An On/Off Circular Dichroism Signal Reveals a pH Dependent Competition between a Cyclodextrin and a Polyelectrolyte for an Atropisomeric Aromatic Guest

Sung Yun Yang, Mark M. Green,* Gerald Schultz, Salil K. Jha, and Axel H. E. Müller†

Herman F. Mark Polymer Research Institute
Polytechnic University, Six Metrotech Center
Brooklyn, New York 11201
Institute of Physical Chemistry, University of Mainz
Welderweg 15D-55099 Mainz, Germany
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In the following paper, we show how the pH dependent hydrophobic characteristics of poly(methacrylic acid) (PMA) may be used to develop a reversible supramolecular complex between a cyclodextrin and an atropisomeric aromatic group bound as a label to the PMA. The system is monitored by a chiral optical signal which is sensitive not only to the pH at the time of measurement but also to both the pH and time history of the sample.

The complexes between cyclodextrins[1] and naphthalene derivatives cause a large induced circular dichroism (ICD) effect associated with the naphthalene chromophore perturbed by the asymmetric cyclodextrin internal cavity.[2] However an aqueous solution of polymethacrylic acid (PMA), 0.6% of whose monomer units were esterified with 4-bromomethyl-1,1′-binaphthyl[3] (**1**) showed no circular dichroism signal on addition of even large excesses of γ-cyclodextrin. When the pH is raised above 6, however, the expected induced circular dichroism (ICD) appears signaling the incorporation of the aromatic chromophore in the cyclodextrin cavity. The binding constant for this complex is 1250 L/M at pH 10.[4] This ICD instantly disappears on reducing the pH below near to 6 and reappears when the pH is raised above this point.[5,6] Figure 1 exhibits this interplay between the pH and the ICD and, to be discussed below, the pH dependencies of the inherent viscosity of the polymer solution and the fluorescence intensity of the binaphthyl residues in **1**.

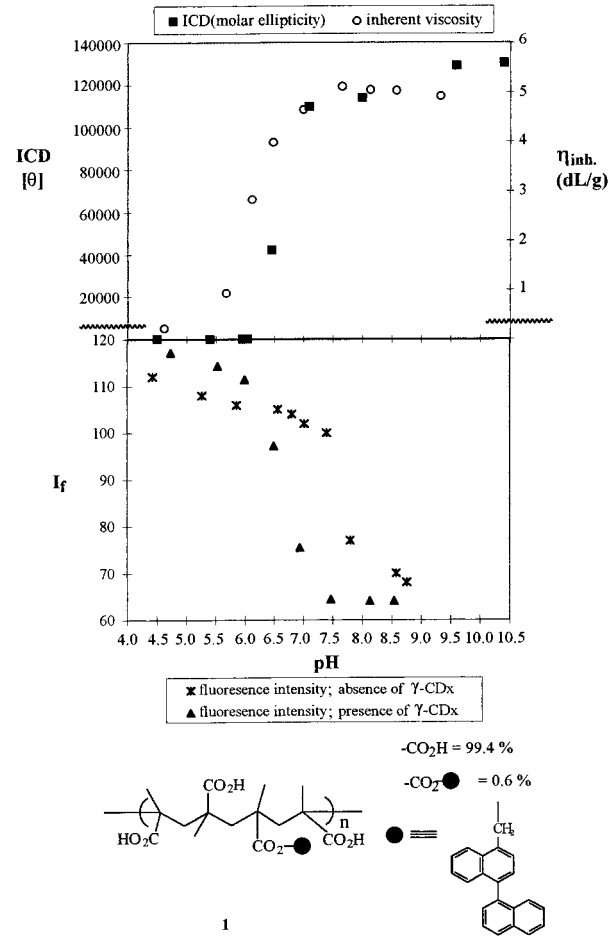

Figure 1. Induced circular dichroism (ICD), inherent viscosity (η_{inh}) and fluorescence intensity (I_f) as a function of pH for **1**. See text and ref 7. All solutions for ICD and I_f contain 0.01 M in monomer residues of **1**; for the ICD and one of the I_f measurements, 0.0018 M cyclodextrin. The pH values were obtained by neutralization of the PMA without addition of salt. Concentration for η was 0.04 M in monomer residues of **1**.

At any pH in which the ICD is observed (Figure 1), the circular dichroism signal grows slowly with time. This is shown in the difference between spectra a and b in Figure 2. Figure 2 also includes the circular dichroism spectrum (c) which remains after breaking the complex between the cyclodextrin and the binaphthyl group by lowering the pH. The conclusion that circular dichroism (c) in Figure 2 is associated with a partial resolution of one of the enantiomers of the binaphthyl atropisomer is confirmed by the slow growth of this signal, which with a half-life of 17 h at 20 °C is in line with that expected for the resolution of the twisted enantiomers.[7] This is further confirmed by the shape and intensity of the circular dichroism (c) which fits for an approximate 5% enantiomeric excess of the (*S*)-binaphthyl enantiomer.[8] The circular dichroism arising from the resolution is designated the twist circular dichorism

† University of Mainz.

(1) For a comprehensive and historical account of the very large literature on cyclodextrins, see: *Comprehensive Supramolecular Chemistry*; Lehn, J. M., Ed.; Pergamon Press: Vol. 3.

(2) For general information about induced circular dichroism (ICD), see: Hatano, M. *Induced Circular Dichroism in Biopolymer-Dye Systems*; Springer-Verlag: Berlin, 1986. Schipper, P. E.; Rodger, A. *J. Am. Chem. Soc.* **1983**, *105*, 4541. For ICD in cyclodextrins, see: Bender, M. L.; Komiyama, M. *Cyclodextrin Chemistry*; Springer Publishers: Berlin, 1978. For ICD work on naphthalene derivatives in cyclodextrins, see: Kobayashi, N.; Minato, S.; Osa, T. *Makromol. Chem.* **1983**, *184*, 1983. Shimizu, H.; Kaito, A.; Hatano, M. *J. Am. Chem. Soc.* **1982**, *104*, 7059. Harata, K.; Uedaira, H. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 375. For recent work concerned with ICD and for leading references, see the following: Forman, J. E.; Barrans, R. E., Jr.; Dougherty, D. A. *J. Am. Chem. Soc.* **1995**, *117*, 9213. Jansen, J. F. G. A.; de Brabander-van den Berg, E. M. M.; Meijer, E. W. *Recl. Trav. Chim. Pays-Bas* **1995**, *114*, 225. Kano, K.; Tatsumi, M.; Hashimoto, S. *J. Org. Chem.* **1991**, *56*, 6579. Ueno, A.; Moriwaki, F.; Osa, T.; Murai, K. *J. Am. Chem. Soc.* **1988**, *110*, 4323.

(3) For the synthetic method followed, see: Shimokawa, T.; Suzuki, T.; Nishikubo, T. *Polymer J.* **1994**, *26* (8), 967. The extent of labeling was judged by the UV spectrum of the resulting polymer **1**. The sample of PMA (M_w = 460 000) used for the data reported here was prepared by hydrolyzing (with HCl in refluxing methanol) poly(*tert*-butyl methacrylate) (M_w = 760 000, M_w/M_n = 1.05) prepared (Müller, A. H. E. *Makromol. Chem.* **1981**, *182*, 2863).

(4) The binding constant *K* for the complex between the binaphthyl label in **1** was evaluated from the intensity of the ICD following a published method (Ueno, A.; Moriwaki, F.; Osa, T.; Hamada, F.; Murai, K. *J. Am. Chem. Soc.* **1988**, *110*, 4323) under the following conditions which pertain to all measurements reported in this work: [PMA] = 0.01 M, [K^+] = 0.1 M, 20 °C.

(5) Reference 1, Vols. 1−11. Lehn, J. M. *Supramolecular Chemistry*; VCH Publishers: New York, 1995.

(6) For other reversible supramolecular observations, see: Branda, N.; Grotzfeld, R. M.; Valdés, C.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1995**, *117*, 85. Branda, N.; Wyler, R.; Rebeck, J., Jr. *Science* **1994**, *263*, 1267. Jeon, Y.-M.; Kim, J.; Whang, D.; Kim, K. *J. Am. Chem. Soc.* **1996**, *118*, 9790. Hamann, B. C.; Shimizu, K. D.; Rebek, J., Jr. *Angew. Chem., Int. Ed. Engl.* **1996**, *35* (12), 1326. Okubo, T.; Kuroda, M. *Macromolecules* **1989**, *22*, 3936.

(7) For leading references to the atropisomeric properties of binaphthyl, see: Tsuzuki, S.; Tanabe, K.; Nagawa, Y.; Nakanishi, H. *J. Mol. Struct.* **1990**, *216*, 279. Niciri, J.; Spada, G. P.; Gottarelli, G.; Weiss, R. G. *J. Am. Chem. Soc.* **1987**, *109*, 4352. Gottarelli, G.; Spada, G. P.; Bartsch, R.; Solladie, G.; Zimmerman, R. *J. Org. Chem.* **1986**, *56*, 589. Carter, R. E.; Liljefors, T. *Tetrahedron* **1976**, *32*, 2915. Brownes, P. A.; Harris, M. M.; Mazengo, R. Z.; Singh, S. *J. Chem. Soc. C* **1971**, 3990. For a polymeric example, see: Schulz, V. R. C.; Jung, R. H. *Makromol. Chem.* **1968**, *116*, 190. For work related to chiral recognition of binaphthyls by cyclodextrins, see: Kano, K.; Yoshiyasu, K.; Hashimoto, S. *J. Chem. Soc., Chem. Commun.* **1989**, 1278.

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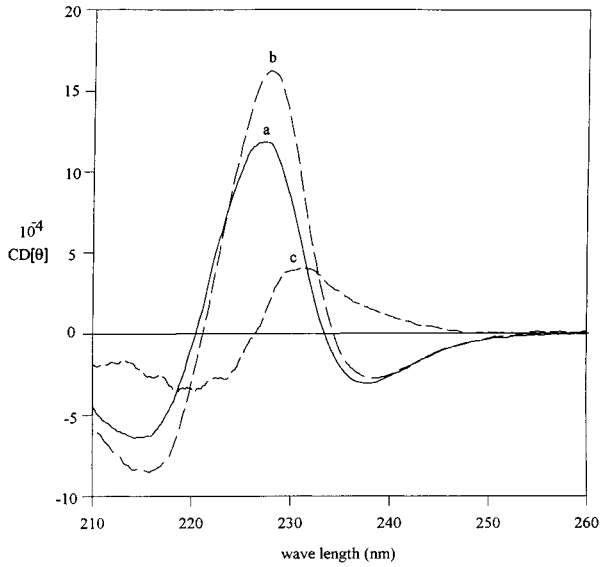

Figure 2. Circular dichorism spectra for the labeled poly(methacrylic acid) **1**: in the presence of γ-cyclodextrin at pH = 10 at (a) time = 0; (b) at time = 120 h; (c) after reduction of the pH to 5.4 following spectrum b.

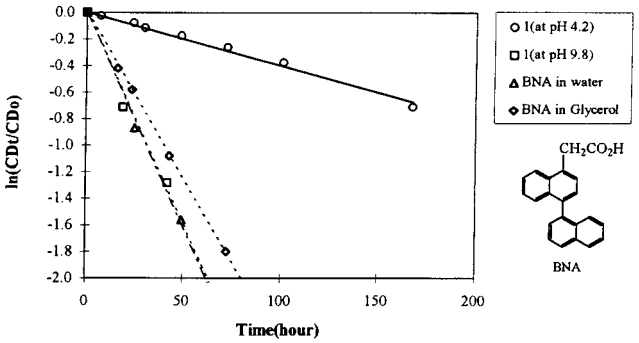

Figure 3. First-order plots of racemization of **1** at pH 4.2 (acetate buffer, $[K^+] = 0.072$ M) and 9.2 (phosphate buffer, $[K^+] = 0.072$ M) and for BNA in water and glycerol.

(TCD) to distinguish it from the ICD discussed above. At low pH, the TCD slowly (see below) decays to zero since the chiral influence of the cyclodextrin is removed, although this decay of the TCD can be immediately reversed by allowing the cyclodextrin complex to reform at higher pH. By change of pH above and below about 6, one can therefore cause the ICD to appear and disappear, respectively, with the intensity of the TCD (added to the ICD above pH 6 but appearing alone below pH 6) depending on the pH and time history of the sample.

The partial resolution allows the study of the racemization kinetics of the binaphthyl label in **1**. Figure 3 shows that the racemization rate at low pH in the dissolved polyelectrolyte **1** is far slower than for high pH[9] where it is similar to the racemization rate of a water-soluble model. The racemization kinetics of 1,1′-binaphthyl are known to be only mildly sensitive to the polarity of the solvent[10] and, as shown in the present work (Figure 3), in glycerol, which is 1400 times the viscosity of water, also only mildly sensitive to the viscosity of the medium. Yet the poly(methacrylic acid) chain, under the conditions where the cyclodextrin is expelled from the binaphthyl label, forces an unprecedented large restriction on the motions responsible for the racemization revealing an unusually closely coupled relationship between backbone chain and label presumably driven by the hydrophobic forces.[11]

Fluorescence measurements of aromatic molecules which show large intensity changes in response to change from non-aqueous to aqueous environments have shown that PMA at low degrees of ionization has a tendency to encapsulate hydrophobic labels protecting them from contact with the aqueous environment, but these capsules are disrupted as the PMA ionization exceeds a critical value.[12,13] Apparently for the binaphthyl group, this local effect is powerful enough to draw the aromatic probe out of the cyclodextrin. This is surprising considering that the overall chain conformation is neither collapsed nor excluding water. Further detail is revealed by the data in Figure 1. While the dependence on pH of the solution viscosity of **1**, characterizing the dimension of the PMA coil (Figure 1), is related to the overall chain properties, the ICD, fluorescence, and racemization rate dependence on pH track the environment around the binaphthyl group. The results show that the expansion of the chain, revealed by the increase of the viscosity, occurs at a lower pH than transfer of the binaphthyl label to the cyclodextrin (appearance of the ICD). This is reasonable since the portion of the chain forming the capsule about the binaphthyl group may be expected to resist exposure to water to higher degrees of ionization than that necessary to expand the bulk of the PMA. The fluorescence data taken in both the presence and absence of the cyclodextrin (Figure 1) beautifully support this picture. They show that in the absence of the cyclodextrin a higher pH is necessary to release the aromatic group from the PMA capsule to a purely aqueous environment (reduction in the fluorescence intensity). In the presence of the cyclodextrin, the fluorescence data closely parallel the pH necessary for the transfer from the hydrophobic PMA cavity into the cyclodextrin cavity shown from the ICD data.

Other water-soluble polymers with hydrophobic properties which undergo temperature-induced phase transitions[14] may be expected to exhibit similar changes of shielding and exposure of aromatic labels to aqueous environments and therefore to reversible complexation with cyclodextrin. In the special case of polyelectrolytes, since illumination may lead to pH changes,[15] a new approach to optical switching may be possible.[16,17]

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(9) For studies at pH higher than 6, the cyclodextrin was removed by precipitation of **1** with concentrated HCl followed by washing with water and dialysis against 1 N KOH.

(10) Colter, A. K.; Clemens, L. M. *J. Phys. Chem.* **1964**, *68*, 651.

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(13) For leading references to this large literature, see: Bednar, B.; Trnena, J.; Svoboda, P.; Vajda, S.; Fidler, V.; Prochazka, K. *Macromolecules* **1991**, *24*, 2054 and references therein.

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(15) McKiernan, J.; Simoni, E.; Dunn, B.; Zink, J. I. *J. Phys. Chem.* **1994**, *98*, 1006.

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(17) For leading references to chiral optical switches see: Agati, G.; McDonagh, A. F. *J. Am. Chem. Soc.* **1995**, *117*, 4425. Jager, W. F.; de Jong, J. C.; de Lange, B.; Huck, N. P. M.; Meetsma, A.; Feringa, B. L. *Angew Chem., Int. Ed. Engl.* **1995**, *34* (3), 348. Zhang, M.; Schuster, G. B. *J. Am. Chem. Soc.* **1994**, *116*, 4852.