Glyco-SAMs by 'Dual Click': Thiourea-Bridged Glyco-OEG Azides for Cycloaddition on Surfaces

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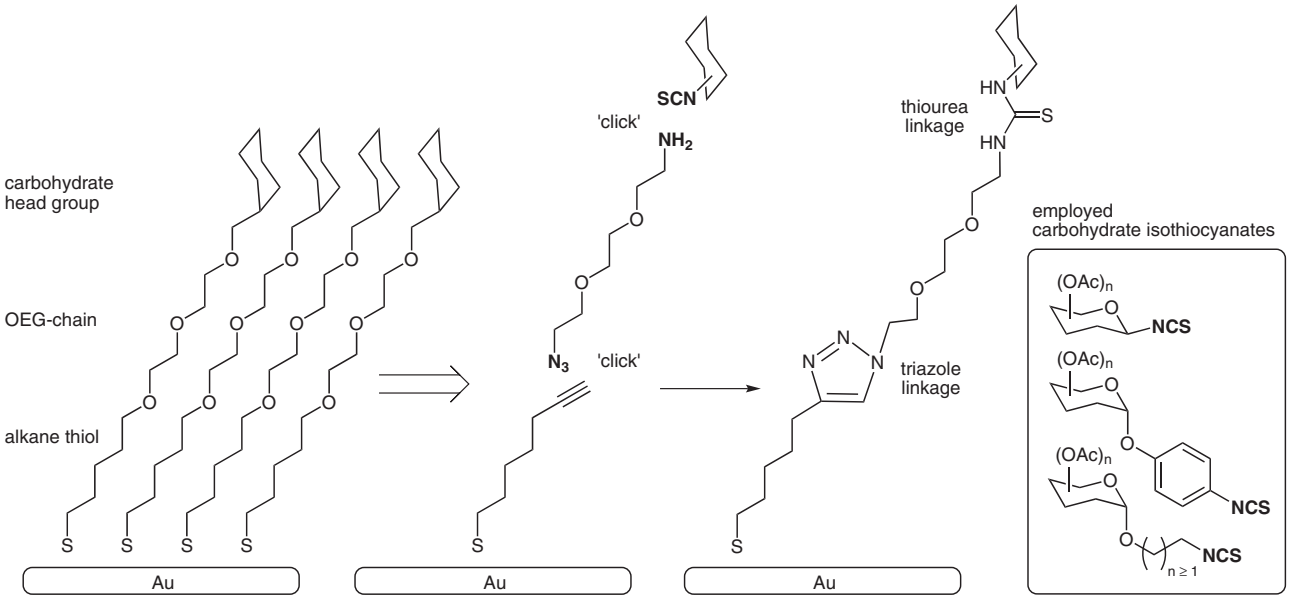
Abstract: A series of NCS-functionalized sugars were synthesized and used in a thiourea-bridging reaction with aminohexa(ethylene glycol) azide [$H_2N(EG)_6N_3$], a bifunctional oligo(ethylene glycol) derivative, which can be used as key intermediate for the fabrication of biorepulsive glyco-SAMs by a 'dual click' approach. Glyco-SAMs can serve as defined glycocalyx models for the study of carbohydrate-protein interactions. The copper(I)-catalyzed 1,3-dipolar cycloaddition reaction of the obtained glyco-OEG azides was exemplified, which can be used to modify preformed monolayers 'on SAM'.

Key words: carbohydrates, self-assembled monolayers, 'click' chemistry, thiourea-bridging

Every eukaryotic cell is covered by a highly complex sugar coat, termed 'glycocalyx', comprised of a variety of complex glycoconjugates. These carbohydrates are of fundamental importance for cell-cell recognition and cell adhesion.[1] To study the details of the molecular recognition processes, that occur on the cell surface, synthetic models are needed, which allow defined variation of the structural set-up of a carbohydrate-coated surface.[2] An ideal system, which offers a reliable as well as flexible construction of ordered glycoarrays are self-assembled monolayers, in short SAMs.[3] SAMs can be functionalized with carbohydrate head groups to obtain 'glyco-SAMs',[4] which allow the study of carbohydrate-protein interactions using different biophysical methods.[5]

Self-assembled monolayers are typically formed with OEG[oligo(ethylene glycol)]-substituted alkane thiols, which chemisorb onto a gold surface (Scheme 1). The alkane thiols that form the monolayer have to be attached to an OEG chain, typically with EG_3 to EG_7, to resist unspecific adsorption of proteins.[6] Protein-repelling properties of the unfunctionalized SAM are a prerequisite for employment of glyco-SAMs in carbohydrate-protein binding studies. Finally, for glyco-SAM construction, molecules of the type $HO(CH_2CH_2O)_n(CH_2)_{11}SH$ have to be functionalized with a carbohydrate head group for carbohydrate-recognition studies.



Scheme 1 Construction of glyco-SAMs has to combine the required alkane thiols with protein-repulsive OEG chains and biorelevant carbohydrate head groups. This is achieved in a chemoselective 'dual click' approach employing an α-amino-ω-azido-difunctionalized OEG [$H_2N(EG)_6N_3$] in 1,3-dipolar addition with alkynes at one end and thiourea-bridging with isothiocyanato-functionalized sugars at the other. Three different types of NCS-functionalized O-acetylated sugars were used in this study.

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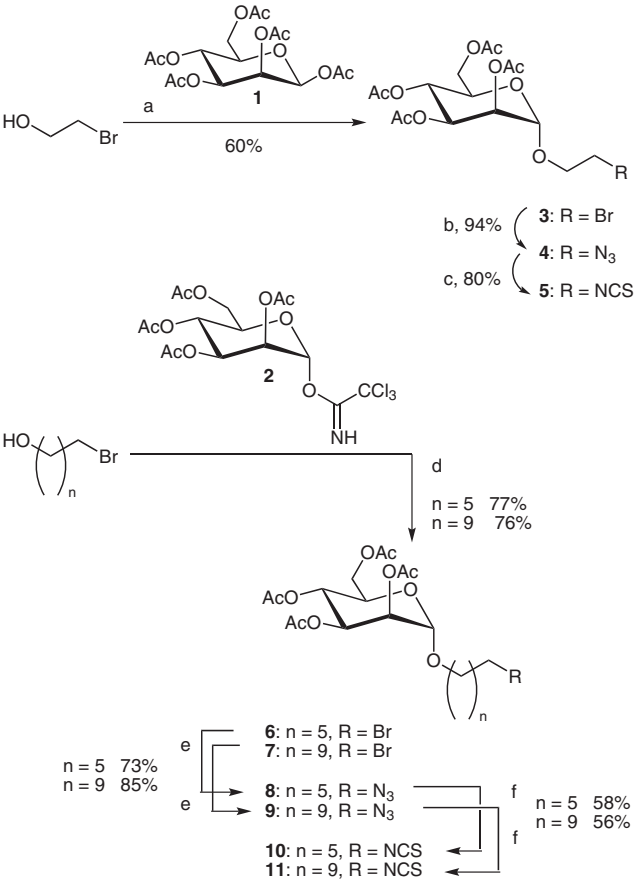
Glyco-SAMs can be constructed in two different ways: (i) either the completely functionalized thiol is synthesized first and subsequently assembled on the gold substrate; or (ii) a basic monolayer is formed first and this blank is then further refined 'on SAM'. The latter concept enables greater flexibility for biological testing, because a particular SAM can be investigated before and after further modification. Thus, 'switching' the condition of a monolayer may allow to draw conclusions about the biological consequences of a specific change, which is not possible otherwise.

We have recently reported on a 'click on SAM' approach,[7] which relies on copper(I)-catalyzed 1,3-dipolar cycloaddition of azides to alkyne-terminated SAMs.[8] This approach can be extended to a 'dual click' concept, in which two essential steps for SAM fabrication are simplified, both OEG functionalization of the alkane thiol as well as the sugar decoration (Scheme 1). The difunctionalized OEG, aminohexa(ethylene glycol) azide [$H_2N(EG)_6N_3$], is the key molecule in this approach which allows 1,3-dipolar addition to alkynes on one hand and the well established thiourea-bridging reaction to isothiocyanates[9] on the other. The sequence of these two operations can be altered according to requirements. In this paper, the facile synthesis of NCS-functionalized glycosides and thiourea-bridging to $H_2N(EG)_6N_3$ is shown and copper(I)-catalyzed cycloaddition to a long-chain alkyne is exemplified.

Three types of NCS-functionalized carbohydrate derivatives were used. Glycosyl isothiocyanates carrying the NCS functionality at the anomeric center were prepared following proven methods.[10] Glycosides, which carry the NCS function on an aromatic or aliphatic aglycone, respectively, have also been described.[11] In addition to known NCS-functionalized sugars, which were employed in this study (Table 1), long-chain alkyl α-D-mannosides, carrying the NCS functionality at the terminus of the aglycone portion, were targeted for the investigation of mannose-specific bacterial adhesion.[12] It has been shown earlier, that the alkyl aglycone of such mannosides can exhibit high affinity to the respective bacterial lectin FimH.[13]

All new glycoside isothiocyanates were synthesized from the corresponding azides in a Staudinger-type reaction employing carbon disulfide and triethyl phosphite.[14] Thus, the 2-azidoethylmannoside **4**[15] was converted into the respective isothiocyanate **5** in good yield (Scheme 2). Whereas the precursor molecule for this synthesis, mannoside **3**,[16] can be obtained by glycosidation of the pentaacetate **1**, this was not possible in case of the longer glycosyl acceptors. 6-Bromohexan-1-ol and 10-bromodecan-1-ol had to be glycosylated using the mannosyl trichloroacetimidate **2** as glycosyl donor.[17] The Lewis acid catalyzed reaction proceeded in good yields, giving the bromo-functionalized mannosides **6** and **7**, which were in turn subjected to nucleophilic displacement with sodium azide to yield **8** and **9**, followed by conversion into the desired isothiocyanates **10** and **11**.

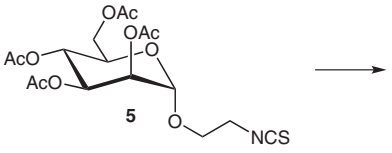
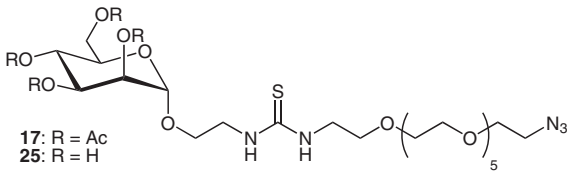
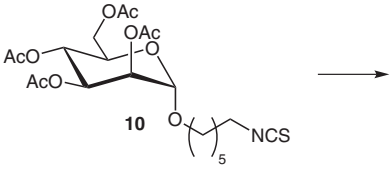
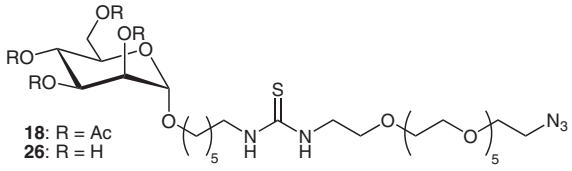
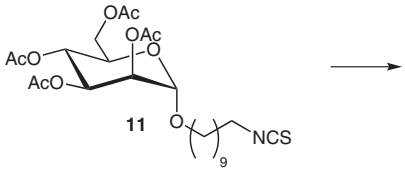
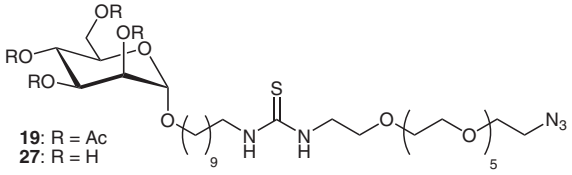
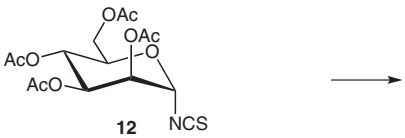
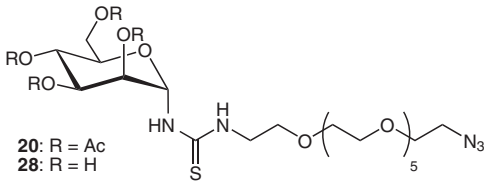
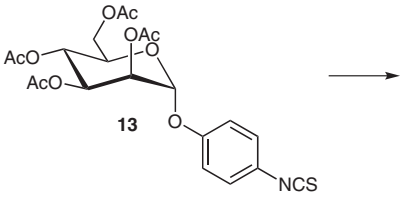
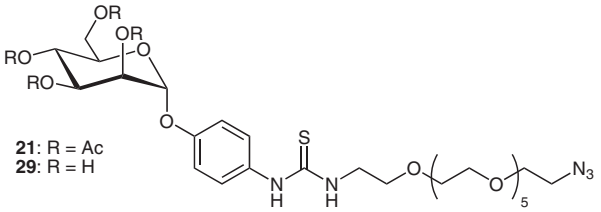
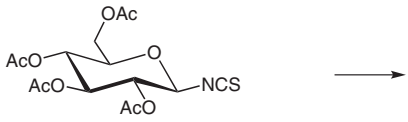
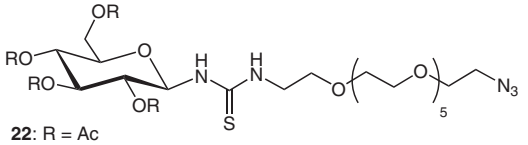
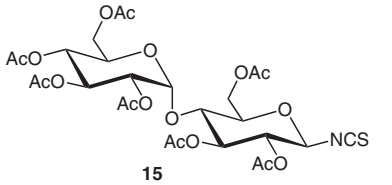
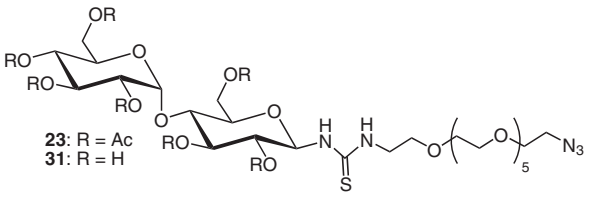
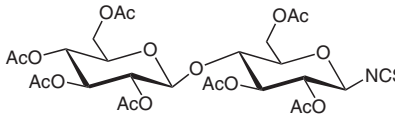
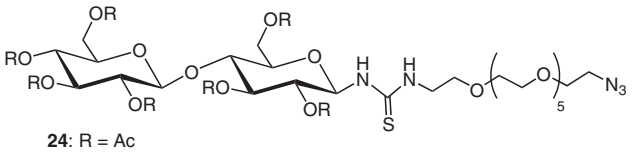


Scheme 2 *Reagents and conditions*: (a) $BF_3{\cdot}OEt_2$, CH_2Cl_2, r.t., 12 h; (b) NaN_3, Bu_4NBr, DMF, 60 °C, 5 h, r.t. 12 h; (c) CS_2, $P(OEt)_3$, toluene, 80 °C, 8 h; (d) 6-bromohexan-1-ol (for n = 5), 10-bromodecan-1-ol (for n = 9), $BF_3{\cdot}OEt_2$, CH_2Cl_2, r.t., 24 h; (e) NaN_3, Bu_4NBr, DMF, 5 h at 60 °C, and 12 h at r.t.; (f) CS_2, $P(OEt)_3$, toluene, 80 °C, 8 h.

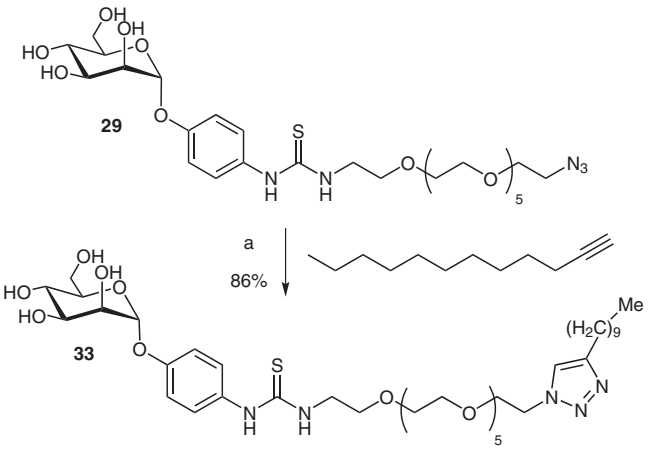
Next, thiourea-bridging with the aminohexa(ethylene glycol) azide [$H_2N(EG)_6N_3$] was done for a series of NCS-functionalized sugars – the glycosides **5**, **10**, **11**, and **13** – and the well-known glycosyl isothiocyanates **12**, **14**, **15**, and **16**[10] (Table 1). The reaction was carried out at room temperature and products were obtained after standard workup. The respective thiourea-bridged glyco-OEG azides were isolated in pure form after column chromatography on silica gel in mostly excellent yields. Deprotection according to Zemplén[18] led to the corresponding unprotected derivatives **25** to **32** in nearly quantitative yields (Table 1).

The carbohydrate-decorated OEG azides **25** to **32** have been designed for 1,3-dipolar cycloaddition to alkyne-terminated SAMs.To test if glyco-OEG azides are suited for the Meldal–Sharpless 'click' reaction,[8] the phenylmannoside-derived OEG azide **29** was reacted with dodec-1-yne under copper(I) catalysis (Scheme 3). This reaction produced the 1,4-triazole **33** in very good yield after column chromatography. The regioselectivity of the cycloaddition reaction was proved by NMR analysis.

Table 1 Synthesis of Thiourea-Bridged Glyco-OEG Azides Employing Aminohexa(ethylene glycol) Azide [$H_2N(EG)_6N_3$]

NCS-functionalized carbohydrates	Thiourea-bridged glyco-OEG-azides	Yield (%)	
		Ligation[a]	Deprotection[b]
 **5**	 **17**: R = Ac **25**: R = H	85	90
 **10**	 **18**: R = Ac **26**: R = H	90	99
 **11**	 **19**: R = Ac **27**: R = H	50	78
 **12**	 **20**: R = Ac **28**: R = H	99	93
 **13**	 **21**: R = Ac **29**: R = H	68	quant
 **14**	 **22**: R = Ac **30**: R = H	93	quant
 **15**	 **23**: R = Ac **31**: R = H	51	99
 **16**	 **24**: R = Ac **32**: R = H	99	82

[a] Reaction conditions: see general procedure.
[b] Reaction conditions: see general procedure.



Scheme 3 *Reagents and conditions*: (a) CuI, MeCN, 70 °C, 18 h.

In conclusion, it was shown that the aminohexa(ethylene glycol) azide [$H_2N(EG)_6N_3$] can be addressed in two subsequent 'click'-type reactions to produce chain-like biorepulsive molecules, which are needed for the construction of glyco-SAMs. This concept implies a highly flexible modular approach for fabrication of carbohydrate-decorated monolayers and their modification. According to the 'dual click' concept, the two chemoselective ligation steps can be applied in any sequence, either in solution or 'on SAM'. Both ligation reactions which were employed – thiourea-bridging and 1,3-diploar cycloaddition of azides and alkynes – are feasible in carbohydrate chemistry. Owing to the chemistry used, either method works equally well in every sugar series, which is important because carbohydrates are the biorelevant head groups in our studies. This project will be further developed towards increasing complexity of the sugar decoration.

All reactions were monitored by TLC on silica gel F_{254} (Merck) with detection by UV light and/or by charring with 10% ethanolic H_2SO_4 and subsequent heating. Flash chromatography was performed on Merck silica gel 60 (0.040–0.063 mm). NMR spectra were recorded at 550 or 600 MHz on Bruker DRX 500 and AV 600 instruments at 298 K. Chemical shifts (δ) are reported in ppm and are relative to Me_4Si (δ = 0) as internal standard. IR spectra were measured with a PerkinElmer FT-IR Paragon 1000 (ATR) spectrometer. ESI-MS measurements were performed on a Mariner instrument, MALDI-TOF mass spectra were recorded on a Bruker Biflex III instrument with 19 kV acceleration voltage and an ionization laser at 337 nm. As matrices 2,5-dihydroxybenzoic acid and α-cyano-4-hydroxycinnamic acid were used. Optical rotations were determined with a PerkinElmer 241 polarimeter at r.t. (10 cm cells, Na D-line: 589 nm). Petroleum ether (PE) used refers to the fraction boiling in the range 30–60 °C.

Thiourea-Bridging; General Procedure

To the O-acetylated NCS-functionalized carbohydrate **5**, **10**–**16** (20–220 mg) dissolved in ice-cold anhyd CH_2Cl_2 (5 mL) were added aminohexa(ethylene glycol) azide [H_2N-$(EG)_6$-N_3, 1 equiv] and DIPEA (1.01 equiv) and the reaction mixture was stirred at 0 °C for 1 h. After removal of the ice bath, stirring was continued at r.t. overnight. Then, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel (Table 1).

De-O-Acetylation; General Procedure

The acetylated thiourea-bridged glyco-OEG-azide **17**–**24** (20–226 mg) was dissolved in anhyd MeOH (10 mL) and a catalytic amount of NaOMe was added at 0 °C. The reaction mixture was stirred at r.t. for 3 h, followed by addition of Amberlite IR120 ion exchange resin for neutralization. After filtration, the filtrate was concentrated under reduced pressure to obtain the pure product (Table 1).

2-Isothiocyanatoethyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (5)

The acetylated azide **4** (450 mg, 1.08 mmol) was dissolved in anhyd toluene (10 mL) and CS_2 (2.79 mL, 46.3 mmol, 43 equiv) and $P(OEt)_3$ (740 μL, 4.32 mmol, 4 equiv) were added. The mixture was stirred for 8 h at 80 °C. Then H_2O (15 mL) was added and the solution was kept at 4 °C for 12 h. After extraction with CH_2Cl_2 (3 × 20 mL), the organic phases were combined and dried ($MgSO_4$). After filtration, the filtrate was concentrated under reduced pressure and the residual syrup purified by flash column chromatography (cyclohexane–EtOAc, 2:1 → 1:2) to give the title compound as a colorless, amorphous solid; yield: 378 mg (80%); R_f = 0.51 (cyclohexane–EtOAc, 1:2); $[\alpha]_D$ +11 (*c* 1.23, $CHCl_3$).

IR (ATR): 2094 (s, NCS), 1730 cm^{-1} (s, C=O).

^1H NMR (600 MHz, $CDCl_3$): δ = 5.36 (dd, $^3J_{2,3}$ = 3.4 Hz, $^3J_{3,4}$ = 10.0 Hz, 1 H, H-3), 5.31 (t, $^3J_{3,4}$ = 10.0 Hz, 1 H, H-4), 5.29 (dd, $^3J_{1,2}$ = 1.8 Hz, $^3J_{2,3}$ = 3.4 Hz, 1 H, H-2), 4.89 (d, $^3J_{1,2}$ = 1.8 Hz, 1 H, H-1), 4.30 (dd, $^3J_{5,6}$ = 5.2 Hz, $^3J_{6,6'}$ = 12.4 Hz, 1 H, H-6), 4.14 (dd, $^3J_{5,6'}$ = 2.8 Hz, $^3J_{6,6'}$ = 12.4 Hz, 1 H, H-6′), 4.09 (m_c, 1 H, H-5), 3.90 (m_c, 1 H, man–OC*H*H), 3.80–3.70 (m, 3 H, man–OCH*H*, CH_2NCS), 2.16, 2.11, 2.05, 2.00 (each s, each 3 H, 4 $COCH_3$).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.5, 169.9, 169.8, 169.7 (4 *C*OCH_3), 134.4 (NCS), 97.9 (C-1), 69.3 (C-5), 69.1 (C-2), 68.9 (C-3), 66.7 (man–OCH_2), 66.0 (C-4), 62.5 (C-6), 45.0 (*C*H_2NCS), 20.8, 20.7, 20.7, 20.6 (4 CO*C*H_3).

MALDI-TOF-MS: *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{23}NO_{10}S$ + Na: 456.09; found: 456.19.

6-Bromohexyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (6)

To an ice-cooled solution of the mannosyl donor **2** (400 mg, 0.815 mmol) and 6-bromohexan-1-ol (107 μL, 0.976 mmol, 1.2 equiv) in anhyd CH_2Cl_2 (10 mL) was added $BF_3{\cdot}OEt_2$ (413 μL, 3.26 mmol, 4 equiv) slowly. After 30 min, the ice bath was removed and the mixture was stirred r.t. overnight. Afterwards, aq $NaHCO_3$ (40 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (2 × 40 mL). The combined organic phases were washed with H_2O (2 × 40 mL), dried ($MgSO_4$), filtered, and the filtrate was concentrated. The product was obtained after column chromatography (PE–EtOAc, 3:2) as a colorless syrup; yield: 320 mg (77%); R_f = 0.43 (PE–EtOAc, 3:2); $[\alpha]_D$ +21 (*c* 0.60, CH_2Cl_2).

IR (ATR): 2937 (s, C–H), 1740 (s, C=O), 1044 cm^{-1} (s, C–Br).

^1H NMR (600 MHz, $CDCl_3$): δ = 5.35 (dd, $^3J_{2,3}$ = 3.5 Hz, $^3J_{3,4}$ = 10.0 Hz, 1 H, H-3), 5.28 (t, $^3J_{3,4}$ = 10.0 Hz, $^3J_{4,5}$ = 10.0 Hz, 1 H, H-4), 5.23 (d, $^3J_{1,2}$ = 1.8 Hz, $^3J_{2,3}$ = 3.5 Hz, 1 H, H-2), 4.80 (d, $^3J_{1,2}$ = 1.8 Hz, 1 H, H-1), 4.28 (dd, $^3J_{5,6}$ = 5.8 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6), 4.12 (dd, $^3J_{5,6}$ = 2.5 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6′), 3.98 (m_c, 1 H, H-5), 3.70 (m_c, 1 H, man–OC*H*H), 3.48–3.44 (m, 1 H, man–OCH*H*), 3.42 (t, ^3J = 6.8 Hz, 2 H, CH_2Br), 2.15, 2.10, 2.04, 2.00 (each s, each 3 H, 4 $COCH_3$), 1.88 (m_c, 2 H, CH_2CH_2Br), 1.88, 1.61, 1.48, 1.40 (each m_c, each 2 H, 3 CH_2).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.6, 170.1, 169.9, 169.7 (4 *C*OCH_3), 97.7 (C-1), 69.7 (C-2), 69.1 (C-3), 68.5 (C-5), 68.3 (man–OCH_2), 66.4 (C-4), 62.6 (C-6), 33.7 (CH_2Br), 32.6

(CH_2CH_2Br), 29.1 (man–OCH_2CH_2), 27.9 ($CH_2CH_2CH_2Br$), 25.3 (man–$OCH_2CH_2CH_2$), 20.9, 20.7, 20.7, 20.7 (4 $COCH_3$).

HRESI-MS: *m/z* [M + Na]$^+$ calcd for $C_{20}H_{31}BrO_{10}$ + Na: 533.0998; found: 533.0993.

10-Bromodecyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (7)

To a solution of the trichloroacetimidate **2** (790 mg, 1.16 mmol) in ice-cooled anhyd CH_2Cl_2 (20 mL) were added 10-bromodecan-1-ol (355 μL, 1.93 mmol, 1.2 equiv) and $BF_3{\cdot}OEt_2$ (410 μL, 3.22 mmol, 2 equiv). After 30 min, the ice bath was removed and the mixture was stirred at r.t. overnight. Afterwards, aq $NaHCO_3$ (40 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (2 × 40 mL). The combined organic phases were washed with H_2O (20 mL), dried ($MgSO_4$), filtered, and the filtrate was concentrated. Column chromatography (cyclohexane–EtOAc, 1:1) gave a colorless syrup; yield: 690 mg (76%); R_f = 0.43 (cyclohexane–EtOAc, 1:1); $[\alpha]_D$ +20 (*c* 0.33, CH_2Cl_2).

IR (ATR): 2929 (s, C–H), 1746 (s, C=O), 1046 cm^{-1} (C–Br).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.34 (dd, $^3J_{2,3}$ = 3.4 Hz, $^3J_{3,4}$ = 10.0 Hz, 1 H, H-3), 5.26 (dd, $^3J_{3,4}$ = 10.0 Hz, $^3J_{4,5}$ = 10.0 Hz, 1 H, H-4), 5.22 (d, $^3J_{1,2}$ = 1.4 Hz, $^3J_{2,3}$ = 3.4 Hz, 1 H, H-2), 4.79 (d, $^3J_{1,2}$ = 1.4 Hz, 1 H, H-1), 4.27 (dd, $^3J_{5,6}$ = 5.3 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6), 4.10 (dd, $^3J_{5,6'}$ = 2.4 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6′), 3.97 (ddd, $^3J_{4,5}$ = 10.0 Hz, $^3J_{5,6}$ = 5.3 Hz, $^3J_{5,6'}$ = 2.4 Hz, 1 H, H-5), 3.68–3.62 (m_c, 3 H, man–OC*H*H, man–OCH_2CH_2), 3.46–3.38 (m, 3 H, man–OCH*H*, CH_2Br), 2.15, 2.10, 2.04, 1.99 (each s, each 3 H, 4 $COCH_3$), 1.84, 1.58 (each m_c, each 4 H, 4 CH_2), 1.45–1.26 (m, 6 H, 3 CH_2).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.7, 170.1, 169.9, 169.8 (4 *C*OCH_3), 97.6 (C-1), 69.8 (C-2), 69.2 (C-3), 68.6 (C-5), 68.4 (man–OCH_2), 66.3 (C-4), 62.6 (C-6), 34.00 (CH_2Br), 32.8 (CH_2CH_2Br), 29.5, 29.4, 29.6, 29.5, 29.3, 29.3, 28.7, 28.2 (8 CH_2), 20.9, 20.7, 20.7, 20.7 (4 CO*C*H_3).

HRESI-MS: *m/z* [M + Na]$^+$ calcd for $C_{24}H_{39}BrO_{10}$ + Na: 589.1624; found: 589.1653.

6-Azidohexyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (8)

To a solution of the bromide **6** (1.26 g, 2.47 mmol) in anhyd DMF (10 mL) were added NaN_3 (802 mg, 12.4 mmol, 5 equiv) and Bu_4NBr (159 mg, 0.494 mmol, 0.2 equiv) and the reaction mixture was stirred at 60 °C for 5 h and overnight at r.t. Then, the mixture was poured into ice water and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the filtrate was concentrated. The residue was purified by flash column chromatography (cyclohexane–EtOAc, 3:2) to obtain the title compound as a colorless syrup, yield: 852 mg (73%); R_f = 0.38 (cyclohexane–EtOAc, 3:2); $[\alpha]_D$ +48 (*c* 0.69, CH_2Cl_2).

IR (ATR): 2093 (s, N_3), 1741 cm^{-1} (s, C=O).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.35 (dd, $^3J_{2,3}$ = 3.4 Hz, $^3J_{3,4}$ = 10.0 Hz, 1 H, H-3), 5.27 (dd~t, $^3J_{3,4}$ = 10.0 Hz, $^3J_{4,5}$ = 10.0 Hz, 1 H, H-4), 5.23 (d, $^3J_{1,2}$ = 1.8 Hz, $^3J_{2,3}$ = 3.4 Hz, 1 H, H-2), 4.80 (d, $^3J_{1,2}$ = 1.8 Hz, 1 H, H-1), 4.28 (dd, $^3J_{5,6}$ = 5.4 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6), 4.12 (dd, $^3J_{5,6'}$ = 2.5 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6′), 3.98 (ddd, $^3J_{4,5}$ = 10.0 Hz, $^3J_{5,6}$ = 5.4 Hz, $^3J_{5,6'}$ = 2.5 Hz, 1 H, H-5), 3.69 (m_c, 1 H, man–OC*H*H), 3.46 (m_c, 1 H, man–OCH*H*), 3.28 (t, ^3J = 6.9 Hz, 2 H, CH_2N_3), 2.15, 2.10, 2.04, 2.00 (each s, each 3 H, 4 $COCH_3$), 1.63 (m_c, 4 H, man–OCH_2CH_2, CH_2N_3), 1.41 (m_c, 4 H, $CH_2CH_2CH_2CH_2N_3$).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.6, 170.1, 169.9, 169.7 (4 *C*OCH_3), 97.6 (C-1), 69.8 (C-2), 69.2 (C-3), 68.5 (C-5), 68.3 (man–OCH_2), 66.4 (C-4), 62.6 (C-6), 51.4 (CH_2N_3), 29.2, 28.8 ($CH_2CH_2CH_2CH_2CH_2CH_2N_3$), 26.5, 25.7 ($CH_2CH_2CH_2CH_2CH_2CH_2N_3$), 20.9, 20.7, 20.7, 20.7 (4 CO*C*H_3).

MALDI-TOF-MS: *m/z* [M + Na]$^+$ calcd for $C_{20}H_{31}N_3O_{10}$ + Na: 496.19; found: 496.28.

10-Azidodecyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (9)

To a solution of the bromide **7** (660 mg, 1.16 mmol) in anhyd DMF (10 mL) were added NaN_3 (379 mg, 5.83 mmol, 5 equiv) and Bu_4NBr (74 mg, 230 mmol, 0.2 equiv). The reaction mixture was stirred at 60 °C for 5 h and at r.t. overnight. Then, the mixture was poured into ice water (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the filtrate concentrated. The residue was purified by flash column chromatography (cyclohexane–EtOAc, 2:1) to give the title compound as a colorless syrup; yield: 520 mg (85%); R_f = 0.36 (cyclohexane–EtOAc, 2:1); $[\alpha]_D$ +43 (*c* 0.55, CH_2Cl_2).

IR (ATR): 2927 (s, C–H), 2094 (s, N_3), 1746 cm^{-1} (s, C=O).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.28 (d, $^3J_{2,3}$ = 3.4 Hz, $^3J_{3,4}$ = 10.0 Hz, 1 H, H-3), 3.21 (t, $^3J_{3,4}$ = 10.0 Hz, $^3J_{4,5}$ = 10.0 Hz, 1 H, H-4), 5.16 (dd, $^3J_{1,2}$ = 1.8 Hz, $^3J_{2,3}$ = 3.4 Hz, 1 H, H-2), 4.73 (d, $^3J_{1,2}$ = 1.8 Hz, 1 H, H-1), 4.21 (dd, $^3J_{5,6}$ = 5.2 Hz, $^3J_{6,6}$ = 12.6 Hz, 1 H, H-6) 4.04 (dd, $^3J_{5,6'}$ = 2.5 Hz, $^3J_{6,6'}$ = 12.6 Hz, 1 H, H-6′), 3.92 (ddd, $^3J_{5,6'}$ = 2.5 Hz, $^3J_{5,6}$ = 5.2 Hz, $^3J_{4,5}$ = 10.0 Hz, 1 H, H-5), 2.61 (dt, ^2J = 9.6 Hz, ^3J = 6.6 Hz, 1 H, man–OCH*H*), 3.57 (t, ^3J = 6.6 Hz, 2 H, CH_2N_3), 3.38 (dt, ^2J = 9.1 Hz, ^3J = 6.6 Hz, 1 H, man–OC*H*H), 2.09, 2.04, 1.98, 1.93 (each s, each 3 H, 4 $COCH_3$), 1.56–1.47 (m, 8 H, 4 CH_2), 1.31–1.19 (m, 8 H, 4 CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.7, 170.2, 170.0, 169.8 (4 *C*OCH_3), 97.6 (C-1), 69.8 (C-2), 69.2 (C-3), 68.6 (man–OCH_2), 68.4 (C-5), 66.3 (C-4), 62.5 (C-6), 51.5 (CH_2N_3), 30.0, 29.4, 29.4, 29.3, 29.2, 28.9, 26.1, 25.7 (8 CH_2), 21.0, 20.8, 20.8, 20.7 (4 CO*C*H_3).

HRESI-MS: *m/z* [M + Na]$^+$ calcd for $C_{24}H_{39}N_3O_{10}$ + Na: 552.2533; found: 552.2528.

6-Isothiocyanatohexyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (10)

To a solution of the azide **8** (363 mg, 0.767 mmol) in anhyd toluene (10 mL) were added CS_2 (1.99 mL, 40.0 mmol, 43 equiv) and $P(OEt)_3$ (530 μL, 3.07 mmol, 4 equiv) were added. The mixture was stirred for 8 h at 80 °C. Then, H_2O (15 mL) was added and the solution was kept at 4 °C for 12 h. After extraction with CH_2Cl_2 (3 × 20 mL), the organic phases were combined, dried ($MgSO_4$), filtered, and the filtrate was concentrated. The crude product was purified by column chromatography (cyclohexane–EtOAc, 3:2) to give the title compound as a colorless syrup; yield: 219 mg (58%); R_f = 0.34 (cyclohexane–EtOAc, 3:2); $[\alpha]_D$ +52 (*c* 0.31, CH_2Cl_2).

IR (ATR): 2098 (m, NCS), 1740 cm^{-1} (s, C=O).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.34 (dd, $^3J_{3,2}$ = 3.4 Hz, $^3J_{3,4}$ = 10.0 Hz, 1 H, H-3), 5.28 (t, $^3J_{3,4}$ = 10.0 Hz, $^3J_{4,5}$ = 10.0 Hz, 1 H, H-4), 5.23 (dd, $^3J_{1,2}$ = 1.8 Hz, $^3J_{2,3}$ = 3.4 Hz, 1 H, H-2), 4.80 (d, $^3J_{1,2}$ = 1.8 Hz, 1 H, H-1), 4.28 (dd, $^3J_{5,6}$ = 5.3 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6), 4.12 (dd, $^3J_{5,6'}$ = 2.5 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6′), 3.98 (ddd, $^3J_{4,5}$ = 10.0 Hz, $^3J_{5,6}$ = 5.3 Hz, $^3J_{5,6'}$ = 2.5 Hz, 1 H, H-5), 3.70 (td, ^3J = 6.4 Hz, ^2J = 9.7 Hz, 1 H, man–OC*H*H), 3.53 (t, ^3J = 6.5 Hz, 2 H, CH_2NCS), 3.46 (m_c, 1 H, man–OCH*H*), 2.16, 2.19, 2.10, 2.00 (each s, each 3 H, 4 $COCH_3$), 1.73, 1.64 (each m_c, each 2 H, 2 CH_2), 1.44 (m_c, 4 H, CH_2CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.6, 170.1, 169.9, 169.7 (4 *C*OCH_3), 105.7 (NCS), 97.6 (C-1), 69.7 (C-2), 69.1 (C-3), 68.5 (C-5), 68.2 (man–OCH_2), 66.3 (C-4), 62.6 (C-6), 45.0 (CH_2NCS), 29.8, 29.1 (2 $CH_2CH_2CH_2$), 26.4, 25.4 ($CH_2CH_2CH_2CH_2CH_2CH_2NCS$), 20.9, 20.7, 20.7, 20.7 (4 CO*C*H_3).

HRESI-MS: *m/z* [M + Na]$^+$ calcd for $C_{21}H_{31}NO_{10}S$ + Na: 512.1566; found: 512.1555.

10-Isothiocyanatodecyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (11)

To a solution of the azide **9** (500 mg, 0.944 mmol) in anhyd toluene (10 mL) were added CS_2 (2.45 mL, 40.6 mmol, 43 equiv) and $P(OEt)_3$ (658 μL, 3.78 mmol, 4 equiv). The mixture was stirred for 8 h at 80 °C. Then H_2O (15 mL) was added and the solution was kept at 4 °C for 12 h. After extraction with CH_2Cl_2 (3 × 20 mL), the organic phases were combined and dried ($MgSO_4$), filtered, and the filtrate was concentrated. The pure product was obtained after column chromatography (cyclohexane–EtOAc, 3:2) as a colorless syrup; yield: 286 mg (56%); R_f = 0.30 (cyclohexane–EtOAc, 3:2); $[\alpha]_D$ +31 (*c* 0.49, CH_2Cl_2).

IR (ATR): 2927 (s, C–H), 2093 (s, NCS), 1744 cm^{-1} (s, C=O).

^1H NMR (500 MHz, $CDCl_3$): δ = 5.28 (d, $^3J_{2,3}$ = 3.4 Hz, $^3J_{3,4}$ = 10.0 Hz, 1 H, H-3), 3.21 (t, $^3J_{3,4}$ = 10.0 Hz, $^3J_{4,5}$ = 10.0 Hz, 1 H, H-4), 5.17 (dd, $^3J_{1,2}$ = 1.7 Hz, $^3J_{2,3}$ = 3.4 Hz, 1 H, H-2), 4.73 (d, $^3J_{1,2}$ = 1.7 Hz, 1 H, H-1), 4.05 (dd, $^3J_{5,6}$ = 5.3 Hz, $^3J_{6,6}$ = 12.6 Hz, 1 H, H-6) 4.04 (dd, $^3J_{5,6'}$ = 2.4 Hz, $^3J_{6,6'}$ = 12.6 Hz, 1 H, H-6′), 3.2 (ddd, $^3J_{5,6'}$ = 2.4 Hz, $^3J_{5,6}$ = 5.3 Hz, $^3J_{4,5}$ = 10.0 Hz, 1 H, H-5), 2.60 (dt, ^2J = 9.6 Hz, ^3J = 6.6 Hz, 1 H, man–OC*H*H), 3.44 (t, ^3J = 6.6 Hz, 2 H, CH_2NCS), 3.38 (dt, ^2J = 9.1 Hz, ^3J = 6.6 Hz, 1 H, man–OCH*H*), 2.09, 2.04, 1.98, 1.93 (each s, each 3 H, 4 $COCH_3$), 1.63, 1.53, 1.35 (each m, each 2 H, 3 CH_2), 1.30–1.21 (m, 10 H, 5 CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.7, 170.2, 170.0, 169.8 (4 C=O), 163.5 (NCS), 97.6 (C-1), 69.8 (C-2), 69.2 (C-3), 68.6 (man–OCH_2), 68.4 (C-5), 66.3 (C-4), 62.5 (C-6), 45.1 (*C*H_2NCS), 29.9, 29.4, 29.3, 29.3, 29.2, 28.8, 26.5, 26.1 (8 CH_2), 20.9, 20.8, 20.7, 20.7 (4 CO*C*H_3).

HRESI-MS: *m*/*z* $[M + Na]^+$ calcd for $C_{25}H_{39}NO_{10}S$ + Na: 552.2192; found: 568.2187.

***N*-[2-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyloxy)ethyl]-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (17)**

The acetylated isothiocyanate **5** (115 mg, 0.266 mmol) was thiourea-bridged according to the general procedure. Column chromatography (EtOAc–MeOH, 30:1) gave the pure product as a colorless oil; yield: 141 mg (68%); R_f = 0.41 (EtOAc–MeOH, 30:1); $[\alpha]_D$ +23 (*c* 1.37, CH_2Cl_2).

IR (ATR): 2358 (s, N–H), 2102 (s, N_3), 1742 (s, C=O), 1078 cm^{-1} (s, C=S).

^1H NMR (600 MHz, $CDCl_3$): δ = 7.00 (br s, 1 H, NH), 6.88 (br s, 1 H, NH), 5.29 (m_c, 1 H, H-3), 5.26 (m_c, 1 H, H-4), 5.24 (dd, $^3J_{1,2}$ = 1.5 Hz, $^3J_{2,3}$ = 3.1 Hz, 1 H, H-2), 4.84 (d, $^3J_{1,2}$ = 1.5 Hz, 1 H, H-1), 4.27 (dd, $^3J_{5,6}$ = 5.4 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6), 4.13 (dd, $^3J_{5,6}$ = 2.4 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6′), 3.99 (m_c, 1 H, H-5), 3.95 (m_c, 1 H, *H*HCNHCS), 3.90 (m_c, 1 H, man–OC*H*H), 3.74–3.60 (m, 28 H, man–OCH*H*, H*H*CNHCS, SCNHCH_2, 6 CH_2OCH_2), 3.39 (t, ^3J = 5.1 Hz, 2 H, CH_2N_3), 2.15, 2.11, 2.05 1.98 (each s, each 3 H, 4 $COCH_3$).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 183.5 (C=S), 170.7, 170.0, 169.9, 169.6 (4 *C*OCH_3), 97.6 (H-1), 70.7–70.0 (CH_2O), 69.4 (C-2), 69.2 (C-3), 68.7 (C-5), 67.2 (man–OCH_2), 66.2 (C-4), 62.5 (C-6), 50.7 (CH_2N_3), 44.7, 44.0 (*C*H_2NHCSNH*C*H_2), 20.8, 20.8, 20.7, 20.6 (4 CO*C*H_3).

MALDI-TOF-MS: *m*/*z* $[M + Na]^+$ calcd for $C_{31}H_{53}N_5O_{16}S$ + Na: 806.31; found: 807.10.

***N*-[6-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyloxy)hexyl]-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (18)**

The isothiocyanate **10** (109 mg, 0.222 mmol) was thiourea-bridged as described in the general procedure. After column chromatography (EtOAc–MeOH, 30:1), the product was obtained as a colorless oil; yield: 117 mg (63%); R_f = 0.38 (EtOAc–MeOH, 30:1); $[\alpha]_D$ +23 (*c* 0.52, CH_2Cl_2).

IR (ATR): 2359 (s, N–H), 2103 (m, N_3), 1743 (s, C=O), 1080 cm^{-1} (s, C=S).

^1H NMR (500 MHz, $CDCl_3$): δ = 6.60 (br s, 1 H, NH), 6.51 (br s, 1 H, NH), 5.34 (dd, $^3J_{2,3}$ = 3.4 Hz, $^3J_{3,4}$ = 10.0 Hz, 1 H, H-3), 5.28 (t, ^3J = 10.0 Hz, 1 H, H-4), 5.23 (dd, $^3J_{1,2}$ = 1.8 Hz, $^3J_{2,3}$ = 3.4 Hz, 1 H, H-2), 4.79 (d, $^3J_{1,2}$ = 1.8 Hz, 1 H, H-1), 4.28 (dd, $^3J_{5,6}$ = 5.3 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6), 4.11 (dd, $^3J_{5,6'}$ = 2.5 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6′), 3.98 (ddd, $^3J_{4,5}$ = 10.0 Hz, $^3J_{5,6}$ = 2.5 Hz, $^3J_{6,6'}$ = 5.2 Hz, 1 H, H-5), 3.73–3.68 (m, 28 H, man–OC*H*H, *H*HCNHCS, CSNHCH_2, 6 CH_2OCH_2), 3.47–3.43 (m, 2 H, man–OCH*H*, H*H*CNHCS), 3.39 (t, ^3J = 5.1 Hz, 2 H, CH_2N_3), 2.16, 2.10, 2.05, 1.99 (each s, each 3 H, 4 $COCH_3$), 1.61 (m_c, 4 H, 2 $CH_2CH_2CH_2$), 1.39 (m_c, 4 H, man–$OCH_2CH_2CH_2CH_2CH_2CH_2CH_2$NHCS).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 182.8 (C=S), 170.6, 170.1, 169.9, 169.7 (4 *C*OCH_3), 97.5 (C-1), 70.7–70.0 (6 CH_2OCH_2), 69.7 (C-2), 69.2 (C-3), 68.6 (C-5), 68.4 (man–OCH_2), 66.3 (C-4), 62.5 (C-6), 50.7 (CH_2N_3), 44.7 (H_2*C*NHCS), 29.1, 29.0 (2 $CH_2CH_2CH_2$), 26.7, 25.9 (man–$OCH_2CH_2CH_2CH_2CH_2CH_2CH_2$NHCS), 20.9, 20.7, 20.7, 20.7 (4 CO*C*H_3).

MALDI-TOF-MS: *m*/*z* $[M + Na]^+$ calcd for $C_{35}H_{61}N_5O_{16}S$ + Na: 862.37; found: 862.22.

***N*-[10-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyloxy)decyl]-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (19)**

The acetylated isothiocyanate **11** (200 mg, 0.367 mmol) was treated according to the general procedure. After purification by column chromatography (EtOAc–MeOH; 30:1), the product was obtained as a colorless oil; yield: 165 mg (50%); R_f = 0.43 (EtOAc–MeOH, 30:1).

^1H NMR (600 MHz, $CDCl_3$): δ = 5.28 (dd, $^3J_{2,3}$ = 3.5 Hz, $^3J_{3,4}$ = 10.0 Hz, 1 H, H-3), 5.21 (dd, $^3J_{3,4}$ = 10.0 Hz, $^3J_{4,5}$ = 10.0 Hz, 1 H, H-4), 5.16 (dd, $^3J_{1,2}$ = 1.8 Hz, $^3J_{2,3}$ = 3.5 Hz, 1 H, H-2), 4.73 (d, $^3J_{1,2}$ = 1.8 Hz, 1 H, H-1), 4.22 (dd, $^3J_{5,6}$ = 5.3 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6), 4.13 (dd, $^3J_{5,6}$ = 2.4 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6′), 3.99 (ddd, $^3J_{5,6'}$ = 2.4 Hz $^3J_{5,6}$ = 5.3 Hz, $^3J_{4,5}$ = 10.0 Hz, 1 H, H-5), 3.63–3.53 (m, 28 H, man–OC*H*H, H*H*CNHCS, SCNHCH_2, 6 CH_2OCH_2), 3.37 (m_c, 2 H, *H*HCNHCS, 1 H, man–OCH*H*), 3.32 (t, ^3J = 5.1 Hz, 2 H, CH_2N_3), 2.09, 2.04, 1.98, 1.93 (each s, each 3 H, 4 $COCH_3$), 1.56–1.47 (m, 4 H, man–OCH_2CH_2, SCNHCH_2CH_2), 1.30–1.18 (m, 12 H, 6 CH_2).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 182.5 (C=S), 170.7, 170.1, 169.9, 169.8 (4 *C*OCH_3), 97.6 (H-1), 70.7–70.0 (6 CH_2OCH_2), 69.7 (C-2), 69.2 (C-3), 68.6 (man–OCH_2), 68.4 (C-5), 66.3 (C-4), 62.5 (C-6), 50.7 (CH_2N_3), 44.8 (*C*H_2NHCS), 29.5, 29.5, 29.4, 29.3, 29.2, 27.5, 27.0, 26.1 (8 CH_2), 20.9, 20.8, 20.8, 20.7 (4 CO*C*H_3).

HRESI-MS: *m*/*z* $[M + Na]^+$ calcd for $C_{39}H_{69}N_5O_{16}S$ + Na: 918.4358; found: 918.4352.

***N*-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (20)**

The acetylated isothiocyanate **12** (216 mg, 0.557 mmol) was thiourea-bridged according to the general procedure. Column chromatography (EtOAc–MeOH, 30:1) gave the pure product as a colorless oil; yield: 352 mg (85%); R_f = 0.40 (EtOAc–MeOH, 30:1).

IR (ATR): 2359 (s, N–H), 2104 (s, N_3), 1742 (s, C=O), 1048.7 cm^{-1} (s, C=S).

^1H NMR (500 MHz, $CDCl_3$): δ = 7.42 (br s, 1 H, NH), 7.32 (br s, 1 H, NH), 5.84 (br s, 1 H, H-1), 5.30–5.25 (m, 3 H, H-2, H-3, H-4), 4.33 (dd, $^3J_{5,6}$ = 5.2 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6), 4.13 (dd, $^3J_{5,6}$ = 2.3 Hz, $^3J_{6,6'}$ = 12.2 Hz, 1 H, H-6′), 4.02 (m, 1 H, H-5), 3.82 (m, 2 H, SCNHCH_2), 3.73–3.62 (m, 24 H, 6 CH_2OCH_2), 3.39 (t, ^3J = 5.1 Hz, 2 H, CH_2N_3), 2.16, 2.09, 2.05, 2.02 (each s, each 3 H, 4 $COCH_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 183.3 (C=S), 170.7, 169.9, 169.9, 169.5 (4 *C*OCH$_3$), 80.3 (C-1), 70.7–70.5 (6 CH_2OCH_2) 70.0 (C-5), 69.1 (C-3), 68.8 (C-2), 66.4 (C-4), 62.2 (C-6), 50.7 (CH_2N_3), 45.2 (SCNH*C*H$_2$), 20.8, 20.8, 20.7, 20.7 (4 CO*C*H$_3$).

HRESI-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{49}N_5O_{15}S$ + Na: 762.2844; found: 762.2869.

N-[4-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyloxy)phenyl]-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (21)

The NCS-functionalized mannoside **13** (120 mg, 250 μmol) was thiourea-bridged according to the general procedure. After purification by column chromatography (EtOAc–MeOH, 30:1), the product was obtained as a colorless oil; yield: 206 mg (99%); R_f = 0.39 (EtOAc–MeOH, 30:1); $[\alpha]_D$ +47 (*c* 0.62, CH_2Cl_2).

IR (ATR): 2358 (s, N–H), 2103 (s, N_3), 1744 (s, C=O), 1506 (m, C=C), 1085 cm^{-1} (m, C=S).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.98 (br s, 1 H, NH), 7.29 (d, ^3J = 8.8 Hz, 2 H_{arom}, Hx, Hx′), 7.10 (d, ^3J = 8.8 Hz, 2 H_{arom}, Hy, Hy′), 6.70 (br s, 1 H, NH), 5.54 (dd, $^3J_{2,3}$ = 3.5 Hz, $^3J_{3,4}$ = 10.0 Hz, 1 H, H-3), 5.49 (d, $^3J_{1,2}$ = 1.8 Hz, 1 H, H-1), 5.43 (dd, $^3J_{1,2}$ = 1.8 Hz, $^3J_{2,3}$ = 3.5 Hz, 1 H, 2-H), 5.38 (dd~t, $^3J_{3,4}$ = 10.0 Hz, $^3J_{4,5}$ = 10.0 Hz, 1 H, H-4), 4.29 (m_c, 1 H, H-6), 4.10 (m_c, 2 H, H-5, H-6′), 3.83 (br s, 2 H, CSNHC*H*$_2$), 3.60–3.58 (m, 24 H, 6 CH_2OCH_2), 3.37 (t, *J* = 5.2 Hz, 2 H, CH_2N_3), 2.20, 2.06, 2.05, 2.04 (each s, each 3 H, 4 $COCH_3$).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 181.5 (C=S), 170.5, 169.9, 169.9, 169.7 (4 *C*OCH$_3$), 153.9 (man–OC_{ar}), 142.8 (C_{ar}–NH), 126.6 (aryl-C_x), 117.4 (aryl-C_y), 96.1 (C-1), 70.7–70.0 (6 CH_2OCH_2), 69.3 (C-5), 69.3 (C-2), 68.8 (C-3), 65.9 (C-4), 62.1 (C-6), 50.7 (CH_2N_3), 44.9 (SCNH*C*H$_2$), 21.0, 20.8, 20.7, 20.7 (4 CO*C*H$_3$).

HRESI-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{35}H_{53}N_5O_{16}S$ + Na: 854.3106; found: 854.3162.

N-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (22)

Glycosyl isothiocyanate **14** (125 mg, 0.321 mmol) was thiourea-bridged as described in the general procedure. Column chromatography (EtOAc–MeOH, 30:1) gave the pure product as a colorless oil; yield: 213 mg (90%); R_f = 0.35 (EtOAc–MeOH, 30:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.47 (br s, 1 H, NH), 7.23 (br s, 1 H, NH), 5.89 (br s, 1 H, H-1), 5.32 (dd~t, $^3J_{2,3}$ = 9.4 Hz, $^3J_{3,4}$ = 9.4 Hz, 1 H, H-3), 5.07 (dd~t, *J* = 9.5 Hz, 1 H, H-4), 5.01 (dd~t, $^3J_{1,2}$ = 9.4 Hz, $^3J_{2,3}$ = 9.4 Hz, 1 H, H-2), 4.31 (dd, $^3J_{5,6}$ = 4.4 Hz, $^3J_{6,6'}$ = 12.4 Hz, 1 H, H-6), 4.09 (dd, $^3J_{5,6'}$ = 2.2 Hz, $^3J_{6,6'}$ = 12.4 Hz, 1 H, H-6′), 3.84 (ddd, $^3J_{4,5}$ = 10.1 Hz, $^3J_{5,6}$ = 4.4 Hz, $^3J_{5,6'}$ = 2.2 Hz, 1 H, H-5), 3.73–3.59 (m, 26 H, CSNHC*H*$_2$, 6 CH_2OCH_2), 3.39 (t, *J* = 5.2 Hz, 2 H, CH_2N_3), 2.06, 2.03, 2.03, 2.00 (each s, each 3 H, 4 $COCH_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 184.2 (C=S), 170.8, 169.8, 169.9, 169.6 (4 *C*OCH$_3$), 82.5 (C-1), 73.5 (C-3), 73.2 (C-5), 70.1 (C-2), 70.7–70.0 (6 CH_2OCH_2), 69.9 (NHCH$_2$), 68.4 (C-4), 61.8 (C-6), 50.7 (CH_2N_3), 20.7, 20.7, 20.7, 20.5 (4 CO*C*H$_3$).

MALDI-TOF-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{49}N_5O_{15}S$ + Na: 762.28; found: 763.45.

N-(2,2′,3,3′,4′,6,6′-Hepta-*O*-acetyl-β-D-maltosyl)-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (23)

The acetylated disaccharide **15** (100 mg, 148 mmol) was thiourea-bridged according to the general procedure. Column chromatography (cyclohexane–EtOAc, 1:5) gave the pure product as a colorless oil; yield: 77 mg (51%); R_f = 0.15 (cyclohexane–EtOAc, 1:5).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.32 (br, 1 H, NH), 7.10 (br, 1 H, NH), 5.82 (br, 1 H, H-1), 5.34–5.27 (m, 3 H, H-1′, H-3, H-3′), 4.99 (t, $^3J_{3,4}$ = 9.9 Hz, $^3J_{4,5}$ = 9.9 Hz, 1 H, H-4′), 4.81–4.77 (m, 2 H, H-2, H-2′), 4.36 (dd, $^3J_{5,6}$ = 2.3 Hz, $^3J_{6,6}$ = 12.1 Hz, 1 H, H-6a), 4.19 (dd, $^3J_{5,6'}$ = 4.2 Hz, $^3J_{6,6'}$ = 12.1 Hz, 1 H, H-6b), 4.14 (dd, $^3J_{5,6'}$ = 3.6 Hz, $^3J_{6,6'}$ = 12.5 Hz, 1 H, H-6a′), 3.98 (dd, $^3J_{5,6}$ = 2.3 Hz, $^3J_{6,6}$ = 12.5 Hz, 1 H, H-6b′), 3.93 (t, $^3J_{3,4}$ = 9.3 Hz, $^3J_{4,5}$ = 9.3 Hz, 1 H, H-4), 3.85 (m_c, 1 H, H-5), 3.77 (ddd, $^3J_{4,5}$ = 9.4 Hz, $^3J_{5,6}$ = 2.3 Hz, $^3J_{5,6'}$ = 3.6 Hz, 1 H, H-5′), 3.74–3.48 (m, 26 H, 6 CH_2OCH_2, CSNHC*H*$_2$), 3.31 (t, ^3J = 5.0 Hz, 2 H, CH_2N_3), 2.05, 2.03, 2.00, 2.96, 2.04, 1.93, 1.92 (each s, each 3 H, 7 $COCH_3$).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 184.1 (C=S), 170.7, 170.5, 170.5, 170.4, 169.8, 169.8, 169.7, 169.5 (7 *C*OCH$_3$), 95.5 (C-1′), 82.0 (C-1), 76.0 (C-3′), 73.5 (C-5′), 72.7 (C-4), 71.3 (C-2, C-2′), 70.6–70.0 (6 CH_2OCH_2, glc–OCH_2), 69.3 (C-3), 68.4 (C-5), 67.9 (C-4′), 62.9 (C-6), 61.7 (C-6′), 50.6 (CH_2N_3), 20.8, 20.8, 20.7, 20.7, 20.6, 20.6, 20.6 (7 CO*C*H$_3$).

MALDI-TOF-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{41}H_{65}N_5O_{23}S$ + Na: 1050.36; found: 1050.92.

N-(2,2′,3,3′,4′,6,6′-Hepta-*O*-acetyl-β-D-cellobiosyl)-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (24)

The acetylated isothiocyanate **16** (22.6 mg, 34.0 μmol) was thiourea-bridged according to the general procedure. After column chromatography (EtOAc–MeOH, 5:1), the compound was obtained as a colorless, amorphous solid; yield: 37 mg (99%); R_f = 0.58 (EtOAc–MeOH, 5:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.51 (br s, 1 H, NH), 7.10 (br s, 1 H, NH), 5.77 (br s, 1 H, H-1), 5.26 (t, $^3J_{2,3}$ = 8.6 Hz, $^3J_{3,4}$ = 8.6 Hz, 1 H, H-3), 5.12 (t, $^3J_{2,3}$ = 9.4 Hz, $^3J_{3,4}$ = 9.4 Hz, 1 H, H-3′), 5.06 (t, $^3J_{3,4}$ = 9.4 Hz, $^3J_{4,5}$ = 9.4 Hz, 1 H, H-4′), 4.92 (m_c, 2 H, H-2, H-2′), 4.49 (d, $^3J_{1,2}$ = 7.9 Hz, 1 H, H-1′), 4.46 (m_c, 1 H, H-6a), 4.35 (dd, $^3J_{5,6}$ = 4.2 Hz, $^3J_{6,6}$ = 12.4 Hz, 1 H, H-6b), 4.13 (dd, $^3J_{5,6'}$ = 4.2 Hz, $^3J_{6,6'}$ = 12.1 Hz, 1 H, H-6a′), 4.20 (dd, $^3J_{5,6'}$ = 2.0 Hz, $^3J_{6,6'}$ = 12.4 Hz, 1 H, H-6b′), 3.79–3.55 (m, 29 H, H-4, H-5, H-5′, 6 CH_2OCH_2, CSNHC*H*$_2$), 3.37 (t, ^3J = 5.0 Hz, 2 H, CH_2N_3), 2.09, 2.08, 2.02, 2.01, 2.00, 1.99, 1.97 (each s, each 3 H, 7 $COCH_3$).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 184.1 (C=S), 170.7, 170.5, 170.2, 170.2, 169.5, 169.3, 169.0 (7 *C*OCH$_3$), 100.5 (C-1), 82.2 (C-1′), 76.4 (C-4), 74.1 (C-5), 72.9 (C-3, C-3′), 71.9 (C-5′), 71.5 (C-2, C-2′), 70.8–69.8 (6 CH_2OCH_2), 67.8 (C-4′), 62.0 (C-6), 61.6 (C-6′), 50.6 (CH_2N_3), 20.9, 20.8, 20.7, 20.5 (7 CO*C*H$_3$).

MALDI-TOF-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{41}H_{65}N_5O_{23}S$ + Na: 1050.36; found: 1050.78.

N-[2-(α-D-Mannopyranosyloxy)ethyl]-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (25)

The acetylated mannoside **17** (80 mg, 102 μmol) was deprotected according to the general procedure to give a colorless oil; yield: 56 mg (90%); $[\alpha]_D$ +24 (*c* 0.75, MeOH).

IR (ATR): 3324 (br, O–H), 2918 (s, C–H), 2106 (s, N_3), 1087 cm^{-1} (s, C=S).

^{1}H NMR (600 MHz, CD_3OD): δ = 4.82 (d, $^3J_{1,2}$ = 1.6 Hz, 1 H, H-1), 3.89 (m_c, 1 H, H-6), 3.87 (dd, $^3J_{1,2}$ = 1.6 Hz, $^3J_{2,3}$ = 3.1 Hz, 1 H, H-2), 3.76–3.66 (m, 33 H, H-3, H-4, H-6′, man–OCH_2, man–OCH_2CH_2, 6 CH_2OCCH_2, CSNHC*H*$_2$), 3.58 (ddd, $^3J_{4,5}$ = 9.8 Hz, $^3J_{5,6}$ = 2.3 Hz, $^3J_{5,6'}$ = 5.9 Hz, 1 H, H-5), 3.42 (t, ^3J = 5.1 Hz, 2 H, CH_2N_3).

^{13}C NMR (150 MHz, CD_3OD): δ = 182.8 (C=S), 101.7 (C-1), 74.7 (C-5), 72.5 (C-3), 72.0 (C-2), 71.6–71.1 (6 CH_2OCH_2), 68.5 (C-4), 67.3 (man–OCH_2), 62.87 (C-6), 51.8 (CH_2N_3), 45.3, 45.2 (*C*H$_2$NHCS, SCNH*C*H$_2$).

HRESI-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{45}N_5O_{12}S$ + Na: 638.2678; found: 638.2701.

***N*-[6-(α-D-Mannopyranosyloxy)hexyl]-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (26)**

The acetylated mannoside **18** (226 mg, 269 μmol) was deprotected according to the general procedure. A colorless oil was obtained; yield: 178 mg (99%); $[\alpha]_D$ +29 (*c* 0.52, MeOH).

IR (ATR): 3314 (br, O–H), 2922 (s, C–H), 2104 (s, N_3), 1552 (s, N–H), 1077 cm^{-1} (s, C=S).

^{1}H NMR (600 MHz, CD_3OD): δ = 4.74 (d, $^3J_{1,2}$ = 1.7 Hz, 1 H, H-1), 3.82 (dd, $^3J_{5,6}$ = 2.4 Hz, $^3J_{6,6'}$ = 11.8Hz, 1 H, H-6), 3.79 (dd, $^3J_{1,2}$ = 1.7 Hz, $^3J_{2,3}$ = 3.4 Hz, 1 H, H-2), 3.71 (dd, $^3J_{5,6'}$ = 5.9 Hz, $^3J_{6,6'}$ = 11.8 Hz, 1 H, H-6′), 3.69–3.64 (m, 29 H, 6 CH_2OCH_2, SCNHCH_2, man–OCH_2, H-3), 3.61 (t, ^3J = 9.6 Hz, 2 H, CH_2NHCS) 3.51 (ddd, $^3J_{4,5}$ = 9.5 Hz, $^3J_{5,6}$ = 2.0 Hz, $^3J_{5,6'}$ = 6.0 Hz, 1 H, H-5), 3.51 (dd, $^3J_{3,4}$ = 6.2 Hz, $^3J_{4,5}$ = 9.5 Hz, 1 H, H-4), 3.40 (t, ^3J = 5.0 Hz, 2 H, CH_2N_3), 1.66–1.56 (m, 4 H, $CH_2CH_2CH_2CH_2$), 1.46–1.36 (m_c, 4 H, man–$OCH_2CH_2CH_2CH_2CH_2CH_2NHCS$).

^{13}C NMR (150 MHz, CD_3OD): δ = 170.4 (C=S), 101.6 (C-1), 75.1 (C-5), 73.1 (C-3), 72.7 (C-2), 72.0–71.2 (6 CH_2OCH_2), 69.1 (C-4), 68.9 (man–OCH_2), 63.4 (C-6), 52.2 (CH_2N_3), 44.6, 45.5 (CH_2NHCS, SCNHCH_2), 31.0, 28.2, 27.6 (4 CH_2).

HRESI-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{53}N_5O_{12}S$ + Na: 694.3304; found: 694.3299.

***N*-[10-(α-D-Mannopyranosyloxy)decyl]-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (27)**

The acetylated mannoside **19** (165 mg, 184 μmol) was deprotected according to the general procedure to give a colorless oil; yield: 105 mg (78%); $[\alpha]_D$ +32 (*c* 0.57, MeOH).

IR (ATR): 3330 (br, O–H), 2922 (s, C–H), 2102 (s, N_3), 1550 (s, N–H), 1083 cm^{-1} (C=S).

^{1}H NMR (500 MHz, CD_3OD): δ = 4.73 (d, $^3J_{1,2}$ = 1.6 Hz, 1 H, H-1), 3.82 (dd, $^3J_{5,6}$ = 2.4 Hz, $^3J_{6,6}$ = 11.7 Hz1 H,, H-6), 3.78 (dd, $^3J_{1,2}$ = 1.6 Hz, $^3J_{2,3}$ = 3.3 Hz, 1 H, H-2), 3.66–3.27 (m, 31 H, H-3, H-4, H-6′, man–OCH_2, 6 CH_2OCH_2, C*H*HNHCS, SCNHC*H*H), 3.52 (ddd, $^3J_{4,5}$ = 9.4 Hz, $^3J_{5,6}$ = 2.4 Hz, $^3J_{5,6'}$ = 5.7 Hz, 1 H, H-5), 3.44–3.40 (m, 2 H, C*H*HNHCS, SCNHC*H*H), 3.38 (t, ^3J = 4.9 Hz, 2 H, CH_2N_3), 1.52–1.44 (m, 4 H, 2 CH_2), 1.30–1.24 (m, 12 H, 6 CH_2).

^{13}C NMR (125 MHz, CD_3OD): δ = 183.7 (C=S), 102.0 (C-1), 75.0 (C-2), 73.1, 72.7 (C-3, C-5), 72.1–71.2 (6 CH_2OCH_2), 69.1 (C-4), 69.0 (man–OCH_2), 63.4 (C-6), 52.2 (CH_2N_3), 45.7, 45.5 (CH_2NHCS, SCNHCH_2), 31.1, 31.1, 31.0, 30.7, 28.4, 27.8 (8 CH_2).

HRESI-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{61}N_5O_{12}S$ + Na: 750.3930; found: 750.3969.

***N*-(α-D-Mannopyranosyl)-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (28)**

The acetylated derivative **20** (116 mg, 0.157 mmol) was deprotected according to the general procedure to give a colorless oil; yield: 83.0 mg (93%); $[\alpha]_D$ +4 (*c* 1.45, MeOH).

IR (ATR): 3297 (br, O–H), 2359 (s, N–H), 2094 (N_3), 1069 cm^{-1} (C=S).

^{1}H NMR (600 MHz, CD_3OD): δ = 5.65 (br s, 1 H, H-1), 3.89 (dd, $^3J_{5,6}$ = 2.3 Hz, $^3J_{6,6'}$ = 11.8 Hz, 1 H, H-6), 3.86 (br s, 1 H, H-2), 3.76 (m_c, 2 H, NHCH_2), 3.73–3.63 (m, 25 H, H-6′, 6 CH_2OCH_2), 3.55 (m_c, 2 H, H-3, H-4), 3.40 (t, ^3J = 5.0 Hz, 2 H, CH_2N_3), 3.32 (m, 1 H, H-5).

^{13}C NMR (150 MHz, CD_3OD): δ = 184.6 (C=S), 83.2 (C-1), 79.6 (C-5), 75.8 (C-3), 72.4 (C-2), 71.6–70.8 (6 CH_2OCH_2), 68.3 (C-4), 63.0 (C-6), 51.8 (CH_2N_3), 45.7 (SCNHCH_2).

HRESI-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{41}N_5O_{11}S$ + Na: 594.2421; found: 594.2416.

***N*-[4-(α-D-Mannopyranosyloxy)phenyl]-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (29)**

Mannoside **21** (300 mg, 361 μmol) was deprotected according to the general procedure. A colorless oil was obtained; yield: 240 mg (quant); $[\alpha]_D$ +76 (*c* 0.89, MeOH).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.17 (d, ^3J = 8.6 Hz, 2 H_{arom}, Hx, Hx′), 7.98 (d, ^3J = 8.6 Hz, 2 H_{arom}, Hy, Hy′), 5.46 (br s, 1 H, H-1), 4.06 (br, 1 H, H-2), 3.96 (dd, $^3J_{2,3}$ = 2.6 Hz, $^3J_{3,4}$ = 9.9 Hz, 1 H, H-3), 3.88 (m_c, 1 H, H-6), 3.76 (m_c, 2 H, NHCH_2), 3.66–3.55 (m, 27 H, H-4, H-5, H-6′, 6 CH_2OCH_2), 3.36 (t, ^3J = 5.1 Hz, 2 H, CH_2N_3).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 181.2 (C=S), 154.5 (man–OC_{ar}), 132.3 (C_{ar}–NH), 126.6 (aryl-C_x), 117.2 (aryl-C_y), 98.5 (C-1), 73.2 (C-5), 71.3 (C-3), 70.6–70.0 (6 CH_2OCH_2), 70.2 (C-2), 69.5 (C-4), 61.1 (C-6), 50.7 (CH_2N_3), 45.0 (SCNHCH_2).

HRESI-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{45}N_5O_{12}S$ + Na: 686.2683; found: 686.2678.

***N*-(β-D-Glucopyranosyl)-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (30)**

Thiourea derivative **22** (37 mg, 0.186 mmol) was deprotected as described in the general procedure to obtain the title compound as colorless oil; yield: quant; $[\alpha]_D$ –3 (*c* 0.81, MeOH).

IR (ATR): 3325 (br, O–H), 2341 (s, N–H), 2100 (s, N_3), 1073 cm^{-1} (s, C=S).

^{1}H NMR (500 MHz, CD_3OD): δ = 5.29 (br s, 1 H, H-1), 3.89 (dd, $^3J_{5,6}$ = 2.3 Hz, $^3J_{6,6'}$ = 12.0 Hz, 1 H, H-6), 3.81 (br s, 2 H, NHCH_2), 3.73–3.67 (m, 25 H, H-6′, 6 CH_2OCH_2), 3.48–3.40 (m, 4 H, H-3, H-5, CH_2N_3), 3.36–3.31 (m, 2 H, H-2, H-4).

^{13}C NMR (125 MHz, CD_3OD): δ = 185.5 (C=S), 85.0 (C-1), 79.2 (C-5), 78.9 (C-3), 74.2 (C-2), 71.0 (C-4), 71.5–70.3 (6 CH_2OCH_2), 62.8 (C-6), 51.8 (CH_2N_3), 45.5 (SCNHCH_2).

HRESI-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{41}N_5O_{11}S$ + Na: 594.2421; found: 594.2416.

***N*-[β-D-Maltosyl]-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (31)**

The acetylated disaccharide **23** (72 mg, 0.068 mmol) was deprotected according to the general procedure to give a colorless oil; yield: 49 mg (99%); $[\alpha]_D$ +37 (*c* 0.10, MeOH).

IR (ATR): 3314 (br, O–H), 2872 (s, C–H), 2104 (s, N_3), 1549 (s, N_3), 1072 cm^{-1} (s, C=S).

^{1}H NMR (600 MHz, CD_3OD): δ = 5.22 (d, $^3J_{1,2}$ = 3.8 Hz, 1 H, H-1), 3.91 (dd, $^3J_{5,6}$ = 1.9 Hz, $^3J_{6,6'}$ = 12.3 Hz, 1 H, H-6a), 3.89 (dd, $^3J_{5,6}$ = 1.8 Hz, $^3J_{6,6'}$ = 12.4 Hz, 1 H, H-6a′), 3.84 (dd, $^3J_{5,6}$ = 4.5 Hz, $^3J_{6,6'}$ = 12.3 Hz, 1 H, H-6b), 3.82–3.78 (m, 2 H, SCNHCH_2), 3.75–3.59 (m, 29 H, 6 CH_2OCH_2, H-3, H-3′, H-2′, H-5′, H-6b′), 3.59 (t, $^3J_{3,4}$ = 9.3 Hz, $^3J_{4,5}$ = 9.3 Hz, 1 H, H-4), 3.51–3.49 (m, 2 H, H-2, H-5), 3.42 (t, ^3J = 5.0 Hz, 2 H, CH_2N_3), 3.32 (t, $^3J_{3,4}$ = 9.3 Hz, $^3J_{4,5}$ = 9.3 Hz, 1 H, H-4′).

^{13}C NMR (150 MHz, CD_3OD): δ = 185.6 (C=S), 102.8 (C-1), 81.0 (C-4), 78.7 (C-5′), 77.8 (C-5), 77.7, 74.7 (C-3, C-3′), 74.1 (C-2), 73.8 (C-2′), 71.6–70.2 (6 CH_2OCH_2), 71.1 (C-4′), 63.0 (C-6), 62.2 (C-6′) 51.8 (CH_2N_3), 45.6 (SCNHCH_2).

HRESI-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{51}N_5O_{16}S$ + Na: 756.2944; found: 756.2944.

***N*-(β-D-Cellobiosyl)-*N*′-[ω-azidohexa(ethylene glycol)] Thiourea (32)**

The acetylated disaccharide **24** (37 mg, 0.033 mmol) was deprotected according to the general procedure to give a colorless oil; yield: 19 mg (82%); $[\alpha]_D$ +36 (*c* 0.31, MeOH).

IR (ATR): 3312 (br, O–H), 2920 (s, C–H), 2108 (s, N_3), 1549 (w, N–H), 1073 cm^{-1} (s, C=S).

^{1}H NMR (600 MHz, CD_3OD): δ = 4.46 (d, $^3J_{1,2}$ = 7.8 Hz, 1 H, H-1), 3.95–9.91 (m, 2 H, H-6a, H-6a′), 3.89 (dd, $^3J_{5,6}$ = 3.9 Hz, $^3J_{6,6'}$ = 12.0 Hz, 1 H, H-6b), 3.73–3.60 (m, 31 H, 6 CH_2OCH_2, $SCNHCH_2$, H-6b′, H-5′, H-4, H-4′, H-3), 3.42 (m~t, 2 H, CH_2N_3), 3.40–3.37 (m, 2 H, H-5, H-3′), 3.28 (dd, $^3J_{1,2}$ = 7.8 Hz, $^3J_{2,3}$ = 9.2 Hz, 1 H, H-2).

^{13}C NMR (150 MHz, CD_3OD): δ = 185.7 (C = S), 108.3 (C-1′), 80.6 (C-5′), 78.2 (C-3′), 78.1, 77.9, 77.9, 77.7, 77.4 (C-2, C-3, C-4, C-4′, C-5), 74.9 (C-2′), 71.62–71.1 (6 CH_2OCH_2, $SCNHCH_2$), 62.5 (C-6), 61.9 (C-6), 51.8 (CH_2N_3).

MALDI-TOF-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{51}N_5O_{16}S$ + Na: 756.29; found: 756.71.

_N_-[4-(α-D-Mannopyranosyloxy)phenyl]-_N′_-[4-decyl-1_H_-1,2,3-triazol-1-ylhexa(ethylene glycolyl)] Thiourea (33)

Azide **29** (38 mg, 58 μmol) and dodec-1-yne (25.0 μL, 116 μmol) were dissolved in degassed MeCN (10 mL). After flushing with N_2, CuI (2.2 mg, 12 μmol, 0.2 equiv) was added and the reaction mixture warmed up to 70 °C for 18 h. After removing the solvent, the residue was purified by flash column chromatography (CH_2Cl_2–MeOH, 5:1). The triazole **33** was obtained as light yellow oil; yield: 40 mg (86%); R_f = 0.52 (CH_2Cl_2–MeOH, 5:1).

^{1}H NMR (500 MHz, CD_3OD): δ = 7.77 (s, 1 H, HC=), 7.26 (d, ^3J = 8.8 Hz, 2 H_{arom}, Hx, Hx′), 7.13 (d, ^3J = 8.8 Hz, 2 H_{arom}, Hy, Hy′), 5.46 (d, $^3J_{1,2}$ = 1.8 Hz, 1 H, H-1), 4.53 (t, ^3J = 4.8 Hz, 2 H, $SCNHCH_2$), 4.01 (dd, $^3J_{1,2}$ = 1.8 Hz, $^3J_{2,3'}$ = 3.4 Hz, 1 H, H-2), 3.90–3.86 (m, 3 H, H-3, $SCNHCH_2CH_2$), 3.78–3.69 (m, 5 H, H-4, H-6, H-6′, CH_2–$C_{triazole}$), 3.66–3.57 (m, 23 H, H-5, OCH_2, 5 CH_2OCH_2), 2.68 (t, ^3J = 7.6 Hz, 2 H, $C_{triazole}$–CH_2), 1.66 (m, 2 H, $C_{triazole}$–CH_2CH_2), 1.34–1.29 (m, 12 H, 6 CH_2), 0.89 (t, ^3J = 7.0 Hz, 3 H, CH_3).

^{13}C NMR (125 MHz, CD_3OD): δ = 182.5 (C=S), 156.0 (man–OC_{ar}), 149.1 (C_{ar}–NH), 133.8 ($C_{triazole}$), 127.6 (aryl-C_x), 124.0 ($CH_{triazole}$), 118.5 (aryl-C_y), 100.4 (C-1), 75.5 (C-5), 72.4 (C-3), 71.9 (C-2), 71.6–70.5 (6 CH_2OCH_2), 68.3 (C-4), 62.7 (C-6), 51.3 ($SCNHCH_2$), 45.5 ($CH_2C_{triazole}$), 33.1 ($C_{triazole}$–CH_2CH_2), 30.7, 30.7, 30.6, 30.5, 30.5, 30.3 (6 $CH_2CH_2CH_2$), 26.3 ($C_{triazole}$–CH_2), 23.8 (CH_2), 17.5 (CH_2CH_3).

MALDI-TOF-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{39}H_{67}N_5O_{13}S$ + Na: 836.46; found: 836.82.

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