Understanding the folding process of synthetic polymers by small-molecule folding agents

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Abstract.   Two acceptor containing polyimides PDI and NDI carrying pyromellitic diimide units and 1,4,5,8-naphthalene tetracarboxy diimide units, respectively, along with hexa(oxyethylene) (EO6) segments as linkers, were prepared from the corresponding dianhydrides and diamines. These polyimides were made to fold by interaction with specifically designed folding agents containing a dialkoxynaphthalene (DAN) donor linked to a carboxylic acid group. The alkali-metal counter-ion of the donor carboxylic acid upon complexation with the EO6 segment brings the DAN unit in the right location to induce a charge–transfer complex formation with acceptor units in the polymer backbone. This two-point interaction between the folding agent and the polymer backbone leads to a folding of the polymer chain, which was readily monitored by NMR titrations. The effect of various parameters, such as structures of the folding agent and polymer, and the solvent composition, on the folding propensies of the polymer was studied.

Keywords.   Polyimides; NMR titration; foldamer; folding agent.

1. Introduction

Control of polymer conformation in solution is an exciting challenge as this confronts the entropy-driven proclivity for long chain molecules to adopt a random conformation. Inspiration for such an endeavour comes from biology, wherein much of the function derived from biomacromolecules depends on their conformational control and regulation, which in turn is achieved through specific intra-chain inter-segment interactions that provides the enthalpic contribution to overcome the entropic barrier associated with the adoption of a specific folded form.

Conformational control in biological macromolecules depends largely on reversible H-bonding interactions, further supported by electrostatic, aromatic π-stacking and hydrophobic interactions. Many efforts have been directed towards the design of oligomeric systems that are coerced to adopt specific conformation in solution[1] by the co-operative use of a wide range of such weak reversible interactions; a term *foldamer*[2] was coined by Gellman to refer to such class of oligomeric molecules. Several excellent reviews describe the structurally diverse range of foldamers that have been studied so far.[1,3–8] It is

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evident from these reviews that a majority of these systems utilize H-bonding as the primary structure-directing interaction and, more importantly, the backbone of most of the foldamers have been designed to possess restricted conformational freedom.

Use of alternate weak interactions co-operatively to generate folded structures remains an exciting challenge, particularly in relatively flexible high molecular weight polymeric systems. Iverson and co-workers were the first to utilize charge–transfer interactions between electron rich aromatic donors and electron–deficient aromatic acceptors in oligomeric systems to stabilize a specific folded conformation.[9] In their design an added solvophobic motivation was provided by the inclusion of a hydrophilic carboxylic acid group in the spacer segment. Subsequently, a few other examples of such donor–acceptor containing oligomers have been described in the literature.[10] The use of oligooxyethylene (OE-n) segment as linkers has also been extensively studied in the context of sensors[11–13] and more recently with regard to foldamers.[14–17] In these systems, the complexation of the OE segment by a metal-ion leads to either a spectroscopic modulation (sensing) or it leads to the formation of a specific folded conformer.

A vast majority of the studies thus far have utilized precisely defined oligomeric systems, while relatively

few studies have dealt with high molecular weight polymers. Two years ago, we described the design and synthesis of a class of donor–acceptor polyimides containing oligooxyethylene (OE-n) linkers. These polymers exhibited a preference to adopt specific folded conformations in relatively polar medium in the presence of appropriate alkali-metal ions.[14–16] Extensive studies demonstrated that the folding propensities of these polymers can be modulated by varying the size of alkali-metal ion, confirming that they exhibit similar selectivity as seen in small molecule podants.[18–19] Subsequently, a simpler and more readily accessible system, wherein a polyimide containing pyromellitic diimide (PDI) acceptors linked by OE6 spacers, was explored.[16] In this polymer, folding is induced by interaction with a small-molecule *folding agent* that contains a dialkoxynaphthalene (DAN) donor unit linked to an ammonium group. The complexation of the ammonium group with the OE6 segment restricts the conformation of the flexible oxyethylene segment in a manner so as to form an A-D-A type sandwich complex, and consequently leads to the folding of the polymer backbone. The role of the halide counter-ion in these systems was shown to be minimal, suggesting that they were mere bystanders in the folding process.

In an effort to enhance the driving motivation for the folding process, an alternate design for the folding agent was conceived. The new design utilizes a DAN donor that is linked to a carboxylic acid group instead of the amine. This design was conceived with two potential advantages in mind – one is that the alkali-metal counter-ion of the carboxylic acid can complex with OE segment and can bring the DAN unit between two adjacent PDI units of the polymer backbone. This provides an active role for the counter-ion (alkali-metal) unlike in the previous ammonium-ion containing folding agent, wherein the perchlorate had little role to play.[16] The second advantage is that the relatively loose electrostatic interaction between the DAN carboxylic acid and the alkali-metal counter-ion would allow a greater degree of adaptability to permit the optimum geometry for the A-D-A charge–transfer complex.

In the present investigation, a few different DAN containing folding agents were synthesized, wherein the length and nature of the terminal alkoxy group were varied to enhance their solubility. The folding of the polyimide that contain PDI acceptors and hexa(oxyethylene) spacers was examined in the presence of the different folding agents to gain a better understanding of the various factors that govern the efficacy of the folding process. Further, a new polyimide containing a naphthlane dimide (NDI) unit possessing a larger aromatic core was also synthesized to enhance the charge–transfer interaction with the DAN donor.

2. Experimental

2.1 *General methods*

Hexaethyleneglycol, diethyleneglycol monomethylether obtained from Sigma-Aldrich, *p*-Toluenesulfonyl chloride obtained from Fluka were used as such without purification. 1,5-Dihydroxynaphthalene obtained from Sigma-Aldrich was sublimed under vacuum at 170°C prior to use. Pyromellitic dianhydride and 1,4,5,8-napthalene tetracarboxydianhydride were refluxed with dried acetic anhydride (dried over P_2O_5); pyromellitic dianhydride was further purified by sublimation at 200°C under vacuum. All other chemicals were purchased from Ranbaxy or SD Fine Chemicals or Spectrochem. All the solvents were dried following the standard procedures. NMR was recorded using a 400 MHz Bruker NMR spectrometer. Hexaethyleneglycol diamine was synthesized as reported in elsewhere.[15–16]

2.1a *1-Methoxy-5-hydroxy naphthalene (1):*
1,5-Dihydroxynaphthalene (5·0 g, 31·3 mmol) was dissolved in ethanol and to it was added 8·6 ml (94 mmol) of purified dimethyl sulfate. The contents were immersed in an ice–water bath and stirred. Sodium hydroxide (1·5 g, 37·5 mmol) in ethanol was added drop-wise to it. The contents were allowed to warm-up to room temperature and stirred further for 18 h. Excess sodium hydroxide (~ 2·0 g in 20 ml water) was then added and the contents were stirred for 30 min to destroy the unreacted dimethyl sulfate. The ethanol was removed using a rotary evaporator and the residue was taken in water and acidified with conc. HCl. The crude product was filtered and purified on a silica gel column using Pet. ether/chloroform/ethyl acetate. Yield: 45%. m.p. 122–124°C. NMR: (in CDCl₃) δ (ppm): 7·82 (*d*, 1H, Ar-<u>H</u>, *p*-OCH₃), 7·72 (*d*, 1H, Ar-<u>H</u>, *p*-OH), 7·42 (*t*, 1H, Ar-<u>H</u>, *m*-OCH₃), 7·32 (*t*, 1H, Ar-<u>H</u>, *m*-OH), 6·86 (*d*, 2H, Ar-<u>H</u>, *o*-OCH₃ and *o*-OH both protons appear at same position), 4·00 (*s*, 3H, –O<u>CH</u>₃).

2.1b *1-(1-Methoxy-5-napthyloxy)ethyl acetate (2):* Compound **1** (1 g, 5·74 mmol) was dissolved in 20 ml dry acetonitrile and to it were added K_2CO_3 (3·2 g, 23 mmol), a catalytic amount of KI and ethyl bromoacetate (1·15 g, 6·89 mmol). The contents were purged with dry nitrogen and refluxed for 24 h under a nitrogen atmosphere. The reaction mixture was cooled, filtered and the residue was washed with 3 × 15 ml of acetonitrile. The combined filtrate was concentrated to get the crude product. The crude product was taken in alkaline sodium hydroxide solution (pH ~10) and stirred for half an hour and extracted with 3 × 20 ml diethyl ether. The combined organic layer washed with distilled water and dried over sodium sulfate and concentrated to yield the product. Yield = ~ 100%, m.p. 64–66°C. NMR: $CDCl_3$, δ (ppm): 7·94 (*d*, 1H, Ar-<u>H</u>, *p*-OCH$_3$), 7·90 (*d*, 1H, Ar-<u>H</u>, *p*-OCH$_2$COOCH$_2$CH$_3$), 7·40 (*t*, 1H, Ar-<u>H</u>, *m*-OCH$_3$), 7·34 (*t*, 1H, Ar-<u>H</u>, *m*-OCH$_2$COOCH$_2$CH$_3$), 6·87 (*d*, 1H, Ar-<u>H</u>, *o*-OCH$_3$), 6·76 (*d*, 1H, Ar-<u>H</u>, *o*-OCH$_2$COOCH$_2$CH$_3$), 7·40 (*s*, 1H, Ar-<u>H</u>, *m*-OCH$_3$), 7·34 (*t*, 1H, Ar-<u>H</u>, *m*-OCH$_2$COOCH$_2$CH$_3$), 4·79 (*s*, 2H, –O<u>CH$_2$</u>COOCH$_2$CH$_3$), 4·32–4·27 (*q*, 2H, –OCH$_2$COO<u>CH$_2$</u>CH$_3$), 3·99 (*s*, 3H, –O<u>CH$_3$</u>), 1·31 (*t*, 3H, –OCH$_2$COOCH$_2$<u>CH$_3$</u>).

2.1c *1-(1-Methoxy-5-napthyloxy) acetic acid (DAN-Ia):* Compound **2** (1 g, 3·8 mmol) was taken in 10 ml of 4 : 1 methanol/water (*v/v*) and 1 ml of DCM in a RB, along with lithium hydroxide (1·57 g, 57 mmol) and the neck was sealed with a wired septum. The contents were stirred at 50°C for 24 h. After the reaction, the solvent was removed and water was added. The precipitate was filtered and then acidified with aq. HCl to obtain the product acid. Yield: 85%, m.p. 181–183°C.

NMR: $CDCl_3$, δ (ppm): 7·93–7·88 (*m*, 2H, Ar-<u>H</u>, *p*-OCH$_3$ and *p*-OCH$_2$COOH), 7·42 (*t*, 1H, Ar-<u>H</u>, *m*-OCH$_3$), 7·42 (*t*, 1H, Ar-<u>H</u>, *m*-OCH$_2$COOH) 6·89 (*d*, 1H, Ar-<u>H</u>, *o*-OCH$_3$), 6·79 (*d*, 1H, Ar-<u>H</u>, *o*-OCH$_2$COOH), 4·87 (*s*, 2H, –O<u>CH$_2$</u>COOH), 4·00 (*s*, 3H, –O<u>CH$_3$</u>).

2.1d *Potassium salt preparation:* DAN-Ia (500 mg, 2·15 mmol) was dissolved in minimum amount of dry tetrahydrofuran (THF) and a methanolic solution of KOH (108 mg, 1·935 mmol) was added to it slowly. The precipitate was centrifuged, washed with dry THF and dried to obtain the product in nearly quantitative yield. m.p. 264–265°C. NMR: DMSO-d_6, δ (ppm): 7·80 (*d*, 1H, Ar-<u>H</u>, *p*-OCH$_3$),

7·62 (*d*, 1H, Ar-<u>H</u>, *p*-OCH$_2$COOK), 7·38–7·28 (*m*, 2H, Ar-<u>H</u>, *m*-OCH$_3$ and *m*-OCH$_2$COOK), 6·96 (*d*, 1H, Ar-<u>H</u>, *o*-OCH$_3$), 6·74 (*d*, 1H, Ar-<u>H</u>, *o*-OCH$_2$COOK), 4·28 (*s*, 2H, –O<u>CH$_2$</u>COOK), 3·95 (*s*, 3H, –O<u>CH$_3$</u>).

2.1e *Synthesis of the polyimides (PDI):* Hexaethyleneglycol diamine (306 mg, 1·4 mmol) was taken along with 3 ml of freshly distilled *m*-cresol in RB fitted with a nitrogen purger. Pyromellitic dianhydride (392 mg, 1·4 mmol) was then added to it and the contents were stirred at 80°C for 6 h with continuous nitrogen purge. After cooling to room temperature, 2 ml of *m*-cresol, 5 ml of toluene and 8 drops of isoquinoline (catalyst) were added. The contents were stirred at 180°C for 8 h with continuous removal of water using a Dean–Stark apparatus, which collected the toluene-water azeotrope. The contents of the flask were cooled, concentrated and precipitated in methanol. The polymer was dissolved in ca. 5 ml chloroform and re-precipitated in ca. 50 ml methanol. Yield: 70%. Polymer NDI was also prepared in 72% yield using a similar procedure using 1,4,5,8-tetracarboxy dianhydride. The ^{1}H-NMR spectra of both the polymers are shown in figure 1.

3. Results and discussions

The structures of the polyimides and the folding agents are shown in scheme 1.

The synthesis of the polymers was readily achieved using standard polyimide polymerization conditions, wherein pyromellitic dianhydride is condensed with an equimolar quantity of the hexaethylene glycol diamine (scheme 2). The first step was
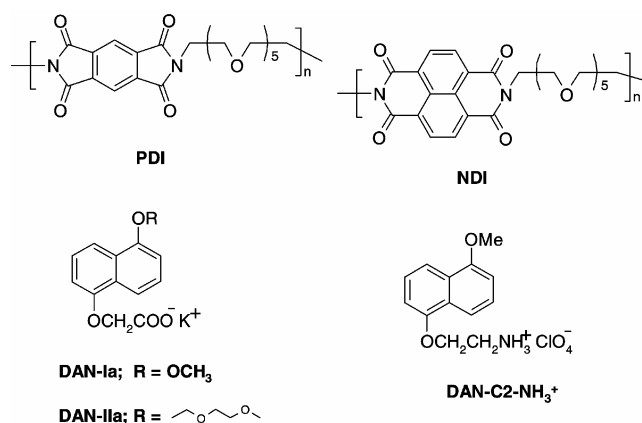
Scheme 1. Structures of the polymers and folding agents.
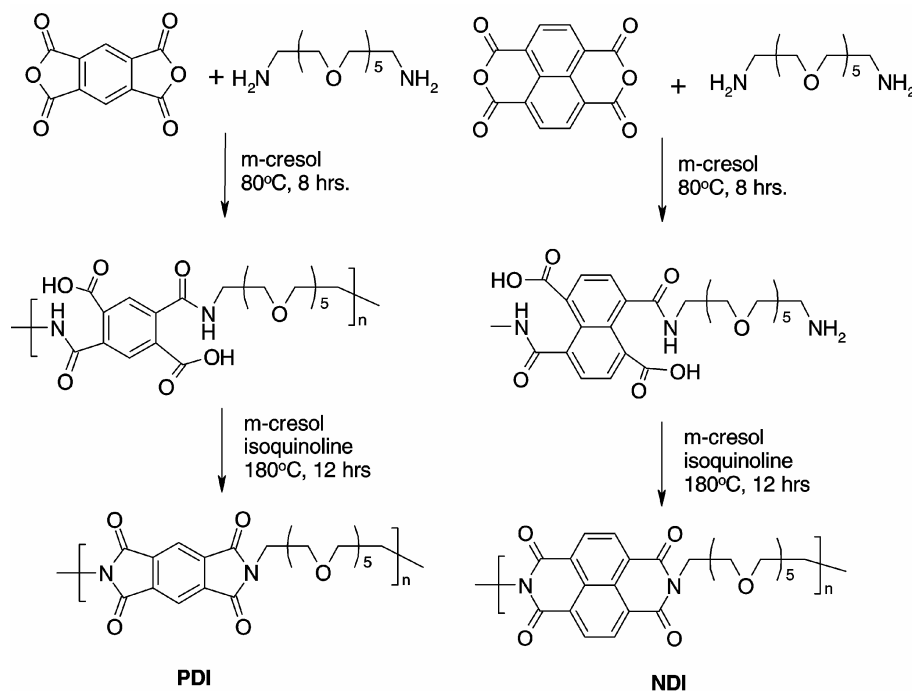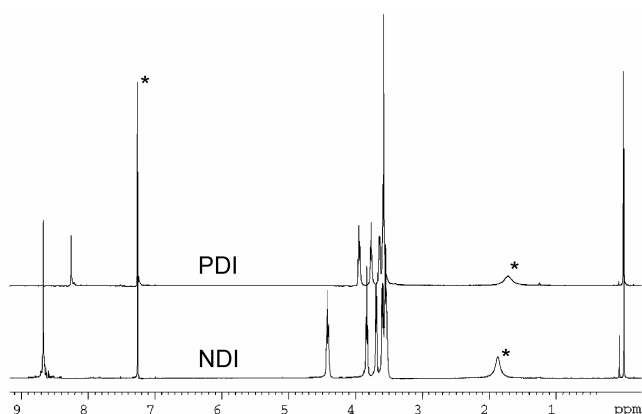
Scheme 2. Synthetic scheme for the polyimides.

**Figure 1.** ^{1}H-NMR spectra of PDI and NDI in CDCl₃. Peaks marked by * are due to solvent/water.

carried out in m-cresol at 80°C to generate the poly-amic acid, which was dehydratively cyclized at 180°C (after addition of toluene and isoquinoline) by continuous azeotropic removal of water. NDI-EO6 was also synthesized under similar conditions using naphthalene tetracarboxydianhydride. PDI-EO6 was obtained as an off-white fluffy powder after two re-precipitations, while NDI-EO6 was obtained as a deep-red hard transparent solid. The ^{1}H-NMR spectra of the two polymers are shown in figure 1. In both cases the aromatic protons due to PDI/NDI appear as a single peak, while those from OE6 spacer appear with the expected intensity in the region between 3·4 and 4·6 ppm.

The DAN folding agents were synthesized by first preparing the mono-alkylated derivative of 1,5-dihydroxynaphthalene, which was then further alkylated using ethyl bromoacetate followed by hydrolysis (scheme 3). The appropriate alkali-metal salt of the carboxylic acid was prepared by suitable neutralization. The proton NMR spectra of the folding agents confirmed their structure (see supplementary material).

3.1 *Folding studies*

From previous studies it was established that EO-6 spacers in polymers form complexes most effectively with K^{+} ions.[15] Furthermore, the folding of PDI-EO6 using DAN-C2-NH₃^{+} was shown to be most effective, i.e. when the ammonium group was linked to the naphthalene donor via a 2-carbon spacer.[16] Based on these observations, we designed a folding agent DAN-Ia, wherein the carboxylic acid group is linked to the naphthalene by a single methylene unit – this should provide roughly the same 2-carbon distance of the donor from the coordinating metal-ion. The potassium salt of the carboxylic acid was used so that the complexation of the metal-ion with the OE-6 loop will bring the naphthalene donor
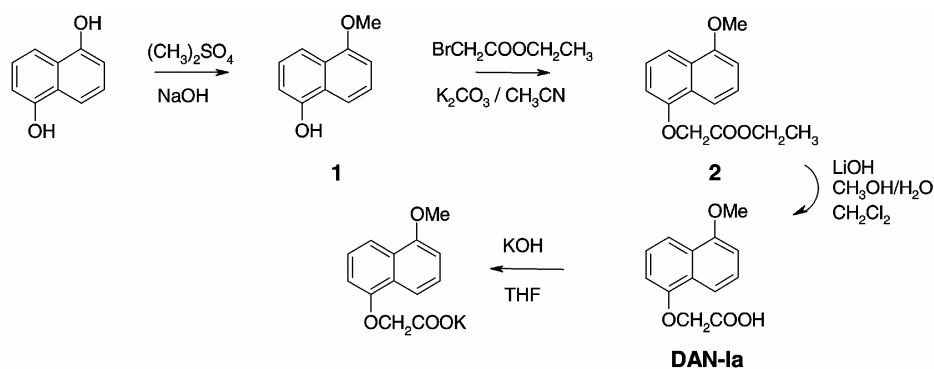
Scheme 3. Synthesis of folding agent DAN-Ia.
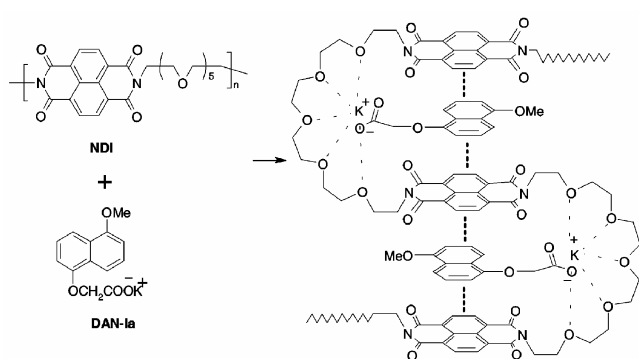
Scheme 4. Folding of NDI in the presence of DAN-Ia.

in the right location to form a charge–transfer complex with two adjacent acceptor units, as depicted in scheme 4.[20]

NMR titration studies were carried out to follow the folding process. As was shown earlier, the formation of a DA type charge–transfer complex causes the chemical shift of the acceptor (aromatic) ring proton in PDI-EO6 to experience an up-field shift, while the sandwiching of the donor between two acceptor units in a ADA type arrangement leads to a further up-field shift.[15] In the PDI–DAN-C2-NH$_3^+$ system the maximum shift of the acceptor proton was around 0·6 ppm.[16] Unlike in previous studies, the present investigations were carried out in CDCl$_3$–MeOH mixtures instead of CDCl$_3$–CH$_3$CN because of the poor solubility of the DAN salt in acetonitrile. This further imposes an upper limit to the methanol composition as the NDI polymer precipitates out beyond 40% methanol. Therefore, the range of solvent composition that was studied was from 20–40% (*v/v*) MeOH in CdCl$_3$ (in PDI up to 50% was tolerated).

A typical spectral variation seen during NMR titration of PDI-EO6 with DAN-Ia (K$^+$ salt) is shown

in figure 2. It is evident that the single acceptor proton (most down-field peak) undergoes a significant up-field shift with increasing amounts of DAN-Ia. The remaining peaks, whose intensities are seen to increase, belong to the DAN donor whose relative concentration increases during the titration. A similar variation was also seen in the case of NDI-EO6 polymer (figure 2), but in this case the extent of shift was seen to be significantly larger. This is in accordance with the expectation that the NDI donor with a larger aromatic core would form a stronger C–T complex.

DAN-IIa, having a 2-(2-methoxyethoxy)ethyl substituent, was also prepared because it was expected to have higher solubility, permitting an extended concentration range for study. To investigate the effect of solvent polarity, the NMR titrations were carried out in CDCl$_3$–MeOH mixtures of varying composition. In figure 3, the chemical shift of the acceptor protons of the polymers is plotted as a function of the mole-ratio of folding agent, for different solvent compositions (vol% MeOH). In general, two observations can be made – one is that the solvent composition does not appear to significantly affect the chemical shift of the acceptor protons in pure PDI-EO6, while the acceptor protons of NDI-EO6 shifts up-field as the polarity of the solvent increases. This is a reflection of the greater tendency for the relatively more hydrophobic naphthalene cores in NDI–EO6 to spatially co-locate themselves in polar medium when compared to the pyromellitic cores in PDI–EO6. The second is that the magnitude of up-field shift in case of NDI–EO6 upon interaction with the folding agent is significantly larger than in PDI–EO6. This reflects the stronger predisposition of the acceptor units to intercalate the donors, again because of the greater solvophobic
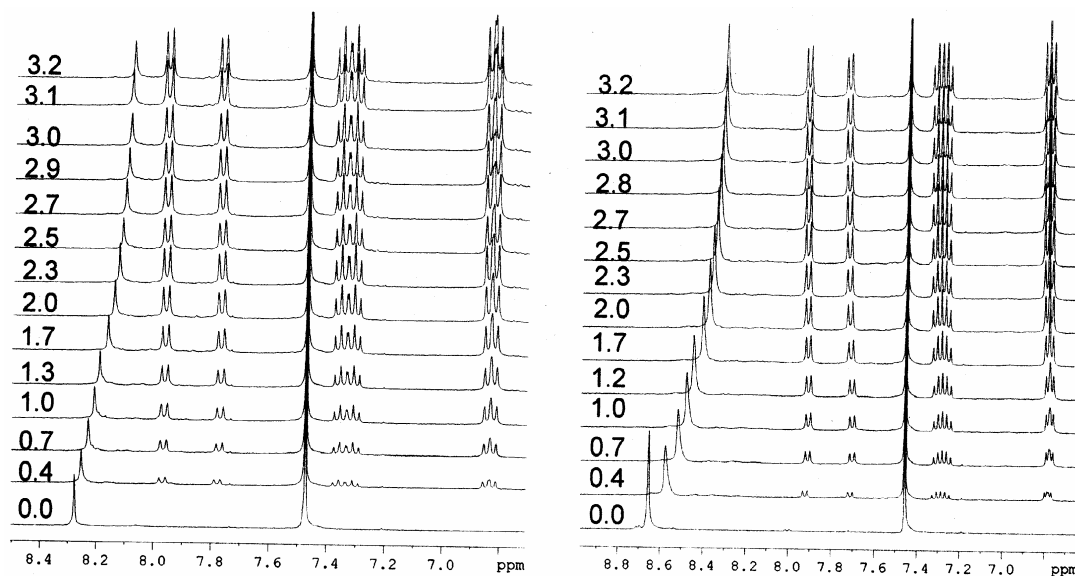
Figure 2. ^{1}H-NMR spectral titration (in CH$_3$OH–CDCl$_3$; 30% *v/v*) of PDI (left) and NDI (right) with varying mole ratios of the folding agent DAN-Ia. Mole ratios of DAN-Ia to polymer repeat unit is listed against each spectrum.
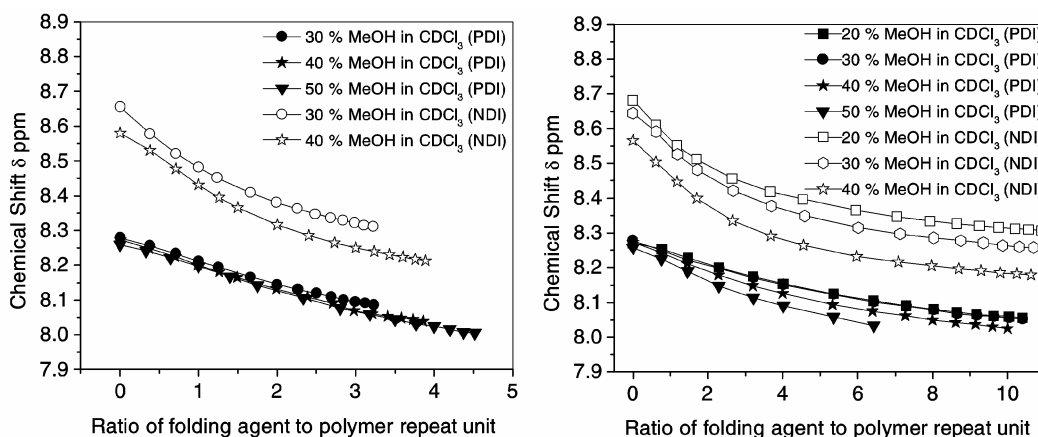

Figure 3. Variation of chemical shift of the acceptor proton as a function of mole-ratio of folding agent DAN-Ia (left) and DAN-IIa (right), recorded in CDCl$_3$–MeOH of varying composition.

driving motivation, in addition to the fact that the larger acceptor core in NDI could lead to a stronger CT interaction.

In an effort to gain a quantitative measure of the folding process, the association constant (K_a) for the charge–transfer complex formation was estimated from the variation of the chemical shifts. Assuming that the free and complexed species are in rapid equilibrium in the NMR time-scale (as evident from the continuously varying single chemical shift for the acceptor proton), a non-linear least-square fitting routine can be used to estimate the K_a for the com-

plex formation. Thus, EQNMR[21] was used to estimate the binding constant assuming a 1 : 1 complexation of the donor and acceptor units. The values thus obtained are listed in table 1.

The association constants clearly confirm our hypothesis that the NDI polymer forms a complex with the DAN donors more effectively than the PDI polymer. As stated earlier, this could be because of the larger aromatic naphthalene ring in NDI and also because of the stronger driving motivation to co-locate themselves in more polar medium as a result of solvophobic association. However, the effect of

Table 1. Association constants (K_a) for the formation of D–A charge–transfer complex determined from the variation seen in the NMR titration experiments.

Sample	Association constant K_a (Mol^{-1})			
	20% MeOH in CDCl$_3$	30% MeOH in CDCl$_3$	40% MeOH in CDCl$_3$	50% MeOH in CDCl$_3$
PDI + DAN-Ia	–*	37	69	64
NDI + DAN-Ia	–*	392	345	–*
PDI + DAN-IIa	60	58	82	98
NDI + DAN-IIa	276	295	319	–*

*Titrations could not be done because of insolubility of either the polymer or the folding agent

increase in solvent polarity on K_a is not very significant, and in some cases we see even a reduction in the association constant at higher solvent polarity. Here it is important to reflect on the two factors that can, in principle, affect the association constant in such systems – one is the intrinsic stability of the charge–transfer complex as a function of solvent polarity and the other is the effect of solvent polarity on the polymer conformation. Several studies of charge–transfer complexation between electron-rich donors and electron deficient acceptors have clearly shown that, in general, charge–transfer complexes are destabilized in polar solvents due to the decrease of energy of electrostatic interaction within the complex.[22–23] However, it is important to recall, that in our polymeric systems, periodically placed aromatic units are linked by relatively hydrophilic EO spacers. The relatively hydrophobic aromatic units would tend to co-locate (cluster) themselves in polar solvents – this effect being larger in the case of NDI than in PDI. Furthermore, the relatively hydrophobic DAN-Ia would have a greater driving motivation to intercalate between two acceptor units of the polymer than DAN-IIa, which has a higher solubility in polar solvents because of the EO unit. This explains both the higher association constant of the donors with NDI and also the observation that DAN-Ia has a higher association constant with the polymers than DAN-IIa; the difference is significantly larger in case of NDI than in PDI. The relatively weak dependence on solvent polarity within a given pair of polymer-donor is possibly a reflection of the interplay between the counter-acting effects – one the intrinsic destabilization of the charge–transfer complex in polar solvents and the other the enhanced solvophobic driving force that drives complex formation.

4. Conclusions

The folding of two polyimides, PDI or NDI, by a two-point interaction with folding agents was examined. The folding agents were designed to possess a dialkoxynaphthalene (DAN) donor linked to a carboxylic acid via a methylene unit. The two-point interaction occurs via the coordination of the EO-6 spacer segment of the polymer with the K$^+$ counterion of the donor carboxylic acid and the charge–transfer interaction of the naphthalene donor with the acceptor units in the polymer backbone. NMR titration studies provided clear evidence for the above stated interaction, as seen from the significant up-field shift of the aromatic protons of the acceptor units. From the chemical shift variation as a function of increasing mole-ratio of the folding agent, the association constants (Ka) were estimated. Correlation of the Ka values with the structures of polymer and folding agent suggests that increasing the size of the aromatic ring of the acceptor units in the polymer from benzene (in PDI) to naphthalene (in NDI) leads to a ca. 4–5-fold increase in the association constant. This increase has been ascribed to the stronger C–T interaction between larger aromatic cores, as well as the greater tendency of the larger and more hydrophobic naphthalene cores to co-locate themselves, thereby enhancing the propensity to form a ADA-type CT complex. The rather weak effect of solvent polarity on the propensity of the polymers to fold by interaction with the folding agent was rationalized as being due to two counteracting factors – one is the intrinsic destabilizing effect of polar solvents on C–T complex formation and the other is the solvophobic effect of polar solvents on the polymer conformation, which may enhance the interaction of the folding agent with the acceptor units in the polymer.

References

1. Hill D J, Mio M J, Prince R B, Hughes T S and Moore J S 2001 *Chem. Rev.* **101** 3893
2. Appella D H, Christianson L A, Karle I L, Powell D R and Gellman S H 1996 *J. Am. Chem. Soc.* **118** 13071
3. Licini G, Prins L J and Scrimin P 2005 *Eur. J. Org. Chem.* **6** 969
4. Gellman S H 2005 *Polym. Preprints* **46** 169
5. Cheng R P 2004 *Curr. Opin. Struct. Biol.* **14** 512
6. Huc I 2004 *Eur. J. Org. Chem.* **1** 17
7. Sanford A R and Gong B 2003 *Curr. Org. Chem.* **7** 1649
8. Gellman S H 1998 *Acc. Chem. Res.* **31** 173
9. Zych A J and Iverson B L 2000 *J. Am. Chem. Soc.* **122** 8898
10. Gawronski J, Kaik M, Kwit M and Rychlewska U 2006 *Tetrahedron* **62** 7866
11. Arunkumar E, Ajayaghosh A and Daub J 2005 *J. Am. Chem. Soc.* **127** 3156
12. Ajayaghosh A, Arunkumar E and Daub J 2002 *Angew. Chem. Intl. Ed.* **41** 1766
13. Morozumi T, Hama H and Nakamura H 2006 *Anal. Sci.* **22** 659
14. Ghosh S and Ramakrishnan S 2004 *Angew. Chem. Int. Ed* **43** 3264
15. Ghosh S and Ramakrishnan S 2005 *Macromolecules* **38** 676
16. Ghosh S and Ramakrishnan S 2005 *Angew. Chem. Int. Ed.* **44** 5441
17. Zhao X, Jia M-X, Jiang X-K, Wu L-Z, Li Z-T and Chen G-J 2004 *J. Org. Chem.* **69** 270
18. Vögtle F and Weber E 1979 *Angew. Chem. Intl. Ed.* **18** 75
19. Lohr H G and Vögtle F 1985 *Acc. Chem. Res.* **18** 65
20. Earlier studies done using 1,5-dimethoxynaphthalene, even in the presence of NH_4SCN, clearly indicated that direct linkage of the ammonium to the donor is essential for effective folding of the polymer.[16] Furthermore, a control titration was done using NDI and DAN-Ia acid, which indicated that the extent of shift of the acceptor proton was only 0·04 ppm, even at a mole-ratio of acid to polymer repeat unit of 10, confirming the importance of the potassium salt to garner this effect. (see Supplementary Material for NMR titration traces)
21. Hynes M J 1993 *J. Chem. Soc. Dalt. Trans.* 311
22. Deperasinkska I and Prochorow J 1977 *Advances in Molecular Relaxation and Interaction Processes* **11** 51
23. Sinanoglu O 1968 *Molecular associations biology* (ed.) B Pullman (New York: Academic Press)