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Recognition of Stereoregularity of Poly(methacrylic acid)s with γ-Cyclodextrin

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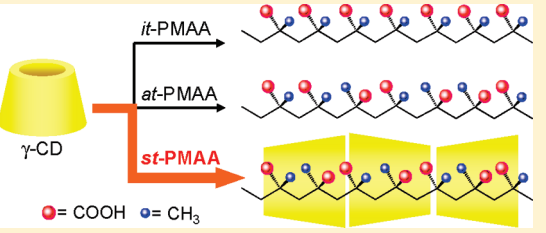
Supporting Information

ABSTRACT: The formation behavior of inclusion complexes between γ-cyclodextrin (γ-CD) and poly(methacrylic acid)s (PMAAs) of different stereoregularities in water was examined by analyzing the precipitate formed by mixing γ-CD with each PMAA in water. When syndiotactic (*st*-) PMAA was used as a guest, a much larger amount of precipitate was formed as compared to isotactic (*it*-) and atactic (*at*-) PMAAs. X-ray diffraction, FT-IR, and ^{1}H NMR measurements of the precipitate indicated that γ-CD effectively formed an inclusion complex with *st*-PMAA. Upon increasing the syndiotacticity of PMAA, the yield and the coverage ratio of the resulting inclusion complexes increased, suggesting that γ-CD more effectively includes PMAA of a higher syndiotacticity. This is the first example of selective inclusion complex formation between CDs and a syndiotactic polymer. By adding γ-CD into a mixture of *st*- and *at*-PMAAs, the selective extraction of *st*-PMAA was successfully achieved through γ-CD−*st*-PMAA inclusion complex formation. Additionally, the formation of a γ-CD−*st*-PMAA inclusion complex in the aqueous solution was confirmed by ^{1}H NMR, NOESY, and dynamic light scattering measurements. By changing the pH of the solution, the formation and dissociation of the γ-CD−*st*-PMAA inclusion complex were reversibly controlled. This pH-controllable inclusion complex can be useful as a novel building block for pH-responsive materials.



INTRODUCTION

Cyclodextrins (CDs) are a class of cyclic oligosaccharides consisting of several D-glucopyranose units linked by α-(1,4)-glucosidic bonds. CDs can form inclusion complexes with guest molecules of the appropriate size and shape in aqueous media via inclusion into the CD cavities. A large number of studies on inclusion complex formation between CDs and polymeric guests as well as low-molecular-weight guests have been carried out.[1−6] In particular, the design and synthesis of supramolecular architectures constructed by inclusion complexes between CDs and polymeric guests, called pseudopolyrotaxanes, have attracted much attention in the material science[7−9] and pharmaceutical fields.[10,11] Harada et al. reported the formation behavior of inclusion complexes of CDs with polymers, and they clarified the relationship between the cavity size of the CDs and the type of guest polymers incorporated.[12] For example, α-CD effectively formed inclusion complexes with poly(ethylene glycol) (PEG),[13−18] but β-CD with a larger cavity size did not form the corresponding inclusion complex. On the other hand, β-CD formed an inclusion complex with poly(propylene glycol) (PPG),[18−20] but α-CD did not. Despite many studies on inclusion complexes between CDs and linear polymeric guests, there have been only a few studies on inclusion complex formation between CDs and stereoregular polymers.[20−22] Harada et al. reported that β-CD forms inclusion complexes with atactic PPG at higher yield as compared with isotactic PPG.[20] Tonelli et al. demonstrated that α- and γ-CDs selectively formed inclusion complexes with isotactic and atactic poly(3-hydroxybutylate)s, respectively.[21] In these cases, it has been considered that the recognition of polymer stereoregularity with the CDs can be ascribed to a better spatial fit between the cross-sectional area of a specific stereoregular polymer and the cavity size of the CD. We recently reported that γ-CD forms an inclusion complex with isotactic poly(methyl methacrylate) (PMMA) more effectively than with syndiotactic PMMA,[22] which has a larger cross-sectional area than the isotactic PMMA.[23] Additionally, it was found that γ-CD can also form an inclusion complex with syndiotactic PMMA in the presence of an excess amount of γ-CD. However, until now, the selective complexation of syndiotactic polymers with CDs has not been achieved. On the basis of our recent findings, we expected that if stereoregular polymers with a smaller cross-sectional area than the corresponding stereoregular PMMAs were chosen as guests, then the selective complexation of the syndiotactic polymer with γ-CD could be achieved.

Generally, it is known that syndiotactic polymers have unique properties different from other stereoregular polymers. Among the stereoregular polystyrenes, syndiotactic polystyrenes have higher crystallinity, which gives them sufficient heat and solvent resistance to be commercialized as engineering plastics.[24−26] Syndiotactic poly(methacrylic acid)s (PMAAs) form stereocomplexes with isotactic PMMAs by the use of good steric fit, in contrast to isotactic and atactic PMAAs, which do not form

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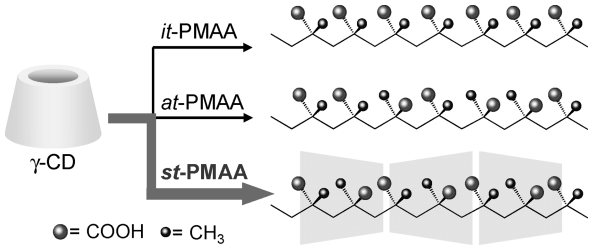

Figure 1. Schematic illustration of selective inclusion complex formation between γ-CD and *st*-PMAA.

stereocomplexes with any stereoregular PMMAs.[27] The resulting stereocomplexes between syndiotactic PMAAs and isotactic PMMAs can be applied to template polymerization systems for the preparation of stereoregular polymers.[28] Thus, the development of a new methodology for the efficient isolation of syndiotactic polymers from a mixture with other stereoregular polymers would be valuable from both academic and practical viewpoints. In this paper, we report the selective inclusion of syndiotactic PMAAs, which are considered to have a smaller cross-sectional area than the corresponding syndiotactic PMMAs, with γ-CD (Figure 1).

EXPERIMENTAL SECTION

Materials. Isotactic (*it*-) PMAA (M_n = 2200, M_w/M_n = 1.4, *mm*:*mr*:*rr* = 82:15:3), syndiotactic (*st*-) PMAA (M_n = 6900, M_w/M_n = 1.5, *mm*:*mr*:*rr* = 2:5:93; M_n = 22 000, M_w/M_n = 1.6, *mm*:*mr*:*rr* = 1:6:93), and PMAA with a lower syndiotacticity (M_n = 16 000, M_w/M_n = 2.4, *mm*:*mr*:*rr* = 3:24:73) were synthesized by the anionic polymerization of trimethylsilyl methacrylate in toluene at −78 °C using *t*-C_4H_9Li,[29] *t*-C_4H_9Li/bis(2,6-di-*tert*-butylphenoxy)methylaluminum,[30] and *t*-C_4H_9Li/tributylaluminum[30] as initiators, respectively, followed by the hydrolysis of the resulting polymers. Atactic (*at*-) PMAA (M_n = 4500, M_w/M_n = 1.6, *mm*:*mr*:*rr* = 7:39:54) was purchased from Aldrich Co. as an aqueous solution of the carboxylate sodium salt and was used after being neutralized with aqueous HCl and then dialyzed. *at*-PMAA with a higher molecular weight (M_n = 29 000, M_w/M_n = 2.2, *mm*:*mr*:*rr* = 5:33:62) was synthesized by radical polymerization in water at 40 °C using VA-044 as an initiator. The number-average molecular weights and their distribution were measured by gel permeation chromatography (Tosoh System HLC-8120GPC) with PMMA standards at 40 °C. Two commercial columns (TSKgel SuperH4000 and TSKgel GMHXL) were connected in series, and tetrahydrofuran was used as an eluent. The characterization of the resulting PMAAs was carried out using the corresponding PMMAs that were prepared by the methylation of all the carboxyl groups of PMAAs with a diazomethane solution. Their tacticities (*mm*:*mr*:*rr*) were estimated from the integral ratio of the α-methyl proton signals of the PMMAs using 400 MHz ^{1}H NMR (in nitrobenzene-d_5, at 110 °C). γ-CD was purchased from Wako Pure Chemical Co. (Tokyo, Japan) and was vacuum-dried prior to use. Pure water was provided by the Milli-Q laboratory system (Millipore).

Evaluation of Inclusion Complex Formation. γ-CD (311 mg, 2.4×10^{-4} mol) was added to an aqueous solution (1.0 mL) of PMAA of the prescribed concentration. The pH values of the mixed solutions were adjusted to 3, where almost all of the carboxylic groups of PMAA should be protonated (the pK_a of PMAA is 5−6[31,32]). After vigorous stirring for 3 h at 80 °C, the solution was cooled to ambient temperature and stirred gently for another 3 days. The resulting precipitate was collected by centrifugal separation and was washed with an aqueous urea solution (0.1 mol L^{-1}) and then pure water. After the lyophilization, the obtained solid was analyzed by X-ray diffraction (XRD), FT-IR, and ^{1}H NMR measurements. On the other hand, inclusion complex formation between γ-CD and *st*-PMAA in a dilute solution (γ-CD, 6.3 mg, 4.9×10^{-6} mol; *st*-PMAA, 2.1 mg, 2.4×10^{-5} unit mol) was evaluated by dynamic light scattering (DLS) as well as by their ^{1}H NMR and NOESY spectra. The XRD patterns were taken by a Rigaku RINT2000. Cu Kα (λ = 0.154 nm) was used as the X-ray source, and it was operated at 40 kV and 200 mA with a Ni filter (Rigaku ultraX18). The FT-IR spectra were measured with a Spectrum 100 FT-IR spectrometer (Perkin-Elmer). The ^{1}H NMR and NOESY spectra were measured with a JEOL JNMECS-400 spectrometer using DSS (sodium 2,2-dimethyl-2-silapentane-5-sulfonate) as an external standard. The DLS spectra were measured with a Zetasizer Nano ZS (Malvern Instruments, UK) after mixing γ-CD and *st*-PMAA in water for a few minutes.

RESULTS AND DISCUSSION

Inclusion Complex Formation between γ-CD and *it*-/*at*-/*st*-PMAA. First, the formation behavior of an inclusion complex between γ-CD and stereoregular PMAAs was examined using *it*-PMAA (M_n = 2200, M_w/M_n = 1.4, *mm*:*mr*:*rr* = 82:15:3), *at*-PMAA (M_n = 4500, M_w/M_n = 1.6, *mm*:*mr*:*rr* = 7:39:54), and *st*-PMAA (M_n = 6900, M_w/M_n = 1.5, *mm*:*mr*:*rr* = 2:5:93) as guest polymers. A mixture of γ-CD (311 mg, 2.4×10^{-6} mol) and each stereoregular PMAA (2.1 mg, 2.4×10^{-5} mol) in aqueous solution was stirred for 3 h at 80 °C and then for 3 days at ambient temperature. The resulting precipitate was washed with an aqueous urea solution (0.1 mol L^{-1}) and then pure water to remove any free PMAA and γ-CD and lyophilized. When *it*- and *at*-PMAAs were used as guests, only a slight precipitate was obtained. On the other hand, when *st*-PMAA was used, a much larger amount of precipitate was formed (Table 1, runs 1−3). When α- and β-CDs were used as hosts instead of γ-CD, no precipitate was formed with any stereoregular PMAAs. These results may suggest that γ-CD can selectively form inclusion complexes with *st*-PMAA. Figure 2 shows the X-ray diffraction (XRD) pattern of the γ-CD−*st*-PMAA precipitate thus obtained. This pattern was clearly different from those of native γ-CD and *st*-PMAA alone. In the XRD pattern of the γ-CD−*st*-PMAA precipitate, two strong peaks at 2θ = 7.4° and 18° were observed. The former peak was characteristic of the channel structure of γ-CD,[33,34] and the latter was also seen in the XRD patterns of inclusion complexes of γ-CD with *it*- and *st*-PMMAs.[22] This result shows that an inclusion complex was formed between γ-CD and *st*-PMAA and that this inclusion complex adopts a columnar structure in its crystalline state. Figure 3 shows the FT-IR spectra of the γ-CD−*st*-PMAA complex and free *st*-PMAA. The C═O stretching vibration band at 1695 cm^{-1} in the spectrum of *st*-PMAA was shifted to 1705 cm^{-1} upon complex formation with γ-CD. This shift can be attributed to the cleavage of the intra- and intermolecular hydrogen bonds between the carboxyl groups of *st*-PMAA by the threading of γ-CD onto the *st*-PMAA chain,[35] supporting the formation of an inclusion complex between γ-CD and *st*-PMAA. To determine the host−guest stoichiometry in the γ-CD−*st*-PMAA complex, the ^{1}H NMR spectrum in D_2O solution including 1 mol L^{-1} NaOD was measured at 25 °C. The stoichiometry estimated from the integral ratio of the H_4 proton signal of γ-CD to the α-methyl proton signal of *st*-PMAA was 1:2.7 (γ-CD:MAA unit) (Figure 4). In our previous report on the γ-CD−*it*-PMMA inclusion complex, the stoichiometry (γ-CD:MMA unit) of the γ-CD−*it*-PMMA inclusion complex increased with an increasing amount of γ-CD added and became almost

Table 1. Precipitate Formation between γ-CD and Stereoregular PMAAs

		PMAA						
run	γ-CD, mg (mol)		mg (unit mol)	M_n	*mm*:*mr*:*rr*	yield,[a] mg	composition[b] CD:MAA unit	coverage ratio,[b] %
1	311 (2.4×10^{-4})	*it*-PMAA	2.1 (2.4×10^{-5})	2200	82:15:3	<0.1		
2		*at*-PMAA		4500	7:39:54	<0.1		
3		*st*-PMAA		6900	2:5:93	0.4 (0.1)	1:2.7	~100
4	311 (2.4×10^{-4})	PMAA(HM)-93[c]	6.7 (7.8×10^{-5})	22000	1:6:93	4.7 (0.7)	1:2.8	96
5		PMAA(HM)-73		16000	3:24:73	1.4 (0.3)	1:3.5	77
6		PMAA(HM)-62		29000	5:33:62	0.8 (0.2)	1:3.8	71

[a] The yield of the precipitate obtained after the washing process. The weight of PMAA in the precipitate is shown in a parentheses. [b] Estimated from ^{1}H NMR spectra. [c] Added at the same molar ratio of polymer/γ-CD as run 3.

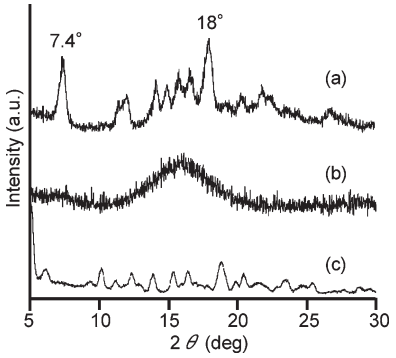

Figure 2. XRD patterns of (a) γ-CD−*st*-PMAA precipitate, (b) *st*-PMAA (M_n = 6900, M_w/M_n = 1.5, *mm*:*mr*:*rr* = 2:5:93), and (c) native γ-CD (cage-type assembly).

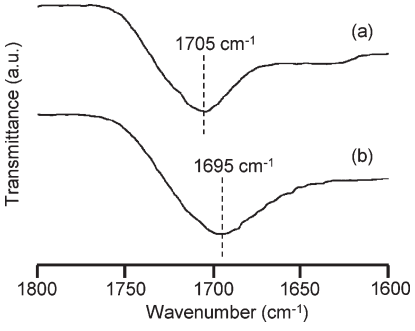

Figure 3. FT-IR spectra of (a) γ-CD−*st*-PMAA precipitate and (b) *st*-PMAA (M_n = 6900, M_w/M_n = 1.5, *mm*:*mr*:*rr* = 2:5:93).

constant at 1:2.5.[22] From the molecular modeling study, this stoichiometry (1:2.5) appeared to correspond to the full coverage of the *it*-PMMA chain by the γ-CD molecules. The stoichiometry of the γ-CD−*st*-PMAA complex estimated in this work (1:2.7) was almost the same as the value for the full coverage of the γ-CD−*it*-PMMA complex (1:2.5), suggesting that *st*-PMAA should be fully covered with γ-CD molecules (the coverage ratio is almost 100%). These results indicate that γ-CD can effectively form an inclusion complex with *st*-PMAA, in contrast to the cases of *it*- and *at*-PMAAs. This γ-CD−*st*-PMAA inclusion complex is also the first example of an inclusion complex between native CD and an anionic polymer.[35]

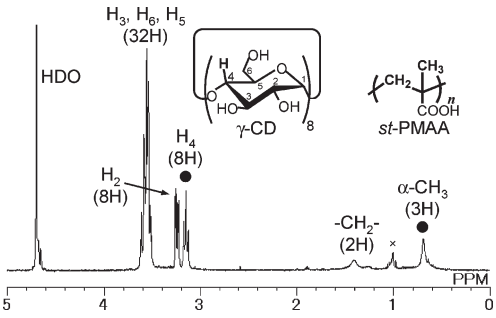

Figure 4. ^{1}H NMR spectrum of the γ-CD−*st*-PMAA inclusion complex in D_2O (including 1 mol L^{-1} NaOD) at 25 °C.

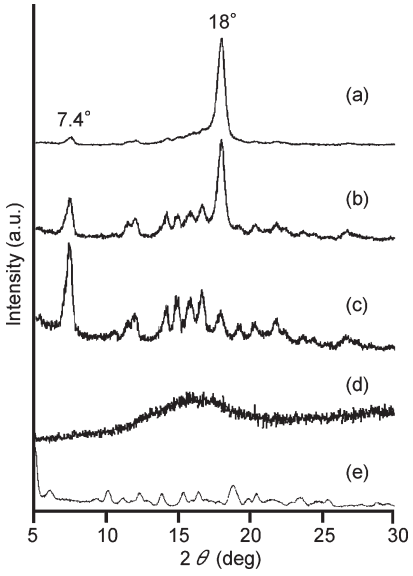

Figure 5. XRD patterns of precipitates formed by mixing γ-CD with PMAAs of different syndiotacticities: (a) PMAA(HM)-93, (b) PMAA-(HM)-73, and (c) PMAA(HM)-62, (d) PMAA(HM)-93, and (e) native γ-CD (cage-type assembly).

Effects of Molecular Weight and Tacticity of *st*-PMAA on Inclusion Complex Formation. Next, using higher-molecular-weight PMAAs of different syndiotacticities (*rr* ratios) (M_n = 22 000, M_w/M_n = 1.6, *mm*:*mr*:*rr* = 1:6:93, M_n = 16 000; M_w/M_n = 2.4, *mm*:*mr*:*rr* = 3:24:73; M_n = 30 000, M_w/M_n = 2.2, *mm*:*mr*:*rr* = 5:33:62),

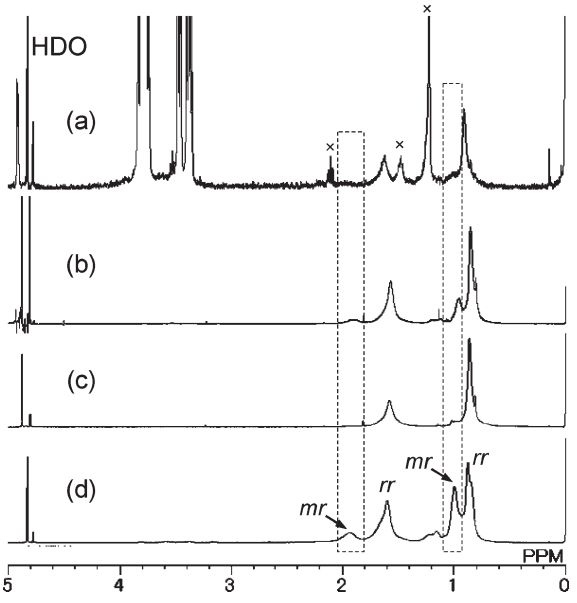

Figure 6. ^{1}H NMR spectra of (a) the precipitate formed by adding γ-CD into a mixture of *at*-PMAA and *st*-PMAA, (b) a mixture of *at*-PMAA and *st*-PMAA, (c) *st*-PMAA, and (d) *at*-PMAA in D_2O (including 1 mol L^{-1} NaOD) at 25 °C.

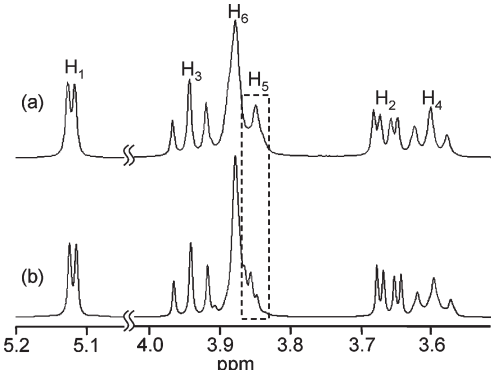

Figure 7. ^{1}H NMR spectra of γ-CD in the (a) presence and (b) absence of *st*-PMAA in D_2O at 25 °C.

which were abbreviated as PMAA(HM)-93, PMAA(HM)-73, and PMAA(HM)-62, respectively, the formation behavior of inclusion complexes with γ-CD was examined. In all cases, a precipitate was formed after mixing each PMAA with γ-CD in water. These precipitates were washed with an aqueous urea solution and then pure water and lyophilized (Table 1, runs 4−6). The yield of the precipitate obtained using PMAA(HM)-93 was much higher than that obtained using lower-molecular-weight *st*-PMAA of almost the same tacticity (Table 1, runs 3 and 4). It is noteworthy that larger amounts of precipitates were formed when PMAAs of higher syndiotacticities were used. In the XRD patterns of the precipitates, peaks at 2θ = 7.4° and 18° were observed, indicating the formation of inclusion complexes of γ-CD with PMAA(HM)-93, PMAA(HM)-73, and PMAA(HM)-62 (Figure 5). Intriguingly, the higher the syndiotacticity of PMAA, the stronger the peak intensity at 2θ = 18° was observed. From the ^{1}H NMR spectra, the coverage ratios (%) of inclusion complexes of γ-CD with PMAA(HM)-93, PMAA(HM)-73, and PMAA(HM)-62 were estimated to be 96%, 77%, and 71%,

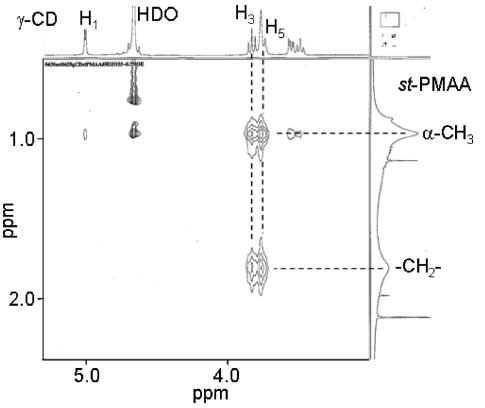

Figure 8. Partial NOESY spectrum of a mixed solution of γ-CD and *st*-PMAA in D_2O at 25 °C.

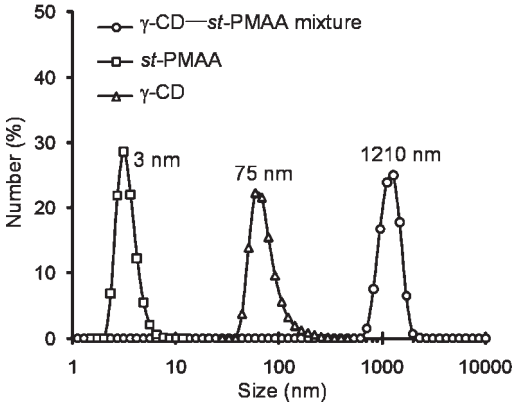

Figure 9. Size distribution of the γ-CD−*st*-PMAA aggregate, γ-CD, and *st*-PMAA in water at 25 °C.

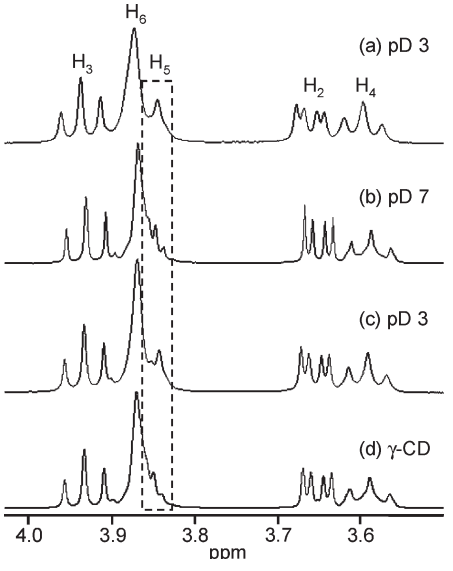

Figure 10. ^{1}H NMR spectral changes observed for γ-CD with pH changes in a γ-CD−*st*-PMAA mixed D_2O solution at 25 °C.

respectively, assuming that the coverage ratio of the inclusion complex of γ-CD with the low-molecular-weight *st*-PMAA (M_n = 6900, M_w/M_n = 1.5, *mm*:*mr*:*rr* = 2:5:93) was 100% (Table 1, runs

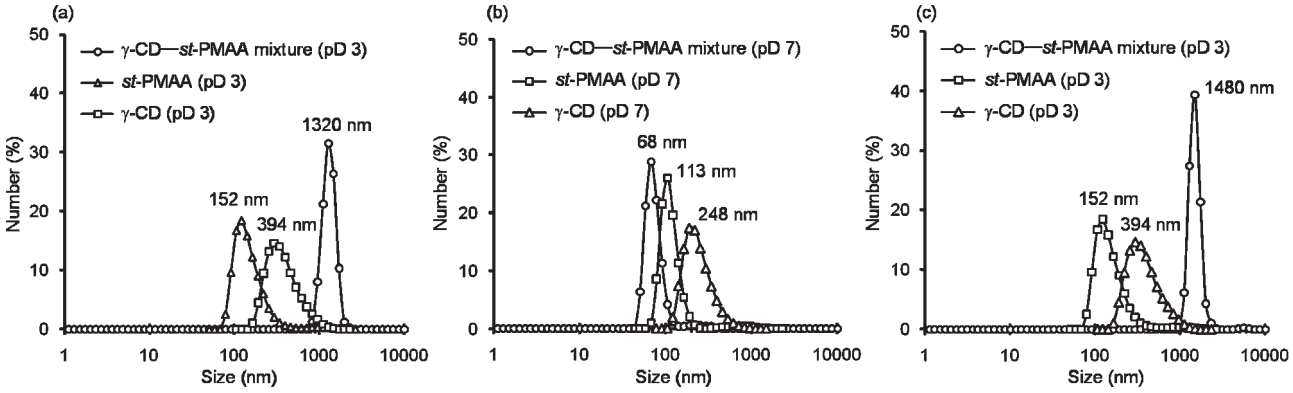

Figure 11. Size distributions of γ-CD−*st*-PMAA aggregates in a solution of (a) pD 3, (b) pD 7, and (c) pD 3 at 25 °C.

4−6 and Figures S1−S3, Supporting Information). This result indicates that the coverage ratio of the inclusion complex increases with increasing syndiotacticity of the PMAA. These findings clearly show that γ-CD more effectively includes PMAA of a higher syndiotacticity, strongly supporting the selective formation of the inclusion complex of γ-CD with *st*-PMAA. The detailed mechanism for selective inclusion of *st*-PMAA by γ-CD is not clear at present, but it can be assumed that hydrogen-bonding interactions between carboxyl groups of *st*-PMAA and hydroxyl groups of γ-CD as well as better spatial fit of the *st*-PMAA chain into the γ-CD cavity play an important role in the selective inclusion.

Selective Extraction of *st*-PMAA from a Mixture with *at*-PMAA. Based on the above-mentioned results, the selective extraction of *st*-PMAA (M_n = 6900, M_w/M_n = 1.5, *mm*:*mr*:*rr* = 2:5:93) from a mixture with *at*-PMAA (M_n = 4500, M_w/M_n = 1.6, *mm*:*mr*:*rr* = 7:39:54) through the inclusion complex formation with γ-CD was tested. The inclusion complex formation was carried out according to the same procedure described above, except that an aqueous solution (1.0 mL) of equal amounts of *at*-PMAA and *st*-PMAA (2.1 mg, 2.4×10^{-5} unit mol of each) was used instead of each polymer solution. In the XRD patterns of the precipitate formed, peaks at 2θ = 7.4° and 18° were observed, confirming the inclusion complex formation between γ-CD and PMAA (Figure S4, Supporting Information). In the ^{1}H NMR spectrum of the precipitate, the intensity of the signals at 1.0 and 1.9 ppm, which correspond to the α-methyl and methylene protons of *at*-PMAA (*mr*), respectively, decreased remarkably as compared with those in the mixture of equal amounts of *at*-PMAA and *st*-PMAA in the absence of γ-CD (Figure 6). This result indicates that the formed precipitate consists mainly of an inclusion complex of γ-CD with *st*-PMAA, and thus the selective extraction of *st*-PMAA from a mixture with *at*-PMAA can be realized through inclusion complex formation with γ-CD.

Interactions between γ-CD and *st*-PMAA in Water. We also examined the inclusion complex formation between γ-CD and *st*-PMAA in aqueous solution by ^{1}H NMR and NOESY measurements of a dilute D_2O solution (1.0 mL, pD 3) including *st*-PMAA (2.1 mg, 2.4×10^{-5} unit mol) and γ-CD (6.3 mg, 4.9×10^{-6} mol) at a molar ratio of 1:5 (γ-CD:MAA unit). Figure 7 shows the ^{1}H NMR spectrum of the γ-CD−*st*-PMAA solution, together with that of the free γ-CD solution. The proton signals of γ-CD in the presence of *st*-PMAA were broadened in comparison with those of free γ-CD. In particular, the H_5 proton signal of γ-CD was markedly broadened, and additionally, this proton signal was shifted upfield. Figure 8 shows the NOESY spectrum of the γ-CD−*st*-PMAA solution. The H_3 and H_5 protons of γ-CD, which are located inside the CD cavity, clearly correlated with both the α-methyl and methylene protons of *st*-PMAA. On the other hand, no correlation was observed between the H_1, H_2, and H_4 protons of γ-CD, which are located outside the cavity, and any of the protons of *st*-PMAA. These results show that the *st*-PMAA chain is included inside the γ-CD cavity, and thus γ-CD can form a water-soluble inclusion complex with *st*-PMAA.[36,37] Moreover, the size distribution of the γ-CD−*st*-PMAA inclusion complex in water was measured by dynamic light scattering (DLS). In a mixed solution of γ-CD and *st*-PMAA, larger aggregates (average size = 1210 nm) were observed, as compared to the γ-CD solution (average size = 75 nm) and the *st*-PMAA solution (average size = 3 nm) (Figure 9). The formation of these larger aggregates in a mixed solution of γ-CD and *st*-PMAA can be explained by considering the aggregation of γ-CD−*st*-PMAA inclusion complexes through hydrophobic and/or van der Waals interactions between the CDs threading onto the *st*-PMAA chain. This aggregation may also be caused by the lower water solubility of γ-CD−*st*-PMAA inclusion complexes as compared to γ-CD and *st*-PMAA alone. These results imply that DLS measurement is a useful method to evaluate inclusion complex formation in solution.

Effects of pH on the Inclusion Complex Formation. The γ-CD−*st*-PMAA inclusion complex formation is expected to be strongly affected by the pH of the solution, since *st*-PMAA has pH-responsive carboxylic groups (the pK_a of PMAA is 5−6[31,33]). Here, we examined the effects of pH on inclusion complex formation between γ-CD and *st*-PMAA. When γ-CD and *st*-PMAA were mixed in a pH 7 aqueous solution where most of the carboxylic groups of *st*-PMAA should dissociate into carboxylate ions, no precipitate of the inclusion complex was formed. Furthermore, in this solution, inclusion complex formation between γ-CD and *st*-PMAA was not observed by ^{1}H NMR, NOESY, and DLS measurements. On the other hand, in the pH 3 solution where most of the carboxylic groups of *st*-PMAA should be protonated, inclusion complex formation was clearly observed by the NMR and DLS spectra of the solution as well as the precipitate formation. Using this pH-responsive property, controlling the formation and dissociation of the inclusion complex by changing the pH of the solution should be possible. The pD of a D_2O solution (1.0 mL) including γ-CD (6.3 mg, 4.9×10^{-6} mol) and *st*-PMAA (2.1 mg, 2.4×10^{-5} unit mol) was alternately changed to 3 (nondissociation of *st*-PMAA) and 7 (dissociation

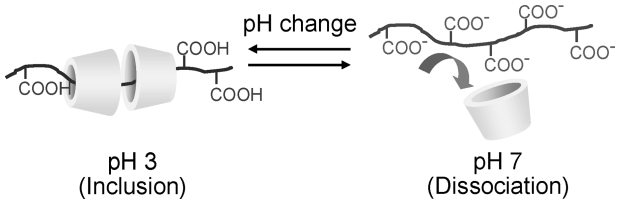

Figure 12. Schematic illustration of pH-controlled inclusion complex formation between γ-CD and *st*-PMAA.

of *st*-PMAA) by adding DCl and NaOD solutions, respectively, in the presence of a constant concentration of NaCl (1.0 wt %). Figure 10 shows the ^{1}H NMR spectral changes for γ-CD with the pD changes (pD 3 → pD 7 → pD 3) in the γ-CD−*st*-PMAA mixed solution. At pD 3, the H_5 proton signal of γ-CD was clearly broadened and shifted upfield as compared to the free γ-CD. When the pD of the solution was changed to 7 by adding NaOD, the signal shift diminished, giving the same spectrum as free γ-CD. The addition of DCl into this solution to change the pD from 7 to 3 caused the shift of H_5 proton signal of γ-CD again, suggesting that the inclusion complex was clearly formed in solution. In the NOESY spectra of the pD 3 solution (Figure S5a,c, Supporting Information), the H_3 and H_5 protons of γ-CD clearly correlated with both the α-methyl and methylene protons of *st*-PMAA, in contrast to the case of the pD 7 solution, where no correlation between the γ-CD and *st*-PMAA protons was observed (Figure S5b, Supporting Information). Additionally, in the DLS spectra of both pD 3 solutions, the formation of larger aggregates (average sizes = 1320 and 1480 nm, respectively), which would be attributed to the aggregation of the γ-CD−*st*-PMAA inclusion complexes, was observed. On the other hand, in the pD 7 solution, such characteristic aggregation was not observed (Figure 11). These results indicate that the acid form of *st*-PMAA, where most of the carboxylic groups are protonated, effectively forms an inclusion complex with γ-CD in water, whereas the dissociated form of *st*-PMAA does not (Figure 12). In addition, it was found that inclusion complex formation between γ-CD and *st*-PMAA in solution is reversibly controlled by the pH changes. This inclusion complex can be used as a novel building block for pH-responsive materials.

CONCLUSIONS

We demonstrated that γ-CD forms an inclusion complex with *st*-PMAA more effectively than with other stereoregular PMAAs in water. The selective extraction of *st*-PMAA from a mixture with *at*-PMAA in water was successfully achieved by inclusion complex formation with γ-CD. This is the first example of selective formation of an inclusion complex of a syndiotactic polymer with CD. The selective recognition ability of γ-CD toward *st*-PMAA can be applied to an efficient separation system of *st*-PMAA from a mixture with other stereoregular PMAAs. It was also revealed that the formation and dissociation of γ-CD−*st*-PMAA inclusion complex in aqueous solution could be reversibly controlled by changing the pH. This inclusion complex can be useful as a novel building block for pH-responsive materials such as pH-responsive hydrogels and nanoparticles.

ASSOCIATED CONTENT

Supporting Information. ^{1}H NMR spectra of inclusion complexes between γ-CD and PMAAs of different syndiotacticities, XRD patterns of the precipitate formed by adding γ-CD into a mixture of *at*-PMAA and *st*-PMAA, and NOESY spectra of a mixture of γ-CD and *st*-PMAA in D_2O solutions of alternately changed pDs. This material is available free of charge via the Internet at http://pubs.acs.org.

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