Formation of Inclusion Complexes of Isotactic and Syndiotactic Poly(methyl methacrylate)s with γ-Cyclodextrin

Toshiyuki Kida, Akira Kikuzawa, and Mitsuru Akashi*
Department of Applied Chemistry, Graduate School of Engineering, Osaka University, 2-1 Yamadaoka, Suita, Osaka 565-0871

(Received July 29, 2008; CL-080737; E-mail: akashi@chem.eng.osaka-u.ac.jp)

We report here inclusion complex formation between γ-cyclodextrin (γ-CD) and stereoregular poly(methyl methacrylate)s (PMMAs). γ-CD was found to form an inclusion complex with isotactic (it) PMMA more effectively than with syndiotactic (st) PMMA. The formation of an inclusion complex between γ-CD and st-PMMA was strongly influenced by the amount of γ-CD added, and the addition of an excess amount of γ-CD was required for γ-CD–st-PMMA complex formation.

Cyclodextrins (CDs) are a class of cyclic oligosaccharides consisting of several α-(1,4)-linked D-glucopyranose units. The inclusion ability of CDs has been studied extensively, and applied to widespread fields including the food, cosmetic, and pharmaceutical industries.[1] CDs can form inclusion complexes with polymers as well as low-molecular-weight compounds. Considerable effort has been devoted to the design and synthesis of supramoleculer architectures constructed by complexes between CDs and polymers. Harada reported a variety of polymer-inclusion complexes with CDs,[2] and they clarified the relationship between the type of polymers incorporated and the cavity size of the CDs. On the other hand, much less attention has been paid to the inclusion complex formation of stereoregular polymers with CDs, except for a few reports by Harada et al.[3] and Tonelli et al.,[4] where the complex formation of isotactic poly(propylene glycol) with β-CD and the complex formation of isotactic poly(3-hydroxylbutylate)s with α-CD were reported, respectively. Recently, Ohya et al. reported chiral recognition of poly(L-lactic acid) by α-CD.[5]

Among the CDs, γ-CD has a unique inclusion property. γ-CD can form inclusion complexes with polymeric guests with substituents on the main chain, such as poly(vinyl acetate)[6] and poly(dimethylsiloxane),[7] more effectively than with linear polymers such as poly(ε-caprolactone)[8] and polyethylenimines.[9] This is due to the larger cavity size of γ-CD as compared to α- and β-CDs. Despite the fact that most of the guest polymers with substituents on the main chain can possess potential stereoregularity, the complexation of stereoregular polymers with γ-CD has not been reported yet. Using γ-CD as a host, the formation of an inclusion complex even with a syndiotactic polymer, which is normally more bulky than the corresponding isotactic polymer, would be possible.

Poly(methyl methacrylate) (PMMA) has found many applications in the biomedical field, due to its excellent biocompatibility. A stereoregular PMMA stereocomplex can be formed by mixing isotactic (it) PMMA and syndiotactic (st) PMMA in specific solvents, with different stoichiometries of it:st = 2:1, 1:1, and 1:2 depending on the preparation conditions.[10] Due to these unique assembly properties, stereoregular PMMAs can act as useful building blocks for supramolecular architectures, like DNA.[11] In this letter, we report the formation behavior of inclusion complexes of it- and st-PMMAs with γ-CD.

it-PMMA ($M_n = 5500$, $M_w/M_n = 1.27$, mm:mr:rr = 95:4:1) and st-PMMA ($M_n = 6900$, $M_w/M_n = 1.30$, mm:mr:rr = 0:9:91) were synthesized by conventional anionic polymerization using MMA monomers and the appropriate initiators (t-C_4H_9MgBr and t-$C_4H_9Li/(C_2H_5)_3Al$ for it- and st-PMMAs, respectively).[12] First, the formation of the inclusion complex of it-PMMA with γ-CD was examined. On the basis of a previous report[13] where inclusion complex formation between atactic PMMA and γ-CD was carried out in 1,4-dioxane/H_2O (10:1), we used 1,4-dioxane as a solvent. Three milligrams of it-PMMA (3.0×10^{-5} unit mol) was dissolved in 1.0 mL of 1,4-dioxane, and 39 mg of γ-CD powder (3.0×10^{-5} mol) was added at 80 °C. After vigorous stirring for 3 h at 80 °C, the suspension was cooled to ambient temperature and stirred gently for another 3 days. The precipitate was collected by centrifugal separation, and washed with 1,4-dioxane and H_2O to remove any free it-PMMA and uncomplexed γ-CD. After lyophilization, the obtained solids (5.7 mg) were analyzed by X-ray diffraction (XRD) and ^{1}H NMR. On the other hand, when it-PMMA alone was stirred in 1,4-dioxane under the same conditions, no precipitation was observed. Figure 1 shows the XRD pattern of the γ-CD–it-PMMA precipitate formed, together with those of free γ-CD and it-PMMA. The XRD pattern of the γ-CD–it-PMMA precipitate was clearly different from those of the corresponding free host and guest polymer, suggesting that this precipitate corresponds to the inclusion complex between γ-CD and it-PMMA. ^{1}H NMR measurements of the precipitates were carried out in DMSO-d_6 to determine the host–guest stoichiometries. Figure 2 shows the ^{1}H NMR spectrum of the γ-CD–it-PMMA precipitate (in DMSO-d_6 at 25 °C). The stoichiometry (γ-CD:MMA units) estimated from the integration ratio of the anomeric protons of γ-CD to the methylene protons of it-PMMA was 1:3.1.

Next, we examined the effects of the amount of γ-CD added

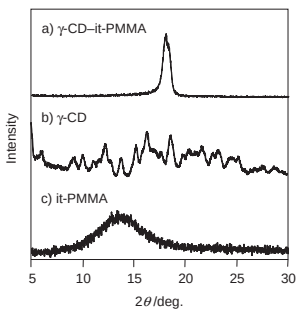

Figure 1. XRD patterns of a) γ-CD–it-PMMA precipitate, b) γ-CD, and c) it-PMMA.

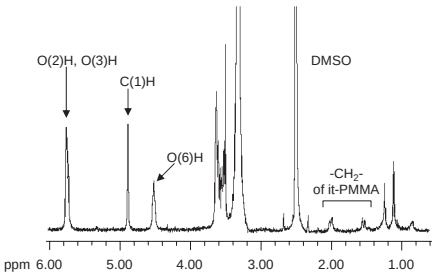

Figure 2. ^{1}H NMR spectrum of the γ-CD–it-PMMA precipitate in DMSO-d_6 at 25 °C.

Table 1. Precipitate formation between γ-CD and stereoregular PMMAs (guests)

γ-CD/mg	Guests	Precipitation (mg)[a]	Composition[b] (γ-CD:MMA units)
19.5	it-PMMA	○ (3.8)	1:13.2
39	(3.0 mg)	○ (5.7)	1:3.1
195		○ (10.5)	1:2.8
390		○ (12.7)	1:2.5
19.5	st-PMMA	×	—
39	(3.0 mg)	×	—
195		○ (3.9)	1:7.0
390		○ (5.2)	1:6.6

[a]After washing with 1,4-dioxane and H_2O. [b]Estimated from the ^{1}H NMR spectra.

on the yield and host–guest stoichiometry of the γ-CD–it-PMMA inclusion complex. Different amounts of γ-CDs (19.5, 39, 195, and 390 mg) were added to the it-PMMA in 1,4-dioxane (Table 1). In all cases examined, inclusion complex formation between γ-CD and it-PMMA was observed. Both the yield of the γ-CD–it-PMMA complex and the number of γ-CD units threading onto the it-PMMA chain were low when only a half equiv of γ-CD (19.5 mg, 1.5×10^{-5} mol) to the monomer units of it-PMMA was added. The stoichiometry (the molar ratio of γ-CD to MMA units) of the inclusion complex increased with increasing amount of γ-CD added, and became almost constant at 1:2.5 (γ-CD:MMA units).

In the case of st-PMMA, the precipitate formation with γ-CD was strongly influenced by the amount of γ-CD added (Table 1). The precipitate was not formed when an equimolar (or less) amount of γ-CD to the monomer units of st-PMMA was added, in contrast to the cases of it-PMMA. On the other hand, γ-CD–st-PMMA precipitation was observed upon addition of an excess amount of γ-CD (more than 5 times the unit mole of st-PMMA). The XRD pattern of the γ-CD–st-PMMA precipitate was similar to that of γ-CD–it-PMMA, indicating that the precipitate corresponded to the γ-CD–st-PMMA inclusion complex (see the Supporting Information[14]). The C=O stretching vibration band at 1723 cm^{-1} in the FT-IR spectrum of st-PMMA was shifted to 1727 cm^{-1} upon complex formation with γ-CD. This observation supports the hypothesis that the st-PMMA polymer chains are included inside the cavity of γ-CD. Here the peak shift ($\approx$4 cm^{-1}) was smaller as compared to the γ-CD–it-PMMA complex ($\approx$7 cm^{-1}). The number of γ-CD units threading onto the polymer chain in the case of the γ-CD–st-PMMA inclusion complex was also lower than in the case of γ-CD–it-PMMA complex. These results show that the cavity size of γ-CD is more appropriately fitted to the cross-sectional size of it-PMMA as compared to st-PMMA.

In conclusion, we demonstrated that γ-CD forms an inclusion complex with stereoregular PMMAs. γ-CD was found to form inclusion complexes with it-PMMA more effectively than with st-PMMA. The formation of an inclusion complex between γ-CD and st-PMMA was strongly influenced by the amount of γ-CD added, and the addition of an excess amount of γ-CD was required for γ-CD–st-PMMA complex formation. To the best of our knowledge, this is the first example of inclusion complex formation between γ-CD and a syndiotactic polymer.

This study was partially supported by Research Fellowships of the Japan Society for the Promotion of Science, a Grant-in-Aid for Scientific Research (No. 18550125) from the Japan Society of Promotion of Science, and a grant from the Shorai Foundation for Science and Technology.

References and Notes

1 a) G. Wenz, *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 803. b) K. A. Connors, *Chem. Rev.* **1997**, *97*, 1325. c) M. V. Rekharsky, Y. Inoue, *Chem. Rev.* **1998**, *98*, 1875. d) R. Breslow, S. D. Dong, *Chem. Rev.* **1998**, *98*, 1997. e) E. Rizzarelli, G. Vecchio, *Coord. Chem. Rev.* **1999**, *188*, 343. f) W.-H. Chen, S. Hayashi, T. Tahara, Y. Nogami, T. Koga, M. Yamaguchi, K. Fujita, *Chem. Pharm. Bull.* **1999**, *47*, 588.
2 A. Harada, *Coord. Chem. Rev.* **1996**, *148*, 115.
3 A. Harada, M. Okada, J. Li, M. Kamachi, *Macromolecules* **1995**, *28*, 8406.
4 X. Shuai, F. E. Porbeni, M. Wei, T. Bullions, A. E. Tonelli, *Macromolecules* **2002**, *35*, 3778; K. L. B. Chang, J. Lin, *Carbohydr. Polym.* **2000**, *43*, 163.
5 Y. Ohya, S. Takamido, K. Nagahama, T. Ouchi, T. Ooya, R. Katoono, N. Yui, *Macromolecules* **2007**, *40*, 6441.
6 A. Harada, J. Li, M. Kamachi, *Chem. Lett.* **1993**, 237.
7 H. Okumura, M. Okada, Y. Kawaguchi, A. Harada, *Macromolecules* **2000**, *33*, 4297.
8 Y. Kawaguchi, T. Nishiyama, M. Okada, M. Kamachi, A. Harada, *Macromolecules* **2000**, *33*, 4472.
9 H. S. Choi, T. Ooya, S. C. Lee, S. Sasaki, M. Kurisawa, H. Uyama, N. Yui, *Macromolecules* **2004**, *37*, 6705.
10 J. Spěváček, B. Schneider, *Adv. Colloid Interface Sci.* **1987**, *24*, 81.
11 Y. He, T. Ye, M. Su, C. Zhang, A. E. Ribbe, W. Jiang, C. Mao, *Nature* **2008**, *452*, 198.
12 a) K. Hatada, K. Ute, K. Tanaka, Y. Okamoto, T. Kitayama, *Polym. J.* **1986**, *18*, 1037. b) T. Kitayama, T. Shinozaki, T. Sakamoto, M. Yamamoto, K. Hatada, *Makromol. Chem.* **1989**, *15*, 167. c) K. Hatada, T. Kitayama, *Polym. Int.* **2000**, *49*, 11.
13 X. Shuai, F. E. Porbeni, M. Wei, T. Bullions, A. E. Tonelli, *Macromolecules* **2002**, *35*, 2401.
14 Supporting Information is also available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

Published on the web (Advance View) October 4, 2008; doi:10.1246/cl.2008.1120