

# Grafted Copolymer Based on Chitosan and Poly(N-Isopropylacryl Amide) via Click Technique. I. Synthesis and Characterization

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**Abstract:** As chitosan's solubility represents a drawback for further applications, the functionalization of chitosan became attractive by a variety of chemical methods. The present study deals with the chemical modification of chitosan by using click chemistry technique as versatile tool being easy to perform with high yields and no additional by products. The approach used herein was to attach a responsive moiety (e.g. NIPAAm, HEMA or DMAEMA) on the macromolecular chain of chitosan via an azide-alkyne coupled reaction. More specifically, the reaction occurred between azide-chitosan and alkyne terminated responsive polymer. The method includes the modification of chain transfer agent with alkyne terminated groups, polymerization of responsive monomer, azidation steps of chitosan and final click reaction between two end products. Structure of end products and intermediaries were confirmed by the FT-IR and H-NMR spectra. Thermal characterization was performed showing different thermal behavior with the chemical modification. As main outcome, chitosan-g-PNIPAAm was obtained, the structure being confirmed by the disappearance of azide group and the presence of triazole moiety within the final product. The new approach of advancing the reaction via alkyne terminated-PNIPAAm, synthesized by RAFT, seemed to be successful as verified by <sup>1</sup>H-NMR. Thermal properties revealed a better thermal stability for the new polymeric materials as the structure was more complex.

**Key-Words:** Click chemistry, Chitosan, Phthaloylation, PNIPAAm, Alkyne terminated PNIPAAm, Triazole ring, Graft copolymer

## 1 Introduction

Advanced chemical modification techniques attracted much attention opening new alternatives in generating of polymeric materials with tailored properties. The main focus of contemporaneous reports was to use environmental friendly methods, easy to perform in mild conditions. Additionally, they should ensure obtaining high chemoselectivity with a variety of functionalities without generating toxic by-products.

In last 10 years click chemistry technique became a very convenient and powerful tool to generate functionalized polymeric materials in various fields. "Click chemistry" was reported for first time by Kolb et al. [1] as a method to tailor and to generate molecules in a fast and reliable manner by joining

small modular units. Among the different approaches made for the "click chemistry" reactions, Cu(I)-catalyzed azide alkyne Huisgen cycloaddition (CuAAC) was favored because of its high regioselectivity, quantitative yield, and milder reaction conditions without generation of by-products [2].

The reaction between the two main functional groups (i.e. alkyne and azide groups) was reported to occur rapidly and selectively in mild and aqueous conditions. [1, 3-7].

The variety of materials resulted from click reactions could easily find applications in biosciences [8-10], drug discovery [11] and material science [12].

Beside the benefit of being easy and high yielded, functionalization of polysaccharides e.g. chitosan,

hyaluronan, etc. started to be developed more due to their unique properties [13]. Among all the attempts, “clicked” chitosan enabled the design of various chitosan-based materials *via* one-step reaction. This new approach may overcome the limitations of chitosan as a natural based polymer, such as low solubility in many solvents and poor physical-chemical properties. Moreover, this method could be considered that is very efficient in the way that “clicked” polysaccharides with more complex architectures are formed without affecting the stability of the polysaccharide’s backbone during the modification technique [14-16].

Cheaburu-Yilmaz *et al.* [7] reported the general accepted mechanisms for click reaction specific for chitosan modification. Various attempts of chemical modification were presented within the review showing that usually the first step prior to the CuAAC reaction is the functionalization of the polysaccharide with either azide or alkyne. The synthesis of 6-azido-6-deoxy-chitosan represented one of the widely used approaches where the free primary hydroxyl groups at C6 position are tosylated at low-temperature and subsequently the tosylated groups undergo a nucleophilic displacement with sodium azide ( $\text{NaN}_3$ ). Another method reported was the introduction of azide groups at C6 position, the primary hydroxyl groups being activated by triphenylphosphine ( $\text{Ph}_3\text{P}$ ), followed by a subsequent bromination with tetrabromomethane or N-bromosuccinimide.

Present study presents the preliminary results from a successive study of “clicked” chitosan. The pre-click functionalization of chitosan was done in the way to chemically protect free  $\text{NH}_2$  of chitosan by phthaloylation at C2, followed by bromination and azidation steps at C6. The outcome of the intended studies was to obtain “clicked” chitosan with responsive (temperature and pH) behavior according to the desired application. In this respect, alkyne terminated polymers (e.g. poly N-isopropylacrylamide, etc ) were firstly synthesized by RAFT polymerization in the presence of a CTA agent. Then they were clicked with azidated chitosan and the final polymers comprised both polymers’ properties leading to a new material to be

used in pharmaceutical formulations for topical application.

## 2 Material and Methods

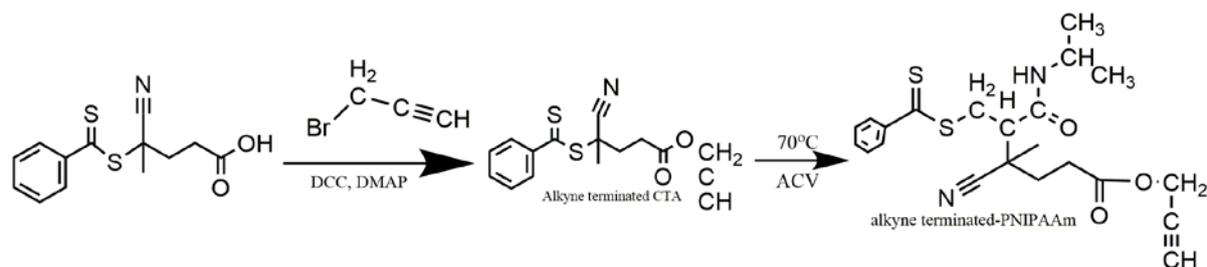
### 2.1 Materials

In the experiments phthalic anhydride (PhA,  $\geq 99\%$ ), N-isopropylacrylamide (NIPAAm, 97%), N,N-dicyclohexylcarbodiimide (DCC), 4-(dimethylamino) pyridine, (DMAP, 99%), methanol (HPLC grade), diethylether (extra pure), acetone, N-methyl pyrrolidone (NMP) were purchased from Sigma-Aldrich and were used as received. The initiator 4,4-Azobis(4-cyanovaleric acid, Sigma) (ACV, 98%) was used as achieved. N,N-Dimethylformamide (DMF, 99% Sigma) was dried on molecular sieves 4A and distilled under vacuum. The carboxyl-end functional RAFT agent (CTA) used was: 4-cyano-4-(phenylcarbonothioylthio) pentanoic acid. For click technique N-methylpyrrolidone (NMP), triphenylphosphine (TPP), N-bromosuccinimide, sodium azide, triethylamine (TEA) were used, all purchased from Sigma Aldrich.

### 2.2 Preparation methods and characterization

#### 2.2.1 Phthaloylation of chitosan with phthalic anhydride

Click chemistry method debuts with the modification of chitosan in order to obtain chemo-selective chitosan derivatives at C6. For this as first step phthaloyl chitosan was prepared as following: Phthalic anhydride (PhA) in excess (5.5 mmol) was first dissolved in 6 mL of DMF/ $\text{H}_2\text{O}$  95/5 v/v% added into a 2 neck-balloon of 20 mL; followed by addition of chitosan powder (1.86 mmol). The system was closed and the dissolved  $\text{O}_2$  was removed by purging  $\text{N}_2$  for prolonged time 1h. The solution was heated up to 120 °C and kept for 8h for complete reaction. The final light brown product was obtained by precipitation from ice-water and washing with methanol repeatedly; the yield of final product was 87 %. The efficiency of the N-phthaloylation of chitosan (CS-Ph) was evaluated by FT-IR, H-NMR and elemental analysis.



**Scheme 1.** Proposed mechanism for preparation of PNIPAAm -alkyne terminated compound.

### 2.2.2 Preparation of the Br-modified derivative, 6-bromo-6 deoxy N-phthaloyl chitosan

Bromination at C6 in the presence of N-methyl-2-pyrrolidone (NMP), N-bromosuccinimide, and triphenylphosphine was considered. For this purpose 1.18 mmol (e.g. 0.2 g) of phthaloyl chitosan was dispersed in 100 mL of NMP. N-bromo succinimide (11.5 mmol- 1.78g) and 11.5 mmol of triphenyl phosphine (2.63 g) were added over an ice bath. The mixture was heated up at 80°C and stirred for 1 h under N<sub>2</sub> flow. The final product was isolated from ethanol and extra purified with ethanol via Soxhlet extractor and dried in vacuum oven at 40°C. The structure of 6-bromo-6 deoxy N-phthaloyl chitosan (CS-Br) was identified by FT-IR, H-NMR and characterized by means of DSC, TGA and elemental analysis.

### 2.2.3 Preparation of Azide-modified derivative, 6-bromo-6 deoxy N-phthaloyl chitosan (CS-N3)

Azidation of the 6-bromo-6-deoxy-N-phthaloyl chitosan was achieved by a nucleophilic displacement reaction of the bromine group with sodium azide. For this purpose, previously obtained 6-bromo-6-deoxy-N-phthaloyl chitosan (1 mmol) were dispersed in NMP and sodium azide (NaN<sub>3</sub>) in excess was added (10 mmol). The mixture was stirred at 80°C under N<sub>2</sub> atmosphere and kept for 24h. The mixture was filtered to remove the salts and the filtrate was precipitated in ethanol to isolate the newly obtained CS-azide product. The azidated derivative was isolated by centrifugation at 4°C and 4000 rpm during 20 min. The final washed product was dried in vacuum oven at 40°C.

### 2.2.4 Preparation of alkyne terminated P(NIPAAm)

Click technique can take place between an azide containing molecule and an alkyne terminated one according to the general accepted mechanism [7].

In the study, a novel approach has been employed for the click reaction. To obtain a PNIPAAm grafted chitosan, an alkyne terminated PNIPAAm was synthesized via RAFT polymerization with an alkyne modified CTA. Then alkyne-PNIPAAm was

clicked with the previously synthesized 6-azido-6-deoxy-N-phthaloyl- chitosan. Below the details of the each step are given.

#### 2.2.4.1 Functionalization of CTA with propargyl alkyne

Esterification of CTA with propargyl bromide was performed according to the mechanism proposed in Scheme 1.

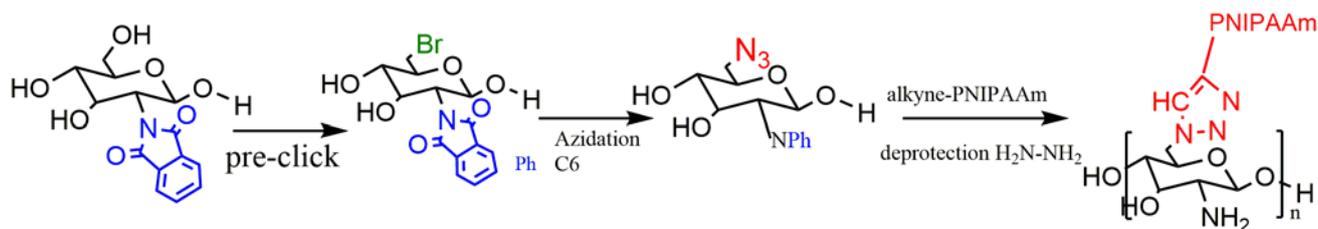
An amount of 5.5 mmol of CTA (M<sub>w</sub>-279g/mol) was mixed in CH<sub>2</sub>Cl<sub>2</sub> with DCC and DMAP. Propargyl bromide was added drop-wise over an ice bath and the reaction continued for 48h at room temperature (RT). The solvent was removed by evaporation by using a Rota-evaporator device. The final product was washed several times with acidic water and dried under vacuum. The resulting product had a pale pink color due to the presence of CTA.

#### 2.2.4.2 Synthesis of alkyne terminated-PNIPAAm

The synthesis of alkyne terminated-PNIPAAm was done according to the Scheme 1. For this purpose CTA-alkyne was mixed with NIPAAm and initiator, ACV in 10 mL of dried DMF. The ratio between CTA and initiator was selected to be optimum as 5:1. Reaction was stirred at 70 °C for 48 h under N<sub>2</sub> atmosphere. The final product was isolated from diethylether, centrifuged at 4°C, 4000 rpm for 20 minutes. The final obtained product had a yellowish color.

#### 2.2.7 Click reaction between 6-azido-6-deoxy-N-phthaloyl-chitosan and PNIPAAm-CTA-alkyne

The proposed mechanism for the click reaction was illustrated in Scheme 2. The “clicked” compound was prepared by mixing 0.64 mmol CS-N<sub>3</sub> with 0.033mmol CuSO<sub>4</sub> pentahydrate and sodium ascorbate (last two dissolved in 0.2 ml distilled water) in DMF. Furthermore tri-ethylene amine was added (1.1 mL). Reaction mixture was heated up at 70°C and stirred for 48 h under N<sub>2</sub> atmosphere. The product was collected from diethyl ether by centrifugation and dried under vacuum.



**Scheme 2.** Proposed mechanism for click reaction between CS-azide from step 1.2 and alkyne terminated – PNIPAAm

## 2.3 Characterizations

### 2.3.1 FT-IR spectroscopy

The chemical characterization of the obtained intermediary and final products was performed by using a Perkin Elmer Spectrum-100 instrument, through reflexion on a diamond crystal with an angle of 45 degrees, resolution of  $4\text{ cm}^{-1}$

### 2.3.2 Elemental analysis

Elemental analyses were performed by Leco TruSpec Micro CHNS (Leco, St. Joseph, MI, USA); experimental results were further compared with the theoretical values

### 2.3.3 NMR spectroscopy

The nuclear magnetic resonance,  $^1\text{H-NMR}$  spectra were recorded by using a AS400 Mercury Plus NMR Varian (Varian Inc., Palo Alto, CA, USA) (400 MHz) in deuterated DMSO and  $\text{D}_2\text{O}$

### 2.3.4 Differential scanning calorimetry

A DSC (differential scanning calorimetry) (Perkin Elmer DSC-8000, Waltham, MA) instrument was used to examine the thermal behavior of the dried synthesized samples and pure components of samples. The samples were sealed in aluminum pans and placed in DSC. DSC analysis was conducted under nitrogen flow (20 mL/min) within a temperature range of 30 and  $300\text{ }^\circ\text{C}$  at a heat rate of  $10\text{ }^\circ\text{C}/\text{min}$  under nitrogen flow.

### 2.3.5 Thermogravimetry

Thermogravimetric studies were performed by using a Perkin Elmer TGA 4000 device. The temperature program was set as from 30 to  $500\text{ }^\circ\text{C}$  with a heating rate of  $10\text{ }^\circ\text{C}/\text{min}$  under  $\text{N}_2$  flow.

## 3 Results and Discussion

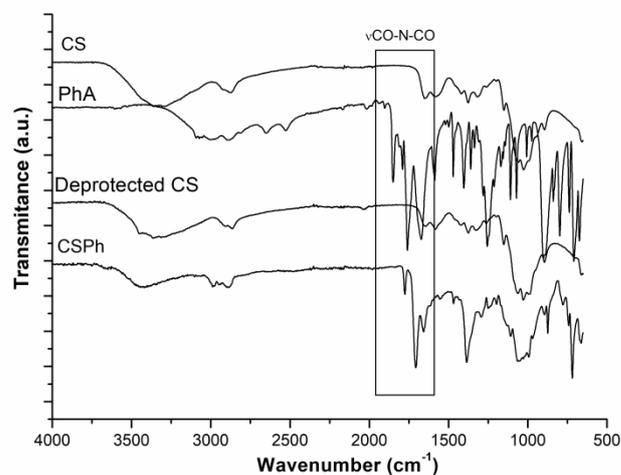
### 3.1 FTIR spectra

Structure identity of the each step's intermediary and the final obtained products were assessed mainly by FT-IR spectra assigning the characteristic

vibration bands for each modified functional group. The obtained spectra were grouped by each performed step during the synthesis.

Phthaloylation of chitosan was assessed in terms of reliability of the modification. Figure 1 shows the IR spectra of phthaloylated chitosan.

The characteristic peaks of chitosan was observed at  $2921\text{--}2887\text{ cm}^{-1}$  ( $-\text{CH}_3$ ,  $-\text{CH}_2$ ),  $1636\text{ cm}^{-1}$  ( $\text{C}=\text{O}$  stretch vibration),  $1548\text{ cm}^{-1}$  (secondary amide),  $1655\text{ cm}^{-1}$  corresponding to the amidic band I;  $1068\text{--}1020\text{ cm}^{-1}$  ( $\text{C-O}$  stretching of saccharide moiety). The structure of N-modified chitosan could be evidenced by the presence of characteristic bands for phthalic anhydride at  $1778\text{--}1760\text{ cm}^{-1}$  which corresponds to the formation of the imide 5-atoms ring ( $\nu_{\text{CO-N-CO}}$ ) and phthalic anhydride at  $1770\text{--}1850\text{ cm}^{-1}$ .

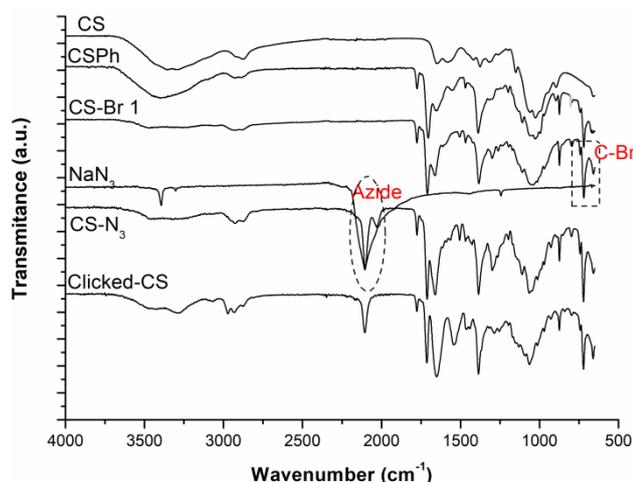


**Figure 1.** FTIR spectra of Phthaloylation of chitosan

Additionally, experiments of de-protection of phthaloylated chitosan were performed in order to double check the removal of phthaloyl group. The FT-IR spectrum of the deprotected-CS was added to Fig.1 for comparison. Phthaloyl chitosan, lost its specific groups from  $1760\text{ cm}^{-1}$  but also part of acetyl groups from the original chitosan structure as result of action of hydrazine monohydrate. The main outcome of this procedure is to obtain free  $\text{NH}_2$

which are well-known that confers pH-responsivity to the final polymer.

FT-IR spectra of 6-bromo-6 deoxy N-phthaloyl-derivative (Fig. 2) showed the specific vibration bands corresponding to the two precursors: a vibration band at 690-515  $\text{cm}^{-1}$  was found being assigned to the formed halo compound with C-Br bonds. Additionally it can be observed that the characteristic vibration bands of phthaloyl chitosan remained at C2 while the bromination took place in the position C6 of the macromolecular unit.

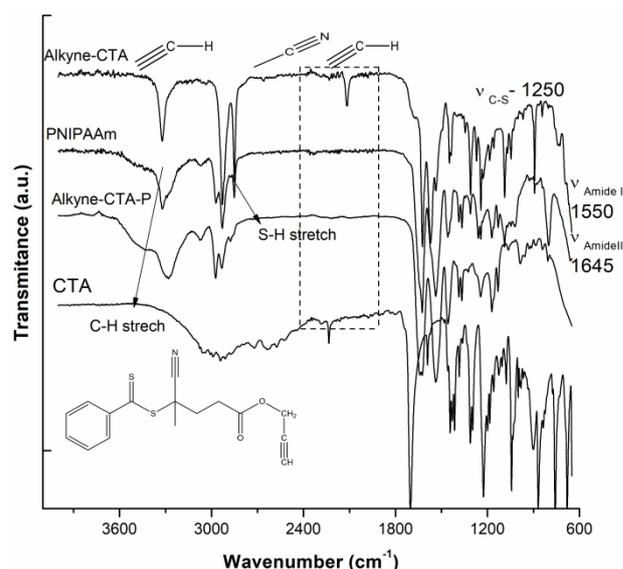


**Figure 2.** FT-IR spectra of functionalized chitosan and its intermediaries by click method

Within the FT-IR spectrum of 6-azido-6-deoxy-N-phthaloyl-chitosan (CS-N3)-Fig. 2, strong vibration band of azide at 2160-2120  $\text{cm}^{-1}$  was observed, showing the success of azidation. In the case of azidated compound it can be also observed that the structure of the functionalized polymer kept the characteristic vibration bands of phthaloyl chitosan indicating that the azidation occurred at C6. Additional intermediary compounds could be formed, in ionized state as the characteristic vibration band specific to azide in the region 2000-2200  $\text{cm}^{-1}$  were observed. Moreover, in the same spectral range similar peaks assigned to  $-\text{C}=\text{N}=\text{N}-$  as side species were also detected.

FT-IR spectrum of alkyne terminated CTA, presented within Fig. 3, showed the main characteristic vibration bands of the CTA, 4-cyano-4-(phenylcarbonothioylthio)pentanoic acid:  $-\text{COOH}$  ( $\sim 2900 \text{ cm}^{-1}$  broad),  $-\text{C}=\text{S}$  ( $\sim 1250 \text{ cm}^{-1}$ );  $\text{C}=\text{O}$  (aliphatic- $\text{COOH}$ ): 1725-1700; intramolecular H bond: 1670-1650  $\text{cm}^{-1}$ . By attaching alkyne group, the final alkyne terminated RAFT agent (CTA) presented the specific vibration bands of alkyne:  $\text{C}\equiv\text{C}-\text{H}$  stretch, at 2900  $\text{cm}^{-1}$  the stretch of  $\text{C}-\text{H}$ , 2120  $\text{cm}^{-1}$  stretch of  $-\text{C}\equiv\text{C}$ , at 1440  $\text{cm}^{-1}$  scissoring

of  $\text{C}-\text{H}$  and the bend of  $-\text{C}\equiv\text{C}-\text{H}$  at 650  $\text{cm}^{-1}$ . Additionally in the spectra of the alkyne terminated CTA the  $\text{C}=\text{S}$  and  $\text{S}-\text{H}$  vibration bands from CTA could be observed. The nitrile ( $-\text{C}\equiv\text{N}$ ) vibration bands were found to be overlapped with the stretch of  $-\text{C}\equiv\text{C}$ .



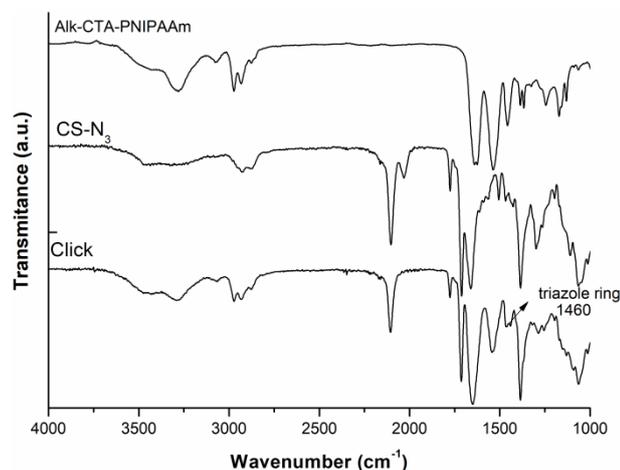
**Figure 3.** FT-IR spectra of alkyne terminated CTA - PNIPAAm

The success of the polymerization of NIPAAm in the presence of alkyne terminated CTA was also confirmed by FT-IR spectra- Fig. 3. The final compound containing the characteristic vibration bands of both CTA and alkyne moieties, additionally contains the characteristic vibration bands of PNIPAAm. Particularly, the vibration bands specific for amide-I at 1550  $\text{cm}^{-1}$  and 1645  $\text{cm}^{-1}$ . The intensity of the characteristic vibration band of alkyne at 2100  $\text{cm}^{-1}$  was found to be decreased and become almost invisible. This is due to the formation of the poly-N-isopropylacrylamide (PNIPAAm).

The FT-IR spectrum of the product PhCS-g-PNIPAAm generated from the click reaction of  $\text{CS}-\text{N}_3$  and alkyne terminated-PNIPAAm was presented within Fig. 2 and 4.

By assessing these spectra, it was observed that the stretching vibration peak of the azide group at 2050  $\text{cm}^{-1}$  disappeared. Except the azide and alkyne vibration peaks, there is still a vibration band at 2100  $\text{cm}^{-1}$  which could be assigned to the remaining alkyne groups from CTA's structure and ionized isonitrile side-groups overlapping. At 1460  $\text{cm}^{-1}$  a vibration band assigned to the  $\text{C}=\text{N}$  bond in the triazole ring could be observed. Furthermore, the stretching vibration absorption peak of the unsaturated  $\text{C}-\text{H}$  bond in the triazole ring, assumed

at near  $3130\text{ cm}^{-1}$ , was overlapped by the hydrogen bond of the hydroxyl group from chitosan. The stretching vibration peak of the N–N bond in the triazole ring, assumed at near  $1020\text{ cm}^{-1}$ , was overlapped by the broad stretching vibration absorption peak of C–N and C–O bonds from the polysaccharide backbone.



**Figure 4.** FT-IR spectra of product generated from click reaction

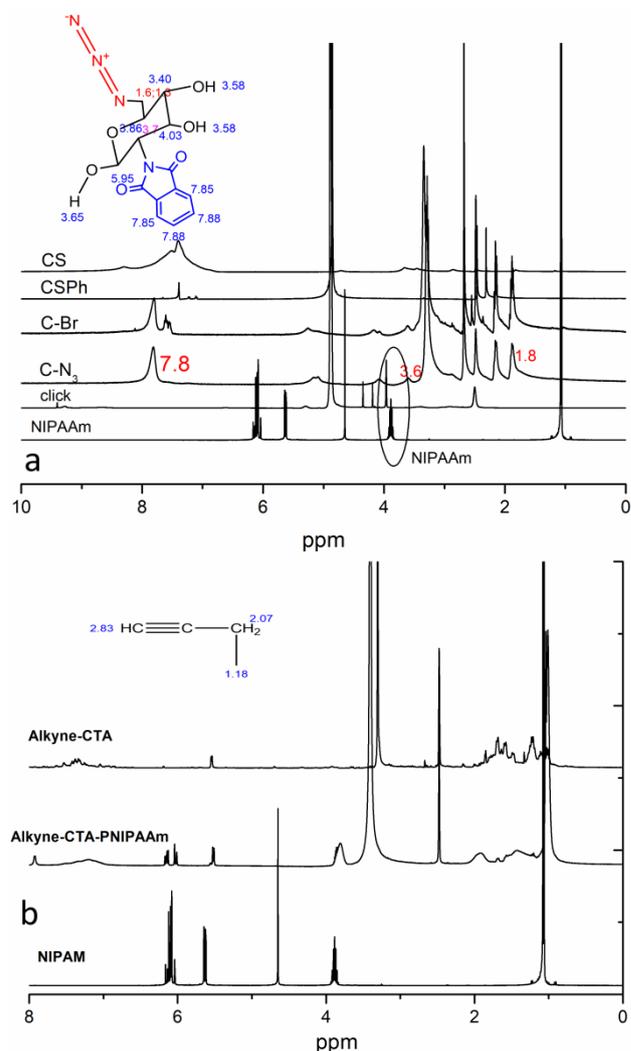
### 3.2 Elemental analysis results

The success of the phthaloylation of the obtained derivative was investigated by elemental analysis to determine the substitution degree from C/N ratio. The results obtained from elemental analysis are shown in Table 1. The degree of deacetylation of pure chitosan and the degree of substitution with phthaloyl groups were determined by comparing the theoretical and experimental C/N ratios.

As determined and summarized within Table 1, the degree of substitution was 92% from the total amount of chitosan used. As concerning the further pre-click functionalization, the brominated derivative and azidated compound were analyzed in terms of determining the differences which occur as a consequence of chemical modification. The degree of substitution of OH groups with Br from C6 was determined as 82% from C/N ratio found and with azide group 84%. The results obtained supported the differences found within the FT-IR spectra once the chemical modifications took place.

### 3.3 $^1\text{H-NMR}$ spectra

The  $^1\text{H-NMR}$  spectra brought additional proof of chemical modification. Figure 5a described the assessment of the pre-click functionalization and the spectrum of the final “clicked” product.



**Figure 5.** Structural identification of chitosan and its functionalized derivatives, precursors for the click reaction by  $^1\text{H-NMR}$  spectra in DMSO- $d_6$  (a) pre-click and click functionalization (b) RAFT esterification of NIPAAm from CTA.

**Table 1.** Elemental analysis results

Sample	Experimental			Theoretical content			C/N ratio*	
	N (%)	C (%)	H (%)	N (%)	C (%)	H (%)	Exp	Theoretical
Chitosan	7.413	40.17	7.2	7.4295	40.923	6.1348	5.406	5.508
Phthaloil Chitosan	5.7615	53.365	5.3045	5.3654	54.12	4.921	9.26	10.08
CS-Br	6.351	49.43	4.79	5.01	47.24	4.87	7.78	9.43 <sup>a</sup>
CS-N <sub>3</sub>	14.65	53.11	5.04	17.71	53.17	3.82	3.55	3 <sup>b</sup>

\*DS= 92%; \*\*DA of chitosan= 98%; <sup>a</sup>DS EA – 82%; DS<sub>grav</sub> 83.3%; <sup>b</sup>DS% -84%

As observed from Fig. 5a, at 7.8 ppm it was observed the chemical shift due to the presence of the azide group on the phthaloyl macromolecular chains. The chemical shifts due to bromide presence within product CS-Br is visible as a small peak at 7.6 ppm due to the effect of Br from position 3 on the chemical shifts of the H2 of the phenyl group of the phthaloyl chitosan. With the azidation, this peak disappeared confirming that the introducing of azide group was successful. "Clicked" chitosan showed additional peaks marking the presence of NIPAAm and the H of triazole from 4, 5 and 8 ppm. The alkyne terminated compound's spectrum was presented in Fig. 5b. As it was observed at 2.5 ppm the H of alkyne terminated was overlapped with the signal of the DMSO used as solvent. Additionally the characteristic peaks of NIPAAm were observed within the spectrum of alkyne terminated -CTA-NIPAAm which indicated the presence of PNIPAAm. The structures of newly synthesized materials were confirmed also by FT-IR spectra-Fig. 3 and 4 and mass spectra, not presented herein.

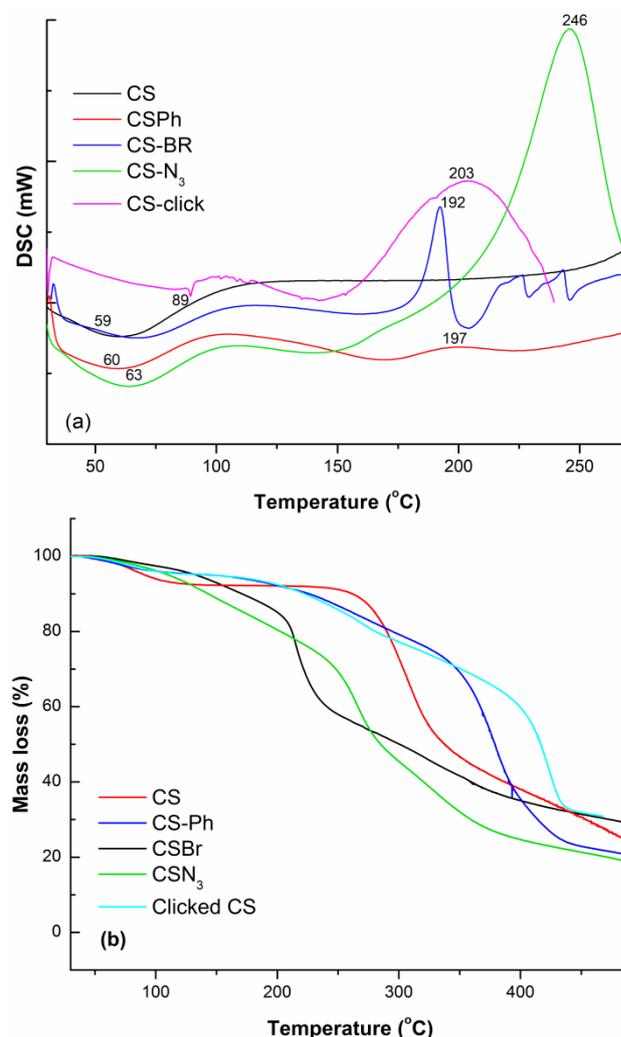
### 3.4 Thermal analysis

Thermal behavior of the brominated and azidated compounds was evaluated by means of DSC and TGA analyses. The study of the thermal behavior is important as it gives information at the glance on the homogeneity of the synthesized substance and by comparison with pure components; details on the degradation behavior are obtained. The DSC thermograms and TGA curves are presented within Fig. 6a and b.

As it is shown in Fig. 6a, the endothermic peak about 50-60 °C was observed and it could be assigned to the water and moisture loss from internal structure. By comparison with phthaloyl chitosan 6-bromo-6 deoxy N-phthaloyl chitosan showed three exothermic peaks at 192, 224 and 242 °C which might be due to the presence of bromide. A wide exothermic peak was observed in the case of azide derivative after the endothermic peak of internal water loss. The second exothermic peaks could be correlated with the exothermic effect combined with decomposition. TGA analysis was performed between 30-500 °C and the weight loss curves were represented in Fig. 6b.

By modifying the structure into a Br-based the thermodegradation behaviour is different; it was found three-four degradation steps at 73, 142, 214 and 321 °C as the structure become more complex by compared with the thermal degradation behaviour of chitosan and phthaloyl chitosan, the starting materials. Azidated derivative seemed to be more stable thermally as the peak from 142 °C

disappeared and the degradation onset temperature are shifted to slightly higher temperatures (71, 229 and 327 °C). The thermogravimetric results supported the findings from DSC analysis.



**Figure 6.** Thermal characteristics for functionalized materials for click reaction (a) DSC thermograms (b) TGA curves

## 4 Conclusion and perspectives

Chitosan was primarily modified with phthalic anhydride giving phthaloyl chitosan in order to block the NH<sub>2</sub> from C2 position of saccharide chains. The main purpose was to modify chitosan at C6 then to release the free NH<sub>2</sub> for pH-responsivity characteristics. The degree of substitution, Ds, was of 0.92 being confirmed by <sup>1</sup>H-NMR and elemental analysis. Phthaloylated chitosan was considered an important precursor for many types of chemical modification e.g. ATRP, RAFT and click. Further functionalization with bromide and azide lead to final graft onto copolymers with confirmed structures by the FT-IR and HNMR spectra. In the

case of alkyne terminated moiety was proved that the polymerization of NIPAAm in the presence of CTA alkyne terminated was successful. Thermal characterization was reported and it confirmed the modification of phthaloyl chitosan as different thermal behaviour was observed.

The reaction of azide chitosan with a newly prepared alkyne-terminated thermoresponsive polymer such as poly N-isopropylacrylamide (PNIPAAm) led to grafted copolymers via a triazole group confirmed spectroscopically. These graft copolymers should possess both properties of chitosan and responsive moieties attached on side positions of main chain. The perspectives of these materials are to be tested as drug delivery systems and the future outcome will be presented in a future study.

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**Author Contributions:** Author C.N.C.Y conceived the idea, performed the experiments and some part of physical chemical analysis, analysed the results and wrote the manuscript; author S.Y.K. hosted the studies within the Department of Pharmaceutical Technology, Faculty of Pharmacy, Ege University, Izmir, Turkey making some administrative arrangements; Author O.Y. performed some physical chemical characterization, analysed the results and contributed to the drafting of the paper.

**Conflicts of Interest:** The authors declare no conflict of interest.

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