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A Molecular Chameleon: Chromophoric Sensing by a Self-Complexing Molecular Assembly**

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In supramolecular chemistry[1]—the domain of chemistry where noncovalent bonding interactions[2] become important—the concept of self-assembly[3] is being increasingly exploited to create molecular-based architectures at the nanoscale level. Over the last decade, numerous researchers have harnessed the power of the noncovalent bond to produce aesthetically pleasing molecular assemblies[4] as well as supramolecular arrays. In recent years, we have employed the molecular recognition[2] that exists between π electron rich aromatic rings (e.g. hydroquinone, 1,5-dioxynaphthalene) and π electron deficient aromatic units (e.g. bipyridinium, diazapyrenium) coupled with C–H···O and O–H···π interactions to assist in the self-assembly of catenanes,[5] rotaxanes,[6] and pseudorotaxanes.[7]

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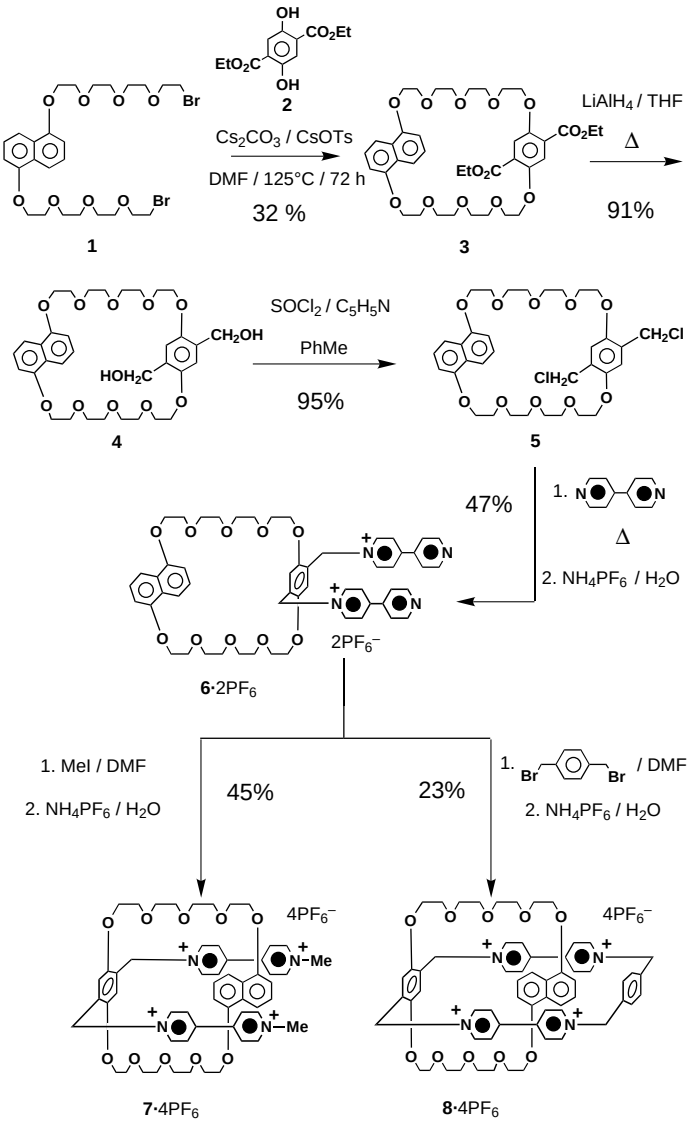
[**] We thank the Eusko Jaurlaritza Unibersitate, Hizkuntza, eta Ikerketa Saila in the Basque Country (Spain) for the award of a predoctoral fellowship (to M.G.-L). The research was funded in the UK by the Engineering and Physical Sciences Research Council.

Here we report the four-step synthesis of an intermediate dicationic salt $\mathbf{6}\cdot 2PF_6$ (see Scheme 1), and the potential of the AB_2-type[8] monomeric tetracation $\mathbf{7}^{4+}$ possessing complementary recognition sites, which is easily obtained from $\mathbf{6}\cdot 2PF_6$, to self-assemble in the shape of a polysupramolecular dendritic wedge (see Scheme 2a).[9] Furthermore, we report on a related attempt to construct from $\mathbf{6}\cdot 2PF_6$ a polycatenane that is reminiscent of an anchor chain; however, the fascinating macrobicyclic tetracation $\mathbf{8}^{4+}$ is formed instead. It is composed of two complementary macrocycles linked together by a common aromatic ring in a manner that allows it to display an intriguing kind of self-complexation,[10] as demonstrated in solution by ^1H NMR spectroscopy and in the solid state by X-ray crystallography. We also describe how $\mathbf{8}^{4+}$ can act in a novel fashion as a chromophoric receptor[11] for tetrathiafulvalene (TTF; see Scheme 3), giving the macrobicyclic tetracation molecular switching[12] properties.

Scheme 1 outlines the synthesis of the key intermediate $\mathbf{6}\cdot 2PF_6$.[13] Reaction of the dibromide **1**[7] with the diester **2**



Scheme 1. The synthesis of the crown ether derivative $\mathbf{7}\cdot 4PF_6$ and the self-assembly of the self-complexing macrobicycle $\mathbf{8}\cdot 4PF_6$. Ts = toluenesulfonyl.

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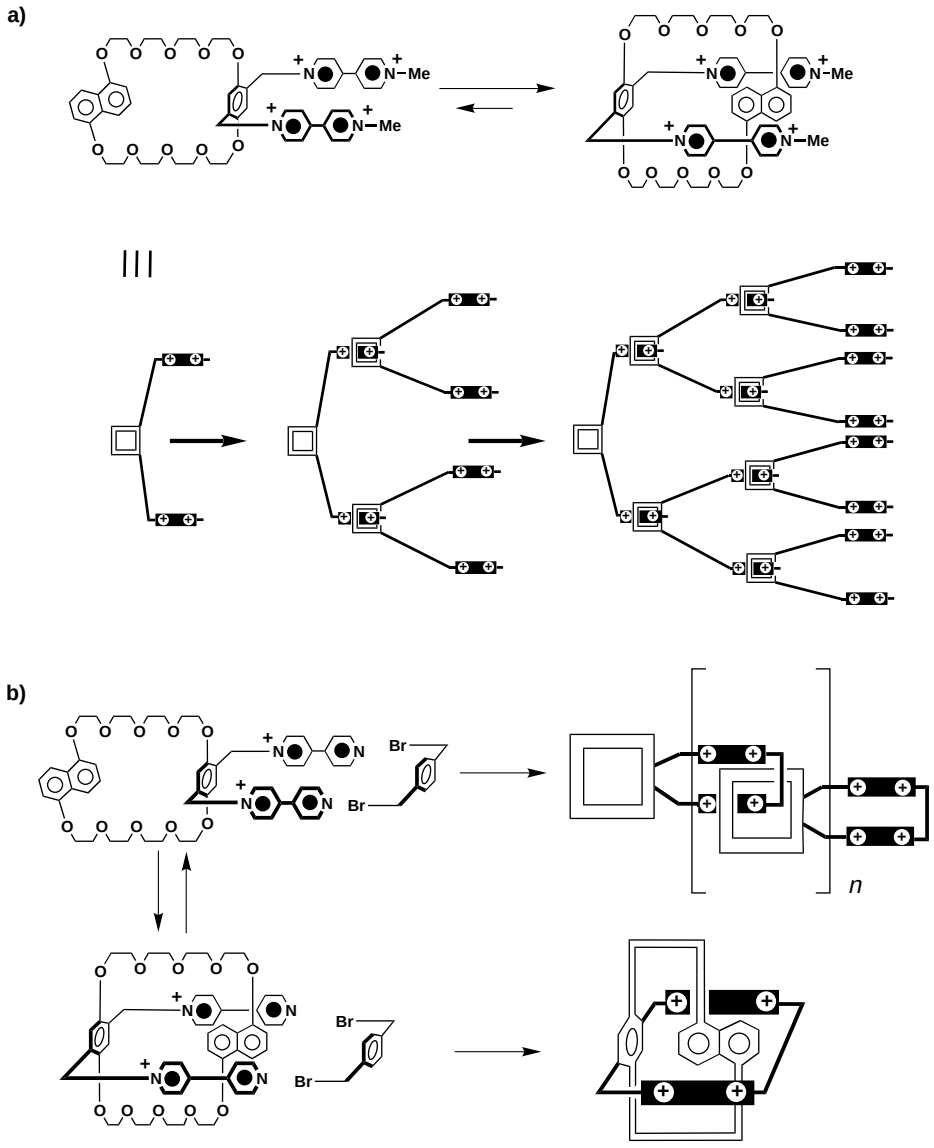
afforded the crown ether **3**. The ester groups in **3** were reduced to give the bis(hydroxymethyl) derivative **4**, which was converted into the corresponding dichloride **5**. Reaction of **5** with 4,4′-bipyridine yielded $\mathbf{6}\cdot 2PF_6$ after counterion exchange. Reaction of this salt with an excess of MeI afforded $\mathbf{7}\cdot 4PF_6$. The template-directed synthesis of $\mathbf{8}\cdot 4PF_6$ was achieved in 23% yield by the reaction of $\mathbf{6}\cdot 2PF_6$ with 1,4-bis(bromomethyl)benzene followed by counterion exchange.

Since the signals in the ^{1}H NMR spectra of $\mathbf{7}\cdot 4PF_6$ recorded in CD_3CN at 304 K show only marginal concentration dependences in a range from 2.76×10^{-2} to 6.10×10^{-4} M, it seems unlikely that dendritic supramolecular arrays, such as those shown in Scheme 2a, are being formed to any significant extent. Comparison of the ^{1}H NMR chemical shifts of $\mathbf{7}\cdot 4PF_6$ with those of model compounds suggests very strongly that $\mathbf{7}^{4+}$ adopts a conformation[13] in CD_3CN in which its 1,5-dioxynaphthalene ring system is sandwiched by its own bipyridinium units (Scheme 2a). Given this situation, it is perhaps hardly surprising that $\mathbf{6}^{2+}$ reacts with 1,4-bis(bromomethyl)benzene to give $\mathbf{8}^{4+}$ as the exclusive catenated product. In fact, no oligocatenanes in the series of the anchor-chain-like polycatenane (see Scheme 2b) appeared to be formed during this reaction. Nonetheless, the macrobicyclic tetracation is a fascinating self-complexing species in its own right. In this communication we report its structure and demonstrate its chameleonlike[14] properties.

The X-ray analysis[15] of a crystal obtained by vapor diffusion of iPr$_2$O into a solution of $\mathbf{8}\cdot 4PF_6$ in acetone revealed that the salt crystallized in a space group that imposes a crystallographic inversion center in the middle of the 1,5-dioxynaphthalene ring, thus requiring the structure to be disordered (Figure 1). However, two alternative orientations for the polyether linkages were clearly resolved, thereby permitting a straightforward analysis of the crystal structure.



Scheme 2. Schematic representation of a) a supramolecular dendrimer derived from $\mathbf{7}^{4+}$ and b) a polycatenane or macrobicycle derived from $\mathbf{6}^{2+}$ and 1,4-bis(bromomethyl)benzene.

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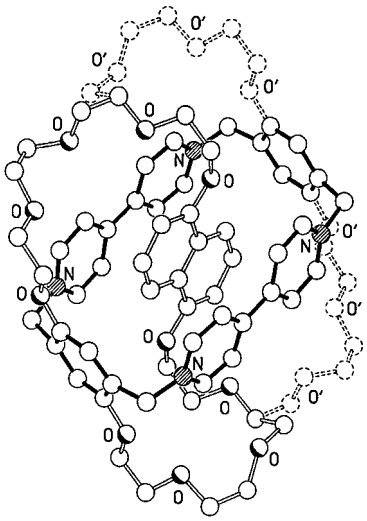
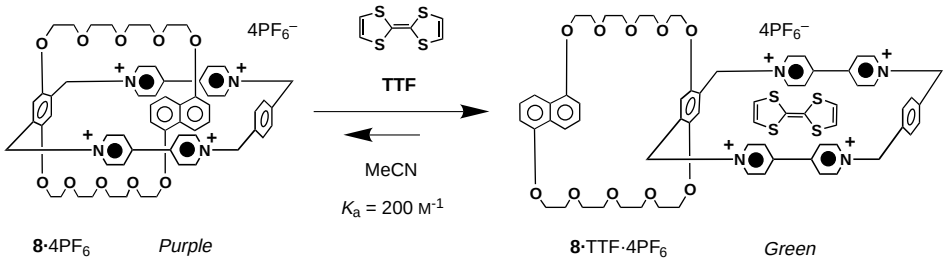


Figure 1. The solid-state structure of $\mathbf{8}^{4+}$. The broken bonds and atoms indicate alternative symmetry-imposed orientations for the polyether linkages.

The 1,5-dioxynaphthalene ring is sandwiched in a conventional manner between the two bipyridinium units[16] (mean interplanar separation 3.35 Å). The O-$C_{10}H_6$-O vector is inclined by 52° to the mean plane of the cyclophane component (as defined by the four methylene carbon atoms). The overall conformation is stabilized by π–π stacking interactions and by C–H···O hydrogen bonds involving the α- and β-bipyridinium hydrogen atoms of one of the pyridinium rings and the second and third oxygen atoms of one of the polyether linkages. The associated C···O and H···O distances are 3.25 and 2.38 Å, respectively, for the α-bipyridinium hydrogen atom and 3.28 and 2.38 Å, respectively for the β-bipyridinium hydrogen atom; the corresponding C–H···O angles are 150° and 157°. In addition, there are C–H···π interactions between the naphthalene hydrogen atoms on C-4 and C-8 and their proximal *p*-xylyl rings (the distance between the H atom and the π electron plane is 2.56 Å, and the C–H···π angle 150°). There are no intermolecular stacking interactions.

Although the resonances in the ^{1}H NMR spectrum of $\mathbf{8}\cdot 4PF_6$ recorded in CD_3CN at 304 K are very broad, they become sharp on cooling the sample down to 233 K. All the protons which are nonequivalent in the tetracation have been assigned with the aid of two-dimensional COSY and NOESY techniques. For example, eight signals[17] can be observed for the α- and β-bipyridinium protons, and the chemical shifts for the H-4 and H-8 protons on the 1,5-dioxynaphthalene ring system resonate at very high field ($\delta = 2.14$, 2.67). This indicates that the ring system is located inside the tetracationic cyclophane, as in the solid-state structure. The resonances for these protons coalesce at 309 K (T_c) as a result of a site-exchange process in which the 1,5-dioxynaphthalene ring system leaves the cavity of the tetracationic cyclophane by a process that involves rotation about the -$CH_2C_6H_2R_2CH_2$- axis of the disubstituted *p*-xylyl residue, undergoes a reorientation as a result of a pedalling motion about the axis defined by the naphthalene ring junction, and reenters the cavity of the tetracationic cyclophane. The free energy of activation $\Delta G_c^{\neq}$ for this process[18] was calculated[19] from the k_c value of 490 s^{-1} to be 14.3 ± 0.1 kcal mol^{-1}.

Addition of one molar equivalent of TTF to the solution of $\mathbf{8}\cdot 4PF_6$ in CD_3CN (Scheme 3) results in a dramatic change in the color of the solution from purple to green. This reflects a shift in the absorbance maximum, corresponding to the charge-transfer band associated with donor–acceptor interactions, from $\lambda_{max} = 537$ nm (when the 1,5-dioxynaphthalene ring system is the donor) to $\lambda_{max} = 846$ nm (when TTF is the donor). Spectrophotometric titration[20] of TTF with $\mathbf{8}\cdot 4PF_6$ in acetonitrile afforded a K_a value[21] of $200 \pm 10\ M^{-1}$ for the 1:1 complex $[\mathbf{8}\cdot TTF]\cdot 4PF_6$. The ^{1}H NMR spectrum of this complex recorded in CD_3CN displays signals at $\delta = 6.57$, 7.25, and 7.53 for the naphthalene ring protons, indicating that the



Scheme 3. The formation of the intermolecular 1:1 complex between $\mathbf{8}\cdot 4PF_6$ and tetrathiafulvalene (TTF) illustrates how the self-complexing macrobicycle acts as a chromophoric receptor.

1,5-dioxynaphthalene ring system has been expelled from the cavity and is rotating freely about the naphthalene ring junction axis. By contrast, the TTF ring protons resonate in the spectrum as a singlet at $\delta = 5.68$, which reflects their being shielded within the cavity of the tetracationic cyclophane. The switching action[22] between a molecular state and a supramolecular one is characterized by its efficiency and simplicity.

It is clear from the results reported here that the principle of maximum site occupancy[1] along with unfavorable entropy factors[3, 23] will always conspire, in the case of compounds like $\mathbf{7}\cdot 4PF_6$ and $\mathbf{8}\cdot 4PF_6$, against the formation of extended supramolecular arrays and large molecular assemblies. To favor their formation, self-complexation[24] has to be avoided at all costs.

Experimental Section

$\mathbf{6}\cdot 2PF_6$: The crown ether **5** (200 mg, 0.29 mmol) was added to a solution of 4,4′-bipyridine (940 mg, 6.0 mmol) in dry MeCN (120 mL). The reaction mixture was heated under reflux for 14 h. After evaporation of the solvent the mixture was purified by column chromatography (SiO_2, MeOH/$MeNO_2$/2 M NH_4Cl aq 7/1/2). Counterion exchange (NH_4PF_6/H_2O) produced a yellow solid precipitate, which was dried in vacuo to afford $\mathbf{6}\cdot 2PF_6$ as a yellow powder (165 mg, 47 %). M.p. > 270 °C (decomp); FAB-MS: *m*/*z* (%) = 1214 (5) [M^+], 1069 (100) [$M - PF_6$]$^+$; ^{1}H NMR (400 MHz, CD_3CN, 25 °C): $\delta = 8.90$ (d, $J = 7$ Hz, 4H), 8.78 (br s, 4H), 8.08 (d, $J = 7$ Hz, 4H), 7.66 (br s, 4H), 7.53 (d, $J = 8$ Hz, 2H), 7.06 (t, $J = 8$ Hz, 2H), 6.61 (d, $J = 8$ Hz, 2H), 6.56 (s, 2H), 5.65 (d, $J = 14$ Hz, 2H), 5.19 (d, $J = 14$ Hz, 2H),

  1433-7851/98/3707-0977 $ 17.50+.50/0

3.60 – 4.17 (m, 32H); ^{13}C NMR (100.6 MHz, CD_3CN, 25 °C): $\delta = 150.5$, 147.5, 147.2, 147.8, 143.7, 139.1, 133.1, 132.7, 132.6, 129.7, 129.6, 127.6, 127.3, 126.2, 115.5, 114.9, 106.1, 77.1, 70.8, 70.6, 70.2, 70.1, 69.4, 69.1, 68.6, 52.5; HR-MS (LSI-MS) calcd for $C_{54}H_{60}N_4O_{10}PF_6$ $[M - PF_6]^+$: 1069.3951, found: 1069.3988.

7·4PF$_6$: The salt **6**·2PF$_6$ (35 mg, 0.029 mmol) was dissolved in MeCN (20 mL). MeI (100 mg, 0.70 mmol) was added, and the mixture heated under reflux for 14 h. The solvent of the dark red solution was evaporated in vacuo. The reaction mixture was purified by column chromatography (SiO_2; MeOH/$MeNO_2$/2 M NH_4Cl aq 7/1/2 and then original eluent/DMF 3/1). Counterion exchange (NH_4PF_6/H_2O) yielded a red solid, which was isolated by filtration and washed with H_2O. The solid was dried in vacuo to afford **7**·4PF$_6$ as a brown powder (20 mg, 45 %). M.p. > 270 °C (decomp); FAB-MS: $m/z = 1557$ $[M+Na]^+$, 1534 $[M^+]$, 1389 $[M - PF_6]^+$, 1245 $[M - 2PF_6]^+$, 1100 $[M - 3PF_6]^+$; ^{1}H NMR (400 MHz, CD_3CN, 25 °C): $\delta = 9.07$ (d, $J = 7$ Hz, 4H), 8.73 (d, $J = 7$ Hz, 4H), 8.20 (d, $J = 7$ Hz, 4H), 8.14 (d, $J = 7$ Hz, 4H), 7.40 (d, $J = 8$ Hz, 2H), 6.97 (s, 2H), 6.86 (t, $J = 8$ Hz, 2H), 6.50 (d, $J = 8$ Hz, 2H), 5.70 (d, $J = 14$ Hz, 2H), 5.30 (d, $J = 14$ Hz, 2H), 4.35 (s, 6H), 3.60 – 4.17 (m, 32H;); ^{13}C NMR (100.6 MHz, CD_3CN, 25 °C): $\delta =$ 158.8, 154.7, 151.8, 150.2, 147.5, 147.1, 127.6, 127.2, 126.8, 126.1, 124.3, 115.8, 114.9, 106.1, 70.9, 70.6, 70.4, 70.0, 69.9, 69.2, 68.9, 68.6, 61.7, 49.5, 30.9; HR-MS (LSI-MS) calcd for $C_{56}H_{66}N_4O_{10}P_1F_6$ $[M - 3PF_6]^+$: 1099.4421, found: 1099.4449.

8·4PF$_6$: The salt **6**·2PF$_6$ (81 mg, 0.067 mmol) was dissolved in MeCN (10 mL). 1,4-Bis(bromomethyl)benzene (19 mg, 0.072 mmol) was added, and the reaction mixture stirred at room temperature for 26 d. The dark purple solution was concentrated in vacuo, and the reaction mixture purified by column chromatography (SiO_2; MeOH/$MeNO_2$/2 M NH_4Cl aq 7/1/2 and then original eluent/DMF 2/1). Counterion exchange (NH_4PF_6/H_2O) produced a dark purple solid, which was isolated by filtration and washed with H_2O. The solid was dried in vacuo to afford **8**·4PF$_6$ as a purple powder (25 mg, 23 %). M.p. > 270 °C (decomp); FAB-MS: $m/z = 1632$ $[M+Na]^+$, 1609 $[M]^+$, 1463 $[M - PF_6]^+$, 1318 $[M - 2PF_6]^+$, 1173 $[M - 3PF_6]^+$; ^{1}H NMR (400 MHz, CD_3CN, −40 °C): $\delta = 9.19$ (d, $J = 7$ Hz, 1H), 9.14 (d, $J = 7$ Hz, 1H), 8.80 (d, $J = 7$ Hz, 1H), 8.77 (d, $J = 7$ Hz, 1H), 8.76 (d, $J = 7$ Hz, 1H), 8.68 (d, $J = 7$ Hz, 1H), 8.63 (d, $J = 7$ Hz, 1H), 8.50 (d, $J = 7$ Hz, 1H), 7.98 (s, 2H), 7.92 (s, 2H), 7.91 (s, 1H), 7.48 (dd, $J = 7$, 2 Hz, 1H), 7.40 (dd, $J = 7$, 2 Hz, 1H), 7.34 (dd, $J = 7$, 2 Hz, 1H), 7.33 (s, 1H), 7.32 (dd, $J = 7$, 2 Hz, 1H), 7.27 (dd, $J = 7$, 2 Hz, 1H), 7.23 (dd, $J = 7$, 2 Hz, 1H), 7.06 (dd, $J = 7$, 2 Hz, 1H), 7.02 (dd, $J = 7$, 2 Hz, 1H), 6.39 (d, $J = 8$ Hz, 1H), 6.36 (d, $J = 8$ Hz, 1H), 6.12 (t, $J = 8$ Hz, 1H), 6.09 (d, $J = 13$ Hz, 1H), 5.99 (d, $J = 13$ Hz, 1H), 5.75 (d, $J = 13$ Hz, 1H), 5.67 (d, $J = 13$ Hz, 1H), 5.65 (d, $J = 13$ Hz, 1H), 5.47 (t, $J = 8$ Hz, 1H), 5.28 (d, $J = 13$ Hz, 1H), 5.26 (d, $J = 13$ Hz, 1H), 3.45 – 4.55 (m, 32H), 2.67 (d, $J = 8$ Hz, 1H), 2.14 (d, $J = 8$ Hz, 1H); ^{13}C NMR (100.6 MHz, $(CD_3)_2CO$, −40 °C): $\delta = 153.0$, 152.3, 151.8, 150.8, 147.6, 146.0, 145.9, 145.8, 145.4, 145.0, 144.3, 143.9, 138.0, 137.5, 131.9, 131.7, 131.5, 131.3, 129.6, 127.9, 126.5, 126.2, 125.8, 125.1, 125.0, 124.9, 124.8, 124.6, 124.0, 114.0, 109.2, 108.3, 105.9, 105.4, 72.8, 72.6, 71.0, 70.2, 69.9, 69.7, 69.1, 68.8, 68.3, 68.1, 67.9, 65.4, 65.0, 60.2, 60.0; HR-MS (LSI-MS) calcd for $C_{62}H_{68}N_4O_{10}P_3F_{18}$ $[M - PF_6]^+$: 1463.3861, found: 1463.3912.

Received: September 29, 1997 [Z 10979 IE]
German version: *Angew. Chem.* **1998**, *110*, 1018 – 1022

Keywords: chromophores · molecular devices · nanostructures · receptors · supramolecular chemistry

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[13] Both **6**·2PF$_6$ and **7**·4PF$_6$ exhibit planar chirality; the ring inversions between their enantiomers are slow on the ^{1}H NMR time scale at room temperature. In the case of **6**·2PF$_6$, the ^{1}H NMR spectrum (400 MHz) recorded in CD_3CN at 304 K exhibits an AB system ($J_{AB} =$ 14 Hz) with δ values of 5.22 and 5.62 for the diastereotopic benzylic methylene protons. Upon increasing the temperature of the solution in CD_3CN, the AB system broadens and finally coalesces ($T_c = 369$ K) to a singlet centered on $\delta = 5.47$. A rate constant k_c of 372 s^{-1} was calculated at T_c with the approximation $k_c = \pi[(\upsilon_a - \upsilon_b)^2 + 6J_{ab}^2]^{1/2}/2^{1/2}$ where $\upsilon_a - \upsilon_b = 164$ Hz. The Eyring equation was then used with k_c and T_c to obtain a value of 17.4 ± 0.2 kcal mol^{-1} for $\Delta G_c^{\neq}$. Although **3** – **5** also possess planes of chirality, their enantiomers are inverting quickly on the ^{1}H NMR time scale at room temperature.

[14] The macrobicyclic tetracationic host **8**$^{4+}$ not only has the capacity to turn itself inside out but, in the presence of an appropiate guest (e.g. TTF), it also changes color. Since **8**$^{4+}$ is a changeable entity, both in terms of its conformation and color, we like to refer to it as a "molecular chameleon". The term "catenane chameleons" has already been used: D. A. Leigh, K. Moody, J. P. Smart, K. J. Watson, A. M. Z. Slawin, *Angew. Chem.* **1996**, *108*, 326-331; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 306 – 310.

[15] Crystal data for **8**·4PF$_6$ ($C_{62}H_{68}N_4O_{10}P_4F_{24} \cdot Me_2CO$): $M_r = 1667.2$, monoclinic, space group $P2_1/n$, $a = 14.218(2)$, $b = 21.164(2)$, $c =$ 14.890(2) Å, $\beta = 112.59(1)°$, $V = 4136.8(9)$ Å^3, $T = 203$ K, $Z = 2$ (the "molecule" has crystallographically imposed C_i symmetry), $\rho_{calcd} =$ 1.338 g cm^{-3}, $\mu(Cu_{K\alpha}) = 18.1$ cm^{-1}, $F(000) = 1712$. Data for the crystal of dimensions $0.13 \times 0.23 \times 0.60$ mm were collected on a Siemens P4/RA diffractometer ($2\theta \leq 110°$), ω scans, graphite-monochromated $Cu_{K\alpha}$ radiation. Of 5190 independent reflections measured, 3205 with $I > 2\sigma(I)$ were considered to be observed. The data were corrected for Lorentzian and polarization effects, but not for absorption. The structure was solved by direct methods, and the non-hydrogen atoms refined anisotropically. Because the space group requires the molecule

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to possess an inversion center, the structure has to be disordered. Two alternate orientations for eight of the atoms in each polyether linkage were identified. These atoms were refined with occupancies of 0.5. A ΔF map revealed the inclusion of one molecule of Me_2CO for each "molecule" of $\mathbf{8}\cdot 4PF_6$. The non-hydrogen atoms of this solvent were refined isotropically. Hydrogen atoms were placed in calculated positions, assigned isotropic thermal parameters $U(H) = 1.2\,U_{eq}(C)$ [$U(H) = 1.5\,U_{eq}(CMe)$], and allowed to ride on their parent carbon atoms. The structure was refined by full-matrix least squares based on F^2 to give $R_1 = 0.148$ and $wR_2 = 0.395$ for 557 parameters. The maximum and minimum residual electron densities in the final ΔF map were 1.11 and $-0.48\,e\,Å^{-3}$. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-100741. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[16] The angles of twist and bowing associated with the bipyridinium units[5a] are 5 and 22°, respectively.

[17] ^{1}H NMR: $\delta(\alpha$-bipyridinium-H) = 8.50, 8.63, 8.68, 8.76.8.77, 8.80, 9.14, 9.19; $\delta(\beta$-bipyridinium-H) = 7.02, 7.06, 7.23, 7.27, 7.32, 7.34, 7.40, 7.48.

[18] For a discussion of a very similar process in [2]catenanes, see M. Asakawa, P. R. Ashton, S. E. Boyd, C. L. Brown, R. E. Gillard, O. Kocian, F. M. Raymo, J. F. Stoddart, M. S. Tolley, A. J. P, White, D. J. Williams, *J. Org. Chem*. **1997**, *62*, 877 – 893.

[19] The temperature-dependent ^{1}H NMR spectra were analyzed with the coalescence method; values of k_c at T_c were obtained from the approximation $k_c = \pi\Delta\nu/2^{1/2}$, where $\Delta\nu$ is the limiting value for the difference [Hz] in chemical shifts for the exchanging protons. The Eyring equation was then used to calculate $\Delta G_c^{\neq}$ from k_c at T_c.

[20] The results of spectrophotometric titration were evaluated by a computer-assisted nonlinear least-square curve-fitting program (Ultrafit, Biosoft, Cambridge, **1992**).

[21] The binding constant K_a for the complex formed between TTF and the parent cyclophane cyclobis(paraquat-*p*-phenylene) in MeCN is $7190 \pm 970\,M^{-1}$ ($-\Delta G^\circ = 5.26 \pm 0.07$ kcal mol^{-1}): P.-L. Anelli, M. Asakawa, P. R. Ashton, R. A. Bissell, G. Clavier, R. Gorski, A. E. Kaifer, S. J. Langford, G. Mattersteig, S. Menzer, D. Philp, A. M. Z. Slawin, N. Spencer, J. F. Stoddart, M. S. Tolley, D. J. Williams, *Chem. Eur. J.* **1997**, *3*, 1113 – 1135. In the case of the [$\mathbf{8}^{4+}\cdot$ TTF] complex $K_a = 200 \pm 10\,M^{-1}$ ($-\Delta G^\circ = 3.14 \pm 0.02$ kcal mol^{-1}). It follows that $\Delta\Delta G^\circ = 2.12$ kcal mol^{-1}; this can be interpreted as the difference in free energy between the two extreme gross conformations of $\mathbf{8}^{4+}$, the self-complexed conformation and the "opened-up" conformation in which the two macrocycles incorporated into $\mathbf{8}^{4+}$ are free to associate with complementary guests.

[22] a) For an excellent review on current developments in molecular switches, see M. D. Ward, *Chem. Ind*. **1997**, 640 – 645. b) for our most recent publication on molecular switches, see M. Asakawa, P. R. Ashton, V. Balzani, A. Credi, C. Hamers, G. Mattersteig, M. Montalti, A. N. Shipway, N. Spencer, J. F. Stoddart, M. S. Tolley, M. Venturi, A. J. P. White, D. J. Williams, *Angew. Chem*. **1998**, *110*, 357 – 361; *Angew. Chem. Int. Ed.* **1998**, *37*, 333 – 337.

[23] a) P. R. Ashton, A. Collins, M. C. T. Fyfe, P. T. Glink, S. Menzer, J. F. Stoddart, D. J. Williams, *Angew. Chem*. **1997**, *109*, 59 – 62; *Angew. Chem. Int. Ed. Engl*. **1997**, *36*, 59 – 62; b) M. C. T. Fyfe, J. F. Stoddart, *Acc. Chem. Res*. **1997**, *30*, 393 – 401.

[24] Note added in proof (March 16, 1998): A self-complexing TTF macrocyle that can be switched has just appeared in the literature: see M. B. Nielsen, S. B. Nielsen, J. Becher, *Chem. Commun.* **1998**, 475 – 476.

The First Enantioselective Aza-Diels – Alder Reactions of Imino Dienophiles on Use of a Chiral Zirconium Catalyst**

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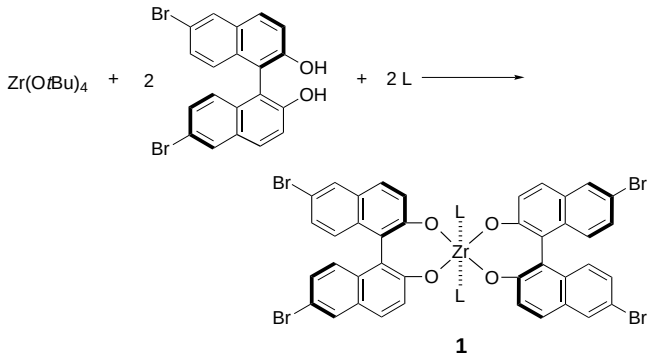
Asymmetric aza-Diels – Alder reactions provide a useful route to optically active heterocycles such as piperidines and tetrahydroquinolines.[1] Although successful examples of diastereoselective approaches have been reported,[2] there have been few accounts of enantioselective reactions. Yamamoto et al. described elegant enantioselective aza-Diels – Alder reactions of aldimines with Danishefsky's diene on using chiral boron compounds; however, stoichiometric amounts of chiral sources were needed.[3] Quite recently, we reported the first example of a catalytic, enantioselective aza-Diels – Alder reaction of azadienes on using a chiral lanthanide catalyst.[4] While high diastereo- and enantioselectivities were attained in the reaction of azadienes with dienophiles, the products obtained were limited to 8-hydroxytetrahydroquinoline derivatives. Here we report the catalytic, enantioselective aza-Diels – Alder reactions of aldimines (imino dienophiles) with Danishefsky's diene for the synthesis of a wide variety of chiral piperidine derivatives; a chiral zirconium compound was used as catalyst.

The chiral zirconium compound **1**[5] was prepared from $Zr(OtBu)_4$, (*R*)-6,6′-dibromo-1,1′-binaphthol [(*R*)-Br-BINOL, 2 equiv],[6] and the ligand L (2 – 3 equiv; Scheme 1). The



1

Scheme 1. Synthesis of **1**. L = ligand.

reaction of aldimine **2**, which is obtained from 1-naphthaldehyde and 2-aminophenol (Nap = naphthyl), with Danishefsky's diene **3**[7] was investigated as the model reaction. The ligand and the solvent influenced the yields and enantiose-

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[**] This work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, Japan, and a SUT Special Grant for Research Promotion. H.I. thanks the JSPS fellowship for Japanese Junior Scientists.