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Coordination Chemistry

Heteroditopic Receptors for Ion-Pair Recognition

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anions · cations · ion pairs · receptors · sensors

Ion-pair recognition is a new field of research emerging from cation and anion coordination chemistry. Specific types of heteroditopic receptor designs for ion pairs and the complexity of ion-pair binding are discussed to illustrate key concepts such as cooperativity. The importance of this area of research is reflected by the wide variety of potential applications of ion-pair receptors, including applications as membrane transport and salt solubilization agents and sensors.

1. Introduction

Cationic and anionic charged species are ubiquitous and their importance in chemical, biological, medical, environmental, and industrial processes cannot be underestimated. For example, many enzymes rely on ionic species for their function, such as iron in heme proteins, and the eutrophication of fresh water systems has been linked to the overuse of fertilizers in agriculture, which leads to a buildup of nitrate and phosphate anions.[1] For many decades there has been considerable interest in the design of synthetic host systems for cations, and more recently for anions. However, these monotopic receptors are designed to bind a cation or anion only. As a consequence, there is an energetic cost that has to be overcome to separate the individual cation or anion from its counterion for binding to take place.[2,3]

The design of heteroditopic receptors containing recognition sites for both the cation and anion, that is, ion-pair recognition, is an emerging field of research.[3,4] Ion-pair recognition has important applications in the development of membrane transport, salt extraction, and salt solubilization agents and sensors.[5,6] The three common designs for ion-pair receptors are shown in Figure 1. In the first design, a cascade complex results from an anionic guest bridging two encapsulated cations (Figure 1a). The other two are heteroditopic receptors where the cation and anion are bound as a separated (Figure 1b) or contact ion pair (Figure 1c). The binding sites for the cation and anion are in close proximity for binding contact ion pairs, whereas they are further apart for binding solvent-separated ion pairs. This Minireview serves to introduce the topic of ion-pair recognition to the newcomer by focusing on the development of heteroditopic ion-pair receptors from the fields of cation and anion coordination chemistry. The concept of cooperativity will also be introduced before finally discussing the varied applications of heteroditopic ion-pair receptors. Examples of heteroditopic receptors have been chosen to highlight key concepts and principles in ion-pair recognition.[7]

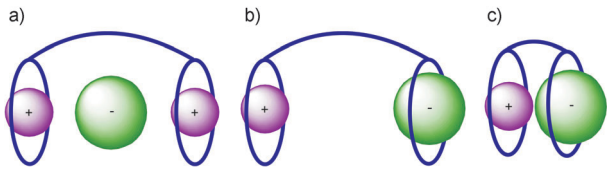

Figure 1. Common designs of ditopic receptors: a) Cascade complex. Heteroditopic receptor for separated ion pairs (b) and contact ion pairs (c).

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2. Heteroditopic Receptors

2.1. Cooperativity

The advantage of heteroditopic receptors over monotopic receptors was demonstrated by Smith et al. The binding affinity of an ion to a monotopic receptor can be reduced with strongly ion-paired species. For example, anion binding to the urea-based anion receptor in Figure 2a was inhibited by the presence of alkali metal cations in [D_6]DMSO, with the largest effect seen with sodium ions, a result of competing ion pairing outside the receptor.[8] This anion binding inhibition could be diminished by modification of the receptor design to include a crown ether for binding the countercation simultaneously (Figure 2b). For example, there was little difference

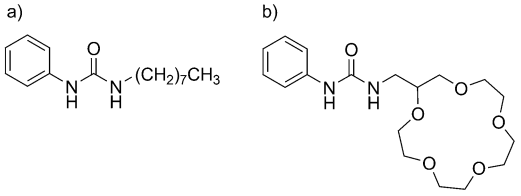

Figure 2. a) Anion receptor and b) ion-pair receptor reported by Smith and co-workers.

in the binding affinity of acetate in the presence and absence of potassium. In some cases, anion binding was even enhanced by the presence of the countercation. For example, acetate is bound 7.5 times more strongly in the presence of cesium.

By taking ion pairing into account, ion-pair recognition is more complicated than anion or cation recognition as a number of equilibria exist in an ion-pair binding system (Figure 3).[9] For example, the anion or cation alone may bind as shown by K_1 and K_3 respectively, the ion pair may bind (K_2) or competing ion pairing outside the receptor (K_{ip}) may occur, thus leading to precipitation of the ion pair. This competing ion pairing and precipitation is particularly a problem in nonpolar solvents where ion-pairing effects are stronger.

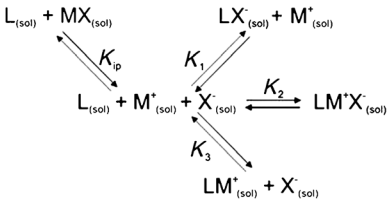

Figure 3. Simplified diagram illustrating the various equilibria that can exist in an ion-pair binding system.

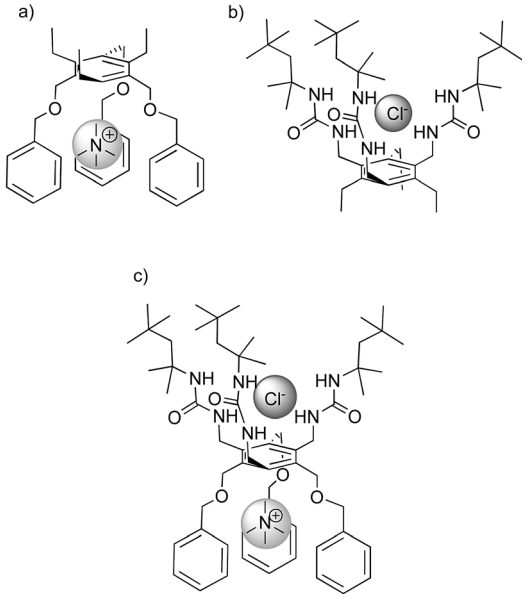

Figure 4. a) Monotopic receptor for cations, b) monotopic receptor for anions, and c) ditopic receptor for ion pairs as reported by Venturi and co-workers.

Cooperativity can also play an important role in an ion-pair binding system since there is more than one binding site. The simplest situation is noncooperative binding where each ion binds independently of the other and therefore, K_2 depends on K_1 and K_3. Often this requires that the cation and anion binding sites are rigid and separated either spatially or by solvent to prevent interactions between the cation and anion. Anticooperative binding occurs when the binding of one ion inhibits the binding of the other, whereas cooperative binding is observed when the binding of one ion enhances the binding of the other. Consequently, K_2 is smaller than the sum of K_1 and K_3 for anticooperative binding, and larger for cooperative binding.[10]

Recently Venturi et al. have discussed the complexity of the equilibria and cooperativity in ion-pair binding systems.[11] They investigated the binding of the ion-pair tetramethylammonium (TMA) chloride to the respective monotopic receptors, that is the receptors designed to bind only the cation (Figure 4a) and only the anion (Figure 4b), as well as binding to the corresponding ditopic receptor (Figure 4c) in 4:1 $CDCl_3/CD_3CN$. In comparing the binding ability of the ditopic receptor to the monotopic receptors, cation binding was enhanced by the presence of the anion, but counterintuitively, anion binding was inhibited by the cation. Therefore ion-pair binding may not always be superior to binding cations or anions individually.

Despite the complicated nature of ion-pair binding, there are many examples of ion-pair receptors that successfully exploit cooperativity. The examples in the following sections will illustrate the factors that contribute to cooperative effects, firstly with a focus on receptors designed to bind separated ion pairs and then receptors designed to bind contact ion pairs.

2.2. Heteroditopic Receptors for Separated Ion Pairs

Many ion-pair receptors designed to bind spatially separated ion pairs exploit cooperativity through conformational and solvent effects. The calix[4]arene-based receptor

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Paul Beer obtained a PhD from King's College in 1982 with Dr. C. Dennis Hall. After a Royal Society European Postdoctoral Fellowship with Professor J.-M. Lehn and a Demonstratorship at the University of Exeter, he accepted a Lectureship at the University of Birmingham in 1984. In 1990 he moved to the Inorganic Chemistry Laboratory, University of Oxford, where he was made a University Lecturer and Tutorial Fellow at Wadham College. He became a Professor of Chemistry in 1998. His research interests include coordination and supramolecular chemistry.

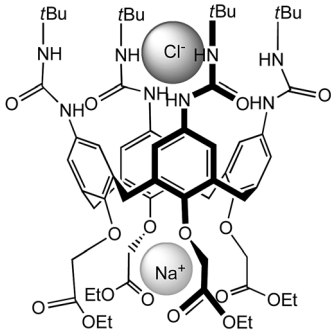

Figure 5. Cation-controlled solubilization of sodium halide ion pairs.

shown in Figure 5 solubilizes sodium halide ion pairs in $CDCl_3$.[12] The sodium cation was essential for binding the anion as cation complexation in the ester cavity preorganizes the urea groups for anion binding. Larger cations such as cesium were too large to fit in the cavity and therefore cesium salts did not bind. Solution studies revealed that NaCl binds most strongly of the sodium halide ion pairs despite its low solubility as a free salt in chloroform, and this is a result of the affinity of the urea anion binding groups for chloride.

The solvent in which the ion-pair recognition event takes place can also affect cooperativity. While the receptor in Figure 6 binds fluoride in the calix[4]pyrrole anion binding cavity in $CDCl_3$, there was no evidence of fluoride binding in 9:1 $CDCl_3/CD_3OD$, and this is most likely due to the stronger solvation of fluoride.[13] However, fluoride binding occurs in this competitive solvent system in the presence of a cesium cation bound within the crown ether cavity, as evidenced by ^{1}H NMR titration experiments and the solid-state structure. While cooperative binding of CsF ion pairs was demonstrated in 9:1 $CDCl_3/CD_3OD$, binding of the two ions was found to be noncooperative in CH_3CN as determined by isothermal calorimetry.

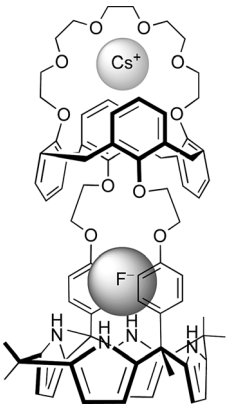

Figure 6. Receptor for CsF ion pairs as reported by Sessler and coworkers.

In the previous examples, the cation and anion binding sites are relatively distant from each other and therefore cooperative through-space electrostatic contributions are expected to be small. Bringing the two sites closer together enables favorable electrostatic interactions, in addition to conformational effects, to be exploited for cooperative binding. A number of groups have reported ion-pair receptors where the cation and/or anion influence ion-pair recognition. In an example of cation controlled ion-pair recognition, the calix[4]arene receptor functionalized with an upper-rim bis(benzo[15]crown-5 ether) amide, reported by Evans and Beer, displays both cooperative and anticooperative binding depending upon the nature of the ion pair (Figure 7).[14] Binding of chloride, benzoate, and dihydrogen phosphate anions to the amide groups was enhanced by up to a factor of

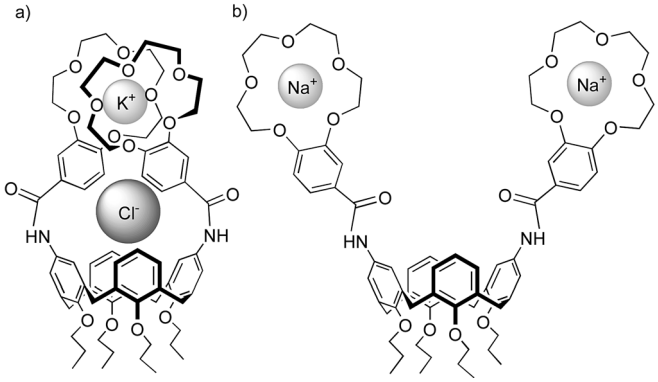

Figure 7. The calix[4]arene-based heteroditopic receptor reported by Beer and co-workers. a) Cooperative binding of KCl and b) anticooperative binding in the presence of two equivalents of sodium.

ten in 1:1 $CD_3CN/[D_6]DMSO$ in the presence of one equivalent of the potassium cation (Figure 7a). This cooperative binding was attributed to the potassium-induced conformational change, which preorganizes the amide groups, resulting from the formation of a 1:1 potassium/bis(benzo[15]crown-5 ether) sandwich complex and favorable electrostatic interactions between the anion and cation. However, anticooperative binding was observed when the two smaller sodium cations bind to the individual crown ether moieties because electrostatic repulsion between the two complexed sodium cations prevents the conformational change favoring anion binding (Figure 7b).

The ditopic receptor reported by Kubo and co-workers was designed to bind a cation in the crown ether and an anion in the thiourea cavity (Figure 8).[15] Binding of diphenylphosphate in CD_3CN was enhanced by a factor of 19 in the presence of potassium because of a dramatic conformational change of the crown ether upon potassium complexation, and the electrostatic interactions between the cation and anion.

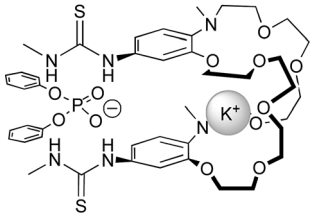

Figure 8. Ditopic receptor reported by Kubo and c-workers.

There are also a number of examples of ion-pair recognition controlled by anion allosteric effects.[16,17] Arduini and co-workers reported a calix[4]arene-based receptor (Figure 9a) wherein anions, such as sulfonate, tosylate, and chloride, hydrogen bond to the phenolic groups, which results in preorganization of the upper rim of the calix[4]arene cavity for binding a TMA cation in $CDCl_3$.[17] Consequently, the highest association constants are observed with TMA ion pairs containing coordinating anions. In contrast, the corresponding receptor with alkyated hydroxy groups binds TMA

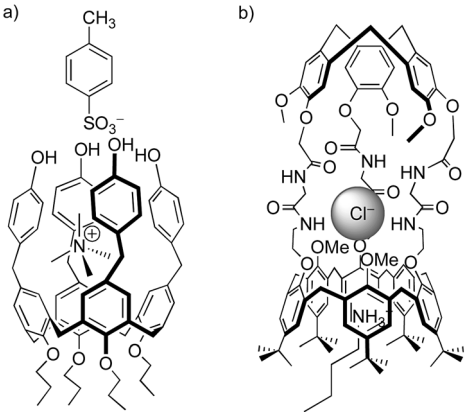

Figure 9. a) Anion-controlled ion-pair receptor reported by Arduini and co-workers and b) the calix[6]cryptamide receptor for alkylammonium chloride ion pairs reported by Jabin and co-workers.

cations with noncoordinating counteranions, such as picrate and trifluoroacetate, more strongly.

Examples of ion-pair recognition controlled by both the anion and cation are rare. Gac and Jabin report on a calix[6]-cryptamide receptor that only binds alkylammonium chloride ion pairs in $CDCl_3$ (Figure 9b).[18] It is proposed that a number of electronic and conformational changes to the receptor can only occur in the presence of both the cation and anion.

Another rare example is the calix[4]pyrrole–calix[4]arene linked receptor in Figure 10 which binds ion pairs in three different recognition modes.[19] The recognition mode adopted is determined by the size of the ion pair in relation to the size of receptor cavity. Since the cation in all cases is cesium, it is the anion that determines the size of the ion pair. When the anion is fluoride, CsF binds to the receptor as a solvent-separated ion pair with a water molecule bridging the cation and anion, and the recognition only takes place when both caesium and fluoride are present (Figure 10a). In contrast, when the anion is chloride an unusual 2:2 complex having two different binding modes is observed in the solid state. Modeling showed that the cavity is too small for a solvent-separated ion pair, but too large for a contact ion pair, thus resulting in a 'solvent-loosened' contact ion pair. The other binding mode observed for CsCl is the spatially separated ion pair shown in Figure 10b. Finally, the largest ion pair, $CsNO_3$, binds to the receptor as a contact ion pair (Figure 10c).

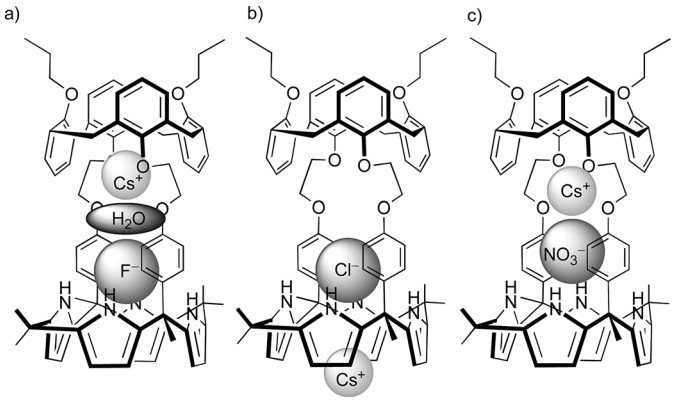

Figure 10. Three different ion-pair binding modes for a single receptor. a) Solvent-separated CsF ion pair; b) spatially separated CsCl ion pair; c) contact $CsNO_3$ ion pair.

2.3. Heteroditopic Receptors for Contact Ion Pairs

Ion-pair recognition can be dramatically enhanced by binding a contact ion pair. This is energetically favorable as it minimizes the Coulombic penalty of unfavorable separation of the two ions upon binding to the receptor.[2,3] The macrobicylic receptor from Smith and co-workers (Figure 11a) exhibited cooperative binding of the contact ion

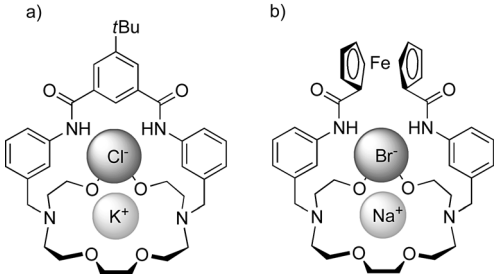

Figure 11. Contact ion-pair receptors reported by a) Smith and co-workers and b) Tuntulani and co-workers.

pairs of KCl and NaCl in $[D_6]$DMSO, and in the less competitive solvent system of 85:15 $CDCl_3$/$[D_6]$DMSO there was an impressive 300-fold enhancement of chloride binding in the presence of potassium.[20] The potential of this receptor for membrane transport and salt solubilization applications will be discussed in the next section. The group of Smith[3] as well as a number of other groups have continued to exploit this motif by varying the anion binding group to include a 2,5-diamidopyrrole,[21] indolocarbazole[22] and ferrocene[23] (Figure 11b). Interestingly, despite having the same cation binding site as the original receptor reported by Smith and co-workers, the ferrocene receptor binds NaBr much more strongly than other sodium and potassium halide ion pairs in 95:5 CD_3CN/$CDCl_3$. The absence of NaCl binding in the solution studies was attributed to competing ion pairing outside the receptor. However, electrochemical studies in 3:2 CH_2Cl_2/CH_3CN revealed that chloride and bromide binding can be sensed electrochemically through cathodic shifts of the ferrocene redox couple, and the magnitudes of these shifts were enhanced in the presence of sodium cations.

Other motifs have also been exploited for contact ion-pair binding such as uranyl salophen (Figure 12).[24] The ditopic receptor binds ion pairs, such as CsCl, in a dimeric supramolecular assembly of two receptors encapsulating two ion-pairs in the solid state. The anion binds to the uranyl

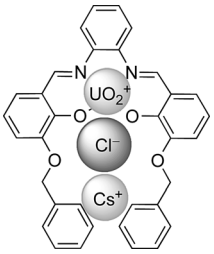

Figure 12. Uranyl salophen receptor for a CsCl contact ion pair.

center and the cation binds through an electrostatic interaction with the anion, as well as through additional stabilizing cation–π interactions with the aromatic side chains.

The calix[6]cryptamide receptor in Figure 13 has recently been reported as the first example of a receptor that is selective for contact alkylammonium fluoride ion pairs in $CDCl_3$.[25] The selectivity for fluoride results from the small size of the anion binding site in the cryptamide cap and it has been demonstrated that the fluoride is necessary for alkylammonium binding. Contact-ion-pair binding was also reversible as protonation of the cap with $MeSO_3H$ triggered the release of the ion pair.

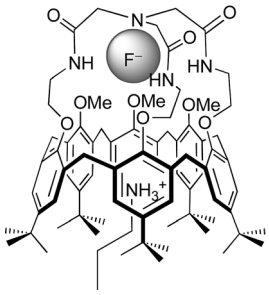

Figure 13. Calix[6]cryptamide receptor that is selective for contact alkylammonium fluoride ion pairs.

Beer and co-workers reported the first contact ion-pair heteroditopic receptors, which require both the cation and the anion for ion-pair recognition in CH_3CN and 98:2 CD_3CN/D_2O (Figure 14).[26] These receptors show little affinity for the cation or anion alone, but there is enhanced binding of contact ion pairs, such as NaCl and NH_4Cl. For this reason they were termed "cooperative AND" ion-pair receptors since the ion-pair recognition follows Boolean AND logic. X-ray crystal structures of the receptor (Figure 14), with and without a bound ion pair, provide insight into the mechanism behind this unique ion-pair recognition behavior. In the absence of the ion pair in the solid state, there is an intramolecular hydrogen bond between one of the quinone oxygen atoms and the amide protons of the isophthalamide anion-binding unit, whereas in the presence of NH_4Cl there is a conformational change with the isophthalamide motif π–π stacking with one of the calix[4]diquinone rings. It was proposed that only ion-pair binding can compensate for the loss of the intramolecular hydrogen-bonding interaction in the free receptor, thus accounting for the low affinity of the receptor for the cation or anion alone.

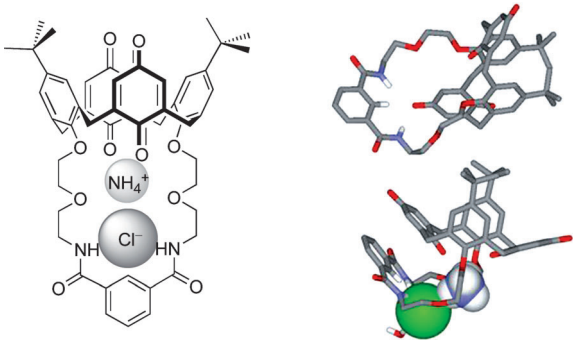

Figure 14. Cooperative AND ion-pair receptor reported by Beer and co-workers, and X-ray crystal structures of the receptor in the absence (upper) and presence (lower) of a bound NH_4Cl ion pair.

3. Applications of Ion-Pair Receptors

Examples of the main types of heteroditopic ion-pair receptors were discussed in the previous sections. This section will focus on the applications of ion-pair receptors, for example as salt extraction, salt solubilization, and membrane transport agents.

3.1. Receptors for Zwitterions

Zwitterions are a special type of ion pair wherein the cation and anion are part of the same molecule. The binding of zwitterions exploits many of the same principles as for binding ion pairs, but has the added design challenge that the distance between the two binding sites has to be complementary in size and shape to the desired zwitterionic guest. For example, the receptor in Figure 15 is able to bind zwitterions through the azacrown and polyammonium functionalities.[27] However, the receptor is unable to discriminate between γ-aminobutyric acid and 6-aminohexanoic acid which differ only in the length of the methylene spacer between the anion and cation ($n = 1$ versus $n = 3$) because of the flexibility of the 1,4-dimethylenebenzene linker group.

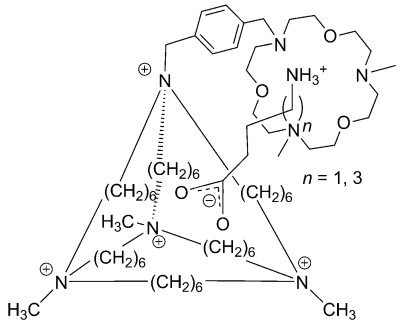

Figure 15. Zwitterion receptor based on a polyammonium cage for binding anions and an azacrown for binding cations.

Zwitterionic recognition has biological importance as often the guests of interest are amino acids, which exist as zwitterions at physiological pH. Therefore chiral discrimination may also need to be considered in the receptor design. The receptor in Figure 16 was able to enantioselectively extract the amino acids L-phenylalanine and L-tryptophan from aqueous solution into CH_2Cl_2.[28] Three complementary noncovalent interactions between the receptor and amino acid guest were proposed to account for the selectivity. The carboxylate group can hydrogen bond to the guanidinium unit, the ammonium group binds in the azacrown, and there are π–π interactions between the naphthalene of the receptor and the phenyl side chain of the amino acid.

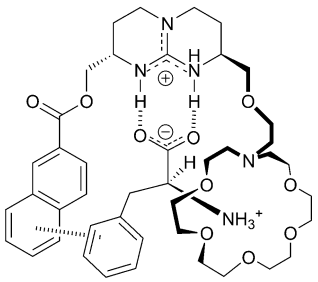

Figure 16. Zwitterion receptor for L-phenylalanine.

3.2. Salt Extraction Agents

An important application of ion-pair receptors is in the development of salt extraction agents since ions play crucial roles in industrial and environmental processes. For example, the extraction of precious metals from ores is of commercial interest, and the design of receptors for the selective extraction and removal of pollutant or radioactive ions is one solution to environmental problems. A particular target ion of environmental relevance is the pertechnetate anion TcO_4^-, which is a toxic radioactive by-product in nuclear waste. Beer and co-workers developed the tren-based ion-pair receptor pictured in Figure 17, and binding studies revealed that binding of chloride, iodide, and perrhenate was enhanced in the presence of a sodium cation in $CDCl_3$.[29] Of particular significance was the 20-fold enhancement of perrhenate binding, since perrhenate is structurally similar to pertechnetate. Pertechnetate extraction experiments demonstrated that the receptor selectively and efficiently extracts sodium pertechnetate under aqueous conditions simulating nuclear waste streams.

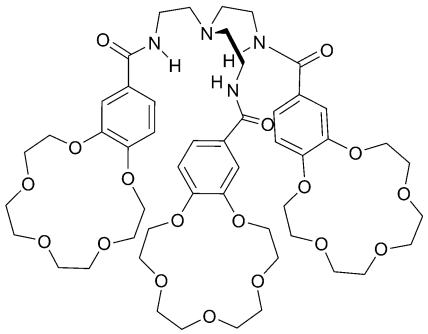

Figure 17. Ion-pair receptor for the extraction of sodium pertechnetate as reported by Beer and co-workers.

Tasker and co-workers have developed a series of salen derivatives for extracting transition-metal salts from aqueous solutions into organic solvents.[30] The zwitterionic form of the ligand efficiently extracts close to a 100% loading of $CuSO_4$ from a pH 3.8 aqueous solution into chloroform (Figure 18).[6] This approach to solvent extraction has several advantages; the pH of the aqueous solution remains unchanged and the loading and stripping of the cation and anion can be controlled by changing the pH value. More recently, they have developed salicylaldoxime-based receptors for extracting MX_2 type ion pairs.[31]

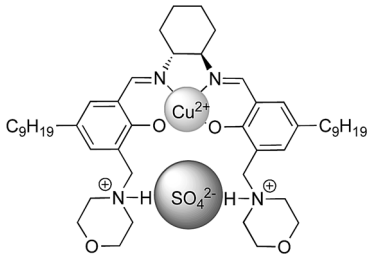

Figure 18. Salen receptor for extracting $CuSO_4$ as reported by Tasker and co-workers.

Polymer-based ion-pair receptors have also shown great promise as salt extraction agents. Sessler and co-workers reported the ability of mixed methyl methyacrylate copolymers with appended calix[4]pyrrole and benzo[15]crown-5 subunits to extract potassium halide salts from aqueous media.[32] This could have important applications in medicine, for example in the control of hyperkalemia.

3.3. Salt Solubilization Agents

The ability of ion-pair receptors to solubilize salts is another important application of ion-pair receptors for the reasons discussed in the previous section. The salt solubilization properties of the calix[4]arene-based receptor in Figure 5 have already been discussed. The related calix[4]semitube also solubilizes alkali-metal halide ion pairs in chloroform and the percentage of solubilization was determined from ^{1}H NMR experiments (Figure 19).[33] These experiments revealed that ion pairs with lower lattice enthalpies are solubilized to a greater extent. For example, KI has the lowest lattice enthalpy, and as a result, 95% solubilization was observed in $CDCl_3$.

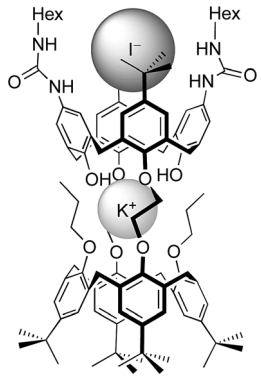

Figure 19. Calix[4]semitube for the solubilization of alkali-metal halide salts.

3.4. Membrane Transport Agents

Related to salt solubilization and salt extraction is the development of membrane transport agents. There are two approaches for transporting an ion pair across a membrane: the dual receptor approach using a mixture of a cation receptor and anion receptor or the heteroditopic receptor

approach. Reinhoudt and co-workers investigated the transport of KCl using these two different approaches with the heteroditopic and monotopic receptors shown in Figure 20.[34] At low salt activity the KCl flux for the heteroditopic receptor (Figure 20a) was similar to that of the mixture of the cation and anion receptors. However, at high salt activity the flux for the heteroditopic receptor was approximately two times slower than for the mixture of the cation and anion receptors because of slow diffusion of the receptor/ion pair complex. Smith and co-workers have proposed that this slow diffusion results from the polarity of the receptor/ion pair complex since the receptor binds KCl as a separated ion pair and the polarity can be minimized by binding a contact ion pair.[35] Smith's ion-pair receptor in Figure 11a binds contact KCl ion pairs and membrane transport studies revealed that the KCl flux is almost double that of the dual receptor mixture at high salt activity. The heteroditopic receptor can also transport alkali halide ion pairs ten times faster than the monotopic cation and anion receptors with a cation selectivity order of $K^+ > Na^+ > Li^+$ and an anion selectivity order of $I^- > Br^- > Cl^-$.

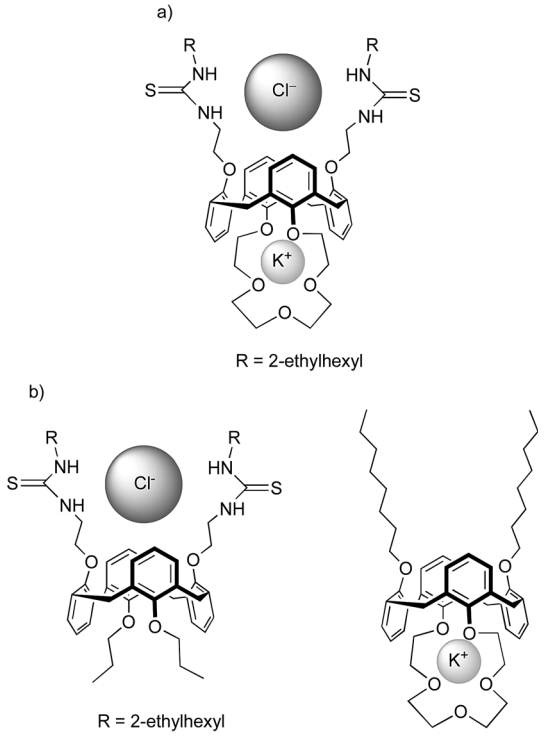

Figure 20. a) Heteroditopic receptor and b) mixture of anion and cation receptors for studying membrane transport of KCl as reported by Reinhoudt and co-workers.

3.5. Sensors

The application of ion-pair receptors as sensors is important for the detection of environmentally and biologically relevant ion pairs. Sensing of ion-pair binding requires the incorporation of a suitable optical or electrochemical reporter group into the receptor design. However, this area of research is relatively underdeveloped because of the complexity of ion-pair binding compared with anion and cation binding alone. This is particularly a problem with electrochemical sensors as the increased competitiveness of the solvent system resulting from the background electrolyte can lead to competing ion pairing outside the receptor and precipitation of the ion pair. For example, electrochemical studies with the copper(II) dithiocarbamate (dtc) receptor (Figure 21) in 4:1 $CHCl_3/CH_3CN$ showed cathodic shifts of

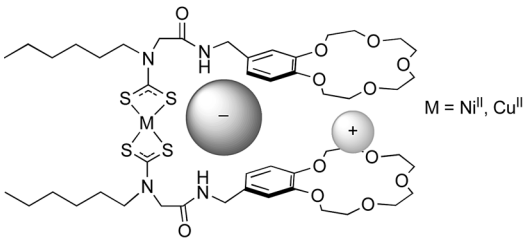

Figure 21. Transition-metal dithiocarbamate ion-pair receptors.

the copper(II)/copper(III) dtc redox couple upon addition of anions, such as acetate and benzoate, and anodic shifts in the presence of alkali-metal cations.[36] Unfortunately, the electrochemical properties of the receptor in the presence of ion pairs could not be studied because of precipitation problems. However, studies in 4:1 $[D_6]DMSO/CD_2Cl_2$ with the corresponding nickel(II) receptor revealed cooperative binding of potassium acetate.

Ferrocene reporter groups have also been exploited to detect ion-pair binding, for example NaCl binding is sensed electrochemically by the receptor in Figure 11b. The related ferrocene-based receptor in Figure 22a displays anodic shifts

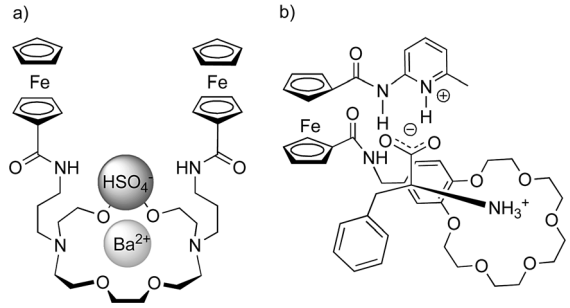

Figure 22. a) Ferrocene ion-pair receptor and b) ferrocene sensor for phenylalanine.

of the ferrocene/ferrocenium redox couple in the presence of cations, such as barium and potassium, and cathodic shifts in the presence of anions, such as chloride and hydrogen sulfate in 10:1 CH_3CN/CH_2Cl_2.[37] The simultaneous binding of ion pairs was demonstrated by cathodic shifts upon addition of anions to the receptor in the presence of a cation and anodic shifts upon addition of cations to the receptor in the presence of an anion. The ferrocene receptor in Figure 22b binds

phenylalanine in acetonitrile through the crown ether and amidopyridine motifs after a proton transfer from the carboxy group of phenylalanine to the amidopyridine group.[38] The binding event was sensed electrochemically in solution through a 129 mV anodic shift of the ferrocene redox couple with a 22 mV larger shift than for the corresponding monotopic receptor without the crown ether binding site.

Molina and co-workers have recently reported the ferrocene/imidazopyrene receptor, which can sense ion-pair binding by both electrochemistry and fluorescence in CH_3CN (Figure 23).[39] Interestingly, the receptor is able to complex ion pairs through a single receptor site, the imidazole ring. Binding of Zn-$(H_2PO_4)_2$ to the receptor was detected by the cathodic shift of the ferrocene/ferrocenium redox couple to 550 mV, a value intermediate between those for the zinc- and phosphate-only complexes with half-wave potentials of 873 mV and 513 mV, respectively. Additionally, the appearance of a band at $\lambda = 422$ nm in the emission spectra indicated the binding of $M(H_2PO_4)_2$ ion pairs where M is Zn, Pb, and Hg.

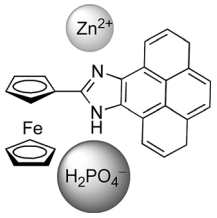

Figure 23. Dual redox and fluorescent ferrocene/imidazopyrene ion-pair receptor.

3.6. Logic Gates

The majority of the ion-pair receptors discussed exploited positive cooperativity for binding ion pairs. Generally anticooperative binding is an unwanted effect but it has an important application in the development of molecular INHIBIT logic devices. The receptor shown in Figure 24

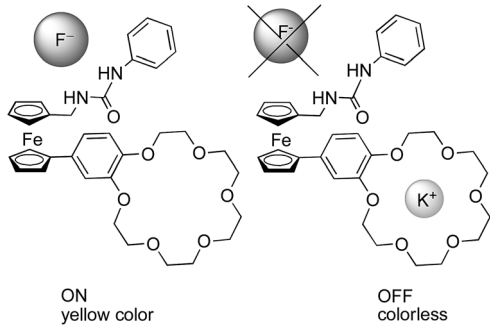

Figure 24. INHIBIT receptor reported by Tucker and co-workers.

was reported by Tucker and co-workers as a colorimetric sensor wherein fluoride binding to the urea group switches the device "ON", as detected by a color change from colorless to yellow in acetonitrile.[40] However, the colorimetric response is turned "OFF" upon addition of potassium. It is proposed that the complexation of potassium in the crown ether weakens fluoride binding to the urea group, presumably through competitive ion pairing.

Kim and co-workers reported the fluorescent calix[4]arene-based INHIBIT gate receptor (Figure 25).[41] The com-

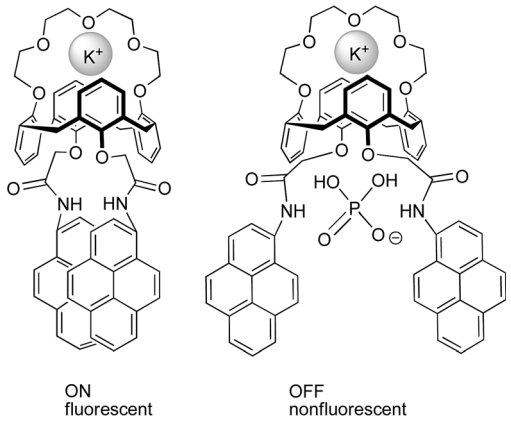

Figure 25. Fluorescent calix[4]arene-based INHIBIT gate as reported by Kim and co-workers.

plexation of potassium within the crown ether causes a conformational change which maximizes π–π stacking interactions between the pyrene units leading to an enhancement of the excimer emission in acetonitrile. However, in the presence of dihydrogen phosphate the excimer emission is switched off as a result of a photoinduced electron transfer (PET) effect.

3.7. Self-Assembly

Ion-pair recognition can also be exploited in self-assembly. TMA halide ion pairs template the formation of resorcin[4]arene molecular capsule, reported by Szumna and Atwood, in 1:1 chloroform/methanol by binding within the cavity through electrostatic, hydrogen-bonding, and cation–π interactions (Figure 26).[42]

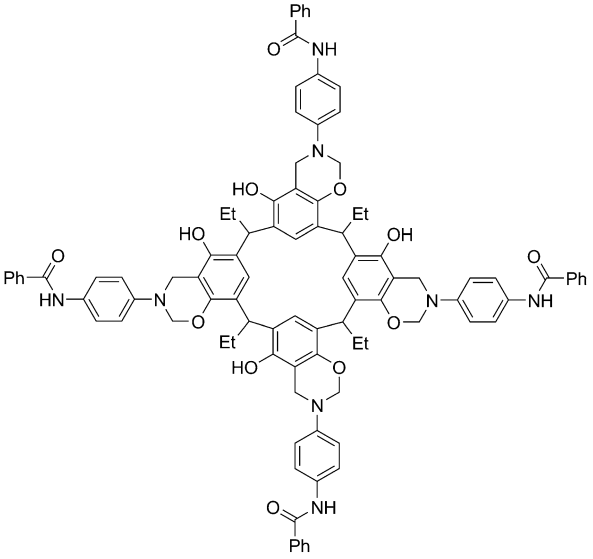

Figure 26. Resorcin[4]arene ion-pair receptor reported by Atwood and co-workers.

Davis and co-workers have reported the self-assembly of hexadecameric ion-pair receptors based on guanosine quadruplexes $(G1)_4$ (Figure 27).[43] Two strontium or barium

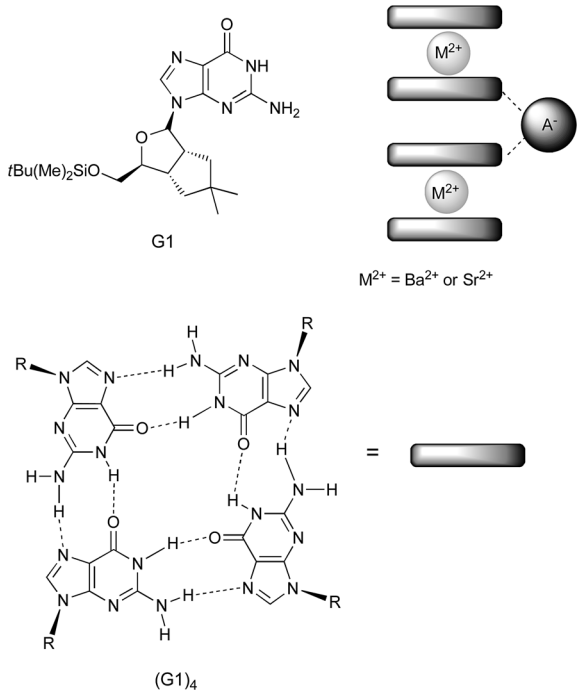

Figure 27. Self-assembled ion-pair receptor reported by Davis and co-workers. A^- = phenolate-containing anion.

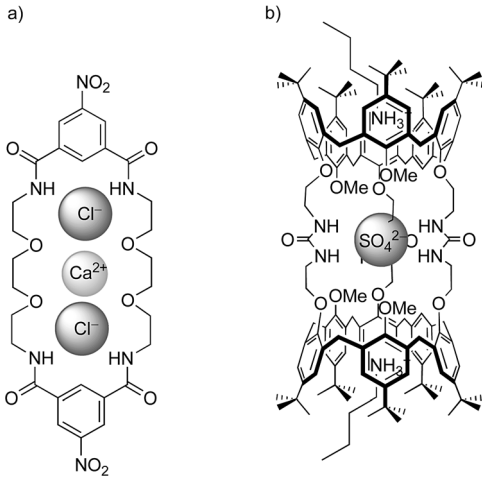

Figure 28. Tritopic receptors reported by a) Lüning and co-workers and b) Jabin and co-wrokers.

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cations bind between pairs of quadruplexes and four phenolate-containing anions hydrogen bond to the exterior of the hexadecamer. More recently, theoretical calculations from Lippert and co-workers have suggested a stacked adenosine quadruplex and guanosine quadruplex can act as a ditopic receptor for NaCl.[44]

4. Summary and Outlook

Ion-pair recognition is a fast growing field of research emerging from cation and anion coordination chemistry. This Minireview has highlighted the different heteroditopic receptor designs for binding separated and contact ion pairs. In comparison to binding a cation or anion alone, ion-pair recognition is more complex with multiple competing equilibria and cooperative effects. Nevertheless, the number of ion-pair receptors being reported is ever increasing and with that a greater understanding of the processes involved in the overall ion-pair recognition event. The scope and relevance of this field of research is illustrated by the potential applications of ion-pair receptors as membrane transport, salt solubilization, and salt extraction agents, and as sensors. Indeed, recent reports of tritopic ion-pair receptors highlight new areas of interest within the ion-pair recognition field. The receptor reported by Lüning and co-workers (Figure 28a) is the first example of a receptor to bind a contact MX_2 ion pair, and it is selective for $CaCl_2$ over $BaCl_2$ and $MgCl_2$ in 95:5 $CDCl_3$/$[D_6]$DMSO.[45] Jabin and co-workers have reported the first metal-free tritopic receptor (Figure 28b) for binding contact M_2X ion pairs (where M is an alkylammonium cation).[46]

[1] P. D. Beer, P. A. Gale, *Angew. Chem.* **2001**, *113*, 502 – 532; *Angew. Chem. Int. Ed.* **2001**, *40*, 486 – 516.
[2] J. M. Mahoney, A. M. Beatty, B. D. Smith, *Inorg. Chem.* **2004**, *43*, 7617 – 7621.
[3] B. D. Smith, *Macrocyclic Chemistry: Current Trends and Future Perspectives*, Springer, Dordrecht, **2005**.
[4] G. J. Kirkovits, J. A. Shriver, P. A. Gale, J. L. Sessler, *J. Inclusion Phenom. Macrocyclic Chem.* **2001**, *41*, 69 – 75.
[5] a) D. M. Rudkevich, J. D. Mercer-Chalmers, W. Verboom, R. Ungaro, F. de Jong, D. N. Reinhoudt, *J. Am. Chem. Soc.* **1995**, *117*, 6124 – 6125; b) N. Pelizzi, A. Casnati, A. Friggeri, R. Ungaro, *J. Chem. Soc. Perkin Trans. 2* **1998**, 1307 – 1311.
[6] D. J. White, N. Laing, H. Miller, S. Parsons, P. A. Tasker, S. Coles, *Chem. Commun.* **1999**, 2077 – 2078.
[7] For a recent comprehensive discussion of types of ion-pair receptors see the review: S. K. Kim, J. L. Sessler, *Chem. Soc. Rev.* **2010**, *39*, 3784 – 3809.
[8] R. Shukla, T. Kida, B. D. Smith, *Org. Lett.* **2000**, *2*, 3099 – 3102.
[9] For a recent publication that considers ion-pairing effects in nonaqueous media in detail, see: H. W. Gibson, J. W. Jones, L. N. Zakharov, A. L. Rheingold, C. Slebodnick, *Chem. Eur. J.* **2011**, *17*, 3192 – 3206.
[10] For a recent comprehensive discussion of the complex topic of cooperativity see: C. A. Hunter, H. L. Anderson, *Angew. Chem.* **2009**, *121*, 7624 – 7636; *Angew. Chem. Int. Ed.* **2009**, *48*, 7488 – 7499.
[11] S. Roelens, A. Vacca, O. Francesconi, C. Venturi, *Chem. Eur. J.* **2009**, *15*, 8296 – 8302.
[12] J. Scheerder, J. P. M. van Duynhoven, J. F. J. Engbersen, D. N. Reinhoudt, *Angew. Chem.* **1996**, *108*, 1172 – 1175; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1090 – 1093.
[13] J. L. Sessler, S. K. Kim, D. E. Gross, C.-H. Lee, J. S. Kim, V. M. Lynch, *J. Am. Chem. Soc.* **2008**, *130*, 13162 – 13166.
[14] A. J. Evans, P. D. Beer, *Dalton Trans.* **2003**, 4451 – 4456.
[15] T. Tozawa, Y. Misawa, S. Tokita, Y. Kubo, *Tetrahedron Lett.* **2000**, *41*, 5219 – 5223.

[16] S. Kubik, *J. Am. Chem. Soc.* **1999**, *121*, 5846 – 5855; A. Arduini, E. Brindani, G. Giorgi, A. Pochini, A. Secchi, *J. Org. Chem.* **2002**, *67*, 6188 – 6194.
[17] A. Arduini, G. Giorgi, A. Pochini, A. Secchi, F. Ugozzoli, *J. Org. Chem.* **2001**, *66*, 8302 – 8308.
[18] S. Le Gac, I. Jabin, *Chem. Eur. J.* **2008**, *14*, 548 – 557.
[19] S. K. Kim, J. L. Sessler, D. E. Gross, C.-H. Lee, J. S. Kim, V. M. Lynch, L. H. Delmau, B. P. Hay, *J. Am. Chem. Soc.* **2010**, *132*, 5827 – 5836.
[20] J. M. Mahoney, A. M. Beatty, B. D. Smith, *J. Am. Chem. Soc.* **2001**, *123*, 5847 – 5848.
[21] J. M. Mahoney, R. A. Marshall, A. M. Beatty, B. D. Smith, S. Camiolo, P. A. Gale, *J. Supramol. Chem.* **2001**, *1*, 289 – 292.
[22] M. K. Chae, J.-I. Lee, N.-K. Kim, K.-S. Jeong, *Tetrahedron Lett.* **2007**, *48*, 6624 – 6627.
[23] C. Suksai, P. Leeladee, D. Jainuknan, T. Tuntulani, N. Muangsin, O. Chailapakul, P. Kongsaeree, C. Pakavatchai, *Tetrahedron Lett.* **2005**, *46*, 2765 – 2769.
[24] M. Cametti, M. Nissinen, A. Dalla Cort, L. Mandolini, K. Rissanen, *J. Am. Chem. Soc.* **2005**, *127*, 3831 – 3837.
[25] A. Lascaux, S. Le Gac, J. Wouters, M. Luhmer, I. Jabin, *Org. Biomol. Chem.* **2010**, *8*, 4607 – 4616.
[26] a) M. D. Lankshear, A. R. Cowley, P. D. Beer, *Chem. Commun.* **2006**, 612 – 614; b) M. D. Lankshear, I. M. Dudley, K.-M. Chan, A. R. Cowley, S. M. Santos, V. Felix, P. D. Beer, *Chem. Eur. J.* **2008**, *14*, 2248 – 2263; c) M. D. Lankshear, I. M. Dudley, K. M. Chan, P. D. Beer, *New J. Chem.* **2007**, *31*, 684 – 690; d) A. J. McConnell, C. J. Serpell, P. D. Beer, *New. J. Chem.* **2012**, *36*, 102 – 112.
[27] F. P. Schmidtchen, *J. Org. Chem.* **1986**, *51*, 5161 – 5168.
[28] A. Galan, D. Andreu, A. M. Echavarren, P. Prados, J. de Mendoza, *J. Am. Chem. Soc.* **1992**, *114*, 1511 – 1512.
[29] P. D. Beer, P. K. Hopkins, J. D. McKinney, *Chem. Commun.* **1999**, 1253 – 1254.
[30] S. G. Galbraith, P. G. Plieger, P. A. Tasker, *Chem. Commun.* **2002**, 2662 – 2663.
[31] R. S. Forgan, J. E. Davidson, F. P. A. Fabbiani, S. G. Galbraith, D. K. Henderson, S. A. Moggach, S. Parsons, P. A. Tasker, F. J. White, *Dalton Trans.* **2010**, *39*, 1763 – 1770.
[32] A. Aydogan, D. J. Coady, S. K. Kim, A. Akar, C. W. Bielawski, M. Marquez, J. L. Sessler, *Angew. Chem.* **2008**, *120*, 9794 – 9798; *Angew. Chem. Int. Ed.* **2008**, *47*, 9648 – 9652.
[33] P. R. A. Webber, P. D. Beer, *Dalton Trans.* **2003**, 2249 – 2252.
[34] L. A. J. Chrisstoffels, F. de Jong, D. N. Reinhoudt, S. Sivelli, L. Gazzola, A. Casnati, R. Ungaro, *J. Am. Chem. Soc.* **1999**, *121*, 10142 – 10151.
[35] J. M. Mahoney, G. U. Nawaratna, A. M. Beatty, P. J. Duggan, B. D. Smith, *Inorg. Chem.* **2004**, *43*, 5902 – 5907.
[36] N. G. Berry, T. W. Shimell, P. D. Beer, *J. Supramol. Chem.* **2002**, *2*, 89 – 92.
[37] P. D. Beer, Z. Chen, M. I. Ogden, *J. Chem. Soc. Faraday Trans.* **1995**, *91*, 295 – 302.
[38] H. Miyaji, G. Gasser, S. J. Green, Y. Molard, S. M. Strawbridge, J. H. R. Tucker, *Chem. Commun.* **2005**, 5355 – 5357.
[39] M. Alfonso, A. Espinosa, A. Tarraga, P. Molina, *Org. Lett.* **2011**, *13*, 2078 – 2081.
[40] H. Miyaji, S. R. Collinson, I. Prokes, J. H. R. Tucker, *Chem. Commun.* **2003**, 64 – 65.
[41] J. K. Choi, K. No, E.-H. Lee, S.-G. Kwon, K.-W. Kim, J. S. Kim, *Supramol. Chem.* **2007**, *19*, 283 – 286.
[42] J. L. Atwood, A. Szumna, *Chem. Commun.* **2003**, 940 – 941.
[43] X. Shi, K. M. Mullaugh, J. C. Fettinger, Y. Jiang, S. A. Hofstadler, J. T. Davis, *J. Am. Chem. Soc.* **2003**, *125*, 10830 – 10841.
[44] T. van der Wijst, C. Fonseca Guerra, M. Swart, F. M. Bickelhaupt, B. Lippert, *Angew. Chem.* **2009**, *121*, 3335 – 3337; *Angew. Chem. Int. Ed.* **2009**, *48*, 3285 – 3287.
[45] J. Eckelmann, V. Saggiomo, F. D. Sonnichsen, U. Lüning, *New J. Chem.* **2010**, *34*, 1247 – 1250.
[46] S. Moerkerke, M. Ménand, I. Jabin, *Chem. Eur. J.* **2010**, *16*, 11712 – 11719.

