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Principles of sequence-recognition in aromatic polyimides†

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Pyrene-based molecular tweezers show sequence-specific binding to aromatic polyimides through sterically-controlled donor–acceptor π-stacking and hydrogen bonding; ^{1}H NMR spectra of tweezer-complexes with polyimides having different sequence-restrictions show conclusively that the detection of long range sequence-information results from multiple tweezer-binding at adjacent imide residues.

The most fundamental mechanisms of biology depend on supramolecular recognition of monomer sequence-information in linear copolymers. This is most evident in the expression of nucleic acid sequences during protein synthesis,[1] but is also crucially important in gene-regulation by proteins,[2] and in the operation of restriction enzymes which cleave DNA at sequence-specified linkages.[3] Recognition of monomer sequences in *synthetic* polymer systems is by contrast relatively unknown,[4] though NMR spectroscopic evidence was very recently obtained for sequence-selectivity in the binding of a molecular tweezer (**1a**) to aromatic co-polyimides.[5] We have now identified the specific interactions associated with this type of binding by crystallographic analysis of a tweezer-complex with a model di-imide. In addition, an analysis of tweezer-complexation with *sequence-restricted* polyimides shows conclusively that long-range sequence effects apparent in the ^{1}H NMR spectra arise from multiple tweezer-binding to adjacent imide residues.

The X-ray structure‡ (Fig. 1) of a 1 : 1 complex between tweezer **1b** and the model di-imide **2** ($K_a = 6 \times 10^3$ M^{-1} in 6 : 1 v/v $CHCl_3$/hexafluoropropan-2-ol) shows that tweezer-binding occurs *via* (i) a double π-stacking arrangement of its electron-rich pyrenyl arms with the electron-poor pyromellitimide unit (mean atom to pyrene-plane distances 3.38, 3.39 Å), (ii) a pair of hydrogen bonds (yellow) between the tweezer amide-NH protons and a pyromellitimide carbonyl oxygen (N···O = 3.13, 3.22 Å), and (iii) di-imide chain folding through *ca.* 180° (as predicted by computational modelling),[5] bringing one of its two 4-chlorophenylenesulfone residues into π-stacking contact with a pyrenyl tweezer-arm (mean C to pyrene-plane distance = 3.66 Å; Cl···pyrene = 3.59 Å). The second ether-sulfone unit does not fold around the tweezer in the same way but adopts a more extended, non-interacting conformation.

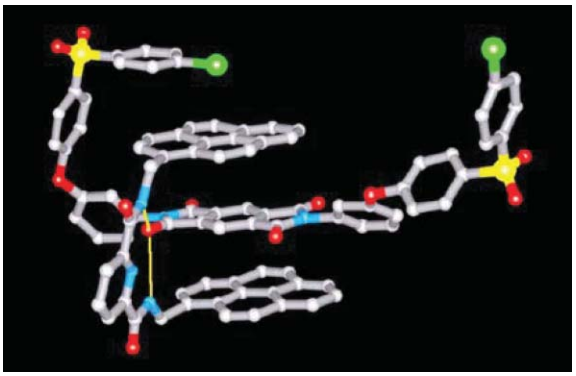
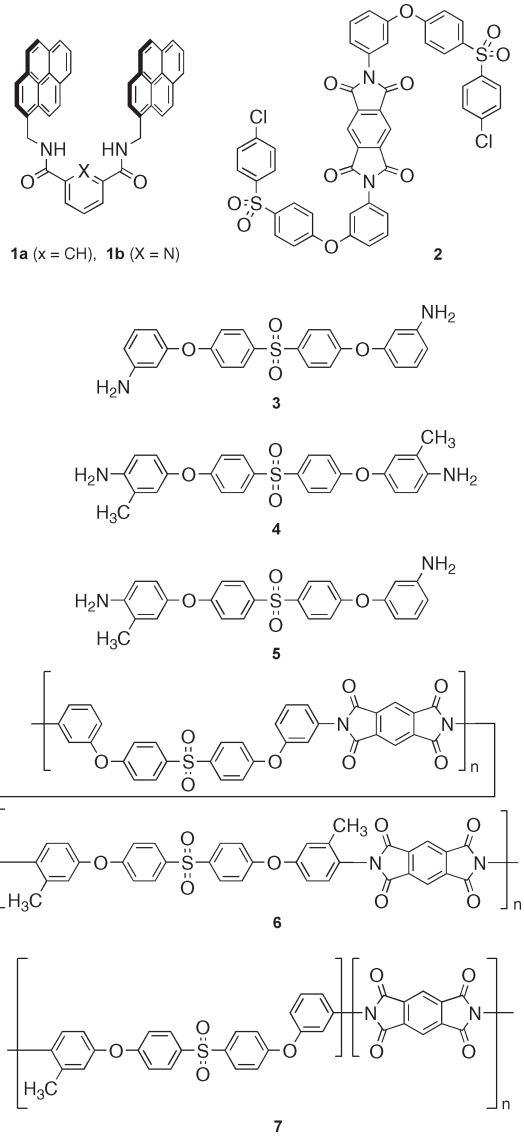


Fig. 1 X-Ray structure of the 1 : 1 complex between tweezer **1b** and the model di-imide **2**. Hydrogen atoms are omitted for clarity.



Development of fine structure in the ^{1}H NMR resonances of tweezer-bound imide residues in high molar mass polyimides has tentatively been ascribed to the amplification of long-range polymer sequence information by the tweezer.[5] Given fast-exchange conditions, a possible mechanism for this involves tweezer-binding at one or both neighbouring imide residues,

† Electronic supplementary information (ESI) available: synthesis and characterisation data for all new materials; binding constant data; ^{1}H NMR data for tweezer–polymer and tweezer–model complexation. See http://www.rsc.org/suppdata/cc/b4/b412801j/

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thereby enhancing the aromatic ring-current shielding effects produced by a tweezer bound at the "observed" site. This would enable differentiation between sequences where the tweezer can bind (i) at neither of the two sites adjacent to the observed binding site, (ii) at one adjacent site or (iii) at both adjacent sites.

We have now subjected this adjacent-binding model to a rigorous experimental test, making use of two novel polyimides with analogous structures but *different sequence-restrictions*. These polymers (**6** and **7**) were synthesised at high molar mass (M_n = 143,000 and 112,000 daltons respectively) by polycondensation of pyromellitic dianhydride with (i) a 1 : 1 mixture of the symmetrical diamines **3** and **4**, and (ii) the unsymmetrical diamine **5** alone. Designating a methylated ring in **6** or **7** as "**H**" (hindered), a non-methylated ring as "**U**" (unhindered), and a di-imide residue as "**I**", then both polymers will contain the three different imide-centred sequences **UIU**, **UIH** (or **HIU**) and **HIH**, one of which (**HIH**) also exists as a pair of non-interconverting conformational isomers (Fig. 2).[6] For both polymers, the sequences **UIU**, **UIH/HIU** and **HIH** should appear in relative abundances 1 : 2 : 1 (on the basis of a random distribution of **U** and **H** residues). As shown in Fig. 3 [spectra (a) and (d)], these abundances are clearly reflected in the imide-resonances (δ 8.4–8.6) observed by ^{1}H NMR spectroscopy.

Spectra (b) and (e) show the effects of adding just 1.25 mol% (relative to imide) of tweezer **1a**. Crucially *only one of the three imide resonances shows a complexation-shift* and is thus assigned to the unhindered sequence **UIU**. This complexation-shift correlates well with that observed for the homopolyimide derived from the unhindered diamine **3** (see ESI). The imide resonance at lowest field is unshifted and can be confidently assigned to the doubly hindered sequence **HIH**, leaving the central resonance assignable as **HIU/UIH** – its twofold degeneracy agreeing with the relative intensity of this resonance. Increasing the proportion of tweezer to 5 mol% leads to a further upfield shift of the **UIU** resonance, but although this remains a sharp singlet for polymer **7**, it broadens and separates into an apparent 1 : 2 : 1 triplet for copolymer **6** (see ESI for more detailed spectroscopic data). As outlined below, these observations clearly demonstrate that higher-order sequence information relating to the environment of **UIU** is being expressed in the 1 : 1 copolymer **6**, but, as a result of inbuilt sequence-restrictions, *not* in polymer **7**.

Designating the residues from monomers **3**, **4**, and **5** as **U–U**, **H–H** and **H–U** respectively, the symmetrical nature of **3** and **4** means that in copolymer **6** the strongly-binding triplet **UIU** can occur only within the following restricted range of sequences:

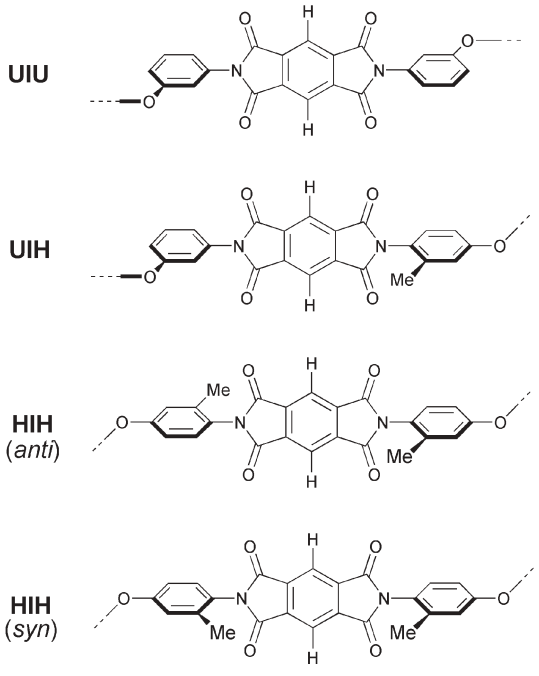

Fig. 2 Imide-centred triplet sequences in polymers **6** and **7**.

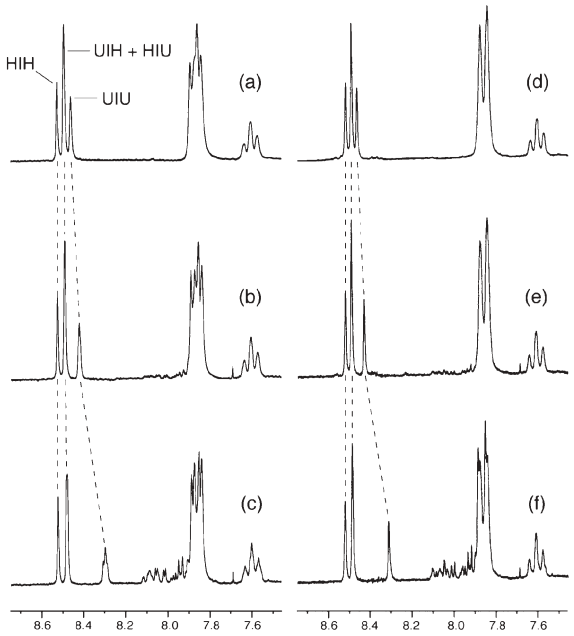

Fig. 3 ^{1}H NMR spectra of polyimides **6** and **7**; (a)/(d) pure polymer, (b)/(e) polymer plus tweezer **1a** (1.25 mol% relative to imide residues), and (c)/(f) polymer plus tweezer **1a** (5 mol% relative to imide).

HIU–UIU–UIH (provides **no** adjacent UIU binding site)
HIU–UIU–UIU (provides **one** adjacent UIU binding site)
UIU–UIU–UIH (provides **one** adjacent UIU binding site)
UIU–UIU–UIU (provides **two** adjacent UIU binding sites)

The emergence of a 1 : 2 : 1 imide-resonance-pattern for **UIU** in copolymer **6** is thus entirely consistent with the idea that supramolecular tweezer-binding induces resolution of long-range sequence-information in the ^{1}H NMR spectra of polyimides. In polymer **7** however, the use of an unsymmetrical diamine places *different* restrictions on sequences higher than triplets so that the only allowed **UIU**-centred three-triplet sequences are now:

HIH–UIU–HIH (provides **no** adjacent UIU binding site)
HIH–UIU–HIU (provides **no** adjacent UIU binding site)
UIH–UIU–HIH (provides **no** adjacent UIU binding site)
UIH–UIU–HIU (provides **no** adjacent UIU binding site)

There are thus again three different sequence-environments for **UIU** in polymer **7**, but the adjacent-binding theory now predicts that the imide resonance arising from this sequence will show *no higher-order splitting* in the presence of the tweezer, since adjacent tweezer-binding is sequence-forbidden. This prediction is clearly borne out by the spectra shown in Fig. 3 (d–f). Even more remarkably, for polymer **7** at higher tweezer : imide ratios (> 1 : 1), additional development of fine structure is observed in the imide resonances of the *non-binding* (**HIH**) and *weakly-binding* (**HIU**) sequences, as shown in Fig. 4. Enumeration of the possible **HIU**-centred sequences in polymer **7** (below) shows equal populations of sequences in which strong tweezer-binding can and cannot occur at an adjacent imide residue, so clearly accounting for the splitting of the **HIH** resonance into an apparent 1 : 1 doublet.

UIU–HIU–HIU (provides **one** adjacent UIU binding site)
UIU–HIU–HIH (provides **one** adjacent UIU binding site)
HIU–HIU–HIU (provides **no** adjacent UIU binding site)
HIU–HIU–HIH (provides **no** adjacent UIU binding site)

A similar analysis (below) of the possible **HIH**-centred sequences in polymer **7** shows that **HIH** can occur in three distinct environments, with relative populations 1 : 2 : 1:

UIU–HIH–UIU (provides **two** adjacent UIU binding sites)
UIU–HIH–UIH (provides **one** adjacent UIU binding site)
HIU–HIH–UIU (provides **one** adjacent UIU binding site)
HIU–HIH–UIH (provides **no** adjacent UIU binding site)

Although an apparent 1 : 2 : 1 triplet would therefore be predicted, a *pair* of such "triplets" is in fact observed (Fig. 4). This is however readily accounted for on the basis that, as noted above

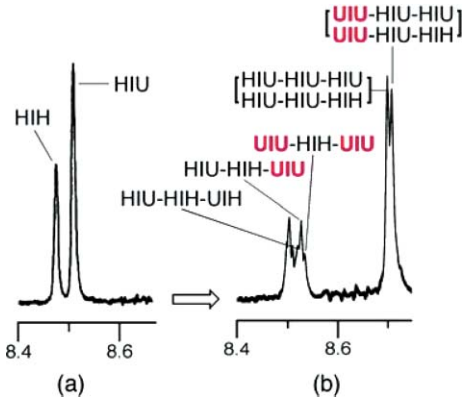

Fig. 4 Partial ^{1}H NMR spectra of polyimide **7** in the presence of the tweezer **1a**; (a) 5 mol% tweezer relative to imide (*cf.* Fig. 3f), and (b) 100 mol% tweezer relative to imide. Assignments refer to the protons of the central di-imide residue (I) in each sequence shown. The **HIH**-centred sequence-assignments shown in spectrum (b) refer to the *syn*-isomer of this sequence and are repeated for the corresponding resonances at lower field assigned to the *anti*-isomer.

and shown in Fig. 2, the sequence **HIH** exists as a pair of non-interconverting conformational isomers. The *syn* isomer, with both methyl groups on the same side of the imide unit, can in principle interact weakly, *via* its unhindered face, with a single pyrene unit of the tweezer. In contrast, each face of the *anti* isomer is blocked by a methyl group and so an even weaker interaction with the tweezer would be expected. A small upfield shift for the *syn*- and an even smaller shift for the *anti*-**HIH** resonance would thus be predicted, accounting for the splitting of this resonance at high tweezer concentrations (Fig. 4).

A control experiment (ESI, Fig. S5) using the homopolyimide from diamine **4** and pyromellitic anhydride, in which every imide unit is of the type "**HIH**", shows exactly the same 1 : 1 splitting of the imide resonance, the same very small interaction-shifts but *no* fine-structure development.

Finally, a corresponding analysis of the environments of **HIU** and **HIU** in copolymer **6** predicts that at high tweezer : imide ratios the corresponding resonances should both split to give simple doublets. As shown in the ESI (Fig. S2) this is indeed the pattern of resonances observed.

It is clear that: (i) the aromatic ring-current shift induced by a tweezer-type molecule such as **1a** represents a powerful tool for identifying polyimide chain-sequences by ^{1}H NMR, (ii) in a polymer "triplet" sequence, only small variations in the steric requirements of the flanking monomer residues are needed to achieve high selectivity in supramolecular recognition of the central residue, (iii) more extended polyimide sequences (triplets of triplets) can be assigned in detail by ^{1}H NMR, through the effects of singly- or doubly-adjacent tweezer-binding, and (iv) these effects result from strong tweezer-binding to unhindered di-imide residues, through a combination of electronically-complementary, π–π stacking (involving polymer chain-folding) and N–H···O hydrogen bonding between the amide groups of the tweezer and a carbonyl oxygen of the imide residue.

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Notes and references

‡ Previous work[7] has shown that tweezers **1a** and **1b** adopt essentially identical binding-geometries with pyromellitimides. In the present study, crystal quality led to **[1b + 2]** being chosen for X-ray analysis. Single crystals of the complex were grown by vapour diffusion of an equimolar solution of the two components in chloroform/hexafluoropropan-2-ol (6/1 v/v) with diethyl ether as non-solvent. **[1b + 2]**: $C_{87}H_{53}Cl_2N_5O_{12}S_2{\cdot}3C_3H_2F_6O{\cdot}CHCl_3$ M_r = 2118.9, triclinic, *P*-1, a = 10.9503(4), b = 17.6840(10), c = 23.9264(12) Å, α = 104.520(2), β = 96.031(3), γ = 91.682(3)°. V = 4452.9(4) Å^3, T = 120 K, Z = 2, D_c 1.58 g cm^{-3}, μ(Mo-κα) = 0.32 mm^{-1}, F (000) = 2152. Independent measured reflections 9168. R_1 = 0.139, wR_2 = 0.391 for 6742 independent observed reflections [$2\theta \leqslant 20.8°$, $I > 2\sigma(I)$]. Average $I/\sigma(I)$ 15.5. CCDC 248234. See http://www.rsc.org/suppdata/cc/b4/b412801j/ for crystallographic data in .cif or other electronic format.

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