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Synthesis of glucose-substituted poly(*p*-phenylene)s with twisted main-chain in one direction due to induced axial chirality

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Summary

The peracetylated and free glucose-substituted poly(*p*-phenylene)s were synthesized by the coupling polymerization of a dibromobenzene monomer using Ni complex and the subsequent deacetylation by hydrazine monohydrate. The polymerization was carried out using bis(1,5-cyclooctadiene)nickel(0) ($Ni(COD)_2$) as a coupling agent with 2,2'-bipyridyl (bpy) and 1,5-cyclooctadiene (COD) in a mixed solvent of DMF and toluene. The structure of the product was confirmed by ^1H and ^{13}C NMR measurements to be the poly(*p*-phenylene) having peracetylated glucose residues. The M_n values were estimated by GPC analysis with DMF as eluent to be 7300 - 9800. The fluorescence analysis of the polymer was carried out in comparison with that of the dimeric model compound. The CD spectrum of the polymer indicated that the main-chain was twisted and immobilized in one direction due to the chirality and bulkily of the peracetylated glucose residues. The deacetylation using hydrazine monohydrate completely took place to give the free glucose-substituted poly(*p*-phenylene).

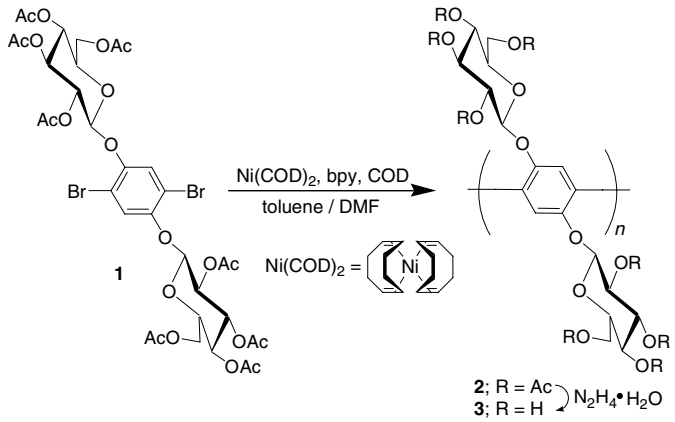
Introduction

Fully conjugated polymers have attractive much attention because of a large number of applications in electronic conductivity and optoelectronics [1]. Moreover, interests and applications of the conjugated polymers have been extended to the biological fields, such as utilizing as cell-specific culture substrates, as well as targeting drug delivery systems. For the viewpoints, the functional sugar-substituted conjugated polymers were synthesized, which had the main-chain structures of polyacetylene [2], polyaniline [3], polyisocyanide [4], poly(*p*-phenylene ethynylene) [5], polythiophene [6], and poly(*p*-phenylene vinylene) [7].

Poly(*p*-phenylene) (PPP) is one of the most useful polymers for organic conducting materials and organic polymeric ferromagnets due to the planar conjugated π system, along with high strength, high heat resistance, and other structural unique properties [8]. Although non-substituted PPP has solubility problem in the solvents, introduction of flexible side chains on the aromatic rings has been effective to solve the problem.

Since π-conjugated polymers containing chiral side chains, such as polythiophenes [9], have been interesting to exhibit a high chiroptical activity, the optically active PPPs having the chiral alkoxy side chains have also been prepared in a previous literature [10].

Recently, synthesis and fluorescent properties of PPP-type glycopolymers have been reported [11,12]. In these studies, the flexible spacers such as oligo(ethylene glycol) and alkyl chains were introduced between sugar side groups and PPP main-chains of the glycopolymers. We have been interested in PPP-type glycopolymers having more rigid natures, in which the sugar side groups are directly connected to the main-chains. Because chirality of the sugar side groups may affect the higher-ordered structures of the PPP main-chains in such polymers. In various methods for synthesizing PPP developed in the previous publications [8], one of the simplest ways to production of PPP is the coupling reaction of dihalobenzenes catalyzed by Ni-complexes [13]. In this study, we employ this reaction manner leading to the desired PPP, because this type of homocoupling reaction of one monomer can exclude complication of monomer synthesis. In this paper, we report the synthesis of acetyl-protected and free glucose-substituted PPPs by the coupling polymerization of a dibromobenzene derivative **1** having peracetylated-glucose side groups using bis(1,5-cyclooctadiene)nickel(0) ($Ni(COD)_2$) as a coupling agent and the subsequent deacetylation (Scheme 1). In addition, the CD analysis of those polymers is also disclosed to indicate that the main-chains were twisted in one direction due to the induced axial chirality by the glucose residues.



Scheme 1. Coupling polymerization of **1** using $Ni(COD)_2$ and deacetylation of **2** using hydrazine monohydrate.

Experimental

Materials

Monomer **1** was prepared according to the literature procedure by reaction of 2,5-dibromohydroquinone with penta-*O*-acetyl-β-D-glucose in the presence of BF_3OEt_2 in dichloromethane at room temperature [7], which was purified by recrystallization from methanol. Toluene and DMF of solvents were purified by distillation. Other reagents were used as received.

*Polymerization of **1***

A typical polymerization procedure was as follows (entry 6, Table 1). Under argon, a mixture of **1** (0.21 mmol, 0.203 g), 1,5-cyclooctadiene (0.82 mmol, 0.10 mL), bis(1,5-cyclooctadiene)nickel(0) (0.81 mmol, 0.222 g), and 2,2'-bipyridyl (0.92 mmol, 0.144 g) in a mixed solvent of toluene (1.5 mL) and DMF (1.5 mL) was heated at 80°C for 40 h. The resulting solution was diluted with chloroform and washed three times with water. After the chloroform layer containing the insoluble precipitate was separated, the precipitate was filtered and washed with methanol. The methanol solution was combined with the chloroform filtrate and the combined solution was evaporated and dried under the reduced pressure to give the crude product. The product was dissolved in DMF (0.50 mL) and acetic anhydride (4.23 mmol, 0.40 mL) and pyridine (0.80 mL) were added to the solution. After the mixture was stirred at 40°C for 7 h. it was poured into water and the precipitate was isolated by filtration and dried under the reduced pressure. The product was dissolved in a small amount of ethyl acetate and subjected by column chromatography on silica gel with hexane / ethyl acetate (1 : 3, vol/vol) to separate the low molecular weight fractions, followed by eluting with methanol, giving the polymeric fractions. The polymeric fractions were collected, evaporated, and dissolved in a small amount of chloroform. The solution was poured into a mixture of hexane and diethyl ether (1 : 1) to precipitate the purified polymer. The product was isolated by filtration and dried in vacuo to give **2** (0.11 mmol, 0.0911 g) in 53. 8 % yield.

*Synthesis of **4***

Under argon, bromohydroquinone (2.16 mmol, 0.409 g) and penta-*O*-acetyl-β-D-glucose (5.23 mmol, 2.043 g) were dissolved in dichloromethane (10 mL), and BF_3OEt_2 (4.73 mmol, 0.60mL) was added to the solution at room temperature. After the mixture was stirred for 7 h at that temperature, the resulting solution was washed successively three times with sat. $NaHCO_3$ aq. and with water. The organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated. The product was purified by column chromatography on silica gel with ethyl acetate / hexane (2 : 3, vol/vol) to give bis-glucosylated monobromobenzene derivative (0.93 mmol, 0.821 g) in 43.1 % yield.
The coupling reaction of this material (0.0589 mmol, 0.0519 g) was carried out in the presence of 1,5-cyclooctadiene (0.163 mmol, 0.020 mL), bis(1,5-cyclooctadiene)nickel(0) (0.241 mmol, 0.0664 g), and 2,2'-bipyridyl (0.230 mmol, 0.0359 g) in a mixed solvent of toluene (1.5 mL) and DMF (1.0 mL) at 80°C for 24 h under argon. The reaction mixture was diluted with chloroform and washed three times with water. After the chloroform layer containing the insoluble precipitate was separated, the precipitate was filtered and washed with methanol. The methanol solution was combined with the chloroform filtrate and the combined solution was evaporated and dried under the reduced pressure to give the crude product. The product was dissolved in DMF (0.50 mL) and acetic anhydride (2.12 mmol, 0.20 mL) and pyridine (0.40 mL) were added to the solution. After the mixture was stirred at 40°C for 5 h, it was poured into water and the precipitate was isolated by column chromatography on silica gel with ethyl acetate : hexane (3 : 1, vol/vol) to give **4** (0.0175 mmol, 0.0281 g) in 29.7 % yield.
^{1}H NMR (DMSO-d_6, 70°C): δ 1.86 – 2.03 (s, CH_3, 48 H), 405 – 4.19 (m, H5, 6, 12H), 4.80 – 5.43 (m, H1-4, 16H), 6.77 – 7.13 (m, aromatics, 6H).

*Synthesis of **5***

Under argon, hydroquinone (2.36 mmol, 0.259 g) and penta-*O*-acetyl-β-D-glucose (5.16 mmol, 2.008 g) were dissolved in dichloromethane (10 mL), and BF_3OEt_2 (4.73 mmol, 0.60mL) was added to the solution at room temperature. After the mixture was stirred for 8 h at that temperature, the resulting solution was washed successively three times with sat. $NaHCO_3$ aq. and twice with water. The organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated. The product was purified by recrystallization from methanol to give **5** (0.421 mmol, 0.3381 g) in 17.8 % yield.
^{1}H NMR ($CDCl_3$): δ 2.04 – 2.09 (s, CH_3, 24H), 3.83 – 3.90 (m, H5, 2H), 4.17 (d, J = 12.6 Hz, $H6_a$, 2H), 4.29 (m, $H6_b$, 2H), 4.99 (d, J = 7.2 Hz, H1, 2H), 5.16 – 5.30 (m, H2-4, 6H), 6.93 (s, aromatics, 4H).

*Deacetylation of **2***

A typical deacetylation procedure was as follows. To a solution of **2** (0.0133 mmol, 0.0106 g) in THF (0.50 mL) was added hydrazine monohydrate (6.2 mmol, 0.30 mL) at 0°C, and the mixture was stirred at room temperature for 20 h. Then, the reaction mixture was diluted with methanol and the solution was poured into a hexane with vigorous stirring. After the solution was kept in refrigerator for 40 h, it was slightly evaporated to precipitate the product. The precipitate was isolated by filtration, which was purified by freeze dry with water (5 mL) to give **3** (0.00775 mmol, 0.0036 g) in 58.6 % yield.

Measurements

NMR spectra were recorded on a JEOL ECA 600 spectrometer. Gel permeation chromatographic (GPC) analyses were performed by using a Shimadzu LC-6A with RI detector under the following conditions: Shodex K-803 column with DMF as the eluent at a flow rate of 1.0 mL/min. The calibration curve was obtained using polystyrene standards. CD and UV-vis spectra were measured in a quartz cell (thickness 1 cm) at room temperature using a Jasco J-820 spectropolarimeter and Shimadzu UV160A spectrophotometer, respectively. Fluorescence spectra were recorded on a Jasco FP-6300 fluorometer. Fluorescence quantum yields were calculated by using quinine sulfate in 0.1 mol/L sulfuric acid as the reference absolute quantum efficiency (Φ_n = 55 %).

Results and Discussion

For the coupling polymerization of **1**, we selected $Ni(COD)_2$ as the coupling agent, because this was reported to be effective for the coupling polymerization of dibromoaromatic monomers in the previous studies [14,15]. Thus, the reaction was carried out using this coupling agent with 2,2'-bilyridyl (bpy) and 1,5-cyclooctadiene (COD) in a mixed solvent of toluene and DMF at 80 – 100°C (Table 1). Since the ^{1}H NMR spectrum of the crude product indicated occurrence of partial deacetylation during the polymerization, its acetylation was performed by acetic anhydride. The thin layer chromatographic (TLC) analysis on silica gel (eluent: ethyl acetate : hexane = 4 : 1)

exhibited that the acetylated products contained not only polymeric materials but also low molecular weight compounds. After the latter fractions were separated off by column chromatography on silica gel, the polymeric fractions were purified further by precipitation into a mixed solution of diethyl ether and hexane (1 : 1). Figure 1 shows the ^{1}H NMR spectrum of the isolated polymer in $CDCl_3$, which sufficiently supports the structure **2** of the product by the following assignments and integrated ratios; δ 1.88 – 2.18 due to methyl protons of the acetyl groups (24H), δ 3.88, 4.21, and 5.10 – 5.32 due to H5, H6, H1-4 protons of glucose residues (total 14H), and δ 6.92 – 7.25 due to aromatic protons of the main-chain (2H). The ^{13}C NMR spectrum of the same sample also supported the polymer structure **2** as follows; δ 20.2 – 20.7 (CH_3), 61.8 (C6), 67.9 – 68.4, 71.0 – 71.1, 71.7 – 71.8, 72.4 – 72.6 (C2-5), 99.2 – 100.5 (C1), 118.1 – 120.1 (C-H of aromatics), around 129.7 (phenylene carbons), 149.4 – 152.5 (C-O of aromatics) and 168.8 – 170.5 (C=O). Specifically, appearance of the signals at around δ 129.7 due to the phenylene carbons of the main-chain strongly suggested the PPP structure of the product.

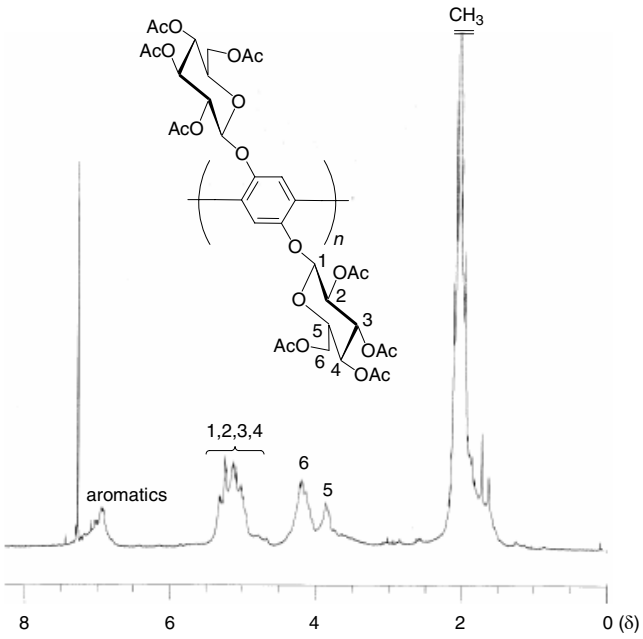


Figure 1. ^{1}H NMR spectrum of **2** in $CDCl_3$.

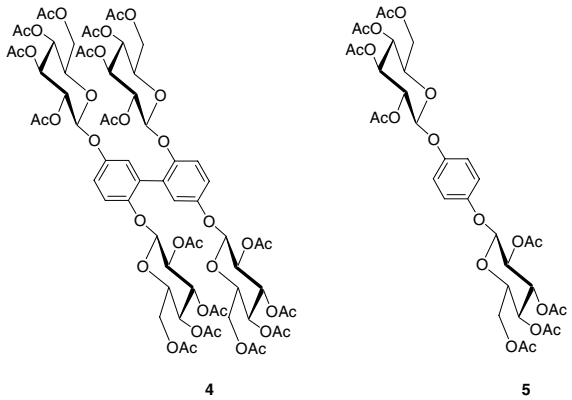
Table 1 shows the selected results of the polymerization. The M_n values of the products were estimated by GPC measurements with DMF as eluent using polystyrene standards to be 7300 – 9800. When the polymerization was carried out under the conditions of entry 1, the yield of **2** was low (8.3 %). The higher concentration of the reaction solution gave a higher yield (15.2 %, entry 2). However, the higher reaction temperature was not effective for increasing the polymer yield (entry 3). The use of the larger amount of $Ni(COD)_2$ affected to increase the yield, which reached 53.8 % under the conditions of entry 6.

Table 1. Polymerization of **1** using $Ni(COD)_2$ in a mixed solvent of toluene and DMF

Entry	[**1**] : [$Ni(COD)_2$] : [bpy] : [COD]	Concentration[a] (mol/L)	Temp (°C)	Time (h)	Yield[b] (%)	M_n[c]
1	1.0 : 2.3 : 2.3 : 1.6	0.029	80	24	8.3	7300
2	1.0 : 2.3 : 2.3 : 1.6	0.050	80	24	15.2	8000
3	1.0 : 2.3 : 2.3 : 1.6	0.040	100	40	7.7	7900
4	1.0 : 4.6 : 4.6 : 3.5	0.050	80	24	18.4	9700
5	1.0 : 4.6 : 4.6 : 3.5	0.084	80	26	47.5	8700
6	1.0 : 3.8 : 4.4 : 3.9	0.084	80	40	53.8	9800

[a] Monomer **1** / (toluene + DMF).
[b] Fraction insoluble in hexane / diethyl ether (1 : 1) after acetylation and purification by column chromatography of the crude product.
[c] Determined by GPC with DMF as eluent using polystyrene standards.

Figure 3 shows the CD and UV-vis spectra of **2**, **4**, and **5** in a mixed solution of methanol and chloroform (7 : 3). The UV-vis spectrum of the polymer **2** (Figure 3(d)) exhibited very week π-conjugation compared with other PPP derivatives. This is probably due to the twisted nature of the main-chains, which was confirmed by the following CD analysis. The CD analysis of **2** was performed to reveal the secondary-ordered structure of the main-chain. Figure 3(a) shows the CD spectrum of **2** at room temperature in comparison with that of dimeric and monomeric derivatives **4** and **5** (Figure 2). Interestingly, the split Cotton effects appear at around 240 nm in the CD spectra of **2** and **4** (Figure 3(a) and (b)), which are reasonably based on induced axial chirality attributed to the peracetylated glucose residues [16]. On the other hand, the CD spectrum of a monomeric derivative **5** does not exhibit the split Cotton effect (Figure 3(c)). These data indicate that the main-chain of **2**, as well as that of **4**, is probably twisted in one direction due to the induced axial chirality and immobilized by the bulkily of the peracetylated glucose residues. The ^1H NMR spectra of **2** and **4** in DMSO-d_6 measured at room temperature showed the broader signals, whereas the sharpness of the signals was observed in the measurements of the same samples at higher temperature like 70°C. The temperature effect in the NMR measurement was attributed to the flexibility of the phenylene linkages, which in turn supported the



4 **5**

Figure 2. Structures of model compounds **4** and **5**.

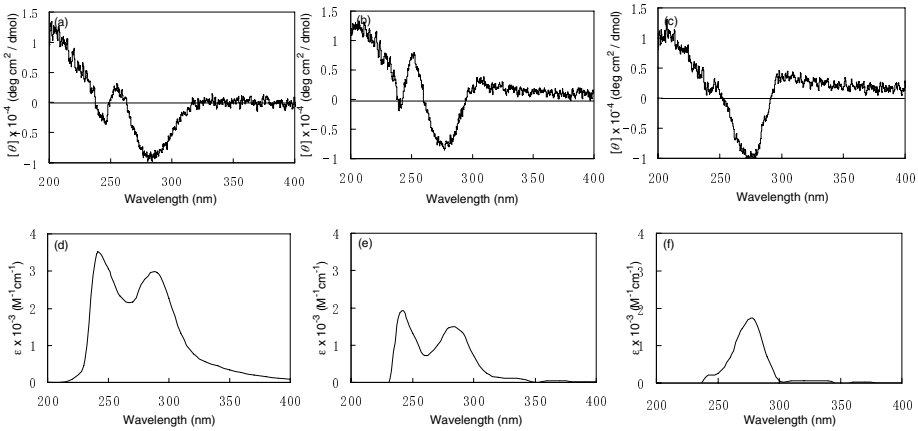


Figure 3. CD spectra of **2** (a), **4** (b), and **5** (c) and UV-vis spectra of **2** (d), **4** (e), and **5** (f) in a mixed solution of methanol and chloroform (7 : 3).

immobilized main-chain in **2** at room temperature. All the above results indicated that the polymerization of **1** proceeded with the formation of twisted main-chain in one direction by the chirality of glucose residues.

Figure 4 shows the fluorescence spectra of **2** and **4** excited at 366 nm in chloroform. Both materials **2** and **4** exhibited emission maximum peaks at 418 nm and 438 nm, respectively, which were ascribed to the π-π* transition of the conjugated backbone. The fluorescence intensity of **2** was much higher than that of **4**. Fluorescence quantum yields of **2** and **4** were 27 % and 19 %, respectively, calculated by using quinine sulfate as reference absolute quantum efficiency.

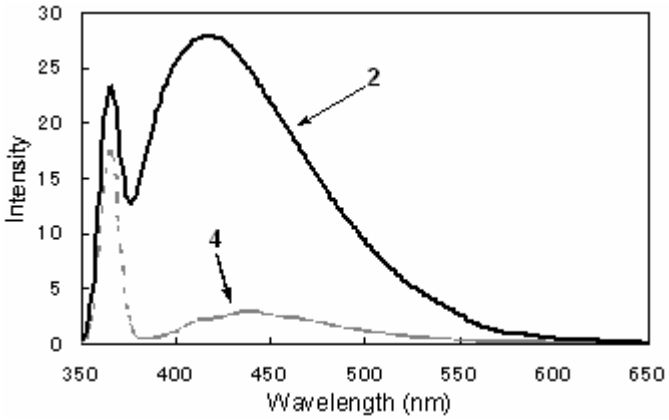


Figure 4. Fluorescence spectra of **2** (a) and **4** (b) in chloroform. Excitation wavelength was 366 nm.

Deacetylation of **2** was carried out using hydrazine monohydrate in THF at room temperature. The product was isolated by precipitation into hexane to give the deacetylated PPP **3**. The ^{1}H NMR spectrum (D_2O) of the product in Figure 5(a) shows

the signals at δ 3.17 – 3.71 (br, H2 – H6 of glucose, 12H), δ 4.72 – 5.01 (br, H1 of glucose, 2H overlapping with a solvent signal), and δ 7.00 – 7.15 (br, aromatics, 2H). No observation of the signals due to the methyl protons of the acetyl groups and due to the acetylated sugar protons indicated occurrence of the complete deacetylation, giving PPP **3** having free-glucose residues. The molar ratio of the glucose residues to the main-chains in the deacetylated polymer **3** was confirmed by the integrated ratio of the anomeric signals to the aromatic signals measured in DMSO-d_6 (Figure 5(b)). The CD spectrum of **3** also exhibited the pattern like split Cotton effect although it was not obvious compared with that in Figure 3(a). This suggested that the free glucose residues as the side groups probably affected immobilization of the main-chian. The detailed studies for this deacetylated polymer **3** are now going on.

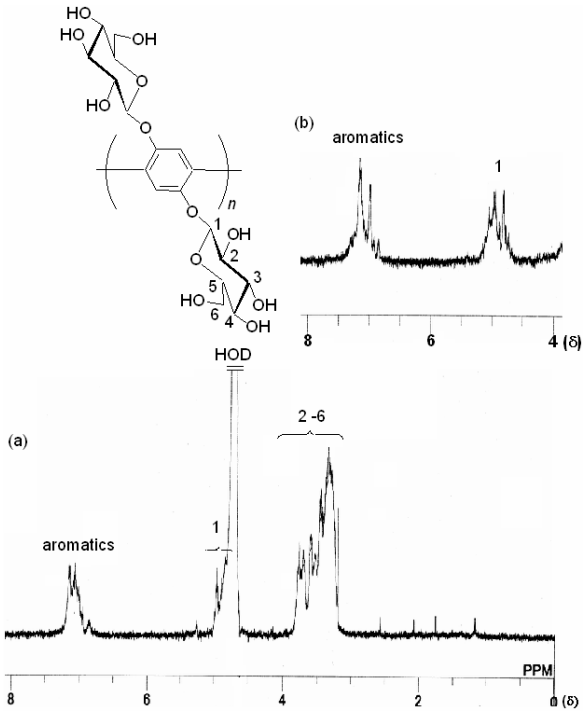


Figure 5. ^{1}H NMR spectra of the deacetylated polymer **3** in D_2O (a) and DMSO-d_6 (b).

Conclusion

We have synthesized the PPP **2** having the peracetylated glucose residues by the Ni-catalyzed coupling polymerization of the dibromobenzene monomer **1**. The structure **2** of the isolated polymer was confirmed by the ^{1}H and ^{13}C NMR spectra and the M_n values estimated by GPC analysis were ranging between 7300 and 9800. The CD analysis of **2** as well as that of the dimeric compound **4** indicated that the main-chain of **2** was twisted and immobilized in one direction, attributed to the chirality and the bulkily of the peracetylated glucose residues. The deacetylation completely took place using hydrazine monohydrate in THF to give the PPP **3** having the free-glucose residues. The further investigations concerning the present study, for example,

evaluation of the detailed higher-ordered structures and the biological functions are now in progress in our research group.

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