1 $R^1 = n\text{-Bu}$ $R^2 = H$ $R^3 = H$

2 $R^1 = Me$ $R^2 = NO_2$ $R^3 = H$
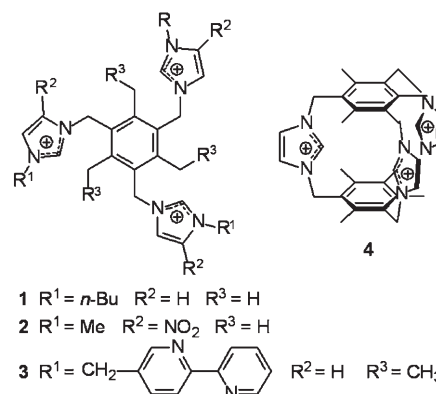
3 $R^1 = CH_2-$ (bipyridine) $R^2 = H$ $R^3 = CH_3$

Anion Receptors

A Metal-Based Trisimidazolium Cage That Provides Six C−H Hydrogen-Bond-Donor Fragments and Includes Anions**

Valeria Amendola, Massimo Boiocchi, Benoît Colasson, Luigi Fabbrizzi,* Maria-Jesús Rodriguez Douton, and Franco Ugozzoli

Dedicated to Professor Vincenzo Balzani on the occasion of his 70th birthday

There is increasing interest in the design of anion receptors, because of the relevance of anions in physiology, environmental disciplines, and food science. In most cases, anion receptors, either neutral or positively charged, contain N−H fragments (from amides, ureas, pyrroles, ammonium cations, or guanidinium cations), which behave as hydrogen-bond donors toward the anion.[1] However, the C−H fragment, when polarized by a proximate positive charge, can also act as a hydrogen-bond donor toward anions. A recent, intriguing case involves a receptor containing the imidazolium subunit.[2] In the first example, **1**, three imidazolium fragments are appended to a 1,3,5-trialkylbenzene platform.[3]

[*] Dr. V. Amendola, Dr. B. Colasson, Prof. L. Fabbrizzi,
    Dr. M.-J. Rodriguez Douton
    Dipartimento di Chimica Generale
    Università di Pavia
    via Taramelli 12, 27100 Pavia (Italy)
    Fax: (+39) 0382-528-544
    E-mail: luigi.fabbrizzi@unipv.it

    Dr. M. Boiocchi
    Centro Grandi Strumenti
    Università di Pavia
    via Bassi, 27100 Pavia (Italy)

    Prof. F. Ugozzoli
    Dipartimento di Chimica Generale ed Inorganica
    Università di Parma
    Parco Area delle Scienze 17/A, 43100 Parma (Italy)

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

The formation of stable 1:1 complexes of **1** with halides in MeCN was ascertained through ^{1}H NMR spectroscopic titration experiments. Of the various tripodal receptors that have since been reported, the highest anion affinity was observed for **2**, in which the hydrogen-bond-donating abilities of the C−H fragments are enhanced by the proximate NO_2 substituent on each imidazolium ring.[4] The 1,3,5-trialkylbenzene platform is known to favor the formation of a cavity suitable for the inclusion of anions.[5] However, the flexible nature of the pendant arms is expected to depress the stability of the hydrogen-bonded complex, owing to a loss in the conformational entropy of the receptor, and to provide only moderate binding selectivity, in view of the tendency of the tripodand to adapt its cavity to the steric requirements of the anion. Both disadvantages could be eliminated, or substantially reduced, by moving from an open to a closed cavity, that is, from a tripod to a cage. Indeed, a trisimidazolium cage equipped with two 1,3,5-trialkylbenzene caps, **4**, has been synthesized, but no evidence of the inclusion of an anion into the cavity has been reported. Moreover, in all of the crystal structures of tribromide salts of **4**, the cavity is empty and the anions are far from the cage.[6] The cavity opening is probably too small to include an anion.

Thus, we decided to prepare a trisimidazolium cage by following a different approach. First, we appended a 2,2′-bipyridine (bpy) subunit to each imidazolium fragment of the tripod to give **3**-$(PF_6)_3$. Then, the **3**-$(PF_6)_3$ salt was treated with $Fe^{II}(CF_3SO_3)_2$ to give a red-violet complex, which was precipitated as $[Fe^{II}(\mathbf{3})](PF_6)_5$. The Fe^{II} ion is known to form a very stable 1:3 complex of octahedral geometry with bpy. Moreover, the low-spin d^6 electronic configuration of the metal center affords substitutional inertness to the complex. Molecular modeling suggested that the spherical trisimidazolium cavity in the $[Fe^{II}(\mathbf{3})]^{5+}$ complex could be suitable for anion inclusion.
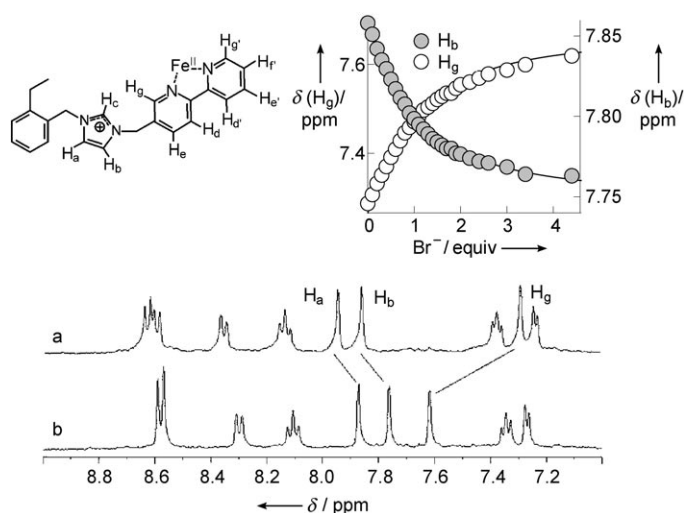
Titration experiments in a variety of media indicated a definite tendency of the $[Fe^{II}(\mathbf{3})]^{5+}$ receptor to include halide ions (see Supporting Information). Figure 1 displays the ^{1}H NMR spectra of a solution of $[Fe^{II}(\mathbf{3})](PF_6)_5$ in CD_3CN/D_2O (4:1 v/v) in the absence and presence of 4.4 equiv of $[Bu_4N]Br$. Upon anion addition, a distinct downfield shift in the signal of the H_g hydrogen atoms was observed, indicating a direct interaction with the anion. Note that the signal of the H_c hydrogen atoms was not observed, probably owing to fast

Figure 1. Titration of a 1.00×10^{-3} M solution of [Fe^{II}(**3**)](PF$_6$)$_5$ in CD$_3$CN/D$_2$O (4:1 v/v) with [Bu$_4$N]Br, monitored by ^{1}H NMR spectroscopy: labeling scheme (top left); titration profiles for the H$_b$ and H$_g$ signals (top right); aromatic regions of the spectra recorded prior to the addition of [Bu$_4$N]Br (a) and after the addition of 4.4 equiv of [Bu$_4$N]Br (b).

Figure 2. Molecular structure of the [Fe^{II}(**3**)$\cdots$Br]$^{4+}$ complex. Only hydrogen atoms involved in hydrogen bonds (thin lines) with the anion are shown. Selected interatomic contacts [Å]: Br$\cdots$H10 2.640(10), Br$\cdots$H27 2.716(10), Br$\cdots$H44 2.786(11), Br$\cdots$H21 3.026(8), Br$\cdots$H38 3.106(9), Br$\cdots$H55 3.059(9).

exchange with D$_2$O. However, the involvement of the C−H$_c$ fragments in anion binding was indirectly suggested by the moderate, yet well distinguishable upfield shift in the signals of the H$_a$ and H$_b$ hydrogen atoms of the imidazolium ring. Nonlinear least-squares treatment of the titration data, using dedicated software,[7] indicated the formation of an [Fe^{II}(**3**)$\cdots$Br]$^{4+}$ complex with an association constant of $\log K = 3.26 \pm 0.02$. Moreover, unambiguous information on the nature of the receptor–anion complex came from X-ray diffraction studies on a single crystal of the red-violet [Fe^{II}(**3**)$\cdots$Br](PF$_6$)$_4 \cdot 2$H$_2$O$\cdot$MeCN salt.

Figure 2 shows a view of the [Fe^{II}(**3**)$\cdots$Br]$^{4+}$ complex: the Br$^-$ ion is included within the trisimidazolium cavity and participates in three hydrogen bonds with the C−H$_c$ fragments from each of the imidazolium subunits (H$_c$ = H10, H27, H44; average H$_c\cdots$Br 2.714(10) Å) and three hydrogen bonds with the C−H$_g$ fragments of the nearest pyridine rings (H$_g$ = H21, H38, H55; average H$_g\cdots$Br 3.063(10) Å). Thus, the coordination of the anion by the C−H$_g$ fragments, which was preliminarily inferred from the ^{1}H NMR spectroscopic titration, has been demonstrated by X-ray diffraction. The hydrogen-bond-donating tendencies of the C−H$_g$ fragments from the neutral heterocyclic rings have been activated by the coordination of adjacent nitrogen atoms to the Fe^{II} center. The metal-induced polarization of a C−H fragment of an isoquinoline unit has been observed in a Pt^{II}-based receptor containing isoquinoline and urea subunits.[8] The [Fe^{II}(**3**)$\cdots$Br]$^{4+}$ complex represents the first example of anion coordination by six C−H fragments. Noticeably, the Br$^-$ ion sits near the line that connects the centroid of the 1,3,5-triethylbenzene platform and the Fe^{II} ion. In particular, the displacement of the Br$^-$ ion from the line is only 0.06(5) Å, the Br$\cdots$centroid(C$_6$) distance is 3.81(1) Å, and the Br$\cdots$Fe distance is 4.76(1) Å. The three C−H$_c$ and the three C−H$_g$ fragments do not point directly towards the Br$^-$ ion, probably
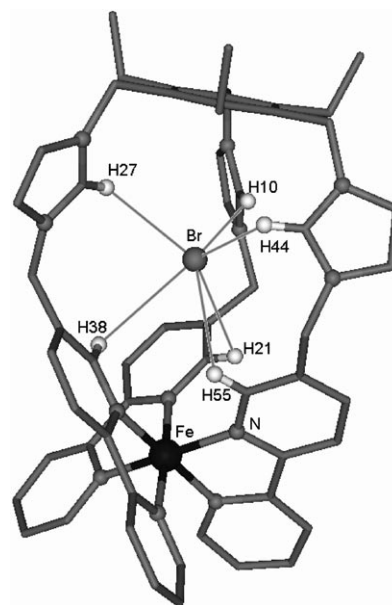
because of steric constraints imposed by the coordination of the bpy subunits to the metal center. The six coordinated hydrogen atoms occupy the corners of a slightly distorted trigonal prism (twist angle = 12.4°). Pseudo-octahedral coordination by amide N−H fragments has been previously observed for an F$^-$ ion included within a bistren (tren = tris(2-aminoethyl)amine) amine–amide cryptand.[9]

An ^{1}H NMR spectrum similar to that observed with [Bu$_4$N]Br was obtained upon titration of a solution of [Fe^{II}(**3**)](PF$_6$)$_5$ in CD$_3$CN/D$_2$O (4:1 v/v) with [Bu$_3$BnN]Cl, and an association constant of $\log K = 3.80 \pm 0.03$ was determined. Moreover, inclusion of the Cl$^-$ ion could also be followed in UV/Vis spectra. In particular, the intensity of the band centered at 300 nm and ascribed to a π–π^* transition in the bpy framework decreases upon addition of [Bu$_3$BnN]Cl. A multiwavelength least-squares treatment of the spectrophotometric titration data gave an association constant of $\log K = 3.9 \pm 0.1$, in good agreement with that obtained from the ^{1}H NMR spectroscopic titration experiment. Similar titration experiments were carried out with the I$^-$ ion, but little change was observed in the UV/Vis spectra, indicating that no complex with an association constant of $\log K > 2$ forms in this case.

To evaluate solvation effects on complex formation, titration experiments were carried out in pure MeCN. With Cl$^-$ and Br$^-$ ions, the spectrophotometric titration profiles obtained were very steep, indicating an association constant of $\log K > 7$ in each case. In contrast, upon titration of [Fe^{II}(**3**)](PF$_6$)$_5$ with [Bu$_4$N]I, a smooth profile was obtained, from which an association constant of $\log K = 4.40 \pm 0.03$ was determined (Figure 3). No spectral modifications were observed upon titration with [Bu$_4$N]H$_2$PO$_4$ or [Bu$_4$N]HSO$_4$, even after the addition of a large excess of the titrant.
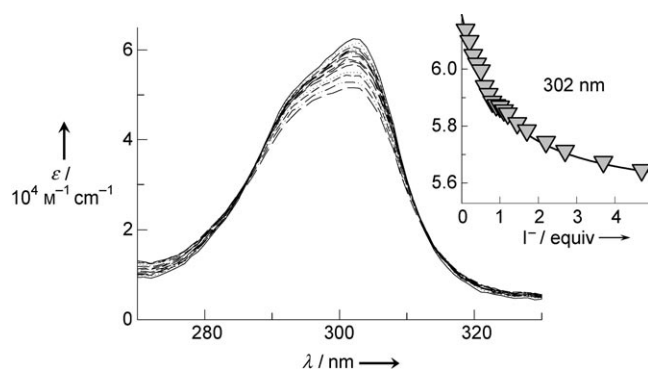
Figure 3. Titration of a 1.00×10^{-4} M solution of [Fe^{II}(**3**)](PF$_6$)$_5$ in MeCN with [Bu$_4$N]I, monitored by UV/Vis spectrophotometry: spectra recorded over the course of the titration; titration profile at $\lambda = 302$ nm (inset).


Figure 4. Titration of a 1.00×10^{-3} M solution of [Fe^{II}(**3**)](PF$_6$)$_5$ in CD$_3$CN with NaN$_3$ in CD$_3$OD, monitored by ^{1}H NMR spectroscopy: aromatic regions of spectra recorded over the course of the titration.

These results disclose an interesting selectivity pattern: [Fe^{II}(**3**)]$^{5+}$ is able to include the spherical, monoatomic halide anions with the affinity sequence Cl$^-$ > Br$^-$ > I$^-$. This sequence may reflect a decrease in the hydrogen-bond-accepting ability of the anion, or a decrease in its ability to fit into the cavity with increasing size. On the other hand, the "spherical" H$_2$PO$_4^-$ and HSO$_4^-$ ions seem to be too large to be accommodated in the [Fe^{II}(**3**)]$^{5+}$ receptor. The geometrical selectivity for a spherical shape was verified by investigating other anions. No spectral modifications were observed upon addition of an excess of the triangular NO$_3^-$ ion to a solution of [Fe^{II}(**3**)]$^{5+}$ in MeCN/H$_2$O (4:1 v/v).

Nevertheless, a well-defined interaction pattern was observed upon titration of [Fe^{II}(**3**)]$^{5+}$ with the rodlike anions N$_3^-$, NCO$^-$, and NCS$^-$. Figure 4 shows ^{1}H NMR spectra taken over the course of the titration of a solution of [Fe^{II}(**3**)](PF$_6$)$_5$ in CD$_3$CN with a solution of NaN$_3$ in CD$_3$OD: a distinct downfield shift of the H$_g$ signal was observed. In particular, the titration profile indicated the formation of a 1:1 complex, but the absence of curvature prevented the determination of the association constant. A value of log$K$ = 5.7 ± 0.1 was calculated from a spectrophotometric titration experiment carried out on a solution 1.00×10^{-4} M solution of [Fe^{II}(**3**)]$^{5+}$ in MeCN/H$_2$O (4:1 v/v), in which the decrease in the intensity of the π–π* band at 300 nm was monitored.

Most significantly, red crystals of the complex salt [Fe^{II}(**3**)···N$_3$](PF$_6$)$_4$·1.5 H$_2$O·3 MeCN that were suitable for X-ray diffraction studies formed from the slow diffusion of diethyl ether into a MeCN/MeOH solution containing equimolar amounts of [Fe^{II}(**3**)](PF$_6$)$_5$ and NaN$_3$. In the crystal structure, the N$_3^-$ ion is statistically distributed over two different orientations within the host cavity (see Supporting Information). Therefore, the mutual attraction between the two charged species occurs in two different ways. In one case, the N$_3^-$ ion accepts seven hydrogen bonds from the receptor (Figure 5). In particular, the terminal N13A atom participates in three hydrogen bonds: two with the two H$_c$ hydrogen atoms H10 and H27 and one with the H$_g$ hydrogen atom H38. The terminal N15A atom is stabilized by two hydrogen bonds, one with the H$_c$ hydrogen atom H44 and one with the H$_g$ hydrogen atom H55. This hydrogen-bonding arrangement is consistent
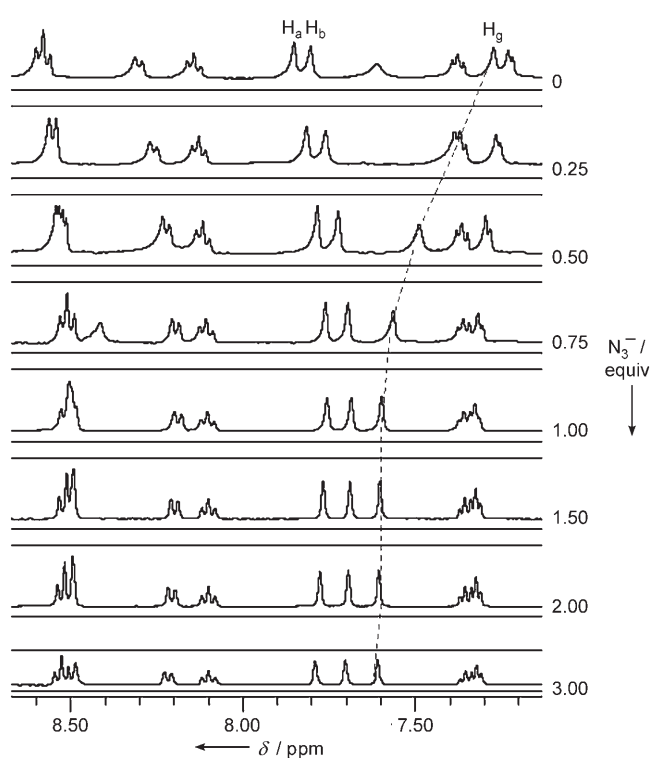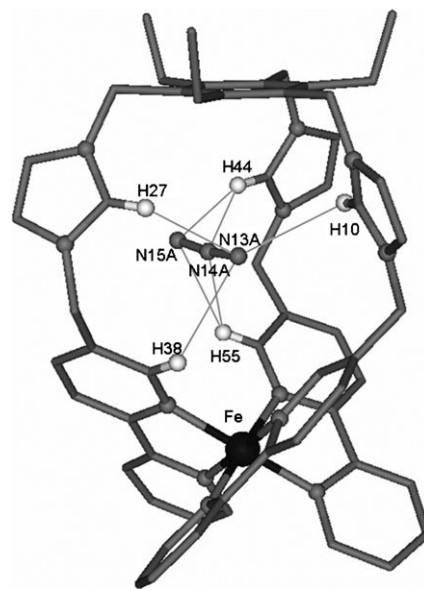
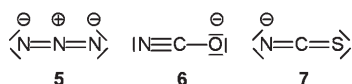**Figure 5.** Molecular structure of the [Fe^{II}(**3**)···N$_3$]$^{4+}$ complex with the N$_3^-$ ion in one of the two disordered orientations. Only hydrogen atoms involved in hydrogen bonds (thin lines) with the anion are shown. Selected interatomic contacts [Å]: N13A···H10 2.707(5), N13A···H38 2.733(5), N13A···H27 2.598(5), N14A···H44 2.571(6), N14A···H55 2.711(5), N15A···H44 2.155(5), N15A···H55 2.579.

with the Lewis structural formula of the N$_3^-$ ion (**5**), in which a formal negative charge is located at each terminal nitrogen atom.

$$\langle \overset{\ominus}{N} = \overset{\oplus}{N} = \overset{\ominus}{N} \rangle \quad |N \equiv C - \overset{\ominus}{\underset{..}{O}}| \quad \langle \overset{\ominus}{N} = C = \overset{..}{S} \rangle$$

$$\mathbf{5} \qquad\qquad \mathbf{6} \qquad\qquad \mathbf{7}$$

However, the central nitrogen atom of the N_3^- ion is also involved in the hydrogen-bond network: N14A interacts with H44 and H55 (which produce bifurcate hydrogen bonds). Interestingly, a plot of the molecular electrostatic potential (MEP) onto the molecular isodensity surface (at 0.002 e$Å^{-3}$) of the N_3^- ion, obtained from an ab initio calculation (at the HF/6-311G* level), demonstrates that a negative electrostatic potential is distributed over the whole surface of the ion, even if the central nitrogen atom is distinctly less negative (see Supporting Information). It is anticipated that the form illustrated in Figure 5 should correspond to the inclusion complex present in solution.

In the other form of the $[Fe^{II}(\mathbf{3})\cdots N_3]^{4+}$ complex, the molecular axis of the N_3^- ion is still normal to the line connecting the centroid of the 1,3,5-triethylbenzene platform and the Fe^{II} center, but the molecule is displaced toward the outside of the cavity (see Supporting Information). The N_3^- ion is bound to the receptor through only three hydrogen bonds, but one terminal nitrogen atom protrudes outside the cavity just enough to form a hydrogen bond with a water molecule. This water molecule plays a pivotal role in the solid state; it bridges two N_3^- ions belonging to different complexes through hydrogen bonds and, thus, directs the self-assembly of the complexes into dimers. It is assumed that this dimeric species is formed only in the solid state, whereas the structure illustrated in Figure 5 better reflects the binding arrangement of the inclusion complex in solution. The stability of the monomeric form is ascribed to the multipoint hydrogen bonds established by all of the nitrogen atoms of the anion with C−H fragments of the receptor.

In spectrophotometric titrations of solutions of $[Fe^{II}(\mathbf{3})]^{5+}$ in MeCN/H_2O (4:1 v/v) with the rodlike anions NCO^- (**6**) and NCS^- (**7**), the formation of 1:1 inclusion complexes with association constants $\log K = 4.2 \pm 0.1$ and 4.09 ± 0.02, respectively, was ascertained. The lower affinity of the NCO^- and NCS^- ions toward the $[Fe^{II}(\mathbf{3})]^{5+}$ receptor, compared to the N_3^- ion, in absence of definite structural details, can be tentatively ascribed to the fact that the formal negative charge in these two anions is not symmetrically distributed over the two terminal atoms, as it is in the N_3^- ion. Indeed, an asymmetric distribution of the electrostatic potential of both anions was indicated by ab initio calculations (see Supporting Information). Such an asymmetric arrangement of the electrical charge could decrease anion tendencies to take full benefit of the coordinating properties of the receptor.

The symmetric encapsulation of an N_3^- ion by a bistren hexammonium receptor, with the formation of six N−H···N hydrogen bonds (three for each terminal nitrogen atom), was observed by Lehn and co-workers in the early days of anion coordination chemistry.[10] Positively charged cages capable of establishing hydrogen bonds with both N−H and C−H fragments have also been described.[11] On the other hand, an imidazolium-functionalized acyclic [$Ru^{II}(bpy)_3$]$^{2+}$ receptor has recently been investigated for anion sensing in aqueous

MeCN.[12] Moreover, a triple-helicate complex containing terminal {$Fe^{II}(bpy)_3$}$^{2+}$ subunits and benzamide spacers has been shown to incorporate one Cl^- ion in solution by ^{1}H NMR spectroscopic titration experiments.[13]

This work has demonstrated that the $C−H_c$ fragment of the imidazolium subunit is a powerful hydrogen-bond donor toward anions, even in aqueous media. It has also shown that the combination of a 1,3,5-trialkylbenzene platform and an {$Fe^{II}(bpy)_3$}$^{2+}$ subunit generates a versatile cavity for anion encapsulation. In particular, the coordination of the bpy nitrogen atoms to the d^6 metal center activates the proximate $C−H_g$ fragments, which contribute to the unprecedented coordination of an anion by six C−H groups. The rodlike N_3^- ion profits to the largest extent from inclusion within the "spherical" cavity of the $[Fe^{II}(\mathbf{3})]^{5+}$ receptor (giving an inclusion constant 80 times larger than that observed for the spherical Cl^- ion), because of its inherent tendency to establish multipoint hydrogen bonds.

From another point of view, the high stability of the investigated complexes could be ascribed to the occurrence of strong electrostatic interactions between the charged $[Fe^{II}(\mathbf{3})]^{5+}$ receptor and the X^- anion: short $H\cdots X^-$ distances, as well as significant shifts in the signals of the $H_a, H_b,$ and H_g hydrogen atoms in the ^{1}H NMR spectra, would result from the close proximity to the anion imposed by the strictly delimited space. However, even if purely electrostatic interactions, enhanced by space restrictions, contribute to the high solution stabilities of the investigated complexes, it seems that hydrogen bonding also plays a major role. In fact, the crystal structures reveal that the included anions lie at a relatively large distance from the metal center (Fe$\cdots$Br$^-$ 4.76 Å, Fe$\cdots$centroid(N_3^-) 4.57 Å), compared to distances of 2.6–2.7 Å from the C−H hydrogen atoms. Moreover, the fact that the N_3^- ion forms a distinctly more stable complex than the NCO^- and NCS^- ions suggests that the charge distribution on the anion plays a significant role in complex formation, which points to a directional interaction, that is, hydrogen bonding.

Finally, it should be noted that systems such as $[Fe^{II}(\mathbf{3})]^{5+}$ offer the unique possibility of controlling the reactivity of a d^6 metal center with a close (and caged) anion. This possibility would be especially interesting if a photoactive {$Ru^{II}(bpy)_3$}$^{2+}$ capping subunit were combined with a caged anion with a tendency to undergo oxidation or reduction. We are currently studying this prospect.

Experimental Section

The experimental details can be found in the Supporting Information, this includes details of the syntheses of $\mathbf{3}$-(PF$_6$)$_3$ and [$Fe^{II}(\mathbf{3})$](PF$_6$)$_5$, crystallographic data for [$Fe^{II}(\mathbf{3})\cdots$Br](PF$_6$)$_4\cdot$2$H_2O\cdot$MeCN and [$Fe^{II}(\mathbf{3})\cdots N_3$](PF$_6$)$_4\cdot$1.5$H_2O\cdot$3MeCN, and ab initio calculations on the N_3^-, NCO^-, and NCS^- ions.

[1] a) V. Amendola, D. Esteban-Gómez, L. Fabbrizzi, M. Licchelli, *Acc. Chem. Res.* **2006**, *39*, 343–353; b) K. Bowman-James, *Acc. Chem. Res.* **2005**, *38*, 671–678; c) R. Martínez-Máñez, F. Sancenón, *Chem. Rev.* **2003**, *103*, 4419–4476.

[2] J. Yoon, S. K. Kim, N. J. Singh, K. S. Kim, *Chem. Soc. Rev.* **2006**, *35*, 355–360.

[3] K. Sato, S. Arai, T. Yamagishi, *Tetrahedron Lett.* **1999**, *40*, 5219–5222.

[4] H. Ihm, S. Yun, H. G. Kim, J. K. Kim, K. S. Kim, *Org. Lett.* **2002**, *4*, 2897–2900.

[5] J. W. Steed, *Chem. Commun.* **2006**, 2637–2649.

[6] a) M. V. Baker, M. J. Bosnich, C. C. Williams, B. W. Skelton, A. H. White, *Aust. J. Chem.* **1999**, *52*, 823–825; Y. Yuan, H. Zhou, Z. Jiang, J. Yan, R. Xie, *Acta Crystallogr. Sect. C* **2000**, *56*, e34–e35.

[7] C. Frassineti, S. Ghelli, P. Gans, A. Sabatini, M. S. Moruzzi, A. Vacca, *Anal. Biochem.* **1995**, *231*, 374–382.

[8] C. R. Bondy, P. A. Gale, S. J. Loeb, *J. Am. Chem. Soc.* **2004**, *126*, 5030–5031.

[9] S. O. Kang, D. Powell, K. Bowman-James, *J. Am. Chem. Soc.* **2003**, *125*, 10152–10153.

[10] B. Dietrich, J. Guilhem, J.-M. Lehn, C. Pascard, E. Sonveaux, *Helv. Chim. Acta* **1984**, *67*, 91–104.

[11] C. A. Ilioudis, D. A. Tocher, J. W. Steed, *J. Am. Chem. Soc.* **2004**, *126*, 12395–12402.

[12] M. S. Vickers, K. S. Martindale, P. D. Beer, *J. Mater. Chem.* **2005**, *15*, 2784–2790.

[13] S. Goetz, P. E. Kruger, *Dalton Trans.* **2006**, 1277–1284.