

Cyclophanes with Self-recognising Components

Pier-Lucio Anelli,^a Masumi Asakawa,^b Peter R. Ashton,^b George R. Brown,^c Wayne Hayes,^b Oldrich Kocian,^b Santiago Rodríguez Pastor,^b J. Fraser Stoddart,^{*b} Malcolm S. Tolley,^b Andrew J. P. White^d and David J. Williams^d

^a BRACCO, via Egidio Folli 50, 20134 Milano, Italy

^b School of Chemistry, University of Birmingham, Edgbaston, Birmingham, UK B15 2TT

^c ZENECA Pharmaceuticals, Mereside, Alderley Park, Macclesfield, Cheshire, UK SK10 4TG

^d Chemical Crystallography Laboratory, Department of Chemistry, Imperial College, South Kensington, London, UK SW7 2AY

High dilution techniques have been employed to construct a series of charged flexible cyclophanes comprised of π -electron-rich hydroquinone and π -electron-deficient bipyridinium residues linked by polyether spacer units of varying length: significant conformational changes, leading to intramolecular and intermolecular interactions between the π -donors and π -acceptors, have been observed—as evidenced by X-ray crystallographic and variable temperature ^1H NMR and 2D ROESY spectroscopic investigations—within the series of the cyclophanes both in the solid and solution states as a result of increasing the lengths of the polyether spacer units.

Investigations of the complexation of π -electron deficient species such as the paraquat dication by crown ethers¹ such as bis(*p*-phenylene)-34-crown-10 (BPP34C10), and π -electron rich units such as 1,4-dimethoxybenzene by, for example, the tetracationic cyclophane² cyclobis(paraquat-*p*-phenylene) tetrakis(hexafluorophosphate), led ultimately to the efficient self-assembly³ of a [2]catenane.⁴ Self-assembly processes have been used to create in an efficient manner mechanically-interlocked molecular systems possessing nanoscale dimensions⁵ and a variety of physical properties.^{6,7} Several research groups have investigated intermolecular and intramolecular π -donor- π -acceptor interactions by employing systems incorporating a variety of π -electron donors and bipyridinium units as the π -electron acceptors.^{8,9} Recently, cyclophanes possessing bipyridinium units and several different π -electron-rich ring systems have been constructed to investigate the dynamics of charge recombination processes within excited charge-transfer states.¹⁰ Cyclophanes of this type have also been shown to possess the ability to complex metal ions.¹¹ Some years ago, we identified and designed a model cyclophane system (Fig. 1) which combines key molecular recognition and structural features of both BPP34C10 and cyclobis(paraquat-*p*-phenylene) tetrakis(hexafluorophosphate) in order to probe the nature of the intramolecular π -donor- π -acceptor interactions, investigate the effects of the polyether spacer length upon the solid and solution state characteristics of the cyclophanes, and to develop novel supramolecular architectures featuring this type of molecular recognition motif. Here we report our findings on the effects of varying the length of the polyether spacer upon the conformations of the resulting cyclophanes. We describe the synthesis of a series of bipyridinium-hydroquinone cyclophanes possessing flexible polyether spacers, the X-ray crystal structures^{†‡} of two of the cyclophanes, the variable temperature ^1H NMR and two-dimensional NMR spectroscopic investigations of the dicationic cyclophanes' solution-state conformations, and the UV

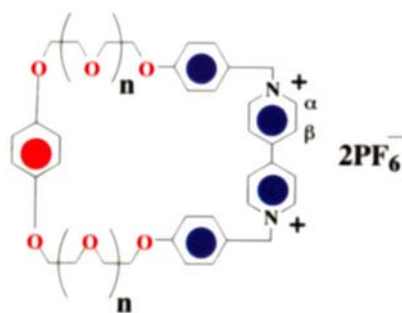
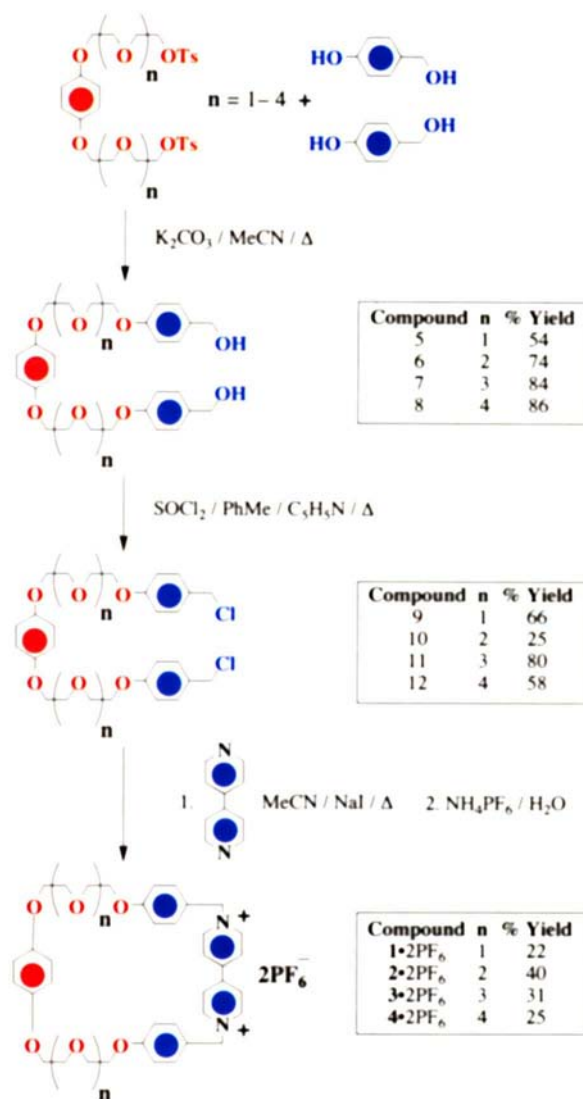


Fig. 1 The series of dicationic cyclophanes 1–4·2PF₆

spectrophotometric characteristics of these dicationic cyclophanes.

The dicationic cyclophanes (1–4·2PF₆) were synthesised as described in Scheme 1. The ditosylates were prepared according to a literature procedure⁴ and then subsequently reacted with 4-hydroxybenzyl alcohol to yield the corresponding diols 5–8, which were then converted into the respective benzylic dichlorides 9–12 with thionyl chloride in refluxing toluene. The



Scheme 1 Syntheses of the series of dicationic cyclophanes 1–4·2PF₆

desired dicationic cyclophanes **1–4**·2PF₆ were prepared under identical high dilution¹² conditions wherein equimolar amounts of 4,4'-bipyridine and the benzylic dichlorides **9–12** were dissolved in separate dry MeCN aliquots (150 ml). The resulting solutions were added during 12 h to refluxing dry MeCN (200 ml), which contained a catalytic amount of NaI. When the dropwise addition was complete, the reaction was maintained under reflux with vigorous stirring for 4 days. Column chromatography (on SiO₂ with MeOH–2 mol dm⁻³ NH₄Cl–MeNO₂ as eluent) and anion exchange with aqueous saturated solutions of NH₄PF₆ afforded the desired dicationic cyclophanes (**1–4**·2PF₆) as orange or orange-red solids. The cyclophanes were characterised subsequently by ¹H and ¹³C NMR spectroscopy as well as by FAB mass spectrometry.

Temperature-dependent ¹H NMR spectroscopic studies on the series of dicationic cyclophanes (**1–4**·2PF₆) in CD₃COCD₃ revealed changes in the chemical shift values of the protons associated with the π-electron-rich and π-electron-deficient recognition units in all the cyclophanes. Significant upfield shifts were observed for the hydroquinone proton resonances in the cyclophanes **2–4**·2PF₆, the largest upfield shift (Δδ –1.04 ppm) being observed†† for **4**·2PF₆, the cyclophane possessing the longest polyether chains. As the CD₃COCD₃ solutions of **2–4**·2PF₆ were cooled down, downfield shifts were also observed for the α-bipyridinium proton resonances in the cyclophanes. Indeed, the magnitudes of the chemical shift changes were analogous to those observed for a dicationic cyclophane previously reported in the literature.¹⁰ The trends in the chemical shift changes observed from the temperature-dependent ¹H NMR spectroscopic studies are consistent with findings from studies involving mechanically-interlocked systems⁴ featuring the same recognition motifs. Thus, it may be concluded that, in the dicationic cyclophanes **2–4**·2PF₆ in the solution state, the π-electron-rich and π-electron-deficient recognition units are in close proximity. Two-dimensional ROESY experiments, carried out in CD₃COCD₃ solutions of **1–4**·2PF₆, also indicated the close proximity of the π-electron-rich and π-electron-deficient recognition units. Significant ROE cross-peaks between the hydroquinone protons and the tolyl spacer unit protons for **2–4**·2PF₆ became evident as the

CD₃COCD₃ solutions were cooled down (Fig. 2), indicating that the hydroquinone ring resides in close proximity to the bipyridinium unit. However, there were only low intensity ROE cross-peaks evident between the hydroquinone and the tolyl spacer unit protons in **1**·2PF₆ when the CD₃COCD₃ solution was cooled down to 193 K. The small temperature-dependent chemical shift changes and low intensity ROE cross-peaks at 193 K in the case of **1**·2PF₆ indicate that this dicationic cyclophane possesses an 'open' conformation in the solution state.

The X-ray analysis of **1**·2PF₆ shows the dicationic cyclophane to have an open 'box-like' structure (Fig. 3) with crystallographic C₂ symmetry about an axis passing through the centre of the hydroquinone ring and the centre of the bond linking the two pyridinium units. The distance between the centre of the hydroquinone ring and the centre of the bond linking the two pyridinium rings of the bipyridinium unit is



Fig. 3 Ball-and-stick representation of the solid state structure of **1**·2PF₆

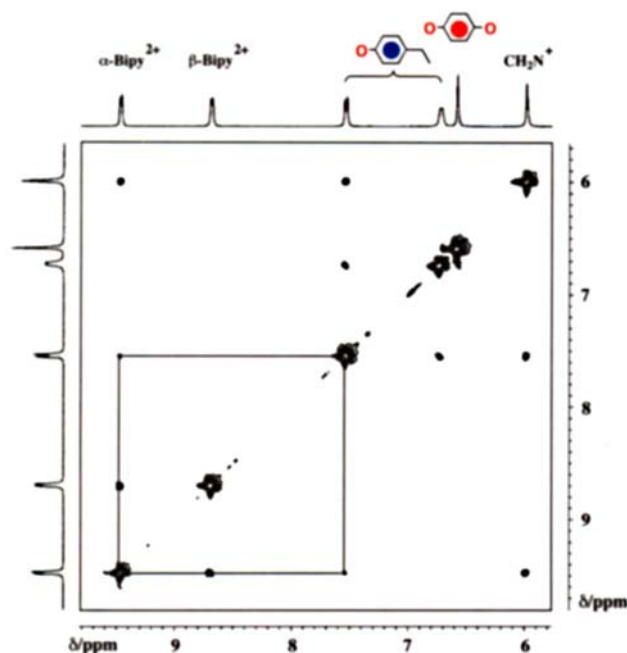


Fig. 2 The two-dimensional ROESY spectra of **2**·2PF₆ in CD₃COCD₃ solution at 223 K

9.5 Å and the transannular separation of the two tolyl oxygen atoms is 13.0 Å. The bipyridinium unit is non-planar and exhibits a small twist angle of 12.8° between the two pyridinium rings and in addition is slightly bowed with the two NCH₂ bonds subtending an angle of 10.6°. In common with numerous solid-state structures of systems incorporating BPP34C10, there is a retention of coplanarity of the two phenoxy ethyl groups with their associated hydroquinone ring.⁴ The dicationic cyclophane molecules pack to form channels that extend in the crystallographic *c* direction. Alternate molecules in the stack are reversed with respect to each other and are offset slightly, thereby restricting the channels. The included acetonitrile molecules lie within these channels. The tolyl units of adjacent stacks are arranged in a parallel fashion and are within π - π interaction distances of each other (interplanar separation = 3.5 Å, ring centroid-ring centroid distance = 3.8 Å). This π - π stacking interaction produces sinuous chains of molecules that extend in the crystallographic *a* direction (Fig. 4). There is a marked absence of the expected complementary π - π stacking interactions between the π -electron-rich hydroquinone ring and π -electron-deficient bipyridinium unit. This situation is a result of the interposition in the crystals of the hexafluorophosphate counterions between these potential recognition sites.

Sample 3·2PF₆ crystallises with two crystallographically independent C₂ symmetric molecules in the asymmetric unit (Fig. 5). Extension of the polyether linkage in 1·2PF₆ to give 3·2PF₆ results in a dramatic change in the conformation of the dicationic cyclophane. Instead of the rigid 'box-like' structure observed for 1·2PF₆, in 3·2PF₆, the π -electron-rich hydroquinone component is 'curled back' inwards and is positioned in a π - π stacking arrangement with respect to the π -electron-deficient bipyridinium unit. Both the twisting and bowing of the bipyridinium unit are more marked, the twist angle between the two pyridinium rings being increased to *ca.* 27°, with the NCH₂ bonds subtending angles of *ca.* 15°. The transannular separation of the two tolyl oxygen atoms is reduced to *ca.* 12.3 Å. It is interesting to note that the -OC₆H₄O- axis of each hydroquinone ring is skewed with respect to the N...N axis of its associated bipyridinium unit, producing a geometry very similar to that observed in other supramolecular systems containing these two components.⁴ Furthermore, crystallographically independent molecules are stacked along the *b* direction (Fig. 6) such that the bipyridinium unit of one molecule inserts itself into the cleft formed by the inwardly-folded hydroquinone ring of another to form an extended π -electron-donor- π -electron-acceptor stack. The intramolecular hydroquinone...bipyridinium distance is *ca.* 4.0 Å, whilst the equivalent intermolecular separation is 3.7 Å. The noticeably larger intramolecular hydroquinone ring...bipyridinium unit separation compared with the shorter intermolecular distance indicates that the polyether linkages in 3·2PF₆ may still be too short to permit optimal complementary intramolecular π - π stacking interactions. The inability of the dicationic cyclophane to optimise these interactions is further reflected in the crystal structure, where there is a degree of lateral disorder in the

hydroquinone ring and attached polyether linkages. This disorder is still present at low temperatures.‡

The UV absorption characteristics of the series (1-4·2PF₆) of dicationic cyclophanes were examined under identical conditions (1 mmol in MeCN at 293 K) and found to exhibit similar characteristics with Gaussian-shaped bands centred on 335 nm. The extinction coefficients for 1·2PF₆, 2·2PF₆, 3·2PF₆ and 4·2PF₆ are 1550, 2260, 1540 and 1350 cm⁻¹ mol⁻¹, respectively. These bands can be assigned to charge-transfer transitions within the confines of donor-acceptor complexes in which electronic charge is transferred^{8,10} from the hydroquinone rings to the bipyridinium units of the dicationic cyclophanes.

The solid and solution state studies carried out on this series of dicationic cyclophanes have revealed the effects of varying the lengths of the polyether chains upon the resulting cyclophane conformations and their abilities to form supramolecular arrays in the solid state. A surprising observation was the formation of channels and sinusoidal arrays in the solid state of 1·2PF₆ resulting from π - π stacking between the tolyl units

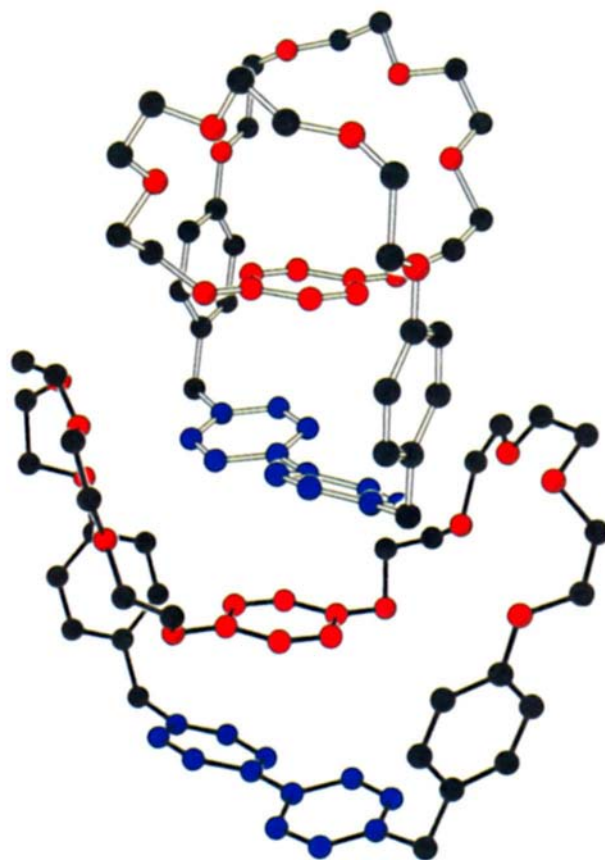


Fig. 5 Ball-and-stick representation of the two crystallographically independent forms of 3·2PF₆ in the solid state

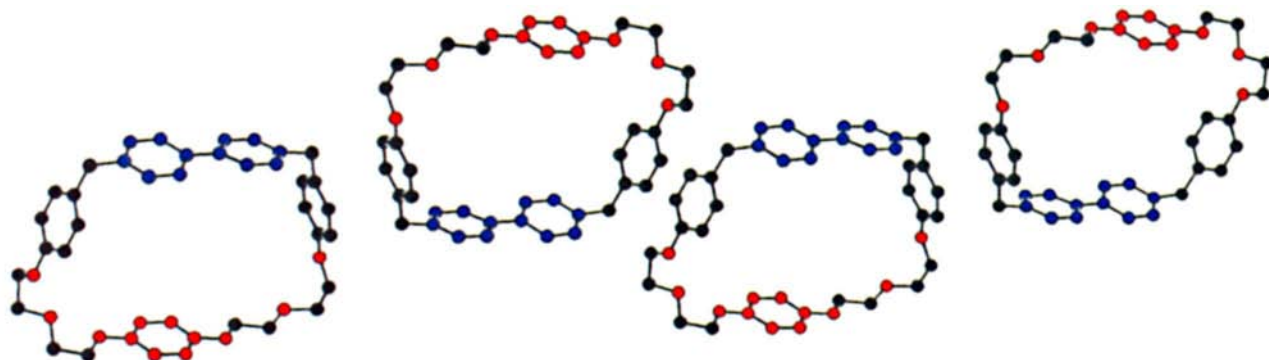


Fig. 4 Ball-and-stick representation of the sinusoidal array arising from the π - π stacking between the tolyl units in 1·2PF₆

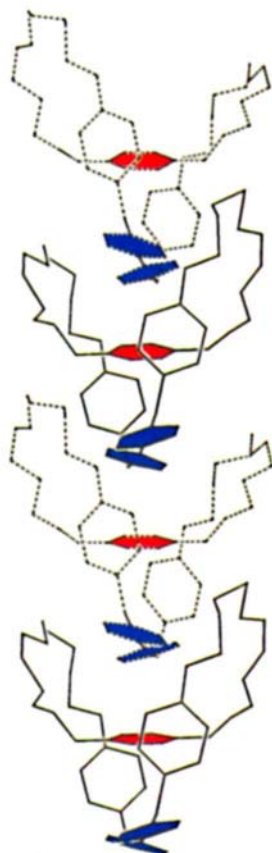


Fig. 6 Part of the infinite polar stack of the dicationic cyclophane **3-2PF₆** in the crystal illustrating the alternating sequence of π -electron-deficient and π -electron-rich aromatic moieties

instead of π - π interactions between the π -electron-rich and π -electron-deficient recognition units as predicted.^{1,2} However, as forecast, the increased flexibilities associated with the longer polyether chains permit greater intra- and inter-molecular π - π stacking between the π -electron-rich and π -electron-deficient recognition units as evidenced by the observations of 'folded' self-complexed conformations for this type of dicationic cyclophane both in the solid and solution states and also the formation of continuous linear stacked arrays for **3-2PF₆** in the solid state. The ability to predict and control molecular conformations,¹³ as well as solid state superstructures with molecules of this type, bodes well for the construction of new materials¹⁴ and also for the development of molecular and supramolecular devices.³

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Footnotes

† Crystal data for **1-2PF₆**: C₃₈H₄₀N₂O₆·2PF₆·1.5MeCN, *M* = 972.3, monoclinic, space group *C2/c*, *Z* = 4 (the molecule is disposed about a two-fold axis), *a* = 27.463(4), *b* = 17.633(3), *c* = 10.106(3) Å, β = 90.21(1)°,

U = 4894(7) Å³, *D_c* = 1.32 g cm⁻³, μ (Cu-K α) = 16.0 cm⁻¹, *F*(000) = 2004. 3303 independent reflections ($2\theta \leq 116^\circ$) were measured on a Nicolet R3m diffractometer with Cu-K α radiation (graphite monochromator) using ω -scans. 2610 had $|F_o| > 3\sigma(|F_o|)$ and were considered to be observed. The structure was solved by direct methods. The non-hydrogen atoms were refined anisotropically. Refinement was by block-cascade full-matrix least-squares to *R* = 0.061 and *R_w* = 0.067 [*w*⁻¹ = $\sigma^2(F) + 0.00081F^2$]. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

‡ Crystal data for **3-2PF₆**: C₄₆H₅₆N₂O₁₀·2PF₆·MeCN, *M* = 1127.9, monoclinic, space group *C2/c*, *Z* = 8 (there are two crystallographically independent *C*₂ symmetric molecules in the asymmetric unit), *a* = 26.770(11), *b* = 15.324(4), *c* = 29.447(12) Å, β = 110.73(3)°, *U* = 11298(7) Å³, *D_c* = 1.33 g cm⁻³, μ (Cu-K α) = 15.3 cm⁻¹, *F*(000) = 4688. 5815 independent reflections ($2\theta \leq 100^\circ$) were measured on a Siemens P3/PC diffractometer with Cu-K α radiation (graphite monochromator) using ω -scans at 293 K. 2685 had $|F_o| > 4\sigma(|F_o|)$ and were considered to be observed. There is disorder in the polyether chains and the hydroquinone rings of both of the crystallographically independent molecules; the disorder was resolved into two partial occupancy linkages (50:50 relative occupancy for one crystallographically independent molecule and 65:35 for the other). Because of the shortage of observed data, only the full occupancy nitrogen, oxygen, fluorine and phosphorous atoms were refined anisotropically. The final residuals are consequently somewhat high with *R*₁ = 0.141 and *wR*₂ = 0.386 for the observed data. Computations were carried out on a Silicon Graphics Iris Indigo using the SHELXTL-IRIS program system. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1. A second data set was collected at 198 K for a crystal from a different batch of **3-2PF₆**. The structure showed, despite the reduced temperature, similar disorder in the polyether chains and the hydroquinone rings. The final residual for this data set was slightly inferior than that for the room temperature study detailed above, probably reflecting the poorer crystal quality.

§ Spectroscopic data for **1-2PF₆**: FABMS: *m/z* 910, 765 and 620, corresponding to [M]⁺, [M - PF₆]⁺ and [M - 2PF₆]⁺, respectively; ¹H NMR (CD₃COCD₃, 400 MHz) δ 3.76–3.83 (8 H, m), 3.93–3.95 (4 H, m), 4.16–4.18 (4 H, m), 6.02 (4 H, s), 6.70 (4 H, s), 6.97 (4 H, AA'), 7.61 (4 H, XX'), 8.66 (4 H, d), 9.39 (4 H, d); ¹³C NMR (CD₃COCD₃, 75 MHz) δ 65.6, 68.5, 68.9, 70.2, 70.5, 115.6, 116.2, 126.4, 128.3, 131.8, 146.2, 151.1, 153.8, 161.3.

¶ Spectroscopic data for **2-2PF₆**: FABMS, *m/z* 998, 853 and 708, corresponding to [M]⁺, [M - PF₆]⁺ and [M - 2PF₆]⁺, respectively; ¹H NMR (CD₃COCD₃, 300 MHz) δ 3.63–3.76 (12 H, m), 3.80–3.85 (4 H, m), 3.90–3.95 (4 H, m), 4.18–4.22 (4 H, m), 6.07 (4 H, s), 6.70 (4 H, s), 7.05 (4 H, AA'), 7.62 (4 H, XX'), 8.72 (4 H, d), 9.41 (4 H, d); ¹³C NMR (CD₃COCD₃, 75 MHz) δ 65.4, 68.6, 68.7, 70.1, 70.3, 71.5, 116.0, 116.4, 125.9, 128.2, 131.9, 146.4, 150.9, 153.8, 161.2.

|| Spectroscopic data for **3-2PF₆**: FABMS, *m/z* 1086, 941 and 796, corresponding to [M]⁺, [M - PF₆]⁺ and [M - 2PF₆]⁺, respectively; ¹H NMR (CD₃COCD₃, 300 MHz) δ 3.55–3.73 (16 H, m), 3.69–3.73 (4 H, m), 3.79–3.83 (4 H, m), 3.90–3.95 (4 H, m), 4.15–4.21 (4 H, m), 6.08 (4 H, s), 6.71 (4 H, s), 7.08 (4 H, AA'), 7.62 (4 H, XX'), 8.72 (4 H, d), 9.41 (4 H, d); ¹³C NMR (CD₃COCD₃, 75 MHz) δ 65.4, 68.6, 68.7, 68.8, 70.1, 70.2, 70.3, 71.1, 71.2, 71.4, 116.2, 116.5, 125.8, 128.2, 131.9, 151.0, 153.8, 161.3.

** Spectroscopic data for **4-2PF₆**: FABMS, *m/z* 1029 and 884, corresponding to [M - PF₆]⁺ and [M - 2PF₆]⁺, respectively; ¹H NMR (CD₃COCD₃, 300 MHz) δ 3.48–3.64 (24 H, m), 3.69–3.74 (4 H, m), 3.79–3.84 (4 H, m), 3.89–3.94 (4 H, m), 4.17–4.22 (4 H, m), 6.03 (4 H, s), 6.60 (4 H, s), 7.07 (4 H, AA'), 7.66 (4 H, XX'), 8.66 (4 H, d), 9.36 (4 H, d); ¹³C NMR (CD₃COCD₃, 75 MHz) δ 65.4, 68.6, 68.7, 70.2, 70.3, 71.0, 71.1, 71.1, 71.2, 71.3, 71.4, 116.1, 116.5, 125.8, 128.1, 131.9, 146.3, 150.7, 153.7, 161.3.

†† $\Delta\delta$ values are quoted between the temperature range 293 to 233 K. Significant broadening of the proton resonances in the ¹H NMR spectra of **3-2PF₆** and **4-2PF₆** at lower temperatures prevented accurate chemical shift determination.

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