Chemical Science

EDGE ARTICLE

Enabling tetracationic cyclophane production by trading templates

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Supporting Information

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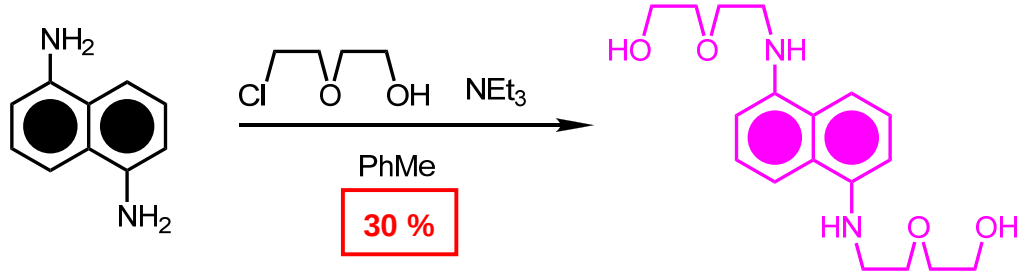
† Electronic Supplementary Information (ESI) available: synthetic methods, 2-D NMR spectrum, isothermal titration microcalorimetry, UV-Vis spectrophotometric titration and crystallographic details. CCDC 764119 and 766073.

Experimental Section

1. General Methods

Chemicals were purchased from commercial suppliers and used as received. All reactions were performed under an argon atmosphere and in dry solvents, unless otherwise stated. Analytical thin-layer chromatography (TLC) was performed on aluminum sheets, precoated with silica gel 60-F_{254} (Merck 5554). Flash chromatography was carried out using silica gel 60 (Silicycle) as the stationary phase. ^{1}H and ^{13}C NMR spectra were recorded on either a Bruker Avance 500 MHz, or a Bruker Avance 600 MHz spectrometer at ambient temperature, unless otherwise noted. The chemical shifts were listed in ppm on the δ scale relative to the signals corresponding to the residual non-deuterated solvents (CD_3CN: δ 1.94 ppm), and coupling constants were recorded in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; b, broad peaks; m, multiplet or overlapping peaks. High resolution electrospray ionization (HR ESI) mass spectra were measured on a Micromass Q-TOF Ultima mass spectrometer. Matrix assisted laser desorption and ionization – time of flight (MALDI-TOF) mass spectrometry was performed, using a Bruker Autoflex III instrument.

2. Synthetic Methods



Scheme S1 The synthesis of BHEAN.

BHEAN: 1,5-Diaminonaphthalene (4.74 g, 30 mmol), 2-(2-chloroethoxy)ethanol (7.95 mL, 75 mmol), and NEt_3 (30 mL) were dissolved in PhMe (70mL). The mixture was heated under reflux in an atmosphere of Ar at 110 ℃ for 3 days. The precipitate was collected and dissolved in CH_2Cl_2 (100 mL), before being washed with brine (50 mL × 2). The organic phase was dried (Na_2SO_4) and the resulting material was recrystallised in EtOAc to afford compound BHEAN as a brown solid (3 g, 30%). ^{1}H NMR (500 MHz, CD_3CN): δ = 7.27 (t, 2H, J = 8.4 Hz), 7.22 (d, 2H, J = 8.4 Hz), 6.62 (d, 2H, J = 8.4 Hz), 5.03 (b, 2H), 3.78 (t, 4H, J = 5.6 Hz), 3.62 (m, 4H), 3.56 (m, 4H), 3.40 (m, 4H), 2.81 (t, 2H, J = 5.6 Hz). ^{13}C NMR (125 MHz, CD_3CN): δ = 44.4, 61.9, 69.8, 73.1, 105.0, 109.9, 125.0, 126.3, 145.2 ppm. HR ESI: calcd for $[M + Na]^+$ m/z =357.1790; found m/z = 357.1787.

3. Analysis of the ^{1}H NMR Spectra of [BHEAN⊂CBPQT]•4PF$_6$

The [BHEAN⊂CBPQT]•4PF$_6$ complex was characterised fully by ^{1}H NMR spectroscopy. Assignments were confirmed and added by ^{1}H–^{1}H gDQF-COSY, recorded on a Bruker Avance 600 MHz spectrometer at 233 K in CD_3CN.

Correlation Spectroscopy Performed on the [BHEAN⊂CBPQT]•4PF$_6$ Complex in CD_3CN at 233K

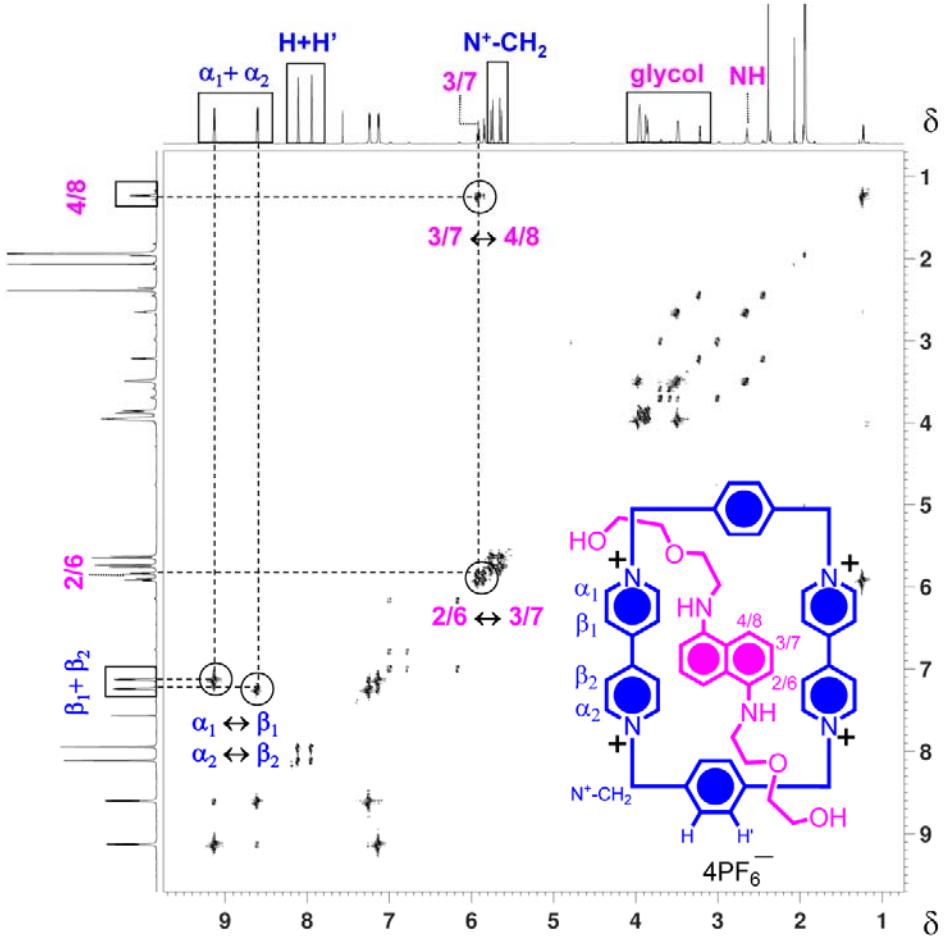


Fig. S1 ^{1}H–^{1}H gDQF-COSY Spectrum (600 MHz) of the [BHEAN⊂CBPQT]•4PF$_6$ complex in CD_3CN at 233 K.

The ^{1}H-^{1}H gDQF-COSY of [BHEAN⊂CBPQT]•4PF_6 (Fig. S1) in CD_3CN at 233K reveals correlation peaks between α and β protons in the AA′BB′ system of the $CBPQT^{4+}$ ring as result of its complexation with the guest BHEAN. The peaks for the protons $H_{3/7}$ and $H_{4/8}$ of the DNP recognition unit that reside inside the electron deficient cyclophane are visible as indicated by 3/7 ↔ 4/8 in the spectrum. The $H_{4/8}$ is shifted upfield to around 1.2 ppm as a result of a [C–H···π] interaction with the $CBPQT^{4+}$ phenylene ring.

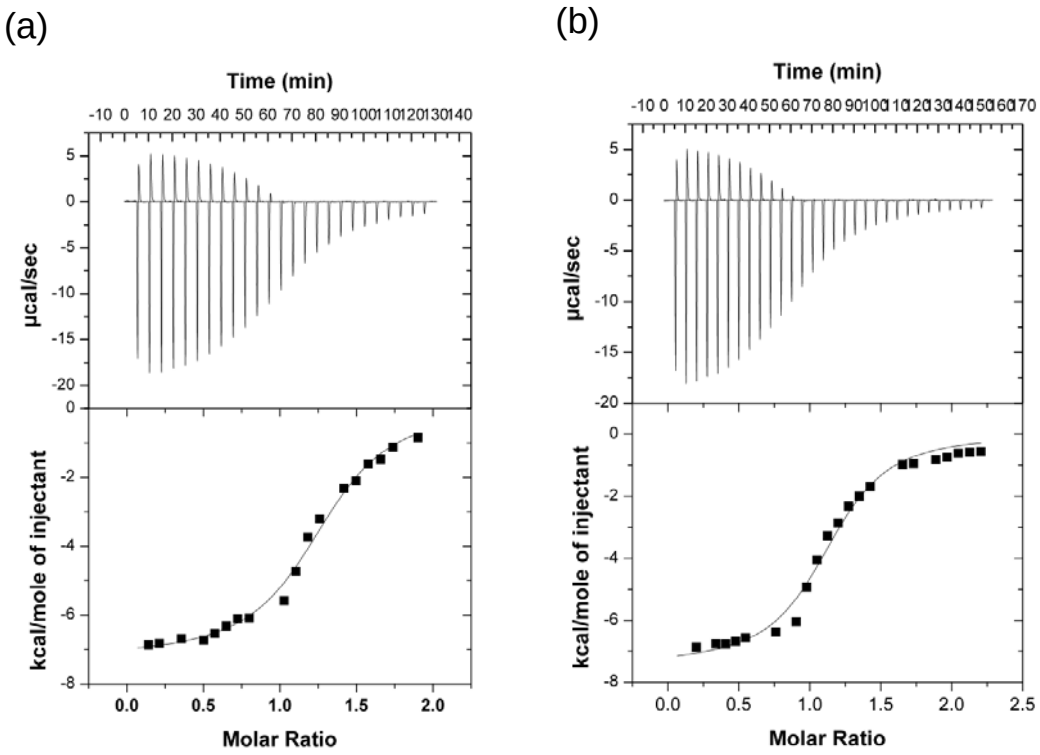


Fig. S2 Binding isotherms of BHEAN with CBPQT•4PF_6 measured by isothermal titration microcalorimetry in MeCN at 298 K. The equilibrium constant K_a for the complexation of [BHEAN⊂CBPQT]•4PF_6 was an average value obtained from the two experiments shown in Fig. S2 (a) and (b).

4. Isothermal Titration Microcalorimetry

Isothermal titration microcalorimetry was employed to determine the thermodynamic binding parameters (K_a, ΔG, ΔH, ΔS) between BHEAN and CBPQT•4PF$_6$ in MeCN at 298 K. The binding isotherms of [BHEAN⊂CBPQT]•4PF$_6$ are shown in Fig. S2. The binding data indicates the complexation of BHEAN with CBPQT•4PF$_6$ (K_a = 58,000 M^{-1}) is comparable to the model compound BHEEN (K_a = 36,400 M^{-1}, Ref. 24).

In order to calculate the amount of BHEAN needed to displace the BHEEN template in the [BHEEN⊂CBPQT]•4Cl complex, we employed the K_a value obtained from the ITC study and made the following assumptions: (1) The relative binding affinity of CBPQT•4Cl to BHEEN and BHEAN in water remains the same as that of CBPQT•4PF$_6$ to BHEEN and BHEAN in MeCN; (2) After the crude reaction mixture has been partitioned between saturated aqueous NH_4Cl solution and CH_2Cl_2, excess of the BHEEN template is washed away and [BHEEN] is equal to [CBPQT•4Cl] in the aqueous layer.

The relative binding affinity is

$$36{,}400 / 58{,}000 = ([\text{BHEEN}\subset\text{CBPQT}\cdot 4\text{Cl}] / [\text{BHEEN}]) / ([\text{BHEAN}\subset\text{CBPQT}\cdot 4\text{Cl}] / [\text{BHEAN}]) \quad (1)$$

The total amount of CBPQT•4Cl and BHEEN (both complexed and uncomplexed) are equal and can be normalized to 1. With x = [BHEAN⊂CBPQT•4Cl] = [BHEEN] and BHEAN is n-fold excess of BHEEN, we may write (1) as

$$\frac{36.4}{58.0} = \frac{(n-x)(1-x)}{x^2} \qquad (2)$$

When n=1, x = 0.56 (56% displacement of BHEEN)

n=5, x = 0.88 (88% displacement of BHEEN)

n=10, x = 0.94 (94% displacement of BHEEN)

Therefore, we concluded that adding a five-fold excess of BHEAN to a solution of the [BHEEN ⊂ CBPQT]•4PF6 complex would result in an approximately 90% displacement of BHEEN from the cavity of the $CBPQT^{4+}$ ring.

5. UV-Vis Spectrophotometric Titration

As a result of charge transfer interactions between the π-electron rich BHEAN as the guest and the π-electron deficient CBPQT•$4PF_6$ as the host, an intense green color develops immediately after the mixing of these two components, indicating the formation of [BHEAN⊂CBPQT]•$4PF_6$ in MeCN. UV-Vis spectroscopy was employed to investigate the

absorption λ_{max} as well as the stoichiometry of the complex formed in solution. The absorption spectrum of a 1:1 mixture of the host and the guest is presented in Fig. S3(b). For comparison purposes the corresponding 1:1 complex of BHEEN and CBPQT•4PF_6 is presented in Fig. S3(a).

In order to determine the stoichiometry of the complex formed, the continuous variations plot illustrated in Fig. S4 was determined by employing total molar concentrations of 10^{-3} M of the host and the guest in MeCN. A maximum value of the absorbance was observed when the molar fraction χ was equal to 0.5, indicating a 1:1 binding stoichiometry.

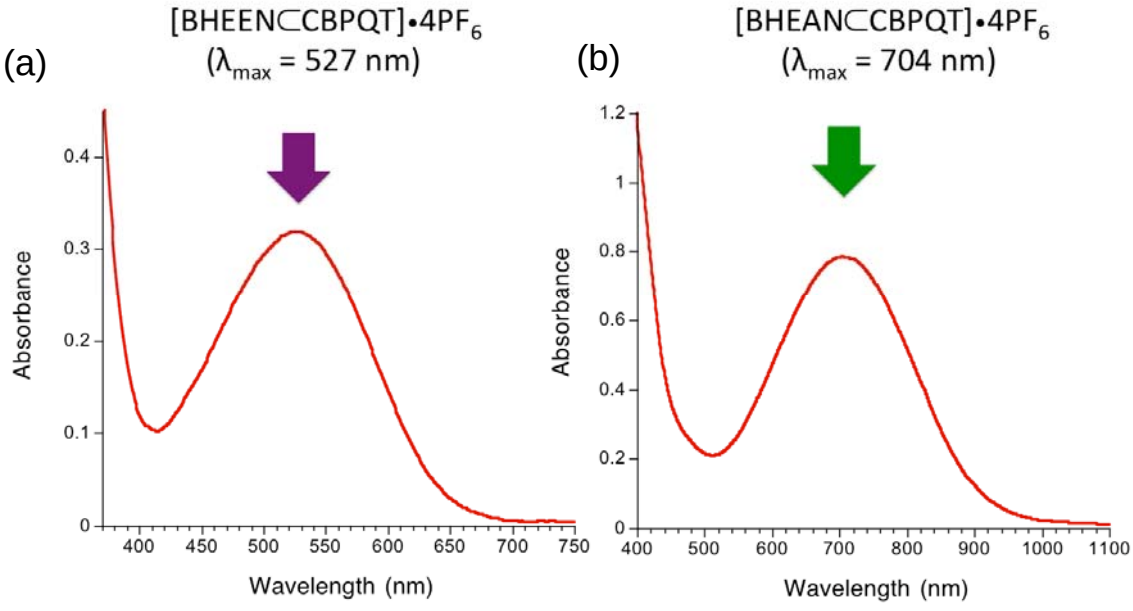


Fig. S3 Absorption maxima of a 1:1 complex of (a) [BHEEN⊂CBPQT]•4PF_6 and (b) [BHEAN⊂CBPQT]•4PF_6, by UV-Vis spectroscopy.

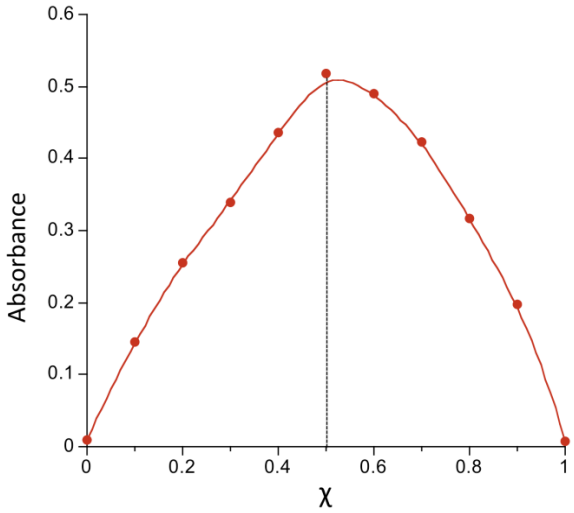


Fig. S4 Continuous variations plots of the absorbance of [BHEAN⊂CBPQT] •$4PF_6$ against the molar fraction χ of the host CBPQT•$4PF_6$. The highest absorbance at $\chi = 0.5$ indicates a 1:1 binding stoichiometry between the host and the guest.

Spectrophotometric titration was performed on the [BHEEN⊂CBPQT]•$4PF_6$ complex with BHEAN, as shown in Fig. S5. In the absence of BHEAN, a charge-transfer complex between BHEEN and $CBPQT^{4+}$ ring is observed with an absorption λ_{max} of 527 nm. Upon addition of BHEAN, a new charge transfer band grows at 703 nm, with the decrease of the band at 527 nm. Upon addition of 5-fold excess of BHEAN, complete disappearance of the band at 527 nm is observed with the subsequent rise of the absorption maxima centered on 703 nm, indicating nearly complete removal of BHEEN from the cavity of the tetracationic cyclophane. Thess data further support our reasoning behind the addition of 5-fold excess of BHEAN during the purification of the $CBPQT^{4+}$ ring in the main text.

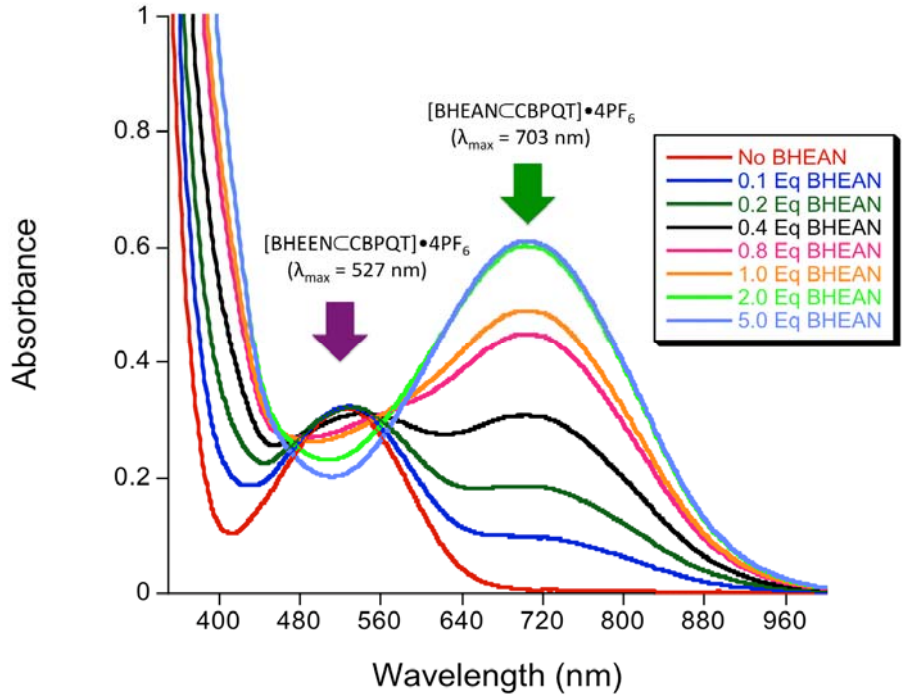


Fig. S5 Spectrophotometric titration of BHEAN with a solution of [BHEEN⊂CBPQT]•4PF_6 in MeCN at 298 K. Upon addition of BHEAN, the λ_{max} at 527 nm disappears and a new band at 703 nm arises, indicating the displacement of BHEEN by BHEAN.

6. X-Ray Crystallography

Single crystals of [BHEAN⊂CBPQT]·4PF_6•3MeCN and CBPQT•4PF_6 were mounted in oil (InfineumV8512) on a glass fiber under a nitrogen cold stream at 100 (2)K. X-Ray diffraction data were collected on a Bruker Kappa diffractometer, equipped with a Cu Kα sealed-tubesource and an APEX II CCD detector. Data were collected, integrated and corrected for decay and Lp effects using BrukerAPEX II software. Final unit cell parameters were obtained through a refinement of all observed reflections during data

integration. A multi-scan absorption correction was performed using SADABS. The structure was solved and refined using the SHELXTL suite of software.

The unit cell of [BHEAN⊂CBPQT]•4PF_6•3MeCN is shown in Fig. S6. Here, we observed a 1:1 complexation in solid state where all the BHEAN molecules are situated inside the cavity of the macrocyclic host. Whereas the 2:1 complex of [BMEEN⊂CBPQT]•4PF_6•2MeCN reported in Ref. 2(d) demonstrated a continuous donor-acceptor stack involving $CBPQT^{4+}$ and BMEEN — present both inside and outside the cavity of the macrocycle — the absence of guest molecules outside of the cavity in the [BHEAN⊂CBPQT]•4PF_6•3MeCN eliminates such extended π-π interaction, resulting in a less dense packing.

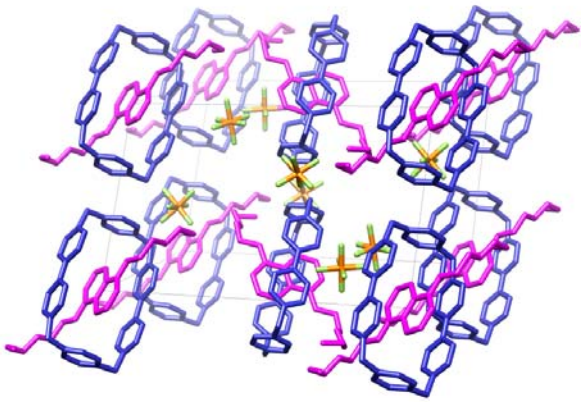


Fig. S6 The unit cell of the inclusion complex [BHEAN⊂CBQPT]•4PF_6 is shown. BHEAN (pink) can be seen bound inside the $CBPQT^{4+}$ cyclophanes (blue). Flexible glycol appendages of BHEAN, extending from the diaminonapthalene cores, 'hug' the cyclophanes through hydrogen bonding. The soft tetrahedral counterions PF_6^- can also be seen (P, orange; F, yellow) in the interstitial regions. Solvent molecules (MeCN) and H atoms have been omitted for clarity.