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Glucosamine- and galactosamine- based monosaccharides with highly fluorinated motifs

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ABSTRACT

Synthesis of modified monosaccharides, derivatives of glucose and galactose, having a highly fluorinated chain, as a library of synthetic building blocks for hyaluronic acid (HA) modified subunits has been developed. "Click" chemistry has been employed as a strategy for the synthesis of these molecules. 1,2,3-triazole ring derivatives were obtained with good to excellent yields.

1. Introduction

Synthetically available carbohydrates are of urgent interest for the development of carbohydrate-based drugs, new drug delivery systems as well as new enzymes inhibitors. In the literature there are described several natural polymers which were successfully used in drug delivery application like: chitosan, dextran, cellulose, alginic acid or collagen [1–3]. One of the polysaccharides of great interest is hyaluronic acid (**1**) (HA) and its derivatives. First isolated from the bovine vitreous body [4], HA is a high molecular weight, natural, linear polysaccharide that consist of the repeating disaccharide subunit composed from 1 to 3 linked β-2-acetamido-2-deoxy-D-glucose-β-(1→4)-D-glucuronic acid (Fig. 1).

Moreover, it's properties like biodegradability, biocompatibility and viscoelasticity make HA a promising drug carrier [5,6]. Naturally occurring molecules are frequently used as starting materials for drugs and drug delivery systems. The advantage of synthetic approach is the possibility of changing its properties to make them more selective, more effective or both. Thereby, an emphasis on the synthesis of hyaluronic acid subunits and their further use for the construction of certain complex structures is made which can potentially act as drugs or drugs delivery platforms in a modern medicine.

Hyaluronan as a therapeutic can act on cancer cells. HA interacts with cell surface receptors CD44 and RHAMM and regulates proliferation, migration and cell adhesion. High molecular weight HA can inhibit proliferation and migration of tumor cells or retard cell migration and metastasis [7,8]. According to the literature, high concentrations of hyaluronan occur in the tumor cells. It's caused by the HA receptors (CD44 and RHAMM) which are overexpressed by most malignant tumor cells. It makes HA an important molecule for cancer targeted drug delivery systems since it could be recognized by the specific target tissue. As highlighted previously, HA is a polymer which consist of disaccharides. The various of chemical groups provides appropriate sites to which drugs could be conjugated e.g. the *N*-acetylglucosamine hydroxyl, the reducing end, carboxylate in glucuronic acid or the acetyl groups (after enzymatic removal). Such diversity of bonds in hyaluronic acid that are biodegradable and hydrolysable makes the combination of this biologically active molecule with potential drug delivery system more promising [1,9–11].

As an example for HA-drug conjugate Paclitaxel, used to treat cancers, can be distinguished. These two molecules, combined together, form a prodrug where HA is a backbone for paclitaxel. By this combination poor aqueous solubility of paclitaxel is overcome. Additionally, HA-Paclitaxel is targeted directly to the cells where HA receptors CD44 are overexpressed [12,13]. Another HA-conjugates were synthesised e.g. HA with 5-fluorouracil and HA-

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0022-1139/

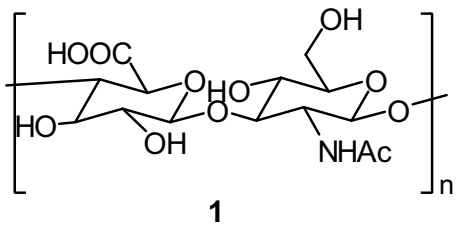


Fig. 1. Hyaluronic Acid.

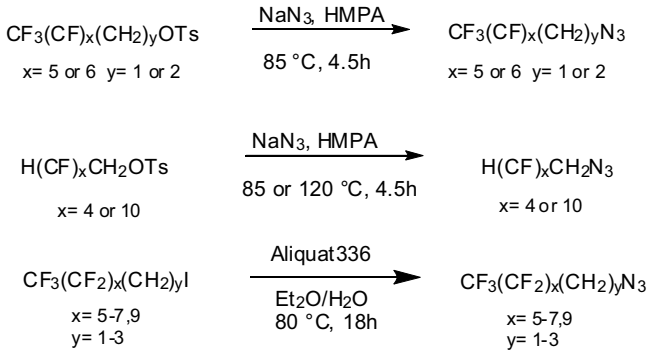
Camphotecin 20-(S). Both compounds shows antitumor activity and are used successfully as an anticancer agent [5,14,15].

On the other hand, growing interest of fluorine and fluorinated products has encouraged the researches for the search of novel and improved methodologies for preparation of new compounds having fluorinated motifs. The long chain of fluorinated fragment attached to the parent molecule improved its lipophilicity, and also quite often its stability. In many cases the incorporation of fluorine to molecules depends on unique properties of this element. We can replace a hydrogen atoms by fluorine because a small size of fluorine atom could not change steric size of molecule and the C—F bond is stronger than C—H bond [16,17].

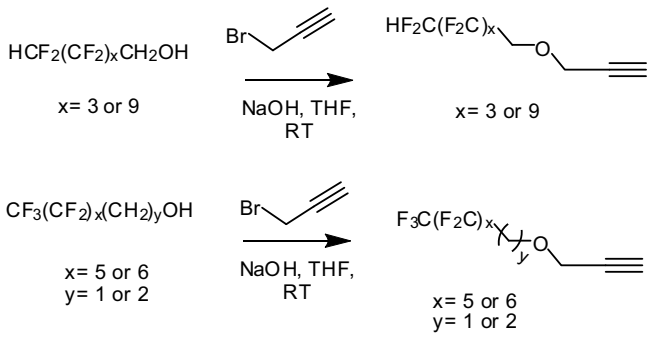
It is worth to mention that some glycosides with perfluoroalkyl chains were tested by Hatanaka et al. [18,19] as a substrate for oligosaccharide biosynthesis. The results of the study showed that the presence of fluorine atoms in saccharide did not cause of toxicity and did not have any damaging effects on the cells. Hatanaka showed that fluorous-tagged saccharide could be used via biosynthetic method. Additionally, higher fluorine content is responsible that the glycosides are more hydrophobic. This results indicate interesting possibilities of application fluorine-containing carbohydrates. [18,19]. However, they decided to investigate cytotoxicity and cellular uptake of some perfluorocarboxylic acid with various chain length from C(6) to C(10). The research suggest that cytotoxicity increased with increasing of perfluoroalkyl chain length. Besides, long-chained acids have stronger affinity to the cell membrane than short-chained acids which in cells were much less. In this case the reason may be high fluorine content [20]. Miethchen [21] mentioned in his work that neutral and non toxic head groups of perfluoroalkylated carbohydrates can represent binding sites for bio-receptors, what is very important information for biomedical uses of fluorinated saccharides. Carbohydrate-based fluorocompounds indicate interesting possibilities of applications e.g. surfactants or liquid crystals [22].

2. Results and discussion

Combination of these two previously mentioned features gives us a rise to develop a synthetic pathway of monosaccharides as building blocks for HA modified subunits having highly fluorinated chain attached to the parent carbohydrate with 8, 13, 15, 17 or 21 fluorine atoms. Our concept was to develop the synthetic method for the synthesis of model monosaccharides and in the next step use it for the synthesis of hyaluronic acid subunits. One of the common modification approach is a strategy using copper catalyzed 1,3 dipolar cycloaddition reaction known as "click" chemistry introduced by Sharpless [23] or Meldal [24]. To do this, a modification of a monosaccharide (building block for HA subunit) is required and next appropriate fluorinated azide (with 13, 15, 17, 21 fluorine atoms) (Scheme 1) or propargyl ether (with 8, 13, 15, 21 fluorine atoms) (Scheme 2) could be attached to the molecule *via* "click" strategy (Scheme 3). In this paper we would like to present our results on synthesis of such new modified units based on glucosamine hydrochloride and galactosamine hydrochloride



Scheme 1. Preparation of fluorinated azides [30–41].



Scheme 2. Preparation of fluorinated propargyl ethers [21,43].

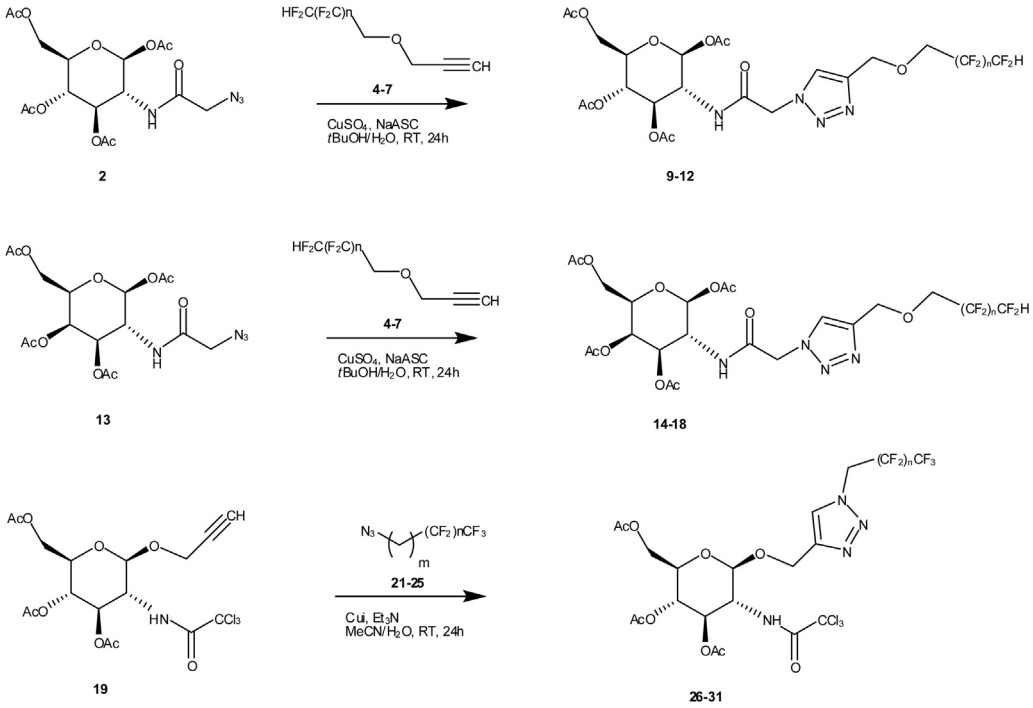
derivatives. It is documented that introduction into the molecule 1,2,3-triazole ring can mimic peptide bond which is naturally occurring bond in our body [25,26]. Undoubtedly, click chemistry impact on drug discovery in recent years has increased due to the mild reaction conditions, chemoselectivity and good or excellent reaction yields [27]. The "click" chemistry has become an efficient tools for different modifications and bioconjugations. This reaction are widely used in polysaccharides [28,29].

There are many contributions describing the access to highly fluorinated azides [30–41] as well as fluorinated propargyl ethers [42,43], nevertheless their synthetic preparation sometimes might be challenging. The synthesis of such species is relatively well documented, however especially fluorinated azides, with per-fluorinated or highly fluorinated groups, are sometimes tricky to be prepared. This is due to the presence of fluorine in reacting molecule, what causes significant change in reactivity and other properties. In general fluorinated alkyl azides were obtained from tosylates or iodides in S_N2 reaction with sodium azide according to known or slightly modified procedures [30–41]. Various azides with different linkers $-CH_2-$ between an azido moiety and fluoroalkylated chain were prepared via known or slightly modified methodologies (Scheme 1).

A fluorinated propargyl ethers have been obtained from corresponding fluorinated alcohols and propargyl bromide (Scheme 2) [42,43].

In this paper we would like to report our studies on preparation of a library of modified monosaccharides as potential HA subunits using as a parent compound 1-*O*-propargyl modified glucosamine reacting with highly fluorinated azides. The second series of molecules are "click" products of glucosamine and galactosamine derived azides with highly fluorinated propargyl ethers.

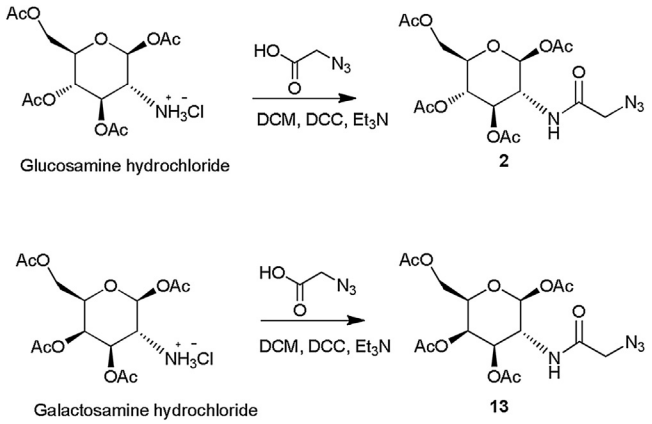
The starting tetraacetylated saccharides are well known and can be prepared from D-glucosamine hydrochloride or D-galactosamine hydrochloride in few steps [44,45]. Preparative



Scheme 3. Synthesized monosaccharides with highly fluorinated motifs.

methodologies leading to insertion of azidoacetylo moiety on glucosamine or galactosamine hydrochloride are already known in literature, however it is worth to note that the synthesis of 1,3,4,6-tetra-*O*-acetyl-*N*-azidoacetylo-D-glucosamine (**2**) and 1,3,4,6-tetra-*O*-acetyl-*N*-azidoacetylo-D-galactosamine (**13**) leads in our case selectively to pure anomer β. In the literature there are different contributions describing mostly the synthesis of these sugars as mixtures of anomers (typically 1:1) [46–49], only in few cases exclusively anomers β [50,51]. Our synthesis of pure β anomer is relatively simple and straitghforwad and uses tetraacetylated glucosamine and galactosamine hydrochlorides as well as azidoacetic acid as starting materials and DCC as coupling reagent (Scheme 4).

The first group of modified monosaccharides we have used as a parent compound are different azides – derivatives glucosamine **2** and galactosamine hydrochlorides **13**. The "click" reactions of monosaccharides with azido group and highly fluorinated propargyl ethers (**4-7**) were performed under standard Sharpless



Scheme 4. Insertion of azidoacetylo moiety on peracetylated glucosamine or peracetylated galactosamine hydrochloride yielding β products **2** and **13.**

conditions with the use of $CuSO_4$ and sodium ascorbate (NaASC) and led us to the library of desired products **9-12, 15–18** with very good yields (Table 1). In each case we had also performed the reaction with non-fluorinated reagent **3** and **20** yielding non-fluorinated triazole derivatives **8** and **14** in order to compare the reaction scope.

Next, the second set of compounds **26-31** was prepared in the reactions of monosaccharide with propargyl moiety **19** and non-fluorinated azide **20** or highly fluorinated azides **21-25**. The starting saccharide **19** was prepared from 1,3,4-tetra-*O*-acetylo-2-deoxy-3-trichloroacetamido-β-D-glucopyranoside with propargyl alcohol and boron trifluoroetherate according to known procedure [52]. These reactions, however, were performed under Meldal conditions with the use of CuI as a catalyst (Table 2). Nevertheless, the reaction yields are much lower compared to the "click" reaction between azidosugar and fluorinated propargyl ether described above (Table 1). Reactions performed under Sharpless conditions were also successful and yielded desired products, however workup and purification was troublesome and product isolation was very difficult, sometimes not possible.

In sugar chemistry in multistage reactions it's necessary to use corresponding protecting groups. For all prepared in this paper acetylated compounds with 1,2,3-triazole ring and partially fluorinated alkyl chains it's possible the deprotection reaction of the acetates protecting groups. In this reaction using solution of sodium methoxide in MeOH the reaction yields are quite good. Below, we would like to present our results on deprotection reaction for some selected acetylated compounds **8**, **12**, **14**, **18**, **26**, **27** (Table 3).

3. Conclusions

Herein we have presented the synthesis of a library of modified monosaccharides with 1,2,3-triazole ring having highly fluorinated aliphatic chain. All compounds were prepared *via "click"* reaction with good yields. Two different "*click*" reaction methodologies has been used: Sharpless or Meldal conditions.

Table 1
"Click" reaction of azidosaccharides **2, 13** with propargyl ethers **3-7**[a].

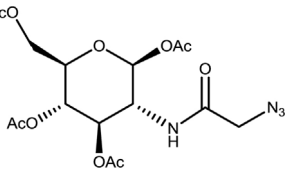
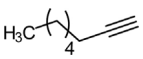
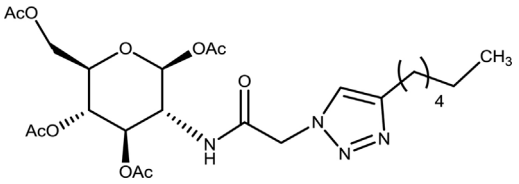
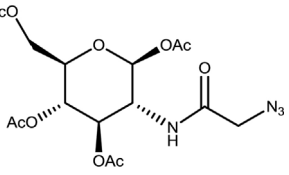
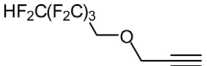
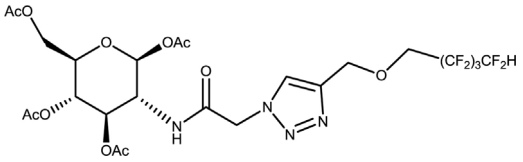
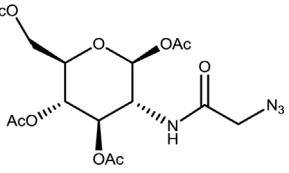
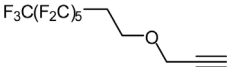
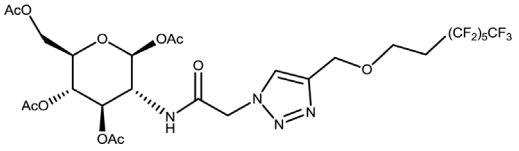
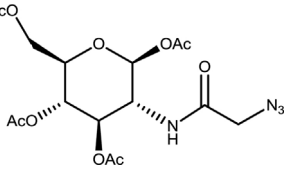
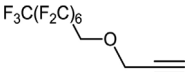
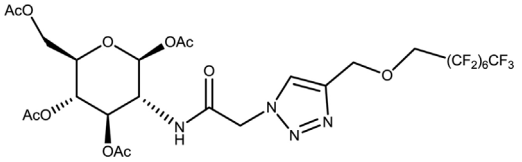
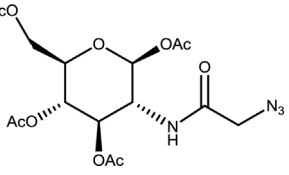
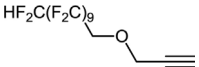
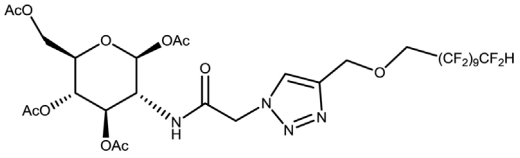
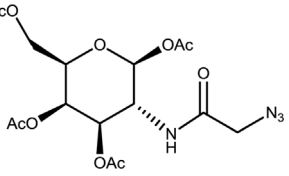
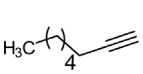
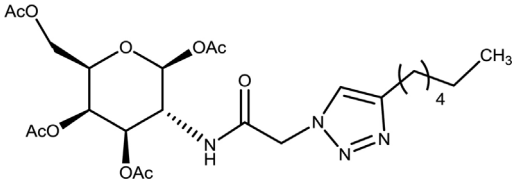
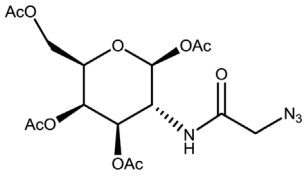
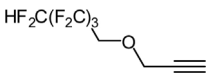
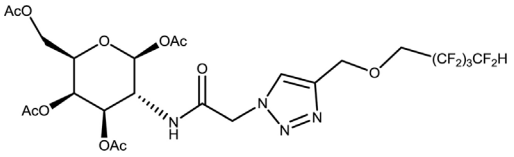
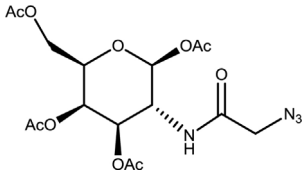
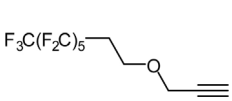
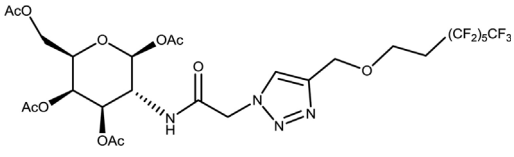
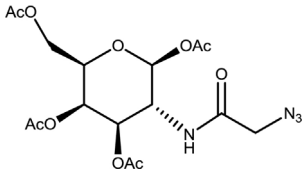
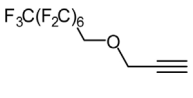
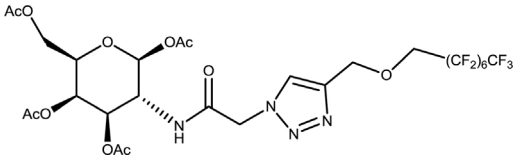
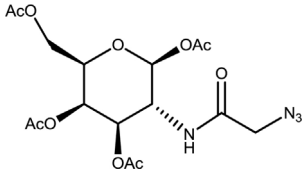
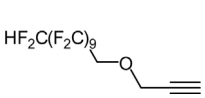
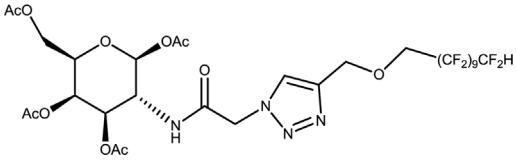
L.P	Starting material	Propargyl ether	Product	Reaction Yield%
1.				91
	2	3	8	
2.				87
	2	4	9	
3.				91
	2	5	10	
4.				88
	2	6	11	
5.				93
	2	7	12	
6.				99
	13	3	14	

Table 1 (*Continued*)

L.P	Starting material	Propargyl ether	Product	Reaction Yield%
7.				80
	13	4	15	
8.				76
	13	5	16	
9.				89
	13	6	17	
10.				99
	13	7	18	

[a] Reactions conditions: $CuSO_4$, NaASC, *t*BuOH/H_2O, rt.

4. Experimental section

All chemicals were reagent grade and used as purchased without further purification. Anhydrous DCM was prepared by pre-drying with anhydrous $CaCl_2$ followed by distillation over CaH_2 under argon atmosphere. Thin-layer chromatography (TLC) was carried out on silica gel plates (Silica gel 60, F254, Merck) with detection by UV light or with stain solution (Cerium Molybdate Stain and Potassium Permanganate). Purification was performed with column chromatography using normal-phase silica gel (Silica gel 60, 70–230 mesh, Fluka). ^1H, ^{13}C, ^{19}F NMR were recorded with a Varian VNMR-S 400 MHz, VARIAN Mercury 300 MHz or Bruker Avance 600 MHz, Bruker ASCEND 600 (600 MHz). Chemical shifts are reported as δ values (ppm). NMR spectra were calibrated using an internal reference: TMS (^1H), $CDCl_3$ (^{13}C) and $CFCl_3$ (^{19}F). Spectra were recorded in deuterated solvents $CDCl_3$ (7.26 ppm (^1H) or 77.0 ppm (^{13}C)), CD_3CN (1.93 (^1H) or 118.2 (^{13}C)) and $(CD_3)_2SO$ (2.49 ppm (^1H) or 39.5 ppm (^{13}C)). Multiplicities of signals are described as follows: s = singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublet of doublets, t = triplet, td = triplet of doublets, tt = triplet of triplets, m = multiplet. Coupling constants (*J*) are given in hertz (Hz). Mass spectra (ESI) were carried out with TripleTOF® 5600 + System, AB SCIEX and Agilent 1200 LC system with Agilent Q-TOF 6540 spectrometer with DUAL AJS ESI source. Optical rotations of sugars were measured with JASCO P-2000 at 20 ± 0.05 °C, D values were determined at 589 nm in MeCN, DCM or DMSO as a solvent. $[\alpha]_D$ values are given in degrees. Melting points were measured with MEL-TEMP® apparatus.

*4.1. Propargyl-3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloracetamido-β-D-glucopyranoside* ***19***

BF_3xOEt_2 (19.3 mL, 152.52 mmol) and propargyl alcohol (9.6 mL, 162.40 mmol) were added to a stirring solution of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (5.00 g, 10.15 mmol) in anhydrous DCM (20 mL), under an argon atmosphere, at room temperature. The reaction mixture was stirred for 48 h. It was subsequently diluted with EtOAc (100 mL) and washed with sat. $NaHCO_3$ (2 × 100 mL). The organic phase was dried over Na_2SO_4 and concentrated to dryness. The crude product was purified by column chromatography (Hex:EtOAc 2:1, v/v) and afforded **19** as a white solid; yield 2.85 g (56%); mp 139–143 °C; $[\alpha]_D = -10.06$ (c 1.05, MeCN); ^1H NMR (403 MHz, $CDCl_3$): δ 6.82 (d, 1H, *J* = 9.0 Hz, NH), 5.38 (dd, 1H, *J* = 9.3 Hz, *J* = 10.7 Hz, H-3), 5.14 (t, 1H, *J* = 9.6 Hz, H-4), 4.91 (d, 1H, *J* = 8.4 Hz, H-1), 4.40 (d, 2H, *J* = 2.4 Hz, CH_2—C≡C), 4.31 (dd, 1H, *J* = 4.7 Hz, *J* = 12.4 Hz, H-6a), 4.17 (dd, 1H, *J* = 2.4 Hz, *J* = 12.4 Hz, H-6b), 4.07-3.99 (m, 1H, H-2), 3.77 (ddd, 1H,

Table 2
"Click" reaction of monosaccharides with propargyl moiety **19** with non-fluorinated azide **20** and fluorinated azides **21-25**[a].

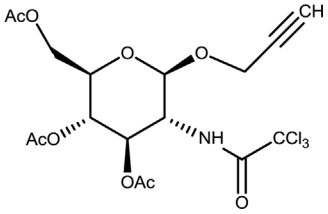
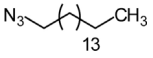
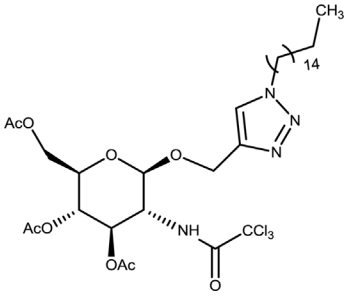
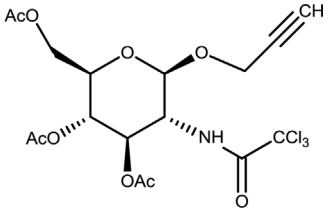
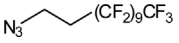
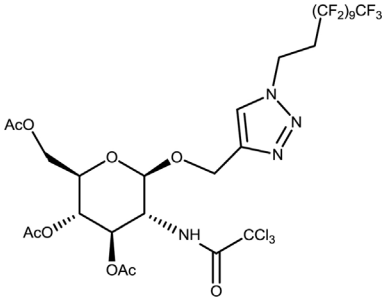
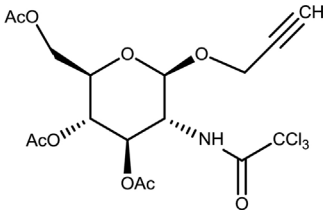
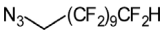
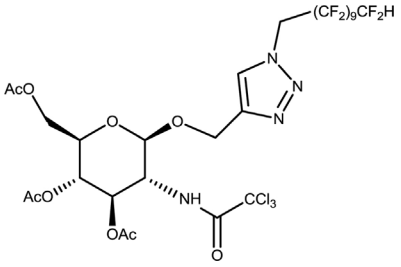
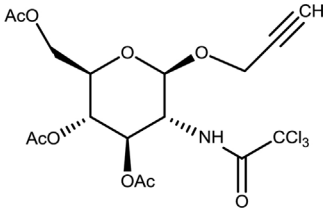
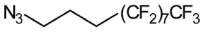
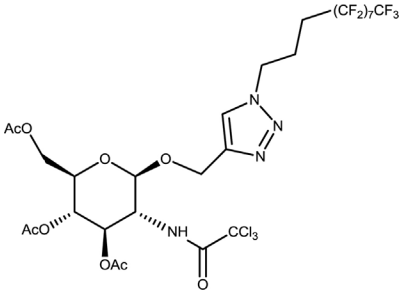
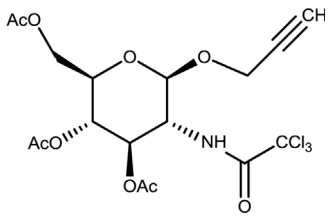
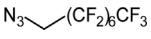
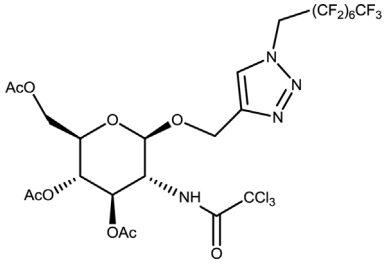
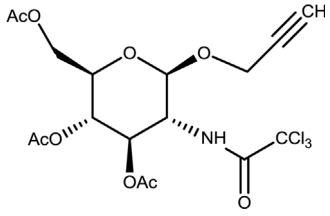
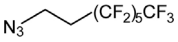
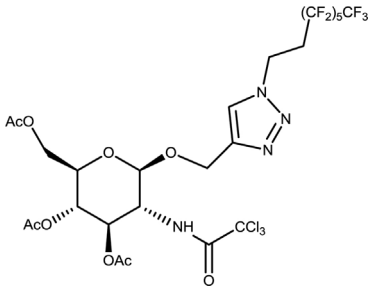
L.P	Starting material	Azide	Product	Reaction Yield%
1.				76
	19	20	26	
2.				91
	19	21	27	
3.				56
	19	22	28	
4.				56
	19	23	29	

Table 2 (*Continued*)

L.P	Starting material	Azide	Product	Reaction Yield%
5.				34
	19	24	30	
6.				38
	19	25	31	

[a] Reaction conditions: CuI, Et_3N, MeCN/H_2O, rt.

J = 2.4 Hz, *J* = 4.7 Hz, *J* = 9.9 Hz, H-5), 2.46 (t, 1H, *J* = 2.4 Hz, ≡CH), 2.11 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.04 (s, 3H, OAc); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.9, 170.6, 169.2, 162.0, 97.9, 92.2, 78.1, 75.7, 72.2, 71.5, 68.2, 61.8, 56.1, 55.6, 20.7, 20.6, 20.5; MS (ESI) *m*/*z* [M +Na]$^+$ calcd for $C_{17}H_{20}Cl_3NNaO_9$: 510.0102; found: 510.0094.

4.2. 1,3,4,6-Tetra-O-acetyl-N-azidoacetylo-β-D-glucosamine **2**

A solution of 2-deoxy-2-amino-1,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl hydrochloride (2 g, 5.22 mmol) in anhydrous DCM (40 mL) was cooled to 0 °C. Next Et_3N (1.06 mL) was added followed by DCC (3.82 g, 18.56 mmol) and 2-azidoacetic acid (3.75 g, 37.1 mmol). The reaction mixture was allowed to warm up to room temperature and stirred overnight. After finishing the precipitate was filtered and the solvents were evaporated. Product was purified by column chromatography (Hex:EtOAc 1:1, v/v) or crystallization EtOAc/CCl_3/Hex gave **2** as white solid; yield 1.79 g (82%); mp 113–117 °C; $[\alpha]_D$ = +16.14 (c 1.02, DCM); ^{1}H NMR (403 MHz, $CDCl_3$): δ 6.65 (d, 1H, *J* = 9.4 Hz, NH), 5.81 (d, 1H, *J* = 8.7 Hz, H-1), 5.30 (dd, 1H, *J* = 9.3 Hz, *J* = 10.5 Hz, H-3), 5.14 (t, 1H, *J* = 9.6 Hz, H-4), 4.29 (dd, 1H, *J* = 2.8 Hz, *J* = 10.6 Hz, H-6a), 4.28-4.22 (m, 1H, H-2), 4.14 (dd, 1H, *J* = 2.3 Hz, *J* = 12.5 Hz, H-6b), 3.92 (s, 2H, CH_2N_3), 3.88 (ddd, 1H, *J* = 2.3 Hz, *J* = 4.7 Hz, *J* = 10.0 Hz, H-5), 2.12 (s, 3H, OAc), 2.10 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.05 (s, 3H, OAc); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.0, 170.6, 169.3, 169.3, 167.1, 92.1, 72.8, 72.1, 67.8, 61.6, 53.0, 52.5, 20.8, 20.7, 20.6, 20.5; MS (ESI) *m*/*z* [M +Na]$^+$ calcd for $C_{16}H_{22}N_4NaO_{10}$: 453.1234; found: 453.1234.

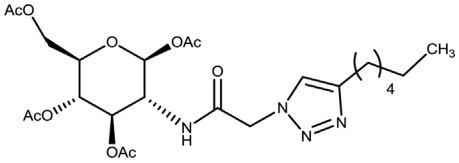
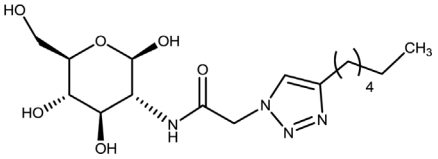
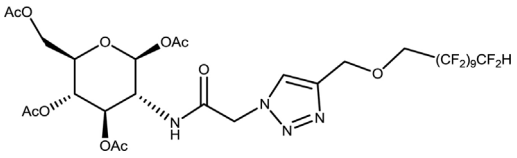
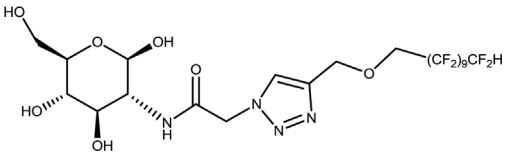
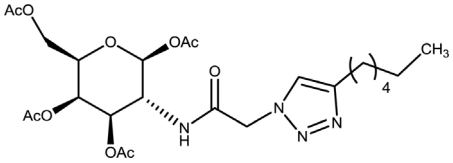
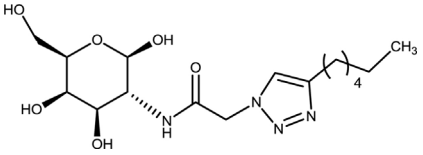
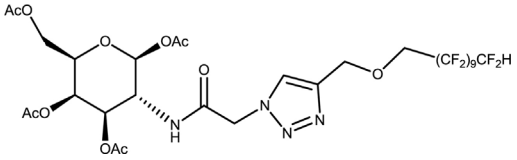
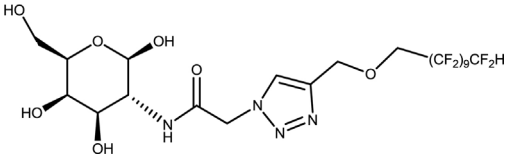
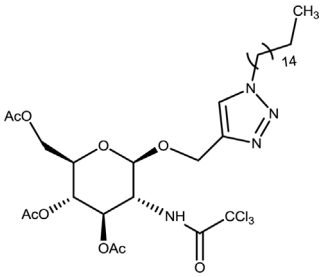
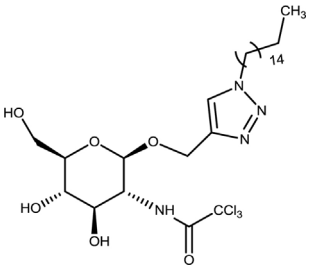
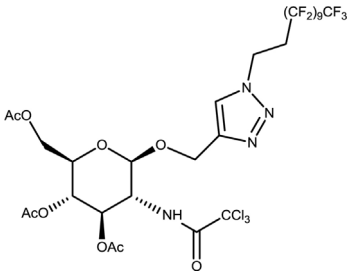
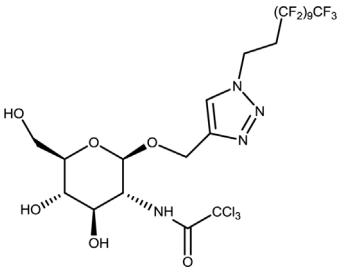
4.3. 1,3,4,6-Tetra-O-acetyl-N-azidoacetylo-D-galactosamine **13**

A solution of 2-deoxy-2-amino-1,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl hydrochloride (2 g, 5.22 mmol) in anhydrous DCM (40 mL) was cooled to 0 °C. Next Et_3N (1.06 mL) was added followed by DCC (2.15 g, 10.44 mmol) and 2-azidoacetic acid (2.11 g, 20.88 mmol). The reaction mixture was allowed to warm up to room temperature and stirred overnight. After finishing the precipitate was filtered and the solvents were evaporated. Product was purified by column chromatography (Hex:EtOAc 1:1, v/v) or crystallization EtOAc/CCl_3/Hex gave **13** as white solid; yield 1.4 g (63%); mp 120–124 °C; $[\alpha]_D$ = +17.04 (c 1.06, DCM); ^{1}H NMR (403 MHz, $CDCl_3$): δ 6.52 (d, 1H, *J* = 9.4 Hz, NH), 5.84 (d, 1H, *J* = 8.8 Hz, H-1), 5.41 (d, 1H, *J* = 2.9 Hz, H-3), 5.26 (dd, 1H, *J* = 3.3 Hz, *J* = 11.3 Hz, H-4), 4.41–4.33 (m, 1H, H-2), 4.21–4.07 (m, 3H, H-6a, H-6b, H-5), 3.93 (s, 2H, CH_2N_3), 2.18 (s, 3H, OAc), 2.14 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.03 (s, 3H, OAc); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 170.4, 170.1, 169.4, 167.3, 92.5, 71.8, 69.9, 66.3, 61.3, 52.6, 50.0, 33.7, 20.8, 20.6, 20.6; MS (ESI) *m*/*z* [M+Na]$^+$ calcd for $C_{16}H_{22}N_4NaO_{10}$: 453.1234; found: 453.1232.

4.4. General procedure for the click reaction of sugar azides: N-azidoacetylo-β-D-glucopyranoside **2** and N-azidoacetylo-β-D-galactopyranoside **13**

1,3,4,6-Tetra-*O*-acetyl-*N*-azidoacetylo-β-D-glucosamine (**2**) (1 equiv) or 1,3,4,6-tetra-*O*-acetyl-*N*-azidoacetylo-D-galactosamine (**13**) (1 equiv) and octyne (**3**) (1.5 equiv) or corresponding propargyl ether (**4**-**7**) (1.5 equiv) were dissolved in the mixture of *t*-BuOH/H_2O (1:1, v/v, 7 mL for 1 mmol of sugar). To the reaction mixture 1 M aq. solution of NaASC (0.1 equiv) and 1 M aq. solution of $CuSO_4 \cdot 5H_2O$ (0.1 equiv) were added and stirred at room temperature for 24 h. The mixture was dissolved in H_2O (2–4 mL) and extracted with Et_2O (3 × 4 mL). Organic phases were combined and washed with 1N HCl (4 mL) and dried over Na_2SO_4. Solvent was evaporated. The crude product was purified by column chromatography (Hex:EtOAc 1:1, v/v) to afford desired products **8,9,10,11,12,14,15,16,17,18.**

Table 3
The deprotection reactions for selected acetylated sugars after "click" reaction **8**, **12**, **14**, **18**, **26**, **27**[a].

L.P	Starting material	Product	Reaction Yield%
1.			79
	8	32	
2.			70
	12	33	
3.			70
	14	34	
4.			82
	18	35	
5.			61
	26	36	
6.			85
	27	37	

[a] Reaction conditions: DCM:MeOH (3:7, v/v), NaOMe 25 wt.% in MeOH, rt.

4.4.1. 1-(1,3,4,6-Tetra-O-acetyl-2-azidoacetamido-2-deoxy-β-D-glucopyranosyl)-4-hexyl-1H-1,2,3-triazole ***8***

1,3,4,6-Tetra-*O*-acetyl-2-azidoacetamido-2-deoxy-β-D-glucopyranoside (**2**) (0.091 g, 0.212 mmol) and 1-octyne (**3**) (0.035 g, 0.318 mmol) gave **8** as a white solid; yield 0.094 g (82%); mp 172–175 °C; $[\alpha]_D$ = +12.98 (c 1.02, DCM); ^{1}H NMR (403 MHz, $CDCl_3$): δ 7.41 (s, 1H, triazole-H), 6.79 (d, 1H, *J* = 8.9 Hz, NH), 5.89 (d, 1H, *J* = 8.7 Hz, H-1), 5.35 (dd, 1H, *J* = 9.4 Hz, *J* = 10.4 Hz, H-3), 5.09 (t, 1H, *J* = 9.6 Hz, H-4), 4.96 (d, 2H, *J* = 3.7 Hz, CH_2triazole), 4.28 (dd, 1H, *J* = 4.6 Hz, *J* = 12.5 Hz, H-6a), 4.14–4.04 (m, 2H, H-6b, H-2), 3.86 (ddd, 1H, *J* = 2.2 Hz, *J* = 4.5 Hz, *J* = 10.0 Hz, H-5), 2.71 (t, 2H, *J* = 7.6 Hz, triazoleCH_2), 2.08 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.97 (s, 3H, OAc), 1.71-1.61 (m, 2H, triazole-CH_2CH_2), 1.40–1.24 (m, 6H, $(CH_2)_3$), 0.88 (t, 3H, *J* = 6.9 Hz, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.6, 170.5, 169.3, 169.1, 165.9, 149.1, 122.1, 91.7, 72.6, 71.8, 67.9, 61.6, 53.8, 53.0, 31.5, 29.2, 28.9, 25.6, 22.5, 20.8, 20.7, 20.5, 14.0; MS (ESI) *m*/*z* $[M+H]^+$ calcd for $C_{24}H_{37}N_4O_{10}$: 541.2509; found: 541.2503; *m*/*z* $[M+Na]^+$ calcd for $C_{24}H_{36}N_4NaO_{10}$: 563.2330; found: 563.2299.

4.4.2. 1-(1,3,4,6-Tetra-O-acetyl-2-azidoacetamido-2-deoxy-β-D-glucopyranosyl)-4-(2,2,3,3,4,4,5,5-octafluorobutylmethoxy)methyl-1H-1,2,3-triazole ***9***

1,3,4,6-Tetra-*O*-acetyl-2-azidoacetamido-2-deoxy-β-D-glucopyranoside (**2**) (0.170 g, 0.395 mmol) and 3-((1-octafluorobutyl) methoxy)prop-1-yne (**4**) (0.160 g, 0.593 mmol) gave **9** as a white solid; yield 0.241 g (87%); mp 164–166 °C; $[\alpha]_D$ = +12.84 (c 0.99, MeCN); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (s, 1H, triazole-H), 6.94 (d, 1H, *J* = 9.1 Hz, NH), 6.07 (tt, 1H, *J* = 5.5 Hz, *J* = 51.9 Hz, HCF_2), 5.89 (d, 1H, *J* = 8.7 Hz, H-1), 5.35 (dd, 1H, *J* = 9.4 Hz, *J* = 10.4 Hz, H-3), 5.11 (dd, 1H, *J* = 9.4 Hz, *J* = 10.4 Hz, H-4), 5.04 (d, 2H, *J* = 5.3 Hz, triazoleCH_2O), 4.82 (s, 2H, CH_2triazole), 4.28 (dd, 1H, *J* = 4.6 Hz, *J* = 12.5 Hz, H-6a), 4.24-4.14 (m, 1H, H-2), 4.15–4.03 (m, 3H, H-6b, $OCH_2(CF_2)_3CF_2H$), 3.89 (ddd, 1H, *J* = 2.2 Hz, *J* = 4.6 Hz, *J* = 10.0 Hz, H-5), 2.09 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.04 (s, 3H, OAc), 1.98 (s, 3H, OAc); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.0, 170.7, 169.4, 169.3, 165.5, 144.3, 124.5, 118.4-104.5, 91.9, 72.7, 72.1, 68.0, 67.0, 65.5, 61.6, 53.7, 53.1, 20.8, 20.7, 20.5, 20.5; ^{19}F NMR (377 MHz, $CDCl_3$): δ −119.79, −125.52, −130.21, −137.30; MS (ESI) *m*/*z* $[M+H]^+$ calcd for $C_{24}H_{29}F_8N_4O_{11}$: 701.1705; found: 701.1702; *m*/*z* $[M+Na]^+$ calcd for $C_{24}H_{28}F_8N_4NaO_{11}$: 723.1525; found: 723.1523.

4.4.3. 1-(1,3,4,6-Tetra-O-acetyl-2-azidoacetamido-2-deoxy-β-D-glucopyranosyl)-4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorohexylethoxy)methyl-1H-1,2,3-triazole ***10***

1,3,4,6-Tetra-*O*-acetyl-2-azidoacetamido-2-deoxy-β-D-glucopyranoside (**2**) (0.120 g, 0.279 mmol) and 3-((2-perfluorohexyl) ethoxy)prop-1-yne (**5**) (0.168 g, 0.419 mmol) gave **10** as a white solid; yield 0.212 g (91%); mp 159–164 °C; $[\alpha]_D$ = +10.48 (c 1.05, MeCN); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (s, 1H, triazole-H), 6.62 (d, 1H, *J* = 9.0 Hz, NH), 5.88 (d, 1H, *J* = 8.7 Hz, H-1), 5.32 (dd, 1H, *J* = 9.4 Hz, *J* = 10.4 Hz, H-3), 5.12 (t, 1H, *J* = 9.6 Hz, H-4), 5.02 (d, 2H, *J* = 3.3 Hz, triazoleCH_2O), 4.70 (s, 2H, CH_2triazole), 4.29 (dd, 1H, *J* = 4.6 Hz, *J* = 12.5 Hz, H-6a), 4.18–4.09 (m, 2H, H-6b, H-2), 3.87 (t, 2H, *J* = 6.7 Hz, OCH_2CH_2), 2.45 (m, 2H, $CH_2(CF_2)_5CF_3$), 2.10 (s, 6H, OAc), 2.05 (s, 3H, OAc), 2.00 (s, 3H, OAc); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.0, 170.7, 169.4, 169.3, 165.7, 145.2, 124.1, 121.7-105.1, 91.8, 72.6, 72.1, 68.1, 64.4, 62.6, 61.7, 53.5, 53.1, 31.3, 20.8, 20.7, 20.5, 20.5; ^{19}F NMR (377 MHz, $CDCl_3$): δ −80.87, −113.47, −121.95, −122.94, −123.73, −126.21; MS (ESI) *m*/*z* $[M+H]^+$ calcd for $C_{27}H_{30}F_{13}N_4O_{11}$: 833.1703; found: 833.1699; *m*/*z* $[M+Na]^+$ calcd for $C_{27}H_{29}F_{13}N_4NaO_{11}$: 855.1523; found: 855.1519.

4.4.4. 1-(1,3,4,6-Tetra-O-acetyl-2-azidoacetamido-2-deoxy-β-D-glucopyranosyl)-4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluoroheptylmethoxy)methyl-1H-1,2,3-triazole ***11***

1,3,4,6-Tetra-*O*-acetyl-2-azidoacetamido-2-deoxy-β-D-glucopyranoside (**2**) (0.108 g, 0.269 mmol) and 3-((1-perfluoroheptyl) methoxy)prop-1-yne (**6**) (0.177 g, 0.404 mmol) gave **11** as a white solid; yield 0.179 g (88%); mp 192–195 °C; $[\alpha]_D$ = +9.97 (c 0.85, MeCN); ^{1}H NMR (600 MHz, CD_3CN): δ 7.80 (s, 1H, triazole-H), 6.79 (d, 1H, *J* = 9.2 Hz, NH), 5.84 (d, 1H, *J* = 8.8 Hz, H-1), 5.29 (dd, 1H, *J* = 9.4 Hz, *J* = 10.7 Hz, H-3), 5.01 (dd, 1H, *J* = 9.4 Hz, *J* = 10.4 Hz, H-4), 4.99 (s, 2H, CH_2triazole), 4.75 (s, 2H, triazoleCH_2O), 4.20 (dd, 1H, *J* = 4.6 Hz, *J* = 12.5 Hz, H-6a), 4.13 (t, 2H, *J* = 14.4 Hz, H-6b, H-2), 4.07–4.02 (m, 2H, $OCH_2(CF_2)_6CF_3$), 3.92 (ddd, 1H, *J* = 2.4 Hz, *J* = 4.8 Hz, *J* = 10.1 Hz, H-5), 2.04 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.95 (s, 3H, OAc); ^{13}C NMR (101 MHz, CD_3CN): δ 171.1, 171.0, 170.4, 169.9, 166.9, 144.0, 126.2, 120.0-107.7, 92.4, 73.2, 72.5, 69.0, 67.2, 65.8, 62.5, 53.8, 52.9, 20.9, 20.79, 20.78, 20.75; ^{19}F NMR (379 MHz, CD_3CN): δ −80.33, −118.92, −121.31, −121.98, −122.55, −125.40; MS (ESI) *m*/*z* $[M+H]^+$ calcd for $C_{27}H_{28}F_{15}N_4O_{11}$: 869.1515; found: 869.1512; *m*/*z* $[M+Na]^+$ calcd for $C_{27}H_{27}F_{15}N_4NaO_{11}$: 891.1335; found: 891.1333.

4.4.5. 1-(1,3,4,6-Tetra-O-acetyl-2-azidoacetamido-2-deoxy-β-D-glucopyranosyl)-4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-eicosafluorononylmethoxy)methyl-1H-1,2,3-triazole ***12***

1,3,4,6-Tetra-*O*-acetyl-2-azidoacetamido-2-deoxy-β-D-glucopyranoside (**2**) (0.150 g, 0.349 mmol) and 3-((1-eicosafluorodecanyl)methoxy)prop-1-yne (**7**) (0.299 g, 0.524 mmol) gave **12** as a white solid; yield 0.325 g (93%); mp 197–199 °C; $[\alpha]_D$ = +9.01 (c 1.02, MeCN); ^{1}H NMR (600 MHz, CD_3CN): δ 7.80 (s, 1H, triazole-H), 6.80 (d, 1H, *J* = 9.2 Hz, NH), 6.47 (tt, 1H, *J* = 51.0 Hz, *J* = 5.1 Hz, HCF_2), 5.84 (d, 1H, *J* = 8.8 Hz, H-1), 5.29 (dd, 1H, *J* = 9.4 Hz, *J* = 10.7 Hz, H-3), 5.01 (dd, 1H, *J* = 9.4 Hz, *J* = 10.4 Hz, H-4), 4.98 (s, 2H, CH_2triazole), 4.75 (s, 2H, triazoleCH_2O), 4.20 (dd, 1H, *J* = 4.8 Hz, *J* = 12.5 Hz, H-6a), 4.12 (t, 2H, *J* = 14.3 Hz, H-6b, H-2), 4.07-4.01 (m, 2H, $OCH_2(CF_2)_9CF_2H$), 3.91 (ddd, 1H, *J* = 2.4 Hz, *J* = 4.8 Hz, *J* = 10.1 Hz, H-5), 2.05 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.95 (s, 3H, OAc); ^{13}C NMR (151 MHz, CD_3CN): δ 172.7, 172.5, 171.9, 171.5, 168.5, 145.7, 127.7, 118.7-108.2, 94.0, 74.9, 74.1, 70.7, 60.9, 67.5, 64.1, 55.5, 54.6, 22.5, 22.4, 22.4, 22.3; ^{19}F NMR (282 MHz, CD_3CN): δ −118.97, −121.09, −121.33, −122.58, −128.74, −137.66, −137.82; MS (ESI) *m*/*z* $[M+Na]^+$ calcd for $C_{30}H_{28}F_{15}N_4NaO_{11}$: 1023.1333; found: 1023.1334.

4.4.6. 1-(1,3,4,6-Tetra-O-acetyl-2-azidoacetamido-2-deoxy-β-D-galactopyranosyl)-4-hexyl-1H-1,2,3-triazole ***14***

1,3,4,6-Tetra-*O*-acetyl-2-azidoacetamido-2-deoxy-β-D-galactopyranoside (**13**) (0.055 g, 0.128 mmol) and octyne (**3**) (0.021 g, 0.192 mmol) gave **14** as a white solid; yield 0.068 g (99%); mp 169–172 °C; $[\alpha]_D$ = +13.95 (c 1.04, DCM); ^{1}H NMR (403 MHz, $CDCl_3$): δ 7.47 (s, 1H, triazole-H), 7.21 (d, 1H, *J* = 8.7 Hz, NH), 5.92 (d, 1H, *J* = 8.8 Hz, H-1), 5.37 (d, 1H, *J* = 3.4 Hz, H-3), 5.33 (dd, 1H, *J* = 3.4 Hz, *J* = 11.1 Hz, H-4), 4.97 (s, 2H, CH_2-triazole), 4.35-4.23 (m, 1H, H-2), 4.17–4.06 (m, 3H, H-6a, H-6b, H-5), 2.70 (t, 2H, *J* = 7.6 Hz, triazoleCH_2), 2.15 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.93 (s, 3H, OAc), 1.70–1.60 (m, 2H, triazoleCH_2CH_2), 1.40-1.24 (m, 6H, $(CH_2)_3$), 0.89 (t, 3H, *J* = 6.9 Hz, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.3, 170.3, 170.1, 169.3, 166.1, 149.0, 122.1, 92.2, 71.6, 69.7, 66.4, 61.3, 52.1, 50.3, 33.9, 31.5, 29.2, 28.9, 25.5, 22.5, 20.8, 20.6, 20.5, 14.0; MS (ESI) *m*/*z* $[M+H]^+$ calcd for $C_{24}H_{37}N_4O_{10}$: 541.2509; found: 541.2500; *m*/*z* $[M+Na]^+$ calcd for $C_{24}H_{36}N_4NaO_{10}$: 563.2329; found: 563.2297.

4.4.7. 1-(1,3,4,6-Tetra-O-acetyl-2-azidoacetamido-2-deoxy-β-D-galactopyranosyl)-4-(2,2,3,3,4,4,5,5-octafluorobutylmethoxy) methyl-1H-1,2,3-triazole ***15***

1,3,4,6-Tetra-*O*-acetyl-2-azidoacetamido-2-deoxy-β-D-galactopyranoside (**13**) (0.060 g, 0.15 mmol) and 3-((1-octafluorobutyl) methoxy)prop-1-yne (**4**) (0.060 g, 0.225 mmol) gave **15** as a white solid; yield 0.084 g (80%); mp 174–178 °C; $[\alpha]_D$ = +5.93 (c 1.01, DCM); ^{1}H NMR (403 MHz, $CDCl_3$): δ 7.73 (s, 1H, triazole-H), 6.73 (d, 1H, *J* = 9.1 Hz, NH), 6.04 (tt, 1H, *J* = 5.5 Hz, *J* = 51.9 Hz, CF_2H), 5.89 (d, 1H, *J* = 8.7 Hz, H-1), 5.37 (d, 1H, *J* = 3.3 Hz, H-3), 5.29 (dd, 1H, *J* = 3.4 Hz, *J* = 11.2 Hz, H-4), 5.01 (s, 2H, CH_2triazole), 4.80 (s, 2H, triazoleCH_2O), 4.34-4.25 (m, 1H, H-2), 4.17-4.02 (m, 5H, H-6a, H-6b, H-5, $CH_2(CF_2)_3CF_2H$), 2.16 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.95 (s, 3H, OAc); ^{13}C NMR (151 MHz, $CDCl_3$); δ 170.6, 170.5, 170.2, 169.5, 165.7, 144.3, 124.5, 117.5-105.6, 92.3, 71.7, 69.8, 67.0, 66.5, 65.5, 61.4, 53.2, 50.5, 33.9, 25.6, 24.9, 20.8; ^{19}F NMR (379 MHz, $CDCl_3$): δ −120.30, −126.02, −130.76, −137.83; MS (ESI) *m*/*z* $[M+H]^+$ calcd for $C_{24}H_{29}F_8N_4O_{11}$: 701.1705; found: 701.1705.

4.4.8. 1-(1,3,4,6-Tetra-O-acetyl-2-azidoacetamido-2-deoxy-β-D-galactopyranosyl)-4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorohexylethoxy)methyl-1H-1,2,3-triazole ***16***

1,3,4,6-Tetra-*O*-acetyl-2-azidoacetamido-2-deoxy-β-D-galactopyranoside (**13**) (0.060 g, 0.15 mmol) and 3-((2-perfluorohexyl) ethoxy)prop-1-yne (**5**) (0.090 g, 0.225 mmol) gave **16** as a white solid; yield 0.095 g (76%); mp 175–178 °C; $[\alpha]_D$ = −31.80 (c 1.02, MeCN); ^{1}H NMR (403 MHz, $CDCl_3$): δ 7.68 (s, 1H, triazole-H), 6.66 (d, 1H, *J* = 8.6 Hz, NH), 5.88 (d, 1H, *J* = 6.4 Hz, H-1), 5.37 (d, 1H, *J* = 3.2 Hz, H-3), 5.28 (dd, 1H, *J* = 3.4 Hz, *J* = 11.2 Hz, H-4), 4.99 (s, 2H, triazoleCH_2O), 4.67 (s, 2H, CH_2triazole), 4.32-4.24 (m, 1H, H-2), 4.18-4.06 (m, 3H, H-6a, H-6b, H-5), 3.85 (t, 2H, *J* = 6.6 Hz, $OCH_2CH_2(CF_2)_5CF_3$), 2.90-2.34 (m, 2H, $CH_2(CF_2)_5CF_3$), 2.16 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.95 (s, 3H, OAc); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.5, 170.4, 170.2, 169.5, 165.8, 145.3, 124.1, 121.1-102.5, 92.3, 71.7, 69.8, 66.5, 64.4, 62.6, 61.3, 53.2, 50.5, 31.4, 20.8, 20.6, 20.5; ^{19}F NMR (379 MHz, $CDCl_3$): δ −81.29, −113.92, −122.41, −123.39, −124.19, −126.66; MS (ESI) *m*/*z* $[M+H]^+$ calcd for $C_{27}H_{30}F_{13}N_4O_{11}$: 833.1703; found: 833.1700; *m*/*z* $[M+Na]^+$ calcd for $C_{27}H_{29}F_{13}N_4NaO_{11}$: 855.1523; found: 855.1516.

4.4.9. 1-(1,3,4,6-Tetra-O-acetyl-2-azidoacetamido-2-deoxy-β-D-galactopyranosyl)-4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluorooctylmethoxy)methyl-1H-1,2,3-triazole ***17***

1,3,4,6-Tetra-*O*-acetyl-2-azidoacetamido-2-deoxy-β-D-galactopyranoside (**13**) (0.040 g, 0.10 mmol) and 3-((1-perfluoroheptyl) methoxy)prop-1-yne (**6**) (0.065 g, 0.15 mmol) gave **17** as a white solid; yield 0.077 g (89%); mp 184–188 °C; $[\alpha]_D$ = +45.06 (c 0.82, DCM); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72 (s, 1H, triazole-H), 6.51 (d, 1H, *J* = 8.6 Hz, NH), 5.87 (d, 1H, *J* = 8.8 Hz, H-1), 5.37 (d, 1H, *J* = 3.3 Hz, H-3), 5.27 (dd, 1H, *J* = 3.3 Hz, *J* = 11.3 Hz, H-4), 5.00 (s, 2H, triazoleCH_2O), 4.82 (s, 2H, CH_2triazole), 4.34-4.22 (m, 1H, H-2), 4.15-4.01 (m, 3H, H-6a, H-6b, H-5), 2.16 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.04 (s, 3H, OAc), 1.96 (s, 3H, OAc); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.6, 170.4, 170.2, 169.5, 165.7, 144.3, 124.4, 119.0-107.0, 92.3, 71.7, 69.8, 67.2, 66.5, 65.6, 61.3, 53.2, 50.5, 33.9, 25.6, 24.9, 20.6; ^{19}F NMR (282 MHz, $CDCl_3$): δ −81.25, −120.10, −122.56, −123.26, −123.77, −126.63; MS (ESI) *m*/*z* $[M+H]^+$ calcd for $C_{27}H_{28}F_{15}N_4O_{11}$: 869.1515; found: 869.1518; *m*/*z* $[M+Na]^+$ calcd for $C_{27}H_{27}F_{15}N_4NaO_{11}$: 891.1335; found: 891.1335.

4.4.10. 1-(1,3,4,6-Tetra-O-acetyl-2-azidoacetamido-2-deoxy-β-D-galactopyranosyl)-4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-eicosafluorononylmethoxy)methyl-1H-1,2,3-triazole ***18***

1,3,4,6-Tetra-*O*-acetyl-2-azidoacetamido-2-deoxy-β-D-galactopyranoside (**13**) (0.060 g, 0.15 mmol) and 3-((1-eicosafluorodecanyl)methoxy)prop-1-yne (**7**) (0.128 g, 0.225 mmol) gave **18** as a white solid; yield 0.150 mg (99%); mp 192–196 °C; $[\alpha]_D$ = +23.49 (c 1.05, DMSO); ^{1}H NMR (403 MHz, DMSO-d_6): δ 8.64 (d, 1H, *J* = 9.3 Hz, NH), 8.08 (s, 1H, triazole-H), 7.22 (tt, 1H, *J* = 5.2 Hz, *J* = 50.1 Hz, HCF_2), 5.71 (d, 1H, *J* = 8.8 Hz, H-1), 5.28 (d, 1H, *J* = 2.7, H-3), 5.13 (dd, 1H, *J* = 3.4 Hz, *J* = 11.3 Hz, H-4), 4.09 (s, 2H, triazoleCH_2O), 4.82 (s, 2H, CH_2triazole), 4.32-4.18 (m, 2H, H-6a, H-6b), 4.18-4.10 (m, 1H, H-2), 4.09-3.97 (m, 2H, H-5, $CH_2(CF_2)_9CF_2H$), 2.10 (s, 3H, OAc), 2.02 (s, 3H, OAc), 1.99 (s, 3H, OAc), 1.91 (s, 3H, OAc); ^{13}C NMR (101 MHz, DMSO-d_6): δ 169.9, 169.88, 169.5, 168.9, 166.1, 142.3, 104.7-118.5, 125.9, 92.2, 70.8, 69.9, 66.4, 65.8, 61.3, 51.7, 48.5, 40.4, 20.49, 20.45, 20.3; ^{19}F NMR (282 MHz, $CDCl_3$): δ −120.08, −122.31, −123.78, −129.76, −137.38, −137.56; MS (ESI) *m*/*z* $[M+H]^+$ calcd for $C_{30}H_{29}F_{20}N_4O_{11}$: 1001.1513; found: 1001.1513; *m*/*z* $[M+Na]^+$ calcd for $C_{30}H_{28}F_{15}N_4NaO_{11}$: 1023.1333; found: 1023.1333.

4.5. General procedure for the click reaction of sugar with propargyl moiety

Propargyl-3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**19**) (1 equiv) and azidohexadecane (**20**) (1.3 equiv) or corresponding fluorinated azide (**21**-**25**) (1.3 equiv) were dissolved in the mixture of MeCN (1.33 mL for 1 mmol of sugar) and H_2O (2.67 mL for 1 mmol of sugar). To the reaction mixture Et_3N (1.3 equiv) and CuI (0.1 equiv) were added and stirred at room temperature for 24 h. The mixture was dissolved in H_2O (3 mL) and extracted with Et_2O (3 × 3 mL). The combined organic layers were washed with brine (3 × 3 mL) and dried over Na_2SO_4. Solvent was evaporated. The crude product was purified by column chromatography (Hex:EtOAc 1:1, v/v) to afford **26,27,28,29,30,31.**

4.5.1. 1-((3,4,6-Tri-O-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl)methoxy)-4-hexadecyl-1H-1,2,3-triazole ***26***

Propargyl-3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**19**) (0.115 g, 0.235 mmol) and azidohexadecane (**20**) (0.082 g, 0.306 mmol) gave **26** as a white solid; yield 0.135 g (76%); mp 128–130 °C; $[\alpha]_D$ = −5.34 (c 1.02, DCM); ^{1}H NMR (403 MHz, $CDCl_3$): δ 7.51 (s, 1H, triazole-H), 7.03 (d, 1H, *J* = 9.0 Hz, NH), 5.30 (dd, 1H, *J* = 9.4 Hz, *J* = 10.7 Hz, H-3), 5.15 (t, 1H, *J* = 9.6 Hz, H-4), 4.97 (d, 1H, *J* = 8.4 Hz, H-1), 4.94 (d, 1H, *J* = 13.1 Hz, OCH_atriazole), 4.83 (d, 1H, *J* = 13.1 Hz, OCH_b-triazole), 4.37-4.24 (m, 3H, H-6b, triazoleCH_2) 4.18 (dd, 1H, *J* = 2.3 Hz, *J* = 12.3 Hz, H-6a), 4.12-4.04 (m, 1H, H-2), 3.79 (ddd, 1H, *J* = 2.3 Hz, *J* = 4.7 Hz, *J* = 9.9 Hz, H-5), 2.12 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.02 (s, 3H, OAc) 1.91-1.77 (m, 2H, CH_2), 1.36-1.28 (m, 6H, $(CH_2)_3$), 1.25 (s, 20H, $(CH_2)_{10}$), 0.88 (t, 3H, *J* = 6.8 Hz, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.9, 170.7, 169.3, 162.0, 144.2, 122.6, 99.9, 92.3, 72.1, 71.9, 68.1, 62.7, 61.9, 55.7, 50.4, 31.9, 30.3, 29.7, 29.65, 29.62, 29.5, 29.4, 29.3, 29.0, 26.5, 22.7, 20.8, 20.6, 20.5, 14.1; MS (ESI) *m*/*z* $[M+H]^+$ calcd for $C_{33}H_{54}Cl_3N_4O_9$: 755.2956; found: 755.2946; *m*/*z* $[M+Na]^+$ calcd for $C_{33}H_{53}Cl_3N_4NaO_9$: 777.2776; found: 777.2762.

4.5.2. 1-((3,4,6-Tri-O-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl)methoxy)-4-(1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-henicosafluorododecyl)-1H-1,2,3-triazole ***27***

Propargyl-3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**19**) (0.046 g, 0.095 mmol) and 1-azido-3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,12-henicosafluorododecane (**21**) (0.073 g, 0.124 mmol) gave **27** as a white solid; yield 0.092 g (91%); mp 177–180 °C; $[\alpha]_D$ = −6.57 (c 0.84, DCM); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59 (s, 1H, triazole-H), 6.84 (d, 1H, *J* = 8.9 Hz, NH), 5.27 (dd, 1H, *J* = 9.4 Hz, *J* = 10.7 Hz, H-3), 5.16 (t, 1H, *J* = 9.6 Hz, H-4), 4.97 (d, 1H, *J* = 13.1 Hz, OCH_atriazole) 4.90 (d, 1H, *J* = 8.3 Hz, H-

1), 4.84 (d, 1H, J = 12.9 Hz, OCH_btriazole), 4.66 (t, 2H, J = 7.4 Hz, triazoleCH_2), 4.31 (dd, 1H, J = 4.7 Hz, J = 12.3 Hz, H-6a), 4.19 (dd, 1H, J = 2.3 Hz, J = 12.3 Hz, H-6b), 4.09-3.98 (m, 1H, H-2), 3.77 (ddd, 1H, J = 2.4 Hz, J = 4.5 Hz, J = 9.8 Hz, H-5), 2.91-2.71 (m, 2H, $CH_2(CF_2)_9CF_3$), 2.12 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc); ^{13}C NMR (151 MHz, $CDCl_3$): δ 170.9, 170.7, 169.3, 162.0, 144.8, 123.3, 117.5-107.7, 100.1, 92.2, 72.3, 71.6, 68.0, 62.8, 61.8, 55.9, 42.4, 31.8, 20.8, 20.6, 20.5; ^{19}F NMR (282 MHz, $CDCl_3$): δ −81.22, −114.63, −122.26, −123.20, −123.91, −126.60; MS (ESI) m/z [M+H]$^+$ calcd for $C_{29}H_{25}Cl_3F_{21}N_4O_9$: 1077.0352; found: 1077.0309; m/z [M+Na]$^+$ calcd for $C_{29}H_{24}Cl_3F_{21}N_4NaO_9$: 1099.0124; found: 1099.0124.

*4.5.3. 1-((3,4,6-O-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopiranosyl)methoxy)-4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9-eicosafluorododecyl)-1H-1,2,3-triazole **28***

Propargyl-3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**19**) (0.097 g, 0.198 mmol) and 1-azido-2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11-eicosafluoroundecane (**22**) (0.143 g, 0.257 mmol) gave **28** as a white solid; yield 0.117 g (56%); mp 158–164 °C; $[\alpha]_D$ = −9.17 (c 1.02, DCM); ^{1}H NMR (403 MHz, $CDCl_3$): δ 7.71 (s, 1H, triazole-H), 6.85 (d, 1H, J = 8.8 Hz, NH), 6.06 (t, 1H, J = 5.0 Hz, J = 51.9 Hz, CF_2H), 5.28 (dd, 1H, J = 9.3 Hz, J = 10.7 Hz, H-3), 5.14 (t, 1H, J = 9.6 Hz, H-4), 5.09-4.96 (m, 3H, OCH_atriazole, $CH_2(CF_2)_9CF_2H$), 4.91 (d, 1H, J = 8.3 Hz, H-1), 4.87 (d, 1H, J = 13.1 Hz, OCH_btriazole), 4.30 (dd, 1H, J = 4.7 Hz, J = 12.4 Hz, H-6a), 4.19 (dd, 1H, J = 2.3 Hz, J = 12.4 Hz, H-6b), 4.10-4.02 (m, 1H, H-2), 3.77 (ddd, 1H, J = 2.4 Hz, J = 4.7 Hz, J = 9.9 Hz, H-5), 2.11 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.0 170.7, 169.3, 162.1, 145.5, 124.5, 117.9-103.1, 100.2, 92.1, 72.2, 71.6, 68.0, 62.7, 61.7, 55.8, 49.3, 20.7, 20.6, 20.5; ^{19}F NMR (379 MHz, $CDCl_3$): δ −17.27, −122.33, −123.39, −123.77, −129.71, −137.39, −137.52; MS (ESI) m/z [M+H]$^+$ calcd for $C_{28}H_{24}Cl_3F_{20}N_4O_9$: 1045.0289; found: 1045.0247; m/z [M+Na]$^+$ calcd for $C_{28}H_{23}Cl_3F_{20}N_4NaO_9$: 1067.0109; found: 1067.0076.

*4.5.4. 1-((3,4,6-O-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopiranosyle)methoxy)-4-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)-1H-1,2,3-triazole **29***

Propargyl-3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**19**) (0.299 g, 0.612 mmol) and 1-azido-4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecane (**23**) (0.400 g, 0.795 mmol) gave **29** as a white solid; yield 0.341 g (56%); mp 161–165 °C; $[\alpha]_D$ = −6.36 (c 1.03, DCM); ^{1}H NMR (403 MHz, $CDCl_3$): δ 7.55 (s, 1H, triazole-H), 6.87 (d, 1H, J = 8.8 Hz, NH), 5.83 (d, 1H, J = 8.7 Hz, H-1), 5.27 (dd, 1H, J = 9.4 Hz, J = 10.7 Hz, H-3), 5.16 (t, 1H, J = 9.6 Hz, H-4), 4.97 (d, 1H, J = 13.1 Hz, OCH_atriazole), 4.92 (d, 1H, J = 8.4 Hz, H-1), 4.84 (d, 1H, J = 13.0 Hz, OCH_btriazole), 4.44 (td, 2H, J = 2.9 Hz, J = 6.8 Hz, triazoleCH_2), 4.31 (dd, 1H, J = 4.7 Hz, J = 12.4 Hz, H-6a), 4.19 (dd, 2H, J = 2.4 Hz, J = 12.3 Hz, H-6b), 4.09-4.01 (m, 1H, H-2), 3.77 (ddd, 1H, J = 2.4 Hz, J = 4.7 Hz, J = 9.9 Hz, H-5), 2.30-2.19 (m, 2H, $CH_2CH_2CH_2$), 2.19-2.08 (m, 2H, $CH_2(CF_2)_7CF_3$), 2.11 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.9, 170.6, 169.3, 161.9, 144.7, 122.7, 120.7-109.4, 100.1, 91.2, 72.2, 71.6, 68.0, 62.8, 61.8, 55.8, 49.2, 28.1, 21.6, 20.7, 20.6, 20.5; ^{19}F NMR (379 MHz, $CDCl_3$); δ −81.24, −114.54, −122.17, −122.40, −123.21, −123.76, −126.62; MS (ESI) m/z [M+H]$^+$ calcd for $C_{28}H_{27}Cl_3F_{17}N_4O_9$: 991.0572; found: 991.0544; m/z [M+Na]$^+$ calcd for $C_{28}H_{26}Cl_3F_{17}N_4NaO_9$: 1013.0392; found: 1013.0370.

*4.5.5. 1-((3,4,6-O-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopiranosyle)methoxy)-4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluorooctyl)-1H-1,2,3-triazole **30***

Propargyl-3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**19**) (0.133 g, 0.272 mmol) and 1-azido-2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluorooctyl (**24**) (0.150 g, 0.353 mmol) gave **30** as a white solid; yield 0.086 g (34%); mp 140–143 °C; $[\alpha]_D$ = −40.24 (c 1.01, MeCN); ^{1}H NMR (403 MHz, $CDCl_3$): δ 7.71 (s, 1H, triazole-H), 6.91 (d, 1H, J = 8.8 Hz, NH), 5.29 (dd, 1H, J = 9.4 Hz, J = 10.7 Hz, H-3), 5.16 (t, 1H, J = 9.7 Hz, H-4), 5.11-4.96 (m, 3H, OCH_atriazole, $CH_2(CF_2)_6CF_3$), 4.92 (d, 1H, J = 8.4 Hz, H-1), 4.87 (d, 1H, J = 13.2 Hz, OCH_btriazole), 4.30 (dd, 1H, J = 4.7 Hz, J = 12.4 Hz, H-6a), 4.19 (dd, 1H, J = 2.3 Hz, J = 12.4 Hz, H-6b), 4.11-4.02 (m, 1H, H-2), 3.78 (ddd, 1H, J = 2.4 Hz, J = 4.7 Hz, J = 9.9 Hz, H-5), 2.11 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.04 (s, 3H, OAc); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.7, 170.7, 169.3, 162.1, 145.6, 124.6, 118.5-106.9, 100.2, 92.2, 72.2, 71.7, 68.2, 62.7, 61.8, 55.8, 49.3, 20.8, 20.6, 20.5; ^{19}F NMR (282 MHz, $CDCl_3$): δ −81.22, −117.31, −122.13, −122.47, −123.27, −123.41, −126.61; MS (ESI) m/z [M+H]$^+$ calcd for $C_{25}H_{23}Cl_3F_{15}N_4O_9$: 913.0291; found: 913.0245; m/z [M+Na]$^+$ calcd for $C_{25}H_{22}Cl_3F_{15}N_4NaO_9$: 935.0111; found: 935.0088.

*4.5.6. 1-((3,4,6-O-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopiranosyle)methoxy)-4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)-1H-1,2,3-triazole **31***

Propargyl-3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**19**) (0.080 g, 0.164 mmol) and 1-azido-3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl (**25**) (0.083 g, 0.213 mmol) gave **31** as a white solid; yield 0.055 g (38%); mp 157–161 °C; $[\alpha]_D$ = −43.87 (c 1.00, MeCN); ^{1}H NMR (403 MHz, $CDCl_3$); δ 7.61 (s, 1H, triazole-H), 6.95 (d, 1H, J = 8.8 Hz, NH), 5.30 (dd, 1H, J = 9.4 Hz, J = 10.7 Hz, H-3), 5.15 (t, 1H, J = 9.6 Hz, H-4), 4.96 (d, 1H, J = 13.4 Hz, OCH_atriazole), 4.92 (d, 1H, J = 8.3 Hz, H-1), 4.84 (d, 1H, J = 13.0 Hz, OCH_btriazole), 4.66 (t, 2H, J = 7.4 Hz, triazole-CH_2), 4.30 (dd, 1H, J = 4.7 Hz, J = 12.4 Hz, H-6a), 4.19 (dd, 1H, J = 2.3 Hz, J = 12.3 Hz, H-6b), 4.07-3.99 (m, 1H, H-2), 3.77 (ddd, 1H, J = 2.4 Hz, J = 4.7 Hz, J = 9.9 Hz, H-5), 2.89-2.74 (m, 2H, $CH_2(CF_2)_5CF_3$), 2.11 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.9, 170.7, 169.3, 162.0, 144.7, 123.3, 121.5-107.2, 100.0, 92.2, 72.2, 71.6, 68.1, 62.8, 61.8, 55.8, 42.3, 31.7, 20.7, 20.6, 20.5; ^{19}F NMR (379 MHz, $CDCl_3$): δ −80.27, −113.67, −121.41, −122.36, −122.98, −125.66; MS (ESI) m/z [M+H]$^+$ calcd for $C_{25}H_{25}Cl_3F_{13}N_4O_9$: 877.0479; found: 877.0462; m/z [M+Na]$^+$ calcd for $C_{25}H_{24}Cl_3F_{13}N_4NaO_9$: 899.0299; found: 899.0252.

4.6. General procedure for the deprotection reaction of acetyl groups in monosaccharides

To a solution of sugars **8**, **12**, **14**, **18**, **26**, **27** (1 eqiuv) in DCM/MeOH (3:7, v/v, 4.7 mL for 1 mmol of sugar) was added 25% sodium methoxide solution (5 equiv) at room temperature. The reaction mixture was stirred overnight and MeOH (3.2 mL for 1 mmol of sugar) was added. Neutralization was achieved with addition of Dowex 50WX8 (50–100 mesh, H$^+$-form). The ion exchange resin was filtered and the filtrate was concentrated in vacuo. The crude product was purified by column chromatography (DCM:MeOH 5:1, v/v) to afford desired products **32**, **33**, **34**, **35**, **36**, **37**.

*4.6.1. 1-(2-Azidoacetamido-2-deoxy-β-D-glucopyranosyl)-4-hexyl-1H-1,2,3-triazole **32***

1-(1,3,4,6-Tetra-*O*-acetyl-2-azidoacetamido-2-deoxy-β-D-glucopyranosyl)-4-hexyl-1H-1,2,3-triazole (**8**) (0.057 g, 0.106 mmol) and 25% CH_3ONa in MeOH (0.029 g, 0.530 mmol) gave **32** as a white solid; yield 0.031 g (79%); ^{1}H NMR (403 MHz, DMSO–d_6); δ 8.24 (d, 1H, J = 7.9 Hz, NH), 7.75 (s, 1H, triazole-H), 5.75 (app s, 1H, H-1), 5.12-4.83 (m, 4H, H-3, H-4, CH_2triazole), 3.95 (ddd, 1H, J = 3.2 Hz, J = 7.5 Hz, J = 12.0 Hz, H-5), 3.62-3.27 (m, 3H, H-6a, H-6b, OH), 3.18-3.05 (m, 1H, H-2), 2.60 (t, 2H, J = 7.6 Hz, triazoleCH_2), 1.62-1.53 (m, 2H, triazole-CH_2CH_2), 1.34-1.22 (m, 6H, $(CH_2)_3$), 0.86 (t, 3H, J = 6.9 Hz, CH_3); ^{13}C NMR (101 MHz, DMSO–d_6): δ 165.6, 146.5,

123.3, 90.5, 72.1, 71.0, 70.5, 61.0, 54.6, 51.4, 31.1, 29.0, 28.3, 25.0, 22.1, 14.0; MS (ESI) *m/z* $[M+H]^+$ calcd for $C_{16}H_{29}N_4O_6$: 373.2087; found: 373.2080; *m/z* $[M+Na]^+$ calcd for $C_{16}H_{28}N_4NaO_6$: 395.1907; found: 395.1900.

4.6.2. 1-(2-Azidoacetamido-2-deoxy-β-D-glucopyranosyl)-4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-eicosafluorononylmethoxy) methyl-1H-1,2,3-triazole ***33***

1-(1,3,4,6-Tetra-*O*-acetyl-2-azidoacetamido-2-deoxy-β-D-glucopyranosyl)-4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-eicosafluorononylmethoxy)methyl-1H-1,2,3-triazole (**12**) (0.081 g, 0.081 mmol) and 25% CH_3ONa in MeOH (0.022 g, 0.405 mmol) gave **33** as a white solid; yield 0.047 g (70%); ^1H NMR (403 MHz, DMSO–d_6); δ 8.30 (d, 1H, *J* = 8.9 Hz, NH), 8.11 (s, 1H, triazole-H), 7.20 (tt, 1H, *J* = 5.1 Hz, *J* = 51.0 Hz, HCF_2), 5.75 (app s, 1H, H-1), 5.43-5.28 (dd, dd, 2H, H-3, H-4), 5.15 (s, 2H, triazoleCH_2O), 4.75 (s, 2H, CH_2triazole), 4.30-4.07 (m, 3H, H-6a, H-6b, H-5), 3.12-3.38 (m, 4H, H-2, OH, $CH_2(CF_2)_9CF_2H$); ^{13}C NMR (101 MHz, DMSO–d_6): δ 165.4, 142.6, 126.1, 119.1-104.5, 99.5, 72.1, 70.5, 66.4-65.1, 64.8-64.1, 54.9, 48.6; ^{19}F NMR (379 MHz, DMSO-d_6): δ −119.38, −122.33, −123.48, −129.48, −138.95; MS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{21}F_{20}N_4O_7$: 833.1091; found: 833.1078; *m/z* $[M+Na]^+$ calcd for $C_{22}H_{20}F_{20}N_4NaO_7$: 855.0910; found: 855.0909.

4.6.3. 1-(2-Azidoacetamido-2-deoxy-β-D-galactopyranosyl)-4-hexyl-1H-1,2,3-triazole ***34***

1-(1,3,4,6-Tetra-*O*-acetyl-2-azidoacetamido-2-deoxy-β-D-galactopyranosyl)-4-hexyl-1H-1,2,3-triazole (**14**) (0.058 g, 0.107 mmol) and 25% CH_3ONa in MeOH (0.029 g, 0.535 mmol) gave **34** as a white solid; yield 0.028 g (70%); ^1H NMR (403 MHz, DMSO–d_6); δ 8.17 (d, 1H, *J* = 8.5 Hz, NH), 7.76 (s, 1H, triazole-H), 5.73 (app s, 1H, H-1), 5.11-4.93 (m, 4H, H-3, H-4, CH_2triazole), 4.75 (s, 1H, OH), 3.82-3.3.64 (m, 2H, H-6a, H-6b), 3.56-3.13 (m, 2H, H-2, OH), 3.98 (ddd, 1H, *J* = 3.2 Hz, *J* = 7.5 Hz, *J* = 12.0 Hz, H-5), 2.63-2.54 (m, 2H, triazoleCH_2), 1.61-1.53 (m, 2H, triazoleCH_2CH_2), 1.33-1.22 (m, 6H, $(CH_2)_3$), 0.86 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR (101 MHz, DMSO–d_6): δ 165.7, 146.5, 122.8, 90.8, 70.5, 68.2, 67.3, 60.6, 51.5, 50.7, 31.1, 29.1, 28.4, 25.1, 22.1, 14.0; MS (ESI) *m/z* $[M+H]^+$ calcd for $C_{16}H_{29}N_4O_6$: 373.2087; found: 373.2086; *m/z* $[M+Na]^+$ calcd for $C_{16}H_{28}N_4NaO_6$: 395.1907; found: 395.1881.

4.6.4. 1-(2-Azidoacetamido-2-deoxy-β-D-galactopyranosyl)-4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-eicosafluorononylmethoxy) methyl-1H-1,2,3-triazole ***35***

1-(1,3,4,6-Tetra-*O*-acetyl-2-azidoacetamido-2-deoxy-β-D-galactopyranosyl)-4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-eicosafluorononylmethoxy)methyl-1H-1,2,3-triazole (**18**) (0.100 g, 0.100 mmol) and 25% CH_3ONa in MeOH (0.027 g, 0.500 mmol) gave **35** as a white solid; yield 0.068 g (82%); ^1H NMR (403 MHz, DMSO–d_6); δ 8.21 (d, 1H, *J* = 8.5 Hz, NH), 8.10 (s, 1H, triazole-H), 7.22 (tt, 1H, *J* = 5.2 Hz, *J* = 50.2 Hz, HCF_2), 5.75 (app s, 1H, H-1), 5.19-5.09 (m, 4H, H-3, H-4, triazoleCH_2O), 4.85 (s, 2H, CH_2triazole), 4.74-4.69 (dd, 1H, H-6a), 4.27-4.16 (app m, 1H, H-6b), 4.02 (ddd, 1H, *J* = 3.2 Hz, *J* = 7.5 Hz, *J* = 12.0 Hz, H-5), 3.60-3.28 (m, 4H, H-2, OH, $CH_2(CF_2)_9CF_2H$); ^{13}C NMR (101 MHz, DMSO–d_6): δ 165.5, 141.9, 125.6, 119.3-104.7, 90.8, 70.5, 68.2, 67.3, 65.7, 64.6, 60.6, 54.9, 48.6; ^{19}F NMR (379 MHz, DMSO-d_6): δ −119.37, −122.32, −123.50, −129.38, −139.01; MS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{21}F_{20}N_4O_7$: 833.1091; found: 833.1067; *m/z* $[M+Na]^+$ calcd for $C_{22}H_{20}F_{20}N_4NaO_7$: 855.0910; found: 855.0900.

4.6.5. 1-((2-Deoxy-2-trichloroacetamido-β-D-glucopyranosyl) methoxy)-4-hexadecyl-1H-1,2,3-triazole ***36***

1-((3,4,6-Tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl)methoxy)-4-hexadecyl-1H-1,2,3-triazole (**26**) (0.030 g, 0.040 mmol) and 25% CH_3ONa in MeOH (0.011 g, 0.200 mmol) gave **36** as a white solid; yield 0.015 g (61%); ^1H NMR (403 MHz, DMSO–d_6); δ 8.33 (s, 1H, triazole-H), 8.14 (app s, 1H, *J* = 8.9 Hz, NH), 5.02-4.93 (br s,1H, OH), 4.88 (dd, 1H, H-3), 4.66 (dd, 1H, H-4), 4.32 (app t, 1H, H-6b), 4.17 (d, 1H, *J* = 7.9 Hz, H-1), 3.71 (m, 1H, H-5), 3.52-3.14 (m, 5H, OH, triazole-CH_2, OCH_atriazole, OCH_btriazole), 3.15-3.00 (m, 2H, H-6a, H-2), 1.83-1.74 (m, 2H, triazoleCH_2CH_2), 1.23 (s, 26H, $(CH_2)_{13}$), 0.85 (t, 3H, *J* = 6.9 Hz, CH_3); ^{13}C NMR (101 MHz, DMSO–d_6): δ 143.7, 124.0, 102.9, 79.2, 77.2, 70.1, 61.7, 61.2, 57.3, 49.3, 31.3, 29.7, 29.1, 29.2, 29.0, 28.9, 28.7, 28.4, 25.9, 22.1, 14.0; MS (ESI) *m/z* $[M+H]^+$ calcd for $C_{27}H_{48}Cl_3N_4O_6$: 629.2639; found: 629.2641; *m/z* $[M+Na]^+$ calcd for $C_{27}H_{47}Cl_3N_4NaO_6$: 651.2459; found: 651.2457.

4.6.6. 1-((2-Deoxy-2-trichloroacetamido-β-D-glucopyranosyl) methoxy)-4-(1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-henicosafluorododecyl)-1H-1,2,3-triazole ***37***

1-((3,4,6-Tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl)methoxy)-4-(1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-henicosafluorododecyl)-1H-1,2,3-triazole (**27**) (0.118 g, 0.110 mmol) and 25% CH_3ONa in MeOH (0.030 g, 0.550 mmol) gave **37** as a white solid; yield 0.087 g (85%); ^1H NMR (403 MHz, DMSO–d_6); δ 8.65 (d, 1H, *J* = 8.5 Hz, NH), 8.07 (s, 1H, triazole-H), 5.11 (sbr, 1H, OH), 4.77 (d, 1H, *J* = 8.4 Hz, H-1), 4.68-4.56 (m, 3H, H-3, H-4, triazoleCH_2), 4.33 (dd, 1H, *J* = 2.5 Hz, *J* = 15.9 Hz, H-6a), 4.24 (dd, 1H, *J* = 2.4 Hz, *J* = 15.9 Hz, H-6b), 3.72 (m, 1H, H-5), 3.58-3.43 (m, 1H, H-2), 3.34 (app s, 3H, OH, OCH_atriazole, OCH_btriazole), 2.93-2.77 (m, 2H, $CH_2(CF_2)_9CF_3$); ^{13}C NMR (101 MHz, DMSO–d_6): δ 161.3, 143.8, 124.4, 118.7-105.9, 99.7, 93.1, 77.1, 73.1, 70.8, 61.6, 61.0, 57.4, 48.6, 30.4; ^{19}F NMR (379 MHz, DMSO-d_6): δ −82.20, −114.77, −123.99, −123.85, −127.35; MS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{19}Cl_3F_{21}N_4O_6$: 951.0035; found: 951.0033; *m/z* $[M+Na]^+$ calcd for $C_{23}H_{18}Cl_3F_{21}N_4NaO_6$: 972.9854; found: 972.9853.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jfluchem.2016.09.002.

References

[1] J.F. Coelho, P.C. Ferreira, P. Alves, R. Cordeiro, A.C. Fonseca, J.R. Góis, M.H. Gil, EPMA J. 1 (2010) 164–209.
[2] N. Goodarzi, R. Varshochian, G. Kamalinia, F. Atyabi, R. Dinarvand, Carbohydr. Polym. 92 (2013) 1280–1293.
[3] B. Posocco, E. Dreussi, J. Santa, G. Toffoli, M. Abrami, F. Musiani, M. Grassi, R. Farra, F. Tonon, G. Grassi, B. Dapas, Mater 8 (2015) 2569–2615.
[4] K. Meyer, J. Palmer, J. Biol. Chem. 107 (1934) 629–634.
[5] A. Mero, M. Campisi, Polym 6 (2014) 346–369.
[6] B. Mangla, S.K. Joshi, K. Khanna, P. Kapoor, I. Kukreja, Biopharm. J. 1 (2015) 64–70.
[7] E.A. Turley, L. Austen, K. Vandelight, C. Clary, J. Cell. Biol. 112 (1991) 1041–1047.
[8] M.A. Selyanin, P.Y. Boykov, V.N. Khabarov, Hyaluronic acid: preparation, properties and application in biology and medicine, in: F. Polyak (Ed.), Medicinal Applications of Hyaluronan, United Kingdom, 2015, pp. 143–192.
[9] Y. Luo, N.J. Bernshaw, Z.-R. Lu, J. Kopecek, G.D. Prestwich, Pharm. Res. 19 (2002) 396–402.
[10] Y.-J. Jin, T. Ubonvan, D.-D. Kim, J. Pharm. Invest. 40 (2010) 33–43.
[11] V.M. Platt, F.C. Szoka, Mol. Pharm. 5 (2008) 474–486.
[12] E. Auzenne, S.C. Ghosh, M. Khodadadian, B. Rivera, D. Farquhar, R.E. Price, M. Ravoori, V. Kundra, R.S. Freedman, J. Klostergaard, Neoplasia 9 (2007) 479–486.

[13] G. Saravanakumar, K.Y. Choi, H.Y. Yoon, K. Kim, J.H. Park, I.C. Kwonc, K. Park, Int. J. Pharm. 394 (2010) 154–161.
[14] Z. Dong, W. Zheng, Z. Xu, Z. Yin, J. Appl. Polym. Sci. 130 (2013) 927–932.
[15] X. Yang, I. Dogan, V.R. Pannala, S. Kootala, J. Hilborn, D. Ossipov, Polym. Chem. 4 (2013) 4621–4630.
[16] B.E. Smart, J. Fluorine Chem. 109 (2001) 3–11.
[17] D. O'Hagan, H.S. Rzepa, Chem. Commun. 7 (1997) 645–652.
[18] M.C.Z. Kasuya, R. Cusi, O. Ishihara, A. Miyagawa, K. Hashimoto, T. Sato, K. Hatanaka, Biochem. Biophys. Res. Commun. 316 (2004) 599–604.
[19] M.C.Z. Kasuya, M. Tojino, M. Mizuno, K. Hatanaka, J. Fluorine Chem. 131 (2010) 655–659.
[20] M.C. Kasuya, K. Hatanaka, J. Fluorine Chem. 188 (2016) 1–4.
[21] C. Zur, A.O. Miller, R. Miethchen, J. Fluorine Chem. 90 (1998) 67–76.
[22] M. Hein, R. Miethchen, Adv. Org. Synth. 2 (2006) 381–429.
[23] V.V. Rostovtsev, L.G. Green, V.V. Fokin, K.B. Sharpless, Angew. Chem. Int. Ed. 41 (2002) 2596–2599.
[24] C.W. Tornøe, C. Christensen, M. Meldal, J. Org. Chem. 67 (2002) 3057–3064.
[25] D.S. Pedersen, A. Abell, Eur. J. Org. Chem. 2011 (2011) 2399–2324.
[26] G.C. Tron, T. Pirali, R.A. Billington, P.L. Canonico, G. Sorba, A.A. Genazzani, Med. Res. Rev. 28 (2008) 278–308.
[27] H.C. Kolb, K.B. Sharpless, Drug Discov. Today. 18 (2013) 1128–1137.
[28] P.-H. Elchinger, P.-A. Faugeras, B. Boëns, F. Brouillette, D. Montplaisir, R. Zerrouki, R. Lucas, Polym 3 (2011) 1607–1651.
[29] K. New, M.W. Brechbiel, Cancer Biother. Radiopharm. 24 (2009) 289–302.
[30] Y.-W. Zhu, W.-B. Yi, Ch. Cai, J. Fluorine Chem. 132 (2011) 71–74.
[31] C.S. Rondestvedt, G.L. Thayer, J. Org. Chem. 42 (1977) 2680–2683.
[32] Y.M. Wu, J. Deng, X. Fang, Q.-Y. Chen, J. Fluorine Chem. 125 (2004) 1415–1423.
[33] P.D. Faurote, J.G. O'Rear, J. Am. Chem. Soc. 78 (1956) 4999–5001.
[34] F.U. Seifert, G.-V. Röschenthaler, J. Fluorine Chem. 68 (1994) 169–174.
[35] S.C. Miller, J. Org. Chem. 75 (2010) 4632–4635.
[36] J. Vastra, L. Saint-Jalmes, US Pat. 6 (992) (2006) 199.
[37] X.-J. Li, D.-X. Sun, Y.-H. Zhang, J. Polym. Res. 21 (2014) 320–333.
[38] B. Boutevin, J.-M. Lusinchi, Y. Pietrasanta, J.-J. Robin, J. Fluorine Chem. 68 (1994) 205–210.
[39] M.E. Ghoul, B. Escoula, I. Rico, A. Latte, J. Fluorine Chem. 59 (1992) 107–112.
[40] M. Allouch, C. Selve, J. Fluorine Chem. 66 (1994) 31–38.
[41] J. Tomaszewska, K. Koroniak-Szejn, unpublished data.
[42] D.V. Francis, D.H. Miles, A.I. Mohammed, R.W. Read, X. Wang, J. Fluorine Chem. 132 (2011) 898–906.
[43] O.A. Radchenko, E.V. Proshakova, A.N. Kotlinskaza, A.Y. Il'chenko, Zh. Org. Khim. 27 (1991) 1463–1473.
[44] M. Bergman, L. Zervas, Ber. Dtsch. Chem. Ges. 64 (1931) 975–980.
[45] D.J. Silva, H. Wang, N.M. Allanson, R.K. Jain, M.J. Sofia, J. Org. Chem. 64 (1999) 5926–5929.
[46] E. Saxon, S.J. Luchansky, H.C. Hang, C. Yu, S.C. Lee, C.R. Bertozzi, J. Am. Chem. Soc. 124 (2002) 14893–14902.
[47] S.T. Laughlin, C.R. Bertozzi, Nat. Protoc. 2 (2007) 2930–2944.
[48] P. Pan, Q. Zhang, J. Hou, Z. Liu, F. Bai, M. Cao, T. Sun, G. Bai, Anal. Bioanal. Chem. 403 (2012) 1661–1670.
[49] D. Fürniss, T. Mack, F. Hahn, S.B.L. Vollrath, K. Koroniak, U. Schepers, S. Bräse, Beilstein J. Org. Chem. 9 (2013) 56–63.
[50] H. Kong, W. Chen, H. Lu, Q. Yang, Y. Dong, D. Wang, J. Zhang, Carbohydr. Res. 413 (2015) 135–144.
[51] M.D. Witte, B.I. Florea, M. Verdoes, O. Adeyanju, G.A. Van der Marel, H.S. Overkleeft, J. Am. Chem. Soc. 131 (2009) 12064–12065.
[52] T. Hasegawa, M. Numata, S. Okumura, T. Kimura, K. Sakurai, S. Shinkai, Org. Biomol. Chem. 5 (2007) 2404–2412.