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Copper(I)-catalyzed azide-alkyne cycloaddition-assisted polymerization of linear glucose-derived co/polymers

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Abstract

The synthesis of linear and controllable oligomers and polymers using sugar-derived monomers is still highly challenging. Herein, we present a method allowing the linear polymerization of a bifunctional glucose derivative as monomer, which contained an azide group at C1 and a propargyl group at C4 position of the glucose ring. The reaction conditions were optimized by grafting the monomer onto the surface of silica nanoparticles (SiNPs) and at the end-modified polyethylene glycol (PEG). For grafting the surface of SiNPs with the monomer, an azide-bearing chlorosilane linker was synthesized and introduced onto SiNPs surface. The copper(I)-catalyzed azide-alkyne cycloaddition using the glucose-derived monomer led to the growth of linear triazole-linked oligosaccharide-mimics on the surface of SiNPs with a degree of polymerization up to 13 and the formation of cyclic trimers and tetramers in the solution. Furthermore, during polymerization of the monomer at end-modified PEG, various linear diblock-copolymers pseudo-cellulose-*block*-PEG and triblock-copolymers pseudo-cellulose-*block*-PEG-*block*-pseudo-cellulose were obtained. The polymerization reactions expired with nearly complete consumption of the monomer and high yields between 88 and 94% were achieved. Obtained block-copolymers showed amphiphilic properties that helped to fractionate obtained polymers into lower and higher molecular weight fractions with narrow polymer dispersity $Đ$.

KEYWORDS

azides, block copolymers, CuAAC, monosaccharides, polymerization

1 | INTRODUCTION

Carbohydrates are a group of bioactive compounds that are structurally highly complex and serve diverse biological functions, such as cell recognition and cell binding.[1] They play an important role in many organisms by participating in signaling events and cell–cell recognition, and they also affect protein structure, function, and stability.[2] Since the purification of well-defined oligosaccharides from natural sources is often difficult or currently even impossible, chemical synthesis is an important way to provide access to them.[3] Their synthesis becomes increasingly complex for oligosaccharides with more than 5–10 monosaccharide units.[3] One approach to simplify the synthesis of longer oligosaccharides is to replace the glycosidic bond with triazole

linkages. For this and many other applications, click chemistry found widespread use in carbohydrate chemistry in the last years.[4]

For instance, sugar backbones from different monosaccharides with introduced azide or alkyne groups were linked together to form oligosaccharides mimics. However, most studies showed the synthesis of cyclic triazole-linked oligosaccharides, ranging from dimers to heptamers.[5,6] In contrast to the synthesis of cyclic oligosaccharide-mimics, the synthesis of linear oligo-/polysaccharide-mimics is still challenging and less investigated. With a convergent approach, the synthesis of linear triazole-linked 1,6-oligomannosides led to linear oligomannosides up to the hexadecamer.[7] Linear 1,5-triazole-linked polygalactosides were synthesized in a topochemical click reaction in the crystal lattice.[8]

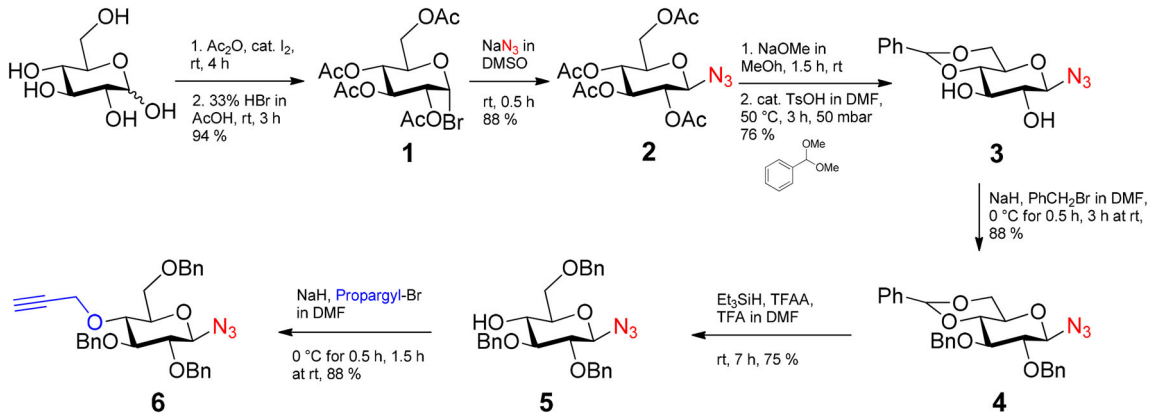
To build linear structures, the use of a starting molecule was proven useful. This starting molecule could contain an azido or an alkyne group, as well as an easily detectable group that is advantageous for further analysis. The chain growth from the starting molecule does not have a second reactive end group, which renders the cyclization impossible. For example, with ethynylferrocene as starter, the Huisgen cycloaddition of *N*-acetylglucosamin-based monomer resulted in linear oligomerization up to the octamer.[9] Such a starter molecule can also be an end-modified polymer, which allows the synthesis of block copolymers with polysaccharide-blocks. Hereby, enzymatic methods were mostly used to polymerize monosaccharides at the end of conventional polymers, such as polystyrene or poly(ethylene glycol).[10] In comparison, direct polymerization of modified monosaccharides gives perfect control over the regioselectivity of newly introduced groups for the introduction of new functionalities into the polysaccharide blocks. However, the choice of monosaccharides for an artificial enzymatic polymerization is limited and modified monosaccharides even may not be polymerizable by enzymes. Therefore, alternative polymerization approaches have been proposed for the polymerization of modified monosaccharides, such as the ring opening polymerization for 4,6-carbonate-linked polyglucoside.[11,12] Such methods allowed the synthesis of block-copolymers by successively adding different monomers, in order to get different functions and properties. So far, linear 1,4-triazole-linked mimics of oligosaccharides or polysaccharides based on glucose-derived monomers have not been reported yet.

Herein, we report the synthesis of linear polysaccharide-mimics using a novel glucose-derived monomer. In the first step, the bifunctional glucose-derived monomer 2,3,6-tris-O-benzyl-4-O-propargyl-β-D-glucopyranosyl azide was synthesized. Furthermore, an azide-bearing chlorosilane linker was synthesized and introduced onto the surface of SiNPs, in order to have starting sites for the polymerization of the glucose-derived monomer. The surface-initiated polymerization was performed under diverse conditions for the growth of longer linear chains. After the Huisgen cycloaddition as copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) is completed, linear oligomers were easily separated from the cyclic compounds, which were formed in the supernatant solution. Linear and cyclic products were separately characterized. After the reaction conditions were optimized for the growth of long linear chains, this established method was further used for the polymerization of the glucose-derived monomer at the end groups of PEG. Hereby, linear amphiphilic block-copolymers with one block of the conventional polymer PEG and novel polysaccharide-mimicking blocks were obtained. Moreover, different solubilities of the two types of blocks were used for the fractionation of block copolymers by chain lengths.

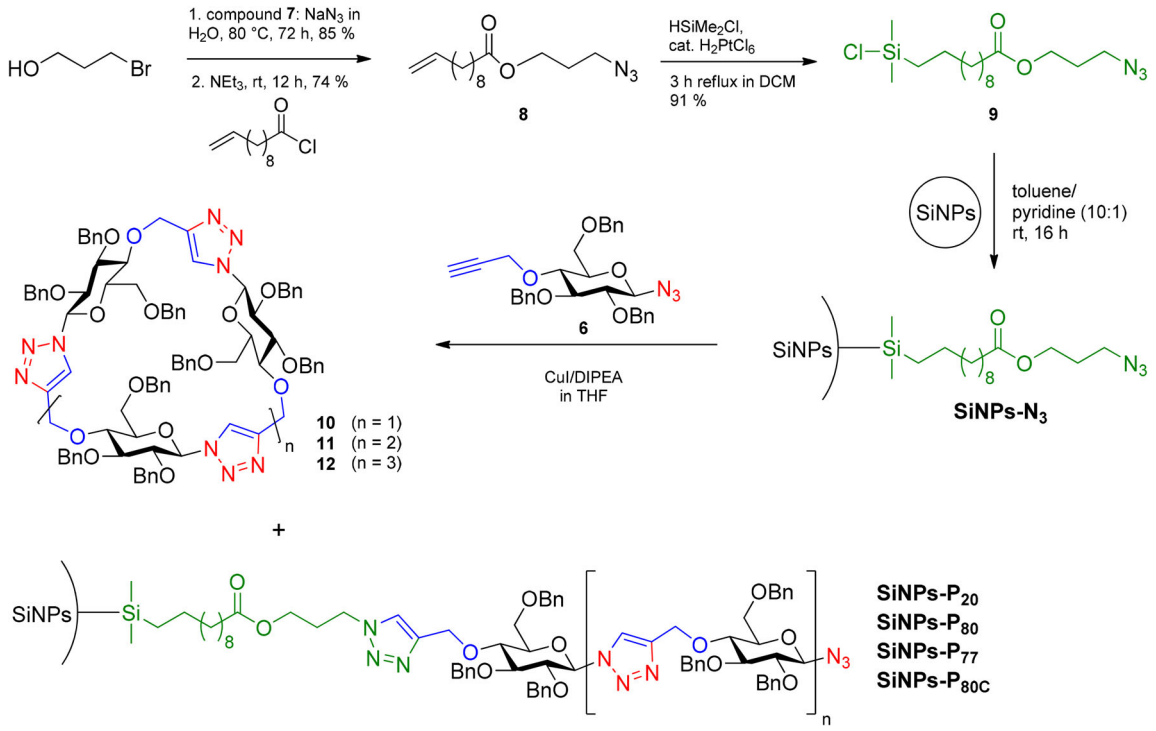
2 | RESULTS AND DISCUSSION

In order to synthesize linear polymers using monosaccharide-derived monomers, a novel glucose-derived monomer **6** was designed and synthesized with high yield (Scheme 1). Hereby, glucose was firstly peracetylated and bromine was introduced at C1 in α-configuration (**1**), which was replaced by an azide group in a following S_N2-type nucleophilic substitution. Then, glucose derivative **2** with an azide group at C1 in β-configuration was deacetylated, leading to glucopyranosyl azide. In the following step, C4 and C6 of the glucopyranosyl azide were protected with benzaldehyde dimethyl acetal (**3**). The remaining hydroxyl groups at C2 and C3 were protected as benzyl ethers (**4**). The selective reductive cleavage of the acetal gave a free hydroxyl group at C4 (**5**), which has not been described before for such glucose derivative. Finally, the glucose-derived monomer **6** bearing an azide group at C1 in β-configuration and a propargyl group at C4 was obtained after the introduction of the propargyl group.

For the click-polymerization on the surface of SiNPs using glucose-derived monomer **6**, azide or alkyne moieties need to be present on their surface. So far, commercially available bromoalkyl silanes have been used for this modification and bromine moieties were substituted by azide moieties in a consecutive reaction step.[13] However, it is generally complicated to monitor the reaction progress of the nucleophilic substitution on the surface and ensure complete conversion of bromine moieties.[14] Therefore, we designed and synthesized a silane linker **9** (Scheme 2) with a terminal azide moiety. Bound to this



SCHEME 1 Schematic representation for the synthesis of the glucose-derived monomer 6 [Color figure can be viewed at wileyonlinelibrary.com]



SCHEME 2 Schematic illustration for the synthesis of the silane linker **9**, azide-bearing silica nanoparticles **SiNPs-N_3**, and subsequent CuAAC. CuAAC, copper(I)-catalyzed azide-alkyne cycloaddition [Color figure can be viewed at wileyonlinelibrary.com]

linker, every chain grafted onto the surface of SiNPs will only contain one azide group.

For the synthesis of the linker with reactive silane species, monochlorosilane was chosen over dichlorosilanes or trichlorosilanes to avoid further crosslinking or branching. Detrimentally for the use of dichlorosilanes and trichlorosilanes is their ability to oligomerize or polymerize, as soon as traces of moisture are present in the reaction system. In comparison, monochlorosilanes dimerize by reacting with water and are consequently deactivated. Hence, monochlorosilanes are advantageous for grafting individual linear chains onto the surface of SiNPs.[15]

In addition, the azide-bearing **SiNPs-N_3** were well dispersed in organic media, such as THF. This dispersibility assures accessibility of the azide groups for the click-catalyst as well as for the polymerization of monomer **6**. This property is attributed to the length of the nonpolar linker as a spacer with 15 atoms between the surface of SiNPs and the terminal azide moieties.

After the grafting process with **9** was finished, unreacted chlorosilane was washed off and the elemental

TABLE 1 Elemental compositions in wt% of **SiNPs-N_3** and SiNPs after the oligomerization of **1** under various reaction conditions, the grafting yields on the SiNPs-surface and the ratios of the peak heights of cyclic oligosaccharide-mimics **11**/**10** in the MALDI mass spectra (Figure 1a)[a]

Sample	C	H	N	DP	Yield on SiNPs-surface	Cyclic compounds	Peak height ratio 11/10
SiNPs-N_3	3.50	1.20	0.46	-	-	-	-
SiNPs-P_{20}	13.90	1.86	1.73	3.46	17.3%	C_{20}	5%
SiNPs-P_{80}	21.30	2.45	2.57	6.62	8.3%	C_{80}	19%
SiNPs-P_{77}	24.80	2.70	2.96	8.44	11.0%	C_{77}	15%
SiNPs-P_{80C}	31.75	3.24	3.73	13.01	16.3%	C_{80C}	0

[a]**SiNPs-P_{20}** represents the sample with the addition of 20 eq. of monomer, **SiNPs-P_{80}** the sample with the addition of 80 eq. of monomer, **SiNPs-P_{77}** the sample with sevenfold of hourly addition using 11 eq. of monomer and **SiNPs-P_{80C}** the sample with the continuous addition of 80 eq. of monomer over a time period of 24 hr.

composition was determined (Table 1). The grafting density of azide groups was calculated to be 109.5 μmol/g based on the nitrogen content. With the BET-surface of 49.25 g/m^2, the density of azide groups on the surface of SiNPs was calculated to be 2.22 μmol/m^2. Compared to previous studies with shorter alkyl chains,[15,16] we achieved 10–20% lower grafting densities due to our longer chlorosilanes **9** with more bulky terminal groups.

Then, linear oligomer chains containing glucose-derived monomers **6** were polymerized on the surface of SiNPs. It is to be expected that the step-growth-type CuAAC polymerization of the monomer **6** starts with the formation of a linear dimer. This dimer bears one reactive azide and one reactive propargyl end group. As the reaction progresses further, the intermediately formed dimers could react with another monomer, dimer or even oligomer, leading to chain growth. In the presence of azide-bearing **SiNPs-N_3**, the monomers, dimers or oligomers can also react with the surface-bound azide groups and form polymer chains on the surface of NPs. Thus, the reaction on the surface of SiNPs and the reaction of monomers in the solution occur parallel. The monomers of the products are connected via β-1,4-triazole linkages, which are different from the β-1,4-glycosidic bonds within cellulose chains. Thus, linear products can be considered to have a pseudo-cellulosic structure.

The chain propagation continues until the reaction is terminated. One possible termination reaction is the intramolecular cyclization, in which the azide end group and propargyl end group of the same oligomer react with each other, forming a stabile triazole bond and leaving no further click-reactive group in the molecule. Hereby, cyclodextrin-analogs with the β-1,4-triazole linkage between monomers are obtained, compared to the α-1,4-glycosidic linkage of cyclodextrins. This termination reaction is not possible for the oligomerization of monomers **6** on the surface of **SiNPs-N_3** bearing pendant azide groups (Scheme 2), which assures the formation of linear oligomer chains on SiNPs. After the reaction, modified SiNPs were separated from the reaction solution via centrifugation.

Because the surroundings of the click reaction were already adapted, we changed the dosage and the feeding frequency of the monomer **6** to tune the lengths of linear oligomers. For the first experiments, 20 equivalents of the monomer **6** were added to 1 equivalent of azide groups on **SiNPs-N_3**. After the reaction, resulting **SiNPs-P_{20}** were separated from the supernatant solution by centrifugation. Oligomer chains with a calculated degree of polymerization (DP) of 3.46 on the surface of **SiNPs-P_{20}** were obtained, according to the results of ELEM. ANAL (Table 1). The CuAAC of the remaining 16.54 equivalents of **6** took place in the solution. MALDI mass spectroscopic analysis of the supernatant showed the presence of oligomers in the mixture **C_{20}** (Figure 1a). To be precise, the mixture **C_{20}** predominantly contained the pseudo-trisaccharide **10** and a minority of the pseudo-tetrasaccharide **11** (Scheme 2).

The asymmetrical stretching vibration of the azide group commonly gives a very strong signal at around 2,100 cm^{-1} in FTIR spectra. In the spectrum of **C_{20}** (Figure 1b), this band cannot be observed. In addition, no signal ascribed to azide group as well as propargyl end group could be detected using proton NMR spectroscopy. Therefore, obtained products should be cyclized compounds.

When a higher amount of 80 equivalents monomer was employed, the content of the cyclic pseudo-tetrasaccharide **11** in the mixtures **C_{80}** slightly increased, but the cyclic pseudo-trisaccharide **10** was still the major cyclic product (Figure 1a). In comparison, the linear oligomers on the surface of **SiNPs-P_{80}** had a higher average DP of 6.62 (Table 1). Compared to the previous experiments of **SiNPs-P_{20}**, the DP of linear oligomers increased by 91%, although a fourfold amount of the monomer was employed. However, the yield of linear oligomers on the

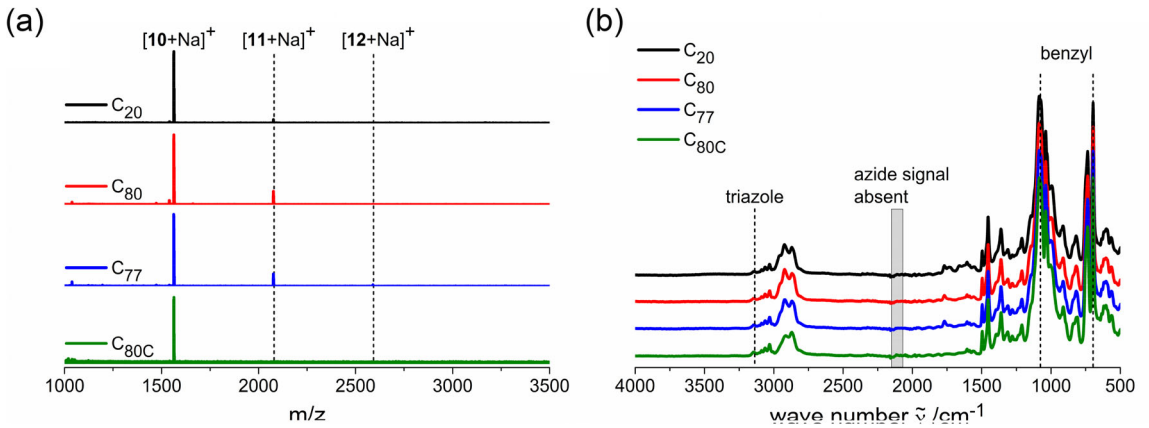


FIGURE 1 (a) Representative MALDI mass spectra of the cyclic oligomers from diverse experiments. The molecular masses of **10** and **11** (Scheme 1) were found with sodium ions as the counterion. (b) FTIR spectra of the cyclic oligomers from diverse experiments [Color figure can be viewed at wileyonlinelibrary.com]

surface of SiNPs decreased from 17.3% for the **SiNPs-P$_{20}$** to 8.3% for **SiNPs-P$_{80}$** (Table 1). It should be noted that the reaction surroundings including the volume of the reaction system were kept constant. This shows that the reaction rate of the cyclic compounds benefits more from the increased monomer concentration than the reaction on the surface of SiNPs. Conversely, the synthesis of linear oligosaccharide mimics on the surface of SiNPs should be favored by lower monomer concentrations.

To prove this hypothesis, CuAAC with 77 equivalents of the monomer that was added in 7 portions hourly was conducted. By doing so, the average monomer concentration was reduced during each click reaction cycle. Following this, the DP of the linear oligomer chains on the surface of **SiNPs-P$_{77}$** increased to 8.44 and the yield increased to 11.0% (Table 1). In contrast, the impact on the obtained cyclic oligomers was minimal, as shown in their MALDI mass spectrum (**C$_{77}$**, Figure 1a). Therefore, a reduced monomer concentration for each single CuAAC step during the whole synthesis will elevate the DP of linear oligomers.

By employing 80 equivalents of the monomer for a continuous addition of the monomer over a time period of 24 hr during the CuAAC reaction, the average active monomer concentration is much lower compared to the previous experiments. After the reaction, the DP of obtained linear oligomers on the surface of resulting **SiNPs-P$_{80C}$** further increased to 13.01 (Table 1). Compared to the previous experiments with the one-time addition with the same amount of the monomer (**SiNPs-P$_{80}$**), the DP increased by 97%. The grafting yield of 16.3% is similar to the first experiment **SiNPs-P$_{20}$**. Moreover, only the cyclic trimer was formed in the solution based on MALDI mass spectrum (Figure 1a).

Cyclic dimerization was not observed in any experiment. The dimer would consist of only two pyranose rings and two rigid triazole rings with a bridging methylene group, which will have a size comparable to cyclodextrins with three to four glucopyranose rings. The synthesis of rings in this size is only possible, when the monosaccharides are locked in the right confirmation.[17] Cyclic dimerization was reported for a galactose-based monomer that differs from **6** by the configuration at C4.[6] Thus, the orientation of the reactive groups at C1 and C4 and the steric hindrance by the bulky benzyl groups should be critical for the cyclic dimerization.

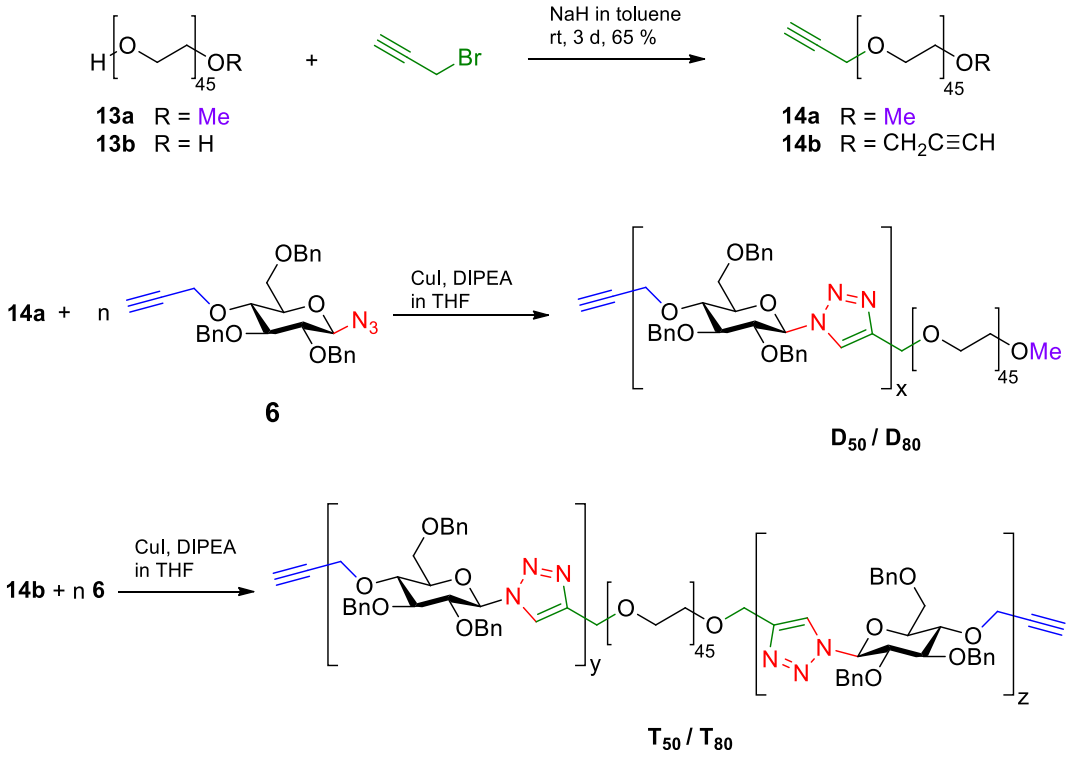
Based on above results, we obtained the cyclic pseudo-trisaccharide **10** as smallest cyclic compound. It was either the main or the only product in the solution after the CuAAC reaction of monomer **6**. The cyclic pseudo-tetrasaccharide **11** was formed to a minor extent, while larger cyclic compounds were not detected at all (Table 1). Moreover, the intramolecular cyclization for **10** and the chain growth by the addition of one more monomer are two competing reactions during the CuAAC oligomerization. Comparing the peak height ratios of **11**/**10** in the MALDI mass spectra (Figure 1a and Table 1), it is visible that more **11** was preferentially formed during reactions with higher monomer concentrations (**C$_{80}$** and **C$_{77}$**).

With lower monomer concentration and therefore higher yield of pseudo-cellulose on the NPs surface, **11** was formed only to a minor extent (**C$_{20}$**) or not formed at all (**C$_{80C}$**). Therefore, the intramolecular cyclization for the synthesis of **10** was preferred with the presence of low amounts of glucose-derived monomers, compared to further chain growth and cyclization to **11**. At the same time, the continuous chain growth of linear oligomers at the surface of SiNPs was preferred as well.

Based on this optimized method, PEG 2000 was further chosen as a polymeric starting molecule to prepare linear polymers. PEG 2000 has an average DP of around 45 and hydroxyl end groups, which can be conveniently converted through an esterification or etherification reaction to various end groups. The excellent solubility of PEG 2000 in a large variety of polar and nonpolar solvents is also an advantage for further reaction steps, which include solvents from water over methanol, ethanol to THF, chloroform, methylene chloride, and toluene. In this report, alkyne groups were introduced into the ends of PEG after the etherification of the hydroxyl groups with propargyl bromide. Hereby, the etherification of monomethoxypolyethylene glycol 2000 (**13a**) gave PEG terminated with one propargyl group (**14a**), while the etherification of PEG 2000 (**13b**) introduced two propargyl end groups (**14b**, Scheme 2). Due to the linear polymer chains of **14a** and **14b**, it can be assumed that the alkyne end groups are not sterically hindered and therefore well accessible to the monomers. The CuAAC-polymerization of the glucose-based monomer **6** was performed in THF, which is a good solvent for the PEG derivatives as well as for the monomer **6**.

A triphenylphosphine-free catalyst system copper(I)-iodide/diisopropylethylamine (DIPEA) was chosen to avoid the Staudinger reaction between the triphenylphosphine and azide groups, which led to a comparatively lower DPs.[18] The reactions were performed with either 50 or 80 equivalents of monomer. Following the reactions, the diblock-copolymers pseudo-cellulose-*block*-PEG (**D_{50}** and **D_{80}**, Scheme 3) and triblock-copolymers pseudo-cellulose-*block*-PEG-*block*-pseudo-cellulose (**T_{50}** and **T_{80}**) were obtained.

The success of the reaction was proven by NMR spectroscopy. The chemical shifts in the NMR spectra of all four polymers are very similar and mainly differ in the intensity of the PEG signals. For the signal assignment, ^{1}H-NMR, ^{1}H, ^{1}H-COSY, and HSQC spectra were recorded and evaluated. The ^{13}C-NMR spectrum of **D_{80}** is exemplarily shown in Figure 2a. C1 gives the most downfield-shifted signal and C6 gives the most highfield-shifted signal of carbon atoms from the glucose ring. Compared to C1 of many polysaccharides, such as cellulose, C1 is not connected to the oxygen atom of the glycosidic bond, but directly with the triazole ring, which causes the highfield-shift of C1 signal. The signals of the methylene groups could not be precisely assigned, because no ^{4}J couplings over the oxygen atoms at C2, C3, C4, C6, and over C9 were observed. For the triazole-carbon atoms C8 and C9, only one set of signals is obtained. Therefore, it can be assumed that the CuAAC



SCHEME 3 Schematic illustration for the end group modification of methoxy-terminated PEG 2000 (**13a**) and PEG 2000 (**13b**), leading to PEG 2000 with one (**14a**) or two (**14b**) propargyl end groups. Further polymerization of **14a** and **14b** with glucose-derived monomer **6** led to diblock-copolymers **D_{50}** and **D_{80}** and triblock-copolymers **T_{50}** and **T_{80}**, respectively [Color figure can be viewed at wileyonlinelibrary.com]

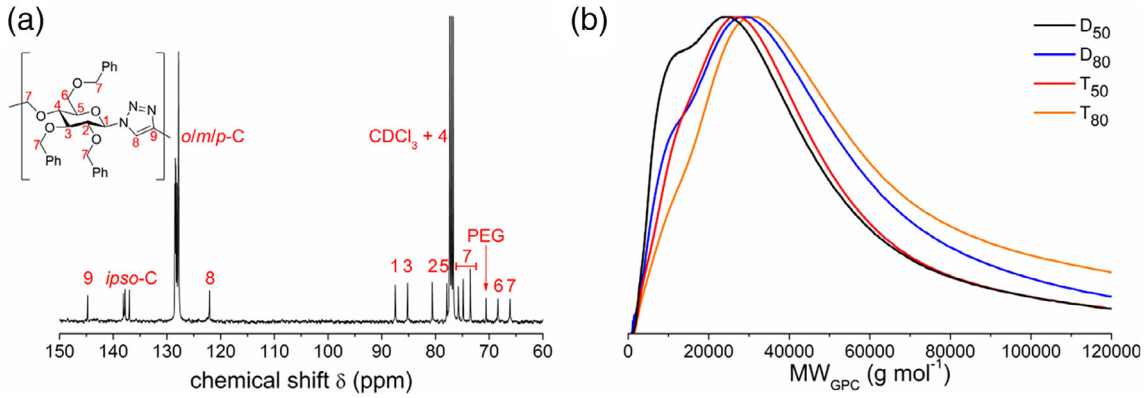


FIGURE 2 (a) ^{13}C-NMR spectrum of D_{80} in $CDCl_3$. (b) GPC curves of D_{50}, D_{80}, T_{50}, and T_{80} [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2 Molecular weights and experimental yields of obtained copolymers

Sample	M_n[a] (kg/mol)	M_w[a] (kg/mol)	$Đ$ (M_w/M_n)	Yield (%)[b]	DP_n[c]
D_{50}	11.5	24.4	2.12	94	48
D_{50L}	8.3	12.3	1.49	34	27
D_{50H}	30.4	42.8	1.41	55	148
D_{80}	12.4	30.6	2.48	90	75
D_{80L}	6.5	9.2	1.41	25	21
D_{80H}	24.0	40.3	1.68	68	123
T_{50}	13.9	28.6	2.05	93	n.p.
T_{50L}	8.8	12.7	1.45	25	n.p.
T_{50H}	29.4	41.3	1.41	65	n.p.
T_{80}	16.5	39.4	2.39	88	n.p.
T_{80L}	6.3	9.0	1.43	11	n.p.
T_{80H}	22.1	41.6	1.88	69	n.p.

Abbreviation: n.p., not possible.
[a]Molecular weights of whole copolymers measured via SEC in THF relative to polystyrene standards.
[b]The combined yields of both polymer fractions are not equal to the overall yields due to minor sample loss during the separation and purification process.
[c]DP_n of pseudo-cellulose blocks calculated from ^{1}H-NMR spectra.

polymerization occurred regioselectively and the 1,4-triazole linkage was obtained after the CuAAC.

The yield and consumption of the monomer was nearly quantitative for all click reactions. The DP_n of both diblock-copolymers (**D_{50}** and **D_{80}**) was calculated to be 48 for **D_{50}** and 75 for **D_{80}** based on their ^{1}H NMR spectra. Hereby, the signal of the methoxy end group of the PEG block was compared to H1 of the pseudo-cellulose blocks. For the triblock-copolymers **T_{50}** and **T_{80}**, the DP could not be calculated using their ^{1}H-NMR spectra due to overlap of signals attributed to protons of PEG and pseudo-cellulose blocks, in particular those of H5, H6a, and H6b. Using the signals of the propargyl end groups for the determination of the DP leads to an overestimation of the DP, which indicates the partial decomposition of propargyl end groups during or after the polymerization reaction. Due to this chain termination, a wider size distribution of the resulting block-copolymer chains can be expected. Cyclic oligomerization was not observed using MALDI mass spectroscopy.

To get a more detailed information of the chain length distribution of the block-copolymers, SEC (Figure 2b). A number-average molecular weight M_n = 11.5 kg/mol with a dispersity $Đ$ = 2.12 was measured for **D_{50}** and M_n = 12.4 kg/mol with a slightly higher dispersity $Đ$ = 2.48 for **D_{80}** (Table 2). For both diblock-polymers a shoulder can be observed in the SEC curves at around 11 kg/mol (Figure 2b). The triblock-

copolymer $\mathbf{T_{50}}$ was synthesized with M_n = 13.9 kg/mol and dispersity $Đ$ = 2.05, while $\mathbf{T_{80}}$ was even larger with M_n = 16.5 and dispersity $Đ$ = 2.39.

Obtained block-copolymers are amphiphilic, consisting of a hydrophilic PEG-block and one or two hydrophobic pseudo-cellulose blocks in one polymer chain. This structural feature and the different solubility of two types of blocks in distinct organic solvents were used for the fractionation of these copolymers. By dissolving the as-synthesized polymers ($\mathbf{D_{50}}$, $\mathbf{D_{80}}$, $\mathbf{T_{50}}$, and $\mathbf{T_{80}}$) in THF and adjusting the amount of methanol added to the solution, precipitation was observed. Compared to the pseudo-cellulose, PEG is well soluble in methanol. As the proof of concept, the polymers were only separated herein in two fractions. The precipitated fraction mostly consists of polymers with longer pseudo-cellulose chains, which means they have a higher molecular weight ($\mathbf{D_{50H}}$, $\mathbf{D_{80H}}$, $\mathbf{T_{50H}}$, $\mathbf{T_{80H}}$, Table 2). The DP_n obtained from NMR measurements of both diblock-copolymers is between 123 and 148. SEC measurements revealed a M_n = 22.1–30.4 kg/mol for all precipitated polymer fractions, while their dispersity $Đ$ was narrowed to 1.41–1.88. In addition, $\mathbf{D_{80H}}$ and $\mathbf{T_{80H}}$ were obtained in higher yields compared to their counterparts from the polymerization with less equivalents of monomer ($\mathbf{D_{50H}}$ and $\mathbf{T_{50H}}$). Polymer chains with a lower molecular weight stayed dissolved ($\mathbf{D_{50L}}$, $\mathbf{D_{80L}}$, $\mathbf{T_{50L}}$, $\mathbf{T_{80L}}$, Table 2) and were collected by the evaporation of solvents. They are considerably shorter with a M_n between 6.3 and 8.8 kg/mol and dispersity $Đ$ of 1.41–1.49. Moreover, the DP_n of the diblock-copolymers is between 21 and 27.

While the yield of linear polymers on the surface of the SiNPs did not exceed 20% even after optimization of the reaction conditions, a yield of over 90% was achieved in the polymerization at PEG end groups. This should be primarily attributed to the catalyst system CuI/DIPEA. This catalyst system is largely dispersed and not dissolved in THF, which means that the reaction is heterogeneously catalyzed. This has the advantage that the catalyst can easily be separated by centrifugation from all dissolved components after the reaction. However, a good solubility of the starting material and monomer seems to be a requirement for the successful use of CuI/DIPEA. Since the modified SiNPs cannot be dissolved in THF, but can only be dispersed, this could have had a negative effect on the catalysis of the reaction on their surface, but not on the catalysis in solution, which led to the formation of cyclic products. This could explain the high yield of cyclic products during the reaction with the SiNPs and the excellent results at end-functionalized PEG.

In previous reports about a step-growth-type CuAAC of monosaccharide-derived monomers, oligomers with DPs of up to 6–8 were often obtained.[9,19] Compared to these results, we obtained significantly enhanced higher average DPs of up to 148. In addition, the separation and purification steps of obtained products are more convenient than the chromatographic methods. Moreover, chain length can be easily tuned in our approach by altering the amount of employed monomer and/or the feeding frequency. Chains of similar length were reported to be accessible by using ring opening polymerization, for example, the synthesis of 4,6-carbonate linked polyglucoside with a DP up to 100.[11] Similar to our results, block-copolymers could be synthesized with this approach, but the monomer design and polymerization technique vastly differs from our approach.

3 | CONCLUSIONS

In conclusion, we developed a novel method for the synthesis of linear polysaccharide analogs with glucose-derived monomers via CuAAC-assisted polymerization. Well soluble linear co/polymers were obtained by using endfunctionlized PEG or to a limited extent on SiNPs surfaces as starter. In particular, this method can also be used for the polymerization of other (saccharide-based) monomers. It further expands the scope for the synthesis of diverse oligo- and polysaccharide-mimics with various functional groups and applications.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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