Abstract: Supramolecular chirality was observed in a charge-transfer (CT) complex formed by self-assembly of β-cyclodextrin-linked pyrene and adamantane-linked pyromellitic diimide in water. In the complex, the pyrene–pyromellitic diimide CT interaction is reinforced several-fold by the strong β-cyclodextrin–adamantane inclusion binding interaction, as confirmed by 1H NMR, absorption, fluorescence and isothermal titration calorimetry studies. The CT complex exhibited high stability, as inferred from the temperature-dependent absorption and NMR studies. The CT absorption band exhibited a positive Cotton effect indicative of supramolecular chirality for the complex. Twisted fibres were observed in TEM, AFM, and SEM experiments. A mechanism involving synergistic binding interactions leading to 2D sheets, followed by twisting of the sheet, is proposed for the formation of twisted fibres. This system offers a chance to investigate a combination of supramolecular CT and supramolecular chirality and explore their synergistic effects.

Introduction

Mixed-stack charge-transfer (CT) complexes formed from aromatic donor (D) and acceptor (A) molecules are not regarded as good materials for electronic applications, as these systems are considered to be insulators or semiconductors. However, a recent study by Tayi et al. has shown that mixed-stack CT crystals could undergo ferroelectric charge switching at room temperature. Density functional calculations and quantum/classical dynamics simulations by Brédas and co-workers also predicted that mixed-stack CT systems have great potential in organic electronics. A major problem associated with mixed-stack CT systems is the very low or moderate association constants for complexation, especially in the case of intermolecular D–A systems, which limit their potential to create structures with long-range order essential for electronic applications.

Recent reports have shown that CT complexes with very large association constants could be prepared by reinforcing the CT interaction with other non-covalent forces such as hydrogen bonding, π-stacking and hydrophobic interactions. This method has emerged as an excellent tool for assembling functional supramolecular nanostructures such as supramolecular gels, vesicles, foldamers and liquid-crystalline materials.

A few supramolecular CT complexes designed in this way were found to also exhibit interesting ferroelectric properties. Kim and co-workers have extensively utilized the host cavity of cucurbiturils, particularly CB[8], to form stable CT complexes between electron-deficient 4,4′-bipyridinium derivatives and electron-rich aromatics. They were successful in making various supramolecular assemblies, such as molecular necklaces, redox-controlled vesicles and rotaxane dendrimers, by using such host-stabilized CT interactions. These design strategies have been adopted to build molecular machines and recognize various biologically relevant molecules. Supramolecular CT complexes thus constructed were found to be chiral only if enantiomerically pure D or A was employed in their construction. Supramolecular chirality has not been observed previously in any mixed-stack CT complexes.

Herein, we report the construction of chiral supramolecular structures by using CT interactions reinforced by β-cyclodextrin (β-CD) inclusion binding in aqueous solution. The constituents of the self-assembly are a pyrene (PY) donor appended to the narrow rim of β-CD through an amide linkage (PYCD) and a pyromellitic diimide (PI) acceptor linked to an N-ethylpyridinium moiety at one end and an adamantyl (AD) group at the other (PIAD). The structures of PYCD and PIAD are shown in Scheme 1. Each of these molecules provides two binding sites for the other, that is, the PY part of PYCD can have CT interaction with the PI unit of PIAD and the AD moiety of PIAD can undergo inclusion binding in the β-CD cavity of PYCD. Both modes of interaction are shown in Scheme 1. For this study we also employed water-soluble pyrene derivative PYP (Scheme 1), which has no inclusion binding site, as a model compound. Although a variety of supramolecular CT complexes have been reported, this is the first report dealing with the amplification of CT interaction by inclusion binding in cyclodextrins. We observed formation of a very stable supra-
Results and Discussion

PIAD and PYCD were prepared as shown in Scheme 2. The intermediates and final products were well characterized by using state-of-the-art spectroscopic methods (see Experimental Section and Supporting Information).

The CT interaction between PY and PI is well characterized with signature absorption in the 400–650 nm region. Figure 1 shows the CT absorption of a 2.5 × 10^{-3} M aqueous solution containing equimolar amounts of PYCD and PIAD (PIAD@PYCD). Although the CT band can be observed even at 2.5 × 10^{-3} M PIAD@PYCD concentration, the reddish brown colour due to the CT complex (inset of Figure 1) could be observed only at concentrations above 10^{-4} M. Temperature dependence of the CT band is also shown in Figure 1. For most PY/PI or PY/naphthalene diimide systems the CT band disappears at temperatures above 80 °C. For the PIAD/PYCD system the CT band was very intense even at 90 °C, which suggests that the CT complex is very stable.

The 1H NMR spectra of PIAD and PYCD in D_2O are shown in Figure 2. In the 1H NMR spectrum of PIAD@PYCD in D_2O, major changes compared to the spectra of the individual components are indicated by arrows. The adamantyl group exhibited three peaks in the region 1.75–2.5 ppm. Upon complexation, peaks at 2.15 and 2.47 ppm coalesced to a broad peak, and the quartet at 1.75 ppm underwent significant changes, suggesting that the adamantyl moiety is encapsulated deeply in the β-CD cavity. The aromatic proton signals of PY are significantly dampened due to π–π stacking due to CT complexation. The sharp singlet at 8.15 ppm corresponding to the aromatic proton of PI undergoes significant dampening and an upfield shift to 6.55 ppm due to π–π stacking. The protons of the pyridinium moiety of PIAD exhibited only small upfield shifts and broadening. All these changes in the 1H NMR signals confirm that inclusion binding and CT interactions take place in the PIAD/PYCD system.
Temperature-dependent $^1$H NMR spectra of PIAD@PYCD are shown in Figure 3. The broad peaks obtained at 25 °C became sharper and better resolved at 80 °C. For example, the aromatic proton signal of PI, which was very broad at 25 °C, became sharper with considerable downfield shift at 80 °C. However, even at 80 °C, the spectrum exhibited considerable differences from the spectra of the individual components shown in Figure 2, suggesting that the complex has not dissociated completely even at this high temperature.

Two-dimensional ROESY experiments performed on the PIAD@PYCD system gave additional proof for the inclusion of the adamantyl moiety inside the β-CD cavity. The H-3 and H-5 protons of β-CD are oriented towards the interior of the CD cavity, and the NMR signals due to these protons are strongly affected when a guest molecule is included in the CD cavity. The H-3 and H-5 protons of β-CD, through-space interactions will occur, and these can be observed as cross-peaks in ROESY experiments. We observed cross-peaks between the adamantyl protons and H-3 and H-5 protons of β-CD in ROESY experiments (Figure S10 in the Supporting Information), which confirm that the AD moiety is located within the β-CD cavity.

Solutions of PIAD@PYCD in [D$_6$]MeOH and [D$_6$]DMSO were colourless, and this suggests that a CT complex is not formed in these solvents. NMR spectra recorded in these solvents (Figures S11 and S12, Supporting Information) also did not show any evidence for CT or inclusion binding. Solutions of model system PIAD@PPY in D$_2$O were slightly coloured, and the NMR spectrum (Figure S13, Supporting Information) showed evidence for π stacking. For example, the aromatic proton of PI (H$_8$ in Figure S13, Supporting Information) undergoes considerable upfield shift and slight broadening upon CT complexation. The NMR signals of the AD protons remain unaffected. All these experiments confirmed that synergistic CT and inclusion binding are essential to bring about the strong PYCD/PIAD complexation observed in the case of the PIAD@PYCD system.

For PY/PI intermolecular systems CT complexation was observed only at high concentrations, and the association constant for CT complex formation was estimated as $K_{ct} < 10^4$ M$^{-1}$.[16,19] For several AD derivatives association constant for inclusion binding in β-CD are $K_{in} \approx 10^4$ M$^{-1}$.[19] For the PIAD/PYCD system the association constant $K_n$ determined by isothermal titration calorimetry (ITC) was $1.82 \times 10^4$ M$^{-1}$ (Figure 4a). Other parameters obtained from the experiment are:

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\Delta H = -5.811 \times 10^4 \text{ J mol}^{-1}, \quad \Delta S = -74.9 \text{ J deg}^{-1} \text{ mol}^{-1}, \quad \Delta G = -35.7 \text{ KJ mol}^{-1},
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and binding stoichiometry $n = 0.82$. The $K_n$ value obtained is approximately equal to $K_{ct} \times K_{in}$, and suggests that both CT and inclusion binding interactions act synergistically in this system. The large negative entropy indicates higher-order assembly of the molecules during formation of the CT complex. When the model compound PYP was employed instead of PYCD in the ITC experiment, small endothermic heat changes were observed (Figure 4b). The observed heat changes may be attributable to a dilution effect. To confirm this, a titration experiment was carried out with water in both cell and syringe, and the ITC curve obtained was very similar to Figure 4b (see Supporting Information, Figure S14). These results indicate a very small $K_n$ value for the PY/PYPI interaction.

The very large association constant observed for the PIAD/PYCD system could be further confirmed by competitive displacement experiments. Adamantane carboxylate (ADC) exhibits very high affinity for the π-CD cavity ($K_n \approx 10^4$ M$^{-1}$).[20] ADC is capable of displacing most organic guests from the β-CD cavity and is often used in competitive displacement experiments.[21] We observed that addition of ADC to PIAD@PYCD did not lead to observable heat changes in the ITC experiment (Figure S15a, Supporting Information), and this suggests that ADC is not capable of displacing PIAD from the cavity of PYCD. On the other hand, addition of PIAD to the ADC/PYCD (1:1) system led to considerable heat changes in the ITC experiment (Figure S15b, S1), which suggest that PIAD is capable of displacing ADC from a β-CD cavity. The ITC experiments thus suggest-

![Figure 3. Temperature-dependent (25–80 °C) $^1$H NMR spectra of PIAD@PYCD in D$_2$O.](image-url)
ed that inclusion of the AD moiety of PIAD in the β-CD cavity of PYCD is the dominant interaction contributing to the very high stability of the PIAD-PYCD system.

To probe the PIAD–PYCD interaction at the molecular level, we recorded the absorption, emission and circular dichroism (CD) spectra of PIAD@PYCD at very low concentrations. Figure 5a shows the absorption spectrum of aqueous PYCD (2.5 × 10⁻⁵ M) in the absence and presence of PIAD (0.5 and 1.0 equiv.). The presence of even very small amounts of PIAD leads to considerable decrease in the intensities of the vibrational bands at 343 and 327 nm and slight increases in intensity below 320 nm and above 348 nm. Formation of the CT band in the 400–650 nm region was also observed at this low concentration (inset of Figure 5a). Figure 5b shows the fluorescence spectra of the above solutions and clearly shows that 1 equiv of PIAD quenches more than 90% of the fluorescence due to PYCD, which is possible only if the quenching is mostly static. This means that even at a low concentration of 2.5 × 10⁻⁵ M almost all the PY residues are π-stacked with PI in PIAD@PYCD to give the CT complex. Control experiments with the model compound PYP at low concentration showed that the absorption and fluorescence are nearly unaffected in the presence of one equivalent of PIAD, and no CT band could be observed (Figure S16, Supporting Information). These studies supported the conclusion reached from the ITC studies that the dominant interaction is the inclusion binding.

The PIAD@PYCD interaction was also probed by CD spectroscopy. Both PY and PIAD are achiral molecules and do not exhibit any Cotton effect. Since β-CD is chiral, an achiral chromophore may exhibit induced circular dichroism (ICD) when associated with β-CD. Figure 6 shows the ICD spectrum obtained for the PIAD@PYCD (2.5 × 10⁻⁵ M) system. The spectrum showed a negative ICD signal in the 300–350 nm region.

The sign of the ICD signal can be used to predict the orientation of the associated molecules with respect to the β-CD axis by using the Kodaka rules,[22] which predict the following: 1) the sign of ICD is positive for a transition polarized parallel to the axis of the β-CD, and negative for one polarized perpendicular to the axis; 2) the sign of ICD is reversed when a chromophore moves from the inside of the β-CD cavity to the outside while keeping the direction of the transition moment unchanged; 3) the absolute value of ICD is greater when a chromophore is located on the outside of the narrower rim than when it is on the outside of the wider rim. Using these rules we can predict the orientation of PY and PI with respect to the β-CD axis in the PIAD/PYCD system. Both PY and PI absorb in the 300–350 nm region. Absorption of PY in this region corresponds to the Sₐ→S₂ transition, which is very intense (ε = 42 000 M⁻¹ cm⁻¹) and polarized along the long axis of pyrene, as shown in Figure S17 (Supporting Information). The absorption due to PI in this region corresponds to the S₂→S₁ transition, which is very weak (ε = 2000 M⁻¹ cm⁻¹) and polarized along the long axis of PI (Figure S18, Supporting Information). Since the absorption transitions of PY and PI in the 300–350 nm region are polarized along the long axes of the molecules, negative ICD signals can arise only from parallel orientations of these molecules outside the cavity or perpendicular orientations inside the cavity. The latter can be ruled out because of geometric restrictions. On the basis of these factors we suggest that the orientations of the PY and PI molecules with respect to β-CD are as shown in Figures S17 and S18 (Supporting Information). These orientations are also in agreement with the possible inclusion and CT binding modes shown in Scheme 1. The absorption contributing to the ICD signal is that due to the complex, which corresponds to the blue spectrum in Figure 5a, and not pure PY.

In Figure 6, the CT band region is very noisy because of the very low absorbance in this region. We recorded the CD spectrum with 5 × 10⁻⁴ M PIAD@PYCD (in a 1 mm cell), as shown in Figure 7a. In this spectrum the negative signal in the 300–350 nm region showed increased intensity but lost the fine structural details. The spectrum clearly shows that the CT band...
also is CD-active, and suggests that the CT complex is also chiral.

Upon increasing the concentration of PIAD@PYCD to $2 \times 10^{-3}\text{ M}$, a positive CD signal could be observed for the CT band (Figure 7b). At this concentration the optical density of the solution below 400 nm is much higher than 1.0, and hence the CD spectrum below 400 nm could not be recorded. We also studied the temperature dependence of the CT-band CD signal, which is also shown in Figure 7b. The CD signal exhibited high stability even at 80 °C (Figure 7b). Temperature dependence of the CD signal is similar to that of the CT-band absorption in Figure 1. The chirality induced in PY or PI by linkage or encapsulation in β-CD is very small, as indicated by the low ICD intensity of the CT band in Figure 6. Thus the intense CD signal in Figure 7b cannot be attributed to transfer of molecular chirality from β-CD to PY or PI, which in turn transfer the chirality to the CT complex. The observed CD spectrum can be due to supramolecular chirality resulting from twisted or helical nanostructures.

To confirm the presence of nanostructures in PIAD@PYCD solutions, Tyndall effect and dynamic light scattering (DLS) experiments were performed (Figure S19, Supporting Information), and these studies confirmed the presence of nanostructures in solution. Subsequently TEM, SEM and AFM images were obtained to identify the nanostructures (Figure 8a–d, more images are given in the SI, Figures S20–S22). The images confirmed the presence of twisted fibre-like nanostructures. These fibres are several micrometres long and have widths of about 750 nm and heights of about 250 nm. The dimensions of the fibres obtained by the different techniques were in very good agreement.

In Scheme 1 the possible CT and inclusion binding interactions in the PIAD@PYCD system are shown. These interactions can repeat several times to give a 2D structure in which the PY and PI residues are assembled in a mixed stack, as shown in Scheme 3. The resulting sheet-like structure can undergo twisting to give the observed twisted fibre-type structures.

![Figure 7.](image1.png) **Figure 7.** a) ICD spectrum of PIAD@PYCD ($5 \times 10^{-4}\text{ M}$) in a 1 mm cuvette. b) CD spectrum of the CT band of PIAD@PYCD ($2 \times 10^{-3}\text{ M}$) and its temperature dependence.

![Figure 8.](image2.png) **Figure 8.** a) TEM, b) SEM, c) AFM images of helical fibres and d) Zoomed portion of the helical fibre. The inset in d) shows the height profile of the fibre.

![Scheme 3.](image3.png) **Scheme 3.** Various stages in the transformation of PIAD@PYCD into chiral supramolecular fibres.
Conclusion

Our approach involving synergistic amplification of CT interaction by inclusion binding resulted in a highly stable mixed-stack CT system. The CT band exhibited an intense CD signal suggesting that the complex exhibits supramolecular chirality. Chiral conductors are still a real challenge for material scientists, and the synergy between chirality and CT in the PIAD®-PYCD system along with its high stability may offer interesting opportunities for chiral optics and chiral electronics.

Experimental Section

Instrumentation and methods

All solvents and reagents were commercially available and used without further purification, unless otherwise specified. All experiments were performed in deionized water at 25 °C. Electronic absorption spectra were recorded with a Shimadzu UV-2600 UV/Vis spectrophotometer, and the emission spectra with a SPECTRO-Fluorolog 3 spectrofluorimeter. ITC data were obtained with a MicroCal ITC 200. The raw data obtained were fitted and analysed by using Origin 7.0 software provided with the instrument. CD experiments were performed in deionized water at 25 °C, unless otherwise specified. All NMR spectra were recorded in D2O or D6-DMSO purchased from Aldrich by static cell holders for variable-temperature studies. All NMR spectra were recorded with a JASCO 810 spectrometer on quartz cuvettes of 1 cm or 1 mm path length, equipped with Peltier thermostatic cell holders for variable-temperature studies. All NMR spectra were recorded in D2O or D6-DMSO purchased from Aldrich by using a 500 MHz Bruker Avance DPX spectrometer. ESI-HRMS mass spectra were recorded with an Orbitrap mass spectrometer (Thermo Exactive). TEM analyses were performed with a FEI-TECNAI T30 G25-TWIN 300 kV HRTEM microscope with an accelerating voltage of 100 kV, and the samples were prepared by drop casting the aqueous solution on a Formvar-coated copper grid (400 mesh) and evaporating excess water. AFM images were recorded with a Multimode SPM (Bruker Nanoscope V) operating in tapping mode. Antimony-doped silicon cantilevers with a resonant frequency of 300 kHz and spring constant of 40 N m⁻¹ were used. Antimony-doped silicon cantilevers with a resonant frequency of 300 kHz and spring constant of 40 N m⁻¹ were used.

Synthesis and characterization

Syntheses of PIAD and PYCD are shown in Scheme 2.

Synthesis of compound 1: PIAD was synthesised by modifying a reported procedure.[21] Pyromellitic dihydride (6.0 g, 27.5 mmol) was dissolved in dry DMF (60 mL) and 1-adamantylamine (4.14 g, 27.5 mmol) was added. After 1 h, 2-aminooethanol (1.68 g, 27.5 mmol) was added and the mixture heated to reflux for 6 h at 140 °C. The reaction mixture, after cooling, was added to ice-cold water and the resulting precipitate was filtered off, dried and purified by column chromatography on silica gel. Elution with methanol/chloroform (5:95) gave 1 (1.68 g, 27.5 %). 1H NMR ([D6]DMSO): δ = 8.22 (s, 2H), 4.17 (t, 2H), 3.65 (t, 2H), 2.52 (d, 6H), 2.19 (s, 3H), 1.74 ppm (q, 6H). 13C NMR ([D6]DMSO): δ = 28.40, 29.06, 38.20, 41.22, 45.8, 128.24, 136.52, 166.05, 167.21 ppm.

Synthesis of compound 2: Compound 2 (0.3 g, 0.74 mmol) and tetrabromomethane (0.27 g, 0.8 mmol) were dissolved in dry tetrahydrofuran under inert atmosphere. Triphenylphosphine (0.21 g, 0.80 mmol) was added to the solution at 0 °C and the mixture stirred at room temperature for 0.5 h. The reaction was quenched with a few drops of water, and the mixture was partitioned between CH2Cl2 (100 mL) and H2O (80 mL). The organic layer was separated and washed with water (3×50 mL) and brine (50 mL). The organic layer was dried over anhydrous Na2SO4, and the solvent was evaporated under reduced pressure. Compound 3 was obtained as a light yellow solid (0.207 g, 67 %). 1H NMR (CDCl3): δ = 8.22 (s, 2H), 4.17 (t, 2H), 3.65 (t, 2H), 2.52 (d, 6H), 2.19 (s, 3H), 1.74 ppm (q, 6H). 13C NMR (CDCl3): δ = 28.40, 29.06, 38.20, 41.22, 45.8, 128.24, 136.52, 166.05, 167.21 ppm.

Synthesis of compound 4: Compound 3 (0.5 g, 1.06 mmol) and pyridine (10 mL) were heated to reflux for 10 h and cooled. The crude product was washed free of pyridine with hexane and re-crystallised from hexane/chloroform to give 4 (0.442 g, 75 %).

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Conflict of interest

The authors declare no conflict of interest.

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[21] Dicyclohexylcarbodiimide (0.180 g, 0.86 mmol) and 1-hydroxybenzotriazole (0.109 g, 0.80 mmol) were added to a cooled solution (−10 °C) of 1-pyreneacetic acid (0.21 g, 0.86 mmol) in DMF (4 mL). The reaction mixture was stirred at −10 °C for 30 min. To the stirred solution 5 (0.45 g, 0.40 mmol) was added and stirring continued at −10 °C for 30 min. The mixture was then heated to reflux at 60 °C for 24 h. The reaction mixture was cooled and DMF was removed under vacuum. The residue obtained was washed with an excess of acetone and dried. The solid obtained was dissolved in DMF and subjected to reverse-phase column chromatography on silica gel. Elution with methanol/water (1:1) gave 6 (0.28 g, 52 %). IR: ν = 3334, 2933, 1651, 1537, 1153, 1029, 945, 848 cm⁻¹; 1H NMR ([D6]DMSO): δ = 8.01–8.39 (m, 10H), 5.66–5.87 (m, 14H), 4.83–4.97 (m, 7H), 4.80 (t, 1H), 4.24–4.50 (m, 7H), 3.54–3.62 (m, 14H), 3.3–3.4 ppm (m, 32H); 13C NMR ([D6]DMSO): δ = 59.84, 72.01, 72.22, 72.40, 72.97, 73.16, 81.39, 81.63, 81.86, 99.49, 101.88, 101.97, 123.90, 124.04, 124.10, 124.68, 124.88, 125.02, 126.13, 126.76, 127.12, 127.37, 128.55, 128.99, 129.64, 130.34, 130.59, 131.06, 131.34, 131.67 ppm; ESI-MS calcd for C60H81NO35: 1376.45 [M+H]+; found: 1376.47.

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Do the twist: A chiral supramolecular charge-transfer complex is formed by the synergistic effect of charge-transfer interaction and inclusion binding between a pyrene-appended β-cyclodextrin donor and an adamantane-linked pyromellitic diimide acceptor in aqueous solution, and formation of twisted fibres was observed by electron microscopy and AFM (see scheme).