Slow Shuttling in an Amphiphilic Bistable [2]Rotaxane Incorporating a Tetrathiafulvalene Unit**

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The mechanically interlocked components of nondegenerate catenanes and rotaxanes[1] can be induced to switch between different ground-state geometries (co-conformations) in response to either physical (light activation) or chemical (redox or pH changes) stimuli.[2] Since the ring and dumbbell components of these highly ordered molecular assemblies can be induced to perform relative motions, such as circumrotation[3] (rotary motion) and shuttling[4] (linear motion), catenanes and rotaxanes[1] are now prime candidates for the construction of artificial molecular machines[5, 6] and the fabrication of molecular electronic devices.[7, 8] In recent years, a number of different protocols, based on self-assembly,[9] have been developed[3, 4, 10] for the template-directed synthesis[11] of rotaxanes. Among the desirable features for the redox-controllable, amphiphilic [2]rotaxanes that have been employed to fabricate single-molecule-thick electrochemical junctions in electronic devices are 1) the siting of redox-active units along the rod section of the dumbbell component and 2) the presence of both hydrophobic and hydrophilic groups as stoppers at the ends of the dumbbell component.

In the context of such devices, the tetrathiafulvalene (TTF) unit (which has found widespread use[12] in materials chemistry) is an ideal redox-active unit in view of its excellent π-electron-donating properties. It forms[13] a strong green 1:1 complex ($K_a = 8000\,\text{M}^{-1}$ in MeCN)[4c] with cyclobis(paraquat-*p*-phenylene)[14] ($CBPQT^{4+}$) for incorporation into a redox-switchable [2]rotaxane also containing a 1,5-dioxynaphthalene (DNP) ring system which also interacts, but somewhat more weakly[15] with $CBPQT^{4+}$ to afford a red color in the process. Although a TTF unit and a DNP ring system have been incorporated[16] into the crown ether ring component of a redox-switchable [2]catenane, which has already been employed in the fabrication of a solid-state electronically reconfigurable switch,[7] no rotaxanes containing these two recognition sites for a $CBPQT^{4+}$ component have been described in the literature.[17] Here, we report the template-directed synthesis of an amphiphilic bistable [2]rotaxane (Figure 1) in which the ring component is $CBPQT^{4+}$ and the dumbbell component—containing a monopyrrolo-TTF unit and a DNP ring system within its rod section—is terminated by a hydrophilic dendritic stopper at one end and a hydrophobic tetraarylmethane stopper at the other end.[18] Furthermore, we demonstrate the separation of the two possible translational isomers and discuss the kinetic and thermodynamic processes involved in the slow interconversion of the two isomers.

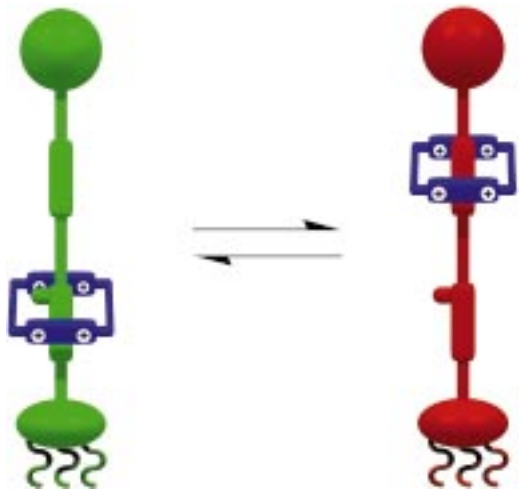

Figure 1. The concept of a slow molecular shuttle with a knob hindering the interconversion between the green and red translational isomers of an amphiphilic bistable [2]rotaxane.

The dumbbell-shaped compound **10** was synthesized as illustrated in Scheme 1. The monotosylate **2** was obtained in 48% yield by reaction of the diol[19] **1** with one equivalent of *p*-toluenesulfonyl chloride (TsCl). Alkylation of the hydrophobic tetraarylmethane-based stopper[10d, 18] **3** with **2** in MeCN in the presence of K_2CO_3 gave (80%) the alcohol **4**, which was subsequently brominated using CBr_4 and Ph_3P in CH_2Cl_2 to afford the bromide **5** in 94% yield. A solution of the recently described[18, 20] asymmetric monopyrrolo-TTF building block **6** in THF was treated with one equivalent of $CsOH \cdot H_2O$. This procedure generated the TTF-monothiolate, which was alkylated with one equivalent of the bromide **5** to afford the TTF derivative **7** in 74% yield. Removal of the tosyl protecting group was carried out in near quantitative yield by refluxing **7** in THF/MeOH (1/1) in the presence of an excess of NaOMe. An 83% yield of compound **10** was obtained following N-alkylation of the pyrrole unit in **8** with the hydrophilic stopper[18] **9** in DMF containing NaH. Self-assembly of the [2]rotaxane $\mathbf{13} \cdot 4\,PF_6$ was achieved (Scheme 2) in 23% yield using **10** as the template for the formation of the encircling $CBPQT^{4+}$ unit from its dicationic precursor[3] $\mathbf{11} \cdot 2\,PF_6$ and 1,4-bis(bromomethyl)benzene (**12**). The molecular shuttle was isolated as an analytically pure brown solid after column chromatography using a solution of NH_4PF_6 in Me_2CO as eluent. The fast atom bombardment mass spectrum (FAB-MS) of this brown solid shows intense peaks at *m*/*z* 2921, 2776, 2631, 1388, 1316, and 1243 which correspond to the $[M - PF_6]^+$, $[M - 2PF_6]^+$, $[M - 3PF_6]^+$, $[M - 2PF_6]^{2+}$, $[M - 3PF_6]^{2+}$, and $[M - 4PF_6]^{2+}$ ions, respectively.

UV/Vis and ^{1}H NMR spectroscopy indicated the presence of the two stable translational isomers present in the isolated product. The UV/Vis spectrum (Figure 2, curve a) recorded in Me_2CO showed a broad charge-transfer (CT) absorption

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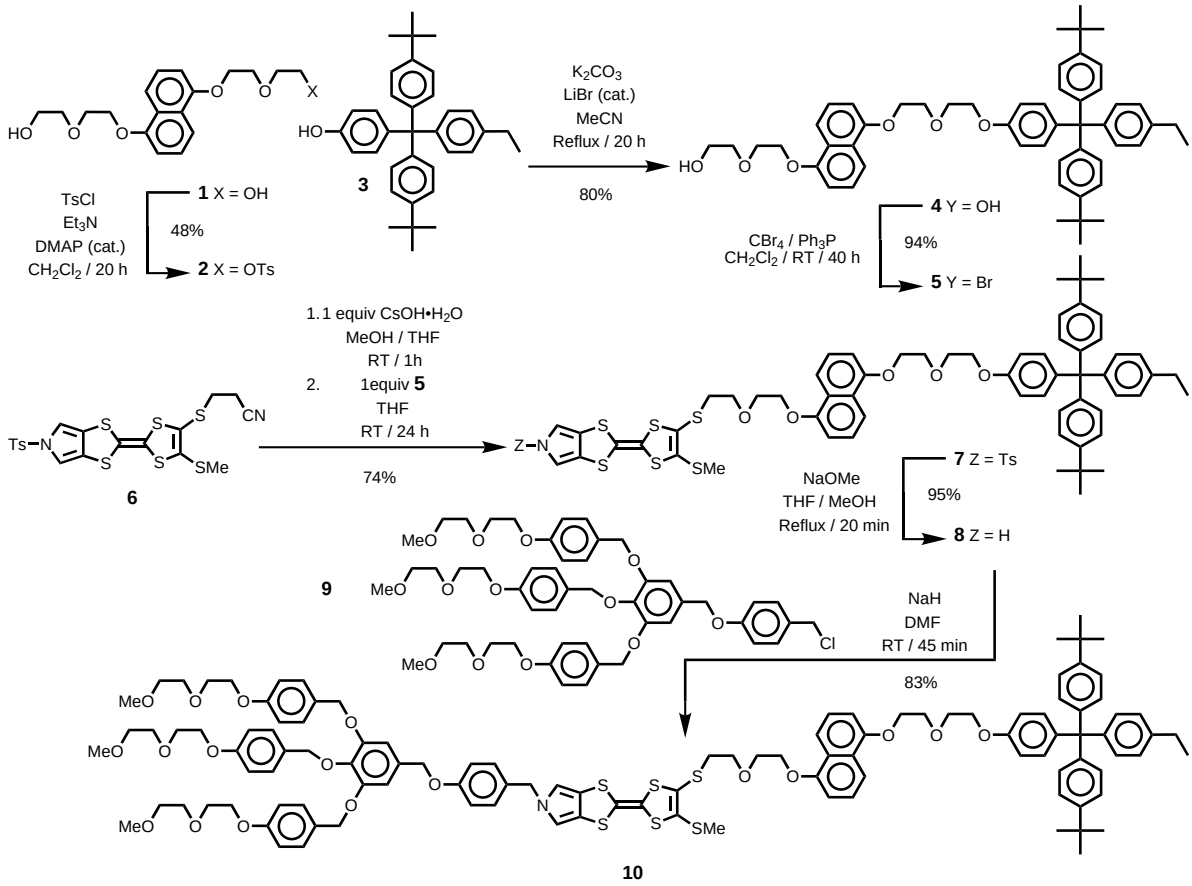
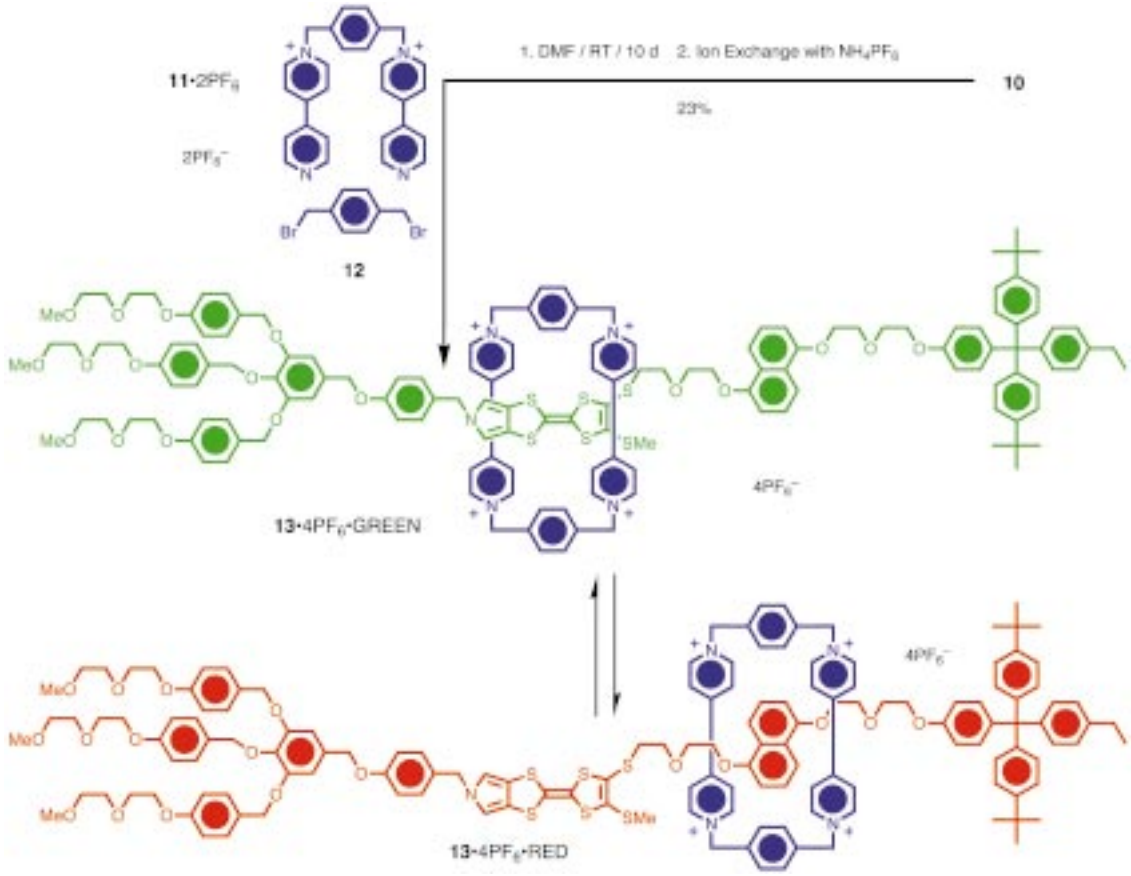


Scheme 1. Synthesis of the dumbbell-shaped compound **10**.



Scheme 2. Template-directed synthesis of the [2]rotaxane **13**·4PF$_6$.

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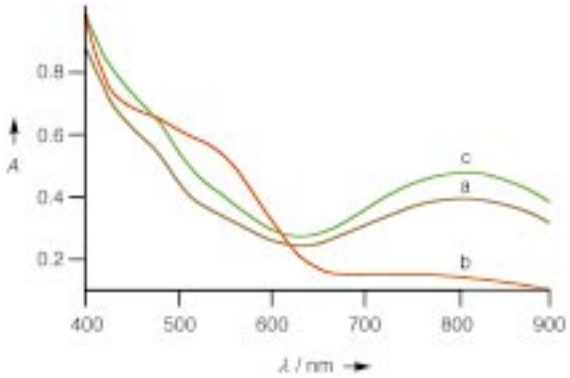

Figure 2. Absorption spectra (Me_2CO, 298 K) recorded on a solution of an equilibrium mixture of the [2]rotaxanes **13**·4PF$_6$·GREEN and **13**·4PF$_6$·RED (curve a) and of the [2]rotaxane **13**·4PF$_6$·RED (curve b) and the [2]rotaxane **13**·4 PF$_6$·GREEN (curve c) immediately after their isolation. Allowing the red solution of **13**·4PF$_6$·RED to stand for 24 h at room temperature regenerates the "original" spectrum (curve a).

band centered on 805 nm ($\varepsilon = 810\,M^{-1}cm^{-1}$)—which is characteristic[13] of co-conformations containing a TTF unit located "inside" CBPQT^{4+}—and a CT absorption band observed as a shoulder at 540 nm ($\varepsilon = 670\,M^{-1}cm^{-1}$)—which results from the DNP moiety being located "inside" the cyclophane.[19, 21] The ^{1}H NMR spectrum (400 MHz) recorded at 298 K in $(CD_3)_2CO$ showed (Figure 3) two singlets at $\delta =$ 2.64 and 2.47, which can be assigned to the SMe resonances

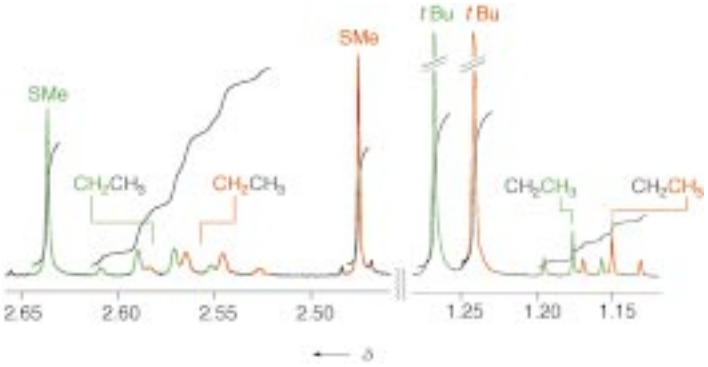

Figure 3. Partial ^{1}H NMR spectrum of an equilibrium mixture of the [2]rotaxanes **13**·4PF$_6$·GREEN and **13**·4PF$_6$·RED recorded at 400 MHz in $(CD_3)_2CO$ at 298 K.

attached to the TTF unit in **13**·4PF$_6$·GREEN and **13**·4PF$_6$·RED, respectively.[22] The ratio of the two translational isomers was estimated from the integrals of the two different SMe resonances to be approximately 1:1.

Thin-layer chromatography (TLC) of **13**·4PF$_6$ showed green and red spots with similar intensities, thus indicating the existence of two isolable translational isomers—one in which CBPQT^{4+} encircles the TTF unit (namely, **13**·4PF$_6$·GREEN) and another in which CBPQT^{4+} encircles the DNP ring system (namely, **13**·4PF$_6$·RED). By employing preparative thin-layer chromatography (PTLC), it was possible (Figure 4) to isolate the red translational isomer (**13**·4PF$_6$·RED). The UV/Vis spectrum (Figure 2, curve b) of **13**·4PF$_6$·RED reveals a CT absorption band which is observed as a shoulder at 540 nm. This band results from the DNP moiety

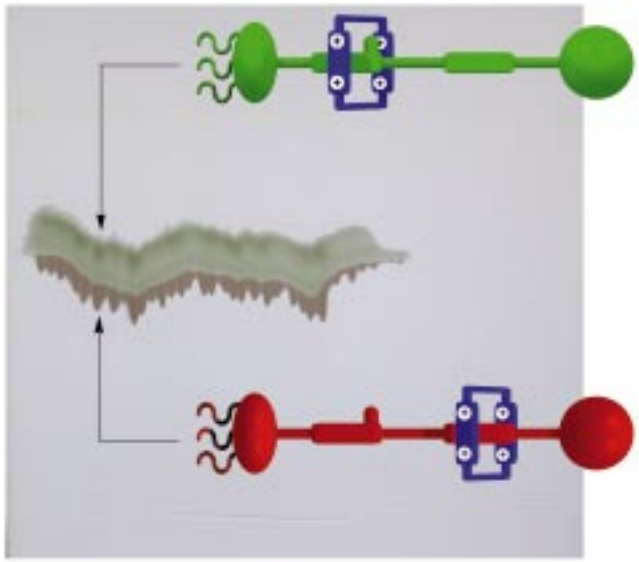

Figure 4. A preparative thin-layer chromatogram (see Experimental Section) showing the separation of **13**·4PF$_6$·RED from **13**·4PF$_6$·GREEN.

being located "inside" CBPQT^{4+}. Furthermore, no absorption band is observed in the region 750–850 nm where the CT interaction resulting from the TTF moiety being located "inside" the tetracationic cyclophane would occur. Leaving the red solution to stand for 24 h at room temperature gives back the "original" spectrum (Figure 2, curve a). The kinetics of the shuttling of CBPQT^{4+} from the DNP recognition site in **13**·4PF$_6$·RED to the TTF recognition site was investigated by ^{1}H NMR spectroscopy. The ^{1}H NMR spectrum (500 MHz) of **13**·4PF$_6$·RED was recorded (Figure 5a) at 230 K in

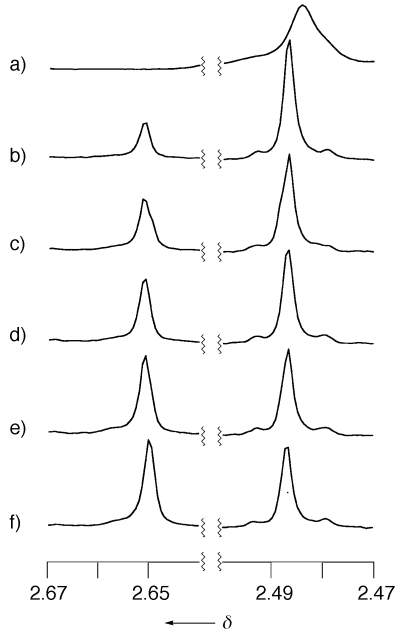

Figure 5. Partial ^{1}H NMR spectra (500 MHz) of the isolated [2]rotaxane **13**·4PF$_6$·RED recorded in $(CD_3)_2CO$ at a) 230 K/0 h, b) 300 K/1 h, c) 300 K/3 h, d) 300 K/5 h, e) 300 K/8 h, f) 300 K/21 h. The singlet at $\delta =$ 2.49 corresponds to the SMe resonance when CBPQT^{4+} encircles the 1,5-dioxynaphthalene ring system and the singlet at $\delta = 2.65$ corresponds to the SMe resonance when CBPQT^{4+} encircles the TTF unit.

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$(CD_3)_2CO$ and shows, as expected, only one signal for the SMe protons as a singlet resonating at $\delta = 2.49$. The sample was heated subsequently to 300 K and the shuttling of $CBPQT^{4+}$ from the DNP recognition site in $\mathbf{13}\cdot 4PF_6\cdot$RED to the TTF recognition site was followed using the SMe resonances as the probe (Figure 5b–f). After 21 h at 300 K, the system had equilibrated and a 1:1 mixture of $\mathbf{13}\cdot 4PF_6\cdot$RED and $\mathbf{13}\cdot 4PF_6\cdot$GREEN was re-established (Figure 5f). As a consequence of these spectroscopic variations the color of the solution changed from red to brown. By employing a first-order kinetic treatment[23] a rate constant of $k = 2\times 10^{-5}\ s^{-1}$ was obtained for the slippage of $CBPQT^{4+}$ over the SMe group, in the direction from $\mathbf{13}\cdot 4PF_6\cdot$RED to $\mathbf{13}\cdot 4PF_6\cdot$GREEN. The corresponding free energy of activation ($\Delta G^{\neq}$) for this isomerization is 24 kcal mol^{-1}.

Although it was not possible to isolate a sufficient amount of $\mathbf{13}\cdot 4PF_6\cdot$GREEN from the PTLC experiment to follow its interconversion into $\mathbf{13}\cdot 4PF_6\cdot$RED by ^{1}H NMR spectroscopy, it proved possible to shift the equilibrium between the two translational isomers from 1:1 to 9:1 in favor of $\mathbf{13}\cdot 4PF_6\cdot$GREEN by heating a solution of the brown 1:1 mixture in $(CD_3)_2SO$ to 425 K. The color of the solution changed from brown to green upon heating to 425 K. The solution was then quenched at 273 K (ice bath) and the conversion of $\mathbf{13}\cdot 4PF_6\cdot$GREEN into $\mathbf{13}\cdot 4PF_6\cdot$RED was followed at 300 K using the signals for the protons on the monopyrrolo-TTF unit and the DNP ring system as a probe. On this occasion, a first-order rate constant of $3\times 10^{-4}\ s^{-1}$ was obtained for the slippage of $CBPQT^{4+}$ over the SMe group in the direction from $\mathbf{13}\cdot 4PF_6\cdot$GREEN to $\mathbf{13}\cdot 4PF_6\cdot$RED. The associated $\Delta G^{\neq}$ value is 22 kcal mol^{-1}.

In summary, we have devised and completed the synthesis of an amphiphilic bistable [2]rotaxane comprising two different recognition sites, a TTF unit and a DNP ring system, for $CBPQT^{4+}$. The steric hindrance exhibited by the SMe group situated between the two recognition sites has made it possible to isolate the translational isomer $\mathbf{13}\cdot 4PF_6\cdot$RED and to study the kinetics of the shuttling of the tetracationic cyclophane between the two recognition sites. The process, which is accompanied by a clearly detectable color change, can also be followed by ^{1}H NMR and UV/Vis spectroscopy. This new amphiphilic rotaxane is currently being assessed for its ability to self-organize into monolayers as a prelude to its introduction into devices.

Experimental Section

5: Ph_3P (0.70 g, 2.67 mmol) was added portionwise to a solution of **4** (1.75 g, 2.20 mmol) and CBr_4 (0.88 g, 2.65 mmol) in anhydrous CH_2Cl_2 (15 mL) at room temperature. The reaction mixture was stirred for 16 h, whereupon additional CBr_4 (0.88 g, 2.65 mmol), followed by Ph_3P (0.70 g, 2.67 mmol) was added and the reaction mixture was stirred for another 24 h. After concentration, the residue was purified by column chromatography (SiO_2, CH_2Cl_2/hexane 2/1). The colorless band ($R_f = 0.3$) was collected and the solvent evaporated to afford a colorless oil, which was repeatedly dissolved in CH_2Cl_2 (3×50 mL) and concentrated to provide **5** (1.77 g, 94%) as an analytically pure white semisolid. ^{1}H NMR ($CDCl_3$, 200 MHz, 298 K): $\delta =$ 1.26 (t, $J = 7.6$ Hz, 3H), 1.33 (s, 18H), 2.65 (q, $J = 7.6$ Hz, 2H), 3.54 (t, $J =$ 6.2 Hz, 2H), 3.94–4.10 (m, 8H), 4.14–4.19 (m, 2H), 4.28–4.36 (m, 4H), 6.80–6.89 (m, 4H), 7.06–7.15 (m, 10H), 7.24–7.42 (m, 6H), 7.90 (d, $J =$ 8.4 Hz, 1H), 7.91 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz, 298 K): $\delta =$ 15.4, 28.3, 30.5, 31.5, 34.4, 63.2 (CAr_4), 67.4, 68.0, 69.8, 70.0, 70.2, 71.6 ($6\times CH_2O$, $1\times CH_2O$ signal missing/overlapping), 105.8 (2 signals), 113.3, 114.7, 114.9, 124.2, 125.2, 125.3, 126.7, 126.8 (2 signals), 130.8, 131.1, 132.3, 139.9, 141.4, 144.3, 144.7, 148.3, 154.3, 154.4, 156.6; FAB-MS: m/z (%): 858 (30) $[M+2]^+$, 856 (27) $[M]^+$; elemental analysis calcd (%) for $C_{53}H_{61}BrO_5$ (857.95): C 74.20, H 7.17; found: C 74.36, H 7.20.

7: A solution of **6**[18, 20] (0.27 g, 0.51 mmol) in anhydrous THF (35 mL) was degassed (Ar, 10 min) before a solution of $CsOH\cdot H_2O$ (0.090 g, 0.54 mmol) in anhydrous MeOH (3.5 mL) was added dropwise by syringe over a period of 1 h at room temperature. The mixture was stirred for 15 min, whereupon a solution of the bromide **5** (0.46 g, 0.54 mmol) in anhydrous THF (5 mL) was added in one portion and the reaction mixture was stirred for 24 h at room temperature. The solvent was evaporated and the resulting yellow residue was dissolved in CH_2Cl_2 (100 mL), washed with brine (100 mL) and H_2O (2×100 mL), and then dried ($MgSO_4$). Removal of the solvent gave a yellowish orange semisolid, which was purified by column chromatography (SiO_2, CH_2Cl_2/hexane 4/1). The broad yellow band ($R_f = 0.3$) was collected and concentrated to afford a yellow semisolid, which was repeatedly dissolved in CH_2Cl_2 (2×20 mL) and concentrated to give **7** (0.47 g, 74%) as an analytically pure yellow semisolid. FAB-MS: m/z (%): 1252 (100) $[M]^+$; elemental analysis calcd (%) for $C_{69}H_{73}NO_7S_7$ (1252.78): C 66.15, H 5.87, N 1.12; found: C 66.34, H 6.02, N 1.05.

8: Compound **7** (0.42 g, 0.34 mmol) was dissolved in anhydrous THF/MeOH (1/1, 50 mL) and degassed (Ar, 10 min) before NaOMe (25% solution in MeOH, 1.1 mL, 0.27 g, 5.0 mmol) was added in one portion. The yellow solution was refluxed for 20 min and cooled to room temperature, whereupon the solvent was evaporated. The yellow residue was dissolved in CH_2Cl_2 (100 mL), washed with H_2O (3×100 mL), and dried ($MgSO_4$). Removal of the solvent gave a yellow semisolid, which was subjected to column chromatography (SiO_2, CH_2Cl_2). The yellow band ($R_f = 0.5$) was collected and concentrated to give **8** (0.35 g, 95%) as an analytically pure yellow solid. FAB-MS: m/z (%): 1098 (100) $[M]^+$; elemental analysis calcd (%) for $C_{62}H_{67}NO_5S_6$ (1098.60): C 67.78, H 6.15, N 1.27; found: C 67.81, H 6.15, N 1.24.

10: Compounds **8** (0.23, 0.21 mmol) and **9**[18] (0.21 g, 0.23 mmol) were dissolved in anhydrous DMF (10 mL) and degassed (Ar, 10 min) before NaH (0.021 g of a 60% suspension in mineral oil, 0.53 mmol) was added. The reaction mixture was stirred for 45 min at room temperature, which resulted in the initial yellow solution becoming more orange. H_2O (40 mL) was added, followed by the addition of brine (40 mL). The yellow precipitate was filtered and dried. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/EtOAc 2/1). The yellow band ($R_f = 0.4$) was collected and the solvent evaporated to afford a yellow oil, which was repeatedly dissolved in CH_2Cl_2 (3×20 mL) and concentrated to yield **10** (0.34 g, 83%) as an analytically pure yellow semisolid. ^{1}H NMR (CD_3COCD_3, 400 MHz, 298 K): $\delta = 1.17$ (t, $J = 7.6$ Hz, 3H), 1.26 (s, 18H), 2.38 (s, 3H), 2.57 (q, $J = 7.6$ Hz, 2H), 3.05 (t, $J = 6.4$ Hz, 2H), 3.26 (s, 9H), 3.45–3.48 (m, 6H), 3.60–3.63 (m, 6H), 3.74–3.79 (m, 6H), 3.81 (t, $J =$ 6.4 Hz, 2H), 3.90–4.00 (m, 6H), 4.05–4.13 (m, 8H), 4.24–4.27 (m, 4H), 4.88 (s, 2H), 4.96 (s, 2H), 5.00 (s, 6H), 6.72 and 6.75 (AB, $J = 2.1$ Hz, 2H), 6.79 (d, $J = 8.8$ Hz, 2H), 6.80 (d, $J = 9.1$ Hz, 2H), 6.83 (s, 2H), 6.88–6.93 (m, 8H) 7.03–7.12 (m, 10H), 7.15 (d, $J = 8.7$ Hz, 2H), 7.22–7.33 (m, 8H), 7.36 (d, $J = 8.8$ Hz, 4H), 7.80 (d, $J = 8.5$ Hz, 1H), 7.82 (d, $J = 8.5$ Hz, 1H); FAB-MS: m/z (%): 1966 (100) $[M]^+$; elemental analysis calcd (%) for $C_{112}H_{127}NO_{18}S_6$ (1967.60): C 68.37, H 6.51, N 0.71; found: C 68.17, H 6.49, N 0.66.

$\mathbf{13}\cdot 4PF_6$: A solution of **10** (0.28 g, 0.14 mmol), $\mathbf{11}\cdot 2PF_6$[3] (0.30 g, 0.42 mmol), and **12** (0.11 g, 0.42 mmol) in anhydrous DMF (10 mL) was stirred for 10 d at room temperature (after approximately 1 d the color changed to dark green and a white precipitate was formed). The green suspension was subjected directly to column chromatography (SiO_2) and recovered **10** was eluted with Me_2CO, whereupon the eluent was changed to Me_2CO/NH_4PF_6 (1.0 g NH_4PF_6 in 100 mL MeCO) and the brown band containing $\mathbf{13}\cdot 4PF_6$ was collected. Most of the solvent was removed under vacuum ($T < 30\,^\circ C$) followed by the addition of H_2O (50 mL). The resulting precipitate was collected by filtration, washed with Et_2O (20 mL), and dried to afford the [2]rotaxane $\mathbf{13}\cdot 4PF_6$ (0.10 g, 23%) as an analytically pure brown solid. M.p. 150 °C (decomposed without melting); FAB-MS: m/z (%): 2921 (4) $[M-PF_6]^+$, 2776 (9) $[M-2PF_6]^+$, 2631 (6) $[M-3PF_6]^+$, 1966 (3), 1388 (10) $[M-2PF_6]^{2+}$, 1315.5 (13) $[M-3PF_6]^{2+}$, 1243 (6) $[M-4PF_6]^{2+}$; elemental analysis calcd (%) for $C_{148}H_{159}F_{24}N_5O_{18}P_4S_6\cdot 2H_2O$

(3068.12): C 57.26, H 5.29, N 2.26; found: C 56.86, H 5.19, N 2.11. Preparative thin-layer chromatography (PTLC) was performed at room temperature on UNIPLATE silica gel PTLC plates with Me_2CO/NH_4PF_6 (1.0 g NH_4PF_6 in 100 mL Me_2CO) as eluent. Immediately after elution, the red band containing $\mathbf{13}\cdot 4PF_6\cdot$RED was extracted into Me_2CO. The solvent was removed under vacuum ($T<10\,^{\circ}C$) and the red residue dissolved in $(CD_3)_2CO$ to give a red solution, which was cooled to $-78\,^{\circ}C$ in a Me_2CO/dry ice bath. Although $\mathbf{13}\cdot 4PF_6\cdot$GREEN seems to be less polar than $\mathbf{13}\cdot 4PF_6\cdot$RED, it was only possible to extract an extremely small amount of $\mathbf{13}\cdot 4PF_6\cdot$GREEN from the silica on the PTLC plate. The UV/Vis spectrum recorded in $(CD_3)_2CO$ at 298 K of this fraction shows, as expected, only a broad charge-transfer (CT) absorption band centered on 801 nm.

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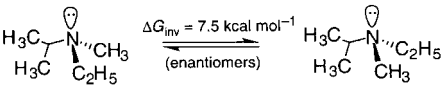
[23] The rate constant k was obtained from the slope of a plot of $\log I$(SMe, **13** · 4 PF_6 · RED) against t, where I(SMe, **13** · 4 PF_6 · RED) denotes the integral of the SMe resonance for the red translational isomer, **13** · 4 PF_6 · RED, and t is the time.

Isolation of an Acid/Base Complex in Solution Puts the Brakes on Nitrogen Inversion**

Paul L. Wash, Adam R. Renslo, and Julius Rebek, Jr.*

Acid/base interactions pervade chemistry and dominate molecular recognition in biology. The isolation of individual acid/base complexes can be achieved in the gas phase at low pressures[1] and in the solid or glassy states within inert matrices. In solution, rapid diffusion permits the frequent exchange of acid/base partners and the characterization of individual complexes requires the fastest of spectroscopic techniques. We have recently introduced a synthetic host that features an inwardly directed carboxy group on its concave surface,[2] and we apply it here to the study of isolated acid/base interactions. The results augur well for the observation and characterization of short-lived intermediates in these receptacles.

The effects are demonstrated with the amine base *N*-ethyl-*N*-methyl-*N*-isopropylamine [**1**, Eq. (1)]. This base features



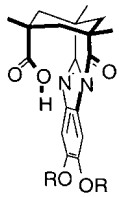
1 (1)

one of the simplest amines with a stereogenic nitrogen atom and its behavior has been closely examined in solution.[3, 4] The nitrogen atom inverts rapidly at room temperature, a motion that can be frozen out at low temperatures. The activation barrier for inversion/rotation—the process that converts the molecule into its mirror image—is approximately 7.5 kcal mol^{-1} at 160 K in $CBrF_3$. Extrapolated to room temperature, the rate of racemization is about 10^7 s^{-1}.

The same amine shows starkly different behavior within the racemic receptacle molecule **2** (Figure 1).[2] The inversion/rotation of **1** within **2** is slow on the NMR timescale at room temperature, and even at 323 K. A portion of the NMR spectrum of **1** in **2** is shown and highlights the consequences of amine complexation: large upfield shifts, emergence of coupling details, an overall expansion of the spectrum, and the doubling of its resonances. The last feature reflects the modest (about 2:1) diastereoselectivity of the racemic receptacle for the amine enantiomers.

The guest exchange rates into and out of **2** are slow on the NMR timescale and separate signals are seen for free and bound guest.[5] Steric barriers—mechanical bonds—isolate the amine from the bulk solution and costly conformational changes (including the rupture of hydrogen bonds) are necessary to allow the passage of molecules into and out of the cavity. The rate of this process for **1**, as measured by an exchange spectroscopy (EXSY) experiment, is 2 s^{-1} at room temperature and corresponds to a barrier of about 17 kcal mol^{-1}. However, EXSY experiments on the bound guest failed to show exchange between diastereomeric complexes, even at 323 K. Accordingly, the lowest energy path for interconversion of diastereomers of the complex involves dissociation to the free components in solution and then their recombination.

What causes the large energetic barrier to the process of Equation (2): the interconversion of the diastereomeric complexes of **1** within **2**? The attractive forces between the acid and base must contribute but they cannot be a large factor. The model (racemic) acid **3** was used as a model for estimating the effects of acid/base attraction. The carboxy groups of both **2** and **3** are derived from Kemp's triacid[6, 7] and are attached to the aromatic residues through an *N*-acylbenzimidazole function; they are inherently chiral. Complexes of **3** with **1** exchange/interconvert rapidly on the NMR timescale in CH_2Cl_2 at ambient temperature, and low temperatures are required to distinguish the diastereomers. Dynamic NMR experiments show an activation barrier of 10.5 ± 0.5 kcal mol^{-1} for the exchange process at the coalescence temperature ($T_c = 230$ K). There is nothing unusual about this acid/base pair: the complex of **1** with 2,2-dimethylpropionic (pivalic) acid also shows a barrier of 10.3 kcal mol^{-1} at $T_c = 230$ K for the inversion/rotation of the amine.



3 (racemic)
R = C_8H_{17}

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