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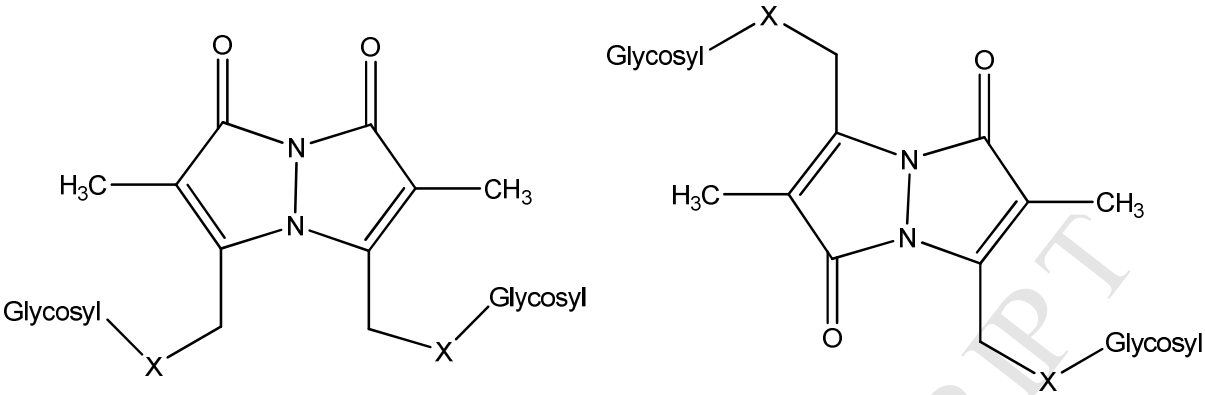

X = S, Se, SS, 1,2,3-triazole

Bivalent glycoconjugates based on 1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione ("bimane") as a central scaffold.

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Keywords:

heteroaromatics, fluorescence, thioglycoside, selenoglycoside, disulfide, 1,2,3-triazole, X-ray structures

Declerations of interest: none.

Abstract

The heteroaromatic fused diazabicyclic "bimane" ring system, discovered four decades ago, is endowed with remarkable chemical and photophysical properties. No carbohydrate derivatives of bimanes have, however,been described thus far. Here we report on the syntheses of a range of bimanes decorated with various glycosyl residues. Mono- and disaccharide residues were attached to *syn*- or *anti*-bimane central cores via thio-, disulfido- or selenoglycosidic linkages to obtain novel fluorescent or nonfluorescent glycoconjugates. Cu(I)-catalyzed cycloaddition of glycosyl azides to a bimane diethynyl derivative furnished further bivalent glycoconjugates with sugar residues linked to the central bimane core via 1,2,3-triazole rings. We have determined the crystal and molecular structures of several glycosylated and non-glycosylated bimanes and report fluorescence data for the new compounds.

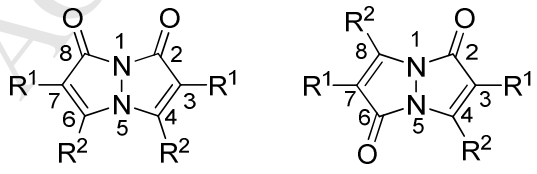
1. Introduction

Cell surface-presented glycans are targets of molecular recognition events in a wide array of physiological processes. Binding of proteins with carbohydrate-recognition domains, such as lectins, to glycan chains anchored to the cell wall play pivotal roles in intracellular signaling, cell-cell-, or cell-extracellular matrix interactions (for recent reviews see references [1,2]). Small molecular weight oligo/multivalent glycoconjugates were often found instrumental to model the glycan partner in experimental settings under *in vitro* conditions [3]. Compounds displaying promising activity in these preliminary tests then qualify them to be carried over to further assays of increasing physiological relevance such as inhibition of lectin binding to cultured cells or histochemical assays in fixed animal tissue sections [4]. Although lectins are exempt of enzymic activity, as a rule (exceptions exist), *O*-glycosidic bonds in lectin-directed glycoconjugates are, however, frequently replaced by non-hydrolyzable (thio-, disulfido- or selenoglycosidic) linkages. This may be regarded as a prudential measure to avoid inhibitor deactivation by glycan hydrolases or other carbohydrate processing enzymes that may be present in complex biological systems used for testing lectin inhibition activities.

A novel class of carbohydrate structures designed along this principle, diglycosyl disulfides and disulfidoglycosides (for a review see reference [5]), received attention recently for their various biological activities. Symmetric diglycosyl disulfides, as one of the first platforms in this line, were found to display lectin inhibition activities in solid phase tests and in tumor cell lines [6,7]. Some oligovalent derivatives featuring mannosyl moieties attached

to benzene central cores by disulfide linkages were shown to bind to concanavalin A with affinities surpassing that of the cognate sugar [8]. Remarkable inhibitory activities against *Trypanosoma cruzi*, the etiologic agent of Chagas's disease, were recorded *in vitro* for similar structures with galacto configurations [9]. Further glycoconjugates with galactose or lactose moieties attached to central naphthalene scaffolds proved to inhibit the binding of a plant agglutinin and different human galectins to tumor cell lines, this bioactivity being preserved when tested in animal tissue sections as well [4]. Exploring the scope for potential biorelevance of sugar mimetics with the glycosidic oxygen substituted with another VIth column heteroatom, selenium, di-*β*-D-galactopyranosyl selenide and -diselenide have been identified to display lectin inhibition efficiency comparable to that of their thio analogs [10]. On the other hand, we have recently observed significant growth inhibiton efficiency of symmetric diglycosyl diselenides against *T. brucei* species, the parasite causing African sleeping sickness [11]. As a further extension of the palette of three-bond interglyosidic connections with two non-oxygen heteroatoms (for a review see reference [5]) we have recently introduced the disulfide analog selenosulfide linkage which is of rare occurrence in carbohydrate chemistry [12].

Building upon various biological activities discussed above we have set out to explore novel glycoconjugates with a central heteroaromatic core called "bimane". Here we wish to report on the syntheses and properties of bivalent glycosyl derivatives based on this remarkable heterocyclic skeleton. The beautifully symmetric heterocyclic ring system, 1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (bimane) was discovered, after some preliminary attempts, by E.M. Kosower et al. in 1978 [13]; an alternative synthesis being reported just recently [14]. Bimanes are fluorescent molecules, the *syn* isomers displaying much stronger effects than the *anti* forms (see Chart 1) [15]. The latter show, on the other hand, low temperature phosphorescence [16,17].



syn-(R_2,R_1)B *anti*-(R_2,R_1)B

Chart 1. *Syn* and *anti* forms of substituted bimanes labeled using the shorthand notation introduced by Kosower et al. [13]

Bimane fluorophores are extensively used in biophysical studies such as for monitoring conformational changes, motions and interactions in proteins [18-21]. We have envisioned that glycoconjugates endowed with fluorescent properties might be further exploited to explore potential interactions with cells or higher organisms. (see, e.g. references [22,23]). Another motivation for our studies was provided by the observation of antiparasitic activity of certain bimane derivatives [24]. Finally, while sugars are vital components of all biosystems and displaying a large variety of biological activities, to some surprise, no carbohydrate derivatives of bimanes have been described thus far to the best of our knowledge.

Haloalkyl-bimanes like the s*yn* and *anti* forms of dibromobimane (**DBB**) derivatives **1a** and **1b** [15] (Chart 2) are reactive species and reactions with thiols are of interest, in particular, for fluorescent labeling in biological systems [18-21].

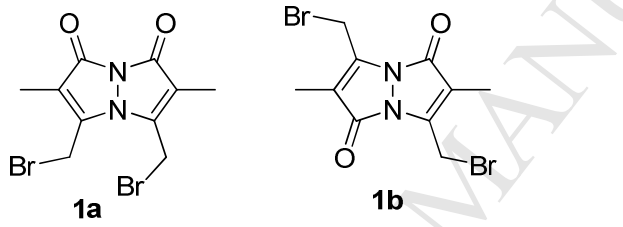
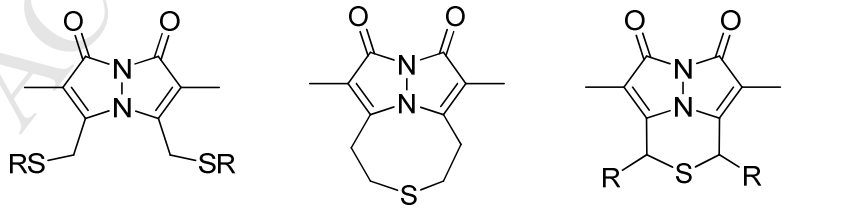


Chart 2. Structures of *syn*-(CH_2Br,CH_3)B (**1a**) and *anti*-(CH_2Br,CH_3)B (**1b**)

Bis-thioether derivatives were obtained in smooth reactions of **DBB** with aliphatic/aromatic thiols, as well as with cysteine [22], substituted cysteines [25] or glutathione [22,26]. Formation of thia-bridged derivatives (Chart 3) as minor side products have also been observed in the reactions with thiols [22,27], with sodium sulfide [27] or H_2S [22].



syn-(RS,CH_3)B[21]

μ-(2-S-trimethylene)-*syn*-(CH_2,CH_3)B[27]

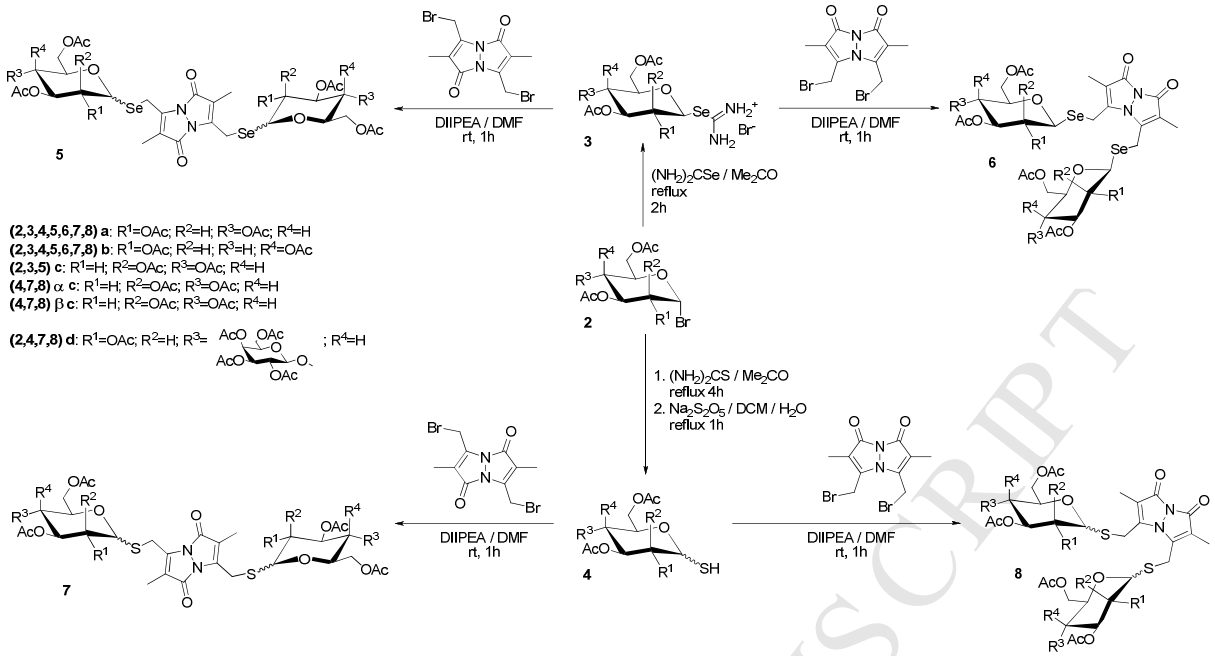
μ-(S)-*syn*-(R,CH_3)B[26]

Chart 3. Bimane thioethers described previously

These reactions have been proposed for the purpose of quantification of glutathione [28], sulfide- or thiol levels or H_2S [22] in physiological concentrations. It is to be noticed that reaction of monochlorobimane (*syn*-(CH_2Cl,Me)B) with selenocysteine did not result in the expected selenoether derivative, *syn*-(Me,Me)bimane was obtained instead via reduction of the CH_2Cl group by Se-cysteine [29].

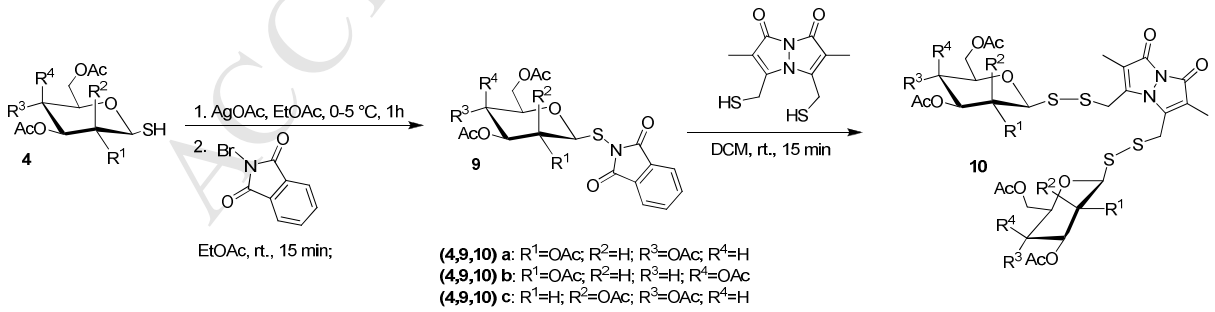
2. Results and Discussion

Dibromobimanes **1a** and **1b** (Chart 2) were found to be suitable starting compounds for the attachment of glycosyl residues to the bimane skeleton. First we have explored reactions of **1a** and **1b** with per-*O*-acetylated glycosyl thiols **4a,b,αc,βc,d** and observed the formation of bis-thioglycosylated bimanes in *syn* (**8a,b,αc,βc,d**) and *anti* forms (**7a,b,αc,βc,d**), respectively, under mild conditions and in good yields (Scheme 1 and Table 1). Reactions with *syn*- and *anti* **DBB (1a, 1b)** occurred with retention of the anomeric configurations of the starting thiols to provide β-glycosylated derivatives as ascertained trivially by the $J_{H1,H2}$ values for the gluco- (**7a, 8a**), galacto- (**7b, 8b**) or lacto (**7d, 8d**) configurations (see Experimental). Availability of mannosyl thiols in both anomeric configurations, α (**4αc**) and β (**4βc**) [30], enabled the preparation of both α and β thioglycosides (**7,8αc** and **7,8βc**, respectively). In these cases the anomeric configurations were deduced from NOESY spectra wherein the presence of crosspeaks between H1/H3 and H1/H5 of the mannosyl moiety clearly indicated β configurations for **7,8βc** whereas such crosspeaks were missing from the spectra of **7,8αc.** ^{1}H chemical shifts of H-5 were, furthermore, found highly diagnostic for the assignment of anomeric configurations of thiomannosides as values for α-anomers are ~ 0.5 ppm larger than those measured in the β-counterparts (see Experimental). Selenoglycosides cannot be prepared in analogy with glycosyl thiols because of the known instability of the corresponding glycosyl selenols [31]. On the other hand, selenoglycosides **6a,b** and **5a,b,c**, respectively, were readily obtained from **1a, 1b** using per-*O*-acetylated glycosyl *iso*selenuronium salts **3a,b,c** as glycosyl-selenenol equivalents following a procedure we have previously described [32] (Scheme 1 and Table 1).



Scheme 1. Syntheses of glycosylated bimanes with thio- or selenoglycoside linkages

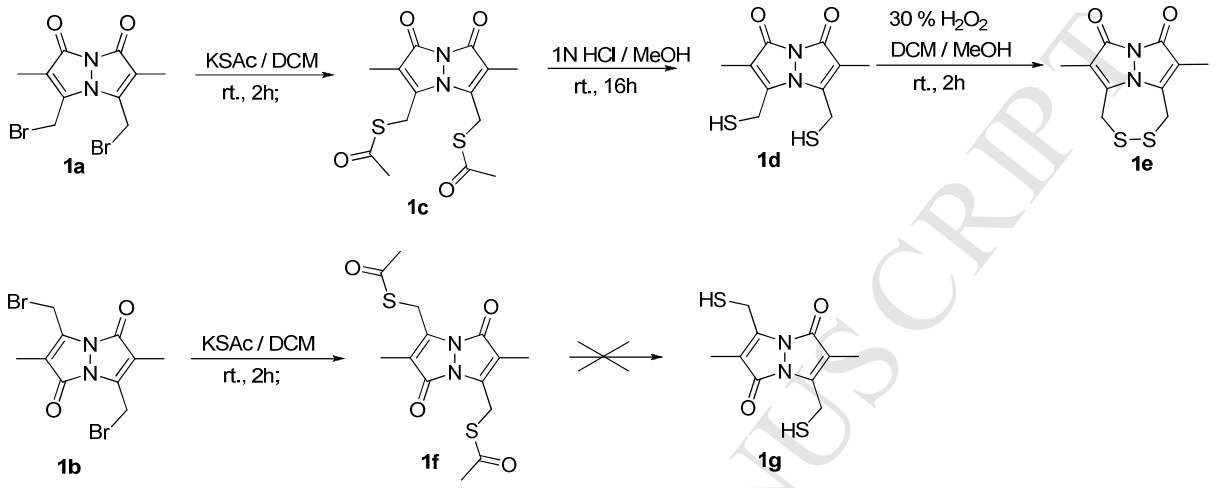
In view of the versatile activities of carbohydrate molecules with disulfide glycosidic linkages observed in interactions with systems of increasing biorelevance [4] we have set out to prepare glycosylated bimanes featuring this type of glycosidic bond. Of the several methods/approaches available to synthesize unsymmetrical disulfides in general [33] and in sugar chemistry, in particular [5,34-37], we have chosen to take advantage of the glycosylsulfenyl-transfer properties of glycosyl sulfenamides (**9**) in reactions with thiols [36]. Indeed, reactions of *syn*-(CH_2SH,CH_3)B (**1d**) with the appropriate *N*-phthalyl-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-glycopyranosyl)sulfonamides [36] furnished the desired bis(glycopyranosyl-dithio) bimane derivatives **10a-c** (Scheme 2, Table 1).



Scheme 2. Syntheses of bis(glycopyranosyl-dithio)bimanes

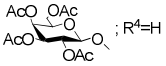
The required *syn*-(CH_2SH,CH_3)B (**1d**) was obtained from **1a** via reaction with potassium thiolacetate followed by acidic deacetylation. No *anti*-thiol (**1g**) could, however, be obtained

from **1b** as treatment of the thiolacetate **1f** with HCl/MeOH resulted in, surprisingly, total decomposition with the formation of polymeric products. Attempted deacetylation of **1f** under basic conditions (ammonia, LiOH) led to similar result. On the other hand, we have observed the formation of internal disulfide **1e** upon oxidation of **1d** with H_2O_2 (Scheme 3, Table 1).



Scheme 3. Reactions to obtain bimane thiols from **DBB**

As a further option to attach glycosyl moieties to the bimane skeleton we have explored approaches by taking advantage of the Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC, "click") reaction (for a review of applications in carbohydrate chemistry, see reference [38]) for this purpose. We have selected the bimane diacetylene derivative **1h** [39] for reactions with glycosyl azides **12a,b,c,d** under "click" conditions and, to our satisfaction, 3,7-disubstituted bimane triazole derivatives **13a,b,c,d** could be obtained in moderate to good yields (Scheme 4 and Table 1).

(12,13) a: R^1=OAc; R^2=H; R^3=OAc; R^4=H
(12,13) b: R^1=OAc; R^2=H; R^3=H; R^4=OAc
(12,13) c: R^1=H; R^2=OAc; R^3=OAc; R^4=H
(12,13) d: R^1=OAc; R^2=H; R^3=  ; R^4=H

Scheme 4. Syntheses of glycosylated bimane triazole derivatives

Table 1. List of the new synthesized compounds

Entry	Compound	Structure*		Yield (%)
		syn / anti	(R_2,R_1)B	
1.	**1c**	*syn*	(CH_2SAc,CH_3)B	62
2.	**1d**	*syn*	(CH_2SH,CH_3)B	87
3.	**1e**	*syn*	(CH_2S*,CH_3)B	63
4.	**1f**	*anti*	(CH_2SAc,CH_3)B	85
5.	**5a**	*anti*	(CH_2Se-β-$GlcAc_4$,CH_3)B	83
6.	**5b**	*anti*	(CH_2Se-β-$GalAc_4$,CH_3)B	59
7.	**5c**	*anti*	(CH_2Se-β-$ManAc_4$,CH_3)B	64
8.	**6a**	*syn*	(CH_2Se-β-$GlcAc_4$,CH_3)B	62
9.	**6b**	*syn*	(CH_2Se-β-$GalAc_4$,CH_3)B	68
10.	**7a**	*anti*	(CH_2S-β-$GlcAc_4$,CH_3)B	80
11.	**7b**	*anti*	(CH_2S-β-$GalAc_4$,CH_3)B	84
12.	**7βc**	*anti*	(CH_2S-β-$ManAc_4$,CH_3)B	98
13.	**7αc**	*anti*	(CH_2S-α-$ManAc_4$,CH_3)B	77
14.	**7d**	*anti*	(CH_2S-β-$LacAc_7$,CH_3)B	95
15.	**8a**	*syn*	(CH_2S-β-$GlcAc_4$,CH_3)B	86
16.	**8b**	*syn*	(CH_2S-β-$GalAc_4$,CH_3)B	77
17.	**8βc**	*syn*	(CH_2S-β-$ManAc_4$,CH_3)B	73
18.	**8αc**	*syn*	(CH_2S-α-$ManAc_4$,CH_3)B	21
19.	**8d**	*syn*	(CH_2S-β-$LacAc_7$,CH_3)B	90
20.	**10a**	*syn*	(CH_2S_2-β-$GlcAc_4$,CH_3)B	81
21.	**10b**	*syn*	(CH_2S_2-β-$GalAc_4$,CH_3)B	71
22.	**10βc**	*syn*	(CH_2S_2-β-$ManAc_4$,CH_3)B	11
23.	**13a**	*syn*	(CH_3,TA-β-$GlcAc_4$)B	97
24.	**13b**	*syn*	(CH_3,TA-β-$GalAc_4$)B	57
25.	**13c**	*syn*	(CH_3,TA-β-$ManAc_4$)B	60
26.	**13d**	*syn*	(CH_3,TA-β-$LacAc_7$)B	57

* For the notation see Experimental

Of the new compounds the structures of glycosylated and non-glycosylated derivatives have been confirmed by crystallographic analyses. For ORTEP views of structures **1c** and **1d** (Figure S1) as well as for details of structure determination and refinement see Supplementary Information (Table S1). **1e** (Figure 1) represents the first example of a bimane structure with an intramolecular disulfide incorporated into a seven-membered ring anellated to the bimane skeleton.

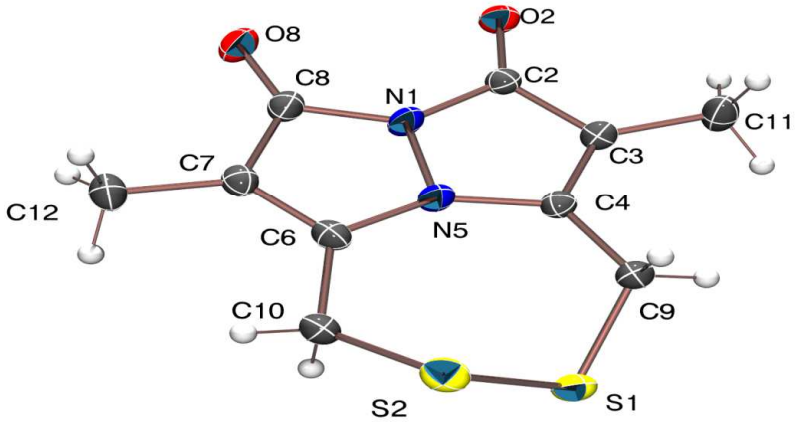


Figure 1. ORTEP View of **1e** at 50% probability level.

In case of **7a** (Figure 2) one half of the molecule occupies the asymmetric unit and the other half is given by a twofold screw axis. For **1c**, **1e** and **8a** (Figure 3) two independent molecules could be found in the asymmetric unit with small conformational differences (Figure S2). Figure 4 shows the molecular structure of triazole derivative **13c**.

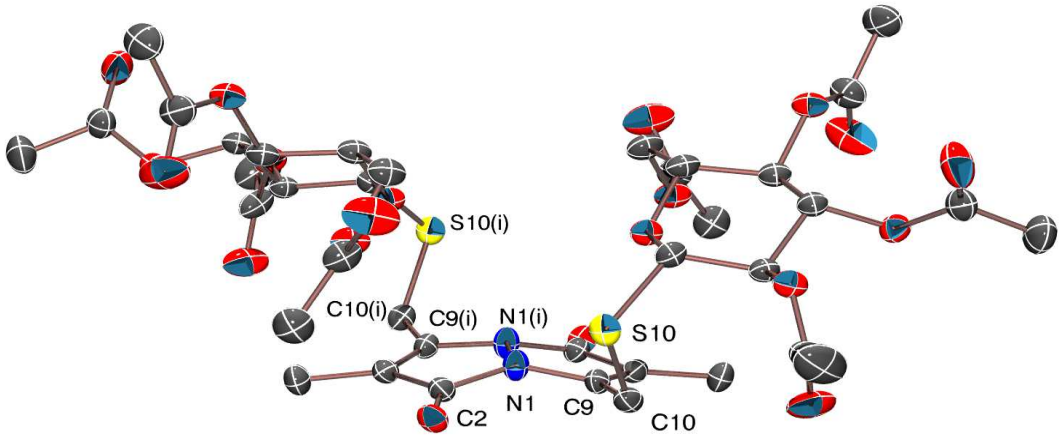


Figure 2. ORTEP view of **7a** at 30% probability level with partial numbering scheme. Hydrogen atoms are omitted for clarity. Symmetry code (i): -y+1, -x+1, -z+3/2.

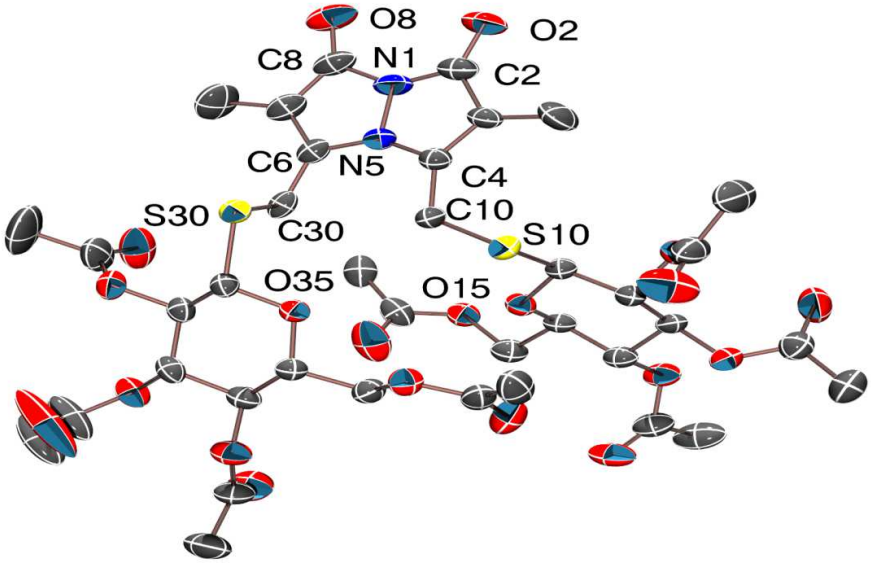


Figure 3. ORTEP view of **8a** with partial numbering scheme at 50 % probability level. Hydrogen atoms are omitted for clarity. Only one of the molecules in the asymmetric unit is shown.

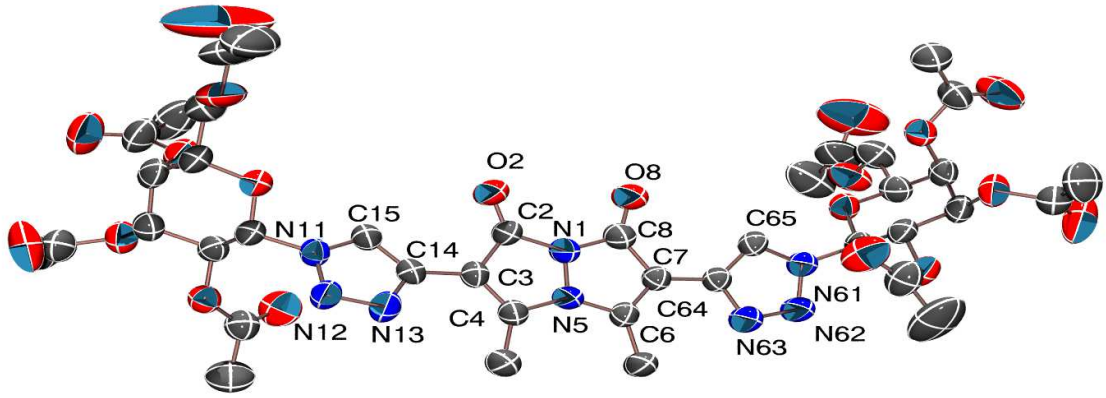


Figure 4. ORTEP view of **13c** at 50% probability level with partial numbering scheme. Hydrogen atoms are omitted for clarity.

Distances between glycosyl units in similar diglycosylated naphthalene derivatives have been shown to matter in sugar-lectin interactions [4]. Compounds **7a** and **13c** represent increasing interglycosidic separations as measured by the through-space distances between the anomeric C-atoms from the crystal structures (Figures 5 & 6).

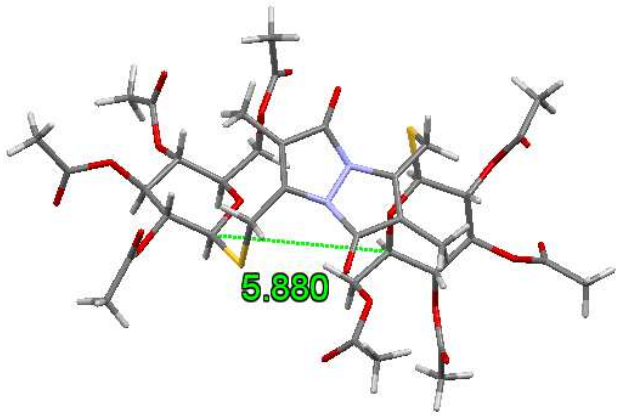


Figure 5. Interglycosidic separation distance (in Å) in **7a.**

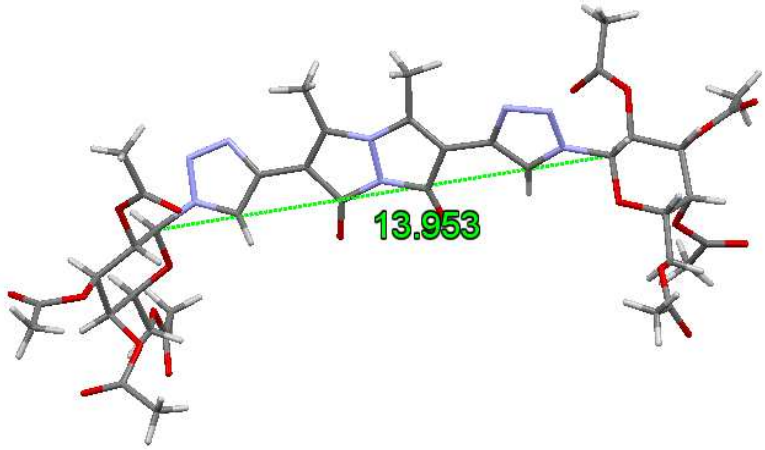


Figure 6. Interglycosidic separation distance (in Å) in **13c**.

Search of the Cambridge Structural Database [40] (Ver. 5.39 updates May, 2018) resulted 28 hits for *syn*- and 11 hits for *anti* bimane structures. Comparison of the bond distance and bond angle data found in the CSD reveals that the corresponding data in our compounds are in the expected range (Table S2). The bimane structures found in the CSD also revealed nonplanarity in several cases, i.e. angles > 0 deg. subtended by the mean planes of the two anellated pyrazolone rings, values being varied between 0 and 50 deg. In the present cases we have often detected two independent molecules in the asymmetric unit of the crystal. It is of note that the extent of nonplanarity within these pairs varied significantly, for example, 13 / 22 deg. in **1c** or 5 / 19 deg. in **8a**. Even for **1e** where the two rings are bridged by a disulfide linkage the respective data are 4.4 / 18.8 deg. (Figure S2 and Table S3). Moreover, this type of bending occurs in both *syn*- (**8a**) and *anti* (**7a**) bimanes (Table S3). These results suggest that the planarity of the bimane backbone is not as prevalent, as it was suggested in early single crystal studies [41, 42]. Further investigations of the same authors had shown the

flexibility of the bimane system [43, 44]. Scatter plot of the N-N distance versus interplanar angles revealed no correlation between these structural descriptors. Should electronic effects, such as overlap of orbitals, govern the interplanar bending, these effects are expected to be very similar for two molecules occupying the same asymmetric unit. However, this is not the case as noted above. We therefore suggest that differences in the deviations from planarity for chemically identical molecules may arise from lattice (packing) constraints in the solid state in these particular structures.

Bimanes are fluorescent compounds with the *syn* isomers displaying distinctly stronger effect than their *anti* counterparts as noted above. As this photophysical property is influenced not only by *syn/anti* relationships but other structural subtleties as well [45,46], it was of interest to investigate the effects, if any, of the pending glycosyl moieties on the fluorescent behavior of these molecules. First, we note that absorption and fluorescence spectra of compounds with the same glycosidic bond type but bearing different sugar moieties (eg. **8a,b,c,d,** see Figures S4 & S7) are practically superimposable therefore data for glucosyl derivatives have only been listed in Table 2. Clearly, the sugar part has no effect on the optical absorption and fluorescence properties of these molecules with absorption/ emission maxima and extinction coefficients similar to those published for non-glycosylated bimane derivatives [15,47]. Data for a*nti*-bimane derivatives are not listed either because, in line with literature reports [15,47], these isomers are non-fluorescent. It is of note, however, that the *syn* selenoglycoside **6a** was found nonfluorescent unlike its thio-analog **8a**. It is known, however, that when "Se is connected to the fluorophore (…) the efficient photoinduced eletron-transfer (PET) process between the Se and fluorophore quenches the fluorescence" [48]. On the other hand, this behavior may also be related to small value of the extinction coefficient (800) for the band used for fluorescent excitation in **6a** in comparison with significantly higher values in other *syn*-bimanes (4 ~ 5000, Table 2).

Table 2. Ultraviolet-visible absorption and emission properties of *syn*-bimanes [*syn*-(R_2,R_1)B]*

Compd. No.	R_2	R_1	Absorbance λ_{abs} (nm) / ε ($M^{-1}\cdot cm^{-1}$)	Excitation λ_{ex} (nm)	Emission λ_{em} (nm)	Quantum yield Φ_F
1c	*CH_2SAc*	*CH_3*	375 / 5600, 238 / 21100	370	445	0.86
1d	*CH_2SH*	*CH_3*	375 / 5400, 237 / 14300	370	445	0.70
1e	*CH_2S-*	*CH_3*	360 /4200, 232 / 13100	370	442	0.74
6a	*CH_2Se-β-$GlcAc_4$*	*CH_3*	360 / 800, 237 / 26100	370	n.d.	-
8a	*CH_2S-β-$GlcAc_4$*	*CH_3*	364 / 5100, 255 / 23100	370	444	0.89
10a	*CH_2S_2-β-$GlcAc_4$*	*CH_3*	378 / 4600, 245 / 13200	370	449	0.57
13a	*CH_3*	*TA-β-$GlcAc_4$*	370 / 3500, 242 / 4400	370	475	0.86

* For the notation, see Experimental

3. Conclusion

In summary we have described the syntheses and characterization of a set of novel derivatives, including those with appended mono- and disaccharide moieties, based on the 1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (bimane) heteroaromatic ring system. Mono- and disaccharide residues were attached to *syn*- or *anti*-bimane central cores via thio-, dithio- or selenoglycosidic linkages to obtain novel fluorescent or nonfluorescent glycoconjugates. Cu(I)-catalyzed cycloaddition of glycosyl azides to a bimane diethinyl derivative furnished further bivalent glycoconjugates with sugar residues linked to the central bimane core via 1,2,3-triazole rings. We have determined the crystal and molecular structures of several glycosylated and non-glycosylated bimanes and report fluorescence data for the new compounds.

4. Experimental

4.1. General information

syn-(CH_2Br,CH_3)B, *anti*-(CH_2Br,CH_3)B [15], *syn*-(CH_3,C≡CTMS)B [39], *N*-phthalyl-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-glycopyranosyl)sulfonamides [36], per-*O*-acetylated-β-D-glycopyranosyl azides [49], 2,3,4,6-Tetra-*O*-acetyl-β-D-glycopyranosyl *iso*selenuronium bromides [31,32], 1-thio-2,3,4,6-tetra-*O*-acetyl-β-D-glycopyranoses [30,50-52] and 1-thio-2,3,6-tri-*O*-acetyl-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranose [53]

were prepared according to literature procedures. TLC was performed on DC-Alurolle Kieselgel F254 (Merck), and the spots on the plates visualized under UV light (254 nm) and by heating. For column chromatography Kieselgel 60 (Merck, particle size 0.063-0.200) was used. NMR spectra were recorded on a Bruker Avance II 500 (500/125 MHz for $^{1}H/^{13}C$) spectrometer. Chemical shifts measured in ppm are referenced to internal Me_4Si (0.00 ppm for ^{1}H), or to the residual solvent signals ($CDCl_3$: 77.23 ppm, DMSO-d_6: 39.51 ppm for ^{13}C). Mass spectra were measured using Bruker microOTOF-Q or Thermo LTQ FT Ultra spectrometers. UV and steady state fluorescence data were determined on a Perkin Elmer Lambda 11 and Jasco FP-8200 spectrometer using 1 µmol solutions in MeCN in a quartz cuvette of 10 mm length The excitation and emission spectra were recorded using 2.5 nm excitation, 5.0 nm emission bandwith and 200 nm/min scanning speed. Quantum yields (Φ) were calculated according to the equation:

$$\Phi F_s = \frac{F_s\,(\varepsilon_{ref}\,c_{ref}\,\Phi F_{ref})}{F_{ref}\,(\varepsilon_s\,c_s)}$$

using *syn*-(CH_3,CH_3)B as reference (ΦF_{ref} = 0.72) [15]. Symbols: F: integrated area under fluorescence curve, s: sample, ref: *syn*-(CH_3,CH_3)B, c: concentration, ε: absorption coefficient.

X-ray diffraction data were collected at 293-298 K using a Bruker-D8 Venture diffractometer equipped with INCOATEC IµS 3.0 dual (Cu and Mo) sealed tube microsources and Photon 2 Charge-integrated Pixel Array detector. For compounds **1c, 1d, 1e** and **13c** Mo Kα (λ = 0.7107 Å) while for **7a** and **8a** Cu Kα (λ = 1.541 Å) radiation was applied. For the software used for data collection and processing see Supporting Information. The structures could be solved using direct methods and refined on F^2 using SHELXL program [54] incorporated into the APEX3 suite. Refinement was performed anisotropicaly for all non-hydrogen atoms.

Hydrogen atoms atoms were placed into geometric positions except the SH protons in **1d** as these hydrogen atoms could be found at the difference electron density map. Tables were extracted from the edited CIF file using publCIF [55]. The PLATON program [56] was used for crystallographic calculations. Further information on the data collection and refinement for the respective compounds can be found in Table S1. CCDC numbers for compounds **1c, 1d, 1e, 7a, 8a, 13c** are 1847474-1847479, respectively. The absolute configurations for compounds **7a, 8a** and **13c** were determined on the basis of the configuration of stereogenic centers in the carbohydrate moiety.

*4.2. syn-(CH_2SAc,CH_3)B, 4,6-bis-[(acetylthio)methyl]-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**1c**)*

To a solution of **1a** (3.50 g, 10.0 mmol) in CH_2Cl_2 (50 mL) potassium thioacetate (3.43 g, 30.0 mmol) was added. The suspension was stirred at room temperature for 1.5 h, then filtered through silica gel (2.00 g), and washed with CH_2Cl_2 (50 mL). The filtrate was evaporated to dryness and the residue crystallized from MeOH, to yield **1c** (2.10 g, 62 %) as yellow needles. R_f 0.48 (9:1 $CHCl_3$-EtOAc), m.p. 131-135 °C, ^{1}H NMR (DMSO-d_6, 500 MHz): δ (ppm) 4.25 (s, 4H, 2xCH_2), 2.43 (s, 6H, 2xCH_3), 1.78 (s, 6H, 2xCH_3), ^{13}C NMR (DMSO-d_6, 125 MHz): δ (ppm) 193.4 (S*C*O), 159.6 (C-2, C-8), 146.9 (C-4, C-6), 114.2 (C-3, C-7), 30.1 (CO*C*H_3), 22.4 (*C*H_2), 6.8 (*C*H_3). HRMS m/z calc. for $C_{14}H_{16}N_2O_4S_2$ $[M+H]^+$: 341.062 Found: 341.062.

*4.3. syn-(CH_2SH,CH_3)B, 4,6-bis-(mercaptomethyl)-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**1d**)*

To a cold (0 °C) mixture of MeOH (65 mL) and acetylchloride (2.6 mL, 36.4 mmol) **1c** (2.60 g, 7.6 mmol) was added. The mixture was allowed to warm to room temperature and

stirred overnight. The precipitated solid was filtered and washed with and recrystallized from MeOH, to yield **1d** (1.70 g, 87 %) as yellow needles. R_f 0.17 (4:1 $CHCl_3$-MeOH), m.p. 169-172 °C, ^{1}H NMR (DMSO-d_6, 500 MHz): δ (ppm) 3.88 (s, 4H, 2xC*H*$_2$), 3.75 (s, 2H, 2xS*H*), 1.79 (s, 6H, 2xC*H*$_3$), ^{13}C NMR (DMSO-d6, 125 MHz): δ (ppm) 160.2 (C-2, C-8), 150.0 (C-4, C-6), 111.7 (C-3, C-7), 17.1 (*C*H$_2$), 6.4 (*C*H$_3$). HRMS m/z calc. for $C_{10}H_{12}N_2O_2S_2$ $[M+H]^+$: 257.041 Found: 257.041.

*4.4. syn-(CH$_2$S,CH$_3$)B, 4,6-(dithiamethylene)-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**1e**)*

To the mixture of MeOH (100 mL) and CH_2Cl_2 (50 mL) **1d** (500 mg, 0.51 mmol), then 30% aq. H_2O_2 (3.6 mL) was added. The solution was stirred at room temperature for 2 h, then the reaction mixture was poured into a solution of 10 % $NaHSO_3$ in water (200 mL) and the water phase extracted with EtOAc (200 mL). The organic phase was washed with water, dried (Na_2SO_4) and evaporated. The crude product was purified by column chromatography (EtOAc) to yield **1e** (310 mg, 63 %) as a yellow solid. Crystals for X-ray diffraction were grown from a solution in THF overlayered with diisopropylether. M.p. 151-157 °C, ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 4.12 (s, 4H, 2xC*H*$_2$), 1.81 (s, 6H, 2xC*H*$_3$), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 159.0 (C-2, C-8), 149.4 (C-4, C-6), 113.1 (C-3, C-7), 36.1 (*C*H$_2$), 6.5 (*C*H$_3$). HRMS m/z calc. for $C_{10}H_{10}N_2O_2S_2$ $[M+Na]^+$: 277.008 Found: 277.007.

*4.5. anti-(CH$_2$SAc,CH$_3$)B, 4,8-bis-[(acetylthio)methyl]-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,7-diene-2,6-dione (**1f**)*

To a solution of **1b** (800 mg, 2.3 mmol) in CH_2Cl_2 (100 mL), potassium thioacetate (784 mg, 6.9 mmol) was added. The suspension was stirred at room temperature for 1.5 h, filtered through silica gel (2.00 g), and washed with CH_2Cl_2 (50 mL). The filtrate was

evaporated, and the residue crystallized from MeOH, to yield **1f** (660 mg, 85 %) as a white solid. R_f 0.64 (4:1 toluene-isopropanol), ^{1}H NMR (ppm) ($CDCl_3$, 500 MHz): δ 4.19 (s, 4H, 2xCH_2), 2.35 (s, 6H, 2xCH_3), 1.93 (s, 6H, 2xCH_3), ^{13}C NMR (DMSO-d_6, 125 MHz): δ (ppm) 194.0 (S*C*O), 160.3 (C-2, C-6), 143.9 (C-4, C-8), 114.3 (C-3, C-7), 30.0 (CO*C*H_3), 22.1 (*C*H_2), 6.7 (*C*H_3). HRMS m/z calc. for $C_{14}H_{16}N_2O_4S_2$ $[M+Na]^+$: 363.045 Found: 363.044.

4.6. General method A for the preparation of seleno- and thio-glycosides

Compound **1a** or **1b** and the appropriate **3(a-c)**, **4(a-d)** were dissolved in DMF with stirring under nitrogen atmosphere at room temperature and triethylamine added through a septum. Stirring was continued at room temperature for 30 min then the reaction mixture was poured into water. A solid deposited, which was filtered, rinsed with water and dried. The crude products were purified by column chromatography (9.5:0.5 toluene-isopropanol) to give **5(a-c)**, **6(a**,**b)** selenoglycosides and **7(a-d)**, **8(a-d)** thioglycosides.

4.7. anti-(CH_2*Se-β-GlcAc*$_4$*,*CH_3*)B, 4,8-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)seleno]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,7-diene-2,6-dione (**5a**)*

According *to general method **A***, the reaction of **1b** (100 mg, 0.29 mmol) with **3a** (313 mg, 0.58 mmol) and triethylamine (0.2 mL, 1.4 mmol) gave **5a** (239 mg, 83 %) as a white solid. R_f 0.52 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 5 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.23 (t, 2H, H-2,2'^{Glc}, $J_{1,2}$ = $J_{2,3}$ = 9.5 Hz), 5.10 (m, 6H, H-3,3'^{Glc}, H-4,4'^{Glc}, H-1,1'^{Glc}), 4.29 (dd, 2H, H-6a,6a'^{Glc}, $J_{5,6a}$ = 4.5 Hz, $J_{a,b}$ = 12.5 Hz), 4.14 (m, 4H, H-6b,6b'^{Glc}, C$H_{2a,a'}^{Bim}$, $J_{CH2a,b}$ = 13.0 Hz), 3.93 (d, 2H, C$H_{2b,b'}^{Bim}$), 3.77 (m, 2H, H-5,5'^{Glc}), 2.09, 2.03, 2.02, 2.01 (s, 24H, 8xCOCH_3^{Glc}), 1.87 (s, 6H, 2xCH_3^{Bim}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.6, 170.1, 169.5 (*C*OCH_3)^{Glc}, 160.7 (C-2, C-6)^{Bim}, 147.2 (C-4, C-8)^{Bim}, 112.6 (C-3,

C-7)^{Bim}, 77.3 (C-1,1')^{Glc}, 76.8 (C-5,5')^{Glc}, 73.5 (C-3,3')^{Glc}, 70.7 (C-2,2')^{Glc}, 68.0 (C-4,4')^{Glc}, 61.8 (C-6,6')^{Glc}, 20.7, 20.6 (CO*C*H$_3$)^{Glc}, 12.6 (*C*H$_2$)^{Bim}, 6.7 (*C*H$_3$)^{Bim}. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}Se_2$ $[M+Na]^+$: 1035.102 Found: 1035.102.

*4.8. anti-(CH$_2$Se-β-GalAc$_4$,CH$_3$)B, 4,8-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)seleno]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,7-diene-2,6-dione (**5b**)*

According to *general method **A***, the reaction of **1b** (200 mg, 0.57 mmol) with **3b** (626 mg, 1.2 mmol) and triethylamine (0.4 mL, 2.9 mmol) gave **5b** (340 mg, 59 %) as a white solid. R_f 0.52 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ + 64 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.47 (d, 2H, H-4,4'^{Gal}, $J_{3,4}$ = 2.5 Hz), 5.26 (t, 2H, H-2,2'^{Gal}, $J_{1,2}$ = $J_{2,3}$ = 10.0 Hz), 5.08 (m, 4H, H-3,3'^{Gal}, H-1,1'^{Gal}), 4.12 (m, 6H, H-6a,6a'^{Gal}, H-6b,6b'^{Gal}, CH$_{2a,a'}^{Bim}$), 3.99 (m, 2H, H-5,5'^{Gal}, CH$_{2b,b'}^{Bim}$), 2.16, 2.05, 2.04, 1.99 (s, 24H, 8xCOC*H*$_3^{Gal}$), 1.88 (s, 6H, 2xC*H*$_3^{Bim}$), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.3, 169.9, 169.8 (*C*OCH$_3$)^{Gal}, 160.6 (C-2, C-6)^{Bim}, 147.1 (C-4, C-8)^{Bim}, 112.5 (C-3, C-7)^{Bim}, 78.2 (C-1,1')^{Gal}, 75.6 (C-5,5')^{Gal}, 71.4 (C-3,3')^{Gal}, 68.0 (C-4,4')^{Gal}, 67.3 (C-2,2')^{Gal}, 61.1 (C-6,6')^{Gal}, 20.7 (CO*C*H$_3$)^{Gal}, 12.9 (*C*H$_2$)^{Bim}, 6.6 (*C*H$_3$)^{Bim}. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}Se_2$ $[M+Na]^+$: 1035.102 Found: 1035.103.

*4.9. anti-(CH$_2$Se-β-ManAc$_4$,CH$_3$)B, 4,8-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-mannopyranosyl)seleno]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,7-diene-2,6-dione (**5c**)*

According to *general method **A***, the reaction of **1b** (50 mg, 0.14 mmol) with **3c** (157 mg, 0.29 mmol) and triethylamine (0.2 mL, 1.4 mmol) gave **5c** (92 mg, 64 %) as a white solid. R_f 0.52 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 18 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500

MHz): δ (ppm) 5.73 (s, 2H, H-1,1'^{Man}), 5.42 (d, 2H, H-2,2'^{Man}, $J_{2,3}$ = 3.5 Hz), 5.34 (t, 2H, H-4,4'^{Man}, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz), 5.23 (dd, 2H, H-3,3'^{Man}), 4.31 (m, 4H, H-6a,6a'^{Man}, H-5,5'^{Man}, $J_{5,6a}$ = 5.0 Hz), 4.16 (dd, 2H, H-6b,6b'^{Man}, $J_{5,6b}$ = 1.9 Hz, $J_{6a,6b}$ 12.0 Hz), 3.96 (dd, 4H, 2xCH_2^{Bim}, $J_{CH2a,b}$ = 13.0 Hz), 2.17, 2.10, 2.06, 1.98 (s, 24H, 8xCOCH_3^{Man}), 1.86 (s, 6H, 2xCH_3^{Bim}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.5, 169.7 (COCH$_3$)^{Man}, 160.1 (C-2, C-6)^{Bim}, 145.4 (C-4, C-8)^{Bim}, 113.7 (C-3, C-7)^{Bim}, 77.9 (C-1,1')^{Man}, 71.1 (C-5,5')^{Man}, 70.6 (C-3,3')^{Man}, 69.8 (C-2,2')^{Man}, 66.1 (C-4,4')^{Man}, 62.3 (C-6,6')^{Man}, 20.9, 20.7 (COCH$_3$)^{Man}, 13.9 (CH$_2$)^{Bim}, 6.8 (CH$_3$)^{Bim}. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}Se_2$ $[M+Na]^+$: 1035.102 Found: 1035.104.

*4.10. syn-(CH$_2$Se-β-GlcAc$_4$,CH$_3$)B, 4,6-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)seleno]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**6a**)*

According to *general method* ***A***, the reaction of **1a** (200 mg, 0.57 mmol) with **3a** (625 mg, 1.2 mmol) and triethylamine (0.2 mL, 1.4 mmol) yielded **6a** (358 mg, 62 %) as a white solid. R_f 0.47 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 5 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.22 (t, 2H, H-2,2'^{Glc}, $J_{2,3}$ = $J_{1,2}$ = 9.5 Hz), 5.08 (t, 2H, H-3,3'^{Glc}, $J_{3,4}$ = 9.5 Hz), 5.07 (t, 2H, H-4,4'^{Glc}), 4.81 (d, 2H, H-1,1'^{Glc}), 4.28 (dd, 2H, H-6a,6a'^{Glc}, $J_{5,6a}$ = 5.0 Hz, $J_{6a,6b}$ = 12.5 Hz), 4.14 (dd, 2H, H-6b,6b'^{Glc}, $J_{5,6b}$ = 1.5 Hz), 4.08 (d, 2H, C$H_{2a,a'}^{Bim}$, $J_{CH2a,b}$ = 13.0 Hz), 3.99 (d, 2H, C$H_{2b,b'}^{Bim}$), 3.73 (m, 2H, H-5,5'^{Glc}), 2.11, 2.06, 2.04, 2.02, (s, 24H, 8xCOCH_3^{Glc}), 1.90 (s, 6H, 2xCH_3^{Bim}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.5, 169.9, 169.4 (COCH$_3$)^{Glc}, 160.0 (C-2, C-8)^{Bim}, 146.2 (C-4, C-6)^{Bim}, 114.2 (C-3, C-7)^{Bim}, 77.4 (C-1,1')^{Glc}, 76.8 (C-5,5')^{Glc}, 73.2 (C-3,3')^{Glc}, 70.3 (C-2,2')^{Glc}, 67.9 (C-4,4')^{Glc}, 61.9 (C-6,6')^{Glc}, 20.7, 20.5 (CH$_2$)^{Bim}, 13.6 (COCH$_3$)^{Glc}, 7.1 (CH$_3$)^{Bim}. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}Se_2$ $[M+H]^+$: 1013.120 Found: 1013.123.

*4.11. syn-(CH_2Se-β-$GalAc_4$,CH_3)B, 4,6-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)seleno]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**6b**)*

According to general method **A**, the reaction of **1a** (100 mg, 0.29 mmol) with **3b** (313 mg, 0.58 mmol) and triethylamine (0.2 mL, 1.4 mmol) furnished **6b** (176 mg, 61 %) as a yellow solid. R_f 0.47 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 75 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.45 (d, 2H, H-4,4'^{Gal}, $J_{3,4}$ = 2.0 Hz), 5.24 (t, 2H, H-2,2'^{Gal}, $J_{1,2} = J_{2,3}$ = 10.0 Hz), 5.06 (dd, 2H, H-3,3'^{Gal}), 4.81 (d, 2H, H-1,1'^{Gal}), 4.11 (m, 8H, H-6a,6a'^{Gal}, H-6b,6b'^{Gal}, 2xCH_2^{Bim}), 3.96 (t, 2H, H-5,5'^{Gal}, $J_{5,6a} = J_{5,6b}$ = 10.0 Hz), 2.19, 2.07, 2.06, 2.00 (s, 24H, 8x$COCH_3^{Gal}$), 1.92 (s, 6H, 2xCH_3^{Bim}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.3, 170.1, 169.8 (COCH_3)^{Gal}, 160.0 (C-2, C-8)^{Bim}, 146.2 (C-4, C-6)^{Bim}, 114.0 (C-3, C-7)^{Bim}, 78.3 (C-1,1')^{Gal}, 76.1 (C-5,5')^{Gal}, 71.2 (C-3,3')^{Gal}, 67.5 (C-4,4')^{Gal}, 67.1 (C-2,2')^{Gal}, 61.3 (C-6,6')^{Gal}, 20.7 (COCH$_3$)^{Gal}, 14.0 (CH_2)^{Bim}, 7.1 (CH_3)^{Bim}. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}Se_2$ $[M+H]^+$: 1013.120 Found: 1013.123.

*4.12. anti-(CH_2S-β-$GlcAc_4$,CH_3)B, 4,8-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thio]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,7-diene-2,6-dione (**7a**)*

According to *general method **A***, the reaction of **1b** (100 mg, 0.29 mmol) with **4a** (219 mg, 0.60 mmol) and triethylamine (0.2 mL, 1.4 mmol) gave **7a** (210 mg, 80 %) as a white solid. R_f 0.56 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ + 6 (c 0.25 $CDCl_3$). Crystals for X-ray diffraction were grown from a solution in *t*BuOH overlayered with cyclohexane. ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.24 (t, 2H, H-2,2'^{Glc}, $J_{1,2} = J_{2,3}$ = 9.5 Hz), 5.12 (t, 2H, H-4,4'^{Glc}, $J_{3,4} = J_{4,5}$ 9.5 Hz), 5.06 (t, 2H, H-3,3'^{Glc}), 4.76 (d, 2H, H-1,1'^{Glc}), 4.24 (dd, 2H, H-6a,6a'^{Glc}, $J_{5,6a}$ = 4.5 Hz, $J_{6a,6b}$ = 10.0 Hz), 4.16 (d, 2H, $CH_{2a,a'}^{Bim}$, $J_{CH2a,b}$ = 14.5 Hz), 4.10 (dd, 2H, H-

6b,6b'^{Glc}, $J_{5,6b}$ = 1.5 Hz), 3.91 (d, 2H, $CH_{2b,b'}$.^{Bim}), 3.75 (m, 2H, H-5,5'^{Glc}), 2.09, 2.04, 2.02, 2.01 (s, 24H, 8xCOCH_3^{Glc}), 1.89 (s, 6H, 2xCH_3^{Bim}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.6, 170.1, 169.4 (COCH$_3$)^{Glc}, 160.5 (C-2, C-6)^{Bim}, 145.9 (C-4, C-8)^{Bim}, 113.8 (C-3, C-7)^{Bim}, 82.5 (C-1,1')^{Glc}, 76.0 (C-5,5')^{Glc}, 73.6 (C-3,3')^{Glc}, 69.8 (C-2,2')^{Glc}, 68.1 (C-4,4')^{Glc}, 61.8 (C-6,6')^{Glc}, 21.7 (CH$_2$)^{Bim}, 20.6 (COCH$_3$)^{Glc}, 6.6 (CH$_3$)^{Bim}. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}S_2$ $[M+Na]^+$: 939.213 Found: 939.215.

*4.13. anti-(CH$_2$S-β-GalAc$_4$,CH$_3$)B, 4,8-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)thio]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,7-diene-2,6-dione (**7b**)*

According to *general method **A***, the reaction of **1b** (100 mg, 0.29 mmol) with **4b** (219 mg, 0.60 mmol) and triethylamine (0.2 mL, 1.4 mmol) gave **7b** (220 mg, 84 %) as a white solid. R_f 0.56 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 40 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.44 (d, 2H, H-4,4'^{Gal}, $J_{3,4}$ = 3.0 Hz), 5.20 (t, 2H, H-2,2'^{Gal}, $J_{1,2}$ = $J_{2,3}$ = 10.0 Hz), 5.07 (dd, 2H, H-3,3'^{Gal}), 4.78 (d, 2H, H-1,1'^{Gal}), 4.08 (m, 10H, H-6a,6a'^{Gal}, H-6b,6b'^{Gal}, 2xCH_2^{Bim}, H-5,5'^{Gal}), 2.16, 2.05, 2.04, 1.98 (s, 24H, 8xCOCH_3^{Gal}), 1.88 (s, 6H, 2xCH_3^{Bim}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.3, 170.1, 169.6 (COCH$_3$)^{Gal}, 160.4 (C-2, C-6)^{Bim}, 145.7 (C-4, C-8)^{Bim}, 113.9 (C-3, C-7)^{Bim}, 83.4 (C-1,1')^{Gal}, 74.5 (C-5,5')^{Gal}, 71.6 (C-3,3')^{Gal}, 67.3 (C-4,4')^{Gal}, (C-2,2')^{Gal}, 61.0 (C-6,6')^{Gal}, 22.3 (CH$_2$)^{Bim}, 20.7, 20.5 (COCH$_3$)^{Gal}, 6.6 (CH$_3$)^{Bim}. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}S_2$ $[M+Na]^+$: 939.213 Found: 939.210.

*4.14. anti-(CH$_2$S-β-ManAc$_4$,CH$_3$)B, 4,8-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-mannopyranosyl)thio]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,7-diene-2,6-dione (**7βc**)*

According to *general method **A***, the reaction of **1b** (100 mg, 0.29 mmol) with **4βc** (219 mg, 0.60 mmol) and triethylamine (0.2 mL, 1.4 mmol) furnished **7βc** (260 mg, 98 %) as a white solid. R_f 0.56 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ + 10 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.47 (d, 2H, H-2,2'^{Man}, $J_{2,3}$ = 3.5 Hz), 5.29 (t, 2H, H-4,4'^{Man}, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz), 5.10 (dd, 2H, H-3,3'^{Man}), 5.04 (s, 2H, H-1,1'^{Man}), 4.24 (dd, 2H, H-6a,6a'^{Man}, $J_{5,6a}$ = 5.0 Hz, $J_{6a,6b}$ = 12.5 Hz), 4.15 (dd, 2H, H-6b,6b'^{Man}, $J_{5,6b}$ = 2.0 Hz), 4.11 (d, 2H, $CH_{2a,a'}^{Bim}$, $J_{CH2a,b}$ = 14.5 Hz), 3.95 (d, 2H, $CH_{2b,b'}^{Bim}$), 3.73 (m, 2H, H-5,5'^{Man}), 2.17, 2.09, 2.04, 1.96 (s, 24H, 8xCOCH_3^{Man}), 1.85 (s, 6H, 2xCH_3^{Bim}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.7, 170.0, 169.5 (COCH$_3$)^{Man}, 160.2 (C-2, C-6)^{Bim}, 145.4 (C-4, C-8)^{Bim}, 114.0 (C-3, C-7)^{Bim}, 81.5 (C-1,1')^{Man}, 76.5 (C-5,5')^{Man}, 71.7 (C-3,3')^{Man}, 69.9 (C-2,2')^{Man}, 65.7 (C-4,4')^{Man}, 62.6 (C-6,6')^{Man}, 22.7 (CH$_2$)^{Bim}, 20.9, 20.7, 20.5 (COCH$_3$)^{Man}, 6.5 (CH$_3$)^{Bim}. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}S_2$ $[M+Na]^+$: 939.213 Found: 939.214.

*4.15. anti-(CH$_2$S-α-ManAc$_4$,CH$_3$)B, 4,8-bis-{1-[(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)thio]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,7-diene-2,6-dione (**7αc**)*

According to *general method **A***, the reaction of **1b** (100 mg, 0.29 mmol) with **4αc** (219 mg, 0.60 mmol) and triethylamine (0.2 mL, 1.4 mmol) furnished **7αc** (201 mg, 77 %) as a white solid. R_f 0.56 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ + 91 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.30 (m, 6H, H-2,2'^{Man}, H-1,1'^{Man}, H-4,4'^{Man}), 5.19 (dd, 2H, H-3,3'^{Man}, $J_{2,3}$ = 3.5 Hz, $J_{3,4}$ = 10.0 Hz), 4.36 (m, 2H, H-5,5'^{Man}), 4.26 (dd, 2H, H-6a,6a'^{Man}, $J_{5,6a}$ = 5.5 Hz, $J_{6a,6b}$ = 12.5 Hz), 4.12 (dd, 2H, H-6b,6b'^{Man}, $J_{5,6b}$ = 2.0 Hz), 3.95 (d, 2H, $CH_{2a,a'}^{Bim}$, $J_{CH2a,b}$ = 14.0 Hz), 3.88 (d, 2H, $CH_{2b,b'}^{Bim}$), 2.13, 2.07, 2.03, 1.94 (s, 24H, 8xCOCH_3^{Man}), 1.85 (s, 6H, 2xCH_3^{Bim}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.4, 169.6 (COCH$_3$)^{Man}, 159.9 (C-2, C-6)^{Bim}, 143.8 (C-4, C-8)^{Bim}, 115.0 (C-3, C-7)^{Bim}, 81.5 (C-1,1')^{Man}, 70.0 (C-5,5')^{Man}, 69.4 (C-

3,3')^{Man}, 69.4 (C-2,2')^{Man}, 66.1 (C-4,4')^{Man}, 62.4 (C-6,6')^{Man}, 22.4 (*C*H$_2$)^{Bim}, 20.8, 20.5 (CO*C*H$_3$)^{Man}, 6.5 (*C*H$_3$)^{Bim}. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}S_2$ $[M+Na]^+$: 939.213 Found: 939.213.

*4.16. anti-(CH$_2$S-β-LacAc$_7$,CH$_3$)B, 4,8-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-galactosyl-(1→4)-2,3,6-tri-O-acetyl-1-thio-β-D-glucosyl)thio]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,7-diene-2,6-dione (**7d**)*

According to *general method **A***, the reaction of **1b** (100 mg, 0.29 mmol) with **4d** (392 mg, 0.60 mmol) and triethylamine (0.1 mL, 0.72 mmol) yielded **7d** (407 mg, 95 %) as a white solid. R_f 0.38 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ + 6 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.34 (d, 2H, H-4,4'^{Gal}, $J_{3,4}$ = 3.5 Hz), 5.22 (t, 2H, H-3,3'^{Glc}, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz), 5.09 (t, 2H, H-2,2'^{Gal}, $J_{1,2}$ = $J_{2,3}$ = 8.0 Hz), 4.95 (dd, 2H, H-3,3'^{Gal}), 4.93 (t, 2H, H-2,2'^{Glc}, $J_{1,2}$ = 9.5 Hz), 4.72 (d, 2H, H-1,1'^{Glc}), 4.48 (m, 4H, H-1,1'^{Gal}, H-6a,6a'^{Glc}, $J_{6a,6b}$ = 12.5 Hz), 4.09 (m, 8H, CH$_{2a,a'}$^{Bim}, H-4,4'^{Glc}, H-6b,6b'^{Glc}, H-6b,6b'^{Gal}), 3.88 (m, 4H, CH$_{2b,b'}$^{Bim}, H-6a,6a'^{Gal}), 3.82 (t, 2H, H-5,5'^{Gal}, $J_{5,6a}$ = $J_{5,6b}$ = 10.0 Hz), 3.64 (m, 2H, H-5,5'^{Glc}), 2.14, 2.12, 2.06, 2.04, 2.03, 2.02, 1.96, 1.84 (s, 42H, 14xCOC*H*$_3^{Lac}$, 2xC*H*$_3^{Bim}$), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.3, 170.0, 169.6, 169.1 (COC*H*$_3$)^{Lac}, 160.5 (C-2, C-6)^{Bim}, 145.8 (C-4, C-8)^{Bim}, 113.8 (C-3, C-7)^{Bim}, 101.0 (C-1,1')^{Gal}, 82.4 (C-1,1')^{Glc}, 76.7 (C-5,5')^{Glc}, 75.9 (C-4,4')^{Glc}, 73.6 (C-3,3')^{Glc}, 71.0 (C-5,5')^{Gal}, 70.7 (C-3,3')^{Gal}, 70.3 (C-2,2')^{Gal}, 69.1 (C-2,2')^{Glc}, 66.6 (C-4,4')^{Gal}, 61.8 (C-6,6')^{Glc}, 60.8 (C-6,6')^{Gal}, 21.9 (*C*H$_2$)^{Bim}, 20.9, 20.8, 20.7, 20.6, 20.5 (CO*C*H$_3$)^{Lac}, 6.6 (*C*H$_3$)^{Bim}. HRMS m/z calc. for $C_{62}H_{80}N_2O_{36}S_2$ $[M+Na]^+$: 1515.382 Found: 1515.390.

4.17. syn-(CH_2S-β-GlcAc$_4$,CH_3)B, 4,6-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thio]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (8a)

According to *general method* ***A***, the reaction of **1a** (100 mg, 0.29 mmol) with **4a** (219 mg, 0.60 mmol) and triethylamine (0.1 mL, 0.72 mmol) yielded **8a** (225 mg, 86 %) as a pale yellow solid. R_f 0.61 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 97 (c 0.25 $CDCl_3$). Crystals for X-ray diffraction were grown from a solution in *t*BuOH overlayered with cyclohexane. ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.24 (t, 2H, H-3,3'^{Glc}, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz), 5.08 (t, 2H, H-4,4'^{Glc}, $J_{4,5}$ = 9.5 Hz), 5.03 (t, 2H, H-2,2'^{Glc}, $J_{1,2}$ = 9.5 Hz), 4.53 (d, 2H, H-1,1'^{Glc}), 4.27 (dd, 2H, H-6a,6a'^{Glc}, $J_{5,6a}$ = 5.0 Hz, $J_{6a,6b}$ = 12.5 Hz), 4.13 (dd, 2H, H-6b,6b'^{Glc}, $J_{5,6b}$ = 1.5 Hz), 4.11 (d, 2H, $CH_{2a,a'}$^{Bim}, $J_{CH2a,b}$ = 14.0 Hz), 4.01 (d, 2H, $CH_{2b,b'}$^{Bim}), 3.73 (m, 2H, H-5,5'^{Glc}), 2.11, 2.06, 2.04, 2.02 (s, 24H, 8xCO*C*H_3^{Glc}), 1.94 (s, 6H, 2x*C*H_3^{Bim}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.5, 170.0, 169.3 (*C*OCH_3)^{Glc}, 159.9 (C-2, C-8)^{Bim}, 144.8 (C-4, C-6)^{Bim}, 115.0 (C-3, C-7)^{Bim}, 81.8 (C-1,1')^{Glc}, 76.5 (C-5,5')^{Glc}, 73.3 (C-3,3')^{Glc}, 69.5 (C-2,2')^{Glc}, 67.9 (C-4,4')^{Glc}, 61.8 (C-6,6')^{Glc}, 22.3 (*C*H_2)^{Bim}, 20.7, 20.6 (CO*C*H_3)^{Glc}, 7.2 (*C*H_3)^{Bim}. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}S_2$ $[M+H]^+$: 917.231 Found: 917.230.

4.18. syn-(CH_2S-β-GalAc$_4$,CH_3)B, 4,6-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)thio]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (8b)

According to *general method* ***A***, the reaction of **1a** (200 mg, 0.57 mmol) with **4b** (438 mg, 1.2 mmol) and triethylamine (0.2 mL, 1.4 mmol) gave **8b** (401 mg, 77 %) as a pale yellow solid. R_f 0.61 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 86 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.45 (d, 2H, H-4,4'^{Gal}, $J_{3,4}$ = 1.5 Hz), 5.20 (t, 2H, H-2,2'^{Gal}, $J_{1,2}$ = $J_{2,3}$ = 10.0 Hz), 5.07 (dd, 2H, H-3,3'^{Gal}), 4.52 (d, 2H, H-1,1'^{Gal}), 4.10 (m, 8H, H-6a,6a'^{Gal}, H-

6b,6b'^{Gal}, $CH_{2a,a'}$^{Bim}, $CH_{2b,b'}$^{Bim}), 3.96 (t, 2H, H-5,5'^{Gal}, $J_{5,6a} = J_{5,6b} = 6.5$ Hz), 2.20, 2.08, 2.07, 2.00 (s, 24H, 8xCOCH_3^{Gal}), 1.96 (s, 6H, 2xCH_3^{Bim}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.2, 169.6 (*C*OCH_3)^{Gal}, 159.8 (C-2, C-8)^{Bim}, 144.8 (C-4, C-6)^{Bim}, 114.6 (C-3, C-7)^{Bim}, 82.7 (C-1,1')^{Gal}, 75.0 (C-5,5')^{Gal}, 71.2 (C-3,3')^{Gal}, 67.0 (C-2,2')^{Gal}, 66.6 (C-4,4')^{Gal}, 61.3 (C-6,6')^{Gal}, 22.6 (*C*H_2)^{Bim}, 20.5 (CO*C*H_3)^{Gal}, 6.9 (*C*H_3)^{Bim}. HRMS m/z calc. for $C_{38}H_{48}O_{20}N_2S_2$ $[M+H]^+$: 917.231 Found: 917.232.

*4.19. syn-(CH$_2$S-β-ManAc$_4$,CH$_3$)B, 4,6-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-mannopyranosyl)thio]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**8βc**)*

According to *general method **A***, the reaction of **1a** (200 mg, 0.57 mmol) with **4βc** (438 mg, 1.2 mmol) and triethylamine (0.2 mL, 1.4 mmol) gave **8βc** (382 mg, 73 %) as a pale yellow solid. R_f 0.61 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 106 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.50 (d, 2H, H-2,2'^{Man}, $J_{2,3} = 3.0$ Hz), 5.26 (t, 2H, H-4,4'^{Man}, $J_{3,4} = J_{4,5} =$ 10.0 Hz), 5.11 (dd, 2H, H-3,3'^{Man}), 5.01 (s, 2H, H-1,1'^{Man}), 4.26 (dd, 2H, H-6a,6a'^{Man}, $J_{5,6a} =$ 6.0 Hz, $J_{6a,6b} = 12.5$ Hz), 4.17 (m, 4H, H-6b,6b'^{Man}, $CH_{2a,a'}$^{Bim}), 3.93 (d, 2H, $CH_{2b,b'}$^{Bim}, $J_{CH2a,b}$ = 15.0 Hz), 3.88 (m, 2H, H-5,5'^{Man}), 2.18, 2.10, 2.02, 1.92 (s, 24H, 8xCOCH_3^{Man}), 1.88 (s, 6H, 2xCH_3^{Bim}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.0, 169.7, 169.3 (*C*OCH_3)^{Man}, 158.7 (C-2, C-8)^{Bim}, 142.6 (C-4, C-6)^{Bim}, 114.9 (C-3, C-7)^{Bim}, 78.7 (C-1,1')^{Man}, 75.8 (C-5,5')^{Man}, 71.0 (C-3,3')^{Man}, 69.8 (C-2,2')^{Man}, 65.2 (C-4,4')^{Man}, 62.5 (C-6,6')^{Man}, 22.8 (*C*H_2)^{Bim}, 20.2 (CO*C*H_3)^{Man}, 6.5 (*C*H_3)^{Bim}. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}S_2$ $[M+H]^+$: 917.231 Found: 917.233.

*4.20. syn-(CH_2S-α-ManAc$_4$,CH_3)B, 4,6-bis-{1-[(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)thio]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**8αc**)*

According to *general method **A***, the reaction of **1a** (176 mg, 0.50 mmol) with **4αc** (376 mg, 1.0 mmol) and triethylamine (0.2 mL, 1.4 mmol) furnished **8αc** (97 mg, 21 %) as a pale yellow solid. R_f 0.61 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ + 4 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.34 (dd, 2H, H-2,2'^{Man}, $J_{1,2}$ = 1.5 Hz, $J_{2,3}$ = 3.5 Hz), 5.30 (t, 2H, H-4,4'^{Man}, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz), 5.18 (dd, 2H, H-3,3'^{Man}), 5.12 (d, 2H, H-1,1'^{Man}), 4.34 (m, 2H, H-5,5'^{Man}), 4.27 (dd, 2H, H-6a,6a'^{Man}, $J_{5,6a}$ = 6.0 Hz, $J_{6a,6b}$ = 12.5 Hz), 4.21 (dd, 2H, H-6b,6b'^{Man}, $J_{5,6b}$ = 2.0 Hz), 4.00 (d, 2H, $CH_{2a,a'}^{Bim}$, $J_{CH2a,b}$ = 15.0 Hz), 3.91 (d, 2H, $CH_{2b,b'}^{Bim}$), 2.17, 2.13, 2.08, 1.99 (s, 24H, 8xCOCH_3^{Man}), 1.92 (s, 6H, 2xCH_3^{Bim}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 169.9, 169.3, 169.0 (*C*OCH_3)^{Man}, 159.0 (C-2, C-8)^{Bim}, 142.9 (C-4, C-6)^{Bim}, 115.6 (C-3, C-7)^{Bim}, 80.0 (C-1,1')^{Man}, 69.6 (C-3,3')^{Man}, 69.1 (C-5,5')^{Man}, 69.0 (C-2,2')^{Man}, 65.6 (C-4,4')^{Man}, 62.1 (C-6,6')^{Man}, 22.6 (*C*H_2)^{Bim}, 20.4, 20.2 (CO*C*H_3)^{Man}, 6.6 (*C*H_3)^{Bim}. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}S_2$ $[M+Na]^+$: 939.214 Found: 939.216.

*4.21. syn-(CH_2S-β-LacAc$_7$,CH_3)B, 4,6-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-galactosyl-(1→4)-2,3,6-tri-O-acetyl-1-thio-β-D-glucosyl)thio]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**8d**)*

According to *general method **A***, the reaction of **1a** (100 mg, 0.29 mmol) with **4d** (392 mg, 0.60 mmol) and triethylamine (0.1 mL, 0.72 mmol) furnished **8d** (383 mg, 90 %) as a pale yellow solid. R_f 0.41 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 81 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.27 (d, 2H, H-4,4'^{Gal}, $J_{3,4}$ = 5.0 Hz), 5.13 (t, 2H, H-3,3'^{Glc}, $J_{2,3}$ = $J_{3,4}$ = 10.0 Hz), 5.01 (t, 2H, H-2,2'^{Gal}, $J_{1,2}$ = $J_{2,3}$ = 10.0 Hz), 4.89 (dd, 2H, H-3,3'^{Gal}), 4.84 (t, 2H, H-2,2'^{Glc}), 4.43 (m, 4H, H-1,1'^{Gal}, H-1,1'^{Glc}), 4.38 (d, 2H, H-6a,6a'^{Glc}, $J_{6a,6b}$ = 10.0 Hz),

3.98 (m, 10H, 2xCH_2^{Bim}, H-6b,6b'^{Glc}, H-6a,6a'^{Gal}, H-6b,6b'^{Gal}), 3.83 (t, 2H, H-4,4'^{Glc}, $J_{4,5}$ = 10.0 Hz), 3.69 (t, 2H, H-5,5'^{Gal}, $J_{5,6a} = J_{5,6b}$ = 9.5 Hz), 3.55 (m, 2H, H-5,5'^{Glc}), 2.07, 2.05, 1.98, 1.97, 1.96, 1.88, 1.83 (s, 42H, 14xCOCH_3^{Lac}, 2xCH_3^{Bim}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.4, 169.9, 169.4, 169.0 (COCH$_3$)^{Lac}, 159.7 (C-2, C-8)^{Bim}, 144.6 (C-4, C-6)^{Bim}, 114.7 (C-3, C-7)^{Bim}, 100.9 (C-1,1')^{Gal}, 81.7 (C-1,1')^{Glc}, 77.4 (C-5,5')^{Glc}, 75.6 (C-4,4')^{Glc}, 73.1 (C-3,3')^{Glc}, 70.8 (C-5,5')^{Gal}, 70.6 (C-3,3')^{Gal}, 69.8 (C-2,2')^{Glc}, 69.0 (C-2,2')^{Gal}, 66.5 (C-4,4')^{Gal}, 61.9 (C-6,6')^{Glc}, 60.7 (C-6,6')^{Gal}, 22.4 (CH$_2$)^{Bim}, 20.5, 20.4 (COCH$_3$)^{Lac}, 7.0 (CH$_3$)^{Bim}. HRMS m/z calc. for $C_{62}H_{80}N_2O_{36}S_2$ $[M+H]^+$: 1493.400 Found: 1493.404.

4.22. General method B for the preparation of disulfido-glycosides

Compound **1d** was dissolved in DMF with stirring under nitrogen atmosphere at room temperature and the appropriate **9(a-c)** added. Stirring was continued at room temperature for 30 min then the reaction mixture was poured into water. The solids deposited were filtered, rinsed with water and dried. The crude products were purified by column chromatography (9.5:0.5 toluene:isopropanol) to give **10(a-c)** disulfido-glycosides.

*4.23. syn-(CH_2S_2-β-GlcAc$_4$,CH_3)B, 4,6-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)dithio]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**10a**)*

According to *general method **B***, the reaction of **1d** (130 mg, 0.51 mmol) with **9a** (650 mg, 1.3 mmol) gave **10a** (406 mg, 81 %) as a pale yellow solid. R_f 0.58 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 161 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.38 (t, 2H, H-2,2'^{Glc}, $J_{1,2} = J_{2,3}$ = 9.5 Hz), 5.29 (t, 2H, H-3,3'^{Glc}), 5.15 (t, 2H, H-4,4'^{Glc}, $J_{3,4} = J_{4,5}$ = 9.5 Hz), 4.59 (d, 2H, H-1,1'^{Glc}), 4.27 (m, 6H, 2xCH_2^{Bim}, H-6a,6a'^{Glc}, $J_{6a,6b}$ = 12.5 Hz, $J_{5,6a}$ = 5.0 Hz), 3.96 (d, 2H, H-6b,6b'^{Glc}), 3.85 (m, 2H, H-5,5'^{Glc}), 2.10, 2.06, 2.03 (s, 24H,

8xCOCH_3[Glc]), 1.97 (s, 6H, 2xCH_3[Bim]), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.5, 169.9, 169.3, 169.0 (*C*OCH$_3$)[Glc], 159.9 (C-2, C-8)[Bim], 144.5 (C-4, C-6)[Bim], 116.1 (C-3, C-7)[Bim], 86.1 (C-1,1')[Glc], 77.3 (C-5,5')[Glc], 73.4 (C-3,3')[Glc], 68.6 (C-2,2')[Glc], 67.8 (C-4,4')[Glc], 61.8 (C-6,6')[Glc], 32.7 (*C*H$_2$)[Bim], 20.6, 20.5 (CO*C*H$_3$)[Glc], 7.4 (*C*H$_3$)[Bim]. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}S_4$ $[M+Na]^+$: 1003.158 Found: 1003.153.

*4.24. syn-(CH$_2$S$_2$-β-GalAc$_4$,CH$_3$)B, 4,6-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)dithio]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**10b**)*

According to *general method **B***, the reaction of **1d** (68 mg, 0.27 mmol) with **9b** (340 mg, 0.67 mmol) gave **10b** (185 mg, 71 %) as a pale yellow solid. R_f 0.58 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 108 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.55 (t, 2H, H-2,2'[Gal], $J_{1,2} = J_{2,3} = 10.0$ Hz), 5.49 (dd, 2H, H-4,4'[Gal], $J_{3,4} = 3.0$ Hz, $J_{4,5} = 0.5$ Hz), 5.12 (dd, 2H, H-3,3'[Gal]), 5.11 (d, 2H, H-1,1'[Gal]), 4.19 (m, 6H, H-6a,6a'[Gal], H-6b,6b'[Gal], CH$_{2a,a'}$[Bim]), 4.06 (td, 2H, H-5,5'[Gal], $J_{5,6a} = J_{5,6b} = 6.5$ Hz, $J_{4,5} = 0.5$ Hz), 4.01 (d, 2H, CH$_{2a,a'}$[Bim], $J_{CH2a,b} = 14.5$ Hz), 2.22, 2.07, 2.05, 2.01 (s, 24H, 8xCOCH_3[Gal]), 1.97 (s, 6H, 2xCH_3[Bim]), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.4, 170.0, 169.4 (*C*OCH$_3$)[Gal], 160.0 (C-2, C-8)[Bim], 144.3 (C-4, C-6)[Bim], 116.2 (C-3, C-7)[Bim], 87.0 (C-1,1')[Gal], 75.5 (C-5,5')[Gal], 71.5 (C-3,3')[Gal], 67.2 (C-2,2')[Gal], 66.1 (C-4,4')[Gal], 61.9 (C-6,6')[Gal], 32.7 (*C*H$_2$)[Bim], 20.7, 20.6 (CO*C*H$_3$)[Gal], 7.5 (*C*H$_3$)[Bim]. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}S_4$ $[M+Na]^+$: 1003.158 Found: 1003.152.

*4.25. syn-(CH$_2$S$_2$-β-ManAc$_4$,CH$_3$)B, 4,6-bis-{1-[(2,3,4,6-tetra-O-acetyl-β-D-mannopyranosyl)dithio]methyl}-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**10c**)*

According to *general method **B***, the reaction of **1d** (130 mg, 0.51 mmol) with **9c** (650 mg, 1.3 mmol) gave **9c** (54 mg, 11 %) as a pale yellow solid. R_f 0.58 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 18 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.53 (d, 2H, H-2,2'^{Man}, $J_{2,3}$ = 3.0 Hz), 5.27 (t, 2H, H-4,4'^{Man}, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz), 5.04 (dd, 2H, H-3,3'^{Man}), 4.97 (s, 2H, H-1,1'^{Man}), 4.29 (m, 6H, H-6a,6a'^{Man}, H-6b,6b'^{Man}, $CH_{2a,a}$'^{Bim}), 3.89 (d, 2H, $CH_{2b,b}$'^{Bim}, $J_{CH2a,b}$ = 14.5 Hz), 3.79 (m, 2H, H-5,5'^{Man}), 2.17, 2.10, 2.07, 1.99 (s, 24H, 8xCOCH_3^{Man}), 1.98 (s, 6H, 2xCH_3^{Bim}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.0, 169.5, 169.1 (*C*OCH_3)^{Man}, 159.6 (C-2, C-8)^{Bim}, 143.7 (C-4, C-6)^{Bim}, 116.4 (C-3, C-7)^{Bim}, 88.9 (C-1,1')^{Man}, 76.7 (C-5,5')^{Man}, 71.0 (C-3,3')^{Man}, 68.8 (C-2,2')^{Man}, 64.8 (C-4,4')^{Man}, 61.9 (C-6,6')^{Man}, 32.2 (*C*H_2)^{Bim}, 20.2, 20.1 (CO*C*H_3)^{Man}, 7.1 (*C*H_3)^{Bim}. HRMS m/z calc. for $C_{38}H_{48}N_2O_{20}S_4$ $[M+Na]^+$: 1003.158 Found: 1003.150.

4.26. General method C for the preparation of triazolo-glycosides

Compound **1g** was dissolved in MeCN under nitrogen at room temperature and the appropriate **12(a-c)**, copper(I)-bromide, copper dust and N,N-diisopropylethylamine were added. Stirring was continued at reflux temperature for 6h then the reaction mixture was evaporated to dryness. Purification by column chromatography (CH_2Cl_2, then EtOAc) yielded the triazolo-glycosides **13(a-d)**.

*4.27. syn-(CH$_3$,TA-β-GlcAc$_4$)B, 4,6-dimethyl-3,7-bis[(1-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-1H-1,2,3-triazol-4-yl)]-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**13a**)*

According to *general method **C***, the reaction of **1g** (100 mg, 0.28 mmol) with **12a** (261 mg, 0.70 mmol), copper(I)-bromide (12 mg, 0.05 mmol), copper dust (16 mg, 0.25 mmol) and N,N-diisopropylethylamine (0.1 ml, 0.57 mmol), yielded **13a** (175 mg, 97 %) as a yellow

solid. R_f 0.43 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 125 (c 0.25 $CDCl_3$). ^1H NMR ($CDCl_3$, 500 MHz): δ (ppm) 8.92 (s, 2H, H-5,5'^{Taz}), 6.25 (d, 2H, H-1,1'^{Glc}, $J_{1,2}$ = 9.5 Hz), 5.97 (t, 2H, H-3,3'^{Glc}, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz), 5.73 (t, 2H, H-4,4'^{Glc}, $J_{4,5}$ = 9.5 Hz), 5.27 (t, 2H, H-2,2'^{Glc}), 4.22 (dd, 2H, H-6a,6a'^{Glc}, $J_{5,6a}$ = 5.5 Hz, $J_{6a,b}$ = 13.0 Hz), 4.13 (m, 4H, H-6b,6b'^{Glc}, H-5,5'^{Glc}), 3.06 (s, 6H, 2xCH_3^{Bim}), 2.07, 2.00, 1.86 (s, 24H, 4xCOCH_3^{Glc}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.6, 169.4, 168.7 (COCH$_3$)^{Glc}, 157.1 (C-2, C-8)^{Bim}, 145.5 (C-4, C-6)^{Bim}, 138.0 (C-4,4')^{Taz}, 122.6 (C-3, C-7)^{Bim}, 107.7 (C-5,5')^{Taz}, 85.2 (C-1,1')^{Glc}, 74.5 (C-5,5')^{Glc}, 73.4 (C-3,3')^{Glc}, 69.8 (C-2,2')^{Glc}, 68.2 (C-4,4')^{Glc}, 61.8 (C-6,6')^{Glc}, 20.7, 20.3 (COCH$_3$)^{Glc}, 13.4 (CH$_3$)^{Bim}. HRMS m/z calc. for $C_{40}H_{46}N_8O_{20}$ $[M+H]^+$: 959.290 Found: 959.292.

*4.28. syn-(CH$_3$,TA-β-GalAc$_4$)B, 4,6-dimethyl-3,7-bis[(1-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-1H-1,2,3-triazol-4-yl)]-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**13b**)*

According to *general method **C***, the reaction of **1g** (100 mg, 0.28 mmol) with **12b** (261 mg, 0.70 mmol), copper(I)-bromide (12 mg, 0.05 mmol), copper dust (16 mg, 0.25 mmol) and N,N-diisopropylethylamine (0.1 ml, 0.57 mmol), yielded **13b** (150 mg, 57 %) as an orange-yellow solid. R_f 0.43 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 123 (c 0.25 $CDCl_3$). ^1H NMR ($CDCl_3$, 500 MHz): δ (ppm) 8.70 (s, 2H, H-5,5'^{Taz}), 6.03 (d, 2H, H-1,1'^{Gal}, $J_{1,2}$ = 9.0 Hz), 5.83 (t, 2H, H-2,2'^{Gal}, $J_{2,3}$ = 9.0 Hz), 5.55 (d, 2H, H-4,4'^{Gal}, $J_{3,4}$ = 2.0 Hz), 5.39 (dd, 2H, H-3,3'^{Gal}), 4.32 (t, 2H, H-5,5'^{Gal}, $J_{5,6a}$ = $J_{5,6b}$ = 5.0 Hz), 4.20 (dd, 2H, H-6a,6a'^{Gal}, $J_{6a,6b}$ = 10.0 Hz), 4.12 (dd, 2H, H-6b,6b'^{Gal}), 3.03 (s, 6H, 2xCH_3^{Bim}), 2.23, 2.00, 1.86 (s, 24H, 4xCOCH_3^{Gal}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.3, 170.0, 168.7 (COCH$_3$)^{Gal}, 157.1 (C-2, C-8)^{Bim}, 145.5 (C-4, C-6)^{Bim}, 138.0 (C-4,4')^{Taz}, 121.9 (C-3, C-7)^{Bim}, 107.7 (C-5,5')^{Taz}, 86.0 (C-1,1')^{Gal}, 73.8 (C-5,5')^{Gal}, 71.2 (C-3,3')^{Gal}, 67.8 (C-2,2')^{Gal}, 67.0 (C-4,4')^{Gal}, 61.4 (C-

6,6')^{Gal}, 20.7, 20.6 (CO*C*H$_3$)^{Gal}, 13.4 (*C*H$_3$)^{Bim}. HRMS m/z calc. for $C_{40}H_{46}N_8O_{20}$ $[M+H]^+$: 959.290 Found: 959.290.

*4.29. syn-(CH$_3$,TA-β-ManAc$_4$)B, 4,6-dimethyl-3,7-bis[(1-(2,3,4,6-tetra-O-acetyl-β-D-mannopyranosyl)-1H-1,2,3-triazol-4-yl)]-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**13c**)*

According to *general method **C***, the reaction of **1g** (100 mg, 0.28 mmol) with **12c** (261 mg, 0.70 mmol), copper(I)-bromide (12 mg, 0.05 mmol), copper dust (16 mg, 0.25 mmol) and N,N-diisopropylethylamine (0.1 ml, 0.57 mmol), yielded **13c** (156 mg, 60 %) as an orange-yellow solid. R_f 0.43 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 127 (c 0.25 $CDCl_3$). Crystals for X-ray diffraction were grown from a solution in *t*BuOH overlayered with CH_2Cl_2. ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 8.43 (s, 2H, H-5,5'^{Taz}), 6.24 (s, 2H, H-1,1'^{Man}, $J_{1,2}$ = 0.5 Hz), 5.67 (dd, 2H, H-2,2'^{Man}, $J_{2,3}$ = 3.5 Hz), 5.38 (t, 2H, H-4,4'^{Man}, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz), 5.31 (dd, 2H, H-3,3'^{Man}), 4.28 (dd, 2H, H-6a,6a'^{Man}, $J_{5,6a}$ = 5.5 Hz, $J_{6a,6b}$ = 13.5 Hz), 4.23 (dd, 2H, H-6b,6b'^{Man}, $J_{5,6b}$ = 2.5 Hz), 3.98 (m, 2H, H-5,5'^{Man}), 2.95 (s, 6H, 2xC*H*$_3^{Bim}$), 2.18, 2.08, 2.07, 1.98 (s, 24H, 4xCOC*H*$_3^{Man}$), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.6, 169.8, 169.4 (*C*OCH$_3$)^{Man}, 157.0 (C-2, C-8)^{Bim}, 145.4 (C-4, C-6)^{Bim}, 137.6 (C-4,4')^{Taz}, 121.3 (C-3, C-7)^{Bim}, 107.4 (C-5,5')^{Taz}, 84.5 (C-1,1')^{Man}, 76.0 (C-5,5')^{Man}, 70.7 (C-3,3')^{Man}, 68.6 (C-2,2')^{Man}, 64.9 (C-4,4')^{Man}, 61.9 (C-6,6')^{Man}, 20.6, 20.4 (CO*C*H$_3$)^{Man}, 13.1 (*C*H$_3$)^{Bim}. HRMS m/z calc. for $C_{40}H_{46}N_8O_{20}$ $[M+H]^+$: 959.290 Found: 959.290.

*4.30. syn-(CH$_3$,TA-β-LacAc$_7$)B, 4,6-dimethyl-3,7-bis[(1-(2,3,4,6-tetra-O-acetyl-β-D-galactosyl-(1→4)-2,3,6-tri-O-acetyl-1-thio-β-D-glucosyl)-1H-1,2,3-triazol-4-yl)]-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione (**13d**)*

According to *general method **C***, the reaction of **1g** (100 mg, 0.28 mmol) with **12d** (464 mg, 0.70 mmol), copper(I)-bromide (12 mg, 0.05 mmol), copper dust (16 mg, 0.25 mmol) and N,N-diisopropylethylamine (0.1 ml, 0.57 mmol), furnished **13d** (247 mg, 57 %) as a yellow solid. R_f 0.27 (4:1 toluene-isopropanol), $[\alpha]_D^{27}$ – 117 (c 0.25 $CDCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 8.49 (s, 2H, C-5,5'^{Taz}), 5.91 (d, 2H, H-1,1'^{Glc}, $J_{1,2}$ = 10.0 Hz), 5.57 (t, 2H, H-2,2'^{Glc}, $J_{2,3}$ = 10.0 Hz), 5.44 (t, 2H, H-3,3'^{Glc}, $J_{3,4}$ = 10.0 Hz), 5.36 (d, 2H, H-4,4'^{Gal}, $J_{3,4}$ = 5.0 Hz), 5.11 (t, 2H, H-2,2'^{Gal}, $J_{1,2}$ = $J_{2,3}$ = 10.0 Hz), 5.00 (dd, 2H, H-3,3'^{Gal}), 4.57 (d, 2H, H-1,1'^{Gal}), 4.50 (d, 2H, H-6a,6a'^{Gal}, $J_{6a,6b}$ = 15.0 Hz), 4.03 (m, 12H, H-4,4'^{Glc}, H-5,5'^{Glc}, H-6a,6a'^{Glc}, H-6b,6b'^{Glc}, H-5,5'^{Gal}, H-6b,b'^{Gal}), 3.00 (s, 6H, 2xCH_3^{Bim}), 2.14, 2.08, 2.05, 2.03, 1.95, 1.84 (s, 42H, 14xCOCH_3^{Lac}), ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 170.4, 170.3, 170.0, 169.7, 168.9 (*C*OCH_3)^{Lac}, 157.1 (C-2, C-8)^{Bim}, 145.6 (C-4, C-6)^{Bim}, 138.1 (C-4,4')^{Taz}, 121.4 (C-3, C-7)^{Bim}, 107.6 (C-5,5')^{Taz}, 101.1 (C-1,1')^{Gal}, 85.5 (C-1,1')^{Glc}, 75.6 (C-5,5')^{Gal}, 75.6 (C-5,5')^{Glc}, 72.7 (C-3,3')^{Glc}, 71.0 (C-3,3')^{Gal}, 70.8 (C-4,4')^{Glc}, 70.6 (C-2,2')^{Glc}, 69.1 (C-2,2')^{Gal}, 66.7 (C-4,4')^{Gal}, 61.8 (C-6,6')^{Gal}, 60.9 (C-6,6')^{Glc}, 20.7, 20.5 (CO*C*H_3)^{Lac}, 13.3 (*C*H_3)^{Bim}. HRMS m/z calc. for $C_{64}H_{78}N_8O_{36}$ $[M+H]^+$: 1535.459 Found: 1535.461.

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References

[1] H-J. Gabius, J.C. Manning, J. Kopitz, S. André, H. Kaltner, Cell. Molec. Life Sci. 73 (2016) 1989-2016.
[2] A. Varki, Glycobiology, 27 (2017) 3-49.
[3] R. Roy, P.V. Murphy, H.J. Gabius, Molecules, 21 (2016) 629.
[4] H. Kaltner, T. Szabó, K. Fehér, S. André, S. Balla, J.C. Manning, L. Szilágyi, H.J. Gabius, Bioorg. Med. Chem. 25 (2017) 3158-3170.
[5] L. Szilágyi, O. Varela, Curr. Org. Chem. 10 (2006) 1745-1770.
[6] S. André, Z.C. Pei, H.C. Siebert, O. Ramström, H-J. Gabius, Bioorg. Med. Chem. 14 (2006) 6314-6326.
[7] S. Martin-Santamaria, S. André, E. Buzamet, R. Caraballo, G. Fernandez-Cureses, M. Morando, J.P. Ribeiro, K. Ramirez-Gualito, B. de Pascual-Teresa, F.J. Canada, M. Menendez, O. Ramström, J. Jiménez-Barbero, D. Solis, H.J. Gabius, Org. Biomol. Chem. 9 (2011) 5445-5455.
[8] B.N. Murthy, S. Sinha, A. Surolia, N. Jayaraman, L. Szilágyi, I. Szabó, K.E. Kövér, Carbohydr. Res. 344 (2009) 1758-1763.
[9] B. Gutierrez, C. Munoz, L. Osorio, K. Fehér, T.Z. Illyés, Z. Papp, A.A. Kumar, K.E. Kövér, H. Sagua, J.E. Araya, P. Morales, L. Szilágyi, J. Gonzalez, Bioorg. Med. Chem. Lett. 23 (2013) 3576-3579.
[10] S. André, K.E. Kövér, H-J. Gabius, L. Szilágyi, Bioorg. Med. Chem. Lett. 25 (2015) 931-935.
[11] J. Franco, F. Sardi, L. Szilágyi, K.E. Kövér, K. Fehér, M.A. Comini, Int. J. Parasitol. Drugs Drug Resist. 7 (2017) 303-313.
[12] T.Z. Illyés, S. Balla, A. Bényei, A.A. Kumar, I. Timári, K.E. Kövér, L. Szilágyi, ChemistrySelect, 1 (2016) 2383-2388.
[13] E.M. Kosower, B. Pazhenchevsky, E. Hershkowitz, J. Amer. Chem. Soc. 100 (1978) 6516-6518.
[14] I. Neogi, P.J. Das, F. Grynszpan, Synlett, 29 (2017) 1043-1046.
[15] E.M. Kosower, B. Pazhenchevsky, J. Amer. Chem. Soc. 102 (1980) 4983-4993.
[16] M. Baba, N. Hirota, E.M. Kosower, J. Phys. Chem. 85 (1981) 1469-1474.
[17] T.S. Chwee, G.S. Lim, Z.C. Wong, M.B. Sullivan, W.Y. Fan, Phys. Chem. Chem. Phys. 18 (2016) 7404-7413.
[18] N.S. Kosower, E.M. Kosower, G.L. Newton, H.M. Ranney, Proc. Nat. Acad. Sci. USA, 76 (1979) 3382-3386.
[19] S.E. Mansoor, D.L. Farrens, Biochemistry, 43 (2004) 9426-9438.
[20] S.E. Mansoor, M.A. DeWitt, D.L. Farrens, Biochemistry, 49 (2010) 9722-9731.
[21] J.W. Taraska, M.C. Puljung, W.N. Zagotta, Proc. Nat. Acad. Sci. USA 106 (2009) 16227-16232.
[22] L.A. Montoya, X.G. Shen, J.J. McDermott, C.G. Kevil, M.D. Pluth, Chem. Sci. 6 (2015) 294-300.
[23] G.L. Newton, R.C. Fahey, M. Rawat, Microbiology-Sgm, 158 (2012) 1117-1126.
[24] E.M. Kosower, A.E. Radkowsky, A.H. Fairlamb, S.L. Croft, R.A. Neal, Eur. J. Med. Chem. 30 (1995) 659-671.
[25] B. Krishnan, A. Szymanska, L.M. Gierasch, Chem. Biol. & Drug Design, 69 (2007) 31-40.
[26] A.E. Radkowsky, E.M. Kosower, D. Eisenberg, I. Goldberg, J. Amer. Chem. Soc. 108 (1986) 4532-4541.
[27] A.E. Radkowsky, E.M. Kosower, J. Amer. Chem. Soc. 108 (1986) 4527-4531.

[28] J. Čapek, M. Hauschke, L. Bruckova, T. Rousar, J. Pharmacol. Toxicol. Meth. 88 (2017) 40-45.
[29] T. Imai, T. Kurihara, N. Esaki, H. Mihara, Anal. Biochem. 532 (2017) 1-8.
[30] M.B. Haque, B.P. Roberts, D.A. Tocher, J. Chem. Soc. Perkin Trans. 1, (1998) 2881-2889.
[31] G. Wagner, P. Nuhn, Arch. Pharm. 297 (1964) 462-473.
[32] A.A. Kumar, T.Z. Illyés, K.E. Kövér, L. Szilágyi, Carbohydr. Res. 360 (2012) 8-18.
[33] M. Musiejuk, D. Witt, Org. Prep. Proc. Int. 47 (2015) 95-131.
[34] L. Szilágyi, T.Z. Illyés, P. Herczegh, Tetrahedron Lett. 42 (2001) 3901-3903.
[35] N. Stellenboom, R. Hunter, M.R. Caira, L. Szilágyi, Tetrahedron Lett. 51 (2010) 5309-5312.
[36] T.Z. Illyés, T. Szabó, L. Szilágyi, Carbohydr. Res. 346 (2011) 1622-1627.
[37] G.R. Morais, B.R. Springett, M. Pauze, L. Schroder, M. Northrop, R.A. Falconer, Org. Biomol. Chem. 14 (2016) 2749-2754.
[38] X.P. He, Y.L. Zeng, Y. Zang, J. Li, R.A. Field, G.R. Chen, Carbohydr. Res. 429 (2016) 1-22.
[39] E.M. Kosower, M. BenShoshan, J. Org. Chem. 61 (1996) 5871-5884.
[40] C.R. Groom, I.J. Bruno, M.P. Lightfoot, S.C. Ward, Acta Cryst. B-Struct. Sci. Crystal Eng. Mater. 72 (2016) 171-179.
[41] E.M. Kosower, J. Bernstein, I. Goldberg, B. Pazhenchevsky, E. Goldstein, J. Amer. Chem. Soc. 101 (1979) 1620-1621.
[42] I. Goldberg, J. Bernstein, E.M. Kosower, Acta Cryst. B-Struct. Sci. 38 (1982) 1990-2000.
[43] I. Goldberg, E.M. Kosower, J. Phys. Chem. 86 (1982) 332-335.
[44] I. Goldberg, J. Bernstein, E.M. Kosower, E. Goldstein, B. Pazhenchevsky, J. Heterocycl. Chem. 20 (1983) 903-912.
[45] D. Huppert, H. Kanety, E. Pines, E.M. Kosower, J. Phys. Chem. 85 (1981) 3387-3390.
[46] E.M. Kosower, H. Kanety, H. Dodiuk, J. Hermolin, J. Phys. Chem. 86 (1982) 1270-1277.
[47] E.M. Kosower, H. Kanety, H. Dodiuk, J. Photochem. 21 (1983) 171-182.
[48] J. He, L. Jia, Y. Li, S. Liu, R. Chen, L. Jin, J. Jin, C. Zheng, Q. Fan, W. Huang, Chem. Commun. (2018).
[49] Z. Györgydeák, L. Szilágyi, H. Paulsen, J. Carbohydr. Chem. 12 (1993) 139-163.
[50] M. Černy, J. Štanek, J. Pacák, Monatsh. Chem. 94 (1963) 291-294.
[51] P.L. Durette, T.Y. Shen, Carbohydr. Res. 81 (1980) 261-274.
[52] D.P. Gamblin, P. Garnier, S. van Kasteren, N.J. Oldham, A.J. Fairbanks, B.G. Davis, Angew. Chem. Int. Ed. 43 (2004) 828-833.
[53] J. Štanek, M. Šindlerová, M. Černy, Collect. Czech. Chem. Commun. 34 (1965) 297-303.
[54] G.M. Sheldrick, Acta Cryst. A, 64 (2008) 112-122.
[55] S.P. Westrip, J. App. Cryst. 43 (2010) 920-925.
[56] A.L. Spek, Acta Cryst. D-Biol. Cryst. 65 (2009) 148-155.

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Thio-, seleno- and disulfido-glycosides

Glycosyltriazolyl bimanes

Molecular and crystal structures by X-ray diffraction