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Extreme Complementarity in a Macrocycle–Tweezer Complex

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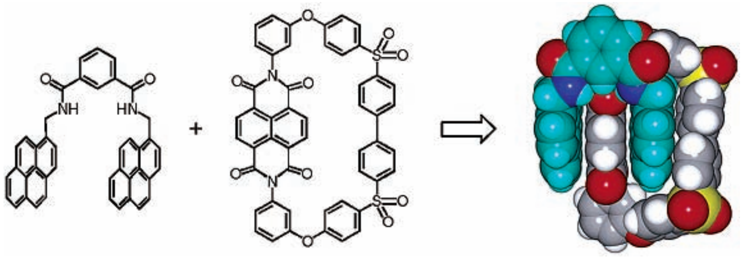
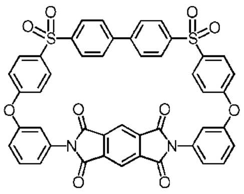
ABSTRACT



Interaction of a novel pyrene-based tweezer molecule with a macrocyclic ether-imide-sulfone results in formation of a strongly bound complex ($K_a = 24\,000$ M^{-1}) in which binding results not only from π–π stacking interactions involving pyrene units as donors and macrocyclic naphthalene-tetracarboximide and biphenylenedisulfone groups as acceptors but also from N–H···O and C–H···O hydrogen bonds and from "reverse" π-stacking of the electron-poor isophthaloyl residue of the tweezer with an electron-rich 3-aminophenoxy residue of the macrocyclic imide.

Intense current interest in the design of multicomponent, nanoscale molecular assemblies has led to the exploitation of many types of intermolecular interaction, including hydrogen bonding,[1] solvophobic effects,[2] metal−ligand coordination,[3] and π-stacking between aromatic donor and acceptor sites.[4] The latter interaction has proved especially valuable for directing the synthesis of supramolecular systems such as catenanes and rotaxanes,[5] thereby enabling the fabrication of nanoscale devices including light- and redox-driven switches[6] and molecular logic gates.[7]

In view of the relatively labile nature of the *N*-benzylpyridinium linkage on which much research into π-stacked molecular assemblies has so far depended, we recently developed a new and much more stable class of *all-aromatic* macrocyclic receptors (e.g., **1** and **2**) by cyclo-imidization of amine-terminated aromatic ether-sulfones.[8]



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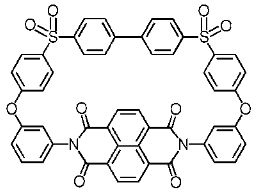

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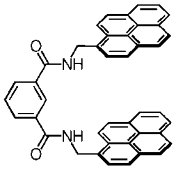

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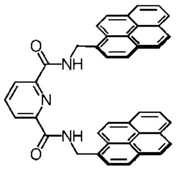

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These macrocycles display extreme thermochemical stability and readily form donor−acceptor complexes in which

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[†] University of Reading.
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(1) For recent examples see: Grieg, L. M.; Philp, D. *Chem. Soc. Rev.* **2001**, *30*, 287. Cantrill, S. J.; Fyfe, M. C. T.; Heiss, A. M.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Org. Lett.* **2000**, *2*, 61. Cantrill, S. J.; Fulton, D. A.; Heiss, A. M.; Pease, A. R.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **2000**, *6*, 2274.
(2) Cubberley, M. S.; Iverson, B. L. *J. Am. Chem. Soc.* **2001**, *123*, 7560 and references therein.
(3) (a) Seidel, S. R.; Stang, P. J. *Acc. Chem. Res.* **2002**, *35*, 972. (b) Vilar, R. *Angew. Chem., Int. Ed.* **2003**, *42*, 1460. (c) Kusukawa, T.; M. Yoshizawa, M.; Fujita, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 1879.

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electron-rich polycyclic hydrocarbons such as pyrene and perylene are bound within the receptors via aromatic π-stacking with the electron-poor diimide and biphenylenedisulfone units. The association constants in solution (800 and 1400 M^{-1} for pyrene and perylene, respectively) are, however, not especially high, and even substrates that might have been expected to complex more strongly with macrocyclic imide-sulfones via "tweezer-type" multiple π-stacking interactions instead afforded only pseudorotaxanes, with similarly low binding constants.[8] There are in fact remarkably few tweezer−macrocycle complexes known, the only examples so far described comprising pseudorotaxanes in which, for example, terminal 1,5-dioxynaphthalene units wrap onto the outer faces of a 4,4′-bipyridinium-based macrocycle.[9] Here we report that a new group of amide-based substrates derived very simply from 1-pyrenemethylamine *do* act as molecular tweezers and complex strongly to macrocyles **1** and **2.** The resulting assemblies are bound through a novel combination of noncovalent interactions including multiple donor−acceptor π-stacking, hydrogen bonding, and "reverse" π-stacking between electronically complementary ring systems.

Reaction of isophthaloyl chloride or pyridine-2,6-dicarbonyl chloride with 1-pyrenemethylamine afforded the novel tweezer molecules **3** and **4**, respectively, in high yield. Interaction of as little as 0.05 molar equiv of tweezer **3** with macrocycle **2** in $CDCl_3$/hexafluoro-propan-2-ol resulted in a very marked broadening and upfield shift of the formerly very sharp ^1H NMR singlet resonance arising from the naphthalene-diimide unit, though other macrocyclic resonances were much less affected (see Supporting Information) This observation suggests both that the kinetics of complexation between **2** and **3** are close to the slow exchange limit and that the naphthalene residue in macrocycle **2** represents the principal binding site for its interaction with **3**. As the tweezer:macrocycle mole ratio progressively increases toward 1:1, very large ring-current-induced complexation shifts are observed in the ^1H NMR spectrum, especially for the resonance arising from the biphenylene protons adjacent to the arene−arene bond ($\delta\Delta$ = 1.60 ppm upfield, for 1:1 stoichiometry). This clearly indicates that the biphenylene unit of the macrocycle, as well as the imide fragment, must be closely involved in the complexation process. Analogous complexation shifts are observed for all four possible combinations of macrocycles **1** and **2** with tweezers **3** and **4**.

Complex **5**, formed between the essentially colorless components **2** and **3**, is deep red in color as a result of a strong charge-transfer absorption band centered at 565 nm. A Job plot based on this absorption, using chloroform/hexafluoro-propan-2-ol (6:1) as solvent, is shown in Figure 1, which affords conclusive evidence for 1:1 complexation.

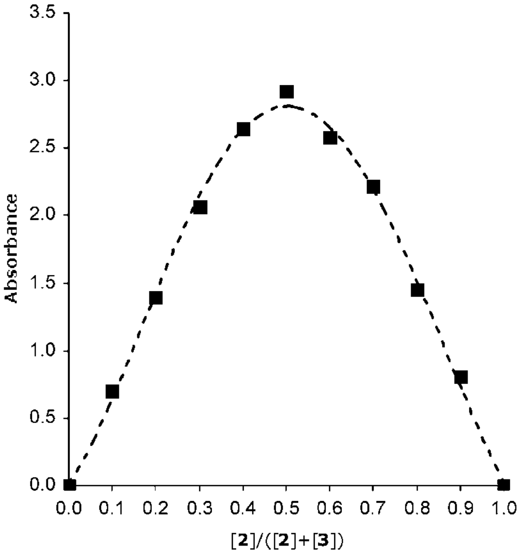

Figure 1. Job plot (based on the charge-transfer absorption at 565 nm) for complexation of macrocycle **2** with tweezer molecule **3** at 25 °C in chloroform/hexafluoro-propan-2-ol (6:1) as solvent.

Measurement of the association constant in the same solvent system using the UV−visible dilution method,[10] again based on changes in the charge-transfer band, gives a value of 24 300 (± 400) M^{-1}, a more than 30-fold increase over the value for pyrene itself.

Complex **5** was obtained in crystalline form by vapor diffusion of diethyl ether into an equimolar solution of the two components in chloroform/hexafluoro-propan-2-ol, and single-crystal X-ray analysis[11] provided an immediate explanation for the extraordinarily high binding constant.

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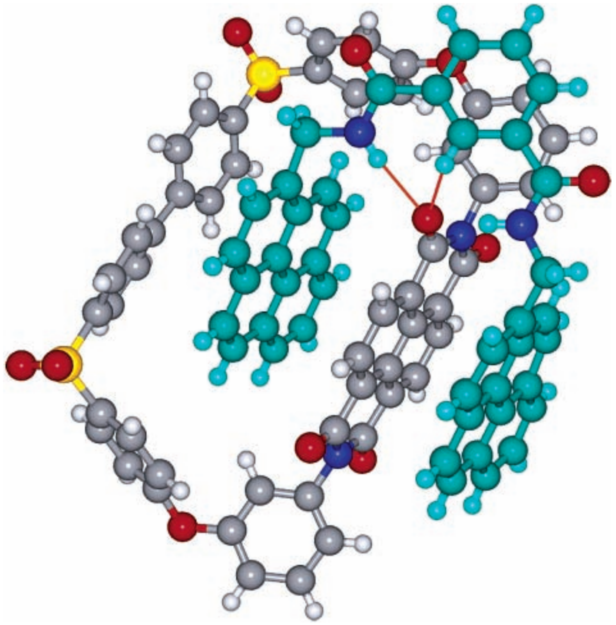

Figure 2. X-ray structure of the 1:1 complex (**5**) formed between **2** and **3**.

As shown in Figure 2, macrocycle **2** is gripped by the tweezer molecule **3** in such a way that the (electron-poor) naphthalene-diimide residue comprising one face of the macrocycle forms a triple donor−acceptor π-stack with the electron-rich pyrenyl ring systems of the tweezer (with interplanar spacings ca. 3.53 Å).[12] In addition, the "inner" pyrene residue π-stacks with the (noncoplanar) biphenylenesulfone unit comprising the opposite face of the macrocycle, with aromatic C···C contacts as short as 3.28 Å. Most unexpectedly, a clear-cut π-stacking interaction (shortest interring C···C contact 3.65 Å) can also be identified between one of the two (electron-rich) 3-aminophenoxy residues in the macrocycle and the (electron-poor) isophthaloyl unit of the tweezer, as shown in Figure 2. In donor−acceptor terms, this last stacking interaction is opposite in direction to that of the other three. So far as we are aware, the present system represents the first example of a π-stacked complex in which the binding is mutually complementary, i.e., each component interacts with the other through both π-donor and π-acceptor sites.

Further interactions that should certainly enhance the binding constant are centered on one of the diimide carbonyl groups, to which two strong hydrogen bonds are formed by the tweezer. As shown in Figure 2, one hydrogen bond is formed from a tweezer amide group (N−H···O═C; H···O = 2.17 Å, N−H−O = 171°) while the other originates from the 2-position of the isophthaloyl ring (C−H···O═C; H···O = 2.31 Å, C−H−O = 124°). The N−H hydrogen of the second amide group, however, appears too far removed from the carbonyl oxygen for hydrogen bonding to be significant (H···O = 2.71 Å, N−H−O = 127°).

Interestingly, the association constant for the corresponding complex (**6**) between tweezer **3** and the *pyromellitimide*-based macrocycle **1** is very much lower than that for complex **5**, at only 9 200 (± 200) M^{-1}. However, computational modeling indicates that the pyromellitimide residue in **1** should hydrogen bond to the tweezer in much the same way as the naphthalimide residue in **2**. The difference in binding constant must therefore reflect a weaker overall set of $\pi-\pi$ stacking interactions in complex **6**, where the pyromellitimide residue offers a substantially smaller aromatic π-system for complexation.

As shown in Figure 3, complex **5** packs in the crystal so that the "outer" pyrene residue of each tweezer forms a yet further π-stack, now with the biphenylenesulfone unit of the adjacent complex. The resulting linear chain comprises an "infinite" sequence of alternating donor and acceptor units, $[P_o\text{-}N\text{-}P_i\text{-}B]_\infty$, where P_o, P_i, N, and B represent the "outer" pyrene, "inner" pyrene, naphthalenedi-imide, and biphenylenesulfone residues, respectively. Somewhat analogous intercomplex π-stacking has previously been reported in the

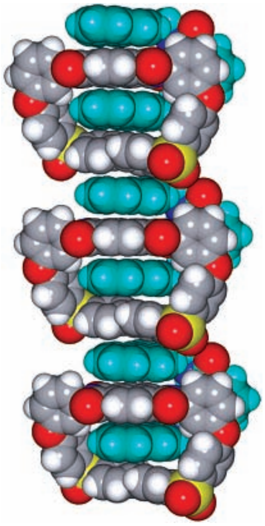

Figure 3. Formation of "infinite" π-stacks between adjacent units of complex **5** in the crystal.

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[11] Crystal data for **5**$\cdot$2.62(CH$_2$Cl$_2$): $C_{50}H_{28}N_2O_{10}S_2\cdot C_{42}H_{28}N_2O_2\cdot 2.62(CH_2Cl_2)$, $M_r = 1696.5$, triclinic, space group *P*-1 (No. 2), $a = 14.482(1)$, $b = 16.014(1)$, $c = 19.382(2)$ Å, $\alpha = 95.388(8)°$, $\beta = 105.608(7)°$, $\gamma = 97.577(6)°$, $V = 4250.0(7)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.325$ g cm^{-3}, μ(Cu Kα) = 2.62 mm^{-1}, $T = 203(2)$ K, red rhombic needles; 12537 independent measured reflections, F^2 refinement, $R_1 = 0.0597$, $wR_2 = 0.144$; 7750 independent observed reflections ($I > 2\sigma(I)$, $2\theta_{max} = 120°$), 1084 parameters. The dichloromethane solvent molecules are disordered over several overlapping partial occupancy sites and could not be resolved. The solvent content was estimated and allowed for using the program SQUEEZE, v.d. Sluis, P.; Spek, A. L. *Acta Crystallogr*. **1990**, *A46*, 194−201. CCDC-211237 contains supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.; fax (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

[12] In the solid state, two alternative orientations (in the ratio 0.61:0.39) are observed for the "outside" pyrene ring of the tweezer unit **3**. Both orientations retain a parallel and overlapping alignment of the pyrene ring systems, but in the former the molecular symmetry of **3** is C_s (as illustrated in Figures 2 and 3) whereas in the latter (minor occupancy orientation) the symmetry is C_2.

crystal structures of catenanes based on 1,5-dioxynaphthalene and either 4,4′-bipyridinium[13] or naphthalenediimide residues.[14]

Although this report focuses on the interaction between macrocycle **2** and tweezer **3**, preliminary investigations of the three remaining combinations of macrocyclic and tweezer-type components described above, i.e., [**2** + **3**], [**1** + **4**], and [**2** + **4**], including a provisional crystallographic analysis of the latter, clearly indicate that in all cases complexes analogous to **5** are formed. More extensive studies of these systems, particularly of their dynamic behavior in solution, are currently in progress.

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Supporting Information Available: Experimental procedures and full characterization data for compounds **3** and **4**. Crystallographic data for complex **5** in CIF format. Space-filling diagrams of complex **5**, showing the range of π-stacking interactions. Complexation shifts in the ^{1}H NMR spectra of macrocycle **2**, showing complexation shifts in the presence of tweezer molecule **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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