Partially-methylated amyloses as effective hosts for inclusion complex formation with polymeric guests†

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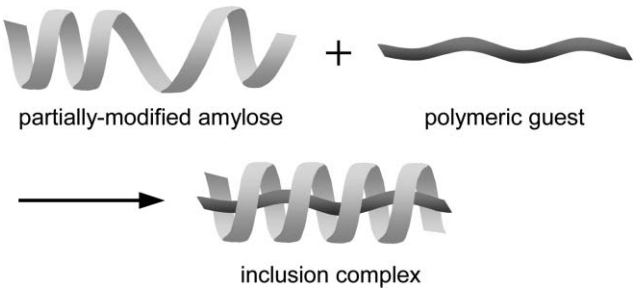
Partially 2,3-*O*-methylated amyloses efficiently form inclusion complexes with polytetrahydrofuran and poly(ε-caprolactone) by simply mixing them in DMSO–H_2O (1 : 9) solution, in contrast to the case of the parent amylose in which the corresponding inclusion complexes are only slightly formed.

In biological systems, biopolymers such as nucleic acids and antibodies effectively function as host molecules to precisely recognize particular guest polymers. The development of artificial host polymers possessing such precise recognition ability towards polymeric guests is of great importance, since these host polymers can be useful for the construction of novel recognition devices.[1] Amylose, which is a linear polysaccharide consisting of α-1,4-linked glucopyranose units and can adopt a left-handed helical conformation with six glucopyranose units per turn,[2] is well known to form inclusion complexes with various types of low-molecular-weight organic molecules[3] and some oligomers[4] in aqueous media by incorporating the guest molecules into its helical cavity *via* hydrophobic interactions. On the other hand, much less attention has been paid to the inclusion complexes formed between amylose and polymeric guests. Although Shogren *et al.* prepared inclusion complexes between amylose and several synthetic polymers, a tedious operation was required to dissolve the amylose into water, and the introduction of a hydrophilic group into the guest polymers was also essential for the complexation with amylose.[5] Recently, Kadokawa *et al.* prepared inclusion complexes of amylose with synthetic polymers by means of the vine-twining polymerization of an α-D-glucose 1-phosphate monomer catalyzed by phosphorylase, but these inclusion complexes were not formed by simply mixing the obtained amylose with the guest polymers.[6] Thus, it can be seen that inclusion complex formation between amylose and polymeric guests is extremely difficult due to the strong tendency of amylose to retrograde,[7] as well as its poor solubility in aqueous media based on the multiple hydrogen bonds between the amylose hydroxyl groups.[8] If these multiple hydrogen bonds can be weakened by the appropriate chemical modification of the amylose hydroxyl groups without significant loss of the helical structure, then the resulting amylose derivatives, which should possess a much weaker retrograde tendency as well as higher solubility in aqueous media compared to the parent amylose, can be expected to easily and effectively form inclusion complexes with polymeric guests in aqueous media (Scheme 1). These amylose derivatives represent the basis for the creation of supramolecular sensors and switches. In this communication, we report the partial modification of amylose hydroxyl groups as a novel and effective strategy for improving the inclusion ability of amylose towards polymeric guests.



Scheme 1 Schematic illustration of inclusion complex formation between partially-modified amylose and a polymeric guest.

We have chosen partially 2,3-*O*-methylated amyloses as the modified amylose (Fig. 1), in which none of the 6-OH groups is methylated, since 6-*O*-methylation of amylose crucially disturbs the helix to give the random coiled structure.[9] Partially 2,3-*O*-methylated amyloses (MAs) were prepared from amylose (M_w = 2.1 × 10^4, M_w/M_n = 1.05) in three steps: selective tritylation of 6-OH groups of amylose,[10] partial methylation of 2,3-OH groups of the resulting 6-*O*-tritylamylose, and detritylation. The MAs showed excellent solubility in water containing more than 10 vol% dimethyl sulfoxide (DMSO). The DMSO–H_2O (1 : 9) solution of MA (4.0 × 10^{-2} mol per monomer unit L^{-1}) generated no

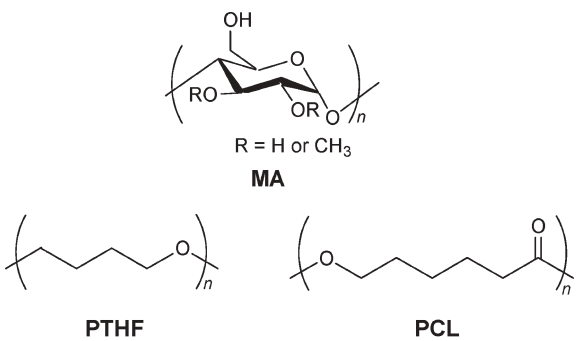


Fig. 1 Structures of partially 2,3-*O*-methylated amylose (MA), polytetrahydrofuran (PTHF), and poly(ε-caprolactone) (PCL).

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† Electronic supplementary information (ESI) available: Synthetic procedures and monomer compositions of partially 2,3-*O*-methylated amyloses (MAs), XRD patterns and ^1H NMR spectra of precipitates between MAs (or amylose) and PTHF (or PCL), DSC thermogram of the precipitate between MA-8 and PCL. See DOI: 10.1039/b616231b

Table 1 Precipitate formation between MAs and guest polymers

Entry	Host[a] (blue value)[b]	Guest polymer	
		PTHF	PCL
1	MA-8 (2.7)	Precipitation	Precipitation
2	MA-20 (0.87)	Precipitation	Precipitation
3	MA-33 (0.070)	None	None
4	MA-50 (0.043)	None	None
5	MA-100 (<0.001)	None	None
6	Amylose (7.8)	Precipitation[c]	Precipitation[c]

[a] MA with *X*% methylation in the 2,3-OH groups was abbreviated as MA-*X*. [b] Blue values were measured in DMSO–H_2O (1 : 9). Blue value = $0.4A_{680}$/[MA/mg mL^{-1}]. [c] The precipitate was almost completely composed of amylose.

precipitate over several weeks, in sharp contrast to the case of the parent amylose whose corresponding solution immediately gave the precipitate. Polytetrahydrofuran (PTHF) (M_w = 2900) and poly(ε-caprolactone) (PCL) (M_w = 1250) were used as guest polymers. Inclusion complex formation was carried out by mixing the guest polymer (PTHF: 8.9×10^{-6} mol per monomer unit, PCL: 6.3×10^{-6} mol per monomer unit) in 100 μL DMSO–H_2O (1 : 9) with MA (4.0×10^{-5} mol per monomer unit) in 900 μL DMSO–H_2O (1 : 9); the mixture was left standing for 12 h at 60 °C and then for 12 h at ambient temperature. The precipitates formed were washed with DMSO–H_2O (1 : 9) solution, methanol (or acetone), and then water to remove the uncomplexed MA and guest polymers. After lyophilization, the obtained solids were analyzed with X-ray diffraction (XRD), differential scanning calorimetry (DSC) and ^{1}H NMR.

Table 1 shows the results of precipitate formation in different combinations of MAs and guest polymers. When MAs with 8 and 20% methylation were used as a host, precipitation with both PTHF and PCL was observed. On the other hand, MAs with more than 33% methylation did not form any precipitate with the guest polymers, possibly due to the lack of a helical structure for these MAs in DMSO–H_2O (1 : 9) solution.

The blue value of the amylose derivative–iodine complex, which is calculated based on the absorbance at 680 nm, provides useful information on the extension of helical segments within the amylose derivative in solution.[11] Fig. 2 shows the UV-Vis spectra of MA–iodine complexes and an amylose–iodine complex in DMSO–H_2O (1 : 9) solution including 0.002% I_2/KI. The blue value calculated from the absorbance at 680 nm (A_{680}) for each complex is shown in Table 1. The blue value decreased with an increase in the degree of methylation of MA, showing that the content of continuous helical segments within the MA molecule decreases with an increase in the degree of methylation. The blue values of MA-8 and MA-20 clearly indicate that some continuous helical segments exist in these MAs in DMSO–H_2O (1 : 9) solution. On the other hand, the blue values of MA-33, MA-50 and MA-100, which are less than 0.1, show that there are few continuous helical segments within these MAs.[11a] Thus, the results of precipitate formation between MA and the guest polymers can be explained by considering that some extended helical segments within the MA molecules are essential for the formation of precipitate between MA and polymeric guests.

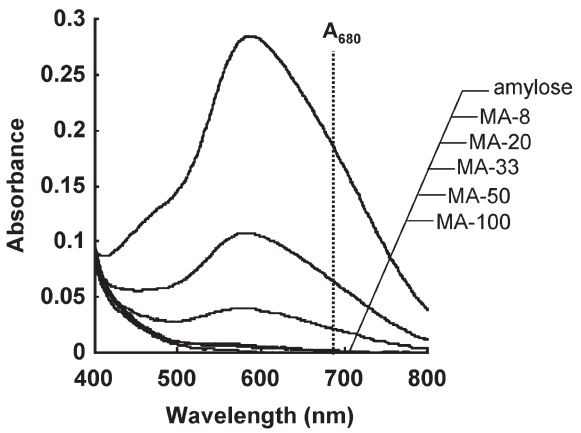

Fig. 2 UV-Vis spectra of MA–iodine complexes and an amylose–iodine complex in DMSO–H_2O (1 : 9) solution including 0.002% I_2/KI. [MA] = [amylose] = 4.7×10^{-7} M.

XRD and DSC analyses are effective methods for evaluating the formation of inclusion complexes between amyloses and guest molecules. Fig. 3 shows the XRD patterns of the MA-8–PTHF precipitate, MA-8 and PTHF. In the XRD pattern of the MA-8–PTHF precipitate, different peaks (2θ = 12.9, 20.1°) from those of MA-8 and PTHF were observed. This pattern is quite consistent with that of amylose–PTHF inclusion complex which was previously prepared by means of the vine-twining polymerization of α-D-glucose 1-phosphate in the presence of PTHF.[6b] This observation suggests that the precipitate corresponds to the inclusion complex between MA-8 and PTHF, in which MA-8 adopts a helical conformation similar to that of V-amylose.[12] In the DSC thermogram of the MA-8–PTHF precipitate, no thermal transition was observed during the course of heating, in sharp contrast to the case of PTHF alone in which an endothermic peak, corresponding to the crystal melting, was observed (Fig. 4). This result shows that no crystalline PTHF exists in the precipitate due to the incorporation of the PTHF chain into the helical cavity of MA-8.

The host–guest stoichiometry in the precipitate was determined by the ^{1}H NMR spectra. Fig. 5 shows the ^{1}H NMR spectrum of the MA-8–PTHF precipitate. The integral ratio of C_β proton (H_β)

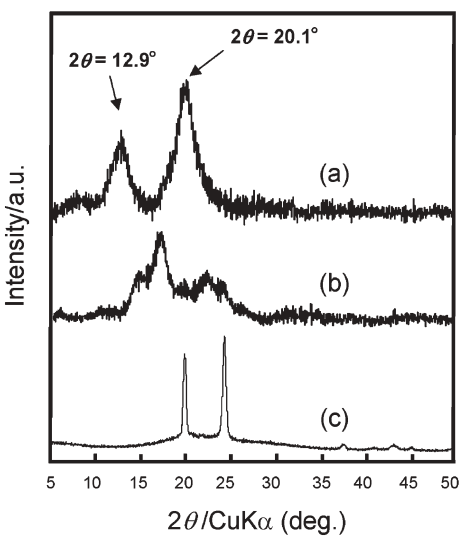

Fig. 3 XRD patterns of (a) the MA-8–PTHF precipitate, (b) MA-8 and (c) PTHF.

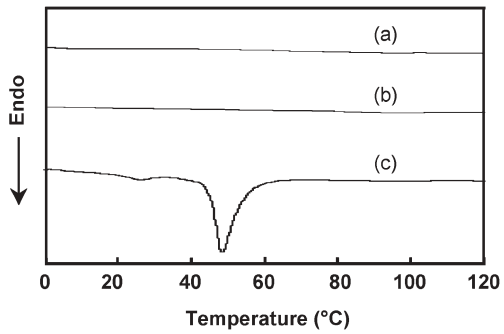

Fig. 4 DSC thermograms (first heating scan at 10 °C min^{-1}) of (a) the MA-8–PTHF precipitate, (b) MA-8 and (c) PTHF.

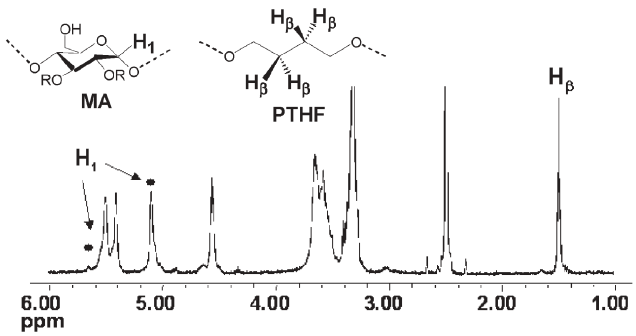

Fig. 5 ^{1}H NMR spectrum of the MA-8–PTHF precipitate in DMSO-d_6.

peaks of PTHF to C_1 proton (H_1) peaks of MA-8, H_β/H_1, was estimated to be 0.82. This value is almost the same as the previously calculated H_β/H_1 value from the synthetic amylose–PTHF inclusion complex (= 0.89).[6b] This result clearly indicates that the inclusion complex between MA-8 and PTHF was successfully formed by simply mixing the polymers. In the cases of MA–PCL precipitates, similar XRD patterns to those of MA–PTHF precipitates were also observed, showing the formation of inclusion complexes between MAs and PCL. The absence of a melting point in the DSC thermogram of the MA-PCL precipitate also supports the inclusion complex formation between them. On the other hand, the parent amylose only slightly afforded the precipitate of inclusion complex with both the guest polymers, while large amounts of retrograded amyloses were precipitated.

In conclusion, we have demonstrated that partially 2,3-*O*-methylated amyloses efficiently formed inclusion complexes with PTHF and PCL by simply mixing them in DMSO–H_2O (1 : 9) solution. The degree of methylation of amylose affected the inclusion ability towards PTHF and PCL: MAs with 8 and 20% methylation formed inclusion complexes with these guest polymers, while MAs with more than 33% methylation formed few inclusion complexes with the guest polymers. Detailed study on the structure of inclusion complex is now in progress. The results of this study are expected to support new applications of amylose as a building block in supramolecular architecture and polymer recognition devices.

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