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COMMUNICATION

Viologen cyclophanes: Redox controlled host-guest interactions

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Viologens can exist in three redox states varying from dicationic to neutral. This work emphasizes the control of the host-guest properties in bis-viologen cyclophanes. Two flexible cyclophanes were prepared by a cyclisation method sensitive to the odd/even number of carbons in the flexible chains linking two viologens. C5 and C7 cyclophanes were characterised by X-ray diffraction in their tetracationic state and their diradical dicationic state. In the presence of tetrathiafulvalene or methyl viologen as guests, inclusion complexes were obtained, including a mixed valence species.

Viologens, or 4,4'-*N,N'*-dimethyl bipyridinium, undergo two reductions at a low redox potentials and with a high degree of reversibility. Three stable redox states are thus accessible, among which the radical cation is of particular interest for its ability to form π-dimers under appropriate conditions.[1] These properties make viologens the perfect candidate for the design of effective redox responsive materials.[2,3,4] During the past decade, viologens have been widely exploited as a key component in redox responsive molecular machines and materials,[5,6] such as liquid crystals,[7] with potential applications in optoelectronics, conductive materials,[8] and information storage.[9] To be fully effective, the π-dimerisation of viologens requires a confined environment and the formation of π-dimers in cucurbiturils was reported.[10] Whereas inclusion in cavities facilitates the π-dimerisation, another strategy is the use of covalent or mechanical link between the species to favour intramolecular π-dimerisation.[3,11] In the search for favoured intramolecular interactions in both flexible and cyclophane structures, the preparation of flexible viologen cyclophanes **1b⁴⁺** and **1d⁴⁺** and their host-guest properties in the solid state are reported hereafter.

Inspired by many approaches developed for the synthesis of the tetracationic cyclophane cyclo(bis(paraquat-*p*-phenylene), or blue-box,[12] two synthetic routes were investigated (routes 1 and 2, Scheme 1). In the first approach, 4,4'-bipyridine (4,4'-bipy) was reacted with an excess of an alkyl dibromide to give a 4,4'-bipyridinium salt appended by two bromoalkyl side chains of a given length. Further cyclisation of viologens **2b²⁺** and **2d²⁺** with a second 4,4'-bipy afforded bis-viologen cyclophanes **1b⁴⁺** and **1d⁴⁺**, respectively, in 7 and 11% yield. Cyclisation did not occur with the

viologen intermediates **2a²⁺**, **2c²⁺** and **2e²⁺** that have butyl, hexyl or octyl chains, respectively.
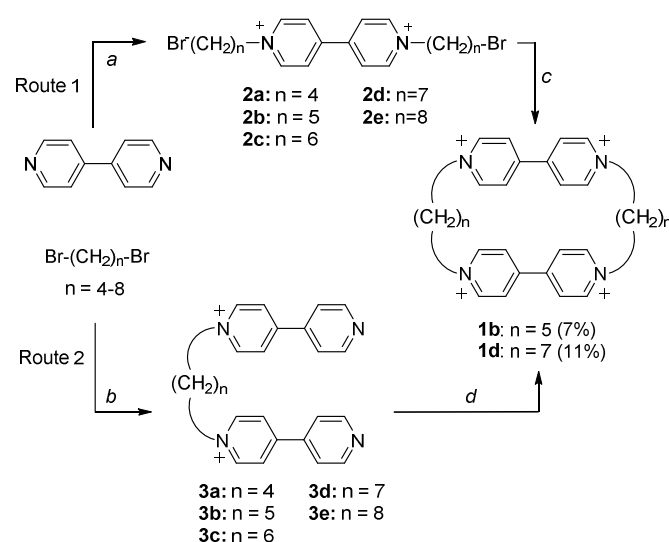
Scheme 1. a) 10 eq. dibromoalkane, CH₃CN, Δ; b) 2.5 eq. 4,4'-bipy, CH₃CN, Δ; c) 1 eq. 4,4'-bipy, CH₃CN, Δ; **1b⁴⁺**: 4%, **1d⁴⁺**: 5%; d) 1 eq. dibromoalkane, CH₃CN, reflux; **1b⁴⁺**: 7%, **1d⁴⁺**: 11%.

In the second synthetic approach (route 2), excess 4,4'-bipy was reacted with alkyl dibromides **2a-e²⁺** to afford the bis-pyridinium salts **3a-e²⁺**. Further reaction of the latter with one equivalent of the corresponding dibromoalkane yielded only cyclophanes **1b⁴⁺** and **1d⁴⁺** in lower yields than by route 1. Once again, cyclisation did not occur for intermediates with an even number of carbon atoms in the linker. Attempts to favour or improve the cyclisation reaction of compounds **3a-e** by using a template effect were unsuccessful in the presence of an electron rich templating guest such as tetrathifulvalene[13] or a naphthalene[14] derivative.

These observations suggest that a cofacial orientation of both bipyridiniums in route 2 is highly disfavoured when the alkyl spacer has an even number of carbon atoms, whereas it is possible with an

odd number of carbon atoms in the chain. Similar restricted mobility effects were observed in liquid crystal derivatives of bis-viologens for which the thermal behaviour was strongly affected by the number of carbons in the alkyl linker.[7] Attempts were made to prepare unsymmetrical cyclophanes via route 2 starting from a linker with an odd number of carbon atoms (C5 and C7) and then performing the cyclisation step with C4 or C6 dibromides. Again, no cyclisation was observed for any of the possible combinations. The same was true when starting with an even linker (C6) and then adding an odd linker (C5 or C7). These trials imply that the gauche configuration of a C4 or C6 alkyl chain is unsuitable for this reaction.

All new compounds were characterized by usual methods and single crystals of the cyclophane [PF_6]⁻ salts were obtained from acetonitrile by diffusion of diisopropyl ether into a solution of the cyclophanes in acetonitrile for **1b**[4+] (Figure 1 left) and as by vapor diffusion of nitromethane for **1d**[4+] (Figure 1 right). Some disorder exists in the structure of **1d**[4+].[15] With the exception of the viologen-viologen distances, the structures of the tetracationic cyclophanes **1b**[4+] and **1d**[4+] are quite similar. The alkyl spacers are in an unconstrained gauche conformation which supports the importance of odd/even effects on the respective orientation of the bipy.[7]

Compared to reported structures of isolated viologens, typical distances between C4 and C4' are observed (1.48 to 1.49 Å) indicating the localization of the electronic density on the aromatic pyridinium moieties that display a dihedral angle of 48° for **1b**[4+] and 41° for **1d**[4+] (ESI). The cavities are characterized by C4-C4 distances of 5.87 Å in **1b**[4+] and 7.96 Å in **1d**[4+] (see SI), whereas their widths are similar (9.7 to 9.9 Å). These distances between positively charged species are quite short and the [PF_6]⁻ counter anions clearly contribute to the close packing of the cyclophanes. In both cases crystal packing shows aligned cyclophane units separated by intermolecular distances of 4.86 Å in **1b**[4+] and 4.13 Å in **1d**[4+], combined with torque angles between each cyclophane of 22° in **1b**[4+] and 15° in **1d**[4+] (ESI).

Whereas the cavity of **1b**[4+] is probably too narrow to host a guest molecule, the size of the cavity of **1d**[4+] is well-adapted to accommodate a guest, such as an electron rich tetrathiafulvalene (TTF). Single crystals were obtained by diffusion of ether in a 1/1 stoichiometric mixture of **1d**[4+]/TTF in CH_3CN. The same inclusion structure was also observed for crystals obtained from a 2/1 stoichiometric ratio of TTF/**1d**[4+] in CH_3CN. The inclusion structure represented in Figure 2 shows that the dicationic character of each viologen remains intact, as shown by the distance of 1.48 Å between the C4 and C4' atoms and pyridinium dihedral angles of 27°. The inclusion is caused only by strong van der Waals interactions leading to a TTF-viologen centroid-centroid distance of 3.82 Å. Compared to the free macrocycle (see SI), the initial height and width of the cavity are only slightly affected (+/– 0.3 Å) by the inclusion of the TTF.
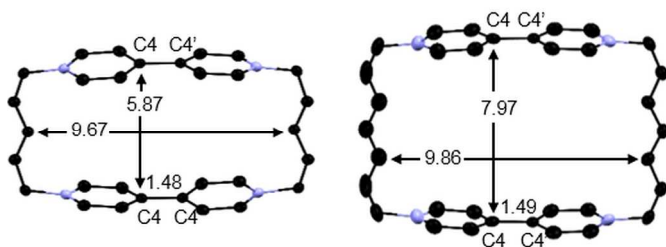

Figure 2. X-ray structure of **1d**[4+]⊂TTF. [PF_6]⁻ counter anions and solvents are omitted for clarity.
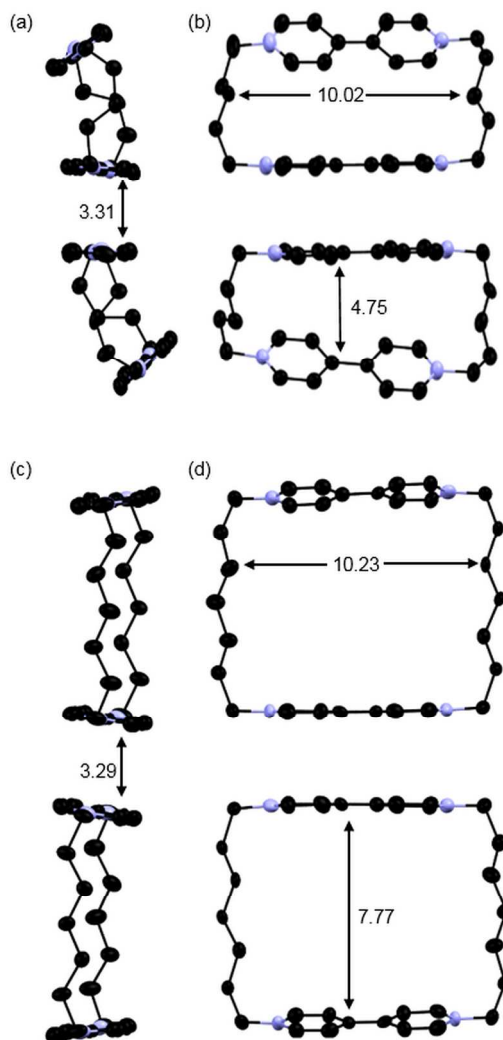
Figure 3. X-ray structure of **1b**[2(+•)] (a) profile and (b) face; X-ray structure of **1d**[2(+•)] (c) profile and (d) face. [PF_6]⁻ anions and solvents are omitted for clarity.

Figure 1. X-ray structure of the empty **1b**[4+] and **1d**[4+]. [PF_6]⁻ counter anions and solvents are omitted for clarity.

Both cyclophane structures were chemically reduced. Upon reduction with zinc powder, crystallization of **1b**[2(+•)] and **1d**[2(+•)] yielded dark blue single crystals which were characterized by X-ray diffraction. In both structures in Figure 3, the width of the cavity is dictated by the flat viologen unit. The perfect coplanar alignment of the pyridinium rings in each viologen unit confirms the delocalization of the radical cations over both pyridiniums connected

by a C4-C4' bond of 1.43 Å. Both cavities are slightly elongated, which is consistent with less intramolecular electrostatic repulsion in the di-radical cation state than in the tetracationic state. For both $1b^{2(+\bullet)}$ and $1d^{2(+\bullet)}$, clear evidence for the intermolecular π-dimerisation is provided by the close proximity of two viologen units located on distinct cyclophanes. The intermolecular distances are comparable in $1b^{2(+\bullet)}$ and $1d^{2(+\bullet)}$ (respectively 3.31 and 3.29 Å) and the cyclo-phanes are arranged in a continuous alignment (see packing in ESI).

Aside from these similar features, the structures differ by the conformation of their alkyl spacers. In the structure of $1d^{2(+\bullet)}$, the gauche conformation of the seven carbon chain forbids any intramolecular interactions. In contrast, the five carbon chain of $1b^{2(+\bullet)}$ is clearly distorted due to the closer intramolecular proximity of the two radical cationic viologen units. The bending of the five carbon alkyl spacers leads to an edge-to-edge distance of 3.90 Å at the shortest point and 4.01 Å at the longest; these distances are consistent with weak van der Waals interactions but are too large for molecular orbital (MO) interactions required for π-dimerisation. In both structures, stabilization through intermolecular interactions is clearly favoured over intramolecular interactions.
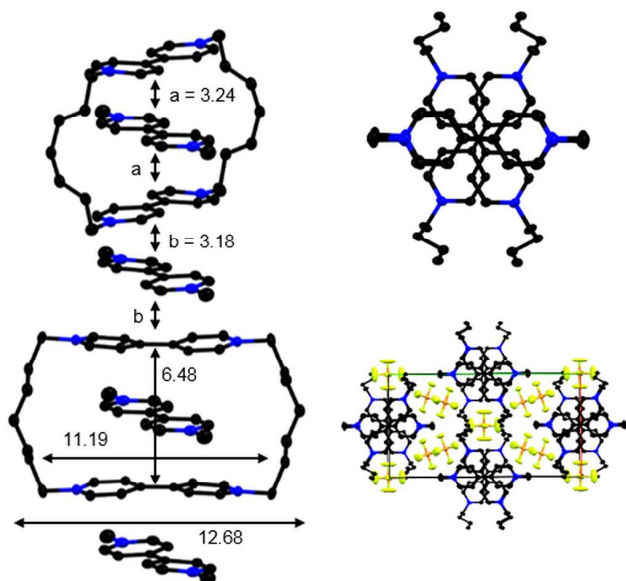

Figure 4. X-ray structure of the mixed valence complex $[(1d)(MV)_2]^{3(+\bullet)(2+)}$. Left: significant distances in the continuous mixed valence stack; $[PF_6]^-$ counter anions and solvents are omitted for clarity. Top right: top view of the continuous stack with $[PF_6]^-$ omitted. Bottom right: top view showing the contribution of $[PF_6]^-$ to the organization.

The solid state structures obtained for both the tetracationic species and the diradical dicationic species also suggest that whereas the C5 cyclophane cavity seems too small for any inclusion, the C7 cyclophane cavity is suitable for the formation of inclusion compounds. Viologens[16] are particularly well suited for solid state self-organization, providing quasi or pseudo-columnar stacks. Various stoichiometric ratios of $1d^{4+}$ and MV^{2+} were mixed in acetonitrile and reduced by an excess of zinc powder. After filtration and addition of degassed diisopropyl ether, dark blue single crystals were obtained from from a 1:2 mixture of $1d^{2(+\bullet)}/MV^{+\bullet}$. The same crystalline material was obtained from a 1:1 mixture, showing that the structure represented in the Figure 4 is highly favoured.

The structure of $1d^{2(+\bullet)}/MV^{+\bullet}$ (Figure 4) show aligned stacks of viologen and bis-viologen units. The number of $[PF_6]^-$ matches a global +5 charge for the four viologen units present in the unit cell, therefore this is a mixed valence species, $[(1d)(MV)_2]^{3(+\bullet)(2+)}$. The

inclusion of $MV^{+\bullet}$ inside the cyclophane cavity generates a columnar set of very similar bipyridinium (BP) subunits. Unlike the inclusion of $MV^{+\bullet}$ in the reduced blue-box reported in the literature, in the structure of $[(1d)(MV)_2]^{3(+\bullet)(2+)}$, the guest is not forced to opt for one side of the box to develop intermolecular interactions and is thus located at equal and shorter distances from the viologen subunits of the cyclophane.[17] The $MV^{+\bullet}$ located outside of the host is not completely flat. The short spacing of the MV units belonging to the cyclophane (C) and the inclusion guest (I) or (C) and the MV (O) sandwiched between the cyclophane first suggests a strong interaction between all species. However, a detailed examination of the intramolecular C-C distances within and between each pyridine or pyridinium rings shows that the extra charge seems unequally distributed over the four viologen units.

Partially reduced species have already been observed with simple MV derivatives and mixed valence scaffolds were characterized for $(MV^{2+})(MV^{+\bullet})$.[16] Due to the single crystalline nature of the structure, partial reoxidation of fully reduced crystalline species can be excluded in our system and the stronger localisation of the partial charge on the MV that is not part of the inclusion complex can be explained by its higher degree of structural freedom.
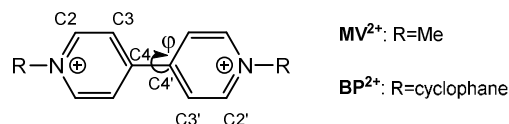

Table 1. Average nitrogen-carbon and carbon-carbon distances in the methyl-viologen (MV) and bipyridinium (BP) subunits depending on their localization in the scaffolds.

MV or BP subunit	C_2-N	C_2-C_3	C_3-C_4	C_4-C_4'	φ(deg)
BP in $1b^{4+}$	1.35	1.37	1.39	1.48	48
BP in $1d^{4+}$	1.34	1.37	1.39	1.49	41
BP in $1d^{4+}⊂TTF$	1.35	1.37	1.39	1.48	28
BP in $1b^{2(+\bullet)}$	1.36	1.36	1.42	1.43	1.6, 2.4
BP in $1d^{2(+\bullet)}$	1.35	1.42	1.42	1.43	1.3
$[(1d)(MV)_2]^{3(+\bullet)(2+)}$					
MV Inside (I)	1.36	1.36	1.43	1.43	0.0
BP (C)	1.37	1.37	1.42	1.44	4.6
MV Outside (O)	1.37	1.37	1.41	1.45	9.2
$[MV^{2+}MV^{\bullet+}]$	1.34	1.38	1.40	1.47	0.6
	1.36	1.36	1.42	1.43	0.0

Remarkably, despite the fact that the mixed valence state in $[(1d)(MV)_2]^{3(+\bullet)(2+)}$ is spread over four viologen units, the interatomic distances between the latter are close to those in π-dimerised radical cations or radical cations observed in mixed valence species. The only significant difference between each viologen unit in the scaffold is the torsion angle (0°, 4.6° or 9.2°) between the pyridinium rings. However, none of these values is close to the 40-50° torsion angle observed in dicationic viologen moieties (e.g. 48° in $1b$ in Table 1).

Interestingly, a mixed valence species $[MV^{2+}MV^{\bullet+}]$ consisting of the radical cation and dication of methylviologen was obtained when attempting to co-crystallize $1b^{2(+\bullet)}$ with $MV^{\bullet+}$. The solid state structure (ESI) of the corresponding $[PF_6]^-$ salt significantly differs from that reported for the $[BF_4]^-$ salt[16a] and a long range, continuous stacking at an interplanar distance of 3.19 Å is observed. Carbon-nitrogen and carbon-carbon distances are given in Table 1 for comparison with the cyclophane scaffolds. The mixed valence structure with $[BF_4]^-$ anions did show long range organization, although it was significantly less regular. Thus, the highly regular organization in viologen stacks reported in this communication seems strongly associated with both the use of $[PF_6]^-$ anions and the flexibility of the cyclophane structures.

Size adjustments are possible in the cavity of the host due to the flexible alkyl chains. Upon inclusion of $MV^{+\bullet}$ the cyclophane's alkyl chains are distorted from the initial gauche conformation. The size of the cavity shrinks from 7.77 x 10.22 Å in the absence of guest to 6.48 x 11.19 Å in the presence of guest. Such adjustments allow a distribution of the electron density over large distances without the pairing effects that are usually observed with rigid spacers.

Flexible cyclophanes of bis-viologens linked by alkyl chains were prepared by a cyclisation method that is sensitive to the odd or even number of carbon atoms in the linker. Two scaffolds in which the viologen moieties are separated by five or seven carbon links were obtained and characterized in their tetracationic and diradical-dicationic forms. In empty diradical-dicationic hosts, intermolecular π-dimerisation is preferred, whereas the largest host co-crystallizes with two $MV^{+\bullet}$ guests to generate a continuum of mixed valence states in which one positive charge is delocalized over four partially reduced viologen units. The viologen inclusion complex $[(\mathbf{1d})(MV)_2]^{3(+\bullet)(2+)}$ is the first solid state characterization of a delocalized mixed valence state in which a dication is surrounded by radical cation species. A continuum of interactions and band structures are determining parameters for the electronic properties of organic materials; thus, investigation of the crystals' electronic properties is in progress, together with the determination of HOMO, LUMO and SOMO levels by DFT calculations. This structure can be considered as one of the missing links in multi-viologen architectures and in depth theoretical studies are needed to investigate the partial charge distribution in this adaptive scaffold. Preliminary electrochemical studies of both cyclophanes in the absence and presence of MV^{2+} have not yet provided reliable results and suggest behaviour that varies depending on the combinations of solvent and counter anions.

Notes and references

1   E. M. Kosower, J. L. Cotter, *J. Am. Chem. Soc.*, 1964, **86**, 5524-5527.

2   A. Trabolsi, N. Khashab, A. C. Fahrenbach, D. C. Friedman, M. T. Colvin, K. K. Coti, D. Benitez, E. Tkatchouk, J.-C. Olsen, M. E. Belowich, R. Carmielli, H. A. Khatib, W. A. Goddard, III, M. R. Wasielewski, J. F. Stoddart, *Nat. Chem.*, 2010, **2**, 42-49.

3   A. Iordache, M. Oltean, A. Milet, F. Thomas, B. Baptiste, E. Saint-Aman, C. Bucher, *J. Am. Chem. Soc.*, 2012, **134**, 2653-2671.

4   C. Zhou, J. Tian, J.-L. Wang, D.-W. Zhang, X. Zhao, Y. Liu, Z.-T. Li *Polym. Chem.*, 2014, **5**, 341-345.

5   K. Wadhwa, S. Nureyyeva, A. C. Fahrenbach, M. Elhabiri, C. Platas-Iglesias, A. Trabolsi, *J. Mater. Chem. C*, 2013, **1**, 2302-2307.

6   Y. Wang, M. Frasconi, W.-G. Liu, Z. Liu, A. A. Sarjeant, M. S. Nassar, Y. Y. Botros, W. A. Goddard III, J. F. Stoddart, *J. Am. Chem. Soc.*, 2015, **137**, 876–885.

7   M. Bonchio, M. Carraro, G. Casella, V. Causin, F. Rastrelli, G. Saielli, *Phys. Chem. Chem. Phys.*, 2012, **14**, 2710-2717.

8   A. C. Fahrenbach, S. Sampath, D. J. Late, J. C. Barnes, S. L. Kleinman, N. Valley, K. J. Hartlieb, Z. Liu, V. P. Dravid, G. C. Schatz, R. P. Van Duyne, J. F. Stoddart, *ACS Nano*, 2012, **6**, 9964-9971.

9   J. C. Barnes, A. C. Fahrenbach, D. Cao, S. M. Dyar, M. Frasconi, M. A. Giesener, D. Benitez, E. Tkatchouk, O. Chernyashevskyy, W. H. Qhin, H. Li, S. Sampath, C. L. Stern, A. A. Sarjeant, K. J. Hartlieb, Z. Liu, R. Carmieli, Y. Y. Botros, J. W. Choi, A. M. Z. Slawin, J. B. Ketterson, M. R. Wasielewski, W. A. Goddard III, J. F. Stoddart, *Science*, 2013, **339**, 429-433.

10   J. W. Lee, I. Hwang, W. S. Jeon, Y. H. Ko, S. Sakamoto, K. Yamaguchi, K. Kim, *Chem.–Asian J.*, 2008, **3**, 1277-1283; T. Zhang, S. Sun, F. Liu, J. Fan, Y. Pang, L. Sun and X. Peng, *Phys. Chem. Chem. Phys.*, 2009, **11**, 11134-11139.

11   a) M. Furue, S. Nozakura; Chem. Lett., 1980, 821-824; b) M. Furue, S. Nozakura, *Bull. Chem. Soc. Jpn.*, 1982, **55**, 513-516; c) A. Deronzier, B. Galland, M. Vieira, *New J. Chem.*, 1982, **6**, 97-100; d) A. Deronzier, B. Galland, M. Vieira, *Electrochim. Acta*, 1983, **28**, 805-811; e) S. J. Atherton, K. T. Tsukahara, R. C. Wilkins, *J. Am. Chem. Soc.*, 1986, **108**, 3380-3385.

12   a) B. Odell, M. V. Reddington, A. M. Z. Slawin, N. Spencer, J. F. Stoddart, D. J. Williams, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 1547−1550; b) J. F. Stoddart, H. M. Colquhoun, *Tetrahedron*, 2008, **64**, 8231−8263.

13   M. Asakawa, P. R. Ashton, V. Balzani, A. Credi, C. Hamers, G. Mattersteig, M. Montalti, A. N. Shipway, N. Spencer, J. F. Stoddart, M. S. Tolley, M. Venturi, A. J. P. White, and D. J. Williams, *Angew. Chem. Int. Ed.*, 1998, **37**, 333-337.

14   a) C. L. Brown, D. Philp, and J. F. Stoddart, *Synlett;* 1991, **7**, 462-464; b) P. R. Ashton, R. Ballardini, V. Balzani, A. Credi, M. T. Gandolfi, S. Menzer, L. Pérez-García, L. Prodi, J. F. Stoddart, M. Venturi, A. J. P. White, and D. J. Williams, *J. Am. Chem. Soc.*, 1995, **117**, 11171-11197.

15   In the structure of $\mathbf{1d}^{4+}$, only three PF_6^- counter ions could be located by X-ray diffraction. The fourth counter-ion was not identified.

16   a) N. Leblanc, N. Mercier, O. Toma, A. H. Kassiba, L. Zorina, P. Auban-Senzier, C. Pasquier; *Chem. Commun.*, 2013, **49**, 10272-10274; b) T. M. Bookman, J. K. Kochi; *J. Org. Chem.*, 1990, **55**, 4127-4135; c) W. W. Porter, T. P. Vaid; *J. Org. Chem.*, 2005, **70**, 5028-5035.

17   A. C. Fahrenbach, J. C. Barnes, D. A. Lanfranchi, H. Li, A. Coskun, J. J. Gassensmith, Z. Liu, D. Benítez, A. Trabolsi, W. A. Goddard III, M. Elhabiri, J. F. Stoddart *J. Am. Chem. Soc.*, 2012, **134**, 3061-3072.