Folded Polymers

Aromatic Donor–Acceptor Charge-Transfer and Metal-Ion-Complexation-Assisted Folding of a Synthetic Polymer[**]

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Synthetic polymers typically adopt a random-coil conformation in solution primarily driven by the tendency to maximize entropy. Generation of well-defined secondary structures in synthetic polymers, therefore, will need to include specific intrachain intersegment interactions that will provide adequate enthalpic contribution to overcome this entropic penalty associated with the formation of well-ordered conformations.[1] The motivation to generate synthetic polymers with a precisely controlled conformation stems from the desire to emulate the elegance of nature on the one hand, while at the same time from the expectation that this will enable one to bridge the gap between the molecular and the macroscopic scales in terms of the evolution of structural order. The term "foldamer"[2] is used to describe synthetic polymers that can be made to adopt well-defined conformations in solution, such as a helix, by inclusion of specific intrachain interactions, such as hydrogen bonding, steric and/or bond-angle constraints along the backbone, solvophobic interactions, etc.[3] Although several examples of synthetic polymers that adopt helical conformations in solutions are known, for example, poly(trityl methacrylate)s,[4] polyisocyanates,[5] *cis*-poly(acetylene)s,[6] polyisocyanides,[7] and poly(1,3-phenylene ethynylene)s,[8] most of these deal with relatively stiff chains that have very limited conformational degrees of freedom as a result of steric and/or bond-angle constraints. There are, however, only very few examples of relatively flexible systems that have been made to adopt a well-defined conformation in solution. Iverson and co-workers[9] described one such system in a series of elegant papers in which they demonstrated the possibility of forming folded structures in specifically designed oligomers by virtue of specific intrachain aromatic donor–acceptor charge-transfer interactions aided by solvophobic effects. Thus far, most studies on flexible foldamers have dealt only with precisely defined oligomers,[10] and to the best our knowledge there are no reports on analogous polymeric systems.[10c] Thus, in an effort to explore directed folding in truly flexible synthetic polymers, we designed and synthesized a segmented donor–acceptor polyimide **3**, which contains three design elements

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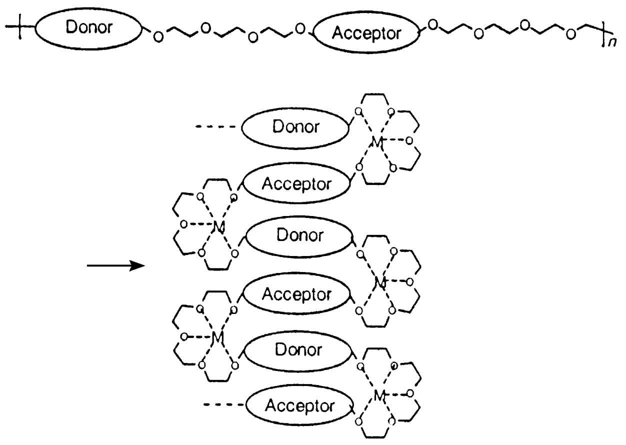
that could induce folding in tandem under appropriate conditions. The three design elements are: 1) alternate placement of aromatic donor and acceptor units that could form an intrachain donor–acceptor charge transfer complex, analogous to the Iverson systems, 2) a hexa(ethylene oxide) linking segment that could impart a solvophobic driving force to folding, and 3) the alkali-metal-ion complexation ability of the flexible oligoethylene oxide segment that could further assist in the formation of folded structures by restricting the conformational freedom of the loop, which in turn should further aid the formation of the donor–acceptor charge-transfer complex.[11] A schematic representation of such a folded structure is shown in Scheme 1.



Scheme 1. The folding process.

Polymer **3** was prepared through standard polyimide synthesis methodology from diamine **1** (which contains the appropriate naphthalene (donor) and oligoethylene oxide moieties) and pyromellitic dianhydride (**2**; Scheme 2). The diamine **1** was synthesized in several steps from 1,5-dihydroxynaphthalene.[12] The polymer was structurally characterized by ^{1}H and ^{13}C NMR spectroscopy and elemental analysis, and its molecular weight was determined to be about 17000 (M_n, PDI ~ 2.0) by GPC in THF, using a triple detector system. The ^{1}H NMR spectrum (Figure 3) clearly shows the presence of the naphthalene protons (3 sets, $\delta = 6.7$–7.6 ppm) and a single signal for the pyromellitic diimide protons ($\delta = 7.9$ ppm), in addition to the oligoethylene oxide proton signals in the aliphatic region (not shown). The polymer was readily solution-cast to give bright red films, which clearly suggests the formation of a strong charge-transfer complex in the solid state.[13]

The formation of intrachain charge-transfer complex between the adjacent donor and acceptor units not only provides the driving force for the formation of the anticipated folded structure but also serves as a spectroscopic probe to examine the formation of such a structure. The UV/Vis absorption spectrum of the polymer in chloroform ($c = 0.23$ mM) is shown in Figure 1. The charge-transfer absorption band is clearly visible at 450 nm, which is well separated from the other absorption bands owing to the individual donor and acceptor units. For comparison, the absorption spectrum of a mixture of model donor and acceptor molecules,[14] at the same concentration as that of the polymer (considering the repeat unit), is also shown in Figure 1. It is clear from the significantly larger charge-transfer absorbance (see inset in Figure 1) that linking of the donor and acceptor units in an alternating fashion along the polymer backbone enhances the formation of the charge-transfer complex.[15] Confirmation that such a complex is indeed formed intramolecularly (intrachain) was obtained by dilution experiments (in the range 0.7–0.06 mM), which shows the expected Beer–Lambert law dependence (inset in Figure 1).

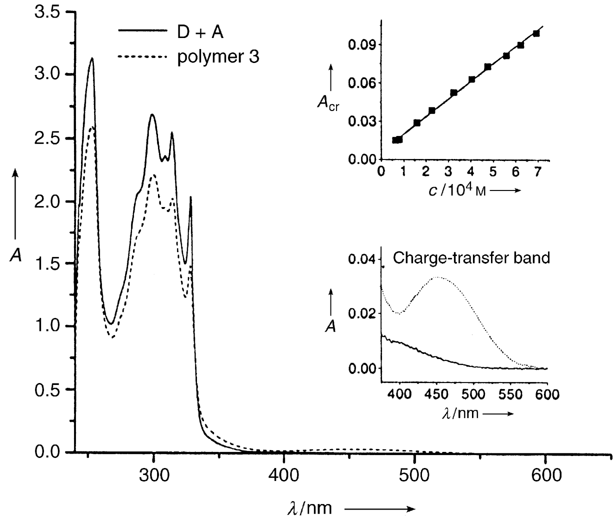
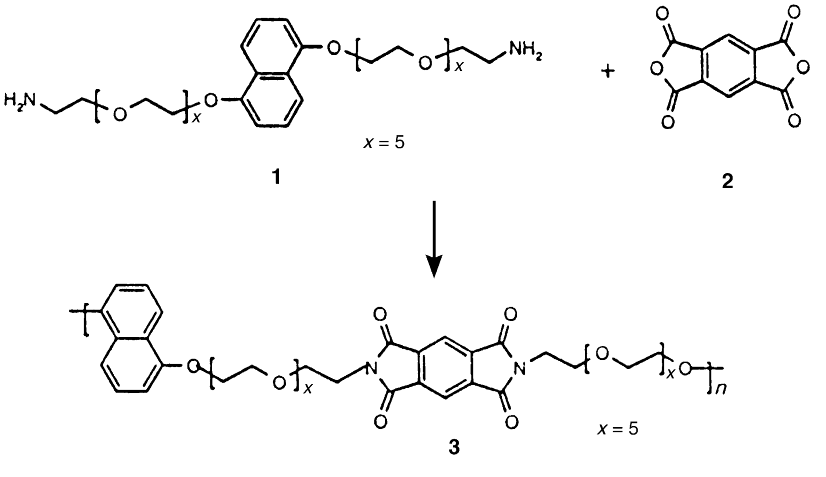


Figure 1. Comparison of UV/Vis spectra of polymer **3** and a mixture of analogous model donor and acceptor compounds in chloroform. Insets: bottom: expanded region of the charge-transfer band; top: variation of charge-transfer absorbance with concentration. D = donor, A = acceptor.



Scheme 2. Synthesis of the polymer **3**.

To examine whether the difference in solubility characteristics between the aromatic units and the oligoethylene oxide loop can be utilized to induce folding (solvophobic effect), we carried out a solvent titration experiment in chloroform/methanol. A noticeable increase in the charge-transfer absorption band intensity with increasing methanol composition is evident from Figure 2. A plot of the concentration-corrected normalized absorbance as a function of solvent composition (inset in Figure 2) shows a small initial decrease in the intensity before the onset of the increase. The initial decrease is ascribed to possible destabilization of the donor–acceptor charge-transfer complex in polar solvents,[16] which is later overcome by the solvent-induced conformational transition of the polymer chain, which apparently forces closer contacts between the donor and acceptor units.[17] An increase in the methanol content beyond a certain value makes the solution visibly cloudy owing to the onset of precipitation. This was also seen from a second abrupt rise in the apparent absorbance (not shown) as a result of scattering losses arising from precipitation. To further confirm that the first increase in the charge-transfer absorbance, prior to precipitation, is indeed due to solvent-induced enhancement in the intrachain charge-transfer complex formation, dilution experiments maintaining the solvent composition as that just prior to precipitation (43 % v/v CH_3OH in $CHCl_3$) were done, which again exhibited the expected Beer–Lambert dependence.

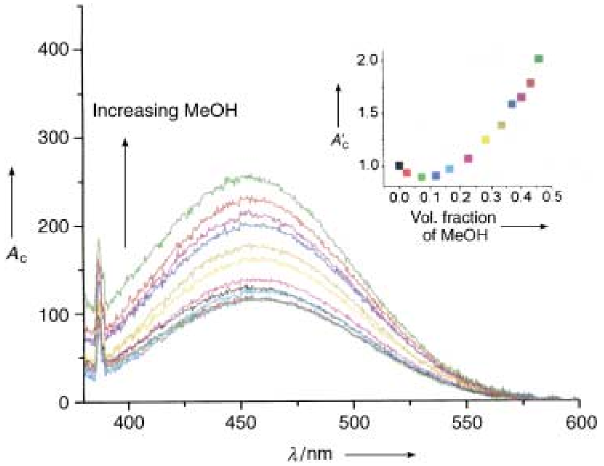


Figure 2. Variation of UV/Vis spectra of polymer **3** in chloroform with increasing amounts of methanol. The inset shows the variation of normalized concentration-corrected charge-transfer absorbance (A_c') as a function of methanol volume fraction. A_c = concentration-corrected absorbance.

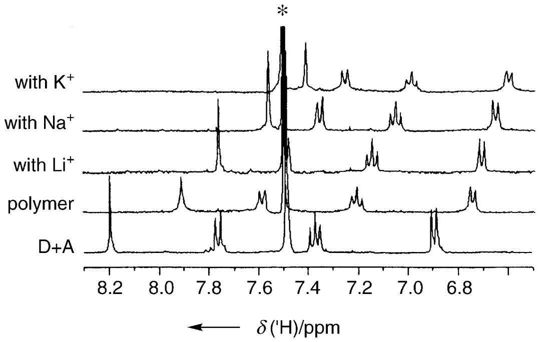


Figure 3. The aromatic region of the ^1H NMR spectra of polymer **3** in the presence of various alkali-metal ions (ca. ninefold excess) in $CDCl_3/CH_3CN$ (1:1 v/v). For comparison, the spectrum of an equimolar mixture of model compounds (D+A) is also given. The peak indicated with the * is due to the solvent.

^1H NMR spectroscopic studies of the polymer provide further unequivocal evidence for the formation of an intrachain donor–acceptor charge-transfer complex. First, it is observed that signal for the acceptor proton ($\delta = 7.9$ ppm) undergoes a considerable upfield shift upon the formation of the charge-transfer complex; the signals for the donor protons also undergo a similar but smaller upfield shift.[18] In Figure 3, we compare the ^1H NMR spectra of a mixture of donor and acceptor model compounds (D+A)[14] with that of the polymer **3**; it is clearly evident that the chemical shift of the acceptor proton in the latter case is significantly shifted upfield relative to the former, reconfirming the greater propensity for the polymer to form a charge-transfer complex. In the presence of a polar solvent such as acetonitrile (50 % v/v CH_3CN in $CDCl_3$), a further upfield shift of signal for the aromatic acceptor proton[19] is seen, and this we ascribe to the solvophobic effect, which was earlier seen in the absorption spectra as well. More importantly, in the presence of an alkali-metal ion, the formation of the charge-transfer complex is further enhanced, as is evident from the variation of the NMR spectrum as a function of increasing amounts of metal ions, such as K^+ (Figure 4).

It is apparent from Figure 4 that the signal for the acceptor proton undergoes the most significant upfield shift, which

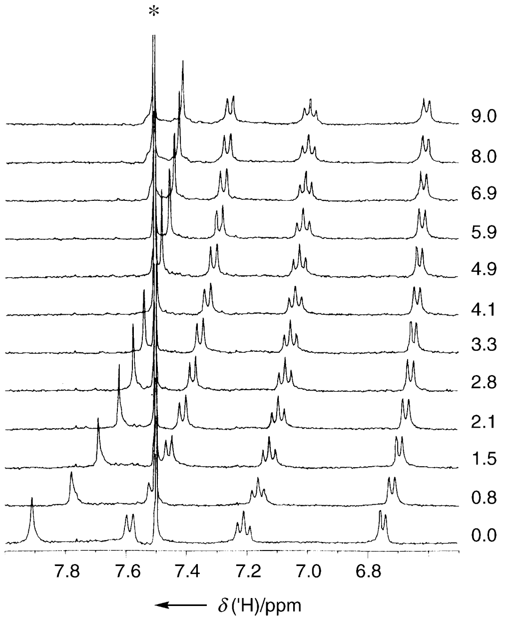


Figure 4. Variation of the aromatic region of the ^1H NMR spectra of polymer **3** with increasing amounts of KSCN in $CH_3CN/CDCl_3$ (50 % v/v). The numbers on the right represent the mole equivalents of the salt with respect to the polymer repeat unit. The peak indicated with the * is due to the solvent.

appears to level off at higher concentrations of K^+ ions. Similar changes in the spectrum are also seen in the presence of both Li^+ and Na^+ ions, but the extent of the change is smaller. In Figure 3, the aromatic region of the spectra in the presence of an excess of different alkali-metal ions (approximately ninefold excess) is compared and clearly reflects these differences. In Figure 5, the variation in the chemical shift of the acceptor proton as a function of the metal-ion concentration for various metal ions, along with a similar comparison of the absorbance of the charge-transfer band in the absorption spectra, is presented. It is clear from this comparison that the extent of variation in both the spectral methods is largest for K^+ followed by Na^+ and Li^+. The variation in chemical shift was used as an indicator of the extent of metal-ion complexation to calculate the apparent association constant K to be 85, 356, and 299 mol^{-1} for Li^+, Na^+, and K^+, respectively.[20] Importantly, the enhanced charge-transfer complex formation in the presence of alkali-metal ions, and the apparent ionic size-dependant complexation ability of the hexaethylene oxide loop, is clear evidence in support of the hypothesis that the aromatic charge-transfer interactions are indeed occurring between adjacent donor and acceptor units along the polymer chain. The changes in the aliphatic region of the NMR spectra in the presence of the metal ion helps to reconfirm that the complexation of the hexaethylene oxide loop indeed occurs with the metal ion, as seen from the considerable downfield shift of several of the signals for the methylene protons along with an enhanced discrimination between the different types of methylene units.[21] In an effort to see if the molecular weight of the polymer has any effect on the folding, the nascent polymer was fractionated and the high-molecular-weight fraction ($M_n = 52000$, PDI = 1.2) was used to carry out two representative experiments. The variations in the ^{1}H NMR and the UV/Vis spectra as a function of K^+ ion concentration was monitored and found to be similar to those exhibited by the nascent polymer (see Figure 5). This helped to confirm that the molecular weight has very little effect on the folding process, at least in the range investigated.

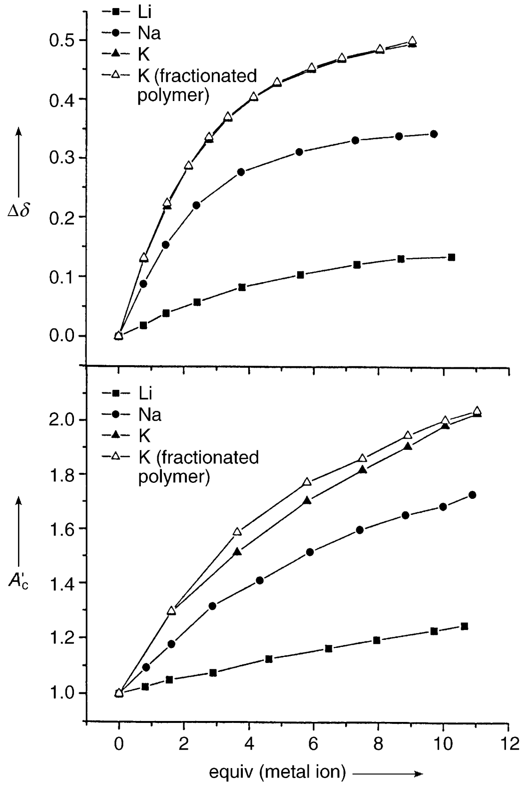


Figure 5. The change in chemical shift (Δδ) of the acceptor proton of polymer **3** (top) and charge-transfer absorbance (bottom) as a function of different alkali-metal ion concentrations. The open symbols represent changes observed in the high-molecular-weight fractionated sample. A_c' = normalized concentration-corrected charge-transfer absorbance.

In conclusion, we have demonstrated that by proper design, flexible synthetic macromolecules can be made to fold under the influence of relatively weak intrachain intersegment interactions, such as charge-transfer complex formation, assisted in tandem by solvophobic effects and metal-ion complexation of a flexible oligoethylene oxide loop—leading to a stacking of aromatic donor and acceptor segments enveloped by the relatively hydrophilic oligoethylene oxide loops that wrap around suitable metal ions by coordination (as depicted in Scheme 1). The maximum probability of such a folded state is seen when all the three effects are present at the same time, which occurs in a relatively polar medium in the presence of an alkali-metal ion. The number of stacked donor and acceptor units, which would be a truer reflection of the extent of folding, remains a difficult question that needs further investigations. Preliminary studies of model compounds of the type donor–oligoethylene oxide acceptor (DA) and analogous DAD and ADA, clearly suggest that the stacking exceeds simple pairing of the donor and acceptor units. Further studies are currently underway to probe this aspect in greater detail with possible inclusion of chirality, which will enable the use of CD methods as a probe for the extent of stacking.

Experimental Section

Polymer **3** was prepared from the diamine **1** and pyromellitic dianhydride **2** under standard polyimide preparation conditions, using *m*-cresol as a solvent during the first step at 80 °C, followed by a polyimidization step at a higher temperature (185 °C), which was done under continuous azeotropic (toluene) removal of water.[12] The polymer formed was purified by repeated reprecipitation from chloroform/methanol. A high-molecular-weight fraction was separated by fractionation with chloroform/methanol, and independently studied to assess the role of molecular weight. Dry and purified solvents were used in all the NMR and UV/Vis spectroscopic experiments. The NMR studies were carried out on a Bruker 400 MHz NMR machine and the UV/Vis spectra were measured on an Hitachi spectrometer. The alkali-metal salts were purified by recrystallization before use. For NMR complexation studies, 1.5 mL of the polymer solution was prepared in 1:1 $CDCl_3/CH_3CN$ (concentration range 1–3 mM) (solution A). A calculated amount of the appropriate alkali-metal salt (≈20–25 equiv with respect to the polymer repeat unit) was added to 0.9 mL of solution A (solution B). Solution A (0.6 mL) was then taken in an NMR tube and titrated with solution B (in 20–100 μL steps), which resulted in a series of solutions with a fixed polymer concentration but varying amounts of the alkali-metal salts. The UV/Vis studies were also carried out in a similar manner, maintaining a fixed polymer concentration of 1 mM, in the same solvent mixture. In the solvent titration experiment, the polymer solution in chloroform was diluted in steps with a measured volume of methanol and the charge-transfer band intensity was monitored. The spectra were then corrected to adjust for the decreasing polymer concentration with dilution. The NMR studies were also done similarly, and the peak positions were monitored with varying composition.

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[12] Experimental details regarding the synthesis and characterization of the monomer and the polymer are available in the Supporting Information.

[13] In contrast, the homopolyimide, which is devoid of the naphthalene unit, prepared from simple amine terminated oligoethylene glycol and pyromellitic dianhydride, is white in colour.

[14] 1,5-Dimethoxynaphthalene was used as the model donor and the pyromellitic diimide prepared from pyromellitic dianhydride with 2-[2-(2-methoxyethoxy)ethoxy]ethylene amine was used as the model acceptor.

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[17] A similar variation in the chemical shift of the acceptor protons, going through a maximum with increasing solvent polarity was noticed, which confirms the initial decrease prior to the increase in the apparent association constant. Detailed NMR spectral evolution as a function of solvent composition is included in the Supporting Information.

[18] Similar upfield shifts of the signals for the donor and acceptor protons upon charge-transfer complex formation was previously reported, and may be ascribed to the perturbation of the aromatic ring current causing a shielding effect: a) Y. Nakamura, S. Minami, K. Iizuka, J. Nishimura, *Angew. Chem.* **2003**, *115*, 3266; *Angew. Chem. Int. Ed.* **2003**, *42*, 3158; see also reference [9c].

[19] The chemical shift value of the acceptor proton in pure $CDCl_3$ is 8.07 ppm as compared to 7.9 ppm in $CDCl_3/CH_3CN$ (1:1 v/v). In contrast, there was no change in the chemical shifts in the case of a mixture of the model compounds at the same concentration.

[20] The program EQNMR version 2.10 was used to calculate the K values from the variation of the chemical shift of the acceptor proton. (Freeware developed by M. J. Hynes, Chemistry Department, University College, Galway, Ireland). It is evident that the association constant does not directly parallel the extent of change seen in either the charge-transfer absorbance or the chemical shift. It may be reasoned that the extent of change experienced by the donor and acceptor units (both in their NMR and UV/Vis spectra), owing to metal-ion complexation by the loop, would greatly depend on the final geometry of the donor–acceptor complex. Thus, formation of a strong complex with the metal ion need not necessarily bring the donor and acceptor units in the optimum geometry for most effective charge-transfer interaction. Further studies are currently being done on model conor–acceptor oligomers to gain better insight into these aspects.

[21] The maximum change is noticed for the methylene protons of the central region of the loop, which move downfield, whereas the methylene protons immediately adjacent to the chromophores move slightly upfield with K^+ and Na^+ and change little in the case of Li^+. A similar variation was reported by Vogtle and co-workers in the case of podands (see reference [11a]). All the spectral variations are included in the Supporting Information.