DOI: 10.1002/ange.200501448

Small-Molecule-Induced Folding of a Synthetic Polymer**

*Suhrit Ghosh and S. Ramakrishnan**

The remarkable range of chemical functions that evolution has elicited from biopolymers has inspired chemists to design synthetic systems that can mimic both the structural and functional features of these elegant long-chain molecules. Although the efforts to mimic functions such as molecular recognition, catalysis, and so forth has led to the development of systems such as molecular-imprint polymers,[1] the attempts to understand and emulate structural features has given rise to the area of foldamers.[2] In most such systems, the core design element utilizes multiple inter- or intramolecular noncovalent interactions that can be stabilized/destabilized by an external trigger. The cooperativity and reversibility of these weak noncovalent interactions are, thus, of paramount importance in the design of synthetic analogues that can emulate biological systems.

Supramolecular science, which deals with the design and utilization of noncovalent interactions to build superstructures with small molecular building blocks, has witnessed intense activity over the past decade.[3] The extension of these ideas has resulted in the generation of supramolecular polymers in solution, formed through multiple hydrogen-bonding interactions[4] or through metal–ion coordination between monomeric building blocks.[5] In the context of conventional polymer molecules, a similar approach in which noncovalent interactions occur between neighboring (or equi-spaced) segments within a single polymer chain, has been explored to stabilize specific conformations (secondary structures) in solution.[2] On the basis of these considerations, several research groups have examined new types of oligomers and polymers, which adopt well-defined conformations in solution guided by hydrogen-bonding interactions along the backbone,[6] steric and/or bond-angle constraints,[7] solvophobic effects, and so forth.[8] Although the large majority of foldamers are based on precisely defined oligomers with relatively rigid backbones, far fewer are based on flexible systems.[9]

Recently, we demonstrated that truly flexible synthetic macromolecules can be designed to fold under the influence

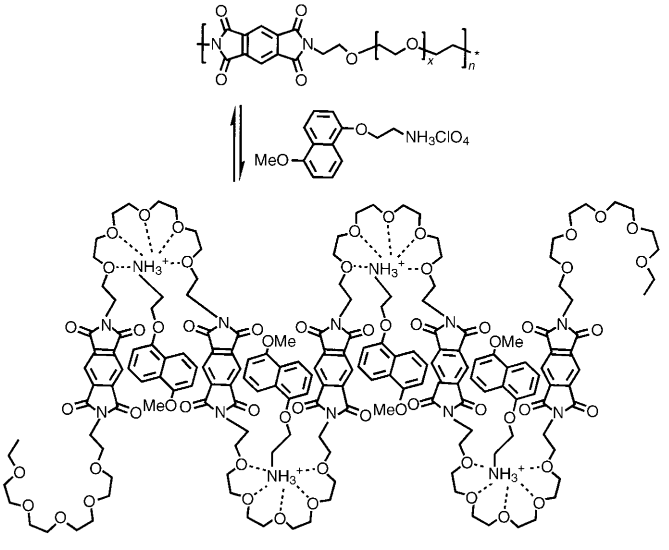
---

[*] S. Ghosh, Prof. S. Ramakrishnan
Department of Inorganic and Physical Chemistry
Indian Institute of Science
Bangalore 560012 (India)
Fax: (+91) 802-360-1552
E-mail: raman@ipc.iisc.ernet.in

[**] We would like to thank DST, New Delhi, and 3M India Ltd, for their financial support.

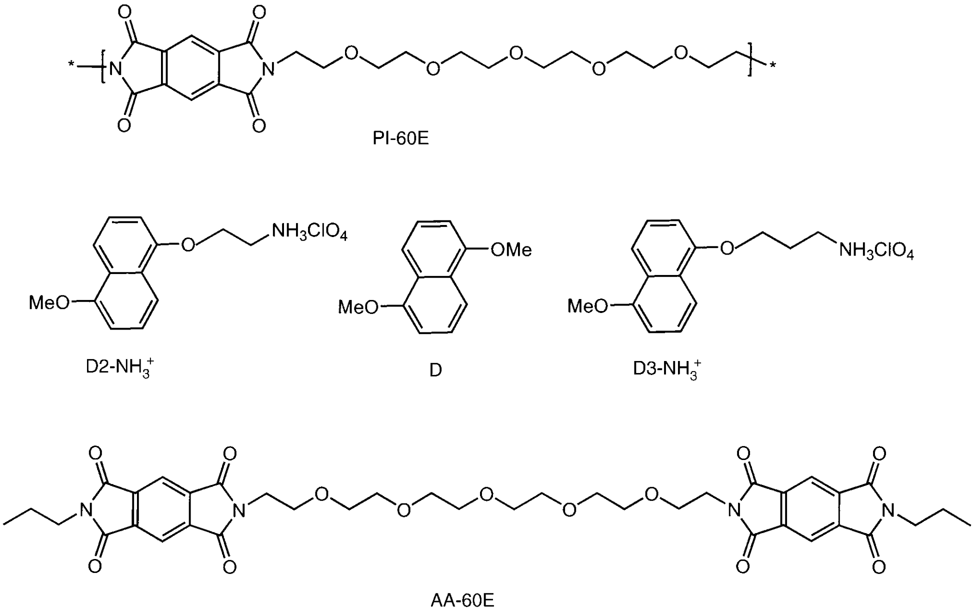
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

of several relatively weak intrachain intersegment interactions, such as formation of a charge-transfer (CT) complex, solvophobic effects, and metal–ion complexation, working in tandem.[10] Detailed spectroscopic studies of these (donor–spacer–acceptor–spacer)$_n$ type polymers, in conjunction with studies of model systems, have suggested the formation of extended donor–acceptor stacks by suitable folding of single polymer chains.[11] In a bid to develop simpler polymeric systems that can fold under similar conditions, we present herein a conceptually new approach for the folding of synthetic polymers based on a polyimide that contains only acceptor units linked by hexaoxyethylene (6OE) spacers of the type (acceptor–spacer)$_n$. In this design, we utilize an external small-molecule folding agent (donor type) that is designed to interact simultaneously with two adjacent segments along the polymer chain so that the polymer folds in a predetermined manner. As depicted in Scheme 1, the design specifically entails the formation of a CT complex between the donors of the folding agent and the acceptors along the polymer chain, in tandem with the complexation of the ammonium group of the folding agent with the 6OE spacer.[12] The latter interaction is expected to restrict the conformation of the flexible OE spacer so that the two adjacent acceptor units along the polymer chain can be brought close enough to form an effective CT interaction with the donor unit in the folding agent. Such a multiple-point interaction, which is key to the development of supramolecular science, has been extensively utilized to enhance associations between small molecules, as well as between polymers and small molecules.[13] An interesting example of the latter is the work of Meijer and co-workers,[14] in which they describe anchoring (clicking-in) small functional molecules onto the periphery of dendrimers through the simultaneous use of electrostatic and hydrogen-bonding interactions.



Scheme 1. Folding of a synthetic polymer aided by two-point interactions with a folding agent.

The polyimide PI-6OE was prepared from the appropriate diamine (derived from hexaethylene glycol)[15] and pyromellitic anhydride under standard conditions for polyimide synthesis.[16] Two folding agents, namely, D2-NH$_3^+$ and D3-NH$_3^+$, that contain a naphthalene donor linked to an ammonium group through a two- or a three-carbon-atom spacer, respectively, were prepared along with 1,5-dimethoxynaphthalene (D) that serves as a model donor which is devoid of the ammonium group (see Scheme 2). The structures of the various model compounds and polymer were confirmed by standard spectroscopic techniques, and the molecular weight M_n of PI-6OE was determined to be 20 500 Da (polydispersity index (PDI) = 1.7) by gel-permeation chromatography (GPC).[17] PI-6OE forms a colorless solution, but an intense yellow color develops in the presence of D2-NH$_3^+$ because of the characteristic CT absorption band at 450 nm.



Scheme 2. Structures of the polymer, model compounds, and folding agents.

The interaction of PI-6OE with the folding agents was investigated by monitoring the intensity of the CT band by UV/Vis spectroscopic analysis and by following the chemical shift of the aromatic protons of the pyromellitic diimide acceptor unit by ^{1}H NMR spectroscopic analysis. Figure 1 depicts the variation in the ^{1}H NMR spectra of PI-6OE with increasing amounts of D2-NH$_3^+$. The signal marked by an arrow, from the pyromellitic diimide unit in the polymer, is seen to move continuously upfield on addition of increasing amounts of the donor species. The remaining signals in the aromatic region are from the naphthalene ring of the folding agent, the intensities of which increase and are accompanied by a small downfield shift.[18]

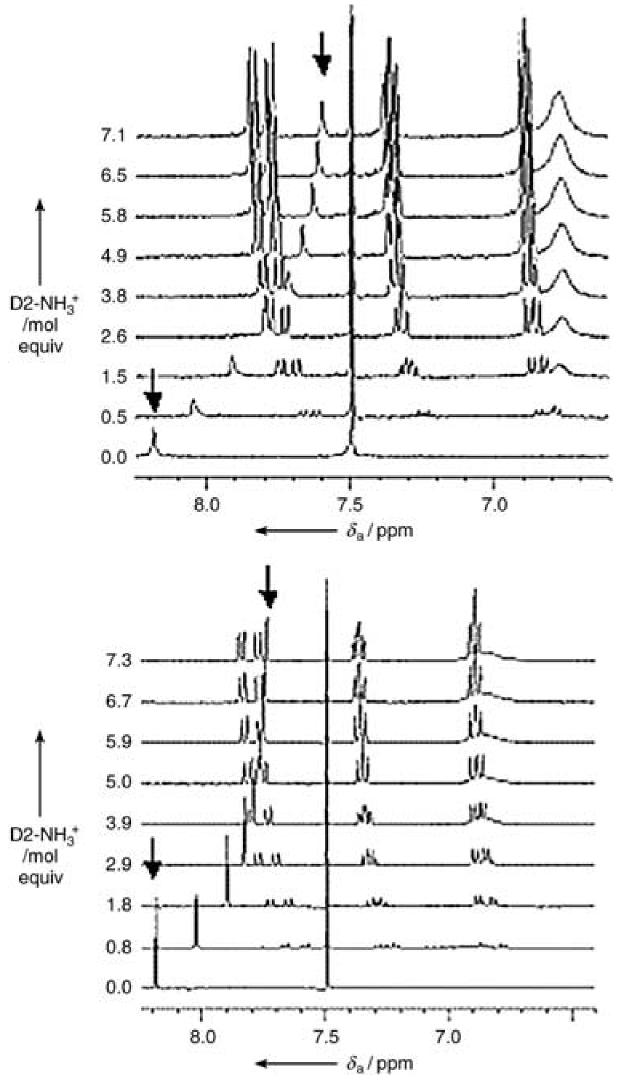


Figure 1. Variation in the aromatic region of the ^{1}H NMR spectra of PI-6OE (top) and AA-6OE (bottom) as a function of the addition of increasing amounts of D2-NH$_3^+$. The signal that arises from the pyromellitic diimide acceptor protons is indicated by an arrow. The solvent used is a CDCl$_3$/CH$_3$CN mixture (1:1, v/v).

A plot of the variation in the chemical shift of the acceptor proton as a function of the concentration of the two different folding agents D2-NH$_3^+$ and D3-NH$_3^+$, along with the simple model donor D as a control experiment, is shown in Figure 2. It is evident that although both the folding agents that contain an ammonium group cause a dramatic change in the δ value, the simple donor molecule that does not contain this group causes only a marginal variation. This upfield shift of the acceptor proton suggests the formation of donor–acceptor CT stacks, as was elaborated in our earlier report.[11] Similarly, a significant increase in the intensity of the CT band in the UV/Vis spectra of the polymer solution occurs in the presence of the two donors that contain ammonium groups while only a marginal increase is seen in the presence of the simple donor (Figure 2), despite the fact that both the control experiments were done in the presence of an equimolar quantity of NH$_4$SCN with respect to D. The independent complexation of the ammonium ion with the OE loop would be expected to at least partially aid the CT interaction with D. These compa-

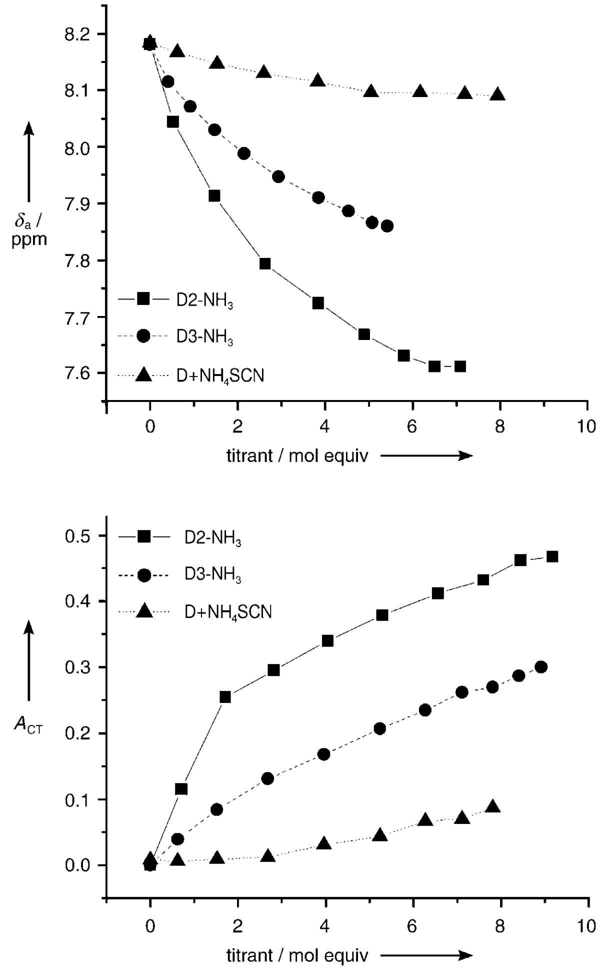


Figure 2. Variation in the chemical shift of the acceptor ring protons δ_a in PI-6OE in the presence of D + NH$_4$SCN, D2-NH$_3^+$, and D3-NH$_3^+$ (top) and variation in the CT band intensity A_{CT} in the presence of D + NH$_4$SCN, D2-NH$_3^+$, and D3-NH$_3^+$ (bottom). The solvent used is CDCl$_3$/CH$_3$CN (1:1). The mole equivalents are calculated with respect to the polymer repeating unit.

rative studies clearly demonstrate the importance of the cooperative two-point interaction, namely, the coordination of the ammonium group with the OE loop and the concomitant CT interaction between the donor and acceptor units, in the generation of the postulated folded structure. Furthermore, as anticipated, the length of the spacer that connects the ammonium group to the naphthalene donor also plays an important role in governing the efficacy of the CT interactions. It is apparent from the variations in the UV/Vis and NMR spectra that D2-NH_3^+ is a more effective folding agent than D3-NH_3^+ (see Figure 2).[19] This dependence on the spacer length reaffirms the importance of the crown ether type complexation of the ammonium group with the OE segment of the polymer in directing the formation of the postulated folded structure.

To probe the extent of the folding, model compound AA-6OE (see Scheme 2) which contains two acceptor units linked by a hexaoxyethylene spacer was synthesized[20] and its interaction with the folding agents studied by both UV/Vis and NMR spectroscopic analysis. The variation in the aromatic region of the ^{1}H NMR spectra of AA-6OE as a function of increasing concentration of the folding agent D2-NH_3^+ is compared with that of the polymer in Figure 1. It is apparent that a significant upfield shift of the acceptor protons is seen in this case as well, although the extent of the shift is clearly smaller in the model compound than in PI-6OE. The variation of the chemical shift of the acceptor proton upon interaction with the two folding agents in the case of the polymer is compared with that of the model compound AA-6OE in Figure 3. For both folding agents, it is clear that the extent of the shift is significantly higher for the polymer than for the model compound. This enhanced shift is clearly a reflection of the fact that the acceptor units in the model can never be sandwiched between two donors, unlike in the case of the polymer in which extended stacking would cause the acceptor units to be sandwiched between two donors. Interestingly, the final chemical shifts of the donor (naphthalene) protons are nearly identical for both the polymer and the model compound (see Figure 1), as expected, because in both cases the donor could become sandwiched between the acceptor units. In addition, as anticipated, the extent of folding exhibits strong temperature dependence, as is evident from the significant upfield shift upon cooling (see inset in Figure 3).[11] Again, it is seen that the polymer exhibits much stronger temperature dependence than the AA-6OE model, thus causing the difference in their chemical shifts to become as large as 0.3 ppm at the lowest temperature probed. We ascribe this difference to the formation of extended stacks in the case of the polymer.[21] To gain further insight into the extent of the stacking, a Job plot was constructed from the absorbance of the CT band, which suggested that the acceptor/donor ratio was 1:0.85 for the polymer PI-6OE (the maximum value in the Job plot was seen at approximately 0.46, see the Supporting Information). Although, in a general sense a ratio of 1:1 need not imply the formation of an extended stack, in our case, however, it can be reasoned that it does confirm the formation of a stack. It is apparent in the present system that the interaction of the ammonium group with the OE spacer is essential for the formation of a CT complex and, more importantly, leads to the sandwiching of the donor between two adjacent acceptors to form an acceptor-donor-acceptor type unit. Evidence for this sandwiching also comes from the Job plot of the model compound AA-6OE, which suggests the formation of an exact 1:1 complex (see the Supporting Information for details). Thus, an acceptor/donor ratio of 2:1 in case of the polymer would suggest the formation of only acceptor–donor–acceptor-type interactions with no extended stacking. On the other hand, if all the OE spacer sites form complexes with the ammonium group of the folding agent, as expected with an acceptor/donor ratio of 1:1, then the formation of an infinitely extended stack is implied. Although the exact scale of the stacking continues to be a challenging problem, a rough estimate on the basis of the Job plot of our polymer suggests the formation of stacks that consist of six donor–acceptor pairs on average.

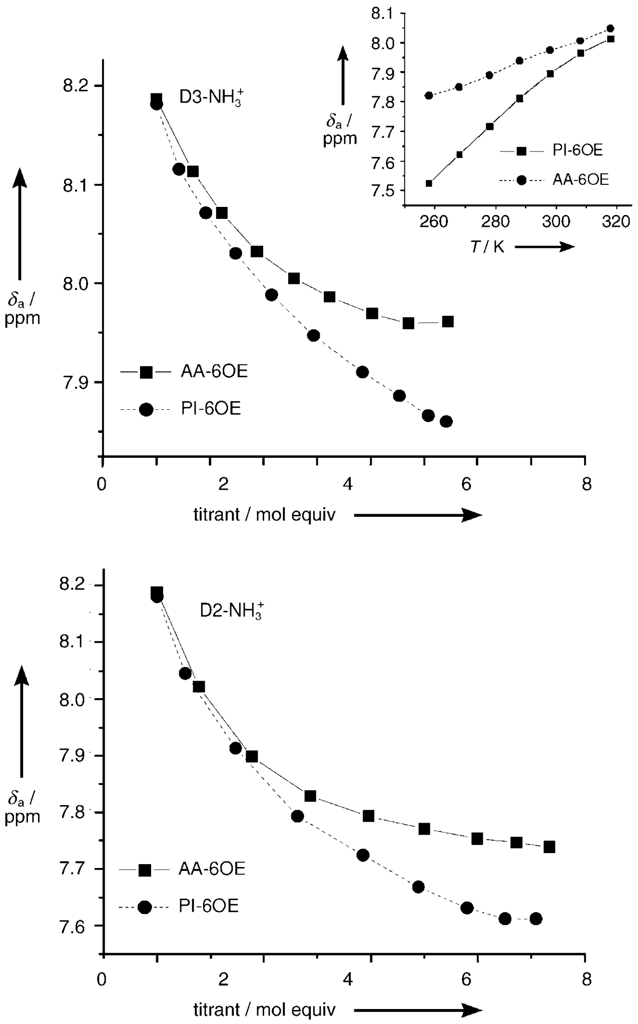


Figure 3. Variation in the chemical shift of the acceptor ring protons δ_a in PI-6OE and AA-6OE in the presence of D3-NH_3^+ (top) and D2-NH_3^+ (bottom). Inset: Effect of temperature on the chemical shift of PA-6OE and AA-6OE in presence of D3-NH_3^+ (the ratio of D3-NH_3^+ to polymer repeating unit/model compound was 4:1).

To test the reversibility of such an interaction-induced folding, an experiment to extricate the folding agent with a crown ether was carried out. Thus, PI-6OE in the folded state (in the presence of 8 equiv of D2-NH_3^+) was titrated with [18]crown-6, which is known to bind very strongly with ammonium ions.[22] In Figure 4, the variation of the chemical shift is plotted, first for the addition of increasing amounts of the folding agent to the polymer and subsequently for the addition of increasing amounts of [18]crown-6. It is clear from the plot that there is a complete reversal of the chemical shift, as a signal with nearly the same value as that for the unfolded polymer is observed, although slightly more than one equivalent of [18]crown-6 was required to effect this complete reversal. The color of the solution changes from deep yellow to nearly colorless at the end of the titration with the crown ether, which is consistent with the complete disappearance of the CT band in the UV/Vis spectra (Figure 4). These experiments clearly confirm that the folding is completely reversible and also suggest that the folding/unfolding equilibrium can be controlled by an appropriate external agent.

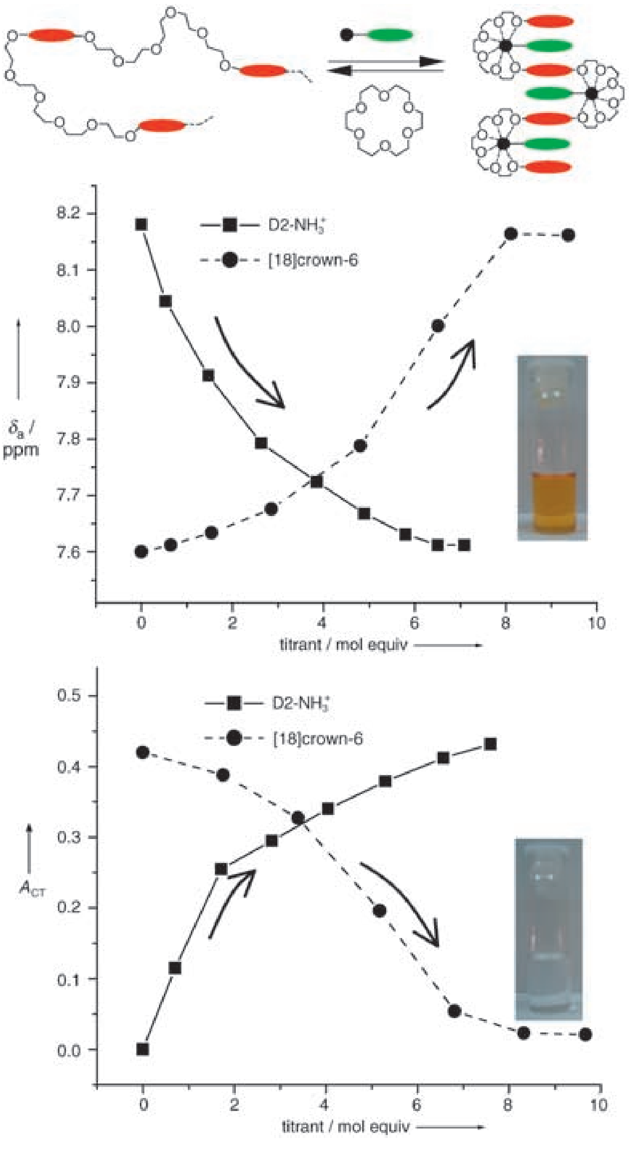


Figure 4. Reversal of the chemical shifts of the acceptor protons δ_a of PI-6OE (top) and the disappearance of CT absorption band (bottom) in the presence [18]crown-6. The mole equivalents were calculated with respect to the polymer repeating unit.

In conclusion, we have demonstrated a new approach to folding a flexible synthetic polymer in solution by utilizing a small molecule as a folding agent. The folding agent was designed to interact cooperatively with two adjacent segments of the polymer chain, such that one interaction facilitates the other, thus leading to the formation of a stacked structure. An ammonium cation in the folding agent forms a complex with a hexaoxyethylene spacer thereby aiding the CT interaction between a naphthalene donor and a pyromellitic diimide acceptor in the polymer. Control experiments with a model naphthalene donor, along with an equimolar amount of an ammonium salt, clearly helped delineate the importance of linking the two interacting subunits in the folding agent, and thereby confirmed the importance of cooperativity in such a folding process. Importantly, the folding was also shown to be completely reversible and the polymer unfolds when the folding agent is extricated by formation of a stronger complex with [18]crown-6. Further work to explore the generality and utility of such a small-molecule-induced folding of synthetic polymers would be of great interest and is currently being studied.

Experimental Section

Pyromellitic dianhydride and 1,5-dihydroxynaphthalene were purchased from the Aldrich Chemical Co. and were purified by sublimation and recrystallization (from nitromethane), respectively. Dry and purified solvents were used in all the syntheses and spectroscopic studies. All the solvents and common synthetic reagents were purified according to standard procedures.[23] The NMR experiments were performed using a Bruker 400 MHz spectrometer and UV/Vis spectra were measured using a Ocean Optics spectrometer. The molecular weights were determined by GPC with chloroform as the eluent at 35 °C, two PL-gel mixed-bed columns were used for separation, and a Viscotek TDA Model 300 was used as the detector. The universal calibration method based on a polystyrene standard was used to estimate the molecular weights. Isothermal titration calorimetry (ITC) experiments were performed with a VP-ITC Microcal LLC instrument in a $CHCl_3/CH_3CN$ solvent mixture (1:1). Mass-spectrometric data were obtained on a Q-TOP Micromass spectrometer. Elemental analysis was performed with a Carlo Erba 1106 CHN analyzer.

Folding studies: In a typical NMR titration experiment, a polymer solution (1.5 mL, 1.92 mM) was prepared in $CDCl_3/CH_3CN$ (1:1 v/v; solution A). An aliquot of this solution (0.6 mL) was placed in the NMR tube and a large excess ($\approx$10–15 equiv) of donor molecule was dissolved in the remaining solution (solution B). Solution A was then titrated with solution B (20–150-μL steps), which resulted in a series of solutions of fixed polymer concentration but with various amounts of donor. Similarly, the UV/Vis experiments were performed in $CHCl_3/CH_3CN$ (1:1).

In the experiment with the crown ether, a solution containing a polymer/donor mixture in a 1:7 ratio in $CHCl_3/CH_3CN$ (1:1) was titrated with a solution of [18]crown-6 in $CHCl_3/CH_3CN$ (1:1) that also contained a polymer/donor mixture in a 1:7 ratio. Therefore, the concentration and relative molar ratios of the polymer and donor molecules were kept constant, and the only variable was the concentration of [18]crown-6. The Job plot experiment based on UV/Vis spectroscopic analysis was performed in $CHCl_3/CH_3CN$ (1:1), and the total concentration (polymer + folding agent) was maintained at 12 mM for the polymer and 6 mM for the model compound.

Synthesis of the polymer: Hexaethylene glycol diamine[15] (0.494 g, 1.76 mmol) was placed in the reaction vessel and dissolved in freshly distilled *m*-cresol (3 mL). The purified pyromellitic dianhydride (0.384 g, 1.76 mmol) was added to this solution in one portion, and the reaction mixture was stirred at 85 °C for 2 h under a continuous flow of N_2 gas. The reaction mixture was cooled to room temperature, and *m*-cresol (2 mL), dry toluene (5 mL), and isoquinoline (8 drops) were added. The reaction mixture was stirred at 185 °C for another 6 h in an inert atmosphere with continuous azeotropic removal of water. The reaction mixture was cooled to room temperature, and the viscous liquid was poured into methanol (50 mL). The fine powdery precipitate was centrifuged, redissolved in a minimum volume of chloroform, and reprecipitated from methanol to obtain the desired polymer as a white fibrous material. The product was dried under vacuum at 100 °C for 3 h. Yield: 62 %.

For fractionation, methanol was added dropwise to a solution of the polymer (150 mg) in chloroform (10 mL) until the solution became cloudy. The mixture was stirred for another 15 min as a colorless oil separated and stuck to the walls of the vessel. The supernatant was decanted, and the oil was dissolved in chloroform (1 mL) and reprecipitated from methanol to form the fibrous colorless polymer. The product was dried under vacuum for 3 h at 100 °C, and the recovery was found to be approximately 30 %.

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.257$ (s, 2H, Ar-H), 3.950 (t, 4H, N-CH_2), 3.768 (t, 4H, N-CH_2-CH_2-), 3.658–3.581 ppm (m, 16H, rest of the oligoethylene protons); ^{13}C NMR: $\delta = 166.17$, 137.26, 118.27, 70.59, 70.53, 70.03, 67.68, 37.93 ppm. Elemental analysis (%) calcd for $C_{22}H_{26}N_2O_9$: C 57.14, H 5.66, N 6.06; found: C 56.82, H 5.51, N 5.93.

Received: April 27, 2005

Keywords: charge transfer · crown compounds · donor–acceptor systems · polymer folding

---

[1] a) G. Wulff, *Chem. Rev.* **2002**, *102*, 1; b) K. Haupt, K. Mosbach, *Chem. Rev.* **2000**, *100*, 2495; c) *Molecularly Imprinted Polymers, Man-Made mimics of Antibodies and their Application in Analytical Chemistry* (Ed.: B. Sellergren), Elsevier, New York, **2001**; d) S. C. Zimmerman, N. G. Lemcoff, *Chem. Commun.* **2004**, 5.

[2] a) S. H. Gellman, *Acc. Chem. Res.* **1998**, *31*, 173; b) D. J. Hill, M. J. Mio, R. B. Prince, T. S. Huges, J. S. Moore, *Chem. Rev.* **2001**, *101*, 3893; c) C. Schmuck, *Angew. Chem.* **2003**, *115*, 2552; *Angew. Chem. Int. Ed.* **2003**, *42*, 2448.

[3] a) J. M. Lehn, *Supramolecular Chemistry—Concepts and Perspectives*, Wiley-VCH, Weinheim, **1995**; b) C. A. Schalley, A. Lutzen, M. Albrecht, *Chem. Eur. J.* **2004**, *10*, 1072.

[4] a) J.-M. Lehn, *Supramolecular Polymers* (Ed.: A. Cifferi), Marcel Dekker, New York, **2000**, p. 615; b) S. C. Zimmerman, P. S. Corbin, *Struct. Bonding (Berlin)* **2000**, *96*, 63; c) L. Brunsveld, J. A. J. M. Vekemans, J. H. K. K. Hirschberg, R. P. Sijbesma, E. W. Meijer, *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 4977; d) R. P. Sijbesma, E. W. Meijer, *Chem. Commun.* **2003**, 5; e) L. Brunsveld, B. J. B. Folmer, E. W. Meijer, R. P. Sijbesma, *Chem. Rev.* **2001**, *101*, 4071; f) V. Berl, M. Schmutz, M. J. Krische, R. G. Khoury, J.-M. Lehn, *Chem. Eur. J.* **2002**, *8*, 1227.

[5] a) D. Yu-Bin, W. Peng, H. Ru-Qi, D. S. Mark, *Inorg. Chem.* **2004**, *43*, 4727; b) U. S. Schubert, C. Eschbaumer, *Angew. Chem.* **2002**, *114*, 3016; *Angew. Chem. Int. Ed.* **2002**, *41*, 2892; c) H. Hofmeier, U. S. Schubert, *Chem. Soc. Rev.* **2004**, *33*, 373; d) P. R. Andres, U. S. Schubert, *Adv. Mater.* **2004**, *16*, 1043; e) B. J. Benjamin, J. J. R. Stuart, *J. Am. Chem. Soc.* **2003**, *125*, 13922.

[6] a) Y. Hamuro, S. J. Geib, A. D. J. Hamilton, *J. Am. Chem. Soc.* **1997**, *119*, 10587; b) Y. Hamuro, S. J. Geib, A. D. J. Hamilton, *J. Am. Chem. Soc.* **1996**, *118*, 7529; c) J. Zhu, R. D. Parra, H. Zeng, E. Skrzypczak-Jankun, X. C. Zeng, B. Gong, *J. Am. Chem. Soc.* **2000**, *122*, 4219; d) L. Yuan, H. Zeng, K. Yamato, A. R. Sanford, W. Feng, H. S. Atreya, D. K. Sukumaran, T. Szyperski, B. Gong, *J. Am. Chem. Soc.* **2004**, *126*, 16528.

[7] a) V. Berl, I. Huc, R. G. Khoury, J. M. Lehn, *Nature* **2000**, *407*, 720; b) A. Petitjean, L. A. Cuccia. J. M. Lehn, H. Nierengarten, M. Schmutz, *Angew. Chem.* **2002**, *114*, 1243; *Angew. Chem. Int. Ed.* **2002**, *41*, 1195.

[8] a) A. Tanatani, M. J. Mio. , J. S. Moore, *J. Am. Chem. Soc.* **2001**, *123*, 1792; b) R. B. Prince, L. Brunsveld, E. W. Meijer, J. S. Moore, *Angew. Chem.* **2000**, *112*, 234; *Angew. Chem. Int. Ed.* **2000**, *39*, 228; c) J. C. Nelson, J. G. Saven, J. S. Moore, P. G. Wolynes, *Science* **1997**, *277*, 1793; d) J. M. Heemstra, J. S. Moore, *J. Am. Chem. Soc.* **2004**, *126*, 1648; for related polymeric systems, see; e) R. S. Hecht, A. Khan, *Angew. Chem.* **2003**, *115*, 6203; *Angew. Chem. Int. Ed.* **2003**, *42*, 6021; f) L. Arnt, G. N. Tew, *Macromolecules* **2004**, *37*, 1283.

[9] a) W. Wang, L.-S. Li, G. Helms, H.-H. Zhou, A. D. Q. Li, *J. Am. Chem. Soc.* **2003**, *125*, 1120; b) A. D. Q. Li, W. Wang, L.-Q. Wang, *Chem. Eur. J.* **2003**, *9*, 4594; c) E. E. Neuteboom, S. C. J. Maskers, E. W. Meijer, R. A. J. Janssen, *Macromol. Chem. Phys.* **2004**, *205*, 217; d) R. S. Lokey, B. L. Iverson, *Nature* **1995**, *375*, 303; e) J. Q. Nguyen, B. L. Iverson, *J. Am. Chem. Soc.* **1999**, *121*, 2639; f) A. J. Zych, B. L. Iverson, *J. Am. Chem. Soc.* **2000**, *122*, 8898; g) G. J. Gabriel, B. L. Iverson, *J. Am. Chem. Soc.* **2002**, *124*, 15174; h) M. A. Balbo Block, S. Hecht, *Macromolecules* **2004**, *37*, 4761.

[10] S. Ghosh, S. Ramakrishnan, *Angew. Chem.* **2004**, *116*, 3326; *Angew. Chem. Int. Ed.* **2004**, *43*, 3264.

[11] S. Ghosh, S. Ramakrishnan, *Macromolecules* **2005**, *38*, 676.

[12] K^+ and $NH_4{}^+$ ions are known to have similar size-selective preferences on complexation with crown ethers. We have shown that a donor–acceptor polymer that contains a 6OE spacer forms complexes most strongly with K^+ ions.[10,11] Therefore, a polyimide that contains 6OE spacers was chosen in the present study. For reviews of the complexation of crown ethers and podands with cations, see: a) G. K. Gokel, W. M. Leevy, M. E. Weber, *Chem. Rev.* **2004**, *104*, 2723; b) H. G. Lohr, L. F. Vogtle, *Acc. Chem. Res.* **1985**, *18*, 65, and references therein; c) *Comprehensive Supramolecular Chemistry, Vol. 1* (Ed.: G. W. Gokel), Pergamon/Elsevier, Oxford, **1996**; d) R. M. Izatt, J. S. Brad-Shaw, S. A. Nielsen, J. D. Lamb, J. J. Christensen, *Chem. Rev.* **1985**, *85*, 271.

[13] a) G. Kaiser, T. Jarrosson, S. Otto, Y.-F. Ng, A. D. Bond, J. K. M. Sanders, *Angew. Chem.* **2004**, *116*, 1993; *Angew. Chem. Int. Ed.* **2004**, *43*, 1959; b) L. Kovbasyuk, R. Kramer, *Chem. Rev.* **2004**, *104*, 3161; c) F. Ithan, G. K. Blanchette, V. Rotello, *Macromolecules* **1999**, *32*, 6159; d) V. Berl, M. J. Krische, I. Huc, J. M. Lehn, R. Schmutz, *Chem. Eur. J.* **2000**, *6*, 1938.

[14] M. W. P. L. Baars, A. J. Karlsson, V. Sorokin, B. F. W. Waal, E. W. de Meijer, *Angew. Chem.* **2000**, *112*, 4432; *Angew. Chem. Int. Ed.* **2000**, *39*, 4262.

[15] For synthetic details, see the Supporting Information.

[16] J. G. Liu, M. H. He, Z. X. Li, Z. G. Qian, F. S. Wang, S. Y. J. J. Yang, *J. Polym. Sci. A* **2002**, *40*, 1572.

[17] All spectral data and gel-permeation chromatograms are available in the Supporting Information.

[18] The increase in intensity is simply a reflection of the increase in the concentration of the donor species, whereas the downfield shift arises from the mole-fraction weighted average of the free and complexed naphthalene units. It may be recalled that formation of a CT complex generally causes an upfield shift of

both the donor and acceptor units,[11] however, the downfield shift of the donor protons in this case arises from the overwhelming presence of free donor species.

[19] The association constants of the two folding agents with AA-6OE were determined from the variation in the chemical shift of the acceptor ring protons as a function of the folding-agent concentration by using computer program EQNMR version 2.10. (Freeware, M. J. Hynes, Chemistry Department, University College Galway, Ireland). The K values were found to be 850 and 600M^{-1} for D2-NH_3^+ and D3-NH_3^+, respectively, but only 30M^{-1} for $D + NH_4^+$, thus confirming the cooperativity of the interaction, as well as the importance of the spacer length for effective binding and folding. The association constant for D2-NH_3^+ was also determined from ITC and was found to be 1050M^{-1}, which is comparable to that obtained with NMR spectroscopic analysis. Similar attempts to determine the association constant for the polymer with ITC was difficult as a simple plot that assumed a single association constant failed to give a good fit. A probable reason for this failure is that several different values of association constants could, in principle, be required in the case of the polymer. Nevertheless, it is clear from the values of K obtained for the model AA-6OE that linking the two interacting segments in the folding agent is critical for the generation of a folded structure in the polymer.

[20] For synthetic details, see the Supporting Information.

[21] The variable temperature experiment was done using D3-NH_3^+ as the folding agent at a ratio of 4:1 molar equivalents with respect to the polymer repeating unit to ensure that the ammonium salt did not precipitate on cooling.

[22] [18]Crown-6 is known to form a very strong complex with ammonium ions with an association constant K in the order of $10^6\,\text{M}^{-1}$; see reference [12a].

[23] D. D. Perrin, W. L. F. Armarego, D. R. Perrin, *Purification of Laboratory Chemicals*, 2nd ed., Pergamon, Oxford, **1980**.