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Supramolecular Chemistry

A Calix[4]imidazolium[2]pyridine as an Anion Receptor**

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The design and synthesis of efficient receptors capable of binding biologically and environmentally important anionic species is an emerging field in supramolecular chemistry.[1] Anion receptors with amide, pyrrole, urea, ammonium, and guanidinium groups as binding sites form $N-H\cdots A^-$ hydrogen bonds.[2] In contrast, we have studied several benzene- and anthracene-based receptors with two or three imidazolium units which bind effectively with anionic species through $(C-H)^+\cdots A^-$ hydrogen-bonding interactions.[3] The discovery of calix[4]pyrroles as anion receptors has led to detailed studies and further synthetic modifications being carried out for use in a range of applications, including anion sensing and transport.[4] Synthesis of these receptors to selectively sense

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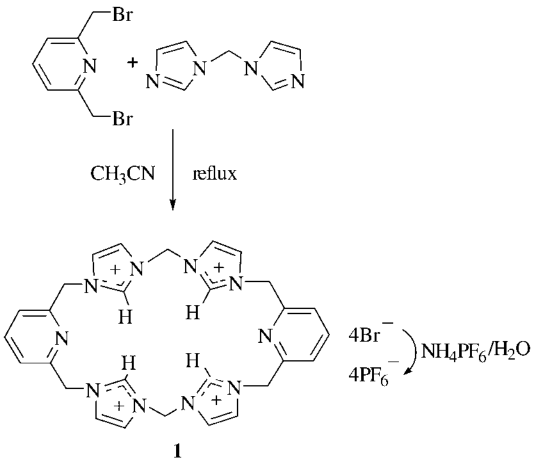
fluoride ions is of special importance because of the unique properties and hygienic importance of the fluoride ion.[5] The ionic hydrogen-bonding interactions formed by the imidazolium moieties, which are stronger than the hydrogen-bonding interactions formed by the pyrrole and urea moieties (see the Supporting Information), could be used to improve the binding affinity of the receptor for the anion. In particular, a receptor designed so that it possessed an array of positively charged imidazolium moieties in a calix form should have an enhanced binding affinity towards anions. The selectivity order of the anions could also be varied by adjusting the cavity size of the receptor. Herein, we report the first example based on this design, calix compound calix[4]imidazolium[2]-pyridine (**1**), and discuss its synthesis, characterization, and recognition abilities.

The reaction of equal quantities of 1-(1*H*-imidazol-1-ylmethyl)-1*H*-imidazole and 2,5-bis(bromomethyl)pyridine in acetonitrile followed by anion exchange with NH_4PF_6 afforded **1**-$(PF_6)_4$ as colorless microcrystals after recrystallization from acetone (Scheme 1). Single crystals of **1**-Br_4 and **1**-$(PF_6)_4$ were obtained from water/ethanol and acetonitrile/acetone solutions, respectively. Macrocycle **1** was characterized on the basis of the spectroscopic data of these salts (see the Supporting Information) and X-ray diffraction analysis.



Scheme 1. Synthesis of **1**.

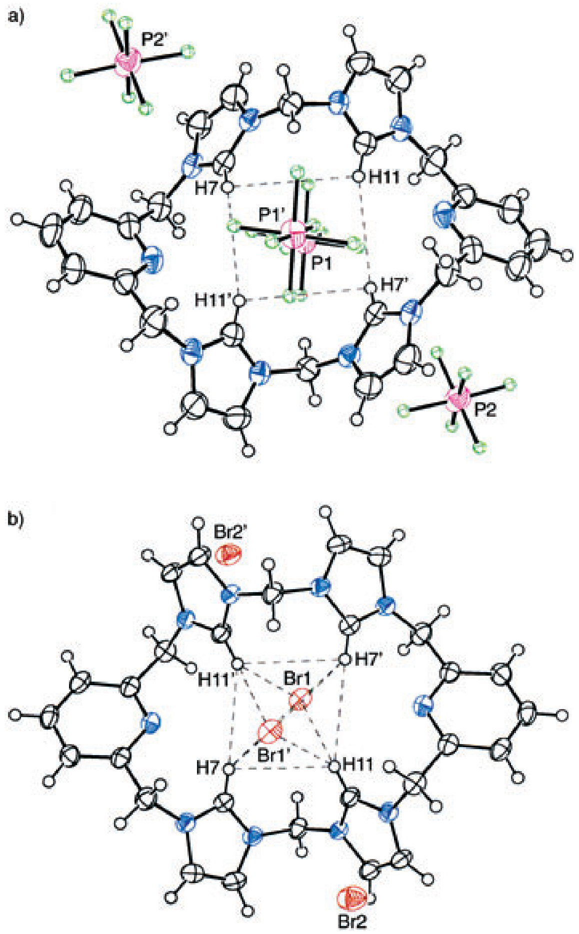


Figure 1. Crystal structures of a) **1**-$(PF_6)_4{\cdot}2\,CH_3CN$ and b) **1**-$Br_4{\cdot}6\,H_2O$. The displacement ellipsoids are given with 50% probability, except for the F atoms in the PF_6^- ion. The CH_3CN and H_2O molecules are omitted for clarity. All the anions (PF_6^- and Br^-) are located outside the cage with no direct interactions with the imidazolium moieties.

Single-crystal structures of **1**-$Br_4{\cdot}6H_2O$ and **1**-$(PF_6)_4{\cdot}2MeCN$ are shown in Figure 1. Macrocycle **1** adopts a chairlike conformation with all four imidazolium $(C{-}H)^+$ groups pointing towards the center of the macrocyclic core. Two of the four counteranions are "sandwiched" between two adjacent macrocycles and the other two are located outside the cage with no apparent interaction with the macrocycle. Compound **1** has many potential hydrogen-bond donor sites and a relatively large cavity; consequently, it is expected to be an interesting complexing agent for various anions.

Binding studies of **1**-$(PF_6)_4$ with various anions (F^-, Cl^-, Br^-, I^-, CH_3COO^-, and HSO_4^-) were carried out in dry CD_3CN and $[D_6]$DMSO by monitoring the changes in the chemical shift of the $(C{-}H)^+$ hydrogen atom in the imidazolium moiety during ^1H NMR spectroscopic titrations. The addition of an equimolar amount of fluoride anions as the tetrabutylammonium salt (tetrabutylammonium fluoride (TBAF)) to **1**-$(PF_6)_4$ induced a large downfield chemical shift $\Delta\delta$ of the positively charged imidazolium $(C{-}H)^+$ hydrogen atom to $\Delta\delta = 3.14$ ppm in CD_3CN, whereas the shift was $\Delta\delta = 1.77$ ppm in $[D_6]$DMSO; further addition caused no other significant changes in the chemical shift. Job-plot analysis showed a maximum change in chemical shift at a mole fraction of 0.5, thus indicating a 1:1 binding stoichiometry (see the Supporting Information). The bridging CH_2 group between the two imidazolium groups also showed $\Delta\delta = 0.87$ and 0.30 ppm in CD_3CN and $[D_6]$DMSO, respectively. The addition of one equivalent of tetrabutylammonium chloride (TBACl) moves the resonance of the $(C{-}H)^+$ hydrogen atom of **1** from $\delta = 9.42$ to 10.02 ppm and up to $\delta = 10.49$ ppm after addition of two molar equivalents in $[D_6]$DMSO, thus inferring a more complicated binding pattern. The association constant K_a, calculated with the HOSTEST program,[6] revealed evidence of strong binding with the fluoride anions in a 1:1 stoichiometry. The titration curves for all the other anions tested were best fit to 1:2 receptor/anion stoichiometries. The association constant for **1**-$(PF_6)_4$ with F^-, Cl^-, Br^-, and I^- ions exceeded $K_a \approx 10^5$ by ^{1}H NMR spectroscopic titrations in CD_3CN, so the highly polar solvent $[D_6]$DMSO was employed for the quantitative analysis of anion binding with **1**-$(PF_6)_4$. The binding constants (M^{-1}) were found to be $K_1 = 28\,900$ for F^- ions, $K_1 = 2030$ and $K_2 = 2790$ for Cl^- ions, and $K_2 \gg K_1$ for Br^-, I^-, and HSO_4^- ions. It should be noted that the binding constant for the F^- ions was obtained in the presence of a trace amount of water which arose from the use of the trihydrate salt. The binding constants for $H_2PO_4^-$ ions were not determined because of the disappearance of the imidazolium $(C{-}H)^+$ hydrogen atom signal after the addition of one equivalent of the anions during ^{1}H NMR spectroscopic titration.

Crystals of the **1**-$F(PF_6)_3$ complex of sufficient quality for X-ray diffraction studies[7] were obtained by the addition of TBAF·3 H_2O to a solution of **1**-$(PF_6)_4$ in acetonitrile (Figure 2). This structure determination further supported the idea that host **1** binds a single fluoride anion. Orientation of all the four $(C{-}H)^+$ groups of **1** towards the cavity anchors the fluoride anion in the center of the macrocyclic core through strong H–F interactions (with distances of 1.991 and 2.082 Å for H7···F and H12···F, respectively; CH_2···F = 2.576 Å).

Interestingly, crystallization of the host complex **1**-$(PF_6)_4$ with TBACl (molar ratio = 1:1) from acetonitrile solution afforded crystals of **1**-$Cl_2(PF_6)_2$ of sufficient quality for X-ray diffraction studies, which showed that the receptor/anion ratio was 1:2 (Figure 3 a).[7] It is of note that the addition of one equivalent of tetrabutylammonium bromide (TBABr) to **1**-$(PF_6)_4$ results in a crystal in which the unit cell contains two layers: one composed of **1**-$Br_2(PF_6)_2$ and the other composed of the free receptor **1**-$(PF_6)_4$ (Figure 3 c). The structure of the **1**-$Br_2(PF_6)_2$ layer is analogous to the structure of **1**-$Cl_2(PF_6)_2$ (Figure 3 b). The chloride and bromide anions, as they are larger and favor nonspherical or surface conformations[8] in order to keep the extra electron in a large empty space, do not fit in the center of the cavity of **1**, unlike the fluoride anion, and the two chloride anions reside 2.194 Å above and below the plane, slightly offset from the center of the macrocyclic core. One chloride anion forms strong interactions with the H(11) and H(7) protons of the imidazolium rings at distances of 2.610 and 2.759 Å, respectively, whereas the other chloride anion is closer to the H(7′) and H(11′) protons and forms interactions with them at distances of 3.075 and 3.498 Å, respectively.

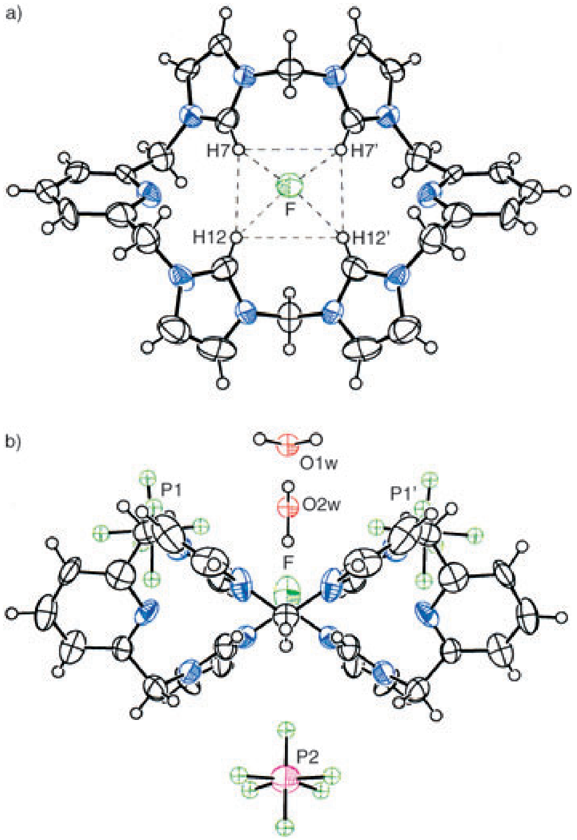


Figure 2. View of the molecular structure of **1**-$F(PF_6)_3$·2 H_2O. a) Top view of the **1**-F unit and b) side view of **1**-$F(PF_6)_3$·2 H_2O, with displacement ellipsoids at 50% probability.

We further investigated the conformations of the free receptor and the receptor/anion complexes using B3LYP/6-31G(+)* density functional calculations (see the Supporting Information). The binding energy of **1** with F^- ions in the gas

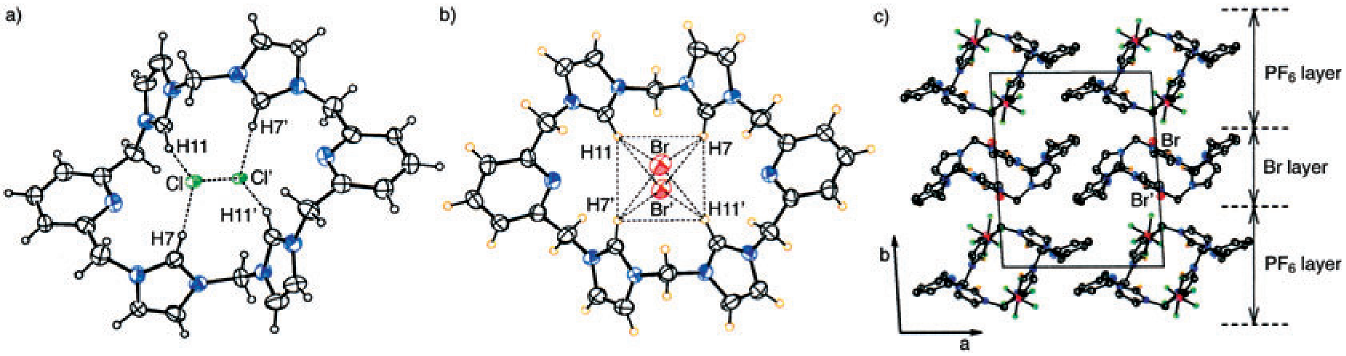


Figure 3. a) Crystal structure of the {**1**-Cl_2} unit from **1**-$Cl_2(PF_6)_2$·2 CH_3CN, with displacement ellipsoids at 50% probability. The PF_6^- ions and CH_3CN molecules are omitted for clarity. b) Single-crystal structure of the {**1**-Br_2} unit from $\mathbf{1}_2$-$Br_2(PF_6)_6$, with displacement ellipsoids at 50% probability. c) Unit cell structure of [**1**-Br_2][**1**-$(PF_6)_2$][PF_6]$_4$·2 CH_3CN, with displacement ellipsoids at 30% probability except for the F atoms in the PF_6^- ion.

phase is 315.9 kcal mol^{-1}, which is larger than those of the Cl$^-$ and Br$^-$ ions (279.2 and 273.3 kcal mol^{-1}, respectively) but is less stable than the **1**:2F complex (537.2 kcal mol^{-1}; Table 1). However, the gain in free energy in DMSO favors the formation of the **1**:F complex over the **1**:2F complex by 1.3 kcal mol^{-1} and the 1:1 complexes of **1** with Cl$^-$ and Br$^-$ ions by approximately 2 and 3 kcal mol^{-1}, respectively. This result is in agreement with the experimental K_a values and the formation of the 1:1 complex from the host **1** and the F$^-$ ions as observed in the crystal structure. The presence of one water molecule associated with the F$^-$ ions lowers the free energy by 0.1 kcal mol^{-1} in DMSO, thus suggesting that the presence of a trace amount of water in DMSO slightly weakens the interactions between the receptor and the fluoride anion, which is in agreement with the experimental results.[2h] However, the 1:2 complexes of **1** with the Cl$^-$ and Br$^-$ ions in DMSO are more stable than the corresponding 1:1 complexes, respectively. The method used for these calculations described herein, although not accurate, helps us to predict the selectivity order of the receptor for the anions and determine whether a 1:1 or 1:2 complex will be formed.

Table 1: Experimental free energies and calculated interaction energies for **1**/anion complexes (kcal mol^{-1}).[a]

Anion	K_a [M^{-1}] ([D$_6$]DMSO)		$-\Delta G_{\text{NMR}}$	$-\Delta E^{\text{gas}}_{\text{calcd}}$	$-\Delta E^{\text{sol}}_{\text{calcd}}$	$-\Delta G_{\text{scaled}}$
	K_1	K_2				
F$^-$	28 900	–	6.08	315.9 (537.2) [304.9]	20.29 (16.14) [19.96]	6.09 (4.84) [5.99]
Cl$^-$	2030	2790	4.51/4.70	279.2(477.9)	13.80(19.52)	4.14(5.86)
Br$^-$	100	10 700	2.73/5.49	273.3(469.7)	10.13(14.97)	3.04(4.49)
I$^-$	130	3330	2.88/4.80	–	–	–
CH_3COO^-	5040	1940	5.05/4.48	–	–	–
HSO_4^-	40	1120	2.18/4.16	–	–	–

[a] The association constants K_a (M^{-1}) were measured using ^{1}H NMR spectroscopic titrations (25 °C). Errors estimated to be $<10\%$. The anions were used as their tetrabutylammonium salts. $\Delta E^{\text{gas}}_{\text{calcd}}$ is the interaction energy in the gas phase at the B3LYP/6-31(+)G* level of theory. $\Delta E^{\text{sol}}_{\text{calcd}} = \Delta E^{\text{sol}}_{\mathbf{1}/\text{anion}} - \Delta E^{\text{sol}}_{\text{sol/anion}} - \Delta E^{\text{sol}}_{\text{TBA anion}}$, where $\Delta E^{\text{sol}}_{\mathbf{1}/\text{anion}}$ is the interaction energy of the **1**/anion complex in DMSO based on the isodensity surface polarized continuum model (IPCM), $\Delta EE^{\text{sol}}_{\text{sol/anion}}$ is the interaction energy of the anion with the solvent molecules in the first solvation shell of an anion. $\Delta EE^{\text{sol}}_{\text{TBA anion}}$ (sol = DMSO) is the interaction energy of the tetrabutylammonium ion with the anion in solution. The countercation correction was applied only to the F$^-$ ions as this effect is not significant for the other anions.[9] The free energy change (ΔG_{scaled}) was obtained approximately by scaling the internal energy change, on the basis of the results of the internal versus the free solvation energy of the halide anions in the first solvation shell.[8] Values in parentheses are for 1:2 complexes, values in square brackets are for a 1:1 complex in which the F$^-$ ions interact with one extra water molecule.

In summary, we have synthesized novel macrocyclic anion receptor **1** that has an array of positively charged imidazolium units and has proved to be an effective receptor for F$^-$ ions. Modification of this system would allow the development of a new class of calix containing many positively charged moieties that would be suitable for anion recognition by ionic hydrogen-bonding interactions and as precursors for N-heterocyclic carbenes for application in metal-coordination chemistry.[10]

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Keywords: anions · calix compounds · halides · ionophores · supramolecular chemistry

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[1] a) P. de Hoog, P. Gamez, I. Mutikainen, U. Turpeinen, J. Reedijik, *Angew. Chem.* **2004**, *116*, 5939–5941; *Angew. Chem. Int. Ed.* **2004**, *43*, 5815–5817; b) J. L. Sessler, D. Seidel, *Angew. Chem.* **2003**, *115*, 5292–5333; *Angew. Chem. Int. Ed.* **2003**, *42*, 5134–5175; c) P. D. Beer, P. A. Gale, *Angew. Chem.* **2001**, *113*, 502–532; *Angew. Chem. Int. Ed.* **2001**, *40*, 486–516; d) *Supramolecular chemistry of anions* (Eds.: A. Bianchi, K. Bowman-James, E. García-España), Wiley-VCH, New York, **1997**; e) J. Y. Kwon, N. J. Singh, H. N. Kim, S. K. Kim, K. S. Kim, J. Yoon, *J. Am. Chem. Soc.* **2004**, *126*, 8892–8893; f) F. P. Schmidtchen, M. Berger, *Chem. Rev.* **1997**, *97*, 1609–1646.

[2] a) C. R. Bondy, P. A. Gale, S. J. Loeb, *J. Am. Chem. Soc.* **2004**, *126*, 5030–5031; b) M. J. Chmielewski, M. Charon, J. Jurczak, *Org lett.* **2004**, *6*, 3501–3504; c) K. A. Nielsen, J. O. Jeppesen, E. Levillain, J. Becher, *Angew. Chem.* **2003**, *115*, 197–201; *Angew. Chem. Int. Ed.* **2003**, *42*, 187–191; d) E. J. Cho, J. W. Moon, S. W. Ko, J. Y. Lee, S. K. Kim, J. Yoon, K. C. Nam, *J. Am. Chem. Soc.* **2003**, *125*, 12376–12377; e) K. J. Wallace, W. J. Belcher, K. F. Syed, J. W. Seed, *J. Am. Chem. Soc.* **2003**, *125*, 9699–9715; f) T. Mizuno, W.-H. Wei, L. R. Eller, J. L. Sessler, *J. Am. Chem. Soc.* **2002**, *124*, 1134–1135; g) M. Haj-Zaroubi, N. W. Mitzel, F. P. Schmidtchen, *Angew. Chem.* **2002**, *114*, 111–114; *Angew. Chem. Int. Ed.* **2002**, *41*, 104–107; h) F. P. Schmidtchen, *Org. Lett.* **2002**, *4*, 431–434; i) G. Cafeo, F. H. Kohnke, G. L. La Torre, A. J. P. White, D. J. Williams, *Angew. Chem.* **2000**, *112*, 1556–1558; *Angew. Chem. Int. Ed.* **2000**, *39*, 1496–1498; j) M. , Sirish, H.-J. Schneider, *J. Am. Chem. Soc.* **2000**, *122*, 5881–5882; k) K. Niikura, A. P. Bisson, E. V. Anslyn, *J. Chem. Soc. Perkin Trans. 2* **1999**, 1111–1114.

[3] a) S. K. Kim, N. J. Singh, S. J. Kim, H. G. Kim, J. K. Kim, J. W. Lee, K. S. Kim, J. Yoon, *Org. Lett.* **2003**, *5*, 2083–2086; b) S. Yun, H. Ihm, H. G. Kim, C. W. Lee, B. Indrajit, K. S. Oh, Y. J. Gong, J. W. Lee, J. Yoon, H. C. Lee, K. S. Kim, *J. Org. Chem.* **2003**, *68*, 2467–2470; c) H. Ihm, S. Yun, H. G. Kim, J. K. Kim, K. S. Kim, *Org. Lett.* **2002**, *4*, 2897–2900; d) K. Sato, S. Arai, T. Yamagishi, *Tetrahedron Lett.* **1999**, *40*, 5219–5222.

[4] a) K. A. Nielsen, W.-S. Cho, J. O. Jeppensen, V. M. Lynch, J. Becher, J. Sessler, *J. Am. Chem. Soc.* **2004**, *126*, 16296–16297; b) P. Piatek, V. M. Lynch, J. L. Sessler, *J. Am. Chem. Soc.* **2004**, *126*, 16073–16076; c) J. L. Sessler, V. Krol, T. V. Shishkanova, P. A. Gale, *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 4848–4853; d) C. Bucher, R. S. Zimmerman, V. Lynch, J. L. Sessler, *J. Am. Chem. Soc.* **2001**, *123*, 9716–9717; e) P. A. Gale, J. L. Sessler, V. Král, V. Lynch, *J. Am. Chem. Soc.* **1996**, *118*, 5140–5141.

[5] a) S. O. Kang, J. M. Llinares, D. VanderVelde, K. Bowman-James, *J. Am. Chem. Soc.* **2003**, *125*, 10152–10153; b) C. J. Woods, S. Camiola, M. E. Light, S. J. Coles, M. B. Hursthouse, M. A. King, P. A. Gale, J. W. Essex, *J. Am. Chem. Soc.* **2002**, *124*, 8644–8652; c) M. Takeuchi, T. Shioya, T. M. Swager, *Angew. Chem.* **2001**, *113*, 3372–3376; *Angew. Chem. Int. Ed.* **2001**, *40*, 3372–3376; d) P. Anzenbacher, K. Jursikova, J. L. Sessler, *J. Am. Chem. Soc.* **2000**, *122*, 9350–9351.

[6] C. S. Wilcox in *Frontiers in Supramolecular Organic Chemistry and Photochemistry* (Eds.: H.-J. Schneider, H. Durr), VCH, Weinheim, **1991**, pp. 123–143.

[7] Crystallographic data for **1**-Br_4·6H_2O: triclinic, space group $P\bar{1}$, $a=7.281(7)$, $b=10.693(1)$, $c=12.749(1)$ Å, $\alpha=71.270(2)$, $\beta=80.668(2)$, $\gamma=83.539(2)°$, $V=925.6(1)$ Å^3, $Z=1$, GOF = 1.001, $R1=0.030$, $wR2=0.0765$. **1**-$(PF_6)_4$·CH_3CN: triclinic, space group $P\bar{1}$, $a=7.905(1)$, $b=11.993(1)$, $c=12.597(1)$ Å, $\alpha=108.540(2)$, $\beta=99.468(2)$, $\gamma=98.131(2)°$, $V=1092.6(2)$ Å^3, $Z=1$, GOF = 1.067, $R1(I>2\sigma(I))=0.0664$, $wR2=0.1838$. **1**-Cl_4·5H_2O: triclinic, space group $P\bar{1}$, $a=7.219(1)$, $b=10.55(1)$, $c=11.805(1)$ Å, $\alpha=100.637(2)$, $\beta=93.709(2)$, $\gamma=101.095(2)°$, $V=862.3(1)$ Å^3, $Z=1$, GOF = 1.100, $R_1(I>2\sigma(I))=0.0282$, $wR_2=0.0782$. **1**-$F(PF_6)_3$·2H_2O: monoclinic, space group Cm, $a=13.901(2)$, $b=20.921(3)$, $c=8.504(1)$ Å, $\beta=93.709(2)°$, $V=2085.8(5)$ Å^3, $Z=2$, GOF = 1.058, $R_1(I>2\sigma(I))=0.0835$, $wR_2=0.2208$. **1**-$Cl_2(PF_6)_2$·2MeCN: triclinic, space group $P\bar{1}$, $a=8.496(1)$, $b=11.494(2)$, $c=12.072(2)$ Å, $\alpha=80.212(3)$, $\beta=71.576(3)$, $\gamma=69.760(3)°$, $V=1047.0(3)$ Å^3, $Z=1$, GOF = 0.996, $R_1(I>2\sigma(I))=0.0933$, $wR_2=0.1187$. {**1**-$Br_2(PF_6)_2$}{**1**-$(PF_6)_4$}: triclinic, space group $P\bar{1}$, $a=12.201(1)$, $b=14.143(1)$, $c=14.204(1)$ Å, $\alpha=96.825(2)$, $\beta=109.519(1)$, $\gamma=90.931(2)°$, $V=2291.3(3)$ Å^3, $Z=2$, GOF = 0.951, $R_1(I>2\sigma(I))=0.0657$, $wR_2=0.0963$. CCDC-234170–234172 and -259317–259319 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[8] a) J. Kim, H. M. Lee, S. B. Suh, D. Majumdar, K. S. Kim, *J. Chem. Phys.* **2000**, *113*, 5259–5272; b) H. M. Lee, D. Kim, K. S. Kim, *J. Chem. Phys.* **2002**, *116*, 5509–5520; c) K. S. Kim, P. Tarakeshwar, J. Y. Lee, *Chem. Rev.* **2000**, *100*, 4145–4186.

[9] J. R. Blas, M. Marquez, J. L. Sessler, F. J. Luque, M. Orozco, *J. Am. Chem. Soc.* **2002**, *124*, 12796–12805.

[10] a) J. Ruiz, M. E. G. Mosquera, G. García, F. Marquinez, V. Riera, *Angew. Chem.* **2005**, *117*, 104–107; *Angew. Chem. Int. Ed.* **2005**, *44*, 102–105; b) X. Hu, I. Castro-Rodriguez, K. Meyer, *Organometallics*, **2003**, 22, 3016–3018; c) W. A. Herrmann, *Angew. Chem.* **2002**, *114*, 1326–1341; *Angew. Chem. Int. Ed.* **2002**, *41*, 1290–1309.