 (d, 1H, $^3J = 8.1$ Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.35, 20.63, 20.68, 20.76, 61.70, 67.90, 69.51, 73.59, 76.21, 87.47, 121.13, 122.38, 125.05, 126.41, 136.11, 154.34, 169.35, 169.37, 170.22, 170.54; ES^+ MS $C_{21}H_{23}NO_9S_3$ (529) *m/z* (%) 530 $[M+H]^+$ (60). HRMS (ESI): $[M+H]^+$ calcd for $C_{21}H_{24}O_9NS_3$, 530.0608; found, 530.0608.
22. Compound **2e**: $[\alpha]_D^{20}$ -110.0 ± 2 (*c* 0.09, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 1.28 (m, 8H), 1.76 (m, 2H), 2.00, 2.02, 2.03, 2.07 (4s, 12H, 4OAc), 2.84 (m, 1H), 3.72 (m, 1H, H-5), 4.13 (dd, 1H, H-6, $J_{6,5} = 2.0$ Hz, $J_{6,6'} = 12.3$ Hz), 4.23 (dd, 1H, H-6′, $J_{6',5} = 4.8$ Hz, $J_{6',6} = 12.3$ Hz), 4.46 (d, 1H, H-1, $J_{1,2} = 9.6$ Hz), 5.09 (dd, 1H, H-4, $J_{4,3} = J_{4,5} = 9.6$ Hz), 5.22 (m, 2H, H-2 and H-3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.69, 20.73, 20.79 (2C), 25.69, 26.00, 26.06, 32.62, 32.73, 50.34, 62.10, 68.06, 69.37, 73.99, 76.01, 88.21, 169.27, 169.50, 170.37, 170.66; ES^+ MS $C_{20}H_{30}NO_9S_2$ (478) *m/z* (%) 501 $[M+Na]^+$ (100). HRMS (ESI): $[M+NH_4]^+$ calcd for $C_{20}H_{34}O_9NS_2$, 496.1669; found, 496.1670.
23. Compound **2g**: $[\alpha]_D^{20}$ -122.5 ± 1 (*c* 1.18, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.86 (t, 3H, $J = 7.2$ Hz), 1.29 (m, 6H), 1.64 (m, 2H), 1.99, 2.01, 2.02, 2.06 (4s, 12H, 4OAc), 2.75 (m, 2H), 3.72 (m, 1H, H-5), 4.13 (dd, 1H, H-6, $J_{6,5} = 2.1$ Hz, $J_{6,6'} = 12.3$ Hz), 4.21 (dd, 1H, H-6′, $J_{6',5} = 4.4$ Hz, $J_{6',6} = 12.3$ Hz), 4.50 (d, 1H, H-1, $J_{1,2} = 9.6$ Hz), 5.09 (dd, 1H, H-4, $J_{4,5} = J_{4,3} = 9.6$ Hz), 5.24 (m, 2H, H-2 and H-3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 13.98, 20.56, 20.60, 20.68 (2C), 22.49, 28.09, 28.82, 31.33, 40.07, 62.01, 67.99, 69.08, 73.83, 75.99, 88.03, 169.15, 169.37, 170.23, 170.52; ES^+ MS $C_{20}H_{32}O_9S_2$ (480) *m/z* (%) 503 $[M+Na]^+$ (100). HRMS (ESI): $[M+NH_4]^+$ calcd for $C_{20}H_{36}O_9NS_2$, 498.1826; found, 498.1825.
24. Compound **2j**: $[\alpha]_D^{20}$ -91.5 ± 1 (*c* 0.84, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 1.95, 1.97, 2.10, 2.13 (4s, 12H, 4OAc), 3.88 (t, 1H, H-5, $J_{5,6} = 6.5$ Hz), 3.95 (d, 2H, $J_{5,6} = 6.5$ Hz), 4.66 (d, 1H, H-1, $J_{1,2} = 9.9$ Hz), 5.04 (dd, 1H, H-3, $J_{3,4} = 3.2$ Hz, $J_{2,3} = 9.9$ Hz), 5.37 (d, 1H, H-4, $J_{3,4} = 3.2$ Hz), 5.41 (dd, 1H, H-2, $J_{1,2} = J_{2,3} = 9.9$ Hz), 7.10 (t, 1H, $^3J = 4.8$ Hz), 8.59 (d, 2H, $^3J = 4.8$ Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.68, 20.72, 20.76, 20.94, 61.24, 67.06, 71.84, 74.72, 88.74, 118.34, 157.78 (2C), 169.63, 170.13, 170.35, 170.36, 170.84; ES^+ MS $C_{18}H_{22}N_2O_9S_2$ (474.08) *m/z* (%) 497 $[M+Na]^+$ (100). HRMS (ESI): $[M+H]^+$ calcd for $C_{18}H_{23}O_9N_2S_2$, 475.0839; found, 475.0842.
25. Compound **2k**: $[\alpha]_D^{20}$ -76.3 ± 1 (*c* 1.84, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 1.22 (d, 3H, $J = 6.1$ Hz), 1.97, 2.03, 2.11 (3s, 9H, 3OAc), 3.94 (d, 1H, $^2J = 12.3$ Hz), 3.98 (d, 1H, $^2J = 12.3$ Hz), 4.05 (m, 1H, H-5), 4.69 (s, 1H, H-1), 5.04 (dd, 1H, H-4, $J_{3,4} = 9.9$ Hz, $J_{4,5} = 9.7$ Hz), 5.13 (dd, 1H, H-3, $J_{2,3} = 3.4$ Hz, $J_{3,4} = 9.9$ Hz), 5.37 (dd, 1H, H-2, $J_{1,2} = 1.5$ Hz, $J_{2,3} = 3.4$ Hz), 7.24–7.30 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.45, 20.74, 20.88, 21.00, 43.81, 68.59, 69.16, 70.24, 70.86, 88.40, 127.71, 128.80 (2C), 129.44 (2C), 136.67, 169.83, 169.99 (2C); ES^+ MS $C_{19}H_{24}O_7S_2$ (428.10) *m/z* (%) 451 $[M+Na]^+$ (100). HRMS (ESI): $[M+NH_4]^+$ calcd for $C_{19}H_{28}O_7NS_2$, 446.1302; found, 446.1297.
26. Compound **2l**: $[\alpha]_D^{20}$ -7.5 ± 1 (*c* 2.01, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.95 (d, 3H, $J = 6.1$ Hz), 1.96, 2.02, 2.11 (3s, 9H, 3OAc), 3.85 (m, 1H, H-5), 5.05 (dd, 1H, H-4, $J_{3,4} = 9.9$ Hz, $J_{4,5} = 9.7$ Hz), 5.16 (dd, 1H, H-3, $J_{2,3} = 3.4$ Hz, $J_{3,4} = 9.9$ Hz), 5.23 (d, 1H, H-1, $J_{1,2} = 1.4$ Hz), 5.40 (dd, 1H, H-2, $J_{1,2} = 1.4$ Hz, $J_{2,3} = 3.4$ Hz),

7.26 (d, 1H, $^3J = 7.3$ Hz), 7.31 (dd, 2H, $^3J = 7.3$ Hz), 7.56 (d, 2H, $^3J = 7.3$ Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 16.96, 20.73, 20.85, 20.96, 68.67, 69.26, 70.26, 70.98, 88.49, 128.06, 129.17 (2C), 130.03 (2C), 136.43, 169.93, 169.95 (2C); ES$^+$ MS $C_{18}H_{22}O_7S_2$ (414.08) m/z (%) 437 $[M+Na]^+$ (100). HRMS (ESI): $[M+NH_4]^+$ calcd for $C_{18}H_{26}O_7NS_2$, 432.1145; found, 432.1149.

27. Compound **2n**: $[\alpha]_D^{20}$ $+22 \pm 1$ (c 1.45, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.94, 2.00, 2.05, 2.16 (4s, 12H, 4OAc), 3.88 (dd, 1H, H-6, $J_{5,6} = 2.0$ Hz, $J_{6,6'} = 12.4$ Hz), 4.30 (dd, 1H, H-6′ $J_{5,6'} = 4.7$ Hz, $J_{6,6'} = 12.4$ Hz), 4.45 (m, 1H, H-5), 5.29 (dd, 1H, H-3, $J_{2,3} = 3.4$ Hz, $J_{3,4} = 9.9$ Hz), 5.36 (dd, 1H, H-4, $J_{3,4} = J_{4,5} = 9.9$ Hz), 5.54 (dd, 1H, H-2, $J_{1,2} = 1.5$ Hz, $J_{2,3} = 3.4$ Hz), 5.57 (d, 1H, H-1, $J_{1,2} = 1.5$ Hz), 7.32 (m, 2H), 7.48 (m, 1H), 7.65 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.65, 20.68, 20.78, 20.92, 61.86, 65.79, 69.28, 69.49, 70.93, 87.98, 110.49, 119.57, 125.03, 125.28, 141.76, 152.52, 161.83, 169.64, 169.81, 169.85, 170.64; ES$^+$ MS $C_{21}H_{23}NO_{10}S_2$ (513.54) m/z (%) 536.1 $[M+Na]^+$ (100). HRMS (ESI): $[M+H]^+$ calcd for $C_{21}H_{24}O_{10}NS_2$, 514.0836; found, 514.0839.

28. Compound **2q**: $[\alpha]_D^{20}$ -200.5 ± 1 (c 1.67, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.23 (d, 3H, $J =$ 5.8 Hz, CH_{3rha}), 1.98, 2.00, 2.00, 2.03, 2.03, 2.04, 2.11 (7s, 21 H, 7OAc), 3.75 (m, 1H, H-5$_{glc}$), 4.00 (m, 1H, H-5$_{rha}$), 4.09 (dd, 1H, H-6$_{glu}$, $J_{6,5} = 1.3$ Hz, $J_{6,6'} = 12.3$ Hz), 4.20 (dd, 1H, H-6′$_{glu}$, $J_{6',5} = 5.5$ Hz, $J_{6',6} = 12.3$ Hz), 4.50 (d, 1H, H-1$_{glu}$, $J_{1,2} = 9.2$ Hz), 5.10 (m, 2H, H-4$_{glu}$ and H-4$_{rha}$), 5.24 (m, 4H, H-2$_{glu}$, H-3$_{glu}$, H-4$_{rha}$ and H-1$_{rha}$), 5.50 (dd, 1H, H-2$_{rha}$, $J_{1,2} = 1.6$ Hz, $J_{2,3} = 3.3$ Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.50, 20.71, 20.73 (3C), 20.74, 20.75, 62.28, 68.26, 68.95, 69.01, 69.16, 70.01, 70.85, 73.69, 76.60, 86.66, 87.87, 169.27, 169.36, 169.78, 169.90, 169.93, 169.98, 170.31; ES$^+$ MS $C_{26}H_{36}O_{16}S_2$ (668) m/z (%) 691 $[M+Na]^+$ (100). HRMS (ESI): $[M+NH_4]^+$ calcd for $C_{26}H_{40}O_{16}NS_2$, 686.1783; found, 686.1784.

29. Compound **2r**: $[\alpha]_D^{20}$ -32.1 ± 1 (c 2.64, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.95, 2.01, 2.05, 2.14 (4s, 24 H, 8OAc), 4.00 (m, 2H, H-6), 4.08 (m, 2H, H-6′), 4.20 (dd, 2H, H-5, $J_{5,6} = 6.1$ Hz, $J_{5,6'} = 10.9$ Hz), 4.54 (d†, 2H, H-1, $J_{1,2} = 9.6$ Hz), 5.05 (dd, 2H, H-3, $J_{3,4} = 3.4$ Hz, $J_{2,3} = 9.6$ Hz), 5.32 (dd, 2H, H-2, $J_{1,2} = J_{2,3} = 9.6$ Hz), 5.41 (d, 2H, H-4, $J_{3,4} = 3.4$ Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.64, 20.71, 20.75, 20.88, 60.77, 66.63, 67.69, 72.17, 74.77, 88.44, 169.46, 170.08, 170.24, 170.36. †Symmetrical disulfide; triplet seen in thio-monosaccharide; ES$^+$ MS $C_{28}H_{38}NO_{18}S_2$ (726) m/z (%) 749 $[M+Na]^+$ (83). HRMS (ESI): $[M+NH_4]^+$ calcd for $C_{28}H_{42}O_{18}NS_2$, 744.1838; found, 744.1841.

30. Compound **3**: $[\alpha]_D^{20}$ -25.0 ± 1 (c 5.23, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.26 (m, 6H, $2CH_3$), 1.98, 2.01, 2.06, 2.08 (4s, 12H, 4OAc), 3.71 (m, 1H, H-5), 4.20 (m, 6H, H-6, H-6′ and $2CH_2$), 4.88 (d, 1H, H-1, $J_{1,2} =$ 9.6 Hz), 4.96 (dd, 1H, H-4, $J_{3,4} = J_{4,5} = 9.6$ Hz), 5.07 (dd, 1H, H-3, $J_{2,3} = J_{3,4} = 9.6$ Hz), 5.22 (dd, 1H, H-2, $J_{1,2} = J_{2,3} =$ 9.6 Hz), 7.19 (br s, 1H, NH); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.34, 14.50, 20.64, 20.68, 20.70, 20.80, 61.97, 62.36, 64.61 (2C), 68.12, 68.32, 73.79, 75.99, 155.59 (CO), 156.05 (CO), 169.43, 169.76, 170.19, 170.87; ES$^+$ MS $C_{20}H_{30}N_2O_{13}S$ (538) m/z (%) 539 $[M+H]^+$ (30), 561 $[M+Na]^+$ (30). HRMS (ESI): $[M+NH_4]^+$ calcd for $C_{20}H_{34}O_{13}N_3S$, 556.1807; found, 556.1809.