Novel 4,4′-Bipyridinium-Based Cationic Mono- and Bicyclic Cyclophanes

Perumal Rajakumar*[a] and Kannupal Srinivasan[a]

Keywords: Charge transfer / Cyclophanes / Electrochemistry / N ligands

The intra-annularly functionalised tetracationic cyclophanes **3a**–**b** were synthesised from the corresponding *m*-terphenyl dibromides and 4,4′-bipyridine by a simple quaternisation methodology. An intra-annularly linked tetracationic cyclophane **10** was synthesised in three steps and it possesses a concave structure and novel intramolecular CT interactions. Synthesis of the tetracationic cyclophanes **13**, **16a** and **16b** containing carbonyl groups was accomplished from the corresponding carbonyl dibromides and 4,4′-bipyridine. Sixfold coupling of a tricarbonyl tribromide with 4,4′-bipyridine afforded a rare hexacationic cyclophane **18**. The cyclophanes **3a** and **3c** form CT complexes with a bis(1*H*-indol-3-yl)-(phenyl)methane compound while the cyclophane **13** forms CT complexes with 1,4-dimethoxybenzene and indole. Electrochemical parameters were obtained for all the cyclophanes. They exhibit two sets of redox peaks and most of them are quasireversible. The smallest-cavity cyclophane **13** has the lowest reduction potentials in the series.

Introduction

Mechanically interlocked compounds such as rotaxanes and catenanes are increasingly attracting synthetic chemists' attention because of their ability to provide the basic elements for constructing nanoscale devices in the future.[1] The Stoddart cyclophane, cyclobis(paraquat-*p*-phenylene), derived from *p*-xylenyl dibromide and 4,4′-bipyridine, has been employed for the construction of a number of rotaxanes and catenanes based on its ability to form inclusion complexes with π-electron-rich aromatic molecules.[2] Replacement of either the bipyridinium recognition sites or the *p*-phenylene spacers of the Stoddart cyclophane with other recognition sites or aromatic spacers has led to novel tetracationic cyclophanes with potential applications.[3] We are interested in incorporating *m*-terphenyl building blocks into cyclophane structures[4] because such cyclophanes possess noncollapsible rigid cavities with intra-annular functionality. Furthermore, the cavities of such cyclophanes would be large and could form complexes with large electron-rich guest molecules. Introduction of carbonyl groups into the aromatic spacers would be more promising because we could study the effect of the electron-deficient carbonyl groups on the complexing ability of such cyclophanes. Herein we report syntheses and electrochemical properties of some novel tetra- and hexacationic cyclophanes possessing mono- and bicyclic structures incorporating the 4,4′-bipyridinium building unit.

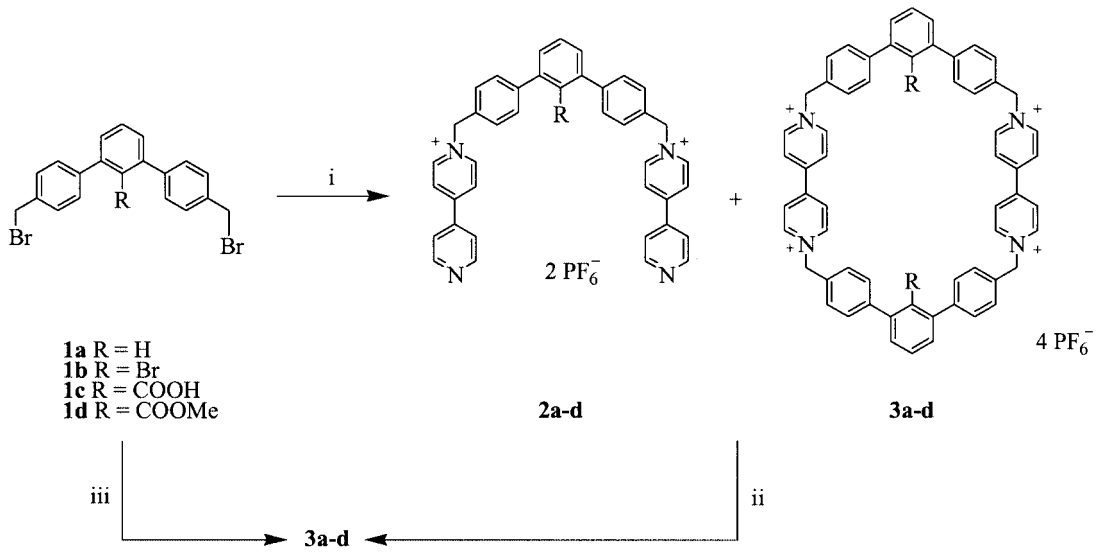
[a] Department of Organic Chemistry, University of Madras, Guindy Campus,
Chennai-600 025, Tamil Nadu, India
Fax: (internat.) + 91−44−2352494
E-mail: perumalrajakumar@hotmail.com

Results and Discussion

Cyclophanes with *m*-Terphenyl Spacers

The synthetic methodology employed for the syntheses of these cyclophanes closely parallels that reported previously by the Hünig[5] and Stoddart[6] groups. Heating one equivalent of one of the *m*-terphenyl dibromides[7] **1a**−**d** with five equivalents of 4,4′-bipyridine in acetonitrile under reflux afforded a mixture of dicationic precyclophanes **2a**−**d** and tetracationic cyclophanes **3a**−**d** in 66−82% overall yields after counterion exchange with NH_4PF_6. The formation of tetracationic cyclophanes may be attributable to the angular nature of the *m*-terphenyl dibromides, which favoured the [2+2] macrocyclisation. Analysis of the ^{1}H NMR spectra of these mixtures revealed that about 10−50% of the tetracationic cyclophanes **3a**−**d** were present along with the dicationic precyclophanes **2a**−**d**. Without separation, the mixtures were heated under reflux with a slight excess of a *m*-terphenyl dibromide under high dilution conditions to afford the tetracationic cyclophanes **3a**−**d** in 16−25% yields after column chromatography and counterion exchange. One-pot syntheses were also carried out by heating equimolar mixtures of **1a**−**d** and 4,4′-bipyridine in acetonitrile under reflux under high dilution conditions, and this method gave the tetracationic cyclophanes **3a**−**d** in yields similar to the two-step procedure (Scheme 1). All the cyclophanes were thoroughly characterised by spectroscopic and analytical data.

MOPAC calculations (PM3) indicated the cavity size of **3a** was 12.8 × 13.2 Å, which was further confirmed by XRD studies.[8] The ORTEP plot of the crystal structure of **3a** is shown in Figure 1. The centrosymmetric macrocyclic tetracation as a whole assumes a chair-like conformation.



Scheme 1. Reagents and conditions: i) 4,4′-bipyridine (5 equiv.), CH_3CN, reflux, 30 h, then NH_4PF_6, CH_3CN, 66−82%; ii) **1a**−**d**, CH_3CN, reflux, 48 h, then NH_4PF_6, H_2O; afforded **3a** (25%), **3b** (19%), **3c** (16%) and **3d** (27%); iii) 4,4′-bipyridine (1 equiv.), CH_3CN, reflux, 48 h, then NH_4PF_6, H_2O; afforded **3a** (18%), **3b** (22%), **3c** (15%) and **3d** (28%)

Two hexafluorophosphate anions are inserted into the cavity of the tetracation and the other two anions are situated away from the cavity. Four water molecules are partly inserted into the cavity. The two outer rings of the *m*-terphenyl unit are twisted from the central ring by 24.7° and 18.9°, respectively, and this flexibility allows the formation of these cyclophanes without the use of any templates in better yields as compared with that of the Stoddart cyclophane.

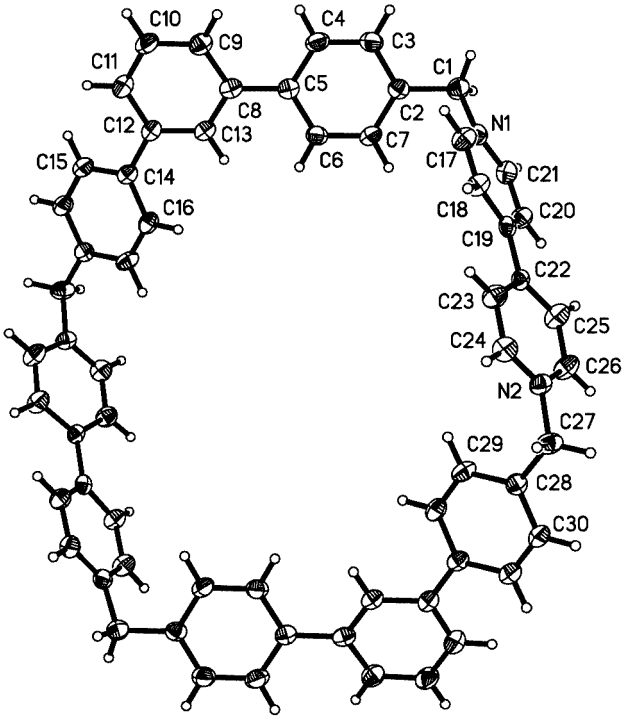
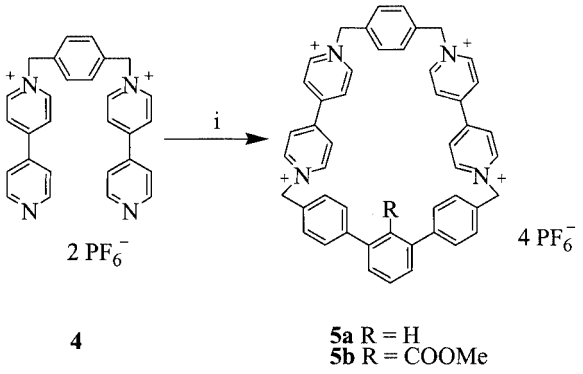


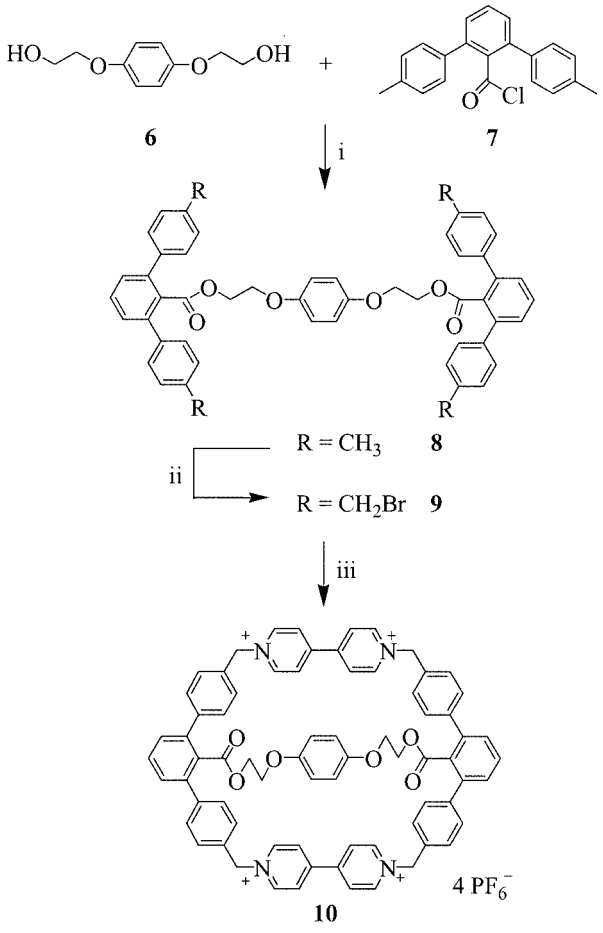
Figure 1. ORTEP plot of the crystal structure of **3a**; the counterions and water molecules are omitted for clarity

We were also interested in replacing one of the *p*-phenylene spacers of the Stoddart cyclophane with a *m*-terphenyl unit for the comparison of their complexation behaviours. Thus, the cyclophanes **5a** and **5b** were synthesised by heating an equimolar mixture of the bispyridinium salt **4** and **1a/1d** under reflux (Scheme 2).



Scheme 2. Reagents and conditions: i) **1a/1d**, CH_3CN, reflux, 48 h, then NH_4PF_6, H_2O; afforded **5a** (23%) and **5b** (27%)

By connecting two *m*-terphenyl units through their 2′-positions with a tethering unit, followed by linking the outer rings with bipyridinium moieties, it is possible to construct bicyclic cyclophanes. The novelty of the resulting bicyclic cyclophanes is twofold. If the tethering unit connecting the two *m*-terphenyl units is long enough, then the cyclophane can be expected to possess a concave nature and, hence, can undergo an umbrella inversion process. Furthermore, if the unit used for the intra-annular connection is electron rich, the cyclophane will have two peripheral electron-deficient layers and an electron-rich middle layer like a capacitor and, hence, can show novel CT interactions.



Scheme 3. Reagents and conditions: i) NaH, DMF, 80 °C, 48 h, 22%; ii) NBS, Bz_2O_2, CCl_4, reflux, 40 h, 80%; iii) 4,4′-bipyridine (2 equiv.), CH_3CN, reflux, 24 h, then NH_4PF_6, H_2O, 60%

Synthesis of an intra-annularly linked bicyclic cyclophane **10** is outlined in Scheme 3. Reaction of the sodium salt generated from 1,4-bis(2-hydroxyethoxy)benzene (**6**) and NaH with two equivalents of *m*-terphenyl acid chloride **7** in DMF gave the diester **8** in 22% yield. Fourfold radical bromination of **8** using NBS and Bz_2O_2 in CCl_4 afforded the tetrabromide **9** in 80% yield. Heating two equivalents of 4,4′-bipyridine with one equivalent of **9** under reflux gave the bicyclic cyclophane **10** in 60% yield after column chromatography and counterion exchange.

MOPAC calculations (PM3) indicated a concave structure for the cyclophane **10** with the hydroquinone ring constituting the bottom portion. Its ^{1}H NMR spectrum showed an upfield change in chemical shift of $\delta = 0.54$ ppm for the hydroquinone protons as compared with the hydroquinone protons in **9** and, hence, there should be intramolecular CT interactions between the hydroquinone unit and the bipyridinium moieties. We tried to investigate the umbrella inversion process of the cyclophane **10** by variable-temperature ^{1}H NMR spectroscopy. The inversion process, however, was too fast on the ^{1}H NMR time scale and no coalescence was observed between the temperatures of 22 °C and 140 °C in DMSO.

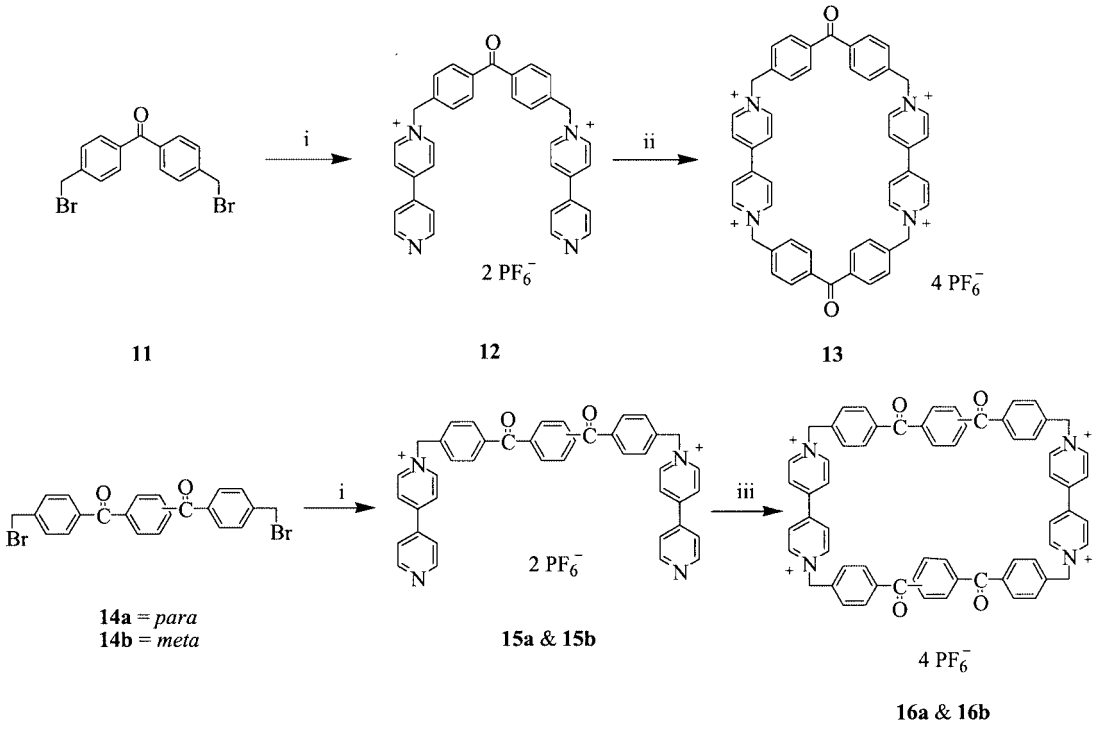
Cyclophanes with Aromatic Carbonyl Spacers

To introduce carbonyl groups into the structures of the tetracationic cyclophanes, the carbonyl dibromides **11**, **14a** and **14b** were chosen to provide the aromatic spacers. These dibromides were prepared by the Friedel−Crafts acylation of the corresponding aromatic acid chlorides with toluene followed by twofold radical bromination with NBS. Reaction of five equivalents of 4,4′-bipyridine with one equivalent of dibromides **11**, **14a** and **14b** in refluxing acetonitrile gave the dicationic precyclophanes **12**, **15a** and **15b** in 68, 80 and 77% yields, respectively, after counterion exchange. These precyclophanes were then heated under reflux with a slight excess of the dibromides **11**, **14a** and **14b** to give the tetracationic cyclophanes **13**, **16a** and **16b** containing carbonyl groups in 16, 12 and 14% yields, respectively, after column chromatography and counterion exchange (Scheme 4).

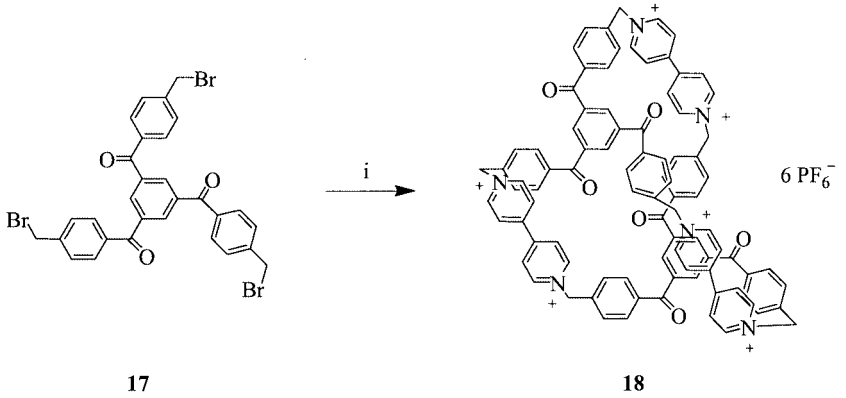
A bicyclic cyclophane **18** with a fascinating tris(paraquat) cage was derived from the tricarbonyl tribromide **17** as shown in Scheme 5. This hexacationic cyclophane was obtained in 3% yield by a sixfold coupling of two equivalents of the tribomide **17** with three equivalents of 4,4′-bipyridine, followed by column chromatography and counterion exchange. It is noteworthy to mention that such cyclophanes with hexacationic cage are rare in the literature. Such cyclophanes in general cannot be detected by mass spectrometry.[9] ^{1}H NMR and ^{13}C NMR spectra, however, supported the proposed cage structure for the cyclophane **18**.

Complexation Studies

We investigated the complexation behaviour of the cyclophanes **3a**−**d** with several electron-rich guest molecules like 1,4-dimethoxybenzene, 1,4-bis(2-hydroxyethoxy)benzene, indole, ferrocene and TTF. The association, however, was much too weak to be measured by either UV/Vis or ^{1}H NMR spectroscopic techniques. Even when one of the *p*-phenylene spacers of the Stoddart cyclophane was replaced by a *m*-terphenyl spacer, as in the case of cyclophanes **5a** and **5b**, formation of CT complexes could not be detected by UV spectroscopy. This phenomenon is due to the large cavity size that nullifies the π−π stacking interactions between the complementary aromatic units of the host and the guest.[10] These cylophanes, however, formed CT complexes with electron-rich guest molecules of larger size. For example, while mixing an equimolar solution of **3a** with bis(1*H*-indol-3-yl)(phenyl)methane in MeCN, a deep red colour developed with a CT band centred around 497 nm ($\varepsilon = 1667$ $M^{-1}cm^{-1}$) with an association constant (K_a) of 12 M^{-1} (determined by Benesi−Hildebrand method[11]). Similarly, the CT complexes of the cyclophane **3c** with bis(1*H*-indol-3-yl)(phenyl)methane gave a value of K_a of 18 M^{-1} at 492 nm ($\varepsilon = 1111$ $M^{-1}cm^{-1}$). The formation of CT complexes was also studied for the cyclophane **13**, which has a relatively smaller cavity. It formed CT complexes with smaller electron-rich guest molecules, like 1,4-dimethoxybenzene and indole with association constants of 0.46



Scheme 4. Reagents and conditions: i) 4,4′-bipyridine (5 equiv.), CH_3CN, reflux, 30 h, then NH_4PF_6, CH_3CN; afforded **12** (68%), **15a** (80%) and **15b** (78%); ii) **11**, CH_3CN, reflux, 48 h, then NH_4PF_6, H_2O, 16%; iii) **14a**/**14b**, CH_3CN, reflux, 48 h, then NH_4PF_6, H_2O; afforded **16a** (12%) and **16b** (14%)



Scheme 5. Reagents and conditions: i) 4,4′-bipyridine (3 equiv. for 2 equiv. of **17**), CH_3CN, reflux, 72 h, then NH_4PF_6, H_2O, 3%

$M^{-1}$and 0.62 M^{-1}, respectively. The smaller magnitudes of these values of K_a could be due to the loss of rigidity of the cavities of the host molecules as well as the minimised $\pi-\pi$ stacking interactions resulting from the presence of carbonyl groups.

Electrochemical Properties

All the cyclophanes exhibited two sets of redox waves that are characteristic of paraquat derivatives. The electrochemical parameters obtained for the cyclophanes are shown in Table 1. Among the cyclophanes containing *m*-terphenyl spacers, the cyclophanes **3a**, **3d** and **10** showed two reversible one-electron redox processes (for which we found the difference between anodic and cathodic peaks ΔE_p = 74 mV vs. Ag/AgCl in DMSO at room temperature) as compared with ferrocene. The quasireversibility of the second redox process of the cylophane **3b**, and both the first and second redox processes of the cyclophane **3c**, may be due to the nature of the intra-annular functional groups. The cyclophanes **5a**−**b** showed two sets of quasireversible peaks because of the presence of nonidentical spacers.

Table 1. The electrochemical parameters obtained for the cyclophanes in DMSO at 25 °C

Cyclophane[a]	E^1_{pc} (mV)	E^1_{pa} (mV)	$E^1_{1/2}$ (mV)	ΔE^1_p (mV)	E^2_{pc} (mV)	E^2_{pa} (mV)	$E^2_{1/2}$ (mV)	ΔE^2_p (mV)
3a	−365	−287	−326	78	−733	−659	−696	74
3b	−364	−278	−321	86	−849	−653	−751	196
3c	−381	−245	−313	136	−907	−641	−774	266
3d	−392	−326	−359	66	−758	−694	−726	64
5a	−375	−252	−314	123	−759	−640	−700	119
5b	−381	−256	−319	125	−777	−648	−713	129
10	−384	−310	−347	74	−755	−669	−712	86
13	−375	−166	−271	209	−778	−563	−671	215
16a	−343	−270	−307	73	−871	−764	−818	107
16b	−355	−235	−295	120	−746	−598	−672	148
18	−505	−296	−401	209	−835	−773	−784	102

[a] E^1_{pc} and E^2_{pc} are the cathodic peak potentials of the first and second redox processes respectively. E^1_{pa} and E^2_{pa} are the anodic peak potentials of the first and second redox processes respectively. $E^1_{1/2}$ and $E^2_{1/2}$ are the averages of the cathodic and anodic peak potentials of the first and second redox processes respectively. ΔE^1_p and ΔE^2_p are the differences between the cathodic and anodic peak potentials of the first and second redox processes respectively.

Among the cyclophanes containing aromatic carbonyl spacers, all the redox processes, except the first redox process of **16a**, were quasireversible because of the presence of carbonyl groups. For the cyclophane **13**, both the first and second redox potentials were shifted to less-negative potentials as compared to other cyclophanes. The electrostatic repulsion between the two positively charged bipyridinium units is maximised in **13** because it has the smallest cavity size in the series. This repulsion was decreased significantly upon reduction and, hence, the ability to accept electrons is greatest for **13**.[12]

Conclusions

Based on Hünig and Stoddart methodology, we have prepared novel mono- and bicyclic tetra- and hexacationic cyclophanes. Because of their large cavity sizes, the cyclophanes **3a** and **3c** form CT complexes only with large electron-rich guest molecules like bis(1*H*-indol-3-yl)(phenyl)-methane. The cyclophane **13**, however, which has a smaller cavity, is able to form CT complexes with smaller electron-rich guest molecules like 1,4-dimethoxybenzene and indole. The concave cyclophane **10** and the hexacationic cage cyclophane **18** are of interest because of their attractive structural features. The electrochemical parameters have been determined for all the cyclophanes. They exhibit two sets of redox peaks and most of them are quasireversible because of the presence of functional groups. The reduction potentials are lowest for the smallest-cavity cyclophane **13**.

Experimental Section

General Remarks: Melting points were determined by the open capillary tube method using a Toshniwal melting point apparatus and were uncorrected. IR spectra were recorded on Nicolet Impact 400 FT-IR and FTIR-8300 spectrophotometers. ^{1}H and ^{13}C NMR spectra were recorded on Jeol 400 MHz, Bruker 300 MHz and Bruker ARX 200 MHz spectrometers. The FAB-MS spectra were recorded on a Jeol SX 102/DA-6000 mass spectrometer. Ultraviolet-Visible (UV) spectra were recorded on a Shimadzu 260 spectrophotometer. Elemental analyses were performed on a Perkin−Elmer 240B elemental analyzer. Electrochemical studies were carried out on a CH Instruments electrochemical analyzer.

General Procedure for the Synthesis of Dicationic Precyclophanes: A solution of the dibromide (2.50 mmol) in dry CH_3CN (25 mL) was added dropwise with stirring to a solution of 4,4′-bipyridine (12.5 mmol) in refluxing dry CH_3CN (20 mL) for 6 h under nitrogen. The reaction mixture was heated under reflux for further 24 h and then cooled to room temperature. The precipitated solid was filtered and washed thoroughly with diethyl ether (20 mL) and $CHCl_3$ (20 mL). The residue was suspended in CH_3CN (20 mL), solid NH_4PF_6 (1.00 g) was added, and the mixture was stirred for 30 min and then filtered. The solvent was removed under vacuum; the residue was washed thoroughly with H_2O and then dried to give the dicationic precyclophane.

Dicationic Precyclophane 2a: From **1a** (1.04 g) and 4,4′-bipyridine (1.95 g), the product (1.50 g, 82%) was obtained as a yellow solid, which contained about 10% of **3a** as revealed by ^{1}H NMR spectroscopy. The product was used in the next step without separation or further characterisation.

Dicationic Precyclophane 2b: From **1b** (1.24 g) and 4,4′-bipyridine (1.95 g), the product (1.43 g, 71%) was obtained as a yellow solid, which contained about 45% of **3b** as revealed by ^{1}H NMR spectroscopy. The product was used in the next step without separation or further characterisation.

Dicationic Precyclophane 2c: From **1c** (1.15 g) and 4,4′-bipyridine (1.95 g), the product (1.28 g, 66%) was obtained as a yellow solid, which contained about 25% of **3c** as revealed by ^{1}H NMR spectroscopy. The product was used in the next step without separation or further characterisation.

Dicationic Precyclophane 2d: From **1d** (1.18 g) and 4,4′-bipyridine (1.95 g), the product (1.35 g, 69%) was obtained as a yellow solid, which contained about 50% of **3d** as revealed by ^{1}H NMR spectroscopy. The product was used in the next step without separation or further characterisation.

Dicationic Precyclophane 12: From **11** (0.92 g) and 4,4′-bipyridine (1.95 g), **12** (1.16 g, 68%) was obtained as a colourless solid after recrystallisation from acetone/H_2O (9:1). M.p. 244 °C. IR (KBr): $\tilde{\nu}$ = 1642 cm^{-1} (C=O). ^{1}H NMR (200 MHz, CD_3CN): δ = 5.85 (s, 4 H, CH_2), 7.60 (d, J = 8.0 Hz, 4 H, Ar-H), 7.83−7.87 (m, 8 H, Ar-H & bipy-3′-H), 8.35 (d, J = 6.2 Hz, 4 H, bipy-3-H), 8.85−8.88 (m, 8 H, bipy-2 & 2′-H) ppm. ^{13}C NMR (50 MHz, CD_3CN): δ = 64.2, 118.1, 122.6, 127.0, 128.3, 129.8, 131.3, 137.9, 141.9, 145.8, 151.6, 195.7 ppm. MS (FAB): m/z = 665 [$M^+ - PF_6$]. $C_{35}H_{28}F_{12}N_4OP_2$ (810.57): calcd. C 51.86, H 3.48, N 6.91; found C 51.72, H 3.50, N 7.12.

Dicationic Precyclophane 15a: From **14a** (1.18 g) and 4,4′-bipyridine (1.95 g), **15a** (1.82 g, 80%) was obtained as a colourless solid after recrystallisation from acetone/H_2O (9:1). M.p. > 208 °C (dec.). IR (KBr): $\tilde{\nu}$ = 1642 cm^{-1} (C=O). ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 6.02 (s, 4 H, CH_2), 7.74 (d, J = 7.8 Hz, 4 H, Ar-H), 7.84−7.86 (m, 8 H, Ar-H), 8.01 (d, J = 4.9 Hz, 4 H, bipy-3′-H), 8.65 (d, J = 6.3 Hz, 4 H, bipy-3-H), 8.86 (d, J = 4.9 Hz, 4 H,

bipy-2′-H), 9.36 (d, J = 6.4 Hz, 4 H, bipy-2-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 62.8, 122.3, 126.3, 129.3, 130.0, 130.8, 137.5, 139.1, 140.2, 141.3, 145.9, 151.2, 153.4, 195.1 ppm. MS (FAB): m/z = 769 [M$^+$ − PF$_6$]. $C_{42}H_{32}F_{12}N_4O_2P_2$ (914.67): calcd. C 55.15, H 3.53, N 6.13; found C 55.43, H 3.70, N 6.05.

Dicationic Precyclophane 15b: From **14b** (1.18 g) and of 4,4′-bipyridine (1.95 g), **15b** (1.77 g, 77%) was obtained as a colourless solid after recrystallisation from acetone/H$_2$O (9:1). M.p. > 195 °C (dec.). IR (KBr): ṽ = 1642 cm^{-1} (C=O). ^{1}H NMR (200 MHz, CD$_3$CN): δ = 5.78 (s, 4 H, CH$_2$), 7.51−8.01 (m, 16 H, Ar-H & bipy-3′-H), 8.26 (d, J = 5.8 Hz, 4 H, bipy-3-H), 8.73−8.82 (m, 8 H, bipy-2 & 2′-H) ppm. ^{13}C NMR (50 MHz, CD$_3$CN): δ = 64.1, 118.0, 122.5, 127.0, 128.3, 129.6, 129.8, 131.4, 134.4, 138.0, 138.8, 140.6, 141.9, 145.8, 151.8, 195.5 ppm. MS (FAB): m/z = 769 [M$^+$ − PF$_6$]. $C_{42}H_{32}F_{12}N_4O_2P_2$ (914.67): calcd. C 55.15, H 3.53, N 6.13; found C 55.22, H 3.65, N 6.15.

General Procedure for the Synthesis of Tetracationic Cyclophanes: The dicationic precyclophane (0.35 mmol) was heated under reflux with a slight excess of the corresponding dibromide (0.40 mmol) in CH$_3$CN (250 mL) for 48 h. The reaction mixture was cooled to room temperature and the solvent was reduced to one-fifth of its volume under reduced pressure. The precipitated solid was collected, dried and purified by column chromatography over SiO$_2$ using CH$_3$OH/H$_2$O/satd. aq. NH$_4$Cl (6:3:1) as eluent. The cyclophane-containing fractions were combined and the solvent was evaporated under vacuum. The residue was dissolved/suspended in H$_2$O (50 mL) and solid NH$_4$PF$_4$ (0.25 g) was added, then the precipitate was filtered, washed thoroughly with H$_2$O and dried to give the pure tetracationic cyclophane.

Tetracationic Cyclophane 3a: From the dicationic precyclophane **2a** (334 mg, 0.35 mmol, based on the amount of **2a** present in the mixture) and **1a** (166 mg, 0.40 mmol), **3a** (158 mg, 25%, based on the amount of **2a** present) was obtained as a pale yellow solid. Single crystals suitable for X-ray studies were grown by vapour diffusion of iPr$_2$O into a solution of **3a** in acetonitrile. M.p. > 210 °C (dec.). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 6.03 (s, 8 H, CH$_2$), 7.60−8.03 (m, 24 H, Ar-H), 8.81 (d, J = 5.9 Hz, 8 H, bipy-3-H), 9.63 (d, J = 5.9 Hz, 8 H, bipy-2-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 63.2, 125.0, 126.6, 127.3, 127.8, 129.5, 129.8, 133.7, 136.5, 140.0, 145.7, 149.1 ppm. MS (FAB): m/z = 1114 [M$^+$ − 2PF$_6$]. $C_{60}H_{48}F_{24}N_4P_4{\cdot}3H_2O$ (1458.98): calcd. C 49.39, H 3.73, N 3.84; found C 49.50, H 3.64, N 3.80.

Tetracationic Cyclophane 3b: From the dicationic precyclophane **2b** (505 mg, 0.35 mmol, based on the amount of **2b** present in the mixture) and **1b** (173 mg), **3b** (283 mg, 19%, based on the amount of **2b** present) was obtained as a pale yellow solid. M.p. > 230 °C (dec.). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 6.01 (s, 8 H, CH$_2$), 7.06−7.67 (m, 22 H, Ar-H), 8.78 (d, J = 6.4 Hz, 8 H, bipy-3-H), 9.56 (d, J = 6.4 Hz, 8 H, bipy-2-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 63.5, 127.9, 128.5, 128.9, 129.8, 131.3, 135.6, 138.3, 143.5, 145.5, 148.3, 149.6 ppm. MS (FAB): m/z = 1272 [M$^+$ − 2PF$_6$]. $C_{60}H_{46}Br_2F_{24}N_4P_4{\cdot}H_2O$ (1580.74): calcd. C 45.59, H 3.06, N 3.54; found C 45.52, H 3.16, N 3.51.

Tetracationic Cyclophane 3c: From the dicationic precyclophane **2c** (421 mg, 0.35 mmol, based on the amount of **2c** present in the mixture) and **1c** (184 mg), **3c** (188 mg, 16%, based on the amount of **2c** present) was obtained as a pale yellow solid. M.p. > 192 °C (dec.). IR (KBr): ṽ = 3415 (O−H), 1711 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 6.02 (s, 8 H, CH$_2$), 7.35−7.68 (m, 22 H, Ar-H), 8.80 (d, J = 6.4 Hz, 8 H, bipy-3-H), 9.59 (d, J = 6.4 Hz, 8 H, bipy-2-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 63.1, 122.4, 126.5, 127.8, 129.3, 130.0, 134.0, 138.4, 141.6, 146.3, 151.4, 153.5, 170.3 ppm. MS (FAB): m/z = 1202 [M$^+$ − 2PF$_6$]. $C_{62}H_{48}F_{24}N_4O_4P_4$ (1492.95): calcd. C 49.88, H 3.24, N 3.75; found C 50.01, H 3.12, N 3.66.

Tetracationic Cyclophane 3d: From the dicationic precyclophane **2d** (642 mg, 0.35 mmol, based on the amount of **2d** present in the mixture) and **1d** (190 mg), **3d** (463 mg, 27%, based on the amount of **2d** present) was obtained as a colourless solid. M.p. > 300 °C (dec.). IR (KBr): ṽ = 1724 cm^{-1} (C=O). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.97 (s, 6 H, CH$_3$), 5.97 (s, 8 H, CH$_2$), 7.36−7.63 (m, 22 H, Ar-H), 8.74 (d, J = 6.4 Hz, 8 H, bipy-3-H), 9.47 (d, J = 5.9 Hz, 8 H, bipy-2-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 51.7, 63.3, 127.4, 128.7, 129.0, 129.6, 130.5, 131.9, 133.9, 138.9, 141.0, 146.0, 149.3, 169.0 ppm. MS (FAB): m/z = 1230 [M$^+$ − 2PF$_6$]. $C_{64}H_{52}F_{24}N_4O_4P_4$ (1521.00): calcd. C 50.54, H 3.45, N 3.68; found C 50.23, H 3.35, N 3.82.

One-Pot Synthesis of the Tetracationic Cyclophanes 3a−d: A mixture of the m-terphenyl dibromides **1a−d** (0.72 mmol) and 4,4′-bipyridine (0.72 mmol) was heated under reflux for 48 h in dry CH$_3$CN (150 mL). The reaction mixture was then cooled to room temperature and the solvent was reduced to one-fifth of its volume under vacuum. The residue was purified as outlined in the general procedure above. The yields of **3a−d** obtained by this method were 18, 22, 15 and 28%, respectively. The cyclophanes **3a−d** obtained by this method were identical in all respects with those obtained by the two-step procedure.

Tetracationic Cyclophane 5a: From **4** (247 mg) and **1a** (166 mg), **5a** (101 mg, 23%) was obtained as a pale yellow solid. M.p. > 300 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 5.90 (s, 4 H, CH$_2$), 5.97 (s, 4 H, CH$_2$), 7.54−7.76 (m, 16 H, Ar-H), 8.68 (d, J = 5.4 Hz, 8 H, bipy-3 & 3′-H), 9.47 (m, 8 H, bipy-2 & 2′-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 63.2, 63.6, 125.8, 127.1, 127.2, 128.1, 128.9, 129.7, 129.9, 130.2, 134.1, 135.5, 140.3, 141.6, 145.6, 145.8, 148.7, 148.9 ppm. MS (FAB): m/z = 962 [M$^+$ − 2PF$_6$]. $C_{48}H_{40}F_{24}N_4P_4{\cdot}2H_2O$ (1288.77): calcd. C 44.73, H 3.44, N 4.35; found C 44.78, H 3.42, N 4.40.

Tetracationic Cyclophane 5b: From **4** (247 mg) and **1d** (190 mg), **5b** (124 mg, 27%) was obtained as a pale yellow solid. M.p. > 300 °C. IR (KBr): ṽ = 1729 cm^{-1} (C=O). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.41 (s, 3 H, CH$_3$), 5.87 (s, 4 H, CH$_2$), 5.95 (s, 4 H, CH$_2$), 7.24 (d, J = 7.8 Hz, 4 H, Ar-H), 7.46−7.52 (m, 6 H, Ar-H), 7.63 (t, J = 7.3 Hz, 1 H, Ar-H), 7.77 (s, 4 H, xyl-H), 8.65−8.67 (m, 8 H, bipy-3 & 3′-H), 9.43 (d, J = 6.8 Hz, 4 H, bipy-2-H), 9.49 (d, J = 6.4 Hz, 4 H, bipy-2′-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 49.2, 61.3, 61.6, 125.1, 125.3, 126.1, 126.5, 127.0, 127.3, 128.0, 128.3, 131.8, 132.3, 133.5, 136.9, 138.9, 143.6, 143.8, 146.8, 166.3 ppm. MS (FAB): m/z = 1020 [M$^+$ − 2PF$_6$]. $C_{50}H_{42}F_{24}N_4O_2P_4$ (1310.77): calcd. C 45.82, H 3.23, N 4.27; found C 45.51, H 3.32, N 4.35.

Tetracationic Cyclophane 13: From **12** (284 mg) and **11** (147 mg), **13** (75 mg, 16%) was obtained as a white solid. M.p. > 275 °C (dec.). IR (KBr): ṽ = 1642 cm^{-1} (C=O). ^{1}H NMR (200 MHz, CD$_3$CN): δ = 5.87 (s, 8 H, CH$_2$), 7.35 (d, J = 7.8 Hz, 8 H, Ar-H), 7.67 (d, J = 7.8 Hz, 8 H, Ar-H), 8.34 (d, J = 6.0 Hz, 8 H, bipy-3-H), 8.89 (d, J = 6.0 Hz, 8 H, bipy-2-H) ppm. ^{13}C NMR (50 MHz, CD$_3$CN): δ = 64.7, 118.0, 128.2, 128.8, 131.1, 138.2, 138.9, 146.8, 195.8 ppm. MS (FAB): m/z = 1018 [M$^+$ − 2PF$_6$]. $C_{50}H_{40}F_{24}N_4O_2P_4$ (1308.76): calcd. C 45.89, H 3.08, N 4.28; found C 45.66, H 3.03, N 4.19.

Tetracationic Cyclophane 16a: From **15a** (320 mg) and **14a** (189 mg), **16a** (65 mg, 12%) was obtained as a colourless solid. M.p.

> 248 °C (dec.). IR (KBr): $\tilde{\nu}$ = 1642 cm^{-1} (C=O). ^1H NMR (400 MHz, CD_3CN/[D_6]DMSO): δ = 6.58 (s, 8 H, CH_2), 8.28−8.56 (m, 24 H, Ar-H), 9.10 (d, *J* = 5.9 Hz, 8 H, bipy-3-H), 9.83 (distorted d, 8 H, bipy-2-H) ppm. ^{13}C NMR (100 MHz, CD_3CN/[D_6]DMSO): δ = 62.6, 117.0, 125.9, 128.8, 129.4, 130.4, 138.1, 139.9, 145.3, 153.6, 194.7 ppm. MS (FAB): *m*/*z* = 1226 [M^+ − $2PF_6$]. $C_{64}H_{48}F_{24}N_4O_4P_4$ (1516.97): calcd. C 50.67, H 3.19, N 3.69; found C 5.53, H 3.27, N 3.47.

Tetracationic Cyclophane 16b: From **15b** (320 mg) and **14b** (189 mg), **16b** (73 mg, 14%) was obtained as a colourless solid. M.p. > 260 °C. IR (KBr): $\tilde{\nu}$ = 1642 cm^{-1} (C=O). ^1H NMR (400 MHz, [D_6]DMSO): δ = 6.03 (s, 8 H, CH_2), 7.77−7.79 (m, 14 H, Ar-H), 7.98 (d, *J* = 7.4 Hz, 8 H, Ar-H), 8.27 (s, 2 H, Ar-H), 8.74 (d, *J* = 5.9 Hz, 8 H, bipy-3-H), 9.51 (d, *J* = 5.9 Hz, 8 H, bipy-2-H) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 61.1, 125.4, 127.2, 127.4, 128.3, 128.5, 132.1, 134.8, 135.5, 136.6, 144.0, 147.4, 192.5 ppm. MS (FAB): *m*/*z* = 1226 [M^+ − $2PF_6$]. $C_{64}H_{48}F_{24}N_4O_4P_4{\cdot}H_2O$ (1534.99): calcd. C 50.08, H 3.28, N 3.65; found C 50.02, H 3.34, N 3.61.

Diester 8: The *m*-terphenylcarbonyl chloride **7** − obtained from of the corresponding acid[7] (5.58 g, 18.48 mmol) and $SOCl_2$ (1.35 mL; 18.48 mmol) using 4−5 drops of pyridine − was added in three portions to the disodium salt of 1,4-bis(2-hydroxyethoxy)benzene [from **6** (1.50 g, 7.56 mmol) and NaH (60% in oil; 0.76 g, 18.94 mmol)] in anhydrous DMF (100 mL) under nitrogen. The mixture was stirred at 80 °C for 48 h and then the DMF was evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 (2 × 100 mL), washed with water (2 × 100 mL), dried (Na_2SO_4) and then the solvents were evaporated to give a dark red solid. Column chromatography (SiO_2; hexane/EtOAc, 9:1, v/v) gave **8** (1.28 g, 22%) as a white solid. M.p. 170 °C. IR (KBr): $\tilde{\nu}$ = 1732 cm^{-1} (C=O). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 12 H, CH_3), 3.63 (t, *J* = 4.0 Hz, 4 H, OCH_2), 4.17 (t, *J* = 4.0 Hz, 4 H, OCH_2), 6.66 (s, 4 H, hq-H), 7.12 (d, *J* = 6.4 Hz, 8 H, Ar-H), 7.30−7.34 (m, 12 H, Ar-H), 7.46 (t, *J* = 6.5 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.4, 63.1, 66.0, 115.5, 128.6, 128.9, 129.2, 129.5, 132.7, 137.4, 137.8, 140.5, 153.0, 169.6 ppm. MS (FAB): *m*/*z* = 766 [M^+]. $C_{52}H_{46}O_6$ (766.94): calcd. C 81.44, H 6.04; found C 81.50, H 6.02.

Tetrabromide 9: NBS (381 mg, 2.14 mmol) was added in four equal portions at 4 h intervals to a solution of **8** (400 mg, 0.52 mmol) in CCl_4 heated at reflux. Each portion was immediately followed by the addition of Bz_2O_2 (a few mg). After heating under reflux for a total of 40 h, the mixture was cooled and the precipitated succinimide removed by filtration. The residue obtained after evaporation of the solvent was chromatographed (SiO_2; hexane/CH_2Cl_2, 1:1, v/v) and the final product was recrystallised (hexane/CH_2Cl_2) to give **9** (452 mg, 80%) as a pale yellow solid. M.p. 106 °C. IR (KBr): $\tilde{\nu}$ = 1729 cm^{-1} (C=O). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.56 (distorted t, 4 H, OCH_2), 4.07 (distorted t, 4 H, OCH_2), 4.37 (s, 8 H, CH_2), 6.61 (s, 4 H, hq-H), 7.25−7.50 (m, 22 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.2, 63.3, 65.7, 115.3, 128.3, 128.5, 128.9, 129.4, 132.3, 137.0, 139.7, 140.4, 152.7, 169.0 ppm. MS (FAB): *m*/*z* = 1083 [M^+ + 1]. $C_{52}H_{42}Br_4O_6$ (1082.53): calcd. C 57.70, H 3.91; found C 57. 55, H 3.74.

Bicyclic Cyclophane 10: A mixture of the tetrabromide **9** (200 mg, 0.185 mmol) and 4,4′-bipyridine (58 mg, 0.37 mmol) was heated under reflux for 24 h in dry CH_3CN (100 mL). The reaction mixture was then cooled to room temperature and the solvent was reduced to one-fifth of its volume under vacuum. The precipitated product was purified by column chromatography as described above to give **10** (183 mg, 60%) as a pale red solid. M.p. > 215 °C (dec.). IR (KBr): $\tilde{\nu}$ = 1725 cm^{-1} (C=O). ^1H NMR (400 MHz, [D_6]DMSO): δ = 3.67 (distorted t, 4 H, OCH_2), 3.88 (distorted t, 4 H, OCH_2), 5.97 (s, 8 H, CH_2), 6.08 (s, 4 H, hq-H), 7.23−8.05 (m, 22 H, Ar-H), 8.62 (d, *J* = 5.9 Hz, 8 H, bipy-3-H), 9.52 (d, *J* = 5.9 Hz, 8 H, bipy-2-H) ppm. ^{13}C NMR (100 Mz, [D_6]DMSO): δ = 63.1, 63.3, 64.9, 115.2, 116.1, 122.2, 126.2, 126.9, 128.0, 129.0, 133.7, 138.8, 141.4, 145.3, 148.6, 150.2, 168.2 ppm. MS (FAB): *m*/*z* = 1509 [M^+ − PF_6]. $C_{72}H_{58}F_{24}N_4O_6P_4{\cdot}3H_2O$ (1709.17): calcd. C 50.60, H 3.77, N 3.28; found C 50.56, H 3.75, N 3.33.

Bicyclic Cyclophane 18: A mixture of the tricarbonyl tribromide **17** (300 mg, 0.45 mmol) and 4,4′-bipyridine (105 mg, 0.67 mmol) was heated under reflux for 72 h in dry CH_3CN (300 mL). The reaction mixture was then cooled to room temperature and the solvent was reduced under vacuum to one-fifth of its volume. The precipitated product was purified by column chromatography in the manner described above to give **18** (15 mg, 3%) as a pale yellow solid. M.p. > 235 °C (dec.). IR (KBr): $\tilde{\nu}$ = 1642 cm^{-1} (C=O). ^1H NMR (400 MHz, [D_6]DMSO): δ = 5.96 (s, 12 H, CH_2), 7.69 (d, *J* = 7.8 Hz, 12 H, Ar-H), 7.86 (d, *J* = 7.81 Hz, 12 H, Ar-H), 8.01 (s, 6 H, Ar-H), 8.61 (d, *J* = 5.9 Hz, 12 H, bipy-3-H), 9.32 (d, *J* = 5.4 Hz, 12 H, bipy-2-H) ppm. ^{13}C NMR (100 Mz, [D_6]DMSO): δ = 62.6, 122.5, 126.2, 129.1, 130.7, 137.3, 139.2, 141.7, 145.8, 153.0, 193.9. $C_{90}H_{66}F_{36}N_6O_6P_6$ (2197.32): calcd. C 49.20, H 3.03, N 3.82; found C 49.34, H 3.25, N 3.63.

Determination of Association Constants by UV/Vis Spectroscopy (Benesi−Hildebrand Method): In a typical experiment, an aliquot (3.5 mL) of a standard stock solution of the cyclophane in MeCN was placed in a quartz cuvette. A known amount of the electron-rich guest molecule was added by incremental amounts and changes in the absorbance of the CT band were recorded. A plot of [concentration of cyclophane]/absorbance vs. 1/[concentration of guest] was linear. From the slope and the intercept, the values of K_a and ε were evaluated. The plots were linear suggesting that the predominant species in solution was a 1:1 complex.

Electrochemical Measurements: Electrochemical experiments were carried out in nitrogen-purged DMSO solutions at room temperature. The solutions for electrochemistry were held at a concentration in the range of 10^{-3} M of the electroactive species. $TBAPF_6$ (0.1 M) was included as a supporting electrolyte. A glassy carbon electrode was used as the working electrode; its surface was routinely polished with a 0.05-μm alumina/water slurry on a felt surface prior to use. All potentials were recorded against a saturated Ag/AgCl electrode and a platinum wire was used as a counter electrode. The potential range was cycled from 0 to −1.2 V at a scan rate of 50 mV/s for all samples.

Acknowledgments

K. S. thanks CSIR, India, for financial support. The authors thank Dr. K. Chinnakali, Department of Physics, Anna University, for XRD studies; Dr. K. Pandian, Department of Chemistry, University of Madras, P. G. Extension Centre, Vellore, for discussions on electrochemistry; RSIC, Madras, for NMR spectra; and RSIC, Lucknow, for FAB-MS.

[1] A. P. Davies, *Nature* **1999**, *401*, 120−121.
[2] [2a] D. B. Amabilino, J. F. Stoddart, *Chem. Rev.* **1995**, *95*, 2725−2828. [2b] M. Asakawa, P. R. Ashton, S. E. Boyd, C. L. Brown, S. Menzer, D. Pasini, J. F. Stoddart, M. S. Tolley, A. J. P. White, D. J. Williams, P. G. Wyatt, *Chem. Eur. J.* **1997**, *3*, 463−481.

[3] For examples see: [3a] M. Asakawa, C. L. Brown, D. Pasini, J. F. Stoddart, P. G. Wyatt, *J. Org. Chem.* **1996**, *61*, 7234−7235. [3b] A. Lorente, M. Fernandez-Saiz, F. Herraiz, J. M. Lehn, J. P. Vigneron, *Tetrahedron Lett.* **1999**, *40*, 5901−5904.
[4] [4a] P. Rajakumar, M. Srisailas, *Tetrahedron Lett.* **1997**, *38*, 5323−5326. [4b] P. Rajakumar, V. Murali, *Tetrahedron* **2000**, *56*, 7995−7999. [4c] P. Rajakumar, M. Srisailas, *Tetrahedron* **2001**, *57*, 9749−9754.
[5] W. Gueder, S. Hünig, A. Suchy, *Tetrahedron* **1986**, *42*, 1665−1677.
[6] B. Odell, M. V. Reddington, A. M. Z. Slawin, N. Spencer, J. F. Stoddart, D. J. Williams, *Angew. Chem.* **1988**, *100*, 1605−1608; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1547−1550.
[7] H. Hart, P. Rajakumar, *Tetrahedron* **1995**, *51*, 1313−1336.
[8] T. Ravishankar, K. Chinnakali, K. Srinivasan, P. Rajakumar, A. Usman, H.-K. Fun, *Acta Crystallogr.* **2002**, *E58*, o1356−o1358.
[9] C. Seel, F. Vogtle, *Angew. Chem.* **1992**, *104*, 542−563; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 528−549.
[10] [10a] M. Asakawa, P. R. Ashton, C. L. Brown, M. C. T. Fyfe, S. Menzer, D. Pasini, C. Scheurer, N. Spencer, J. F. Stoddart, A. J. P. White, D. J. Williams, *Chem. Eur. J.* **1997**, *3*, 1136−1150. [10b] M. Asakawa, P. R. Ashton, S. Menzer, F. M. Raymo, J. F. Stoddart, A. J. P. White, D. J. Williams, *Chem. Eur. J.* **1996**, *2*, 877−893.
[11] H. A. Benesi, J. H. Hildebrand, *J. Am. Chem. Soc.* **1949**, *71*, 2703−2707.
[12] P. L. Anelli, P. R. Ashton, R. Ballardini, V. Balzani, M. Delgado, M. T. Gandolfi, T. T. Goodnow, A. E. Kaifer, D. Philp, M. Pietraszkiewicz, L. Prodi, M. V. Reddington, A. M. Z. Slawin, N. Spencer, J. F. Stoddart, C. Vicent, D. J. Williams, *J. Am. Chem. Soc.* **1992**, *114*, 193−218.

Received August 17, 2002
[O02470]