Fluorogenic and Chromogenic Chemosensors and Reagents for Anions

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Ramón Martínez-Máñez was born in 1963 in Valencia, Spain and graduated in Chemistry from the Universitat de Valencia in 1986. He received the Ph.D. in 1990 with Professor P. Lahuerta on cyclometallation reactions in rhodium complexes. After a postdoctoral period with Professor E. C. Constable at Cambridge (U.K.) working on metallocene-functionalized helicands, he joined the Department of Chemistry at the Universidad Politécnica de Valencia where he started to study electroactive ferrocene-based receptors for cation and anion sensing. He became professor in 2002. His research interest now comprises the development of a wide range of new chemosensors for the sensing of anions, cations, and neutral molecules.

Félix Sancenón was born in 1968 in Manises, Valencia, Spain. He started studying chemistry at the University of Valencia, where he received his diploma in 1991. He stayed for 4 years working with Professor A. Marco in isolation and synthesis of natural products in the Organic Chemistry Department at the University of Valencia. Since 1999, he has been working with Prof. R. Martínez Máñez in the Chemistry Department at the Universidad Politécnica de Valencia in the field of development of chromogenic and fluorogenic chemosensors for cations and anions and obtained the Ph.D. degree in 2003. His current research interest deals with colorimetric and fluorimetric receptors for anion sensing.

1. Introduction

Anions play a fundamental role in a wide range of chemical and biological processes, and numerous

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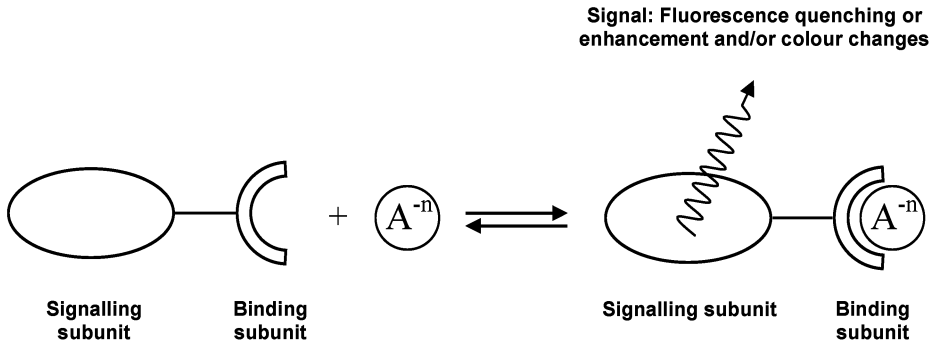


Figure 1. Anion chemosensors based on the binding site-signaling subunit approach.

efforts have been devoted to the development of abiotic receptors for anionic species.[1] This has been especially true during the last 20 years, and there have been a number of reviews describing the chemistry of anion recognition and host molecules for anions.[2−11] In a related advanced supramolecular concept, recognition sites can be coupled to certain groups that are capable of "reporting" the anion coordination process.[12] In this case, the binding process is transduced into a signaling event. Receptors specifically designed for sensing purposes are generally called chemosensors.[13] One basic design principle in these new multicomponent systems is that the sensing event has to be related with an easy-to-measure signal. In fact, many chemosensors display changes in either color[14,15] or fluorescence[16] in the presence of a certain guest although changes in electrochemical properties such as the oxidation potential of redox active groups have also been widely used.[17,18] In this sensing process, information at the molecular level, such as the presence or not of a certain guest in solution, is amplified to a macroscopic level; hence, sensing might open the door to the determination (qualitative or quantitative) of certain guests. These ideas connect in some way with supramolecular concepts such that of molecular devices (in this case sensor devices) in which the final operation (anion signaling) performed by the device results from the sum of the basic functions of the components, the binding site (coordination), and the reporting unit (transduction of the coordination event).

This review deals with the use of fluorogenic and chromogenic reagents for anions sensing. In this sense, it is remarkable that there are relatively few examples on anion sensing when compared with the literature devoted to anion recognition or when compared to cation sensing.[19,20] However, the number of papers on anion sensing has grown considerably. The present review is a comprehensive analysis about signaling of small anions using changes in fluorescence, luminescence, or color (no changes in fluorescence or color using anionic macromolecules such as DNA are included) and will point out how the use of relatively simple molecules is leading to the development of new systems for the selective sensing of target anionic guests. These advances suggest that it would be possible soon to have selective reagents for screening a wide range of anions of environmental, biological, and medical importance.

2. Different Design Principles for Anion Sensing

A general approximation to the development of anion chemosensors is the coupling of at least two units, each one displaying a precise function: the binding site and the signaling subunit. In the former resides the function of coordination to a certain anion, whereas the latter changes some spectroscopic characteristics (color or fluorescence) upon anion coordination. Binding sites and signaling units can be covalently linked (binding site−signaling subunit approach)[21] or not (displacement approach).[22] This general design principle is based on anion coordination events; therefore, both the interaction with the anion and the change in color or fluorescence are in principle reversible. In fact, coordination is a typical reversible chemical reaction in which changes in the concentration of the anion determine the relative amount of coordinated and free guest. In addition to these systems, anion signaling using fluorescence or color changes can also be observed using irreversible reactions. Here, the term chemosensor should not strictly be applied and terms such as reagents, reactants, or chemodosimeters should be used.[23,24] Despite their irreversible nature, recent advances in the area of chemodosimeters for anions have also been included in this review.

2.1. Binding Site−Signaling Subunit Approach

As we will see below, many chemical sensors follow the approach of the covalent attachment of signaling subunits and binding sites as schematically shown in Figure 1.[21] This has been the most widely used approach in the development of anion chemosensors and will surely be a fundamental approach in future developments. As can be seen in Figure 1, the coordination site binds the anion in such a way that the properties of the signaling subunit are changed giving rise to variations either in the color (chromogenic chemosensor) or in its fluorescence behavior (fluorogenic chemosensor).

2.1.1. Anion Binding Sites

As it has been reported many times, the chemistry of anion coordination has some special features that need to be considered.[25] Thus, when making the choice of a receptor for a certain anion, the shape and geometry of the anion to coordinate; its charge, which can be varied as a function of the pH; and its hydrophobicity should be taken into account, among

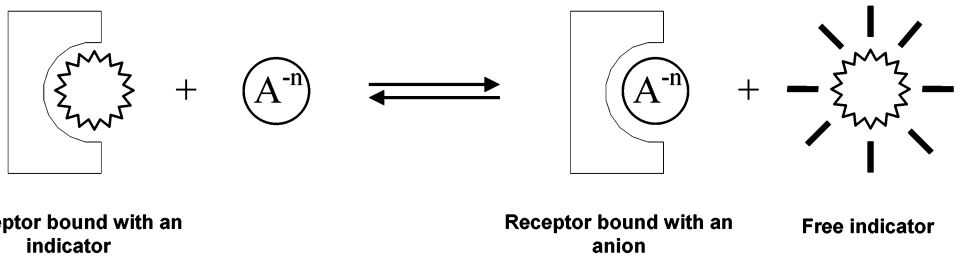


Figure 2. Anion chemosensors based on the displacement approach.

other factors.[10] In general, it can be said that abiotic receptors for anions use similar type of interactions as biological receptors. Those can be classified basically in electrostatic interactions, formation of hydrogen bonds, and interactions with metal centers.

Electrostatic interactions with anions are found when using positively charged receptors having for instance guanidinium groups[26−30] or quaternary ammoniums.[31,32] These two groups have a positive charge that basically does not depend on the pH of the medium. Recently, isothiouronium groups have also been used as anion receptors in fluorogenic chemosensors. Amines can also give electrostatic interactions with anions as they are usually protonated and therefore charged at neutral and acidic aqueous solutions. In fact, polyamines can be synthesized with a large variety of shapes (open chain, cyclic, branched, etc.) and have been widely employed as anion receptors, especially in aqueous environments.[33−36]

Hydrogen-bonding groups have been widely used in binding sites for anion recognition. A hydrogen bond can be established when a hydrogen covalently attached to a highly electronegative atom interacts with another electronegative atom (of the same or different molecule) having lone pairs. Polyamines and guanidinium groups can form hydrogen bonds with anions. Other hydrogen-bonding sites typically used in chromogenic or fluorogenic chemosensors are ureas,[37,38] thioureas,[39,40] calyx[4]pyrroles,[41−43] sapphyrins,[44] porphyrins,[45−47] and amides.[48,49]

Metal complexes have also been used as anion binding sites. Metal complexes can bind anions forming stronger bonds than those generally observed using electrostatic or hydrogen-bonding interactions.[50,51]

A certain binding site may combine several of those binding groups in a proper spatial distribution for the selective coordination of target anions.

2.1.2. Signaling Subunits

The role of the signaling subunits is to act as a signal transducer. That is, it translates chemical information taking place at the molecular level (the anion binding process) into a signal. Here, we will consider the use of spectroscopic signaling subunits able to transduce the coordination event into changes in either color or fluorescence behavior.[52] Other signaling subunits such as electroactive groups have also been used and many times reviewed but will not be considered here.[17,18]

2.2. Displacement Approach

This approach also involves, as in the above case, the use of anion binding sites and signaling subunits. However, in this case, both subunits are not covalently attached but form a coordination complex (molecular ensemble). Then, when a target anion is added to the solution containing the binding site−signaling unit ensemble, there is a displacement reaction; the binding site coordinates the anion whereas the signaling subunit returns to the solution retrieving its noncoordinated spectroscopic behavior (Figure 2). If the spectroscopic characteristics of the signaling subunit in the molecular ensemble are different to those in its noncoordinated state, then the anion binding process is coupled to a signaling event. As it can be inferred, the stability constant for the formation of the complex between the binding site and the signaling subunit has to be lower than that between the binding site and the target anion. Only in this way will the displacement reaction take place; hence, the signaling event indicating the presence of the target anion will be observed. Additionally, selectivity can be achieved by choosing an indicator−binding site couple with a formation stability constant larger than that between the signaling unit and the potentially interfering anions.[22]

2.3. Chemodosimeter Approach

This approach involves the use of specific chemical reactions (usually irreversible) induced by the presence of target anions that are coupled to a color or emission variation.[23,24] If the chemical reaction is irreversible, the use of the term chemosensor cannot strictly be used and we will refer to these systems as chemodosimeters or chemoreactants. Figure 3 shows schematically two examples, one in which the anion reacts with the chemodosimeter remaining covalently bonded to the product and the other in which the anion catalyzes a chemical reaction. In those examples, as the final compound is chemically different to the original one, the spectroscopic characteristics of the solution should change, allowing determination of the anion. The underlying idea of these irreversible systems is to take advantage of the selective reactivity that certain anions may display. Hence, the use of anion-induced reactions has advantages as the high selectivity usually reached and also an accumulative effect that is related directly with the anion concentration.

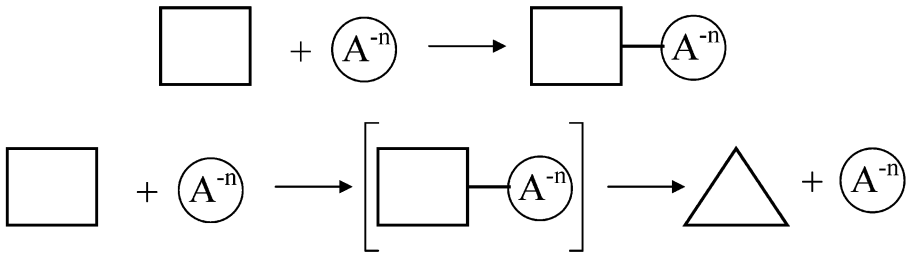


Figure 3. Chemodosimeters or chemoreactands. In the first sequence, the anion reacts with the chemodosimeter and remains covalently attached, and in the second sequence, the anion catalyzes a chemical reaction.

3. Fluorogenic Chemosensors and Reagents for Anions

3.1. Fluorogenic Principles of Sensing

Luminescence can be defined as a spontaneous emission of radiation from an excited state. Depending on the mode of excitation, the terms chemoluminescence, electroluminescence, radioluminescence, sonoluminescence, etc. are used. If we focus our attention in the emission process, the luminescence phenomenon can be classified as fluorescence when the excited molecule results in a new molecule with the same spin multiplicity and as phosphorescence when it involves luminescence with a change in spin multiplicity. What is observed in a fluorescence molecule is that absorption of light at a given wavelength results in an almost instantaneous emission of light at a longer wavelength.[53]

Fluorescence detection has been widely used as a versatile tool in analytical chemistry, biochemistry, cell biology, etc.[54] In relation to the use of fluorescence for sensing or detecting, the principal advantage over other light-based methods such as absorbance is its high sensibility. This is so because the emission fluorescence signal is proportional to the substance concentration whereas in absorbance measurements the substance concentration is proportional to the absorbance, which is related to the ratio between intensities measured before and after the beam passes through the sample. Therefore, in fluorescence, an increase of the intensity of the incident beam results in a larger fluorescence signal whereas this is not so for absorbance. Fluorescence techniques can measure concentrations even one million times smaller than absorbance techniques.

There are excellent reviews dealing with the study of mechanisms involving the photophysics of fluorogenic chemosensors, and it is not our intention to explain exhaustively those mechanisms.[19,20,55,56] However, it is interesting to understand the basis of the nature of the photoinduced processes that are responsible for the photophysical changes upon anion coordination. These effects are specifically related with the use of the binding site−signaling subunit approach and the displacement approach.

3.1.1. Photoinduced Electron Transfer (PET)

This photoinduced process has been extensively studied and widely used for sensing purposes of cations and anions.[55,56] As described above, fluorescence in a molecule is observed when an excited electron, for instance in the lowest unoccupied molecular orbital (LUMO), goes to the highest occupied molecular orbital (HOMO), releasing the excess of energy as light. Over this scheme, it might happen that an orbital from another part of the molecule or from another molecular entity could have energy between that of the HOMO and that of the LUMO of the fluorophore. When this "alien" orbital is full (for instance, if we have a donor group), a PET from this full orbital to the HOMO of the fluorophore can take place. A further electron transfer from the LUMO of the fluorophore to the external orbital retrieves the stable ground state. Following this sequence, fluorescence quenching occurs because the transition from the excited to the ground state takes place following a nonradiative path (see Figure 4). What is macroscopically observed is a decrease of the emission intensity or no fluorescence at all. A similar process can take place when there is an empty orbital from another part of the molecule or from another molecular entity between both the HOMO and the LUMO of the fluorophore. In this case, a PET from the excited LUMO to the empty orbital can occur, followed by a further electron transfer from this orbital to the HOMO of the fluorophore. Again, deexcitation occurs without radiation and fluorescence quenching is observed (see Figure 5). The design of anion chemosensors tries to take advantage of such PET effects in such a way that the presence of the anion should induce the appearance or the removal of energy levels between the HOMO and the LUMO of the fluorophore inducing quenching or enhancement of the fluorescence emission.

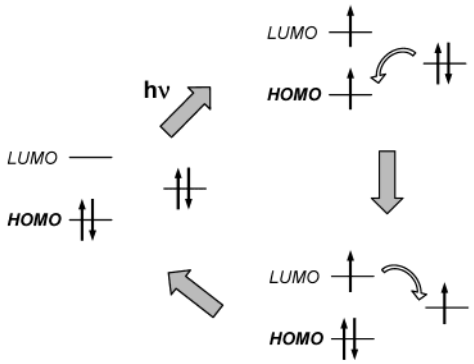


Figure 4. PET process with the participation of the HOMO and LUMO of the fluorophore and an external molecular orbital.

3.1.2. Electronic Energy Transfer (EET)

Another mechanism that may be responsible for the fluorescence quenching by certain molecular

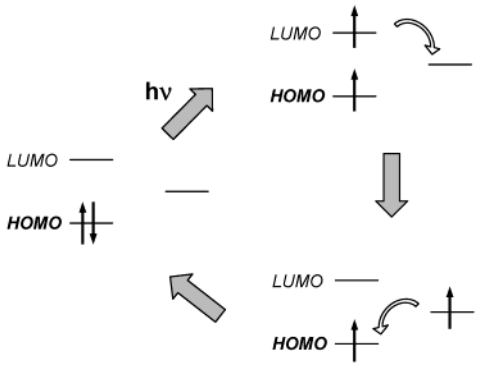


Figure 5. PET process with the participation of the HOMO and LUMO of the fluorophore and an empty external molecular orbital.

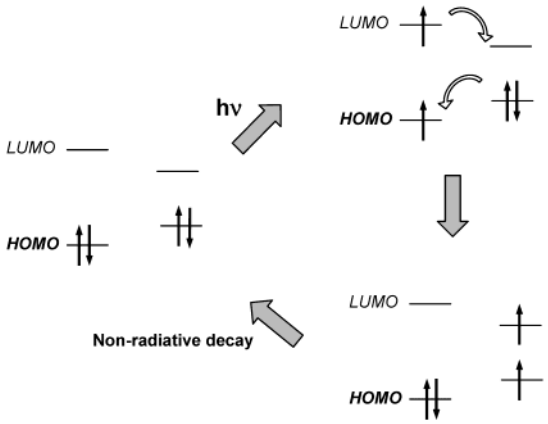


Figure 6. EET process with the participation of the HOMO and LUMO of the fluorophore and an external molecular orbital.

entities is the EET.[55,56] When the external molecular group has some empty or half-filled energy levels between the HOMO and the LUMO of the fluorophore, a simultaneous exchange of two electrons (from the LUMO to the foreign orbital and from the foreign orbital to the HOMO) can occur (see Figure 6). The double electron exchange restores the fluorophore to its ground state following a nonradiative process therefore resulting in a fluorescence quenching. The occurrence of this double and simultaneous electron transfer requires a close contact between the fluorophore and the molecular group. Thus, flexible linkers may favor the occurrence of an intramolecular energy transfer process of this type.

3.1.3. Monomer–Excimer Formation

A phenomenon that can be observed when using fluorophores is the formation of excimers. An excimer can be defined as a complex formed by interaction of a fluorophore in the excited state with a fluorophore of the same structure in the ground state.[56] An important aspect is that the emission spectrum of the excimer is red-shifted with respect to that of the monomer, and in many cases, the dual emission of the monomer and the excimer is observed. Therefore, excimer formation or excimer rupture upon anion addition results in anion sensing by simple monitoring of the emission excimer band. In general, it is assumed that flat highly π-delocalized systems such as pyrene and anthracene show greater tendency to form excimers. An additional requirement for excimer formation is that two monomers need to be in close proximity in order to give stacking interactions and the molecular excimer state. Figure 7 shows an example of anion-induced excimer formation in which anion coordination favors the proximity between two fluorophores.

3.1.4. Rigidity Effect

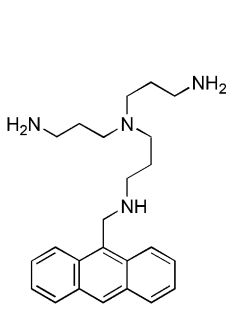
Although there are doubts of the real existence of this effect, it has been many times employed to justify fluorescence enhancement upon anion coordination. As a consequence of the anion coordination, the rigidity of the formed complex increases making the nonradiative decay from the excited state less probable; consequently, the emission intensity increases.[57]

Other less common mechanisms also reported in anion fluorogenic chemosensors are the heavy atom effect, excited state proton transfer (ESPT) mechanisms, and changes in the conformation of the receptors induced by coordination with target anions. These mechanisms have been reported for instance when using the receptors **62**, **64**, **65**, and **67**.

3.2. Following the Binding Site–Signaling Subunit Approach

3.2.1. Fluorescent Chemosensors Based on Polycyclic Aromatic Hydrocarbons

3.2.1.1. Containing Anthracene. Anthracene is a polycyclic aromatic hydrocarbon that has been widely used as a signaling subunit for both cation and anion sensing. This has been so probably due to the commercial availability of a large variety of derivatives, by the fact that its photophysical properties are well-known, and because it is highly fluorescent (quantum yield in acetonitrile is 0.36).[58] Anthracene and anthracene derivatives usually show three well-defined and shaped absorption bands between ca. 340 and 380 nm, and the emission spectrum usually consists of well-defined and structured bands centered at ca. 415 nm.[59] The first specifically designed anion chemosensor containing anthracene was reported by Czarnik in 1989 who published the behavior of receptors **1** and **2**, which



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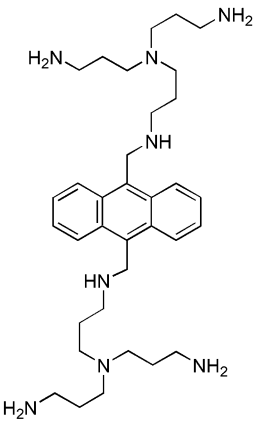

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were capable of sensing the presence of certain anionic species in aqueous environments by changes

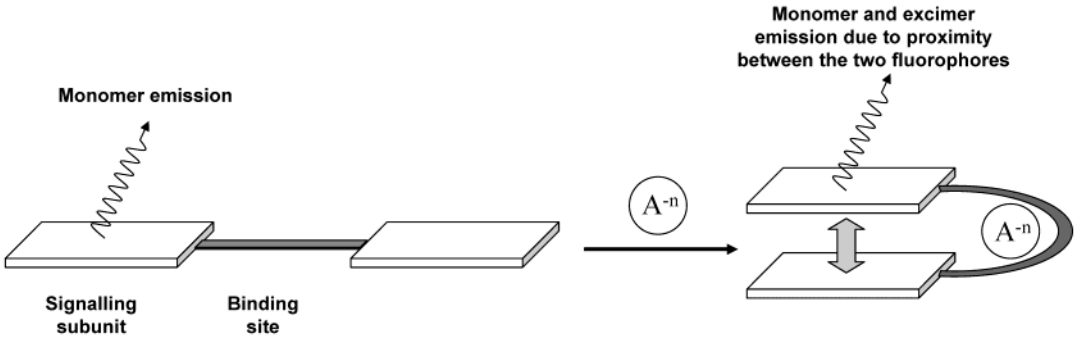


Figure 7. Receptor composed of a flexible coordinating subunit and two "flat" fluorophores. Coordination with an anion induced spatial proximity between the two fluorophores and dual emission from the monomer and the excimer.

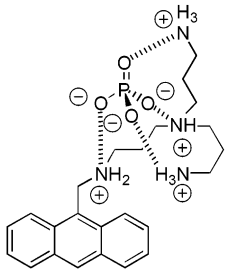
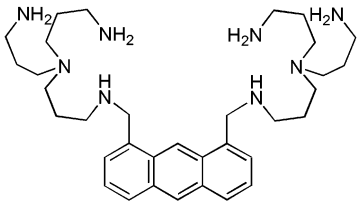


Figure 8. Host−guest binding interaction between receptor **1** and phosphate anion through the formation of hydrogen bonds.

in the fluorescence of the anthracene signaling subunit.[60] Those systems also responded to pH changes, and both pH and anion response were based in the same effect: the inhibition of PET processes. Thus, when the benzilic nitrogens are not protonated, there is a thermodynamically favorable PET from the lone pair of the nitrogen to the excited fluorophore (anthryl group) that induces fluorescence quenching. Upon protonation (or anion coordination), the lone pair of the benzilic nitrogen is engaged, electron transfer does not take place, and an enhancement of the emission intensity is observed. Upon addition of phosphate to aqueous solutions of **1** at pH 6, a remarkable emission intensity enhancement was observed. At this pH, both the polyamine and the phosphate are partially protonated and the fluorescence enhancement could be attributed to a favorable intracomplex proton transfer that leads to the benzilic amine protonation (see Figure 8) (an alternative interpretation would involve favorable formation of hydrogen bonds between one OH group of the phosphate with the lone pair of the benzilic nitrogen that also would inhibit the PET process). The polyamine binding site originates some selectivity due to the formation of a suitable cavity for phosphate. Other anionic species such as ATP, citrate, sulfate, acetate, and dimethyl phosphate gave smaller fluorescence enhancements upon binding with **1**.

Since this earlier work, a number of sometimes closely related anthryl-functionalized polyazaalkanes have been designed as anion sensing fluorophores. For instance, compound **3** illustrates how without changing the signaling subunit (anthracene), the selectivity against anions is controlled by the topology of the binding site. Thus, **3** was able to discriminate between phosphate and pyrophosphate.[61] The two polyammonium arms of the receptor are geometrically disposed for binding the six external oxygen



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atoms of the pyrophosphate anion (see Figure 9). Studies were carried out in water at pH 7. The larger stability constant found for pyrophosphate vs phosphate was in line with the larger fluorescence enhancement in the presence of the former. The recognition mechanism was similar to that described above (PET chemosensor).

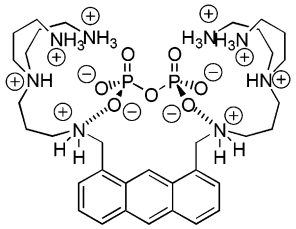
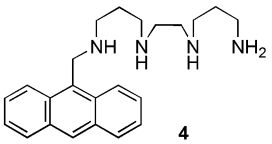


Figure 9. Binding pattern of receptor **3** with pyrophosphate anion by means of hydrogen-bonding interactions.

The fluorescence of the polyazaalkanes bearing anthryl groups **4**−**6** was investigated in water.[62] Free



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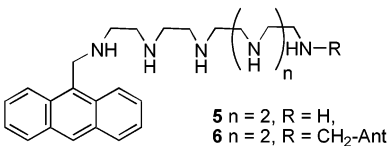
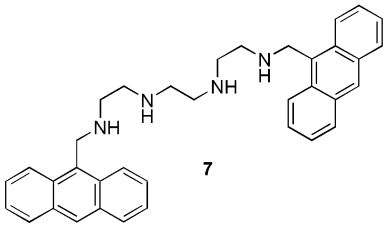


ligands showed typical PET processes with quenched fluorescence at basic pH and revival of the fluorescence at acidic pH. The most interesting feature was the quenching (up to 60%) that ATP induced in all receptors below pH 4. This quenching effect might

be attributed to PET or energy transfer from the ATP to the photoexcited anthracene unit favored by π-stacking interactions between the anthracene and the adenine fragment. ADP also showed a chelation-enhanced quenching with **4** although to a lesser extent than ATP. Other tested anions such as AMP, adenine, and tripolyphosphate did not affect the emission behavior.

The receptors **7** and **8** enhanced in water their emission in the presence of ATP and ADP (maximum



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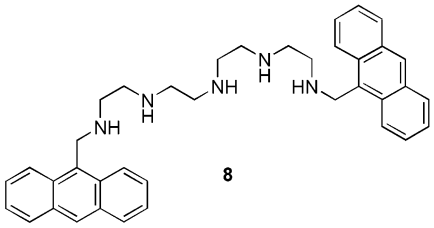

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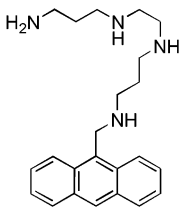
fluorescence enhancement for ATP is centered at pH 6 for both receptors and for ADP at pH 5.5 for receptor **7** and at pH 7 for receptor **8**).[63] Emission enhancement was probably due to inhibition of PET quenching mechanism by hydrogen bonding between the ATP or the ADP anions and the nitrogen atoms attached to the anthrylmethyl groups. In contrast, in acetonitrile−water 70:30 v/v mixtures, a selective quenching of **7** and **8** at acidic pH was observed in the presence of ATP similar to that found for **4**. In this case, the reduction in dielectric constants in acetonitrile−water when compared with water would enhance π-stacking binding modes that would result in quenching of the emission intensity.

Similar anthryl derivatives such as **9**−**12** have been used as receptors for polyanions such as heparin



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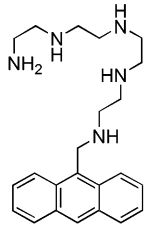

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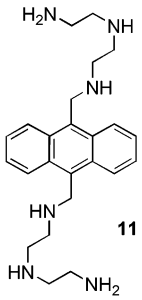

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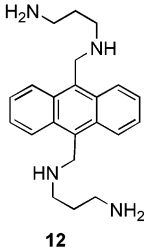

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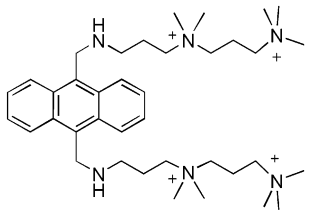
and poly-L-glutamate, ds DNA (double-stranded DNA) and ss DNA (single-stranded DNA) in water.[64] Compound **11** is the most effective in binding to heparin, and it was used to monitor the activity of the enzyme heparinase at pH 5. The most effective binder of polyglutamate was compound **10**, and it was used to follow the activity of the enzyme pronase that hydrolyzes polyglutamate to glutamic acid. Thus, in the absence of polyanion (heparin), the fluorescence of the anthracene was observed. In the presence of heparin, pairs between receptors were formed and emission at 510 nm due to excimer formation was observed. The addition of hydrolytic enzymes (such as heparinase and pronase) caused cleavage of the polyanions, and the fluorescence of the monomer was retrieved.

The fluorescent chemosensor **13** was designed to bind anions (via electrostatic forces) but avoid the



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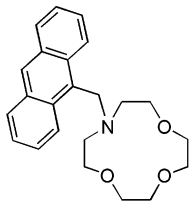
potential interference by transition metal ions (quaternary ammonium does not bind cations and the benzylic amines are protonated at neutral pH).[65] Compound **13** was used to follow the hydrolysis of ss and ds DNA and to evaluate the transition metal activation of *Bal*31 nuclease.

The fluorescent behavior of **14** was studied in acetonitrile in the presence of Cl^-, Br^-, HSO_4^-, and



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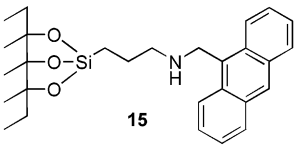
$H_2PO_4^-$.[66] The emission intensity band was not modified in the presence of chloride and bromide. Addition of HSO_4^- produced a slight decrease of the fluorescence intensity whereas the quenching induced by $H_2PO_4^-$ was most noticeable. The quenching was probably induced by electron transfer from the anion to the excited anthracene unit.

Compound **15** is one of the very few examples of functionalized solids designed for anion sensing. The



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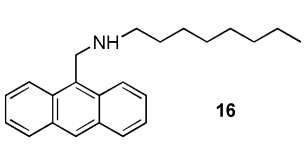

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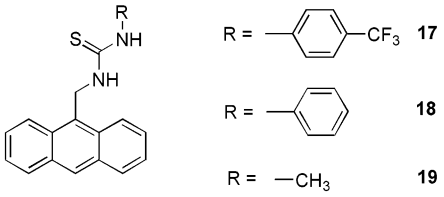
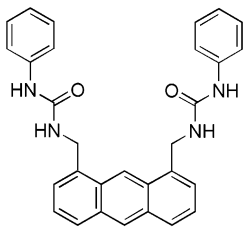
mesoporous solid MCM-41 was used as a support for the covalent anchoring of an anthracene fluorophore-bearing amino group.[67] Water suspensions of **15** were

able to sense ATP in water (pH 2.8) in the micromolar range (ca. 0.5 ppm) showing a notable quenching of the fluorescence intensity. Related hybrid solids to **15** but using silica fume as an inorganic matrix and the molecular-based receptor **16** showed a remarkably poorer response to ATP. The enhancement in the sensitivity for ATP with **15** was attributed to the periodicity of the mesoporous surface that after functionalization formed modulated cavities that fit well with ATP size, charge, and geometry mimicking, in some aspects, active site cavities found in biological receptors.

Apart from polyazaalkanes, other binding domains usually used for anion binding are urea and thiourea groups. Those are well-known anion binding sites that have proven to be good receptors for the recognition of basic anions such as fluoride, acetate, and phosphate. Perhaps the main drawback in their use is that they usually only shows sensing properties in nonaqueous solvents; therefore, their application as chemosensors in water is very limited. In those systems, anion coordination to the urea or thiourea usually results in a quenching of the anthracene emission. Upon anion coordination, the reduction potential of thiourea increases causing PET to become competitively more viable resulting in quenching of the fluorescence emission. Compounds **17**−**23** contain anthracene as signaling subunits and urea or thiourea as anion binding sites. The fluorescence emission spectra of **17**, in dimethyl sulfoxide (DMSO)



solutions, consisted of three sharp bands at 443, 419, and 397 nm (λ_{exc} = 370 nm).[68] Addition of F^-, AcO^-, and $H_2PO_4^-$ caused quenching of ca. 90, 70, and 50%, respectively. Minor quenching was observed on addition of Cl^- and Br^- (<7%). The logarithms of the binding constants for the formation of 1:1 complexes were in line with the quenching behavior observed. For **18**, the same selectivity trend was observed although smaller binding constants were found, due to the reduced acidity of the thiourea protons. For **19**, the order of selectivity was somewhat different; $H_2PO_4^-$ was selectively detected over AcO^-. On the other hand, the bis-urea anthracene derivative **20** in acetonitrile−DMSO 9:1 v/v mixtures displayed a selective fluorescent quenching effect only in the presence of F^- and a relatively small quenching with



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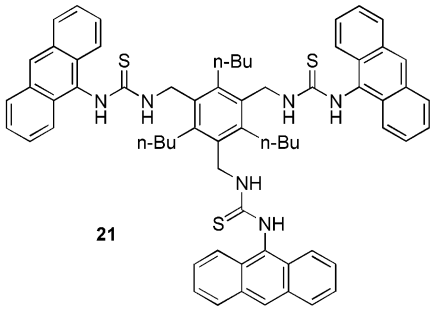
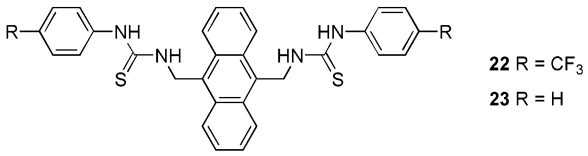
the addition of Cl^-, Br^-, and I^- anions.[69] The response for F^- anion was almost 120 times larger than that for Cl^-. The thiourea derivative with a substituted benzene ring, **21**, showed a typical anthracene emis-



21

sion band centered at 415 nm (acetonitrile solutions and λ_{exc} = 366 nm).[70] This fluorescence emission band was slightly affected by addition of chloride and acetate anions and remarkably quenched upon addition of dihydrogen phosphate (200 equivalents). As stated above, the quenching observed in all of those systems can be ascribed to a PET process enhanced upon anion binding.

The receptors **22** and **23** were especially designed for the recognition of bis-carboxylates such as glut-



arate, malonate, and pyrophosphate.[71] For glutarate, the fluorescence emission of **22** was quenched by ca. 70%; for malonate, the quenching was about 86%; and for pyrophosphate, the quenching was 95%. Similar quenching effects were observed for receptor **23**. These bis-carboxylates form 1:1 complexes with both receptors (see Figure 10). Other anions such as AcO^-, $H_2PO_4^-$, and F^- formed 2:1 anion:receptor complexes and also gave quite large fluorescence emission quenching (ca. 70−98%).

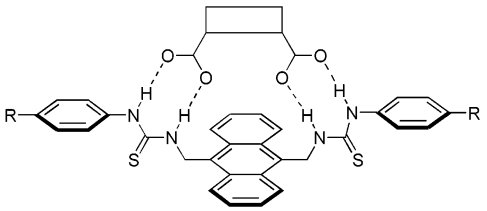
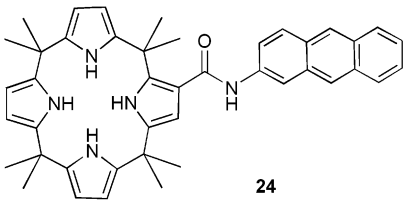


Figure 10. Schematic representation of the interaction of receptors **22** or **23** with bis-carboxylates.

An effective group for hydrogen interactions with anions are the calix[4]pyrrole derivatives, which are known to display remarkable large stability constants via hydrogen bonding with certain anions. Attachment of anthracene signaling subunits to calix[4]-pyrrole binding sites allowed development of fluorogenic chemosensors for fluoride. These chemosensors display sensing properties in organic solvents, but not in water. The calix[4]pyrrole receptors **24**−**26** suf-

fered fluorescence quenching in dichloromethane or acetonitrile upon addition of fluoride.[72] Partial quench-



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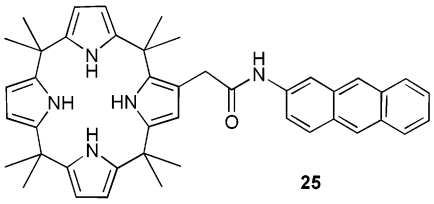

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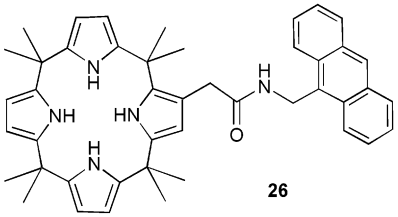

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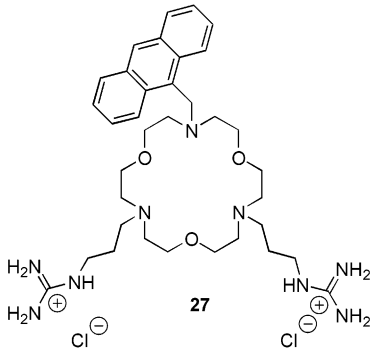
ing was also observed upon addition of other anions such as dihydrogen phosphate and chloride, but fluoride caused the greatest fluorescence quenching.

Receptor **27** was designed for binding amino acids in a 1:1 fashion via ammonium binding with the



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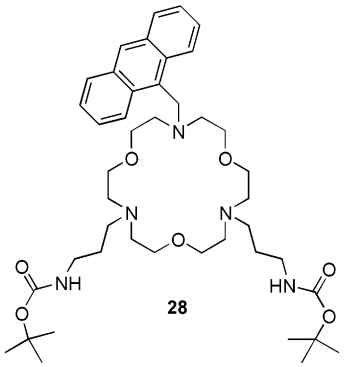
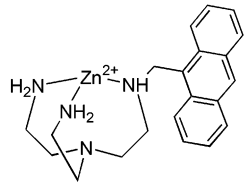


28

triaza-18-crown-6 ether moiety and carboxylate coordination with the guanidinium groups.[73] In receptor **28**, the two guanidinium subunits were exchanged for two carbamate groups, which are not able to interact with carboxylates. The anthracene emission of the two receptors was studied upon addition of amino acids (γ-aminobutiric acid, glycine, lysine, alanine, phenylalanine (phe), valine, serine, glutamine, and arginine) in H_2O/MeOH 1:2 v/v mixtures buffered at pH 9.5. The presence of γ-aminobutiric acid and lysine induced fluorescence enhancements for both receptors whereas only glycine induced enhancement of the emission intensity in the presence of receptor **27**.

Another important group of receptors incorporating anthracene as a signaling subunit involved the use of metal cations as binding sites. That is the case with systems **29**−**35**. The approach in those systems is to have a coordinatively unsaturated metal cation. Coordination of a certain anion to the metal center brings the signaling subunit close enough to the anion, and a quenching is usually observed due to a PET process from the anion to the photoexcited anthracene signaling unit.[50] Metal cations showed generally quite large formation stability constants with anions, and many of those chemosensors work in water or water−organic solvent mixtures.

The Zn^{2+} cation forms the complex **29** with an anthrylmethyl-functionalized tetraamine.[74] Metha-



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nolic solutions of **29** were fluorescent, but addition of *N*,*N*-dimethylaminobenzoate (dmbz) induced a near complete quenching. A similar effect was observed upon addition of other benzoate anions bearing either a donor or an acceptor group. In contrast, addition of anions such as nitrate, thiocyanate, or chloride to the complex **29** did not have any effect. The quenching was ascribed to an intramolecular electron transfer process from the benzoate to the photoexcited anthracene unit. This mechanism was found to be thermodynamically favorable, and the revival of the fluorescence at 77 K demonstrated the electron transfer nature of the quenching (see Figure 11).

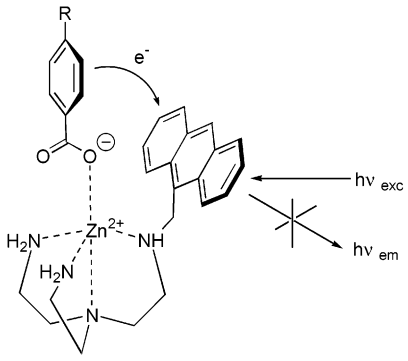
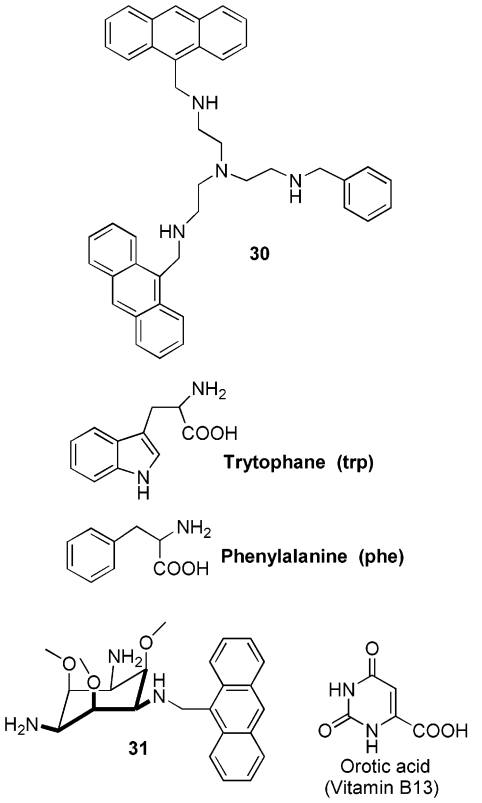


Figure 11. Interaction of complex $[Zn(\mathbf{29})]^{2+}$ with *p*-substituted benzoate anions that induced anthracene emission quenching through an electron transfer path from the benzoate anion to the anthracene subunit.

Similar quenching of the anthracene emission upon anion axial coordination to a metal center was also

observed using the $[Zn(\mathbf{30})]^{2+}$ and $[Zn(\mathbf{31})]^{2+}$ complexes. The entity $[Zn(\mathbf{30})]^{2+}$ formed 1:1 complexes



with natural amino acids (4:1 ethanol/water mixtures buffered at pH 6.8) giving a particular affinity with tryptophane (trp) and phe.[75] The high stability of the complexes $[Zn(\mathbf{30})(trp)]^{2+}$ and $[Zn(\mathbf{30})(phe)]^{2+}$ was due to the formation of a metal−carboxylate bond and π-stacking interaction between aromatic parts of the amino acids and the polyaromatic substituent of the *tren* (tris(2-aminoethyl)amine) framework. $[Zn(\mathbf{30})]^{2+}$ showed the typical monomer emission of anthracene. Among amino acids tested, only trp induced fluorescence quenching due to a through space photoelectron transfer process from the secondary amine nitrogen atom of the trp subunit to the excited anthracene fragment.

The $[Zn(\mathbf{31})]^{2+}$ complex gave a response in the presence of certain organic species in aqueous solutions buffered at pH 7.2.[76] This complex detects oxalate by a 40% decrease in fluorescence emission whereas no effect was observed with various mono- and dicarboxylates of longer chains. The fluorescence emission intensity of $[Zn(\mathbf{31})]^{2+}$ was also effectively quenched by nucleotides containing an imide or amide function. GMP causes strong quenching (42%) whereas TMP (20%) and UMP (23%) produced quenching to a lesser extent. AMP and CMP produced negligible changes in the fluorescence emission intensity. Probably the most noticeable effect was the quenching observed in the presence of orotate anion. Orotic acid (vitamin B13) is an intermediate metabolite in the biosynthesis of pyrimidine nucleotides and has a positive role in heart protection and in decreasing cholesterol levels. The emission intensity of $[Zn(\mathbf{31})]^{2+}$ decreased linearly with the added anion down

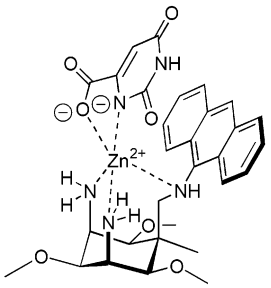
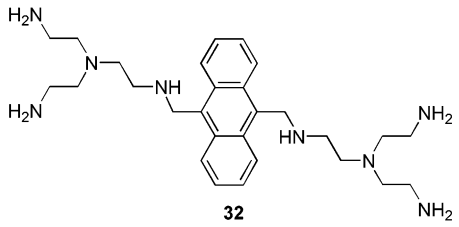
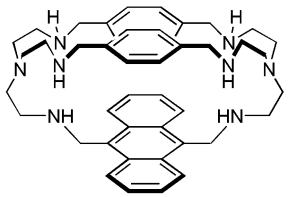


Figure 12. Proposed structure for the adduct formed between the complex $[Zn(\mathbf{31})]^{2+}$ and the orotate anion. The observed emission quenching was due to aromatic stacking between the anthracene moiety and the orotate.

to total quenching after addition of one equivalent of orotate to give the [Zn(**31**)(orotate)] complex. The high affinity of $[Zn(\mathbf{31})]^{2+}$ for the orotate anion was due first to the bidentate character of the orotate that coordinates the Zn^{2+} metal center through the deprotonated amide and the carboxylate group and second to the aromatic stacking between the anthracene moiety and the substrate (see Figure 12). This stacking interaction was responsible for the observed quenching.

Solution studies on receptors **32** and **33** suggested that in the presence of two equivalents of Zn^{2+} the





complexes $[Zn_2(\mathbf{32})]^{4+}$ and $[Zn_2(\mathbf{33})]^{4+}$ were formed. When the imidazolate anions were added to $[Zn_2(\mathbf{32})]^{4+}$ solutions, the $[Zn_2(\mathbf{32})(imidazolate)]^{3+}$ complex was formed in which the imidazolate acts as a bridging anion between the two metal centers.[77] When this complex was formed, there was a quenching of the emission intensity of the anthracene fragment probably due to a photoelectron transfer from an orbital of the electron rich imidazolate to the photoexcited anthracene group. A similar quenching effect was observed upon addition of L-histidine (containing an imidazole ring) to the dizinc(II) complex of **32** at pH 9.6. The dizinc(II) complex of the bis-*tren* cage **33** selectively included the isoestructural N_3^- and NCO^- anions in aqueous solution.[78] The N_3^- anion inclusion was signaled through the quenching of the fluorescence of the anthracene group (see Figure 13). Again, the quenching was probably due to a photoelectron transfer process from the N_3^- anion to the photoexcited anthracene fragment.

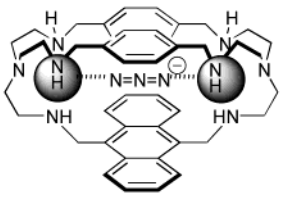
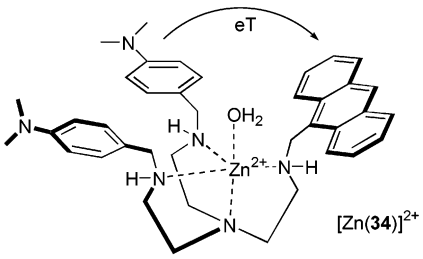


Figure 13. N_3^- anion encapsulation within two zinc(II) atoms in bistren cryptate **33**. The quenching of the anthracene emission was assigned to a photoelectron transfer process from the N_3^- anion.

Titration of solutions of receptor **34** in the presence of equimolar amounts of Zn^{2+} produced a profile in



which the fluorescence intensity decreases in the whole pH range when compared to that of **34** alone.[79] This decrease in intensity was ascribed to formation of the complex $[Zn(\mathbf{34})]^{2+}$, which brings the photoexcited anthracene fragment and the *N*,*N*-dimethylaniline subunits close enough for a through space photoelectron transfer process. When the titration was performed in the presence of one equivalent of triphenylacetate, a sharp enhancement in the fluorescence was observed at pH ≥ 4.5. This enhancement was ascribed to the binding of the triphenylacetate anion to the axial site of the complex $[Zn(\mathbf{34})]^{2+}$ (see Figure 14). The bulky carboxylate acted as a curtain removing the photoelectron transfer process from the aniline to the photoexcited anthracene. It seemed that the anion bulkiness had a remarkable effect in controlling the efficiency of the intramolecular photoelectron transfer in the $[Zn(\mathbf{34})]^{2+}$ complex because other carboxylates such as acetate, cyclohexylcarboxylate, benzoate, and 1-adamantanecarboxylate produced poor or moderate enhancement of the emission intensity.

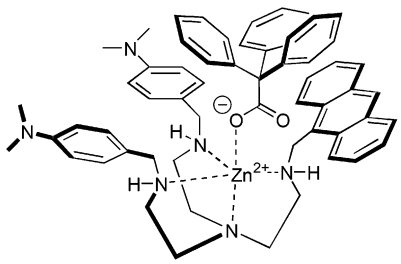
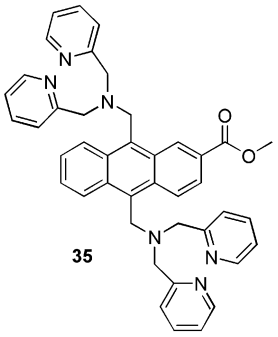


Figure 14. Binding pattern proposed for the interaction between $[Zn(\mathbf{34})]^{2+}$ complex and triphenylacetate anion. This bulky carboxylate acted as a curtain removing the photoelectron transfer process from the aniline to the photoexcited anthracene.

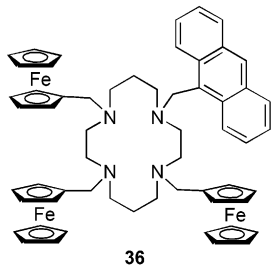
The receptor **35** contains two sets of dipicolylamine subunits and forms the complex $[Zn_2(\mathbf{35})]^{4+}$ that is



35

able to give 1:1 complexes with phosphate and ATP anions.[80] Upon addition of phosphate to aqueous solutions of $[Zn_2(\mathbf{35})]^{2+}$ buffered at pH 7.2, there was a revival of the emission intensity (fluorescence enhancement factor of 2.3). This enhancement was ascribed to a conformational rigidification induced by the cooperative coordination of the two sets of Zn-dipicolylamine to the phosphate species. The presence of acetate, nitrate, sulfate, chloride, and azide did not cause any significant fluorescence intensity change. The presence of ATP induced the largest enhancement in the emission intensity (fluorescence enhancement factor of 3), whereas the presence of ADP and AMP induced minor enhancements. As many times reported, a good correlation was found between fluorescence changes and stability constants, as the affinity of $[Zn_2(\mathbf{35})]^{4+}$ for ATP is 10- and 30-fold larger than that for ADP and AMP, respectively.

The complex $[Cu(\mathbf{36})]^{2+}$ consists of a copper(II) atom in a near square-planar coordination mode with



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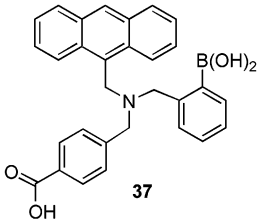
the cyclam unit adopting a configuration with the four N-anchored groups above the N4 plane.[81] The $[Cu(\mathbf{36})]^{2+}$ complex was poorly fluorescent due to energy or electron transfer processes from either the metal atom or the ferrocene to the photoexcited anthryl group. Whereas the presence of chloride, bromide, iodide, and hydrogen sulfate had no effect in the fluorescence emission, nitrate, fluoride, and dihydrogen phosphate induced an emission fluorescence enhancement of 26, 20, and 17%, respectively. Coordination of anion might inhibit partially the quenching effect produced by ferrocene or by the copper(II) cation with a consequent enhancement of the emission intensity.

Receptor **37** showed an enhanced response in the presence of certain anions when incorporated into a polymer.[82] Thus, **37** bound nucleotides and nucleosides in aqueous solutions (pH 7.3) in a very weak manner, and in all cases, there was little or no change

in receptor fluorescence emission. However, there was a remarkable cooperative effect when **37** was attached to the polymer poly(allylamine) PA (MW 50 000−65 000) via amide linkage. Upon titration of PA-**37** in aqueous solution with UTP, there was an emission enhancement due to boronic acid chelation even in the presence of the competing phosphate buffer, whereas uridine, UMP, and UDP produced negligible changes.



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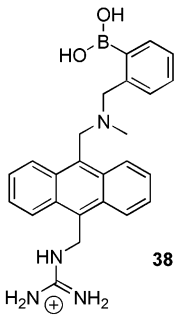
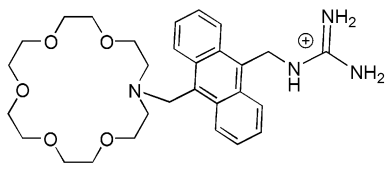
Receptor **38** consists of a boronic acid and a guanidinium unit as recognition subunits attached



38

to the anthracene signaling subunit.[83] Addition of D-glucarate to water:methanol 1:1 v/v solutions at pH 7.4 of receptor **38** induced a 4.5-fold emission enhancement. The presence of D-gluconate and D-sorbitol induced less pronounced enhancements while D-glucuronate and D-glucose induced no changes. These enhancements were reflected in the values of stability constants that gave the order D-glucarate ≫ D-gluconate = D-sorbitol ≫ D-glucose = D-glucuronate. Molecular modeling studies suggested that the two carboxylates of D-glucarate would be bound with the guanidinium unit whereas the hydroxyl groups at the 3,4-positions would bound the boronic acid moiety.

α,ω-Amino acid zwitterions cause fluorescence enhancement of **39** in methanol:water mixtures at



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pH 9.5.[84] The chemosensor consists of a guanidinium group as the cationic receptor for carboxylates and a monoaza-18-crown-6 ether for coordination with the ammonium terminus (see Figure 15). A family of amino acids was tested, and the fluorescence enhancement interestingly depended on the alkylic chain length between the acid and the ammonium

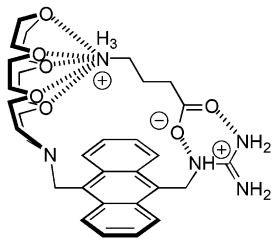
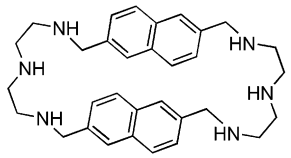


Figure 15. Proposed structure for the adduct formed between receptor **39** and γ-aminobutirate.

group. The largest fluorescence enhancement factor was found for γ-aminobutyric acid, which is a principal neurotransmitter in the brain. γ-Aminobutyric acid also displays the larger binding constant with **39**.

3.2.1.2. Containing Naphthalene. Naphthalene and naphthalene derivatives usually show no well-shaped and poor structured bands centered at ca. 275 nm that upon excitation display an emission broad band at ca. 350 nm.[59] In general, naphthalene derivatives are less fluorescent (quantum yield of naphthalene in acetonitrile is 0.23) than similar compounds containing anthracene. Similar derivatives to those found with anthracene have in general been described with naphthalene.

Compound **40** is the only naphthalene-containing example with a polyamine as an anion binding site.[85]



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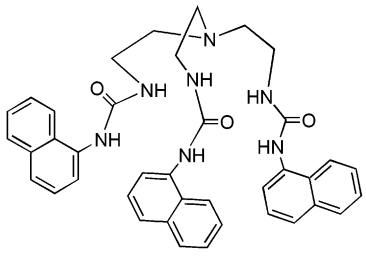
Compound **40** proved to form strong complexes with planar anionic species such as aromatic carboxylates and nucleotides. Nucleotides (AMP, ADP, ATP, GMP, CMP, and UMP) in water at pH 6 induced a non-selective decrease of the fluorescence emission.

The receptor **41** contains multiple coordination sites provided by three urea groups and a ternary

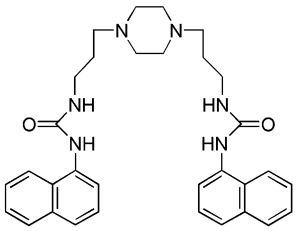


41

amine and exhibits preferential coordination for tetrahedral anions vs spherical ones.[86] In **41**, the ternary amine is strongly donor due to the lone pair and quenches the fluorescence of the naphthalene through a photoelectron transfer process. Upon addition of $H_2PO_4^-$ in dimethyl formamide (DMF) solutions, the **41**$H^+\cdots HPO_4^{2-}$ complex is formed by means of a proton transfer from $H_2PO_4^-$ to the amine of **41**. This process reduces the electron donor character of the amine resulting in an enhancement of

the fluorescence emission intensity. Only a small fluorescence emission increase in the presence of HSO_4^- and no change with Br^- and I^- were observed.

Compound **42** is one of the few known examples able to discriminate between carboxylates of different length.[87] Compound **42** has two urea groups linked



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by a spacer containing amines. The fluorescence intensity of **42** in DMSO was gradually quenched as the dicarboxylate anion concentration was increased, and simultaneously, a new band at 500 nm was observed (see Figure 16). The authors assigned this

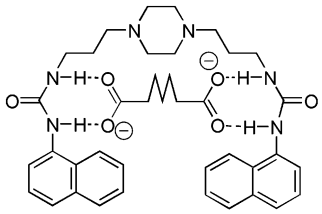
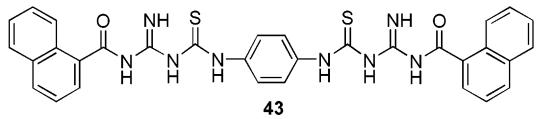


Figure 16. Possible binding model for receptor **42** and the anion pimelate.

red-shifted band to an emission from the complex formed upon interaction of the receptor with the correspondent carboxylate through hydrogen-bonding interactions and not to the formation of an intramolecular excimer. Interestingly, the quenching ability depended on the chain length of the dicarboxylate ($^-OOC-(CH_2)_n-COO^-$); the order of quenching was as follows: pimelate ($n = 5$) > suberate ($n = 6$) = adipate ($n = 4$) > glutarate ($n = 3$) > malonate ($n = 2$).

Upon addition of various anions in a 1000-fold excess to solutions of receptors **43**−**46** in methanol, strong emission fluorescence enhancements were obtained with CO_3^{2-} and HCO_3^-.[88] Other anions such



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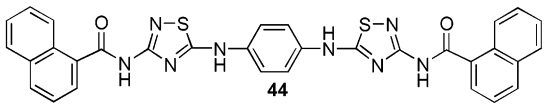

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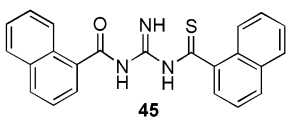

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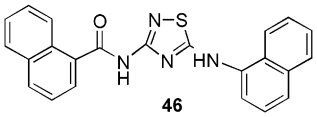
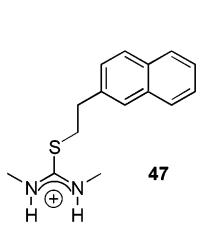


46

as HPO_4^{2-} and HSO_4^- showed a moderate emission enhancement, and the anions ClO_4^-, NO_3^-, and $H_2PO_4^-$ produced negligible changes. The largest variations were obtained for receptors **43** and **45** with CO_3^{2-} (enhancement factors of 53 for **43** and 27 for **45**) and with HCO_3^- (enhancement factors of 39 for **43** and 27 for **45**). The enhancement obtained with the receptors **44** and **46** in the presence of CO_3^{-2} and HCO_3^- was less important because these receptors only contain four and two NH groups capable of forming hydrogen bonds. The enhancement of the fluorescence intensities was attributed to an increase of the rigidity of the receptor molecules upon anion complexation. This complexation takes place basically between the guanidyl or the amido moieties and the corresponding anion through hydrogen-bonding interactions.

Naphthalene functionalized receptors **47**−**49** emit weakly as a result of PET processes from the singlet



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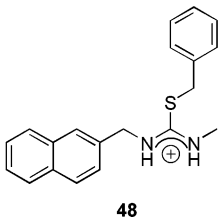

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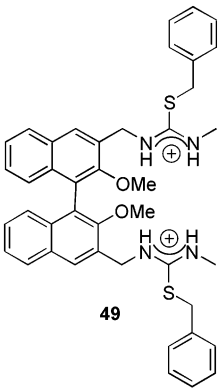
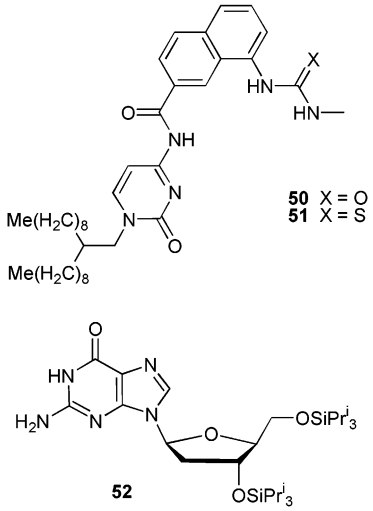


49

state of the excited naphthalene fluorophore to the electron deficient isothiouronium moiety.[89,90] Those isothiouronium binding sites formed 1:1 complexes with anions with association constants comparable to analogous receptors functionalized with guanidinium groups, indicating comparable binding affinities. Upon addition of acetate to **48** and **49**, a significant enhancement of the fluorescence emission intensity of ca. 380% for receptor **48** and ca. 1600% for receptor **49** occurred. This enhancement was attributed to an interaction of the anion acetate with the isothiouronium moiety that reduced the efficiency of the PET process. Weak enhancements were found for both receptors **48** and **49** in the presence of $(Bu^nO)_2PO_2^-$, and no fluorescence changes were found for the two receptors in the presence of Cl^-. The fluorescence emission intensity of receptor **47** was enhanced, in the presence of HPO_4^{-2}, by a factor of 10 in methanol solutions and by a factor of 5 upon binding with AcO^-, and only slight spectral changes were observed upon addition of $H_2PO_4^-$ or Cl^-.[91]

Receptors **50** and **51** contain several hydrogen-bonding sites and are designed to coordinate guanosine derivatives.[92] The coordination of those receptors with the guest **52** was via formation of several hydrogen bonds (see Figure 17). The presence of the lipophilic guanosine derivative **52** in binary mixtures of $CHCl_3$ and DMSO (4:1 v/v) induced a significant quenching of the fluorescence emission of both receptors **50** and **51** (receptor **50** was more appropriate for sensing because **51** was not photostable). The response of an optical sensor based on a membrane containing the ionophore **50**, a plasticizer (bis(ethylexyl)sebacate), tridodecylmethylammonium chloride, and poly(vinyl chloride) (PVC) was tested. A remarkable and stronger quenching of the fluorescence emission was observed for GTP than for ATP.



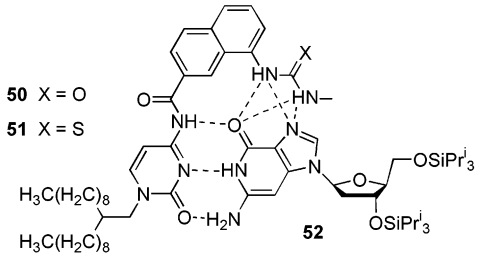
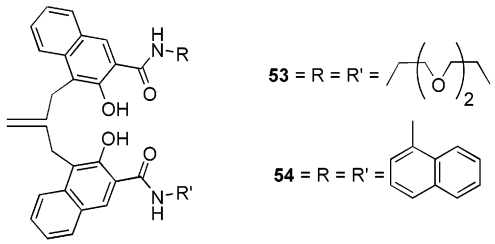
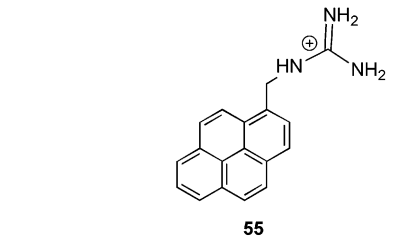


Figure 17. Scheme of the host−guest binding interaction, through formation of multiple hydrogen bonds, between receptors **50**, **51**, and the guanosine derivative **52**.

Other hydrogen-bonding receptors containing naphthalene are **53** and **54** whose fluorescence emission was enhanced and red-shifted upon addition of basic anions such as F^-, $H_2PO_4^-$, and AcO^- in acetonitrile, whereas Cl^-, Br^-, I^-, and ClO_4^- anions gave no response.[93] These spectral changes were associated with a proton transfer process from the hydroxyl group of the host compounds to the guest anion confirmed by the observation of HF_2^- through ^{19}F NMR measurements. Other evidence of the proton transfer was obtained by the reproduction of the emission enhancement by adding sodium hydroxide to solutions of receptor **54**.



3.2.1.3. Containing Pyrene. Pyrene and pyrene derivatives usually show five well-shaped and fine absorption bands between 210 and 330 nm, whereas the emission spectrum usually consists of a broad band centered at ca. 400 nm.[59] The quantum yield of pyrene is 0.65 in acetonitrile solutions. Probably the most interesting feature of pyrene derivatives is their capacity of forming excimers and the ability to give dual monomer−excimer fluorescence. In fact, this monomer−excimer equilibrium has been used as a sensing principle in several pyrene-based receptors. This has been the case for receptors **55**−**58**. Thus, for instance, in the absence of anions, **55** showed a broad emission band centered at 400 nm, which is assigned to the pyrene monomer emission in methanol.[94] In the presence of pyrophosphate ($P_2O_7^{4-}$), a structureless band at 476 nm due to the formation of an intramolecular excimer appeared. The observed behavior is attributed to the formation of the $[(P_2O_7)(\mathbf{55})_2]^{2-}$ complex (see Figure 18). A much less effective response was found upon addition of HPO_4^-, and no change was found with $H_2PO_4^-$, AcO^-, SCN^-, Cl^-, and Br^-.



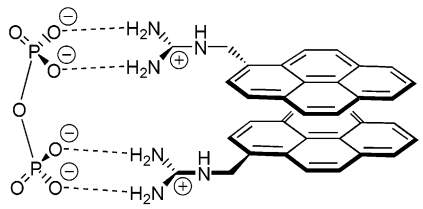
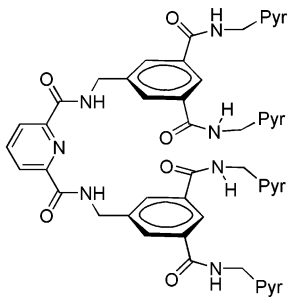


Figure 18. Binding pattern of two molecules of receptor **55** with pyrophosphate anion through formation of hydrogen bonds between the guanidinium subunits of receptor **55** and the pyrophosphate.

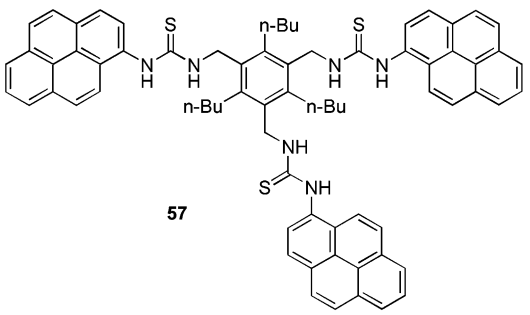
Compounds **56** and **57** contain as anion binding sites amides and thiourea groups, respectively. Receptor **56** shows fluorescence monomer emission at 377 nm and excimer fluorescence emission at 477 nm in tetrahydrofuran (THF):$CHCl_3$ 1:1 mixtures.[95] The organized conformation of **56** due to the $\pi-\pi$ stacking between two pyrene units is responsible for the excimer emission observed. Only in the presence of $H_2PO_4^-$ and PO_4^{3-} does the ratio excimer emission to monomer emission decrease, whereas the anions F^-, Cl^-, Br^-, SCN^-, AcO^-, NO_3^-, ClO_4^-, and HSO_4^- gave no change. This variation was attributed to

encapsulation of phosphate into the core of one molecule of **56** favored by formation of hydrogen bonds with the amido groups. On complexation with $H_2PO_4^-$ or PO_4^{3-}, the pyrene rings would be pushed apart to disfavor the excimer formation.



56

Receptor **57** has a preorganized cavity with three thiourea moieties and three pyrene signaling subunits.[70] Solutions in acetonitrile of receptor **57** showed two emission bands, one centered at 400 nm and ascribed to the pyrene monomer emission and another very broad band centered at 500 nm ascribed to the intramolecular interaction of the pyrene rings. No spectral change occurred upon addition of an excess of the perchlorate anion. With chloride, acetate, and dihydrogen phosphate, an enhancement in fluorescence emission at 500 nm was observed. The fluorescence intensity at 500 nm increased in the order $H_2PO_4^- > AcO^- > Cl^-$, which was also the order of the stability constants determined. The preorganization effect of the tripodal receptor appears to increase the selectivity toward the tetrahedral dihydrogen phosphate anion rather than to the planar acetate anion.



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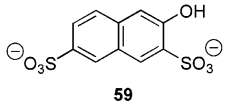
The fluorescence spectrum of the pyrenophane **58** showed a characteristic emission from the excimer due to the close proximity of the two pyrene groups in water−ethylene glycol 3:1.[96] With the addition of the anion **59**, a quenching of the excimer fluorescence

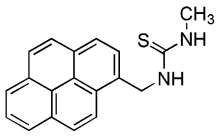


59

58

up to 80% was achieved. Similar quenching phenomena were obtained with nucleotides (AMP, UMP, GMP, and CMP). The quenching was ascribed to π-stacking of the aromatic part of the anions with the pyrene rings that occupy the up and down faces of the cyclophane frame hindering pyrene−pyrene interactions.

Some other thiourea anion receptors containing pyrene are **60** and **61**. Addition of AcO^- to **60**



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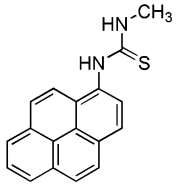
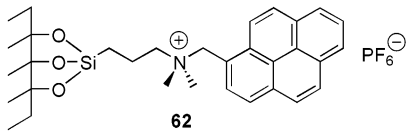


61

produced a significant quenching in acetonitrile.[97] This effect can be rationalized in terms of changes in the redox properties of the thiourea group in a similar manner as described above for compounds **17**−**23**. In acetone, the monomer emission was quenched with the anions AcO^-, $H_2PO_4^-$, and Cl^- and it was also observed an intramolecular emission band at 494 nm that was attributed to an exciplex formed between the pyrene and the thiourea. The magnitude of the quenching in acetone follows the order $AcO^- > H_2PO_4^- > Cl^-$ reflecting the stabilities of the complexes. In the absence of anions, **61** displayed the expected emission band in acetonitrile of the pyrene group at 400 nm.[98] Upon addition of certain anions, a new band appeared at 507 nm probably due to the formation of an excimer. The enhancement of the 507 band was in the order $AcO^- > H_2PO_4^- \gg ClO_4^-$ in agreement with the binding selectivity of **61**.

A quaternary ammonium salt bearing a pyrene fluorophore has been grafted onto the surface of a delaminated zeolite (**62**) and used as a selective

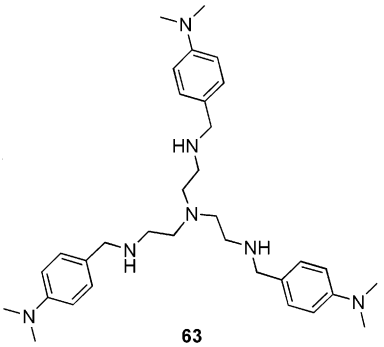


62

chemosensor for iodide.[99] For all of the halides studied, only iodide is capable of quenching the emission intensity of pyrene fluorophore centered at 375 nm (λ_{exc} = 338 nm) by exhaustive ion exchange of the PF_6^- by the iodide anion. The emission quenching was probably due to a heavy atom effect or to a single electron transfer from the iodide atom to the pyrene induced by the interaction of the iodide with the ammonium cation present in **62**.

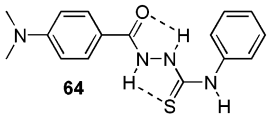
3.2.1.4. Containing Other Aromatic Hydrocarbons. The $[Zn(\mathbf{63})]^{2+}$ complex follows the same sensing principle as **29**−**35**, and thus, its fluorescence was partially quenched in methanol in the presence of aromatic carboxylates (benzoate, 4-nitrobenzoate, and 9-anthracenoate) due to a combination of carboxylate coordination with the Zn^{2+} cation and

π-stacking interactions with the *N*,*N*-dimethylaniline substituents.[100] Aliphatic carboxylates and inorganic anions such as Cl^-, NO_3^-, and ClO_4^- did not induce any modification of the fluorophore emission.



63

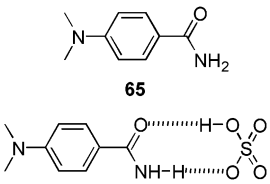
Acetonitrile solutions of **64** showed dual fluorescence at 370 and 520 nm on excitation at 289 nm



64

assigned to the emission from the locally excited (LE) and charge transfer (CT) states, respectively.[101] The presence of AcO^- resulted in quenching of the long wavelength CT emission while enhancing the LE emission, with a clear isoemissive point at 425 nm. This variation in the dual fluorescence profile was assigned to a hydrogen-bonding interaction between the thiourea moiety and the acetate anion. Plots of the CT to LE fluorescence maximum intensity ratio vs anion concentration showed remarkable selectivity toward AcO^- anion over F^- and $H_2PO_4^-$. Binding constants for 1:1 complexes showed the same trend than that observed in fluorescence selectivity and seemed to be related with the basicity of the anions. The authors suggested that a change in the hydrogen bond network of the receptor−anion complex was responsible for the fluorescence response observed. The occurrence of an ESPT within the complex formed induced a shift in the LE to CT equilibrium in the presence of certain anions.

Solutions of *p*-dimethylaminobenzamide **65** in acetonitrile also showed dual fluorescence at 360 and 484 nm assigned to LE and CT states, respectively.[102] A dramatic decrease in the CT to LE fluorescence intensity ratio, I_{CT}/I_{LE}, occurred in the presence of HSO_4^-, whereas the presence of the other anions (for instance $H_2PO_4^-$, AcO^-, and ClO_4^-) exerted much less influence. As for **64**, the quenching observed was

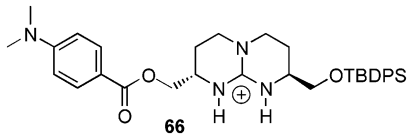


65

Figure 19. Scheme of the hydrogen-bonding interaction between receptor **65** and the anion hydrogen sulfate.

assigned to the existence of a proton transfer in the excited state within the (HSO_4^-)−**64** hydrogen-bonding complex (see Figure 19).

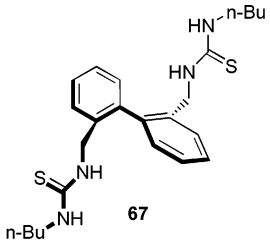
By using receptor **66**, which contains a chiral bicyclic guanidinium subunit linked to a 4-(*N*,*N*-



66

dimethylamino)benzoate fluorophore, it was possible to design a suitable fluorescent probe for the anion sulfate.[103] Upon excitation at 280 nm, acetonitrile solutions of **66** showed dual fluorescence with apparition of two bands centered at 344 and 497 nm and assigned to the LE and twisted intramolecular charge transfer (TICT) states, respectively. The LE band was more intense than the TICT band due to the formation of an intramolecular hydrogen bond between the esther carbonyl oxygen and one of the guanidinium protons. Upon addition of sulfate, the LE band first drops to one-half of the original value on addition of up to 0.5 equivalents and then rapidly increases to form a plateau when 2 equivalents of sulfate were added. In contrast, the TICT band showed an increase until 0.5 equivalents of sulfate and no appreciable changes thereafter. These intricate changes in fluorescence emission were ascribed to the formation of two complexes, first a 2:1 (receptor:anion) and then a 1:1 (receptor:anion) complex.

The fluorescent anion sensor **67**, based on a biaryl−thiourea system, showed a fluorescent emission



67

enhancement in the presence of fluoride.[104] Upon excitation of chloroform solutions of receptor **67** at 276 nm, a fluorescence emission centered at 379 nm appeared. The addition of fluoride induced a hypsochromic shift of the band centered at 379 to 356 nm and an emission enhancement, whereas the addition of chloride, bromide, acetate, hydrogen sulfate, and dihydrogen phosphate did not result in any obvious spectral change. Receptor:anion 1:1 and 1:2 complexes were formed with fluoride (see Figure 20). The formation of the 1:1 complex induced an emission enhancement by conformational restriction whereas the formation of the 1:2 complex gave rise to the loss of rigidity and the emission was quenched. The selectivity for fluoride anion can be explained because of its proper size that gives the more effective hydrogen-bonding interactions with the two thiourea moieties.

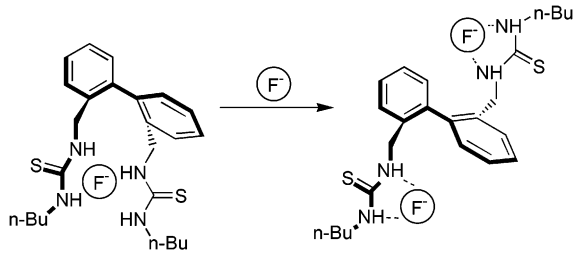
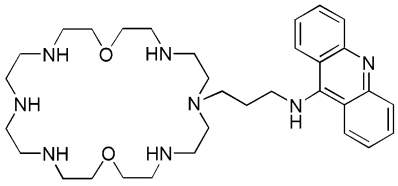


Figure 20. Proposed structures of the 1:1 and 1:2 (receptor:anion) complexes formed between receptor **67** and the fluoride anion.

3.2.2. Fluorescent Sensors Based on Aromatic Heterocycles

3.2.2.1. Containing Acridine and Other Pyridine-Based Derivatives. Acridine has been used as fluorescent signaling subunit in fluorogenic anion chemosensors in combination with polyamines as anion binding sites. Acridine is a high fluorescent unit with the longest wavelength absorption band at ca. 410 nm that upon excitation gave a fluorescence emission at ca. 510 nm.[59] Acridine and acridine derivatives have quantum yields in the range of 0.2−0.5.[105] However, despite this large quantum yield, the use of acridine derivatives as a signaling unit for anion sensing has been quite limited.

In 1988, the use of receptor **68** to sense ATP and CTP over other nucleotides tested (AMP, ADP and



68

GTP) in water at pH 7.6 through an enhancement of the fluorescence emission of the appended acridine fluorophore was reported.[106,107] Fluorescence enhancement in the presence of ATP was more marked than in the presence of CTP. This fluorescence enhancement was attributed to π-stacking interactions between the acridine fluorophore and the aromatic part of the nucleotides in the 1:1 complex formed (see Figure 21). UV/vis and fluorescence properties of **69**

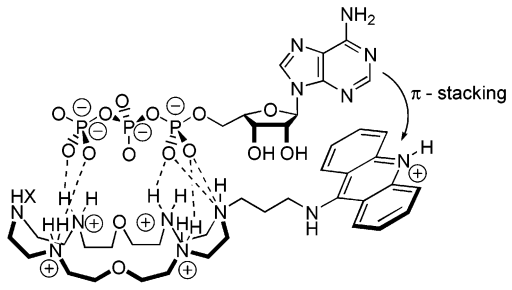
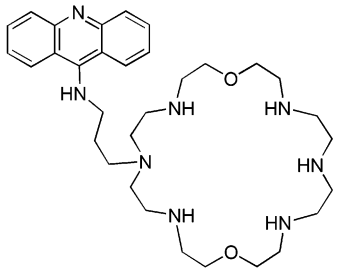


Figure 21. Schematic representation of the complex formed between receptor **68** and ATP by means of hydrogen bonding, electrostatic, and π-stacking interactions. The fluorescence enhancement observed upon ATP binding was adscribed to π-stacking interactions.

and **70** have been studied in the presence of nucleotides in water at pH 6.5. ATP, CTP, UTP, and ADP increased the fluorescence intensity of **69** or **70**, whereas GTP quenched the fluorescence of **69** and slightly increased that of **70**.[108] The largest fluorescence enhancement was found for ATP (fluorescence increase of 150% for **69** and 250% for **70**) probably due to a better stacking interaction between the acridine and the adenine parts. Studies with dinucleotide phosphates were also carried out. NADH has no effect on the fluorescence of the receptor whereas NADPH induced a weak enhancement. That study also described the interaction of the receptors with ds DNA.



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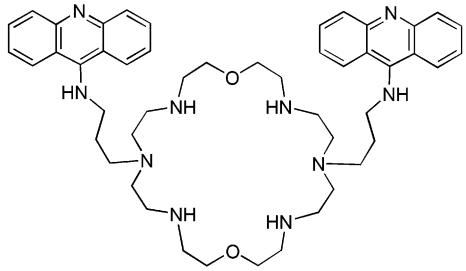
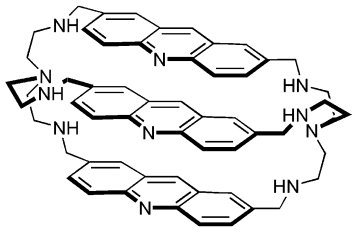


70

A complete study on the effect that anions have on the emission properties of the hexaprotonated form of the macrobicyclic tris-acridine cryptand **71** was



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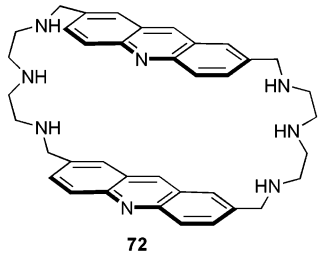
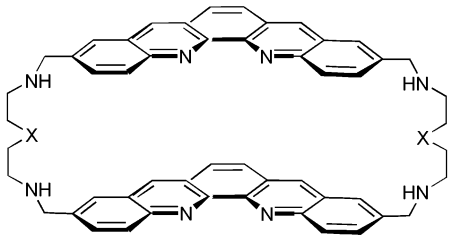


72

carried out in water at pH 6.4.[109] Compound **71** showed very weak fluorescence probably due to intermolecular quenching between acridine groups. Addition of certain anionic substances resulted in the dramatic enhancement of the fluorescence quantum yield. The larger enhancement factors (up to 27) were found for the planar aromatic dicarboxylates terephthalate and metaphthalate probably due to their insertion between the acridine units. This favors $\pi-\pi$-interaction between the aromatic ring of the substrate and the acridines, reducing the intramolecular acridine interactions and favoring the enhancement of the emission intensity. Aliphatic dicarboxylates such as malonate, maleate, etc. gave low or no emission enhancement. ATP, AMP, UMP, and UTP gave moderate enhancement of the quantum yield. A strong increase of the fluorescence (enhancement factor up to 10) of **71** was also observed upon addition of oligodeoxythymidylic acid. In contrast, binding to oligopurinic sequences induced only weak spectral variations. The receptor **72** in its tetraprotonated form (water, pH 6.0) coordinated nuleotides with two types of responses: (i) strong quenching of the fluorescence intensity (about 70−80%) with purine derivatives and (ii) considerable enhancement of the emission intensity (about 70−130%) with pyrimidine derivatives (λ_{exc} = 365 nm, λ_{em} = 430 nm).[110] Both effects were attributed to an interaction between the acridine ring and the nucleobase. In the case of purines, the quenching suggested a conformational change and variation of the interchromophoric distances. In the case of pyrimidines, the authors suggested an insertion of nucleobase between the two acridine moieties, decreasing their mutual interaction and therefore enhancing the fluorescence emission intensity.

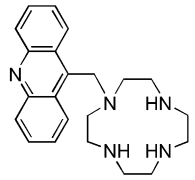
The receptors **73**−**75** are similar to **71** and **72** but contain quinacridine groups as fluorescence signaling



73 X = NH
74 X = O
75 X = CH_2-N(CH_3)-CH_2

units.[111] The addition of gradual quantities of nucleotides (3′,5′-cGMP, 2′,3′-cGMP, GMP, AMP, CMP, UMP, GDP, ADP, GTP, ATP, and UTP) to solutions of receptors **73**−**75** (in their tetraprotonated form) at pH 6.0 induced a progressive decrease in fluorescence intensity. The most important quenching (up to 95%) was achieved on complexation with guanosine derivatives and was attributed to a $\pi-\pi$-stacking interaction between the quinacridine units of the receptor and the nucleobase rings. All nucleoside monophosphates formed 1:2 receptor:nucleobase complexes whereas nucleoside diphosphates and triphosphates gave 1:1 complexes. Guanosine derivatives showed stronger binding constants. Three kinds of interaction governed the formation of 1:2 complexes, electrostatic interactions between the charged polyamine moieties of the receptor and the phosphate groups of the nucleobases, π-stacking interactions between the quinacridine subunits of the receptor and the nucleobase rings, and finally, hydrogen bonding between the two units of nucleoside monophosphate. Receptor **73** showed a similar binding behavior as **74** and was clearly distinct from that observed for receptor **75**. The propylene triamine linkers of **75** enhance the interchromophoric distance relative to the **73** or **74** and should diminish the π-stacking effect. As a consequence, receptor **75** has reduced affinity, in comparison with **73** and **74**, in binding nucleobases.

In another example, a Zn^{2+} complex of the acridine-functionalized cyclen polyazacycloalkane **76** was used



76

as the binding site for molecular recognition of deprotonated nucleobases.[112] In aqueous solution, the Zn^{2+} complex at pH 7.6 was strongly fluorescent due to the presence of the acridine signaling unit. A decay in the acridine fluorescence intensity of [Zn(**76**)]$^{2+}$ was observed in the presence of deoxythymidine and inosine, whereas the presence of 2′-deoxyguanosine, 2′-deoxyadenosine, and 2′-deoxycytidine gave no variation. It was found that the degree of intensity decay increases as the affinity of the Zn^{2+} complex increases for the nucleobase. The authors suggested a stacking interaction to explain the quenching observed (see Figure 22).

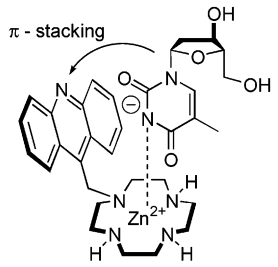
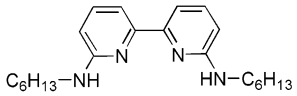


Figure 22. Scheme of the interaction between [Zn(**76**)]$^{2+}$ complex and deprotonated deoxythymidine. π-Stacking interactions are responsible for the emission quenching observed upon coordination.

Although bipyridine and their derivatives are generally nonfluorescents, derivatives bearing amino groups at the 6-position show emission properties with a large quantum yield (up to ca. 0.3). In acetonitrile, addition of diphenyl phosphate to **77**



77

induced the disappearance of the fluorescence band at 390 nm, whereas a new band at ca. 500 nm appears due to the formation of a 1:1 complex in which one of the pyridines was protonated forming the complex $[PO_2(OPh)_2(H\mathbf{77})]$. Compound **77** showed response for diphenyl phosphate but not for carboxylic acids (see Figure 23).[113]

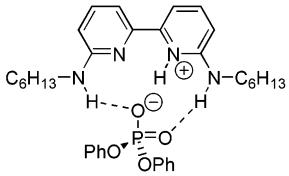
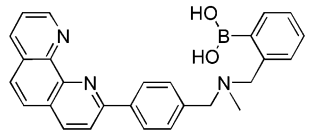


Figure 23. Proposed structure of the complex formed between receptor **77** and diphenyl phosphate anion through hydrogen-bonding interactions.

The receptor **78** binds Zn^{2+} in the 1,10-phenanthroline moiety forming a 1:1 complex at pH 8 in



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aqueous solution.[114,115] This complex is able to recognize and sense uronic carboxylates via coordination through the Zn^{2+} cation and the boronic acid (see Figure 24). Thus, an enhancement in the emission

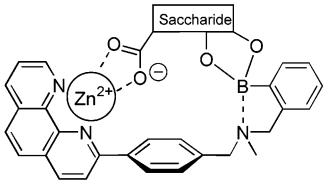
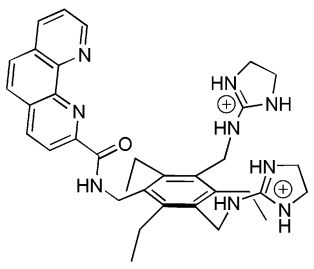


Figure 24. Complexation mode proposed for the binding between $[Zn(\mathbf{78})]^{2+}$ and an uronic carboxylate.

intensity was observed upon complexation with D-glucuronate and D-galacturonate anions. Moderate enhancement was obtained with sialate and neutral monosaccharides D-fructose and D-galactose. The interaction between the complex and the uronic carboxylates produced an inhibition of the PET from the methylamine subunit to the photoexcited 1,10-phenanthroline fluorophore, inducing an enhancement in the emission intensity.

The $[Cu(\mathbf{79})]^{4+}$ complex formed a suitable cavity for citrate inclusion that is coordinated through the metal cation and the guanidinium groups (see Figure



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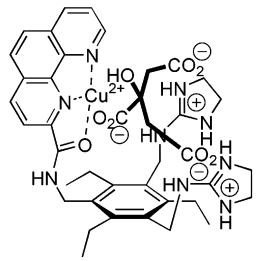
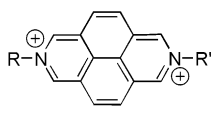


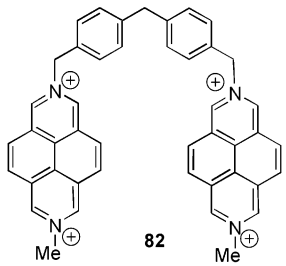
Figure 25. Structure proposed for the adduct formed between complex $[Cu(\mathbf{79})]^{4+}$ and citrate anion.

25).[116] The emission of $[Cu(\mathbf{79})]^{4+}$ increased dramatically upon addition of citrate. This emission enhancement could be attributed to a change in the oxidation−reduction potential of the metal upon citrate coordination, thus changing the extent of electron transfer from metal cation to the 1,10-phenanthroline fluorophore.

3.2.2.2. Containing Diazapyrenium or Phenanthridinium. Diazapyrenium derivatives show strong absorption bands centered at 300−380 nm that upon excitation give well-structured emission at ca. 440 nm. In aqueous solutions, the diazapyrenium cation buffered at pH 7.0 has a quantum yield of 0.63.[117] Phenanthridinium derivatives present strong absorption bands in the UV zone centered at 270−280 and 320−370 nm. Upon excitation at 320−370 nm, an intense fluorescence band centered at 400−520 nm is obtained.[118] The diazapyrenium and phenanthridinium derivatives **80**−**90** have been used as receptors for anions (especially nucleotides). These receptors are conceptually different to those described above in the sense that there are not binding sites and signaling units as separate entities but the diazapyrenium and phenanthridinium signaling subunits also act as anion binding sites as they are positively charged. In contrast with many examples shown above, studies with those fluogenic receptors have been carried out in aqueous environments. Receptors **80**−**90** were pioneers in the development of earlier fluorogenic chemosensors although studies on those compounds were not carried out specifically for sensing purposes but rather as a way to demonstrate their anion coordination ability. For instance, flat anions such as naphthalene-2,6-dicarboxylate caused a strong quenching of the emission intensity of the receptor **81** in water.[119] A small decrease in



80 R = R' = CH_3
81 R = CH_3, R' = $C_6H_5CH_2$



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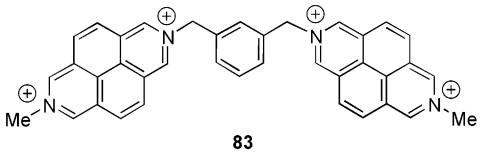

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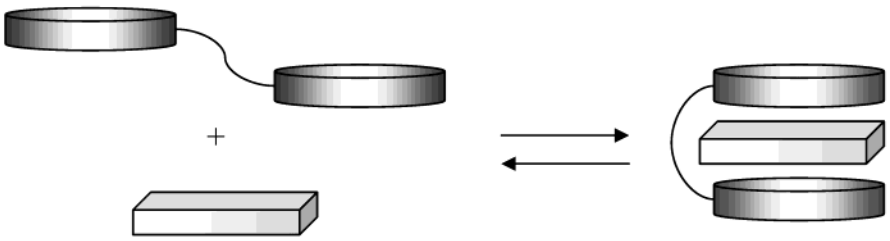
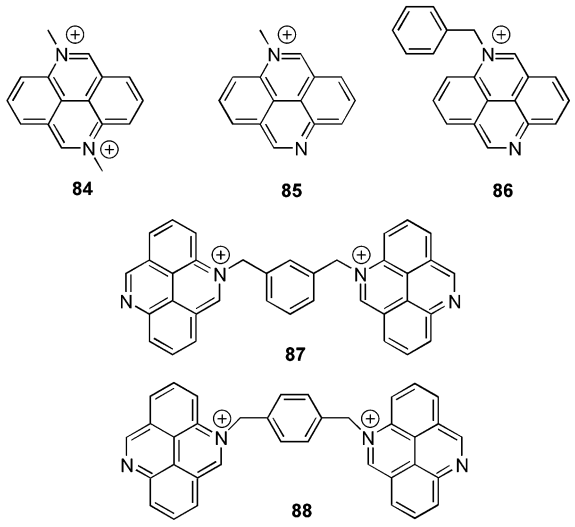


Figure 26. Schematic representation of the 1:1 adduct formed between receptor **83** and nucleotides.

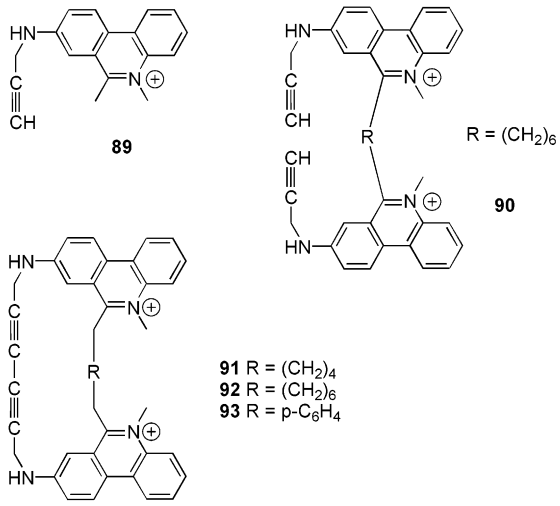
fluorescence emission was observed upon addition of adenide to solutions of receptor **82**.[119] Fluorescence of the diazapyrenium subunits in the receptor **83** was quenched also in water upon addition of nucleotides especially in the presence of ATP and ADP.[120] In these cases, 1:1 complexes were formed and the quenching was ascribed to π-stacking interactions between the diazapyrenium moieties of the receptors and the substrates as shown in Figure 26. Some other anions were also studied, and a wide range of behaviors were observed. Those leading-the-way studies also showed some examples with color changes. Thus, for instance, the addition of indole acetate to **80** caused a change in the color of the solutions from yellow to orange.[119] The absorption band also decreased in intensity and broadened toward longer wavelengths on addition of excess of naphthalene-2,6-dicarboxylate.

In similar studies, the interaction of a family of 4,9-diazapyrenium derivatives **84**−**88** with nucleotides

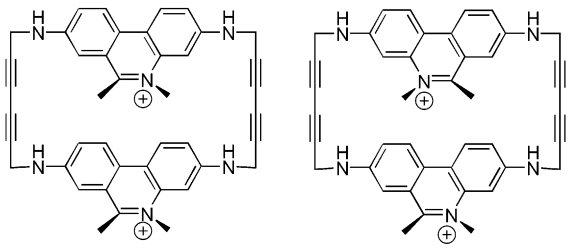


in buffered aqueous solutions at pH 5.0 was studied by means of fluorescence emission measurements.[121] The presence of nucleotides (AMP, ADP, ATP, GMP, and CMP) induced quenching of the fluorescence emission for all of the five receptors. This quenching was assigned to $\pi-\pi$-stacking interactions between the diazapyrenium system and the aromatic part of the nucleotides.

The **89**−**97** receptors containing phenanthridinium groups were also early chemosensors of anions. The phenanthridinium receptor **89** and the bis(phenanthridinium) receptors **90**−**93** suffered fluorescence emission quenching upon addition of increasing amounts of nucleotides (ATP, ADP, AMP, GMP,



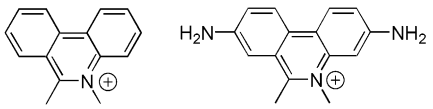
CMP, UMP, and TMP) in aqueous solution buffered at pH 6.[122] The quenching was ascribed to stacking interactions between the two phenanthridinium units and the inserted nucleic base part of the nucleotide. Macrocyclic receptors **94** and **95** containing two



positively charged phenanthridinium units and aminobisacetylenic bridges exhibited low fluorescence in aqueous solutions due to a NH proton transfer to water molecules in the excited state.[123] The addition of AMP induced a ca. 90% emission increase of both receptors. In contrast, the presence of GMP or UMP only induced a very slight emission change. This enhancement in emission intensity contrasted with the quenching of the emission intensity reported for other phenanthridinium cyclobisintercalands (**90**−**93**) upon nucleotide binding. The insertion of the electron rich purine base of AMP between positively charged units of **94** and **95** induced an increase in the emission intensity because the acidity of amino protons decreases and so does the rate of the proton transfer from the NH group to the water molecules.

The presence of all of the nucleotides tested (AMP, ADP, ATP, GMP, and CMP) in buffered aqueous solutions at pH 5.0 induced fluorescence quenching

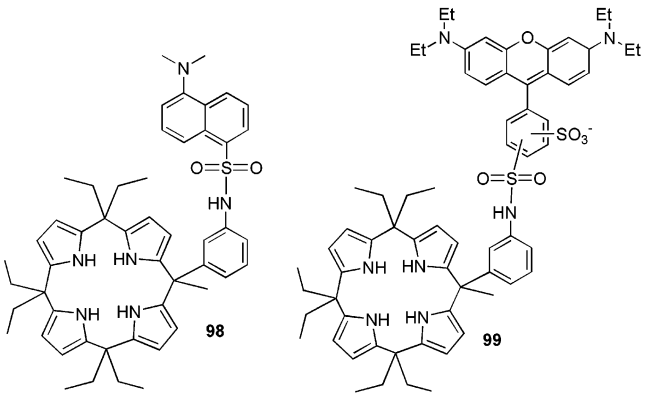
for receptor **96** and fluorescence emission enhancement for receptor **97**.[121] The quenching obtained in



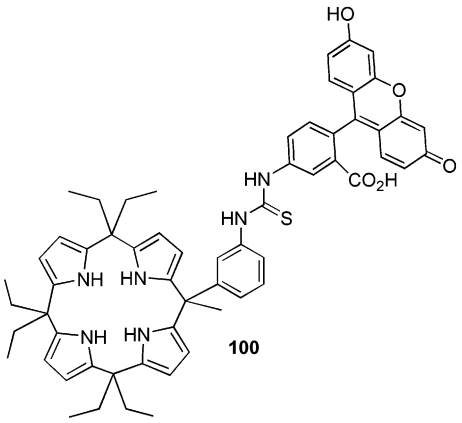
96 **97**

the presence of receptor **96** was ascribed to π-stacking interactions between the phenanthridinium system and the aromatic part of the nucleotides whereas the enhancement observed with receptor **97** was assigned to a suppression of the self-quenching (due to an amino proton transfer to water molecules in the excited state) on complexation with the nucleotide that neutralizes the positive charge of the phenanthridinium system.

3.2.2.3. Miscellaneous. One of the main disadvantages of the chemosensors described above using aromatic hydrocarbons or aromatic heterocycles such as acridines, diazapyrenium, or phenanthridinium is that absorption and emission occur near the UV that is a region where especially serious matrix interference can occur. To get around that problem, systems absorbing and emitting in the visible spectral region have been developed. Those generally involve the use of fluorescent dyes as signaling subunits. Several examples include compounds **98**−**105**. Thus, for instance, in compounds **98**, **99**, and **100**, calixpyrrole



98 **99**



100

units as anion binding sites were functionalized with dansyl, lissamine-rhodamine B, and fluorescein signaling fluorescent cores, respectively.[124] Compounds **98**−**100** contain spacers having sulfonamide and thiourea groups in order to provide additional hydrogen-bonding interactions with the anions (see Figure 27). Receptors **99** and **100** emitted especially in regions of clear analytical advantages (λ_{em} = 575 nm for **99** and λ_{em} = 525 nm for **100**). Anions tested include fluoride, chloride, dihydrogen phosphate, and hydrogen pyrophosphate in acetonitrile. The largest response (emission fluorescence quenching of **98**−**100**) was found for fluoride.

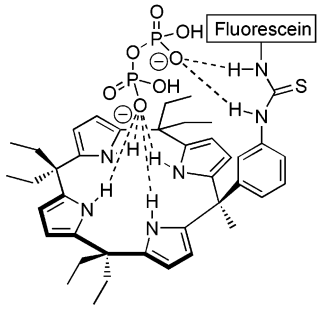
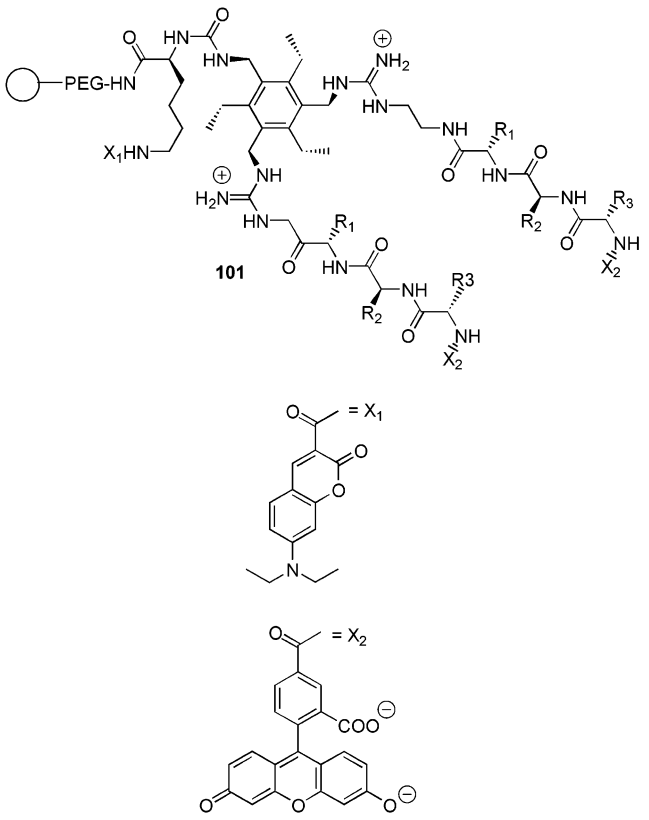


Figure 27. Schematic representation of the proposed multiple hydrogen-bonding interactions between pyrophosphate and **100** that accounts for the high pyophosphate affinity of this receptor.

An interesting applied example designed for sensing AMP was based on a fluorescence resonance energy transfer between fluorescein and rhodamine.[125] The sensor consisted of cAMP-dependent protein kinase in which the catalytic (C) and the regulatory (R) subunits were labeled with fluorescein and rhodamine, respectively. These two dyes were able to give fluorescence resonance energy transfer in the R_2C_2 complex. In this complex, excitation of the fluorescein results in a characteristic emission of the rhodamine at 580 nm. When AMP bound to the regulatory subunits, the C units dissociated, thereby eliminating the energy transfer between dyes. Then, excitation of the fluorescein gave a characteristic fluorescein emission at 520 nm and not at 580 nm (characteristic of the rhodamine). This effect was used to signal cAMP and the activation of the kinase in single living cells.

Receptor **101** was created by combinatorial chemistry to obtain an ATP selective chemosensor.[126] This receptor was composed of a benzene scaffold coupled with two guanidinium functions and two tripeptide arms. Two fluorescent dyes were attached to the structure in order to transduce the binding event in a measurable signal. Finally, all of the system was bound to a resin. Among all tripeptides studied, Ser-Tyr-Ser was the one that displayed the best selectivity and sensitivity toward ATP. This sensor distinguishes between ATP, AMP, and GTP because only the presence of ATP induced a 1.5-fold increase in fluorescence emission upon binding (studies performed in water at pH 7.4). With the combinatorial library of sensors, that allowed to obtain receptor **101** and an indicator displacement assay, an array of sensors was used for the discrimination of structurally similar AMP, GTP, and ATP analytes using pattern recognition algorithms.[127]

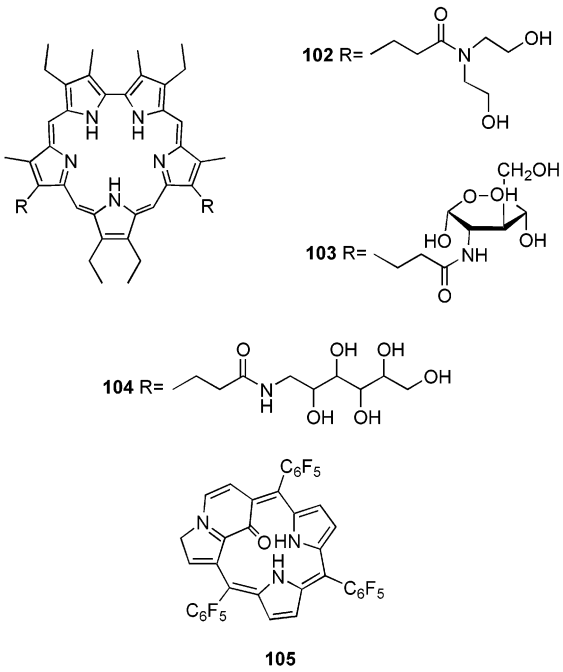
Three mutant PH domains (PH56, PH58, and PH106) were constructed by polymerase chain reaction-based site-directed mutagenesis from rat PLCδ_1. Four fluorophores, 5-iodoacetamidofluorescein (5F),



6-iodoacetamidofluorescein (6F), 6-bromoacetyl-2-dimethyl-aminonaphthalene (DAN), and 2-[4′-(2″-iodoacetamido)phenyl]aminonaphthalene-6-sulfonic acid, were attached at thiol groups present in the PH domains to gave 12 different fluorophore-labeled PH domains.[128] Each fluorophore-labeled PH domain was tested for IP_3 (D-myo-inositol-1,4,5-tris-phosphate is an intracellular second messenger that controls the cellular Ca^{2+} concentration) binding by monitoring changes in fluorescence emission spectra. 6F106 showed an increase in the intensity of fluorescence emission upon addition of IP_3. DAN56 and DAN106 gave quenching of the emission intensity upon addition of IP_3, and the emission maxima were shifted from 490 to 535 nm and from 502 to 525 nm, respectively. All PH58 derivatives and 5F and 6F derivatives of PH56 showed poor spectral changes in response to the concentration of IP_3. The affinity of sensors to IP_3 varied with both the labeled position and the fluorophore.

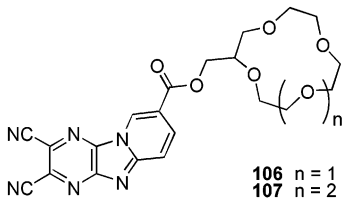
Other examples of receptors absorbing and emitting in the visible spectrum were **102**−**104** and **105**. Thus, the water soluble sapphyrins **102**−**104** were highly aggregated and nonfluorescent at neutral pH.[129] Addition of phosphate solutions enhanced substantially the fluorescence of sapphyrins (water, pH 7.0, $\lambda_{exc} = 450$ nm). These sapphyrins are relatively noncytotoxic and localize well to tumors in models, so it was suggested that those systems may be useful as biological phosphate sensors.

On the other hand, the oxyindolophyrin **105** was capable of binding fluoride via hydrogen-bonding interactions with the inner pyrrolic NH. The UV−visible absorption spectrum of **105** changed slightly upon addition of the anion fluoride (the Soret band at 425 nm was shifted to 431 nm in $CHCl_3$).[130] The



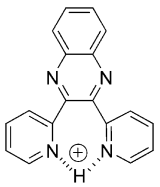
most pronounced changes were obtained in the emission band centered at 631 nm (in $CHCl_3$, $\lambda_{exc} = 425$ nm) that was quenched upon addition of increasing amounts of fluoride anion. These anion binding properties of **105** were specific for fluoride, as other halide anions such as chloride, bromide, and iodide did not cause any remarkable spectral change.

The remaining examples in this section are chemosensors that use particular ultraviolet region absorbing fluorophores. For instance, although **106** and **107**



compounds did not respond by themselves to anions, their Ca^{2+} and Ba^{2+} complexes act as thiocyanate chemosensors in acetonitrile (the fluorescence at 487 nm was dramatically quenched due to a photoelectron transfer from the thiocyanate anion to the excited pyridoimidazopyrazine ring).[131] The quenching was not observed upon perchlorate addition. PM_3 calculations were in agreement with the experimental quenching found for thiocyanate and not for perchlorate.

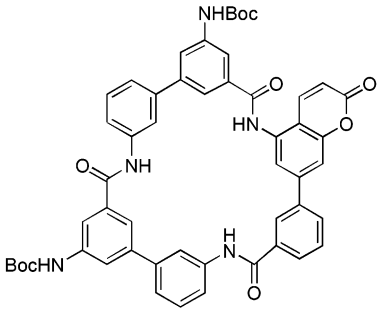
The luminescence of receptor **108** (acetonitrile solutions, $\lambda_{exc} = 332$ nm, $\lambda_{em} = 454$ nm) was quenched



upon addition of small amounts of fluoride, chloride, and dihydrogen phosphate, whereas bromide, iodide,

and hexafluorophosphate gave no response.[132] Anion affinity constants in acetonitrile were determined and followed the order $H_2PO_4^- = F^- > Cl^- \gg Br^- > I^- > PF_6^-$. Quenching was attributed to changes in the conformation of the quinoxaline chromophore upon hydrogen-bonding anion coordination that resulted in fluorescence quenching.

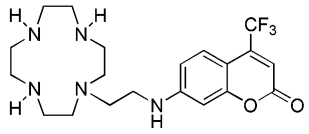
Receptor **109** showed an emission band centered at 430 nm (λ_{exc} = 320 nm, 1:1 DMSO/1,4-dioxane)



109

from an internal CT excited state due to a transfer of negative charge from the nitrogen atom to the coumarine ring.[133] In the presence of $H_2PO_4^-$, an increase in fluorescence intensity and a red shift (10−20 nm) of the CT band was observed and a new band at 560 nm appeared. The intensity enhancement of the band centered at 430 nm may be a consequence of a restriction in the conformational flexibility (rigidity effect). The new band was ascribed to an emission from an ESPT. This excited state involved a proton transfer from the fluorophore excited state to the bound anion, opening a second emission channel. The maximum intensity for the ESPT band was found for the most basic $H_2PO_4^-$ anion, the band intensity was modest for the anion $PhHPO_3^-$, and the band was absent in the presence of the less basic anions such as *p*-TsO^- (*p*-toluensulfonate anion) and Cl^-.

The Cd(II) complex of receptor **110**, [Cd(**110**)]$^{2+}$, acted as an anion chemosensor in aqueous neutral



110

solutions (pH 7.4).[134] Cd(II) was coordinated by the four nitrogen atoms of cyclen and by the aromatic amino group of coumarin. When anions were added to solutions of [Cd(**110**)]$^{2+}$, the aromatic amino group of coumarin was displaced causing changes in its fluorescence spectrum (see Figure 28). While pyrophosphate and citrate anions were detected with high sensitivity, fluoride and perchlorate induced no response. Four nucleotide monophosphates, AMP, GMP, CMP, and UMP, were added to solutions of [Cd(**110**)]$^{2+}$. GMP caused fluorescence quenching (ascribed to PET), whereas the other nucleotides caused red shift of the fluorescence band (this effect was most noticeable for AMP; shift of 40 nm, from 340 to 380 nm). On the basis of the fact that addition of

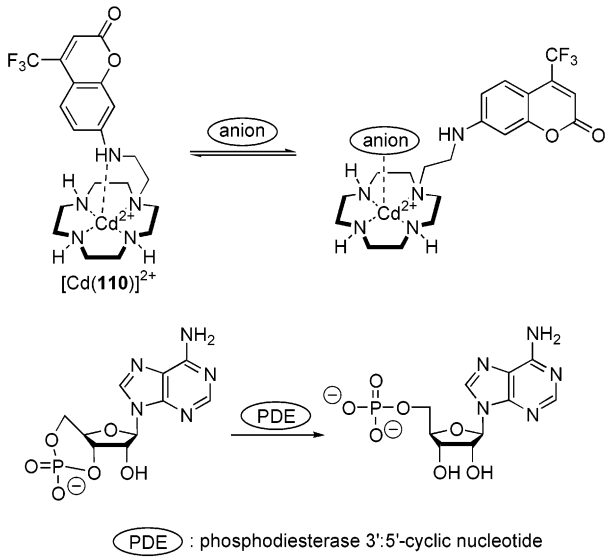
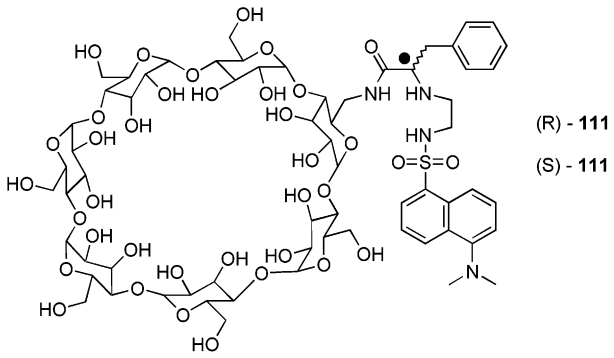


Figure 28. Strucutre of the complex [Cd(**110**)]$^{2+}$ and its interaction with certain anions. This interaction induced the displacement of the aromatic amino group of the coumarin from the metal center and triggers a change in the emission intensity. Also shown is the conversion of cAMP to AMP catalyzed by PDE.

cAMP scarcely changed the fluorescence spectrum of [Cd(**110**)]$^{2+}$, real-time detection of phosphodiesterase 3′:5′-cyclic mononucleotide activity was achieved. This phosphodiesterase catalyzes the conversion of cAMP to AMP. Monitoring the fluorescence increase at 380 nm (band due to the presence of AMP), the activity of this enzyme was detected in real-time.

(*R*)-**111** and (*S*)-**111** receptors were able to discriminate between certain D,L-amino acids. The fluo-



rescence emission of the (*R*)-**111** and (*S*)-**111** dansyl functionalized cyclodextrins (*R* and *S* forms) was quenched upon addition of Cu^{2+} in aqueous solutions at pH 7.3.[135] The two **111** receptors and the Cu^{2+} cation formed 1:1 complexes with the copper coordinated by the amino, amide, and sulfonamide groups. An increase in the fluorescence emission intensity was observed on addition of D- and L-amino acids to these complexes. The complex Cu−(*S*)-**111** showed better discriminating properties than Cu−(*R*)-**111**, being the larger enantioselectivity for D-proline vs L-proline with Cu−(*S*)-**111**. Complex Cu−(*R*)-**111** showed the reverse enantioselectivity because L-proline induced a more pronounced emission enhancement than D-proline. Another significant enantiomeric differentiation was observed for L-phe with

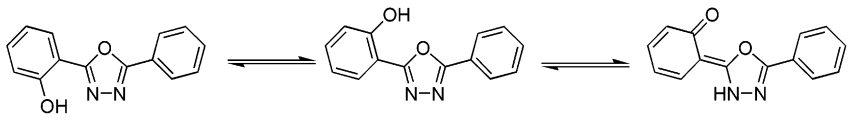
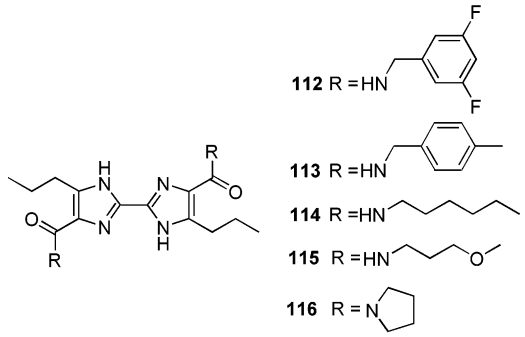


Figure 29. Scheme showing the equilibriums involved in the formation of rotamer (I) and the tautomer (II) forms of receptor **117**.

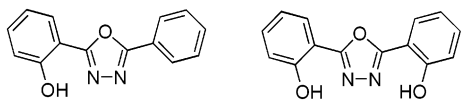
the Cu−(*S*)-**111** complex. The enantioselectivity in the fluorescence enhancement was ascribed to the formation of ternary cyclodextrin:Cu^{2+}:amino acid complexes of different stabilities, but the sensing mechanism was still unclear.

The emission intensity of the biimidazolate diamides **112**−**116** was quenched in the presence of



$H_2PO_4^-$ and Cl^- in dichlorometane solutions (λ_{exc} = 300 nm, λ_{em} = 340 nm).[136] For all **113**−**115** receptors, the presence of $H_2PO_4^-$ induced a larger quenching (for instance, ca. 40% of the initial fluorescence upon addition of 75 equivalents for **113**) than chloride. This was in line with the fact that receptors **113**−**115** formed stronger complexes with $H_2PO_4^-$ than with Cl^-. The coordination of the receptors with these anions came from hydrogen-bonding interactions between the N−H groups of the amide and the imidazole subunits with the corresponding anion.

Receptors **117** and **118** show dual fluorescence in DMF solutions.[137] Upon excitation at 286 nm, the



117 **118**

emission spectrum of receptor **117** was characterized by two bands centered at 354 and 448 nm and ascribed to the forms I and II, respectively (see Figure 29). Similar bands were observed with solutions of receptor **118** (upon excitation at 287 nm, two bands at 365 and 436 nm appeared). Addition of $H_2PO_4^-$ and F^- anions to solutions of receptor **117** in DMF led to strong quenching of the emission band at 448 nm and, simultaneously, enhancement of the emission band at 354 nm. That was attributed to the formation of intermolecular hydrogen bonds between the anions and **117** that shifted the equilibrium from the tautomeric form II to I. In the presence of an excess of $H_2PO_4^-$ and F^- anions (100 equivalents), a new weak emission band centered at 525 nm appeared. This long wavelength emission should be the result of an intramolecular CT between the donor phenolate group and the acceptor 1,3,4-oxadiazole group due to the phenol deprotonation induced by the anion excess. For receptor **118**, only an excess of $H_2PO_4^-$ was capable of inducing the apparition of the CT band centered at 525 nm and this was capable of distinguishing $H_2PO_4^-$ from F^-. Additionally, DMF solutions of both receptors change color from colorless (λ_{max} = 286 nm) to yellow (λ_{max} = 400 nm) upon addition of an excess (0.5 mM) of $H_2PO_4^-$ and F^- anions.

The boradiazaindacene-substituted bipyridyl receptor **119** forms a weakly fluorescent complex with Zn(II).[138] Whereas the boradiazaindacene−bipyridyl ligand is fluorescent, the Zn(II) complex is weakly emissive due to a photoelectron transfer process from the excited fluorophore to the metal-complexed bipyridyl group. Upon addition of anions (F^-, Cl^-, Br^-, HPO_4^{2-}, and AcO^-) to acetonitrile solutions of complex [Zn(**119**)]$^{2+}$, a significant enhancement in the emission intensity (λ_{exc} = 490 nm, λ_{em} = 518 nm) was obtained (the most remarkable enhancement (25-fold) upon addition of HPO_4^{2-}) due to the inhibition of the oxidative PET process upon anion coordination to the metal center (see Figure 30). Anion coordination would partially neutralize the charge on the metal center making the oxidative electron transfer process thermodynamically unfavorable.

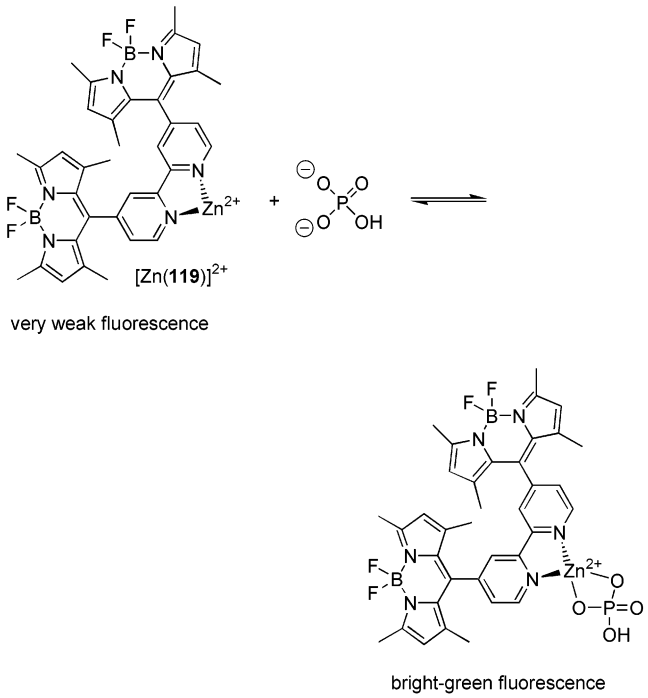
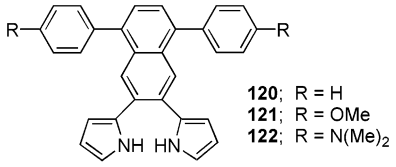


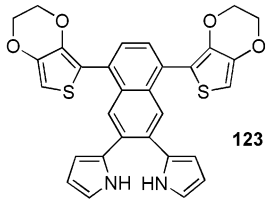
Figure 30. Complexation mode proposed for the binding between complex [Zn(**119**)]$^{2+}$ and phosphate anion.

5,8-Aryl quinoxalines **120**−**123** were suitable fluorescent anion sensors in organic solvents.[139] A dramatic quenching of the fluorescence emission (>95%)

was observed for all of the receptors (dichloromethane solutions) on addition of pyrophosphate and fluoride anions, whereas addition of chloride, bromide, dihydrogenphosphate, and hydrogensulfate did not induce any emission intensity variation (λ_{em} = 500, 502, 590, and 610 nm for **120**, **121**, **122**, and **123**, respectively). The stability constant (for 1:1 stoichiometry complex) found with pyrophosphate was larger than that with fluoride. Addition of fluoride and pyrophosphate anions to dichloromethane solutions of the receptors also induced changes in the UV−visible spectrum because the band in the region of 400−450 nm decreases concomitantly with the apparition of a new band centered at 500−550 nm (color variation from yellow to red).



120; R = H
121; R = OMe
122; R = $N(Me)_2$



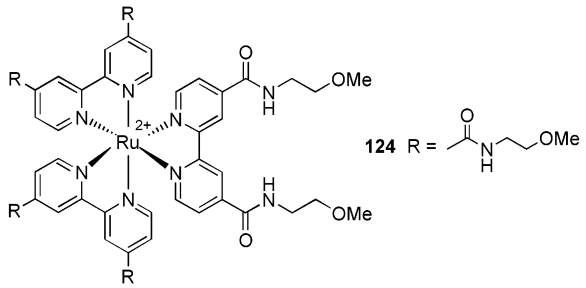
123

3.2.3. Fluorescent Sensors Based on Ruthenium, Iridium, Osmium, and Rhenium Complexes

Among metal-based luminescent systems, the complexes of ruthenium, osmium, and rhenium are very well-known. It is not then surprising that there are a number of chemosensors for anions in which these complexes act as signaling subunits. One attractive feature of these metal-based complexes is that they emit at larger wavelengths, which is a characteristic of clear analytical advantages. As a drawback for their potential application, most of the studies have only been carried out in nonaqueous solvents.

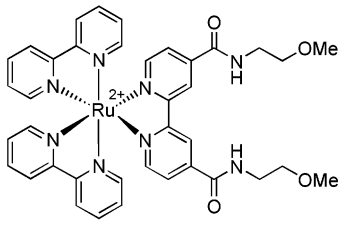
3.2.3.1. Containing $Ru(bipy)_3^{2+}$ Units. The $Ru(bipy)_3^{2+}$ moiety has been the signaling subunit most widely used in the development of fluorogenic anion sensors bearing metal-based fluorescent subunits. The photochemistry of the $Ru(bipy)_3^{2+}$ groups is very well-known. This system shows several absorptions of which the one with the largest wavelength is a metal-to-ligand charge transfer (MLCT) band at ca. 456 nm. Excitation to this band gave emission at ca. 607 nm. Changes in that emission upon addition of anions have been used as output signals for anion sensing, and several coordination sites have been covalently attached to the $Ru(bipy)_3^{2+}$ core. It is also interesting to note that some of those receptors can also recognize electrochemically the presence of anions.[17,18]

In many of the chemosensors studied bearing the $Ru(bipy)_3^{2+}$ core, an emission enhancement was usually observed upon anion binding and attributed to rigidity that adopts the supramolecular anion complex in contrast with the free receptor that lacks structural rigidity. It is argued that the structural rigidity decreases the probability of nonradiative decay and therefore could enhance the quantum yield and the emission intensity. This effect can be seen for instance in compound **124**.[140] The emission peaks



for this receptor showed blue shifts and a significant increase in intensity upon chloride and bromide binding in acetonitrile (λ_{exc} = 464 nm, λ_{em} = 625 nm). The authors suggested that in the uncomplexed form of **124**, the anion coordination amide sites on the bipyridine group were free to rotate, and this lack of structural rigidity increased the chance of nonradiative decay. On complexation, the halide anion was bound by the amide. That imposed a restriction in the rotation, leading to higher quantum yields. Addition of 2.5 equivalents of $H_2PO_4^-$ to solutions of receptor **124** also induced an emission enhancement (1.6-fold) ascribed to structural rigidity upon complexation; however, further addition of $H_2PO_4^-$ caused a reduction in the emission intensity.

A number of compounds (**125**−**145**) have been designed also to contain amides as anion binding sites and $Ru(bipy)_3^{2+}$ cores as signaling units. For instance, **125** and **126** contain two simple amide



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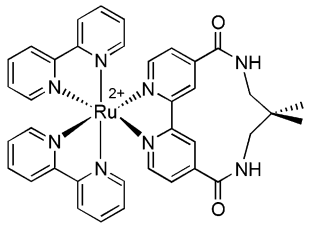
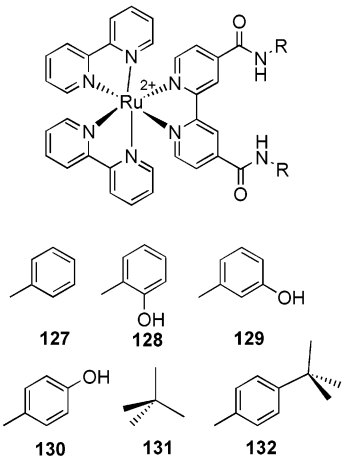


126

groups anchored to a bipyridine fragment.[141] The absorption band intensity was remarkably reduced in the presence of $H_2PO_4^-$ for both receptors **125** and **126** in DMSO solutions. The dihydrogen phosphate anion coordinated via hydrogen bonds to the amide moieties present in both receptors. Fluorescence emission increased in the presence of $H_2PO_4^-$ for receptor **125** with a maximum enhancement factor of 2.6 upon addition of 2.5 equivalents of the anion. The chloride anion provided a much smaller effect.

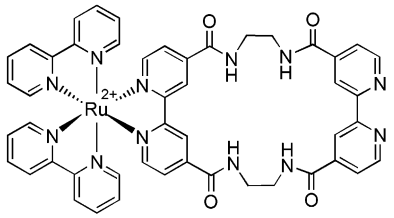
The emission intensity of the more rigid receptor **126** remained unchanged upon addition of either $H_2PO_4^-$ or Cl^- anions. The enhancement in the emission fluorescence of **125** was attributed to rigidity upon complexation as explained above.

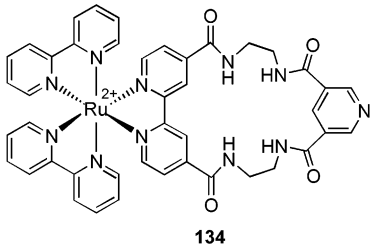
Receptors **127**−**132** were similar to **125** and **126**, but they contained aromatic moieties and their



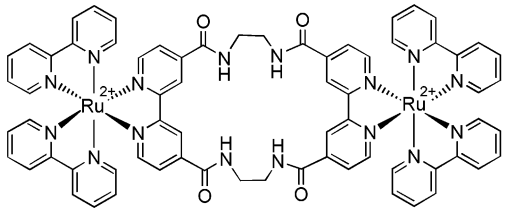
emission behavior was studied in acetonitrile in the presence of halide anions.[142] The receptors coordinated anions via hydrogen bonds with the amide protons. Additionally, for **128**−**130**, the presence of *m*- and *p*-substituted phenols significantly enhanced the strength of anion−receptor complexation via additional hydrogen-bonding interactions. All of the receptors exhibited MLCT emission in the range of 630−650 nm. Chloride or bromide anions induced emission intensity increases. For instance, a 42% increase was observed for **131** with a hypsochromic shift of 8 nm upon chloride addition. This effect was attributed to a rigidity effect. In contrast, iodide causes an emission intensity decrease for all receptors and attributed to a heavy atom effect.

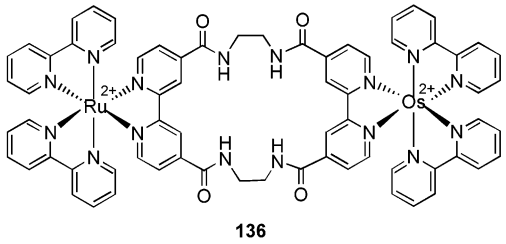
Similar compounds with amides are **133**−**136**.[143] Addition of chloride to acetonitrile solutions of these compounds (λ_{em} = 658 for **133**, **134**, and **135** and 783



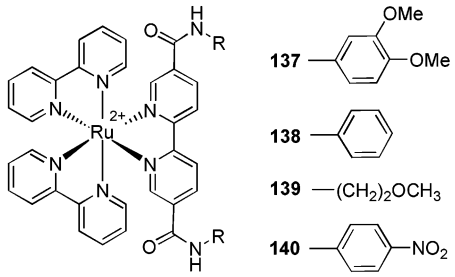


for **136**) resulted in a slight blue shift (5−10 nm) and a marked enhancement of the emission intensity (ca. 30% for **135** and **136**). Chloride formed 1:1 adducts with all of the receptors. The intensity enhancement of the luminescence emission was again explained by the formation of a receptor−anion complex that increased the rigidity of the receptor.



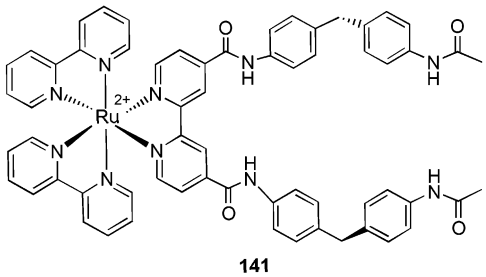


The emission behavior of **137**−**139** was studied in acetonitrile in the presence of chloride and bromide



(λ_{exc} = 428 nm for **137**; 436 nm for **138** and 444 nm for **139**; λ_{em} = 686 nm for **137**, 684 nm for **138**, and 681 nm for **139**), and significant quenching of the emission band was observed.[144] The largest effect was observed when using receptor **137** in the presence of chloride and bromide (10 equivalents) with a percentage of quenching of 24 and 28%, respectively. All of these effects were not observed upon addition of halides to $Ru(bipy)_3^{2+}$. The intensity of the MLCT absorption band was not affected upon addition of anions except for **140** for which an excess of chloride resulted in an increase of the intensity of this band.

Receptor **141** in DMSO solutions showed an interesting behavior as it was capable of optically sensing



the presence of aromatic, linear, and cyclic dicarboxylates by changes in the emission band.[145] The most important results were found with certain cyclic

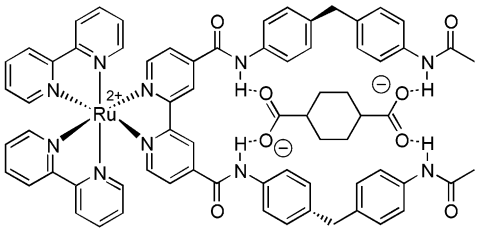
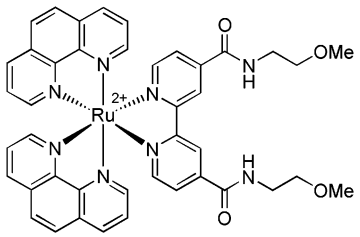


Figure 31. Proposed structure of the complex formed between receptor **141** and 1,4-cyclohexane dicarboxylate via formation of four hydrogen bonds between the carboxylates and the amide moieties in **141**.

dicarboxylates. Thus, addition of *trans*-1,4-cyclohexane dicarboxylate resulted in an enhancement of the emission intensity, whereas the same band diminished upon addition of the cis isomer. The formation of a 1:1 complex between receptor **141** and *trans*-1,4-cyclohexanedicarboxylate induced rigidity of the receptor structure thereby inducing intensity enhancement of the emission band (see Figure 31). In contrast, the authors suggested that the receptor conformation induced by *cis*-1,4-cyclohexanedicarboxylate might open nonradiation decay channels via vibrational relaxation. Addition of iso- or terephthalate resulted in a slight blue shift of the emission band and a marked increase in intensity. Analogous enhancements in fluorescence intensity were obtained with the addition of the linear carboxylates adipate and pimelate.

Receptor **142** was similar to **125** but two bipyridine subunits were replaced by two phenanthrolines.[146]



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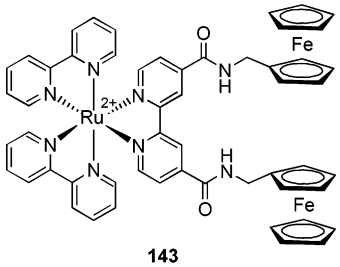
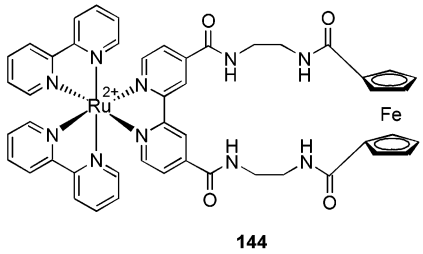


143

Addition of $H_2PO_4^-$ to acetonitrile solutions of receptor **142** induced a significant decrease in the absorption maximum at 263 nm and an increase in the emission intensity ($\lambda_{exc} = 480$ nm, $\lambda_{em} = 648$ nm). This emission enhancement was ascribed to an increase in rigidity of the ligand upon coordination to $H_2PO_4^-$ by a hydrogen-bonding interaction with the amide groups of the receptor.

Ruthenium derivatives containing quenchers such as ferrocene follow an appealing approach to anion sensing. It is well-known that the redox character of the ferrocene can induce quenching of the emission intensity of the $Ru(bipy)_3^{2+}$ core. The design idea in those receptors is that coordination of anionic species may alter the interaction between the $Ru(bipy)_3^{2+}$ excited core and the ferrocene, therefore inducing emission enhancement. For instance, the emission of **143** was completely quenched by the ferrocene moieties via an intramolecular mechanism.[147] Addition of chloride or hydrogen sulfate to acetonitrile solutions of **143** did not induce any emission change, whereas addition of dihydrogen phosphate resulted in a 20-fold increase in emission intensity at 690 nm (assigned to the formation of an excimer) and a smaller increase at 640 nm (usual emission region). Intensity profiles of fluorescence titrations showed formation of 2:1 complexes. In a similar manner, the emission of **144** and **145** (λ_{em} = 636, 638 nm,



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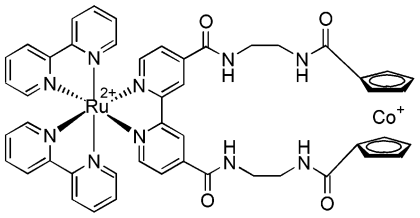
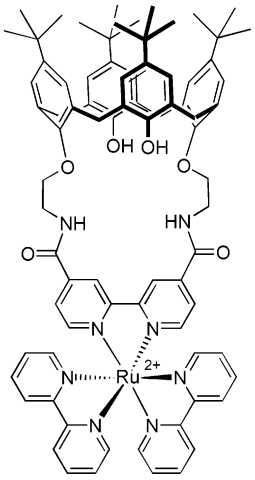


145

respectively) was somehow quenched by the presence of the metallocene moieties.[148] The presence of two new amide moieties and only one metallocene subunit in the structure of receptors **144** and **145** (when compared to **143**) moved their response toward chloride in acetonitrile solutions resulting in a blue shift of the fluorescence emission (ca. 6 nm) and in a remarkable emission intensity enhancement, whereas the presence of $H_2PO_4^-$ resulted in no change. This different selectivity observed with **143** ($H_2PO_4^-$), **144**, and **145** (Cl^-) may be assigned to the presence of a preorganized cavity capable of accommodating spherical anions such as Cl^- in receptors **144** and **145**, whereas the absence of this cavity in **143** resulted in a more flexible receptor that interacts selectively with $H_2PO_4^-$. The observed increase in emission intensity upon anion coordination for receptors **143**−**145** was assigned to a reduction in the energy transfer rate constant upon coordination with chloride anion, indicating a decrease of the electronic interaction between the excited $Ru(bipy)_3^{2+}$ moiety and the appended quencher.

The amide-containing compounds **146**, **147**, **148**, and **149** also contain other potential binding sites such as calixarenes, but they showed a close sensing behavior to that observed for the parent amide containing receptors shown above. Addition of $H_2PO_4^-$ to receptor **146** in DMSO produced a significant



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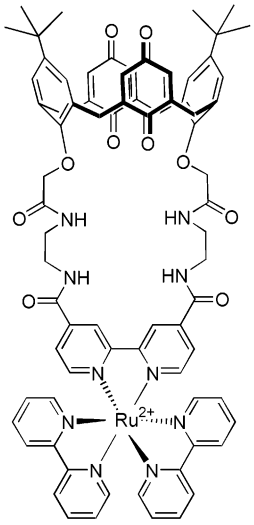

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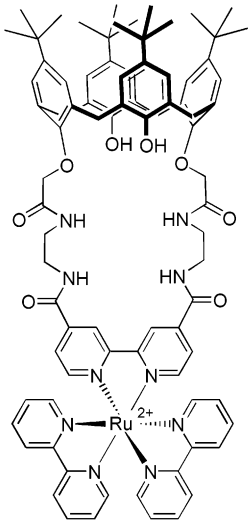

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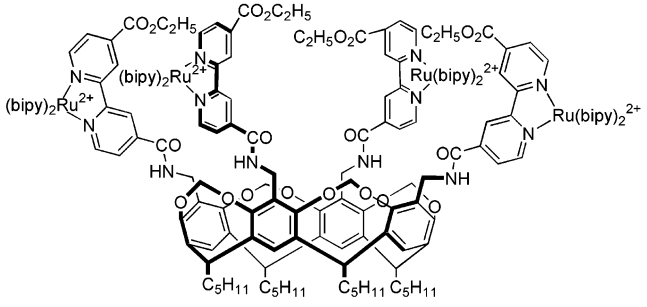
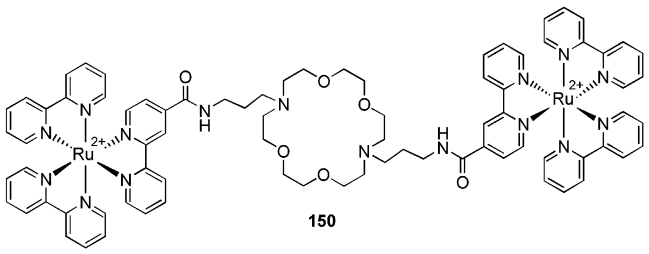


149

increase in the intensity of the MLCT absorption band and an enhancement of the luminescence emission.[141] The dihydrogen phosphate anion was coordinated via hydrogen bonds to the amide and to the calixarene hydroxyl groups, restricting the receptor mobility and therefore resulting in emission enhancement. Receptors **147** and **148** are calix[4]diquinone and calix[4]arene derivatives, respectively, that formed significant strong anion complexes with acetate and chloride and weaker complexes with dihydrogen phosphate.[149] As in **146**, the calixarene or calixdiquinone subunits in conjunction with the $Ru(bipy)_3^{2+}$ center were used to form a cavity in which the bound anion acquires a high thermodynamic stability. The addition of acetate and chloride was found to dramatically affect the luminescence spectrum of all of the receptors in DMSO, and whereas **148** exhibited an emission decrease, acetate addition to acetonitrile solutions of **147** caused a very remarkable intensity increase up to 500%. An also notable 60% emission intensity enhancement was observed for **147** upon chloride addition. It is well-documented that quinones efficiently quench the luminescence emission of the $Ru(bipy)_3^{2+}$ via an oxidative intramolecular electron transfer mechanism. The anion-induced enhancement of the luminescence intensity observed in the case of receptor **147** was related with the decrease of the electron transfer rate constant between the $Ru(bipy)_3^{2+}$ and the quinone due to the formation of a complex that decreased the interaction between the ruthenium center and the quinone moieties. In the case of Cl^- with **148**, the intensity decrease was in line with the decrease in emission lifetime suggesting that the coordination of anions favored nonradiative decay processes.

Addition of acetate, chloride, and benzoate on acetonitrile solutions of **149** ($\lambda_{ex} = 463$ nm, $\lambda_{em} = 636$ nm) resulted in an increase of the fluorescence emission of about 15, 13, and 11%, respectively.[150] This anion-induced enhancement was again explained by an increase of the rigidity upon formation of the receptor−anion complexes by means of hydrogen-bonding interactions between the amide groups and the anions.

Receptor **150** exhibits an MLCT band centered at 452 nm in its UV−visible spectrum.[151] Excitation on

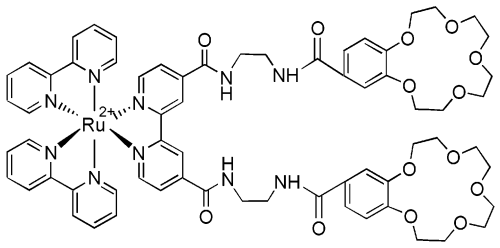


150

this MLCT band produced the typical luminescence MLCT emission centered at 650 nm. The addition of chloride induced a significant enhancement in emission intensity that was attributed to a higher degree of rigidity upon formation of 1:2 (receptor:chloride) complexes. This anion−receptor complex was formed through hydrogen-bonding interactions between the chloride and the amide moieties in the receptor. The same intensity enhancement was obtained with the addition of chloride to solutions of receptor **150** containing potassium cations, although in the presence of potassium the stability constant of the complex formed between receptor **150** and chloride was enhanced.

Addition of Cl^- and $H_2PO_4^-$ to acetonitrile solutions of receptor **151** caused a significant increase of up to 140% in luminescence intensity of the MLCT emission band ($\lambda_{max} = 640$ nm) with a concomitant hypsochromic shift of 7 nm.[152] RMN−^{1}H studies indicated that the amide groups were the sites for anion binding via hydrogen-bonding interactions. In

the presence of one equivalent of K^+, the subsequent addition of $H_2PO_4^-$ had very little effect on either the



151

emission intensity or the position of the maximum. In contrast with Cl^-, a significant enhancement of the emission intensity was observed. This preference for Cl^- over $H_2PO_4^-$ was explained in terms of formation of the 1:1 bis-benzo-15-crown-5-potassium cation intramolecular sandwich complex (see Figure 32) that resulted in the formation of a pseudo-macrocyclic preorganized structure, which enhanced Cl^- recognition but disfavored $H_2PO_4^-$ binding.

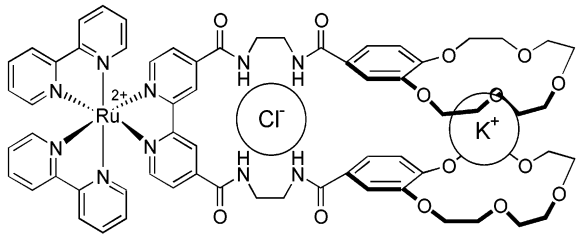
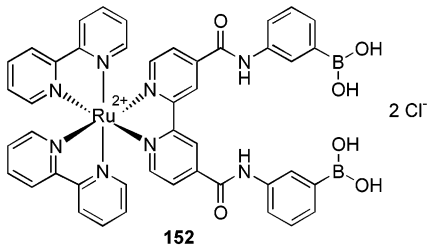


Figure 32. Coordination of receptor **151** with K^+ cation induced a pseudo-macrocyclic preorganized structure with a cavity adequate to incorporate one Cl^- anion.

Receptor **152** combines the presence of amides and boronic acids as binding sites and proved to be a



152

suitable chemosensor for phosphorylated sugars.[153] Compound **152** exhibited the optical properties expected for a ruthenium(II) bipyridyl derivative with the MLCT absorption band centered at 479 nm. The emission intensity of the receptor (λ_{em} = 637 nm) increased in the presence of phosphorylated sugars with fructose-6-phosphate producing the largest enhancement; 1:1 complexes were formed. An explanation for this effect involved an induced fit mechanism, where a phosphate anion bridges the amide group and preorganizes the two pendant boronic acids in a manner that they form bonds with the sugar moiety (see Figure 33). Evidence of this mechanism was obtained from mass spectra analysis.

Compounds **153**−**156** showed a maximum in the emission intensity at pH 5.5. Addition of KH_2PO_4 and Na_2H_2ATP salts to buffered aqueous solutions of **153**−**156** at pH 6 resulted in a partial quenching up

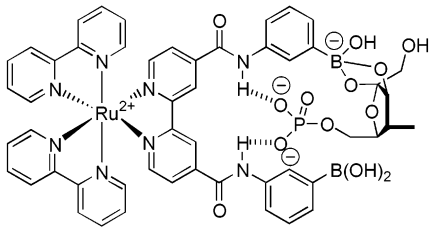
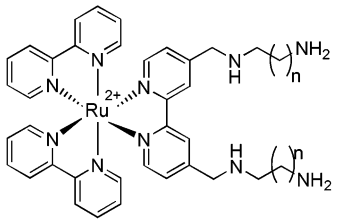
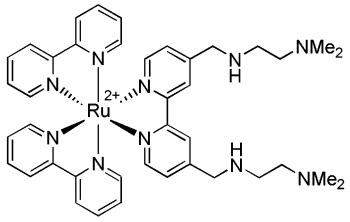


Figure 33. Heteroditopic binding of fructose-6-phosphate by receptor **152**. The saccharide subunit interacts with the receptor through the boronic acid units, whereas the phosphate group forms hydrogen bonds with the amides.

to 15% of the luminescence.[154] Complexes were formed via hydrogen bonding and electrostatic interactions between the protonated amines of the receptor and the correspondent anion. This result was rather different from that shown by ruthenium(II) bipyridyl amide systems that exhibited emission intensity enhancement response to chloride and dihydrogen phosphate anions in DMSO and acetonitrile solutions (for instance, **124**, **128**−**130**, **133**−**136**, and **142**). As the authors suggested, further photophysical investigations are probably needed to determine the nature of the quenching induced upon coordination.

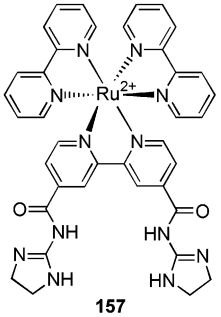


n = 1, **153**
n = 2, **154**
n = 3, **155**



156

Optical sensing of phosphodiesters was demonstrated by means of the luminescent response of **157**.[155] This receptor contains two neutral acylaminoimidazoline binding sites that allowed complexation with phosphodiesters via hydrogen-bonding



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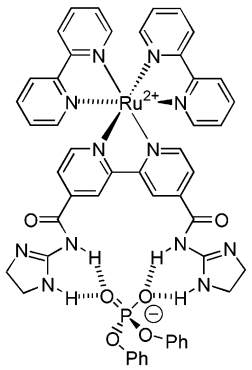
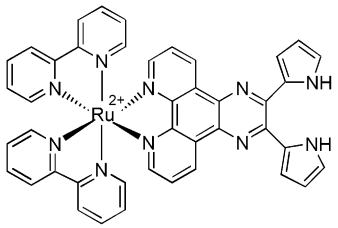


Figure 34. Proposed structures for a 1:1 complex between receptor **157** and diphenyl phosphate.

interactions (see Figure 34). Addition of 10 equivalents of dibenzyl hydrogen phosphate to solutions of **157** in acetone resulted in a 32% reduction of the luminescence intensity that was attributed to intracomplex proton transfer from the dibenzyl hydrogen phosphate to **157**. In contrast, upon addition of 10 equivalents of tetraethylammonium diphenyl phosphate (which do not have a labile proton adequate to give intracomplex proton transfer), a 27% luminescence emission enhancement was observed and attributed to the formation of a rigid complex that reduced the probability of modes of nonradiative decay.

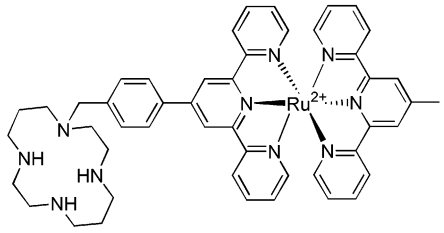
Compound **158** combines the luminescence properties of Ru(II) compounds with the capability of 2,3-



158

di(1*H*-2-pyrrolyl)quinoxalines to form hydrogen bonds with anions.[156] Addition of fluoride, cyanide, and phosphate (in lesser extent) caused a decrease in the MLCT absorption band (centered at 450 nm) with the parallel appearance of a new absorption centered at 530 nm. This new absorption grew in intensity concomitantly with increasing the anion concentration and was a result of anion binding with **158** through the pyrrolylquinoxaline moieties. The MLCT emission band of receptor **158** centered at 594 nm was red-shifted to 610 nm and quenched upon addition of cyanide and fluoride (λ_{exc} = 493 nm in $CH_2Cl_2-CH_3CN$ 98:2 mixtures) and to lesser extension upon addition of chloride and dihydrogen phosphate. This red shift of the emission band upon addition of cyanide and fluoride anions is indicative of a lowering in energy of the excited state and an enhancement of the nonradiative decay process that might account for the emission quenching observed.

3.2.3.2. Containing $Ru(tpy)_2^{2+}$ and $Ir(tpy)_2^{3+}$ Units. The ruthenium containing unit $Ru(tpy)_2^{2+}$ is much less fluorescent than the analogous $Ru(bpy)_3^{2+}$. The low emission of the ruthenium−terpyridine complexes is due to the low energy gap between the MLCT level and the metal-centered level. Excitation to the MLCT (ca. 480 nm) gave emission at ca. 650 nm. Compound **159** and its copper(II) complex are



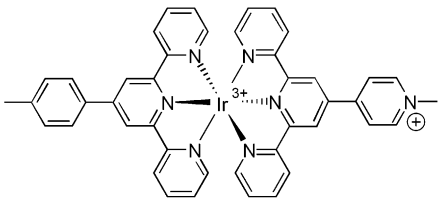
159

the unique described anion chemosensor bearing the $Ru(tpy)_2^{2+}$ unit.[157] ATP addition to **159** in acetonitrile: water 70:30 v/v at pH 3 resulted in a large enhancement of the emission intensity, whereas chloride, sulfate, and phosphate did not induce any emission change. This large and selective enhancement was attributed to a physical phenomenon rather than to coordination and due to the formation of a polyanion−polycation association that would induce structural rigidity.

The Cu^{2+} complex of **159** also displayed anion chemosensing activity.[158] The **159**−Cu^{2+} system was build by a cyclam-Cu^{2+} subunit for anion binding and the $Ru(tpy)_2^{2+}$ core as a signaling reporter. Although the emission intensity of the free **159** is not pH dependent, the [Cu(**159**)]$^{4+}$ complex showed a relative quenching of the mission intensity in the 4−8 pH range via electron transfer or energy transfer processes because of the interaction between the copper(II) atom and the $Ru(tpy)_2^{2+}$ core. In the presence of anions, the fluorescence of the Cu^{2+} complex gave a very varied response. For instance, in the presence of chloride, bromide, and OH^-, a revival of the emission intensity was observed in the 4−8 pH range and attributed to anion axial coordination to the Cu(II) center that would reduce the probability of interaction between the Cu(II) cation and the $Ru(tpy)_2^{2+}$ center with the consequent emission enhancement. The ATP anion also formed complexes with [Cu(**159**)]$^{4+}$ inducing quenching of the fluorescence of the $Ru(tpy)_2^{2+}$ core at pH 9, a pH at which none of the other anions studied (phosphate, sulfate, chloride, bromide, ADP, and GMP) were able to produce any significant effect on the emission of the [Cu(**159**)]$^{4+}$ complex.

Although iridium(III) is a d^6 metal such as ruthenium(II), the photophysical properties of the $Ir(tpy)_2^{3+}$ core are different to those of $Ru(tpy)_2^{2+}$. Thus, the $Ir(tpy)_2^{3+}$ complex is much more emissive than $Ru(tpy)_2^{2+}$ and has a longer luminescent lifetime (about 10^5 times greater). The $Ir(tpy)_2^{3+}$ core shows absorption bands in the UV zone at 250−350 nm and a band in the near visible zone centered at ca. 380 nm. Upon excitation at 380 nm, a well-structured emission is observed at ca. 500 nm.[159] Receptors **160** and **161** are composed of iridium luminescent signaling units and pyridyl subunits for anion coordination.[160] Aqueous solutions of receptors **160** and **161** showed broad emission bands centered at 510 and 525 nm, respectively, upon excitation at 366 nm. Addition of chloride caused emission quenching by a

factor of 3 for receptor **160** and by a factor of 2.5 for receptor **161**. The presence of bromide and iodide also



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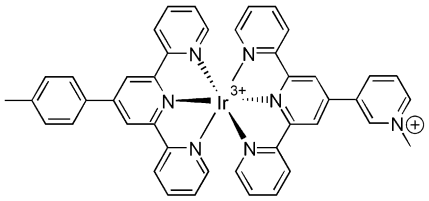
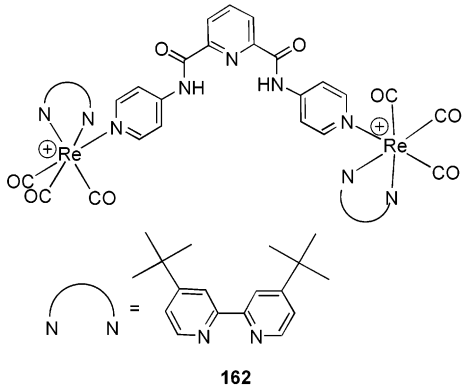


161

quenched the emission efficiently. A modest quenching was observed for acetate and tartrate whereas the presence of nitrate, sulfate, dihydrogen phosphate, hexafluorophosphate, and tetrafluoroborate had no significant effect. It was suggested that the anion chloride (and probably Br^- and I^-) interacted with the *N*-methylpyridyl group and induced emission quenching via a CT process from the anion to the excited fluorophore.

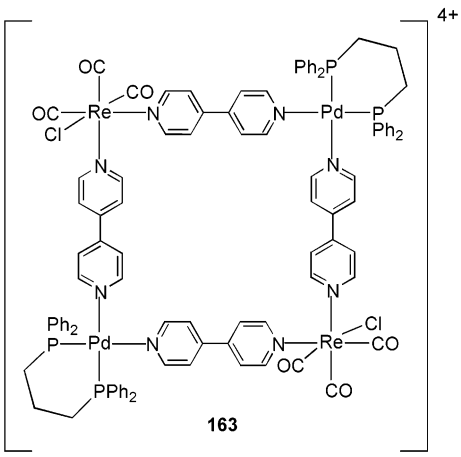
3.2.3.3. Containing Rhenium Complexes. Some examples of anion chemosensors containing rhenium complexes as signaling subunits have been described. Re(I)−polypyridyl complexes show a characteristic and intense ^{1}MLCT absorption band centered around 370 nm, which upon excitation gives emission from a triplet MLCT (^{3}MLCT) excited state in the range of 530−650 nm. Solutions of **162** in dichloromethane



162

exhibited intense absorption bands in the near UV region and very strong luminescence at 536 nm (λ_{ex} = 360 nm, quantum yield of 0.37).[161] Addition of different inorganic anions (CN^-, F^-, I^-, Cl^-, Br^-, AcO^-, $H_2PO_4^-$, NO_3^-, and ClO_4^-) to solutions of **162** caused different degrees of quenching of the luminescence intensity without significant selectivity. Concomitant with the quenching, the luminescence wavelength was slightly red-shifted from 536 to 546 nm. These anions formed 1:1 complexes with receptor **162** by means of hydrogen-bonding interactions with the amide protons. Compound **162** showed strong binding affinities with halides, cyanide, or acetate anions, moderate affinity toward dihydrogen phosphate, and very weak binding affinities to nitrate or perchlorate anions. The red shift in the emission band suggested that emission quenching is associated with a change in the energy of the excited state. As the authors suggested, if the emitting excited state becomes less energetic (red shift of the emission), there would be a greater vibrational overlap with the ground state with the result of an increase in the nonradiative decay process and a parallel quenching of the emissive process.

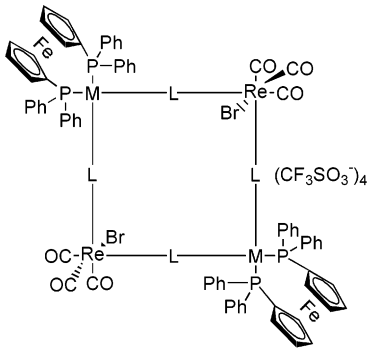
Squares **163**−**168** are luminescent and are able to sense anions. The binding site was the charged square cavity that was capable of encapsulating anions by electrostatic ion pair interactions. Receptors **163**−**168** showed MLCT bands centered at ca. 320−340 nm that upon excitation gave luminescence emission bands centered at ca. 580−630 nm. The quantum yields of this family of receptors were low due to an intramolecular oxidative quenching of the MLCT luminescence by the Pd(II) or Pt(II) centers, and for instance, the emission intensity of **163** is ca.

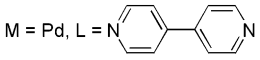


163

25-fold lower than that of *fac*-$Re(CO)_3Cl(4,4'\text{-bpy})_2$. Remarkably, the receptor **163** is the unique chemosensor described for the selective sensing of the poorly coordinating perchlorate anion.[162] The interaction of the perchlorate anion with **163**, via coordination of the anion in the tetracationic cavity, resulted in enhancement of the emission of **163** in acetone. This enhancement in luminescence intensity was related with the perchlorate coordination that induced changes in the intramolecular electron transfer quenching energetics related with the Pd(II) center. Addition of tetrafluoroborate and trifluoromethanesulfonate also produced some enhancement in the emission intensity of **163**. Compounds **164**−**168** are similar to **163** but contain additionally ferrocene groups in their structure that induced a very effective quenching of the MLCT luminescence.[163] Binding studies on **164**−**168** were carried out in acetone solutions and in the presence of the ClO_4^-, AcO^-, TfO^-, PF_6^-, and BF_4^- anions. Only the anions PF_6^- and BF_4^- induced significant changes in the luminescence intensities of the five receptors. The luminescence first decreased with low concentrations of these anions and then increased in the presence of a

larger anion concentration and finally reached a plateau. The authors suggested that the initial binding of anions with these receptors increased the probability of an energy transfer from the MLCT state to the ferrocene-based metal center state, inducing a decrease in luminescence. When more anion was added, the luminescence increase was attributed to a stabilization of the positive charges on Pd(II) reducing the oxidative quenching.





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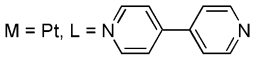

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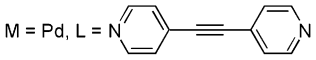

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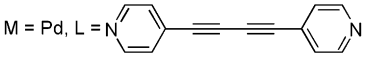

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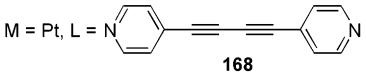
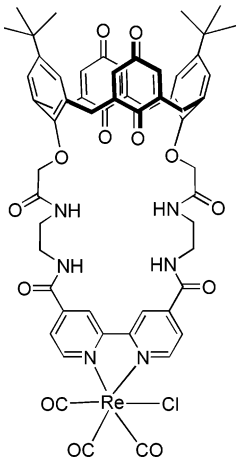


168

Receptors **169** and **170** are analogous to receptors **147** and **148** and formed strong complexes with



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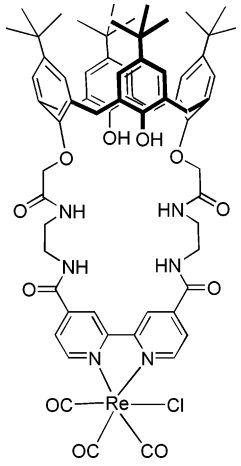


170

acetate and chloride anions and weak complexes with dihydrogen phosphate.[149] Addition of acetate and chloride to solutions of receptor **170** resulted in an enhancement of the emission maxima, whereas with receptor **169**, only acetate was capable of enhancing the emission intensity. The complexes were formed by means of hydrogen-bonding interactions between the amide subunits and the correspondent anion.

3.2.3.4. Containing Lanthanide Complexes. There are a few, although attractive, anion sensing receptors based on lanthanide complexes. Those involve the use of the lanthanide ions Eu and Tb, which show luminescent $^5D_0$ and $^5D_4$ excited states. The direct excitation of the lanthanide ions is very inefficient due to the fact that f−f transitions are Laporte forbidden and therefore very weak (extinction coefficients in the order of 0.5−3 dm^{-3} mol^{-1} cm^{-1}). One solution to this problem is to incorporate near the lanthanide ion a sensitizing chromophore (often called an "antenna"), allowing indirect excitation of the lanthanide. The antenna is usually an organic chromophore that absorbs UV−visible radiation; then, an energy transfer from the antenna to the metal center takes place, and finally, the emission from the long-lived lanthanide center is obtained (see Figure 35). In the receptors shown below, phenanthridine, bipyridine, and pyridine were used as antenna groups.[164]

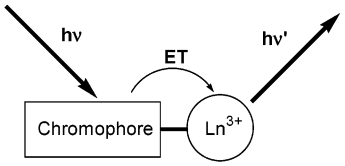
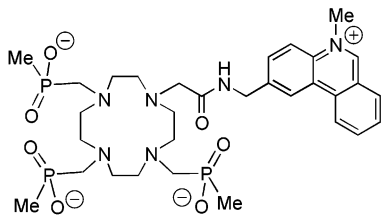


Figure 35. Schematic representation of the modulation of lanthanide emission by an appended chromophore than acts as an "antenna".

Two kinds of mechanisms have been reported for anion sensing with receptors containing lanthanide complexes. For receptors functionalized with antenna chromophores, the binding of anions may perturb the excited state of the chromophore and the rate of the energy transfer to the lanthanide center resulting in quenching of the luminescence intensity. The other mechanism involves the displacement of water molecules bound to the lanthanide center by anions. It is known that one of the causes of quenching in those complexes is due to energy transfer processes from the metal center to the OH oscillators (water molecules bound to lanthanide center). When water molecules are displaced, this quenching mechanism is removed and an enhancement of the emission intensity of the lanthanide complex is observed.[164]

For the [Eu-**171**]$^+$ complex (λ_{exc} = 320 nm), the presence of Cl^-, Br^-, or I^- anions led to a decrease

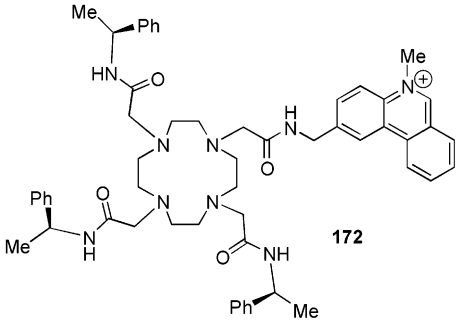


171

in the intensity of the phenanthridinium fluorescence (at 405 nm) and a parallel diminution of the europium luminescence (at 594 and 616 nm) in water

solutions.[165,166] The luminescence quenching observed in the presence of chloride was independent of the pH (in the 1.5−9 range) and was unaffected by the presence of phosphate, citrate, lactate, or bicarbonate, suggesting an attractive and possible application in the development of a sensory system for Cl^- determination in aqueous environments. A similar effect was observed upon addition of Br^- and I^-. Addition of KOH caused a decrease of the europium luminescence (quenching factor > 200) and attributed to the reversible addition of OH^- to the 6-position of the *N*-methylphenanthidinium ion. Cl^- addition to the Tb complex of receptor **171** resulted in a lower quenching of the lanthanide emission. Additionally, the emission of the Tb complex was oxygen sensitive.

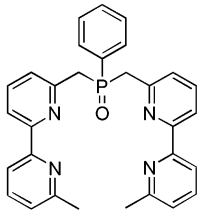
Europium and terbium complexes of **172** also showed dual emission, fluorescence (due to the



172

phenanthridinium unit), and luminescence (due to the europium or terbium) at 405 and 594 nm, respectively, in water (excitation at 320 nm to the phenanthridinium unit).[167] The same halide quenching described for [Eu-**171**]$^+$ was observed with [Eu-**172**]$^{4+}$. The situation with the corresponding terbium complexes was again less favorable because the metal-based emission was rather weak and oxygen sensitive.

Receptor **173** consists of a PhP=O fragment and two methylene-linked bipy subunits.[168,169] The P=O



173

unit and the two bipy fragments formed relatively stable complexes with the Eu^{3+} and Tb^{3+} cations. The bipy subunit acted as a photon antenna able to transfer energy to the lanthanide center with high efficiency. UV−visible titrations confirmed the formation of 1:1 metal-to-ligand complexes. Acetonitrile solutions of [Eu·**173**]$^{3+}$ and [Tb·**173**]$^{3+}$ showed bands centered at 310 nm due to the presence of the bipy moieties. Excitation at 310 nm led to luminescence emission from the metal cations at 615 nm (transition $^5D_0 \rightarrow {}^7F_2$) and 545 nm (transition $^7F_2 \rightarrow {}^5D_4$) for the Eu^{3+} and Tb^{3+} complexes, respectively. Upon the addition of the nitrate anion, an overall increase in the luminescence intensity of the Eu^{3+} and Tb^{3+} complexes was found. The same trend, but less pronounced, was observed with the addition of chloride. For fluoride and acetate, the changes were far less pronounced. This increase in luminescence intensity was first caused by the displacement of solvent molecules of the first coordination shell of the lanthanide cations by coordination of the anion nitrate (or chloride). The coordination of a second nitrate released one bipy arm producing a strong interaction between the metal ion and the bipy moiety that was still coordinated giving a strong increase in the efficiency of the ligand-to-metal energy transfer process and an increase in emission intensity. The addition of the third nitrate produced a little quenching of the emission intensity due to the release of the second bipy arm. The overall effect was an 11% enhancement in emission intensity upon nitrate binding (see Figure 36).

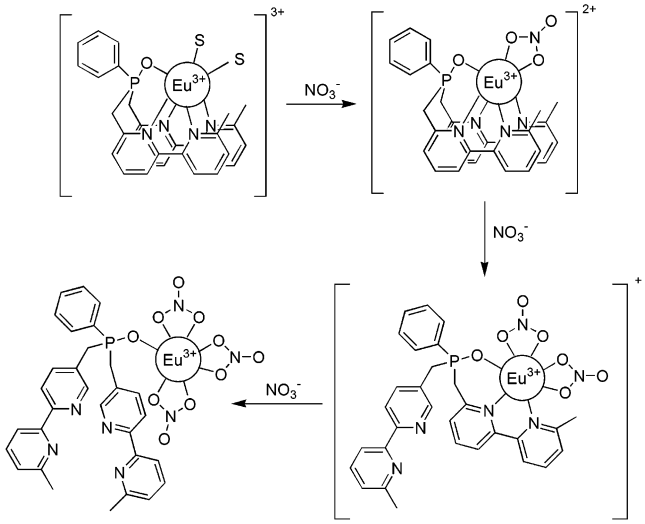
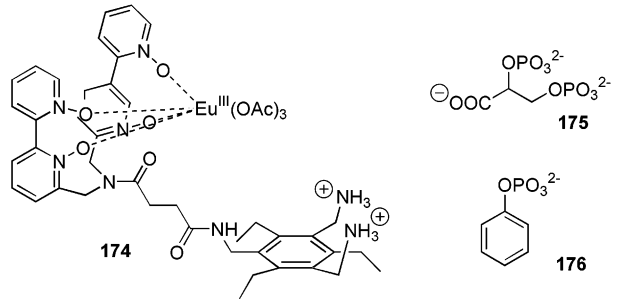


Figure 36. Proposed mechanism for the stepwise coordination of the nitrate anion with the complex [Eu(**173**)]$^{3+}$.

Receptor **174** was designed as a fluorescent sensor for 2,3-bisphosphoglycerate (**175**).[170] Solutions of

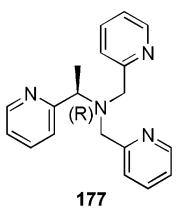


174 **175** **176**

receptor **174** in methanol−acetonitrile 50:50 v/v mixtures showed, upon excitation at 260 nm, six linelike emission bands centered at 577, 590, 610 (stronger peak), 650, 690, and 699 nm. Upon addition of 2,3-bisphosphoglycerate (**175**), 3-phosphoglycerate, 2-phosphoglycerate, phosphoenolpyruvate, and phenyl phosphate (**176**) to solutions of **174**, a decrease in the emission peaks was observed. Compounds **175** and **176** formed 1:1 complexes whereas 3-phosphoglycerate, 2-phosphoglycerate, and phosphoenolpyru-

vate formed 1:2 (host−guest) species. The stability constant for the adduct **174**−**175** was three times greater than that for the adduct **174**−**176**. These differences in the stability constants were explained assuming that **175** binds with receptor **174** through the europium center and the two ammonium subunits whereas **176** only was coordinted by the europium center.

The luminescence spectrum of complexes $[Eu(\mathbf{177})]^{3+}$ and $[Tb(\mathbf{177})]^{3+}$ was measured in aceto-



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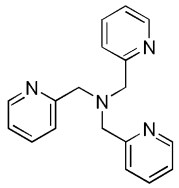

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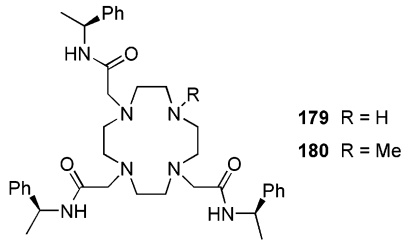
nitrile upon excitation at 260 nm of the pyridine chromophore (that acts as an antenna) in the presence of the anions I^-, Br^-, Cl^-, F^-, ClO_4^-, NO_3^-, SCN^-, AcO^-, HSO_4^-, and $H_2PO_4^-$.[171] The most important enhancement of the intensity of the emission band of the $[Eu(\mathbf{177})]^{3+}$ complex centered at 618 nm was observed upon addition of NO_3^- (about 4.9-fold); modest enhancements were observed upon addition of Cl^- and AcO^-, and no changes were obtained with the rest of the anions tested. The complex $[Tb(\mathbf{177})]^{3+}$ exhibited a selective 5.4-fold enhancement of the emission intensity at 548 nm in the presence of Cl^-. The presence of NO_3^-, SCN^-, and Br^- induced moderate enhancements, whereas the rest of anions induced negligible changes. When the achiral complexes $[Eu(\mathbf{178})]^{3+}$ and $[Tb(\mathbf{178})]^{3+}$ were employed, similar selectivities were found but with lower sensitivities (lower increases in emission intensity). The spectral changes were ascribed to the displacement of solvent molecules by molecules of the corresponding anion.

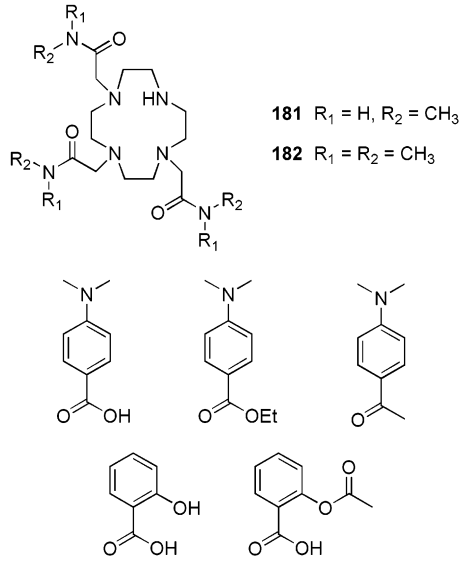
The reversible displacement of the two water molecules coordinated to the lanthanide centers in the complexes $[Eu(\mathbf{179})]^{3+}\cdot 2H_2O$ and $[Tb(\mathbf{179})]^{3+}\cdot$



179 R = H
180 R = Me

$2H_2O$ was used for the design of probes for anion signaling (λ_{exc} = 395 and 355 for europium and terbium complexes, respectively).[172] The emission intensity of the $[Tb(\mathbf{179})]^{3+}$ complex (pH 5.5−6.5) was enhanced in the presence of fluoride, acetate, and sulfate and attributed to the displaced water molecules of the metal coordination shell. In contrast, the anions I^-, Br^-, Cl^-, and NO_3^- (pH 5.5−6.5) did not induce any significant change in the emission behavior. Hydrogen carbonate (pH 6.5) and carbonate (pH 11.0) displaced two water molecules leading to a large change in the measured lifetime and enhancement in luminescence emission. Citrate, malonate, and lactate, which also coordinated the lanthanide center, also induced emission enhancements. Similar results were obtained with $[Eu(\mathbf{179})]^{3+}\cdot 2H_2O$, $[Eu(\mathbf{180})]^{3+}\cdot 2H_2O$, and $[Tb(\mathbf{180})]^{3+}\cdot 2H_2O$ complexes.[167] Another way to detect anions was provided by the relation between the transitions $\Delta J = 2$ and $\Delta J = 1$. Thus, this relation was 4:1, 4:3, and 2:1 for HCO_3^-, F^-, and $H_2PO_4^-$, respectively.

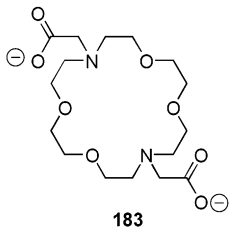
The Tb(III) complexes of receptors **181** and **182** sensed *p*-dmbz and salicylate anions by enhancement



181 R_1 = H, R_2 = CH_3
182 R_1 = R_2 = CH_3

of the lanthanide luminescence in water solutions buffered at pH 7.4.[173] *p*-dmbz and salicylate formed ternary complexes with $[Tb(\mathbf{182})]^{3+}$ displacing two metal-bound water molecules. On excitation at 300 nm (excitation wavelength of the aromatic carboxylates tested that act as sensitizers), an energy transfer between the excited triplet state of the carboxylates and the $^5D_4$ excited state of the Tb(III) ion occurred and the emission of the lanthanide center was enhanced (680-fold). The presence of neither ethyl *p*-dmbz, *p*-*N*,*N*-dimethylacetophenone, nor acetyl salicylate produced enhancement of the $[Tb(\mathbf{182})]^{3+}$ luminescence. The behavior of complex $[Tb(\mathbf{181})]^{3+}$ was the same, but the enhancement of the lanthanide emission was lower (220-fold).

$[Eu(\mathbf{183})]^+$, $[Tb(\mathbf{183})]^+$, and $[Eu(\mathbf{184})]^{2+}$ formed ternary complexes with aromatic carboxylates in



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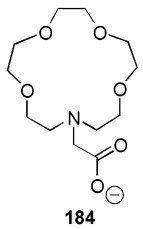


184

aqueous solutions buffered at pH 7.5.[174] Addition of the picolinate anion to solutions of the $[Eu(\mathbf{183})]^+$ or $[Tb(\mathbf{183})]^+$ induced a 250- and 170-fold enhancement in the emission intensity, respectively. The addition of phthalate did not induce any remarkable lumines-

cence intensity change. In the case of $[Eu(\mathbf{184})]^{2+}$, similar enhancements were observed upon addition of picolinate (120-fold) and isophthalate (40-fold) and weak enhancements were observed upon addition of phthalate (20-fold) and benzoate (10-fold). These changes in the emission intensity were assigned to the formation of complexes between $[Eu(\mathbf{183})]^{+}$, $[Tb(\mathbf{183})]^{+}$, or $[Eu(\mathbf{184})]^{2+}$ with the correspondent aromatic carboxylate by displacement of water molecules in the coordinating shell of the lanthanide complexes. The coordinated aromatic carboxylates acted then as an antenna switching on the luminescence of the lanthanide center.

3.3. Following the Displacement Approach

Chloride sensing was achieved by using a displacement reaction by combination of **185** and the 1-dibenzo-24-crown-8.[175] A pseudo-rotaxane was formed between **185** and the crown in dichloromethane. The pseudo-rotaxane can be unthreaded by addition of Cl^- through formation of a strong ammonium chloride (**185**$-Cl^-$) ion pair, while pseudo-rotaxane rethreading can be performed by addition of Bu_3NHPF_6 because Bu_3NH^+ forms a stronger ion pair with Cl^- than **185** (see Figure 37). These processes were followed by remarkable changes in the fluorescence spectra of **185**. Thus, in solutions of **185**$-PF_6^-$ and 1-dibenzo-24-crown-8, the rotaxane was formed and the fluorescence of **185** was observed. Upon addition of 1 equivalent of Cl^-, the fluorescence emission of anthracene disappears due to the formation of the **185**$-Cl^-$ ion pair.

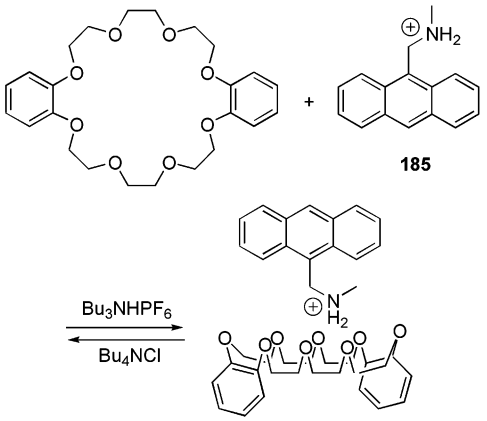
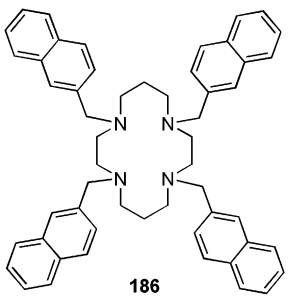


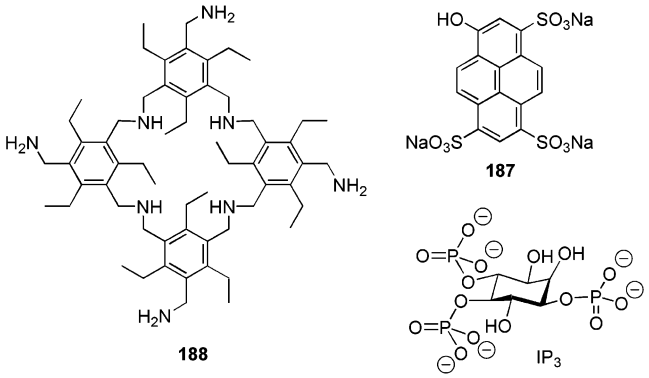
Figure 37. Scheme showing the equilibrium between **185** and the receptor 1-dibenzo-24-crown-8.

When Cu^{2+} was added to THF:water 70:30 v/v solutions of **186**, the $[Cu(\mathbf{186})]^{2+}$ complex was formed and a quenching of the emission of the naphthyl



groups was observed.[176] This quenching was not perturbed by addition of the anions chloride, bromide, or iodide. In contrast, phosphate and especially sulfate induced a revival of the fluorescence at acid pH. The observed enhancement was attributed to a competition between the metal ion Cu^{2+} and the anions to coordinate **186** at acidic pH. The fluorescence of the **186**$-Cu^{2+}$ complex in an nonaqueous solvent (mixtures of THF:acetonitrile) also varied with $H_2PO_4^-$.

By using a competitive assay, the combination of the fluorophore 1-hydroxypyrene-3,6,8-trisulfonate (**187**) and the receptor **188** was used to recognize and



sense of the inositol$-$triphosphate (IP_3) anion.[177] The IP_3 is a short-lived biochemical second messenger that triggers the rapid release of calcium into the cell fluid. IP_3 exists for only a few seconds before being converted into inositol by the action of certain enzymes. Compound **187** forms 1:1 complexes with the azacalixarene **188**. The fluorescence intensity of **187** decreases with increasing concentration of the azacalixarene in aqueous solution at pH 7.2 (λ_{ex} = 390 nm, λ_{em} = 510 nm). Addition of IP_3 to a solution containing the **188**$-$**187** ensemble resulted in an increase of the fluorescence due to the release of **187** into the solution and formation of a complex between **188** and IP_3. Binding constants between **188** and IP_3, fructose-1,6-diphosphate, gluconic acid, and adamantane-1,3-dicarboxylic acid were obtained with this competition assay. The stronger binding constant was obtained for IP_3.

The complex $[Cu_2(\mathbf{189})]^{4+}$ and the fluorescent indicators coumarine 343, fluorescein, or eosine Y (see

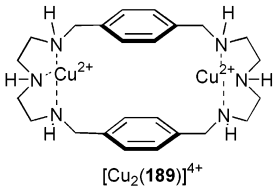


Figure 38) form a chemosensing ensemble that allowed the fluorimetric detection of pyrophosphate by using a displacement approach in aqueous solutions buffered at pH 7.0.[178] The indicators form a complex with the $[Cu_2(\mathbf{189})]^{4+}$ with the two oxygen atoms of the carboxylate groups of each dye bridging the two Cu^{2+} ions. When coordinating to the metal ion, the fluorescence of the indicators was quenched and

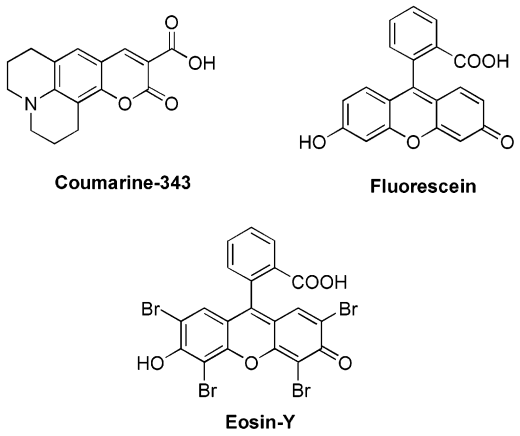


Figure 38. Chemical structures of the indicators coumarine-343, fluorescein, and eosin-y used in displacement assays.

attributed to intramolecular energy or electron transfer processes between the Cu^{2+} atoms and the bound dyes. On addition of pyrophosphate or phosphate anions, a displacement of the bound indicator from the chemosensing ensemble due to the formation of anion−$[Cu_2(\mathbf{189})]^{4+}$ adduct resulted in a significant revival in the fluorescence emission intensity. The $[Cu_2(\mathbf{189})]^{4+}$−(coumarine 343) ensemble did not discriminate between the two phosphates. In the case of $[Cu_2(\mathbf{189})]^{4+}$−(fluorescein) and $[Cu_2(\mathbf{189})]^{4+}$−(eosine Y) ensembles, only the pyrophosphate anion was able to displace the indicator. Remarkably, the last two ensembles allowed detection of pyrophosphate anion in the micromolar range and in the presence of nitrate, sulfate, chloride, cyanate, azide, acetate, benzoate, and phosphate. The same $[Cu_2(\mathbf{189})]^{4+}$− indicator pairs were titrated with some representative L-amino acids (His, Ala, Phe, Leu, Pro, and Gly).[179] For the $[Cu_2(\mathbf{189})]^{4+}$−(coumarine 343) ensemble, both His and Gly displaced the indicator and restored its full emission. The $[Cu_2(\mathbf{189})]^{4+}$−(fluorescein) pair was capable of discriminate His (full recovery of fluorescence emission) from Gly (with a half recovery of fluorescence emission). The best selectivity was achieved with the $[Cu_2(\mathbf{189})]^{4+}$− (eosine Y) ensemble for which only His, among other the amino acids tested, was capable of releasing the indicator from the ensemble. This selectivity toward His was attributed to the deprotonation of the imidazole residue and formation of the imidazolate anion that fits well between the two Cu^{2+} centers of the complex forming an adduct of high stability.

The Zr(IV)−EDTA−flavonol complex **190** exhibited an intense blue fluorescence centered at 460 nm (λ_{exc} = 400 nm) in 20% ethanol−water (v/v) at pH 5.0.[180] The fluorescence intensity decreases upon addition of fluoride anion and attributed to the replacement of flavonol (see Figure 39). With the use of this complex, a detection range from 3.0×10^{-6} to 1.0×10^{-3} mol dm^{-3} was found for fluoride and the lower limit of detection reached was 60 ppb. The presence of Cl^-, HSO_4^-, NO_3^-, $H_2PO_4^-$, and AcO^- did not interfere significantly while metal cations including Al^{3+}, Fe^{3+}, and Cu^{2+} appreciably interfered due to the competing complexation of flavonol with these metals.

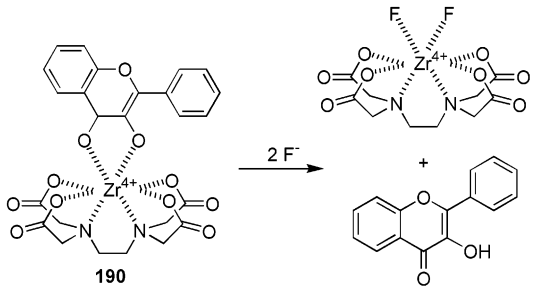
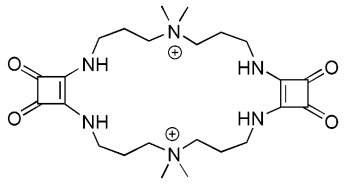


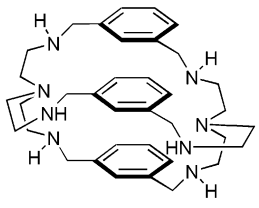
Figure 39. Schematic representation of the ligand exchange reaction between receptor **190** and the fluoride anion.

The **191**−fluorescein couple was able to sense sulfate.[181] Addition of receptor **191** to a solution of



fluorescein in methanol−water mixtures (9:1 v/v) produced a nonfluorescent self-assembled 1:1 complex. The quenching of the fluorescein was probably due to the PET from the donor squaramide rings of **191** to the fluorescein excited singlet state. Upon competitive addition of sulfate, fluorescein was displaced restoring its fluorescence and effectively signaling the presence of sulfate anion. This ensemble proved to be adequate for real-time on-line determination of sulfate in water.

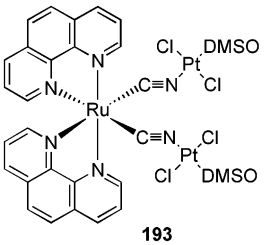
Coumarine 343 is strongly fluorescent in its anionic form (λ_{exc} = 424 nm, λ_{em} = 487 nm, pH 7). Complete quenching of coumarine emission was observed on titrating a solution of coumarine 434 (10^{-7} M) buffered to pH 7.0 with a solution of the complex $[Cu_2(\mathbf{192})]^{2+}$.[182] Fluorescence quenching was ascribed



to an intramolecular energy transfer process involving the photoexcited coumarine fragment and the Cu(II) centers. A chemosensing ensemble containing $[Cu_2(\mathbf{192})]^{2+}$ and coumarine 343 buffered at pH 7.0 was used to sense the HCO_3^-, N_3^-, and NCO^- anions. Competitive binding of $[Cu_2(\mathbf{192})]^{2+}$ with these anions produced the displacement of the coumarine coordinated to $[Cu_2(\mathbf{192})]^{2+}$ observing full regeneration of the coumarine emission. Slight or no enhancement of the fluorescence was obtained with NCS^-, NO_3^-, SO_4^{2-}, HPO_4^-, $HCOO^-$, and AcO^-.

Sensing of certain amino acids was achieved using the neutral trinuclear heterobimetallic cyano-bridged Ru(II)/Pt(II) complex **193**.[183] Compound **193** showed

a weakly intense MLCT emission band centered at 595 nm (upon excitation at 467 nm), in water−DMF 1:1 (v/v) mixtures buffered at pH 7.0, due to coordination of two electron acceptor groups $Pt(DMSO)Cl_2$. Addition of amino acids containing thiol moieties (cysteine, homocysteine, and methionine) induced a red shift of the emission band with a significant enhancement in intensity. Other amino acids tested lacking thiol groups did not induce any variation in the emission profile of the receptor. The emission intensity enhancement was assigned to the binding of the thiol-containing amino acids to the Pt(II) centers of **193** and subsequent cleavage of the receptor structure to give the highly emissive *cis*-$[Ru(phen)_2(CN)_2]$ complex. Gluthatione, a cysteine-containing small pepetide, was also able to induce enhancement of the emission intensity.



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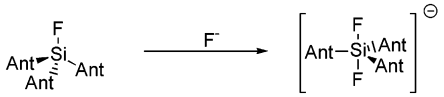
3.4. Following the Chemodosimeter Approach

Despite the attractiveness of the chemodosimeter approach, only some few examples, most of them for fluoride sensing, have been reported by using emission fluorescence variations as output signal. Thus, reaction of fluoride in THF with trianthrylfluorosilane **194** to give **195** (see Figure 40) resulted in a

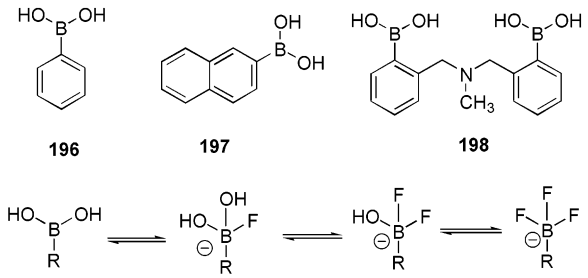


194 **195**

Figure 40. Reaction of the tetrahedral silane receptor **194** with fluoride to give **195** with a trigonal bipyramidal structure.

new band at 10 nm shorter wavelength than that of **194**, along with the disappearance of the absorption band of **194**.[184] In the fluorescence spectrum (in THF, $\lambda_{exc} = 365$ nm) the addition of fluoride anion increased significantly the intensity of the emission with a concomitant 20 nm hypsochromic shift of the emission maximum. The quantum yield increases more than 20 times from **194** (0.033) to **195** (0.64) and attributed to the larger distance between anthryl groups in the bipyramidal **195** than in the tetrahedral **194** with the consequent decrease in the interaction through space between anthryl groups. When other anionic species such as chloride, bromide, iodide, perchlorate, and tetrafluoroborate were added to **194**, no changes were observed.

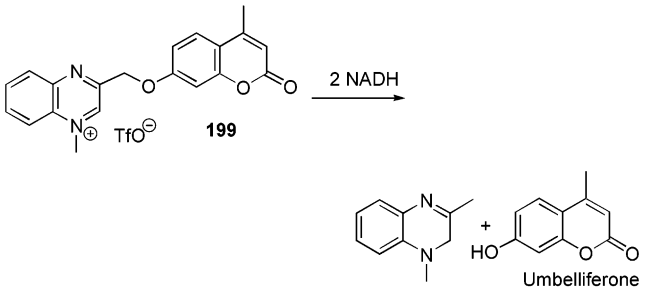
The determination of fluoride using compounds **196** and **197** was based on a chemical reaction between the fluoride anion and the boronic acid groups to form trifluoro tetrahedral boronate anions (see Figure 41) that quenched the fluorescence of the directly attached fluorophore through a PET process.[185] Compound **198** was specifically designed to increase the strength of F^- binding by means of an additional hydrogen-bonding site, which was available when the amine was protonated. Fluorimetric titrations with KCl and KBr showed no change in the fluorescence until very high concentrations of these salts.



196 **197** **198**

Figure 41. Scheme of the consecutive reactions that suffer receptors **196**−**198** with fluoride to give trifluoro tetrahedral boronate anions.

The following example includes detection of NADH by using an irreversible chemical reaction coupled to a fluorescence event.[186] Thus, the reduction of the chemodosimeter **199** by NADH resulted in the release of the fluorescent coumarine umbelliferone (excitation at 350 nm with an emission band at 450 nm) allowing indirect detection of the presence of NADH. The reaction was carried out in aqueous solutions buffered at pH 7.5 (see Figure 42).



199

Figure 42. Reduction reaction of receptor **199** with NADH produced the release of fluorescent umbelliferone allowing indirect detection of NADH.

4. Chromogenic Chemosensors and Reagents for Anions

4.1. Chromogenic Principles of Sensing

Color changes as signaling events have been widely used because it requires the use of inexpensive equipment or no equipment at all as color changes can be detected by the naked eye.[52] In fact, there are many examples of analytical determinations whose final step involves the formation of a colored compound that is indicative of the initial concentration of a certain analyte. This is so basically for cations and in a minor coverage for anions.[14,15] The chromogenic reagents use the same type of design principles as fluorogenic reagents do. Those involve the binding site−signaling subunit approach, the displacement approach, and the chemodosimeter approach.

4.1.1. Dyes as Signaling Subunits

Organic compounds became colored by absorbing electromagnetic radiation in the visible range (from

400 to 700 nm approximately), and investigations related with the correlation between chemical structure and color in organic dyes have been carried out extensively. It was soon recognized that many dyes contain systems of conjugated bonds, and it was the energy gap between the HOMO and the LUMO that is critical in determining the color of a certain organic dye. Thus, many conjugated systems have HOMO to LUMO differences in energy that correspond to visible light and it is well-established that the larger the conjugated system is, the shorter the difference between fundamental and excited states, resulting in a more bathochromic shift of the absorption band of lesser energy.[187] In addition to that basic conjugated backbone related with the length of the conjugated system, there is a chemical mean of modifying the absorption wavelength by anchoring electron donor (NR_2, NHR, NH_2, OH, OMe, O^-, X^-, etc.) or electron acceptor (NO_2, SO_3H, SO_3^-, COOH, C═O, etc.) groups to the conjugated system.[187] When both an electron donor and an electron acceptor group are present and are connected through a conjugated system in a certain molecule, a CT band can be observed. This corresponds to a CT transition where, upon excitation with light, there is an important fraction of electronic charge that is transferred from the donor to the acceptor. What is important related to the design of chromogenic reagents is that the interaction of anions with the donor or acceptors groups in those systems can result in a change in color. Thus, for instance, the interaction of an anion with a donor group will make this more donor, pumping more electrons to the conjugated system, enhancing the conjugation, and inducing a bathochromic shift. For most of the reported chromochemosensors for anions, based on the binding site−signaling subunit approach, containing anion binding sites and acceptor groups such as nitrophenyl, anthraquinone, azo dyes, etc., a shift to longer wavelengths was observed upon anion coordination.

An important effect also found in many dyes is the solvatochromism. A dye that presents a solvatochromic behavior changes its color in solution on changing the polarity of the solvent in which it was dissolved. This solvatochromic effect has been, for instance, extensively used as an indicator of the polarity of the ground and excited state. For sensing purposes, this effect might have some importance as it would allow one to select the initial and final color of certain designed probes.

4.1.2. Metal Complexes as Signaling Subunit

One special feature of transition metal atoms is the presence of partially filled d orbitals in their electronic structure. Molecular orbital diagrams in metal complexes are built by partially filled d orbitals mainly localized in the metal and ligand confined orbitals, both occupied (bonding orbitals) and unoccupied (antibonding orbitals). In such systems, several transitions could be observed upon excitation with light. d−d transitions involve electron jumping from d orbitals in the metal. A second type of band is called ligand to metal (LMCT) or metal to ligand (MLCT) CT bands, and they involve a direct transfer of electrons from filled orbitals of the ligand to unoccupied d orbitals of the metal (LMCT band) or vice versa, a transfer from filled d orbitals of the metal to unoccupied antibonding orbitals of the ligand (MLCT bands). Coordination of certain anions to a metal center in certain transition metal complexes can induce the appearance of new intense CT bands. If the new band is located in the visible region, then a chromogenic sensing of the anion is achieved.[50]

4.1.3. Aggregation–Deaggregation Processes

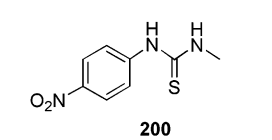
This color sensing principle has special relevance in chromogenic anion chemosensors containing sapphyrin cores.[188] Visible spectra of some sapphyrins are characterized by a Soret band centered at ca. 410 nm due to the formation of aggregates and the four Q bands in the 620−720 nm interval. Upon addition of certain anions, a progressive decrease in the intensity of the 410 nm band was observed with concomitant appearance of two new bands centered at ca. 420 and 450 nm assigned to the dimer and monomer forms of sapphyrins obtained upon anion binding. This deaggregation process can be monitored by the corresponding changes in color of the solutions, and the effect has been used in the development of certain anion chemosensors.

4.2. Following the Binding Site–Signaling Subunit Approach

As in the case of fluorescent chemosensors, the most widely used approach for the development of anion chromogenic chemosensors has been the binding site−signaling subunit approach. In this case, at least one of the atoms of the coordination site is also part of the conjugated system that acts as a signaling unit. Thus, whereas in many cases in fluorescent chemosensors there is a spacer between the binding site and the signaling unit (that preclude any electronic delocalization between both subunits), as a general rule, in chromogenic chemosensors, both signaling and binding units are integrated (absence of spacer). Upon anion coordination, a change in color is produced due to variations in the relative energy between the HOMO and the LUMO orbitals.

4.2.1. Containing Nitrophenyl Groups

The interaction of compound **200** with anions is a typical example of the mechanism outlined above.



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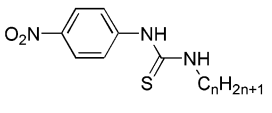

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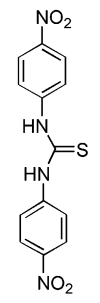


201

Compound **200** consists of a thiourea weak donor group electronically connected via a conjugated sys-

tem with an acceptor nitro group.[189] When **200** (λ_{max} = 340 nm) coordinated basic anions such as acetate via hydrogen-bonding interactions, a bathochromic shift to 365 nm and therefore a change in color of the solutions from colorless to yellow was observed. The coordination of the acetate to the thiourea made the latter to become more electron donor (due to the negative charge of the coordinated anion) therefore enhancing the CT between the thiourea−acetate donor assembly and the nitro acceptor moiety. Some other anions also capable of giving hydrogen bonds such as dihydrogen phosphate and chloride also induced batochromic shifts when added to colorless acetonitrile solutions of **200**. Compounds **201** and **202** are similar to **200**, and they showed a similar response. Compound **201** showed an intramolecular CT absorption band (λ_{max} = 343 nm) in water−acetonitrile 1:99 v/v.[190] With acetate, the CT band shifted to 392 nm with a shoulder at around 450 nm, and the color changed from colorless to yellow (see Figure 43). Compound **201** was applied to the colorimetric determination of acetic acid in a commercially available vinegar with fine results. A slight response was observed upon addition of 1 equivalent of $H_2PO_4^-$, and no changes were observed upon addition of of Cl^-, Br^-, I^-, SCN^-, NO_3^-, HSO_4^-, and ClO_4^-.

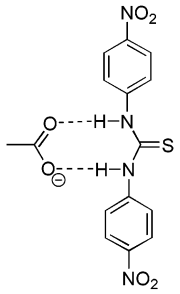
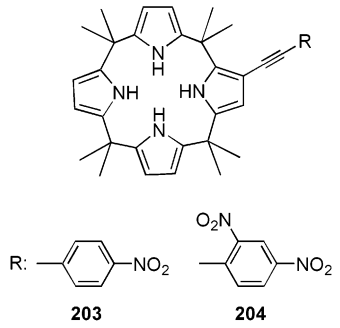


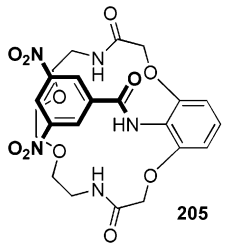
Figure 43. Binding pattern of receptor **201** with the acetate anion by means of hydrogen-bonding interactions.

One drawback in using thioureas as anion binding groups is that the anion signaling is not usually observed in water. To avoid this problem, compounds derived from **202** (n = 1−8) were incorporated to vesicles in order to shield the chromoionophore in a hydrophobic environment and mimic what biological systems do.[191] The spectral changes were examined at pH 7.5. Increasing the anion concentration produced a bathochromic shift in λ_{max} with an enhancement in molar absorptivity. The stronger shifts were obtained with Br^-, $H_2PO_4^-$, and Cl^- anions. The observed selectivity did not follow that expected for thiourea but reflected the Hofmeister series (Br^- > phosphate > Cl^- ≫ HCO_3^- > $MeCO_2^-$), which is linked with the free energy related with the transfer of the anion from the aqueous solution to the membrane phase. Changes in absorption spectra were attributed to anion interaction with the thiourea group via hydrogen bonding or/and changes in the location of the receptor in the vesicle upon anion coordination.

Compounds **203** and **204** also used nitrophenyl groups as acceptor framework combined with a calyx[4]pyrrole as a binding site.[192] Compound **203** showed a maximum at 391 nm that was shifted to 433 nm upon addition of 20 equivalents of fluoride in dichloromethane. A similar behavior was observed upon chloride and dihydrogen phosphate addition, but no changes in color were detected with bromide, iodide, or HSO_4^-. Color changes were attributed to the coordination of the anions with the calyx[4]pyrrole unit. Coordination should enhance the donor characteristics of the calyx[4]pyrrole with a consequent bathochromic shift. Compound **204** showed an adsorption maximum at 441 nm in dichloromethane solutions. Addition of fluoride led to a red shift of the absorption band (λ_{max} from 441 to 498 nm) with a color change from yellow to red. Addition of chloride and $H_2PO_4^-$ transformed the color to orange (shifts from 441 to 483 and 478 nm, respectively), whereas bromide, iodide, and HSO_4^- did not induce any variation.

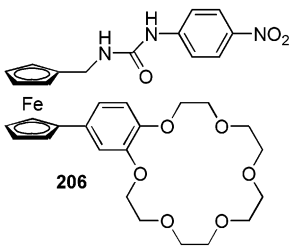


Compound **205** contains the nitrophenyl acceptor backbone connected to NH amide groups as binding



sites.[193] Solutions of receptor **205** in DMSO showed dramatic color changes from colorless to dark blue with F^- (λ = 593, 708 nm) and to yellow upon addition of $H_2PO_4^-$ and AcO^- (λ = 375 and 384 nm, respectively). No color shifts were observed upon addition of Cl^-, Br^-, or HSO_4^- anions. The selectivity trend observed in binding affinities in DMSO solutions were determined to be F^- ≫ AcO^- > $H_2PO_4^-$ > HSO_4^- > Cl^- = Br^- in agreement with the color variations. Interestingly, visual differentiation of F^-, AcO^-, and $H_2PO_4^-$ was enhanced by simple change of the solvent. Thus, in acetonitrile, colorless solutions of **205** turned turquoise upon addition of F^- (λ = 408, 700 nm), yellow with AcO^- (λ = 378 nm), and purple with $H_2PO_4^-$ (λ = 537, 393 nm). These visual changes were consistent with the association constants recorded for **205** in acetonitrile solutions, namely, F^- ≫ $H_2PO_4^-$ ≫ AcO^- > HSO_4^- = Cl^- > Br^-. Coordination of the anion via the N−H amide protons enhanced the amide donor ability and the CT interactions between the amide−anion moiety and the electron deficient 3,5-dinitrobencene group.

Acetonitrile solution of the ditopic ferrocene receptor **206** showed typical nitrobenzene bands centered

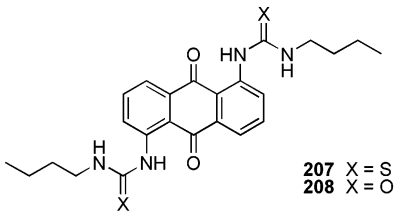


206

at 304 and 332 nm.[194] Addition of 10 equivalents of fluoride gave a new absorbance centered at 472 nm, resulting in a change in color of the solution from colorless to yellow. Addition of the potassium cation (10 equivalents) reversed the change in color, and the solution turned colorless. Reversing the order of the guest addition, first potassium cation and second the fluoride anion, gave similar results. In the two cases, the presence of potassium appeared to inhibit the chromogenic response toward fluoride. NMR studies revealed fluoride coordination to the urea moiety and potassium coordination to the benzocrown unit. The change in color upon fluoride addition was ascribed to the formation of strong hydrogen bonds between the urea NH protons and the fluoride anion. When potassium cation was added, the bound potassium must interact with the fluoride weakening the interaction between the receptor and the fluoride and bleaching was observed.

4.2.2. Containing Anthraquinone

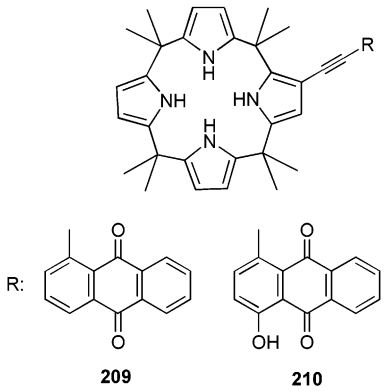
Anthraquinone and anthraquinone derivatives are electron acceptor groups that electronically connected with certain anion binding sites, have proved suitable receptors for the colorimetric sensing of certain anions. For instance, compounds **207** and **208** have



207 X = S
208 X = O

urea and thiourea groups attached to the anthraquinone backbone.[195] As stated above, the urea or thiourea groups are weak electron donors and **207** and **208** are orange (λ_{max} = 495 and 490 nm, respectively, in acetonitrile). Addition of 10 equivalents of fluoride anion to acetonitrile solutions of receptor **207** caused a color shift from orange to brown (λ_{max} = 670 nm). These color changes were ascribed to the enhancement of the donor ability of the thiourea in the presence of fluoride, with the consequent red shift of the CT band between the thiourea−anion donor group and the anthraquinone acceptor moiety. This color change with fluoride was selective, and the addition of chloride, bromide, iodide, nitrate, hydrogen sulfate, dihydrogen phosphate, acetate, benzoate, cyanide, and thiocyanate did not have any effect on the color of **207**. For receptor **208**, addition of 100 equivalents of the corresponding anion in acetonitrile resulted in significant color changes for fluoride, dihydrogen phosphate, cyanide, acetate, and benzoate. As with **205**, selectivity was found to be enhanced by changing the solvent. Thus, solutions of both **207** or **208** receptors in DMSO shifted the color from orange to dark brown selectively in the presence of fluoride (with 2 equivalents of fluoride for **207** and 20 equivalents for **208**).

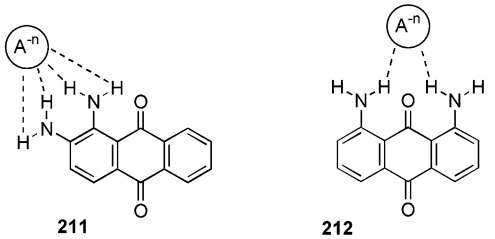
Compounds **209** and **210** showed a band in the visible spectrum at 467 and 526 nm, respectively,



209 **210**

probably due to a CT band between the donor calix[4]pyrrole and the anthraquinone acceptor groups.[196] In the presence of F^-, Cl^-, and $H_2PO_4^-$, a color change was observed and attributed to anion coordination with the calix[4]pyrrole group that enhanced the donor ability of the pyrrole with the consequent red shift of the CT band. Changes for **209** were from 467 nm to 518, 501, and 497 nm in the presence of F^-, Cl^-, and $H_2PO_4^-$, respectively, whereas changes for **210** were from 526 nm to 613, 567, and 549 nm upon addition of F^-, Cl^-, and $H_2PO_4^-$, respectively.

The variation in the absorption spectra of anthraquinone, 1,2-, 1,4-, 1,5-, 1,8-, and 2,6-diaminoanthraquinone as well as 1- and 2-aminoanthraquinone upon the addition of various anions, namely, F^-, Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, AcO^-, BzO^-, CN^-, NO_3^-, SCN^-, and ClO_4^-, was studied in different aprotic solvents (CH_2Cl_2, CH_3CN, and DMSO).[197] All of the anthraquinone derivatives tested changed the color in the presence of F^- in CH_2Cl_2 solutions. Significant bathochromic shifts were also observed for 1,2- and 1,8-diaminoanthraquinone, **211**, and **212**, respectively (see Figure 44) in CH_2Cl_2 in the presence of Cl^-, Br^-, $H_2PO_4^-$, AcO^-, BzO^-, and CN^-. The changes were more remarkable in the case of 1,2-diaminoanthraquinone and less important in the case of 1,8-diaminoanthraquinone. These color changes with **211**



211 **212**

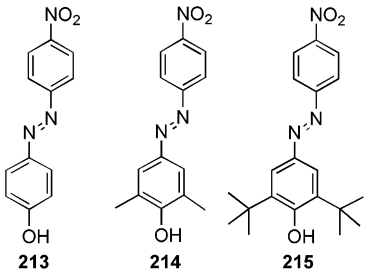
Figure 44. Proposed modes of anion binding for receptors **211** (1,2-diaminoanthraquinone) and **212** (1,8-diaminoanthraquinone) through hydrogen-bonding interactions.

were ascribed to the formation of a CT complex between the amino-anion donor groups and the anthraquinone acceptor moiety. With other anthraquinone derivatives tested (1,4-, 1,5-, and 2,6-diaminoanthraquinone or 1- and 2-aminoanthraquinone), the color variations were not significant. The absence of response with 1,4-, 1,5-, and 2,6-diaminoanthraquinone pointed out how important the spatial disposition of the two amino groups in the formation of the complex between the anion and the receptors was. On changing the solvent from less polar CH_2Cl_2 to the more polar CH_3CN or DMSO, a similar behavior was obtained. Another species was tested for colorimetric anion sensors, especially those containing hydrogen bond donor functionality like NH_2, $CONH_2$, or OH. These species were 4-nitroaniline, 4-nitro-1,2-phenylenediamine, L-leucine-4-nitroanilide, 4-nitrophenol, alizarin, 2,2′-bis(3-hydroxy-1,4-naphthoquinone), 1-(4-nitrophenyl)-2-thiourea, acid blue 45, naphthol AS, 9(10*H*)acridone, and direct yellow 50. The behavior of these systems toward the presence of anions was very similar in the sense that the more basic anions induced a larger color change (F^-, CN^-, $H_2PO_4^-$, AcO^-, and BzO^-). Among those dyes in DMSO solutions, probably that of acid blue 45 showed the most selective behavior because only the presence of 100 equivalents of fluoride anion induced a transformation from blue to colorless.

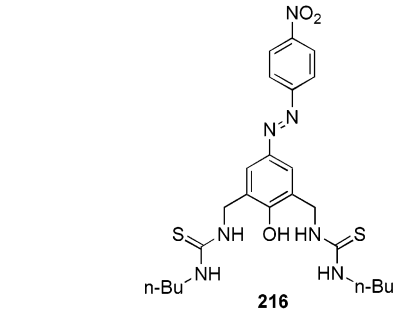
4.2.3. Containing Azo Dyes

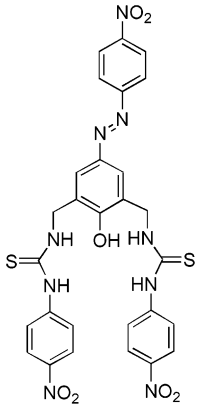
Azo dye derivatives have been used as chromogenic subunits in the development of some chromogenic receptors for anion recognition. The UV−visible spectra of these chromogenic receptors consisted of absorbances in the UV zone due to the presence of the bencenic rings and a CT band, from a donor atom (nitrogen or oxygen) to the acceptor nitro group, centered around 450−480 and responsible for the orange-red color usually observed.[187]

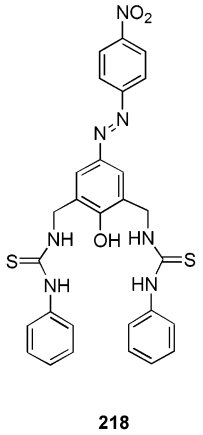
A family of azo-phenol receptors for anion sensing has been developed containing as anion coordination sites one unique phenol (as in **213**−**215**), phenol−

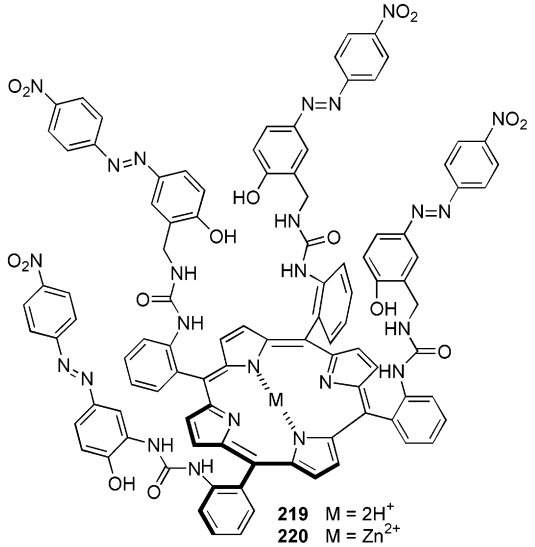


thiourea groups (**216**−**218**), or phenol−urea groups (**219** and **220**). In all cases, the phenol group was connected through a conjugated system with the acceptor nitrophenyl moiety. In the presence of certain anions, coordination with the phenol (via hydrogen bonds) or deprotonation (proton transfer from the phenol to the anion) of the phenolic group was observed. With either coordination or deprotonation, the outcome was an enhancement of the donor character of the phenolic oxygen resulting in a red shift of the CT band. Azophenols **213**−**215** were









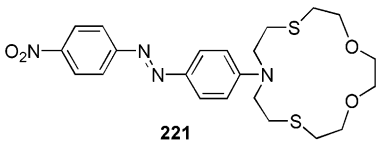
capable of selective detection of F^- over other anions tested ($H_2PO_4^-$, AcO^-, N_3^-, Cl^-, Br^-, and HSO_4^-) in dichloromethane solutions, by a change in color from yellow ($\lambda_{max} = 390$ nm) to bluish purple (for **213**, $\lambda_{max} = 562$ nm) or blue (for **214**, $\lambda_{max} = 615$ nm, and for **215**, $\lambda_{max} = 632$ nm).[198] UV−visible and ^{19}F NMR experiments showed that the new absorption band at 615 nm was due to deprotonation of the phenolic group and formation of HF. Compound **216**, containing two thiourea groups and a phenol as a binding unit, gave color variation in the presence of F^-, $H_2PO_4^-$, and AcO^- in chloroform solutions.[199] Compound **216** showed an absorption maximum at 376 nm, and a new peak at 529 nm was found upon addition of those basic anions. For HSO_4^- and Cl^-, the color change was only detectable upon addition of 10 equivalents, whereas a large excess of Br^- or I^- resulted in no color variation. The color shift was

assigned to the formation of strong complexes between **216** and the anions through hydrogen-bonding interactions between the anions and the protons of the thiourea and the phenolic OH.

The dual receptor **217** contains two backbones susceptible to color variation: the azophenol (as that of **213**) and the thiourea−nitrophenyl (as that of **200**).[200] Compound **217** showed, in the absence of anions, one absorption maxima at 339 nm in chloroform. In the presence of $H_2PO_4^-$, with four oxygen atoms affecting both chromophores via multitopic hydrogen bonds, a pronounced color change was observed, while F^- and AcO^- had a relatively weaker effect. Thus, with $H_2PO_4^-$, the **217** band at 339 nm decreases while a new one gradually appears at 374 nm (due to the anion interaction with the thiourea−nitrophenyl backbone) and at 538 nm (due to anion interaction with the azophenol). The color of the solution changed from light yellow to violet. No detectable color changes were observed upon addition of HSO_4^-, Cl^-, and Br^-. In the case of receptor **218**, color differentiation between the $H_2PO_4^-$, AcO^-, and F^- anions was not feasible because the new absorption band obtained upon complexation of the three anions with **218** was similar and centered at ca. 530 nm.

Among the anions F^-, Cl^-, Br^-, I^-, AcO^-, $H_2PO_4^-$, and HSO_4^-, only the most basic ones, F^-, AcO^-, and $H_2PO_4^-$, formed strong enough complexes with the azophenolic function of the porphyrin-based receptors **219** and **220** and showed noticeable color changes.[201] Thus, yellow solutions of receptor **219** ($\lambda_{max} = 435$ nm) changed to blue upon addition of fluoride ($\lambda_{max} = 600$ nm), to orange-brownish upon addition of acetate ($\lambda_{max} = 525$ nm), and to orange upon addition of $H_2PO_4^-$ ($\lambda_{max} = 515$ nm). Similar color changes were observed with acetonitrile solutions of receptor **220** upon addition of the same anions. The selectivity of the anion-induced color changes for both receptors was determined to be $F^- > AcO^- > H_2PO_4^- \gg HSO_4^-$, Cl^-, Br^-, and I^-.

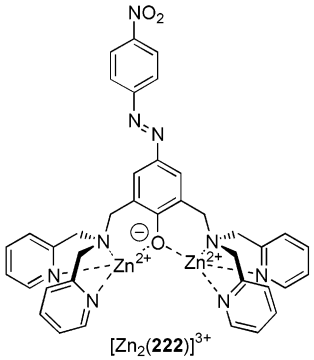
Certain metal complexes of the receptor **221** proved useful for the colorimetric sensing of the poorly



221

coordinating anion nitrate.[202] Acetonitrile solutions of the complexes $[Cu(\mathbf{221})]^{2+}$, $[Fe(\mathbf{221})_2]^{3+}$, and $[Hg(\mathbf{221})_2]^{2+}$ showed a band centered at ca. 525 nm that remarkably changed in a different manner upon addition of certain anions. Thus, acetonitrile solutions of $[Cu(\mathbf{221})]^{2+}$ changed from light red to orange in the presence of the anions F^-, $H_2PO_4^-$, and NO_3^- (λ_{max} at 485 nm) and to dark orange in the presence of Cl^- and HSO_4^- (λ_{max} at 500 nm). In a similar fashion, the red solutions of the $[Fe(\mathbf{221})_2]^{3+}$ complex changed the color to orange upon addition of I^- (λ_{max} at 480 nm) and to yellow with NO_3^- (λ_{max} at 470 nm). The most selective behavior was found for $[Hg(\mathbf{221})_2]^{2+}$ because NO_3^- was the only anion capable of shifting the color from red-orange to yellow (λ_{max} at 470 nm). A π-stacking interaction between the planar nitrate and the also planar azo-dye was suggested as a possible cause for the selective color variation. The $[Hg(\mathbf{221})_2]^{2+}$ complex was employed to determine nitrate concentrations in water samples with reasonable results.

Aqueous solutions (10 mM HEPES buffer, pH 7.4) of complex $[Zn_2(\mathbf{222})]^{3+}$ (in which both Zn^{2+} atoms



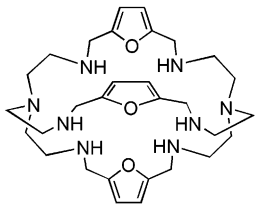
$[Zn_2(\mathbf{222})]^{3+}$

were coordinated with three nitrogen atoms and with the phenolate oxigen) presented an abpsortion band centered at 417 nm responsible for the yellow color observed.[203] Addition of $H_2PO_4^-$, AcO^-, F^-, HCO_3^-, Cl^-, HPO_4^{2-}, and citrate (up to an excess of 100 equivalents) did not induce remarkable spectral changes. However, additon of pyrophosphate causes a bathochromic shift from 417 to 465 nm and a color change from yellow to red. A 1:1 adduct was formed between the complex and the pyrophosphate anion. The binding model between $[Zn_2(\mathbf{222})]^{3+}$ and pyrophosphate involves interaction of two oxygen atoms of pyrophosphate with the zinc atoms in the complex to give two hexacoordinate Zn^{2+} ions in the adduct. It was suggested that the red shift of the emission maxima, induced by pyrophosphate binding, was due to a weakening of the bond between phenolate oxygen and Zn^{2+} atoms that increases the negative charge character of the phenolate oxygen, giving a bathochromic shift in the visible band.

4.2.4. Using Metal Complexes

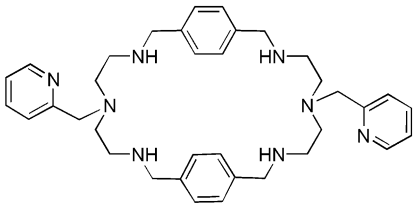
Here are gathered the examples where metal complexes act not only as binding sites but also as signaling units because the color variation resulted from the appearance of new MLCT bands upon anion coordination to the metal center. The examples shown below are based on copper(II) complexes of cryptand-like molecules. In those complexes, two copper(II) cations are coordinated according to a trigonal bipyramidal mode with a vacant axial position available for the coordination of either a solvent molecule or an anion. The selectivity of these bimetallic cryptates toward anions is associated basically with the shape and size of the guest that has to fit between both copper(II) units. For instance, compound **223** formed dicopper(II) complexes in which each metal ion is coordinated by a *tren* subunit.[204] The complex $[Cu_2(\mathbf{223})]^{4+}$ was able to encapsulate halide ions. The formation of 1:1 stoichometries suggested that the anions were included inside the cage. This encapsulation process produced a color

change from pale blue to bright yellow due to the development of an intense band, in aqueous solutions buffered to pH 5.2, upon addition of chloride (410 nm), bromide (430 nm), and iodide (440 nm), but no changes were observed with fluoride. This intense band should result from a $X^- \rightarrow Cu^{2+}$ CT transition. In the presence of N_3^- or SCN^-, there was a color shift from pale a blue to olive green.



223

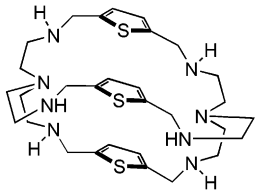
The dicopper(II) complex of the receptor **224** was capable of recognizing imidazolate over other anions



224

tested (N_3^-, NCO^-, NCS^-, and HCO_3^-) by a change in the visible spectra.[205] An aqueous solution with 1 equivalent of **224** and 2 equivalents of Cu^{2+} adjusted to pH 9 presented a blue color ascribed to the $Cu(II)N_4$ chromophore (maximum absorption band at 640 nm). On titration with imidazolate, the pale blue color turned to a more intense blue. The absorption band shifted to 690 nm, and the intensity increased. The imidazolate anion bridged to the two Cu(II) atoms with the simultaneous release of a proton. This binding event induced the appearance of a new CT band (centered at 690 nm) that gives the observed color change. This effect was used to recognize L-histidine (containing the imidazole moiety) visually through the appearance of the blue color in aqueous solution of $[Cu_2(\mathbf{224})]^{4+}$ in the presence of other amino acids (L-glicine, L-proline, L-cysteine, L-valine, L-arginine, L-serine, and L-tryptophan).

The $[Cu_2(\mathbf{192})]^{4+}$ cryptate proved to be an suitable receptor for certain linear anions.[206] Progressive addition of NaN_3 to solutions of $[Cu_2(\mathbf{192})]^{4+}$ at pH = 8.0 resulted in a color change from blue to bright green due to the formation of a new band at around 400 nm assigned to the formation of the inclusion complex $[Cu_2(\mathbf{192})(N_3)]^{3+}$. pH titration studies on the Cu^{2+}/**192** system (2:1 molar ratio) showed that the dominating species at pH = 8.0 was $[Cu_2(\mathbf{192})(OH)]^{3+}$, indicating that the anion coordination equilibrium involved a replacement of OH^- by the N_3^- anion. $[Cu_2(\mathbf{192})]^{4+}$ formed the stronger complexes with linear anions such as N_3^-, NCO^- (λ_{max} = 340 nm), and HCO_3^- (λ_{max} = 360 nm) as their length fits well in the distance between the two copper cations within the cryptate, whereas less stable complexes were formed with SCN^-, SO_4^{2-}, $HCOO^-$, AcO^-, and NO_3^-. A close behavior was found for **225** that formed a bimetallic copper(II) complex that selectively bound



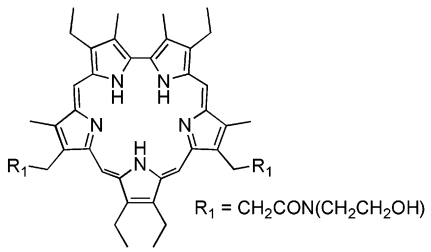
225

N_3^-, NCO^-, and NCS^- over other anions tested in aqueous solutions buffered at pH 6.9.[207] Solutions of the complex $[Cu_2(\mathbf{225})(OH)]^{3+}$ were pale green with two bands centered at 694 and 820 nm. The addition of equimolar quantities of the N_3^-, NCO^-, and NCS^- anions induced the apparition of new absorption bands at 358 and 440 nm from the copper(II)−anion interactions. Negligible variations were observed in the presence of SO_4^{2-}, NO_3^-, HCO_3^-, AcO^-, Cl^-, Br^-, and I^- anions.

4.2.5. Containing Sapphyrins and Porphyrins

Porphyrins and related tetrapyrrolic macrocycles serve a variety of critical roles in living systems and remain among some of the most studied of all macrocyclic systems. Additionally, sapphyrins are one of the most important and studied families of expanded porphyrins.[188] Sapphyrins contain five pyrrolic subunits, are 22 π-aromatic systems, are more basic than porphyrins, and have been reported to host in the protonated form, in the sapphyrin core, anions via hydrogen bonding and columbic interactions. The UV−visible spectrum of the sapphyrins presents the typical Soret-like absorbance centered at ca. 450 nm. A special feature of certain sapphyrins is that they can aggregate or deaggregate upon coordination with certain anions, and this effect is related with changes in the position of the Soret band. This anion-mediated color change in the aggregation−deaggregation process has been used by receptors **226**−**230** to colorimetrically sense certain anions.

Sapphyrin **226** presents a Soret absorption band centered at 410 nm in water at pH 7.0.[208] This band

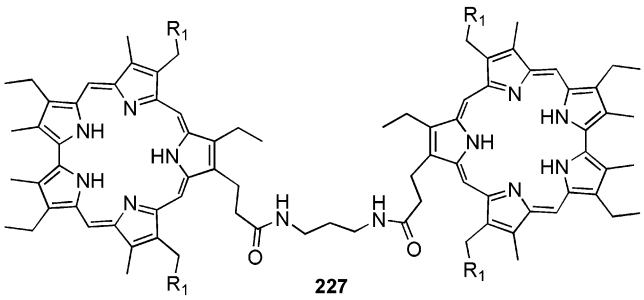


226

was due to the formation of aggregates of **226**. Studies of the interaction of sapphyrin **226** with nucleotides (cCMP, cTMP, cAMP, and cGMP) and polymeric nucleotides (ss DNA and ds DNA) were carried out in water solutions at pH 7.0. With pyrimidine-containing nucleotides (cCMP, cTMP), an absorption band centered at 422 nm was observed and was assigned to the phosphate-bound complex

of the dimer of **226** and the correspondent nucleotide. With purine-containing nucleotides (cAMP, cGMP), the absorption band at 422 nm was partially replaced by a band at 450 nm assigned to the monomeric form of **226** π-stacked with the nucleobase. Interaction of **226** with ds DNA and ss DNA resulted in only one absorption band at 422 nm and two absorption bands at 422 and 450 nm, respectively.

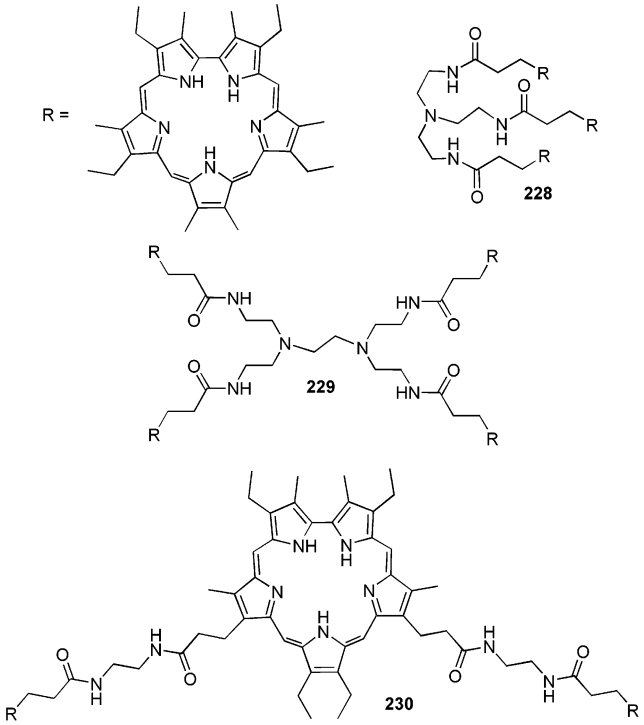
The sapphyrin dimmer **227** showed two absorption bands in methanol at 422 (self-stacked form) and 441



227

nm (nonaggregated form).[209] Addition of dicarboxylate anions to solutions of **227** in methanol caused an intensity enhancement of the band at higher wavelength (nonaggregated form) at the expense of the band at lower wavelength (aggregated form). The results were consistent with a model wherein the dicarboxylate substrates were bound inside the sapphyrin sandwich. Association constants were determined following the increase in relative absorbance at 450 nm with oxalate, malonate, isophthalate, 5-nitroisophthalate, and nitroterephthalate.

Experiments in water:methanol (1:1) were carried out to determine binding constants of receptors **228**–**230** with ADP and ATP.[210] The receptors showed two



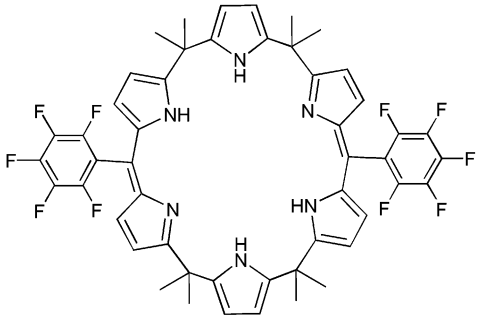
228

229

230

Soret maxima at 420 and 450 nm. The high and low energy transitions corresponded to the aggregate and nonaggregate forms, respectively. Addition of nucleotides resulted in an increase of the band at higher wavelength and a decrease of the intensity of the band at lower wavelength. Following the relative decrease in absorbance at 420 nm as a function of the substrate-to-receptor ratio, association constants were determined. The larger formation stability constants for receptors **228** and **230** were found with ATP whereas for **229**, it was with ADP.

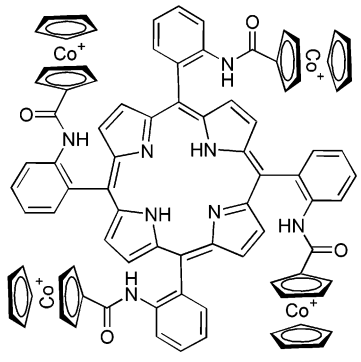
Full conversion of the calix[6]phyrin **231** to the diprotonated form [**231**·$2H^+$] was effected by addition



231

of 90 equivalents of H_2SO_4·30% SO_3 to acetone solutions of **231**.[211] Upon this addition, the band at 449 nm decreased and a new band appeared at 499 nm. The solution changed from yellow to pink. Significant shifts in the band at 499 were seen upon the addition of chloride (red shift of 40 nm), bromide (blue shift of 10 nm), and iodide (blue shift of 20 nm). Full saturation was observed in the presence of 13, 6, and 60 equivalents of these anions, respectively.

In acetonitrile solutions, the Soret band of the receptor **232** at 425 nm was significantly bathochro-

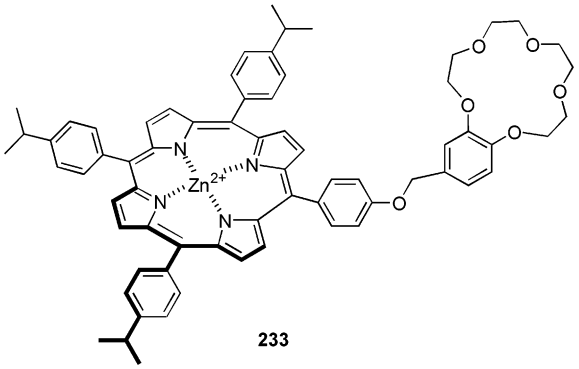


232

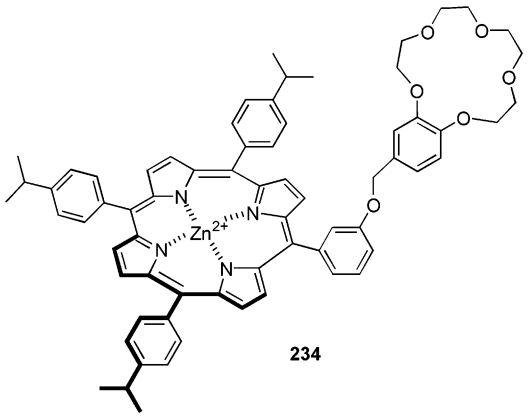
mically shifted ($\Delta\lambda$ = 15 nm) on addition of $H_2PO_4^-$ and hypsochromically shifted with Cl^- ($\Delta\lambda$ = 10 nm) and split into two maxima (430, 440 nm) with HSO_4^-.[212] The anions formed 1:1 complexes via favorable amide hydrogen bonding and electrostatic interactions with the four cobaltocenium moieties.

Changes in color on the Zn(II) complexes of the porphyrins **233** and **234** allowed visual detection of the cyanide anion.[213] Liquid–liquid extraction studies by ^1H NMR revealed that organic solutions of the receptors extracted, in monotopic fashion, sodium cations from water containing the salts NaF, NaCl, NaBr, NaI, NaSCN, and NaH_2PO_4. These extraction

experiments showed that sodium ion was coordinated in the crown ether moiety. Only NaCN was extracted from the water solution in a ditopic fashion by coordination of sodium cation with the crown ether moiety and the cyanide anion with the Zn(II) center of the porphyrin moiety. The high basicity of cyanide anion was responsible of the ditopic extraction of sodium cyanide despite charge separation. This coordination of cyanide induced changes in the color of the solution of the two receptors from red (λ_{max} = 420 nm) to green (λ_{max} = 435 and 550 nm).

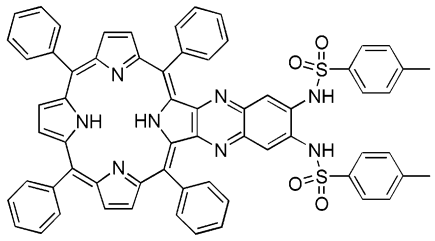


233



234

The anion binding ability of receptor **235** (dichloromethane solutions) was detected by perturbations

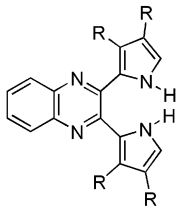


235

of the porphyrin Soret band.[214] This band centered at 422 nm was red shifted 12−16 nm in the presence of different anions. Cl^-, Br^-, I^-, and HSO_4^- formed complexes of 1:1 stoichiometries, whereas F^-, AcO^-, and $H_2PO_4^-$ gave 1:2 (anion-to-ligand) complexes. The selectivity trend observed was $F^- > H_2PO_4^- > AcO^- > Cl^- > HSO_4^- > Br^- > I^-$, which was related with the basicity of the anions. Anion binding interaction consisted of hydrogen bonds between the acidic sulfonamide N−H hydrogens and the anion. The changes in the Soret band were ascribed to an increase in electron density in the receptor (acting as a Lewis acid) upon interaction with the anionic guest.

4.2.6. Containing Dipyrroylquinoxalines

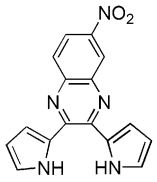
Dipyrroylquinoxalines have been used as chromogenic receptors for anions because they contain two pyrroyl NH groups that could act as anion binding moieties and a quinoxaline ring that might serve as a colorimetric reporter of the binding event. It has been suggested that coordination of the anions with the two pyrrole rings might induce perturbation in the orbital overlap between the pyrrole and the quinoxaline subunits, thereby changing the optical behavior of the dipyrroylquinoxalines upon anion binding. In all cases, a bathochromic shift was observed, suggesting, as an alternative interpretation, an increase in the donor strength of the pyrroyl NH groups upon anion coordination. For instance, solutions of receptor **236** in dichloromethane were



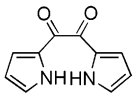
236 R=H
237 R=F

yellow (λ_{max} = 420 nm) and changed to orange (λ_{max} = 470 nm) in the presence of fluoride, whereas other anions such as Cl^-, Br^-, and $H_2PO_4^-$ did not induce any band shift.[215] In contrast, **237** showed color shifts from yellow to orange in the presence of both fluoride and dihydrogen phosphate anions. These results were in line with the determined stability constants (the largest stability constant was for fluoride for both **236** and **237** receptors). Additionally, the presence of four fluorine atoms in **237** led to a remarkable increase of the stability constant with $H_2PO_4^-$.

Compound **238** showed a remarkable color change from yellow (λ_{max} = 455 nm) to purple (λ_{max} = 560



238

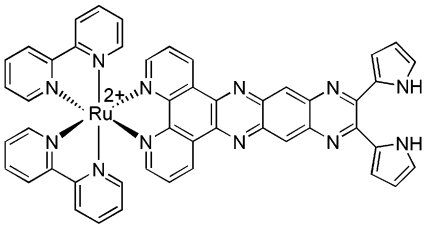


239

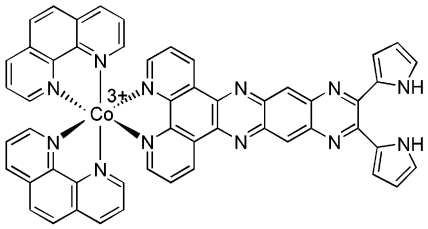
nm) upon fluoride addition in dichloromethane or DMSO, whereas chloride and dihydrogen phosphate did not produce any noteworthy color variation.[216] The sensing of fluoride was also monitored by the quenching of the emission fluorescence observed in the presence of this anion. The color change was in agreement with the quite large stability constant found between **238** and F^- whereas formation constants with chloride and dihydrogen phosphate were much smaller. The diketone **239** gave brightly colored

dichloromethane solution that changed from yellow-green ($\lambda_{max} = 341$ nm) to orange ($\lambda_{max} = 470$ nm) in the presence of fluoride.

The anion binding properties of receptors **240** and **241** in the presence of fluoride, chloride, and dihydrogen phosphate were studied by UV−visible spectroscopy in DMSO.[217] With the two receptors, the band at 525 nm decreased upon addition of fluoride and a new band appeared at 670 nm for receptor **240** and at 652 nm for receptor **241**. Furthermore, the color of the solution changed from red-pink to pale purple. These spectral changes were ascribed to the formation of 1:1 adducts between the metal complexes and the fluoride anion in which the fluoride anion binds, through hydrogen-bonding interactions, with the two dipyrrolylquinoxaline units. Receptor **241** was also studied by cyclic voltammetry, and a clearly reversible redox signal was observed at 160 mV (vs SHE) assigned to the Co(III)/Co(II) reduction. The addition of fluoride led to a complete disappearance of the Co(III)/Co(II) reduction signal due to the formation of a redox inactive strong complex.



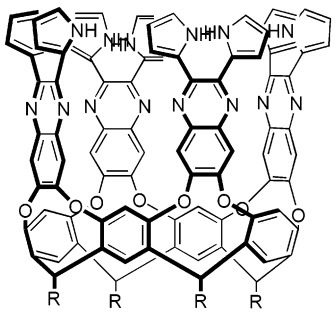
240



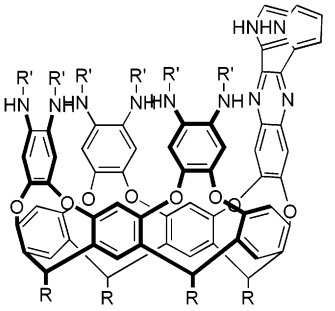
241

Cavitands **242** and **243** were used as visual detectors of fluoride and acetate anions in dichloromethane and acetone.[218] The addition of a 50-fold excess of F^- or Ac^- to acetone solutions of **242** induced the suppression of the band at $\lambda_{max} = 420$ nm (assigned to dipyrroylquinoxaline units) and two new bands at $\lambda_{max} = 350$ and 490 nm emerged (color from yellow to dark red). A similar behavior was observed for cavitand **243**. No chloride and very weak dihydrogen phosphate complexation were detected. ^{1}H NMR measurements showed that the interaction of the anions with these receptors was by means of hydrogen bonding with the pyrrolyl NH groups.

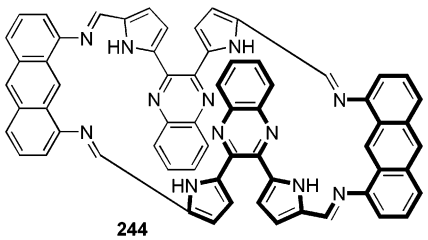
Quinoxaline-bridged porphyrinoid **244** presented two similary sized cavities with six nitrogen atoms.[219] The UV−visible absorption spectrum of receptor **244** recorded in dichloromethane showed two bands at 367 and 427 nm. Upon addition of increasing quantities of F^- anion to yellow solutions of dichloromethane−DMSO 9:1 (v/v), two new bands were observed centered at 329 and 480 nm with a change in color to orange upon addition of 20 equivalents of F^- anion. Similar spectral behavior was observed with $H_2PO_4^-$ but after addition of more equivalents. Addition of more than 300 equivalents of Cl^-, Br^-, NO_3^-, or HSO_4^- to solutions of receptor **244** induced no change in color. F^- and $H_2PO_4^-$ anions coordinated with receptor **244** through a hydrogen-bonding interaction with the N−H pyrrolic moieties forming 2:1 (anion−receptor) adducts. Changes in color are probably due to the enhancement in the donor ability of the N-pyrrolic nitrogens upon anion binding.



242 R = $(CH_2)_{10}CH_3$

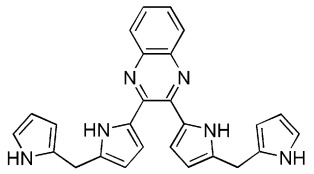


243 R = $(CH_2)_{10}CH_3$
R' = $CO(CH_2)_6CH_3$

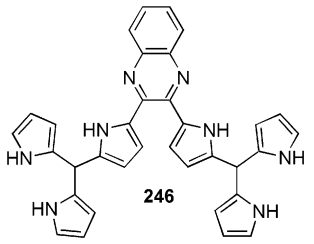


244

Stability constants for the interaction of receptors **245** and **246** with fluoride, chloride, and dihydrogenphosphate were obtained following the changes in the UV−visible abpsortion spectrum.[220] The two receptors form 1:1 complexes with these anions with enhanced affinities when compared to simple dipyrrolylquinoxaline (stability constants obtained for receptor **246** were larger than that for **245**). In the specific case of receptor **245**, it was found that the addition of fluoride to dichloromethane solutions caused a color change from yellow ($\lambda_{max} = 426$ nm) to red (apparition of a broad shoulder arround 500−580 nm).



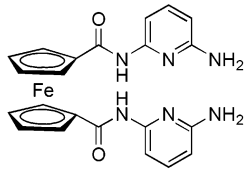
245



246

4.2.7. Miscellaneous

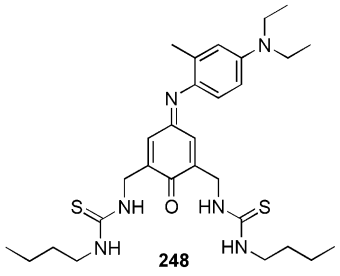
Addition of $H_2PO_4^-$ to acetonitrile solutions of **247** resulted in a 10 nm shift of the d−d ferrocene band



247

at 443 nm and a large increase (500%) in the intensity of this band allowing visual detection the of the dihydrogen phosphate anion.[221] The addition of HSO_4^- caused a negligible response. The different response was associated to the different coordination ability of both anions. Thus, the basic $H_2PO_4^-$ that bound at the amide units close to the ferrocene unit caused a larger perturbation in the UV−visible spectrum. In contrast, HSO_4^- that bound to the receptor at the amine units was more distant from the ferrocene moiety and left its UV−visible spectrum unaffected. Further addition of hydrogen sulfate (5 equivalents) to the **247**−$H_2PO_4^-$ system inhibited the observed response for the $H_2PO_4^-$ anion in agreement with the fact that bound HSO_4^- sterically and electronically hindered $H_2PO_4^-$ binding.

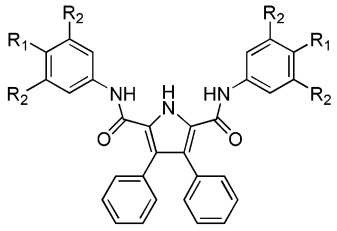
Chloroform solutions of the indoaniline−thiourea receptor **248** are blue-green due to the presence of



248

an absorption band centered at 678 nm.[222] In the receptor **248**, an intramolecular hydrogen bond between the carbonyl oxygen of indoaniline and the two adjacent thiourea NH groups is formed. Upon addition of $H_2PO_4^-$ or HSO_4^-, the color of the solutions changed from blue-green to deep blue due to a hypsochromic shift of the absorption band from 678 to 632 nm. Addition of AcO^- and F^- caused a less intense color change, and no detectable changes were described with Cl^-, Br^-, and I^- anions. Receptor **248** bound $H_2PO_4^-$ and HSO_4^- because these tetrahedral anions gave hydrogen bond interactions with the NH groups of the two thiourea moieties. It was suggested that the complexed anions disturbed the intramolecular hydrogen bond structure of the receptor, therefore inducing spectral absorption changes in the complexes. Interestingly, there was a selective colorimetric detection of $H_2PO_4^-$ and HSO_4^- over F^-.

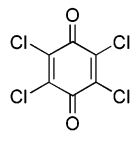
Receptors **249** and **250** were not soluble in acetonitrile; however, addition of anions solubilized them



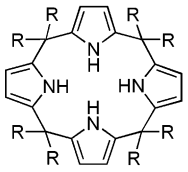
249 $R_1 = NO_2$, $R_2 = H$
250 $R_1 = H$, $R_2 = NO_2$

and induced color changes.[223] In the case of receptor **249**, a yellow color appeared with the addition of F^-, BzO^-, and $H_2PO_4^-$ anions, whereas the addition of Cl^- and Br^- did not show any effect. With receptor **250**, an intense blue color (λ_{max} = 598 nm) was observed upon addition of F^- anion and pale yellow upon addition of BzO^- and $H_2PO_4^-$. The color change observed with receptor **250** induced by the addition of fluoride anion was ascribed to a deprotonation process caused by F^- acting as a base and subsequent CT interaction between the deprotonated pyrrole and the nitoaromatic rings. BzO^- and $H_2PO_4^-$ anions coordinated with receptor **249** and **250** through hydrogen-bonding interactions with the amide moieties.

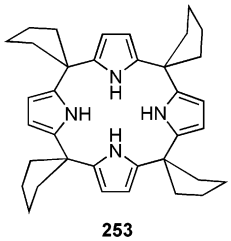
Chloranil (**251**) formed colored CT complexes (1:1 stoichiometries) with the calix[4]pyrroles **252**−**255**.[224]



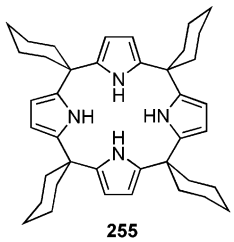
251



252 $R = CH_2CH_3$
254 $R = CH_3$



253

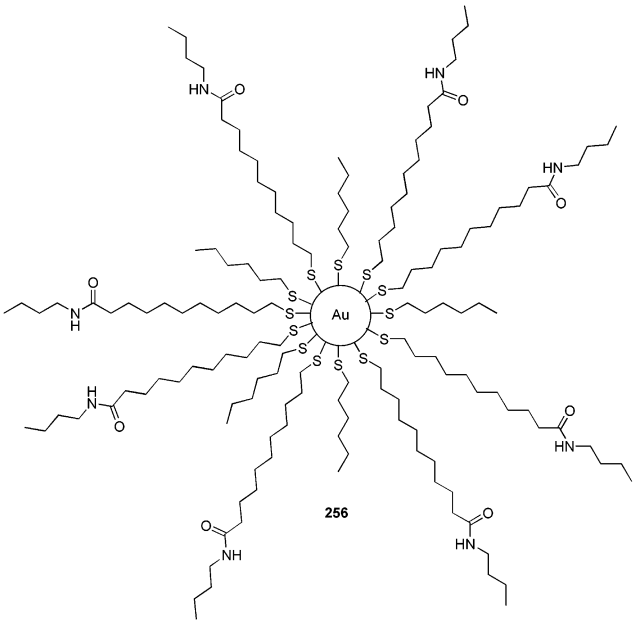


255

Chloranil itself shows an absorption maxima centered at 370 nm in $CHCl_3$. Addition of calix[4]pyrrole **252** produced an increase in intensity of the peak at

370 nm, and the apparition of new band centered at 622 nm that was ascribed to a CT complex. The color of the solution changed from pale yellow to blue. Similarly, the addition of **253** to solutions of chloranil induced a color shift from pale yellow to purple (λ_{max} = 550 nm). In the case of calix[4]pyrroles **254** and **255**, the color of the solutions changed very slowly from pale yellow to greenish yellow (after 16 h, λ_{max} = 470 nm) and dark blue (after 16 h, λ_{max} = 615 nm), respectively. These CT complexes were useful colorimetric receptors for anion sensing. The addition of F^- and $H_2PO_4^-$ anions to a solution of the complex **251**−**252** induced the elimination of the CT band at 622 nm, and new absorptions appeared at 426 and 450 nm changing the color of the solution from blue to orange-yellow. These two new absorption bands were assigned to the formation of calix[4]pyrrole−anion−chloranil adduct in which the anion interacts simultaneously with both the calix[4]pyrrole subunit (via hydrogen bonds with pyrrolic NH) and the chloranil subunit. Negligible perturbation in the UV−visible spectra was obtained upon addition of Cl^-, Br^-, I^-, HSO_4^-, and ClO_4^- anions. Similar results were found with the **251**−**253** and **251**−**255** systems. Preliminary experiments showed that the addition of monophosphate of inosine, uridine, and guanosine to $CHCl_3$−EtOH−H_2O (7:2:1) solutions of the ensemble **251**−**252** induced color change from pale blue to pale yellow.

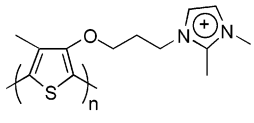
The amide-functionalized gold nanoparticle **256** was used for optical sensing of $H_2PO_4^-$, HSO_4^-, AcO^-,



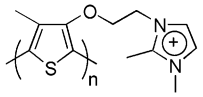
256

NO_3^-, Cl^-, Br^-, and I^- anions.[225] Dichloromethane solutions of **256** are red-wine with a characteristic plasmon band centered at 520 nm. When 0−0.5 equivalents of the anions was added to the solution of **256**, the plasmon band decreased in intensity (about 45−55%) with a slight red shift in wavelength. This marked decrease in the intensity of the band was ascribed to an anion-induced aggregation of **256** through hydrogen bond formation between the anions and the interparticle amide groups. Further addition of anions to **256** solutions caused an increase in intensity reflecting the disaggregation of the supramanoparticles built by **256** and the corresponding anion. The maximum decreasing ratio ($\Delta I_{max} = (I_{min} - I_0)/I_0$) in intensity of **256** upon anion binding showed the preference for $H_2PO_4^-$ and HSO_4^-. These nanoparticles were capable of optically sensing changes in anion concentration at a level of 10^{-6} mol dm^{-3}.

Aqueous solutions of polymer **257** were yellow (λ_{max} = 406 nm) and attributed to a random coil conformation of the polythiophene derivative that leads to a



257



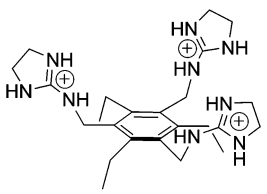
258

decrease in the effective conjugation through the polythiophene chain.[226] Addition of F^-, Cl^-, Br^-, SO_4^{2-}, CO_3^{2-}, HCO_3^-, $H_2PO_4^-$, HPO_4^{2-}, EDTA,$^{4-}$, $(C_6H_5)B^-$, or AcO^- induced negligible changes in the UV−visible spectrum, whereas addition of I^- gave a red shift of the band centered at 406 nm to 543 nm (change in the color from yellow to red-violet). This color variation was ascribed to iodide-induced aggregation and planarization of polymer **257**. Fluorimetric detection of iodide anion was also possible because the fluorescence of **257** in the yellow random coil form (λ_{exc} = 420 nm, λ_{em} = 550 nm) was quenched in the planar aggregated form. The polymer **258** proved to be much less sensitive to iodide than the polymer **257**.

4.3. Following the Displacement Approach

Probably some of the most interesting and potentially applicable results in new chromogenic sensing systems have been described following the displacement approach. Some of the most commonly used dyes in the development of colorimetric displacement assays for anion sensing have been fluorescein derivatives and pyrocatechol violet. Other dyes used were methyl red, resorufin, alizarin complexone, xylenol orange, and methylthymol blue (see Figure 45).

Fluorescein as an indicator has been used with the receptors **259**, **260**, **261**, and **262**. The cocktail 5-carboxyfluorescein−**259** was a chemosensor for citrate



259

in methanol:water 75:25 v/v mixtures buffered at pH 7.4.[227] Addition of the guanidinium receptor **259** to a solution of 5-carboxy-fluorescein resulted in an increase of the absorption band (λ_{max} = 498 nm) of the fluorescein derivative and an enhancement of its fluorescence emission (λ_{em} = 525 nm). This increase

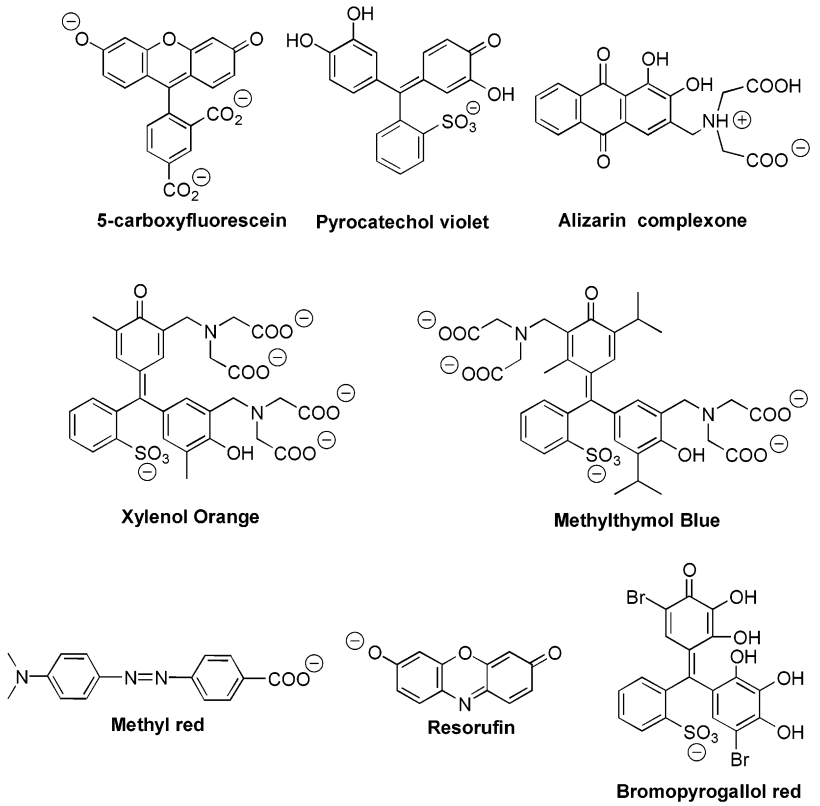
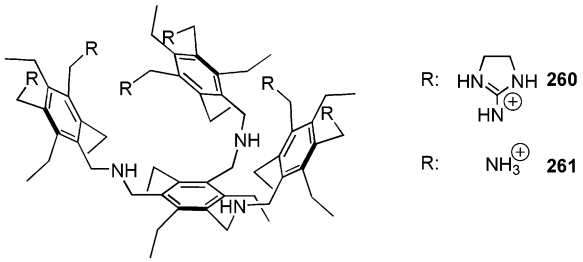


Figure 45. Chemical structures of the dyes 5-carboxyfluorescein, pirochatecol violet, alizarin complexone, xylenol orange, methylthymol blue, methyl red, resorufin, and bromopyrogallol red used in displacement assays.

in absorbance was a result of the increased ionization of the phenol of the xanthene ring due to the positively charged microenvironment that the fluorescein found when coordinating the molecular receptor **259**. Further addition of citrate resulted in a decrease of both the absorbance at 498 nm and the fluorescence intensity assigned to the fact that 5-carboxyfluorescein was expelled from the binding pocket due to the higher binding affinity of citrate toward **259** than that of **259** toward fluorescein. Addition to succinate to the mixture **259** and 5-carboxyfluorescein resulted in a small absorbance and fluorescence change, and the addition of acetate or sugars resulted in no variation. Calibration curves were plotted and used for the citrate determination down to the millimolar level in certain beverages. The same receptor formed 1:1 and 2:1 complexes with the indicators xylenol orange and methylthymol blue.[228] The absorbance of xylenol orange at pH 7.5 increased at 577 nm upon association with **259**, while the absorbance at 445 nm decreased (color of solutions changed from orange to pink-red). Similarly, the absorbance of methylthymol blue at the same pH value increased at 607 nm upon addition of **259** and the absorbance at 454 nm decreased (solutions changed from a light yellow to cobalt blue). These changes in color of the indicators upon binding with receptor **259** were assigned to changes in the pK_a of the indicator due to the positive microenvironment in receptor **259**. Addition of citrate to solutions of these complexes caused a reverse in absorbance of both indicators.

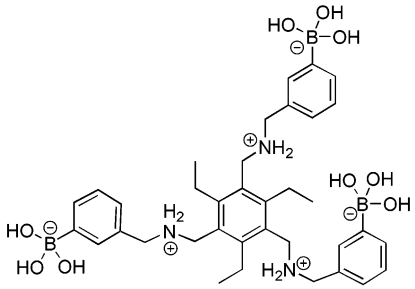
A similar competition assay using 5-carboxyfluorescein and receptors **260** or **261** was used for



monitoring the presence of inositol−triphosphate (IP_3) in water buffered at pH 7.4.[229] The addition of **260** or **261** to 5-carboxyfluorescein resulted in a red shift (12 nm, from 490 to 502 nm) of the absorption band of the fluorescein derivative. Addition of inositol−triphosphate as well as other anionic guests (such as benzene-1,3,5-triphosphate, phytic acid, ATP, fructose-1,6-diphosphate, etc.) to a solution containing **260** or **261** and 5-carboxyfluorescein resulted in a displacement of the fluorescein derivative and subsequent blue shift of the absorption maximum. To enhance the affinity of receptor **260** for inositol−triphosphate, additional studies were carried out in methanol. In this solvent, 5-carboxyfluorescein was in a cyclized form that was colorless and nonfluorescent. Upon addition of **260**, the yellow color of 5-carboxyfluorescein and its fluorescence reappeared because the positive character of the receptor induced a ring opening giving the colored/fluorescent

form of the indicator. Addition of the inositol−triphosphate to a mixture of **260** and 5-carboxyfluorescein resulted in a decrease of the fluorescence and the absorbance due to coordination of **260** with inositol−triphosphate and subsequent release of 5-carboxyfluoresecin into the methanol solution.

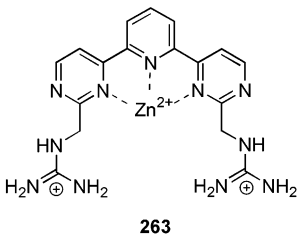
Receptor **262** was employed in a competition assay with 5-carboxyfluorescein with the aim to detect



262

glucose-6-phosphate in water−methanol 70:30 v/v mixtures buffered at pH 7.4.[230] The addition of **262** to solutions of 5-carboxyfluorescein resulted in an increase in the absorbance intensity at 494 nm. Addition of glucose-6-phosphate decreased the absorbance intensity at 494 nm due to a displacement in the 5-carboxyfluorescein-receptor equilibrium, until the absorbance spectrum approached the absorbance spectrum of free 5-carboxyfluorescein. No changes were produced when glucose or sodium phosphate were used instead of glucose-6-phosphate.

The association of the complex **263** and the dye pyrocatechol violet was a suitable combination for

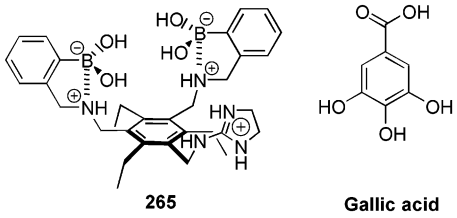


263

sensing of certain amino acids via a displacement approach.[231] Compound **263** formed 1:1 complexes with pyrocatechol violet via coordination with the Zn(II) metal atom. Solutions of the indicator, in water/methanol 1:1 mixtures buffered at pH 7.4, changed the color from yellow (λ_{max} = 445 nm) to deep blue (λ_{max} = 647 nm) upon addition of receptor **263**. This color change was ascribed to changes in the ionization state of the dye. The addition of various amino acids (L-phe, L-valine, glycine, L-asparagine, L-aspartic acid, and L-glutamic acid) to an ensemble of **263**:pyrocatechol violet resulted in a color change from deep blue to yellow indicating the displacement of the indicator and the formation of a 1:1 complex between receptor **263** and the corresponding amino acid. The highest affinity constant was found for aspartate. The affinity of **263** for amino acids was dominated by their interaction with the zinc metal ion, but it was suggested that in the case of aspartate the appended guanidinium moieties surely also played a special role in the binding and selectivity process.

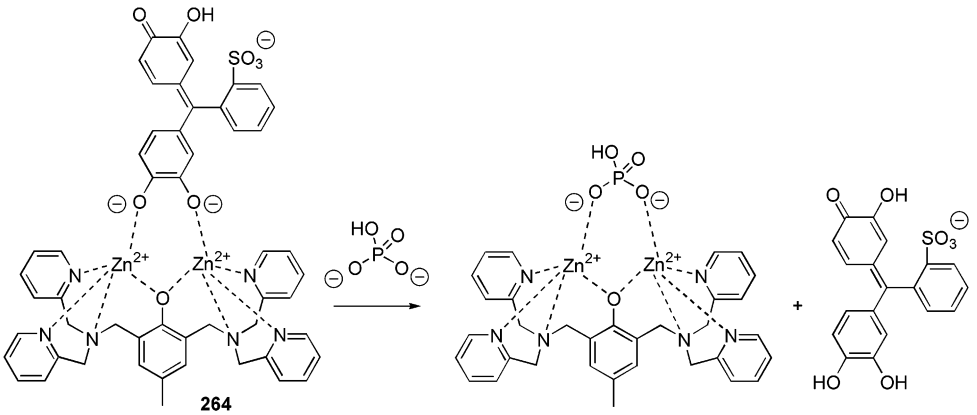
Addition of the complex $[Zn_2(\mathbf{264})]^{4+}$ to aqueous solutions (pH 7) of pyrocatechol violet induced a color change from yellow (λ_{max} = 440 nm) to blue (λ_{max} = 624 nm) ascribed to the binding of pyrocatechol violet with the two Zn^{2+} cations in the complex (see Figure 46).[232] Addition of phosphate to aqueous solutions of the ensemble produced a change in color from blue to yellow due to the release to the solution of the bound pyrocatechol violet upon phosphate binding. The probe exhibited excellent selectivity toward phosphate over the anions acetate, hydrogen carbonate, nitrate, azide, perchlorate, sulfate, fluoride, chloride, and bromide. A quantitative determination of phosphate in a neutral aqueous solution also containing ions commonly found in biological systems (Na^+, Cl^-, AcO^-, and HCO_3^-) was described.

The gallate anion was sensed via a competition mechanism by using a mixture of the receptor **265**



265 **Gallic acid**

and the pyrocatechol violet dye.[233] Addition of receptor **265** to a solution of pyrocatechol violet (25%



264

Figure 46. Scheme of the displacement assay in which the anion phosphate replaces the pyrochatecol violet dye in receptor **264**.

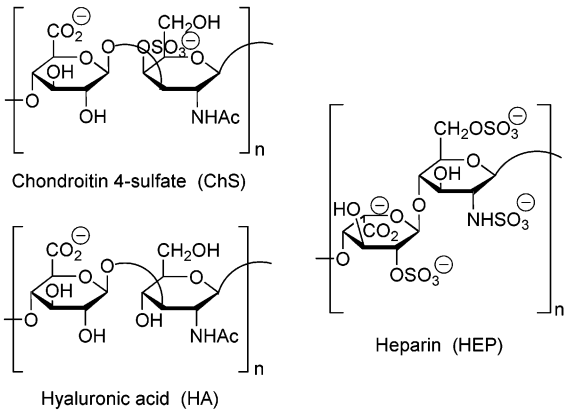
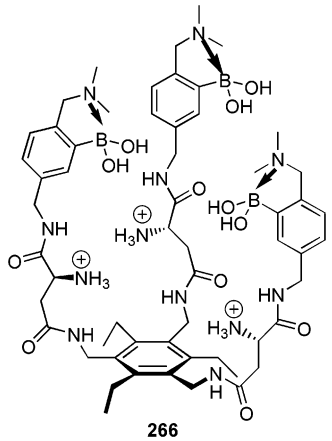


Figure 47. Chemical structures of negatively charged oligosaccharides chondroitin 4-sulfate (ChS), hyaluronic acid (HA), and heparin (HEP).

water−methanol mixtures) resulted in color variations from yellow to maroon due to the encapsulation of the indicator into the receptor and formation of a 1:1 complex. Upon addition of gallate to the sensing ensemble, the color returned to yellow as the indicator was displaced from the complex. This change in absorbance was used to quantify the gallate anion. This sensing ensemble also showed selectivity for analytes having both diols and carboxylate moieties and was used to evaluate the age of several different scotches by determining the amount of gallate and other related anions (caffeate, ellagate, and 3,4-dihydroxybenzoate) following this displacement assay.

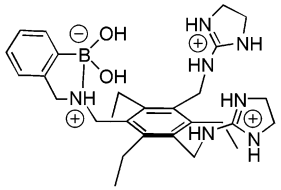
Addition of pyrocatechol violet to water−methanol 1:1 solutions (pH 7.4) of receptor **266** resulted in a



266

decrease of the band at 430 nm and an increase of the band at 526 nm (color change from yellow to grayish purple).[234] Addition of heparin to a solution of the sensing ensemble causes an inverse color change from purple to yellow due to the release of the indicator from the binding cavity of receptor **266** upon heparin binding. Addition of chondroitin 4-sulfate or hyaluronic acid (see Figure 47) to the sensing ensemble also decreases the absorbance at 526 nm (purple band) but to a lesser extent (60 and 10%, respectively, of that in the case of heparin). This selectivity observed was related with the anionic charge density of the glycosaminoglycan analytes, namely, HEP > ChS > HA, suggesting that electrostatic interactions played a dominant role in the binding process.

Compound **267** contains a boronic acid and two guanidinium groups organized to give a cavity of



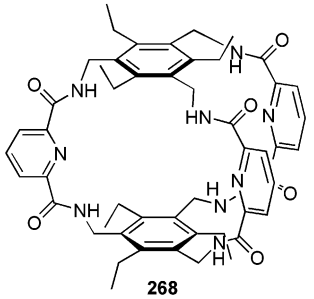
267

correct dimensions for tartrate.[235] Tartrate is a common natural product that can be found in grape-derived beverages. There was a color change from burgundy (λ_{max} = 525 nm) to yellow-orange (λ_{max} = 450 nm) upon addition of the receptor **267** to a solution of alizarin complexone in water−methanol mixtures (75:25 v/v) buffered at pH 7.3. This color variation was ascribed to a change in the protonation state of the phenols of the alizarin upon coordination with the boronic acid moiety present in receptor **267** and formation of a boronate ester. The addition of L-tartrate to a mixture of **267** and alizarin complexone resulted in a color shift from yellow-orange to burgundy due to coordination of **267** with tartarte and release to the solution of the alizarin derivative. Coordination studies and determination of stability constants demonstrated that receptor **267** has an excellent selectivity for tartrate. Only malate showed a similar response than tartrate whereas other possible competing analytes such as ascorbate, succinate, lactate, and sugars did not induce any significant color change. Calibration curves using this method were used to determine tartrate and malate concentrations in grape-derived beverages.

Receptors **267** and **265** were used along with bromopyrogallol red and pyrocatechol violet indicators to develop a multicomponent sensing ensemble to selectively detect and quantify two similar analytes such as tartrate and malate.[236] Receptor **267** was previously found to have a similar affinity for tartrate and malate whereas receptor **265** has greater affinity for tartrate over malate. In this new approach, a number of UV−vis spectra of a mixture of **267**, **265**, and the two indicators were obtained upon addition of various amounts of tartrate and malate. From those data, artificial neuronal networks were used for pattern recognition analysis and simultaneous tartrate and malate determination in mixtures of both analytes, was achieved.

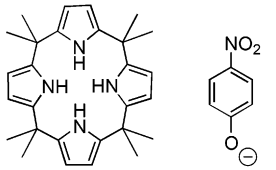
A displacement reaction using the cocktail **268** with the dyes methyl red and resorufin in CH_2Cl_2:MeOH 1:1 v/v was used for nitrate sensing.[237] Addition of the poorly coordinating anion nitrate to solutions containing the receptor **268** and the dye resulted in the formation of a nitrate−**268** complex and subsequent displacement of the indicator with large changes in color. Thus, λ_{max} values for the ensemble **268**−methyl red and **268**−resorufin were 492 and 576 nm, respectively, whereas the free methyl red and re-

sorufin dyes showed λ_{max} values at 500 and 580 nm. These large absorbance changes observed when the free dyes were compared with the **268**−dye ensembles were ascribed to an alteration of the microenvironment of the chromophores upon coordination. Addition of bromide or perchlorate to solutions of **268**−methyl red or **268**−resorufin mixtures also produce changes in the intensity of the bands although in a lesser extension.



268

A competitive method was used for the determination of halide anions in acetonitrile or dichloromethane solutions using a combination of 4-nitrophenolate and **269**.[238] Thus, the yellow color (band



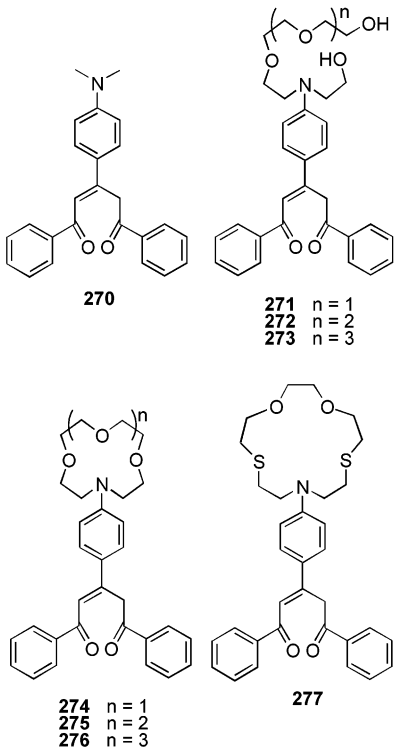
269

at 432 nm) of the 4-nitrophenolate anion disappeared upon complexation with **269** because of coordination, by means of hydrogen bonds, of the 4-nitophenolate anion with the pyrrolic NH of **269** (coordination decreased the electronic density and the donor character of the oxygen atom). Addition of anions to solutions of **269** and 4-nitrophenolate resulted in yellow color revival attributed to a displacement of the 4-nitrophenolate anion from the calix[4]pyrrole anion binding site. The stronger displacement, and therefore the larger absorbance variation, was observed upon addition of fluoride followed by chloride and dihydrogen phosphate. This trend was in line with the affinity of the receptor for those particular anions.

4.4. Following the Chemodosimeter Approach

As explained above, the chemodosimeter approach takes advantage of the use of usually irreversible anion-induced reactions. This approach is an older subject, and thus, most of the commercially available kits for the semiquantitative determination of anions are based on irreversible chemical reactions and not on coordination events. Nevertheless, many of those reactions are not as selective as desired and new advances in this area are still necessary based on new concepts. In fact, in some aspects, this approach for the chromogenic detection of anions is still an unexplored field and very few examples can be found in the recent literature. Recent examples of chromogenic reagents using anion-induced chemical reactions involve the compounds **270**−**290**.

Receptors **270**−**277**, containing the diarylpent-2-en-1,5-dione backbone, have been used as colorimet-



270

271 n = 1
272 n = 2
273 n = 3

274 n = 1
275 n = 2
276 n = 3

277

ric reagents in probes for detection of certain anions in dioxane−water 70:30 v/v mixtures at pH 6.0.[239] Solutions of the receptors **270**−**276** changed the color from yellow (λ_{max} = 380 nm) to magenta (λ_{max} = 550 nm) in the presence of ATP, ADP, and sulfate anions, whereas yellow solutions of receptor **277** selectively turned magenta in the presence of ATP. This change in color was ascribed to the anion-induced cyclization of the diarylpent-2-ene-1,5-dione moiety to the corresponding pyrylium cation. Solutions of the receptor **270** in dioxane−water 70:30 v/v at pH 6.0 changed the color from yellow to magenta in the presence of dicarboxylates with a "tweezers-like" geometry such as oxalate and malonate, whereas in the presence of other dicarboxylates (succinate, glutarate, adipate, pimelate, suberate, acetate, and benzoate) solutions of **270** remained yellow.[240] These changes in color were due to cyclization to give the pyrylium cation promoted by the formation of hydrogen bonds between the hydroxyl group of the enol tautomer of the pent-2-en-1,5-dione moiety and the tweezers-like carboxylates. This tweezers-like effect might lead to the design of colorimetric probes for the discrimination between certain organic isomers. Thus, dicarboxylates such as maleate (cis double bond) induced color changes whereas fumarate (trans double bond) produced no change. Color variation was also obtained with phthalate, whereas the presence of isophthalate and terephthalate induced no change allowing discrimination between the ortho and the meta and para isomers.

The receptor with an aniline−pyrylium backbone, **278**, reacted with the sulfide anion giving an aperture

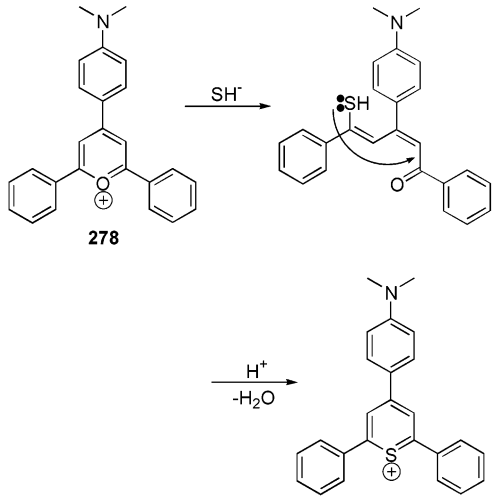
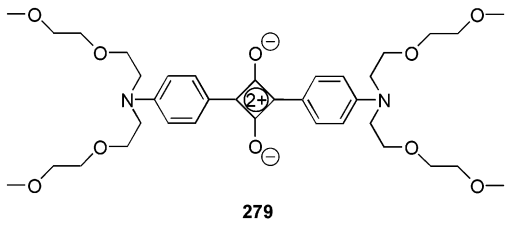


Figure 48. Transformation of receptor **278** in the correspondent thiopyrylium form in the presence of the sulfide anion.

of the pyrylium cycle. Further addition of acid induced cyclization to give the corresponding aniline−thiopyrylium derivative (see Figure 48).[241] This transformation induced a color change in water−acetonitrile 1:1 v/v solutions from magenta (for aniline−pyrylium backbone, λ_{max} = 540 nm) to blue (for aniline−thiopyrylium backbone, λ_{max} = 580 nm) that allows visual recognition of the anion sulfide. Other anions such as fluoride, chloride, bromide, iodide, acetate, benzoate, phosphate, sulfate, and nitrate did not induce any color variation.

Acetonitrile solutions of the squaraine **279** are blue (λ_{max} = 641 nm) due to a CT band from the donor



anilinium group to the central acceptor four-membered cycle and changed to colorless selectively in the presence of the anion cyanide whereas the presence of the anions fluoride, chloride, bromide, iodide, nitrate, dihydrogen phosphate, hydrogen sulfate, acetate, benzoate, and tiocyanate did not have any effect.[242] This bleaching process was ascribed to a nucleophilic attack of the anion cyanide to one carbon of the central four atom ring. This attack would produce both a loss of the acceptor character of the ring and a rupture of the electronic delocalization with the consequent disappearance of the CT band centered at 641 nm. The same bleaching effect was observed in water-containing solutions. This reaction was used for quantification of cyanide in water−acetonitrile 80:20 v/v solutions buffered at pH 9.5 with a detection limit as low as 0.1 ppm.

The dye **280** was used as a chromoreactand in a PVC membrane containing dioctadecylmethylamine and 2-nitrophenyloctyl ether as plasticizer.[243] A color change from pink (λ_{max} = 524 nm) to orange (λ_{max} =

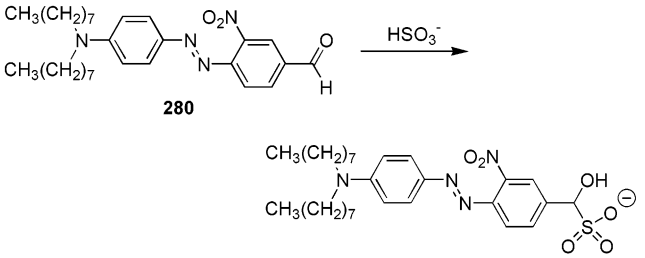
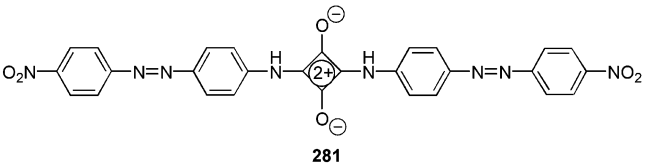


Figure 49. Reaction between the chromoreactand **280** and the anion bisulfite.

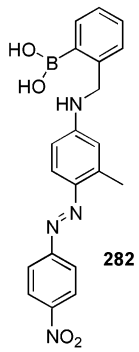
484 nm) was observed when the membrane was in contact with aqueous solutions buffered at pH 4.9 containing the anion bisulfite. This change in color was attributed to a reversible chemical reaction of the anion bisulfite and the formyl group of the dye that produced a change in their electron acceptor strength (see Figure 49). This membrane exhibited high selectivity toward bisulfite and the presence of sulfate, phosphate, chloride, hydroxide, and protons did not induce clear changes in the band centered at 524 nm. Only cyanide concentrations higher than 1 mM at pH 4.9 produced some interference.

An azo dye containing a squaramide (**281**) in DMSO−H_2O solutions proved to be a fine colorimetric



reagent for SO_4^{2-}.[244] Compound **281** (λ_{max} = 530 nm) reacts with SO_4^{2-} at pH 4.3−7.5 with a concomitant color change from red to blue (λ_{max} = 632 nm). A linear relation is held at 0−15 μg SO_4^{2-}/10 mL. Water samples containing sulfate were analyzed with this method, and satisfactory results were obtained.

Solutions of **282** in methanol exhibited an absorption band centered at 450 nm responsible for the



orange color of the solutions.[245] In the presence of chloride, bromide, and iodide, only an increase in intensity of the 450 nm band was observed; in contrast, addition of fluoride resulted in a bathochromic shift from 450 to 563 nm with a simultaneous color shift from orange to claret. This color change was selective for fluoride and attributed to the formation of a tetrahedral boronate anion upon reaction with one equivalent of fluoride (see Figure 50).

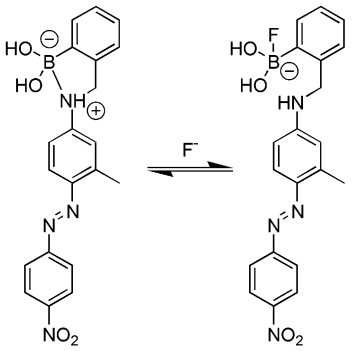
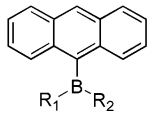
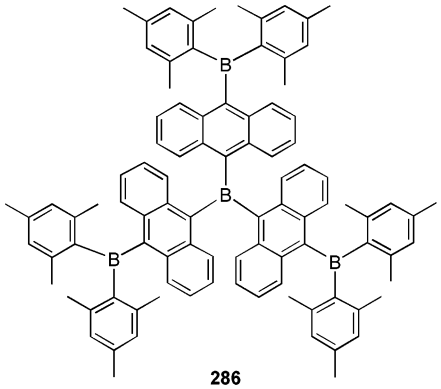


Figure 50. Formation of the boronate anion by coordination of fluoride with receptor **282**. Fluoride coordination induced cleavage of the B−N bond and a change in the color from orange to claret.

THF solutions of **283** were orange, whereas solutions of receptors **284** and **285** showed an intense



283 ($R^1 = R^2$ = 9-anthryl)
284 (R^1 = 9-anthryl, R^2 = mesityl)
285 ($R^1 = R^2$ = mesityl)



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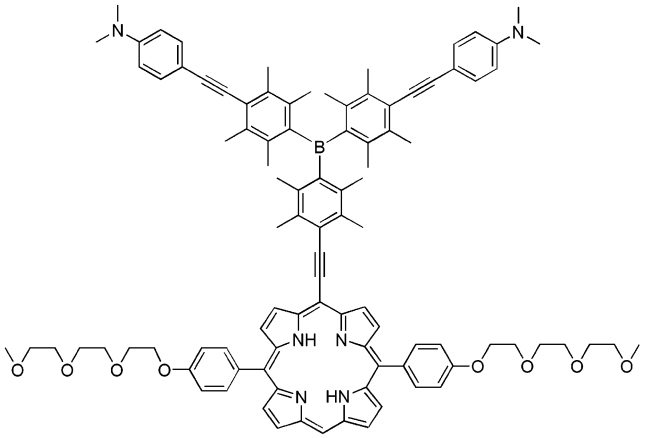
yellow fluorescent color.[246] These colors are due to the presence of extended π-conjugation through the vacant p orbital of the boron atom. In the presence of the anion fluoride, a color modification from orange to colorless was observed for receptor **283** or from yellow to colorless for receptors **284** and **285**. No changes in color were observed with other anions such as AcO^-, OH^-, Cl^-, Br^-, I^-, ClO_4^-, and BF_4^-. This color change was ascribed to the reaction between the fluoride and the boron atom of the receptors that led to an interruption of the π-conjugation. It was suggested that the sterically congested surroundings around the central boron atom might be partly responsible for the highly selective sensing of the small fluoride anion. Compound **286** was intense red in THF solutions and was also capable of sensing the anion fluoride. As the concentration of fluoride increased, the absorption band at 524 nm decreased and a new band appeared at 474 nm and the color of the solution changed from red to orange. The mechanism of the color change was the same as for **283**−**285**.

The triarylborane−porphyrin conjugate receptor **287** showed bands in the UV zone at 303, 322, and



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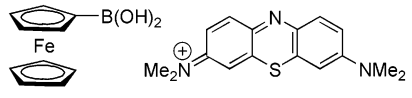
393 nm due to the triarylborane moiety and bands in the visible region at 436 (Soret band) and 580 nm (Q band) due to the porphyrin moiety.[247] Upon addition of increasing quantities of fluoride anion, bathocromic shifts of the Soret (44 nm) and Q band (20 nm) were obtained. These bathochromic shifts were reflected in changes in color of THF solutions of receptor **287** from purple to green. The shifts and changes in color were adscribed to reaction of the fluoride anion with the boron atom with the subsequent sp^2-sp^3 hybridization transformation and the loss of π-conjugation. No changes in color were observed upon exposure of **287** to chloride, bromide, iodide, acetate, and hydroxide anions. Fluorescence measurements of receptor **287** were carried out in THF solutions. Upon excitation at 294 nm where the abpsortion bands are ascribed to the triarylborane subunit, an energy transfer process from the triarylborane to the porphyrin subunit takes place and only the emission of the porphyrin moiety centered at 670 nm was observed. The addition of fluoride anion induced the apparition of two new emission bands centered at 356 (triaryborane moiety) and 692 nm (porphyrin moiety) along with a decrease of the emission centered at 670 nm.

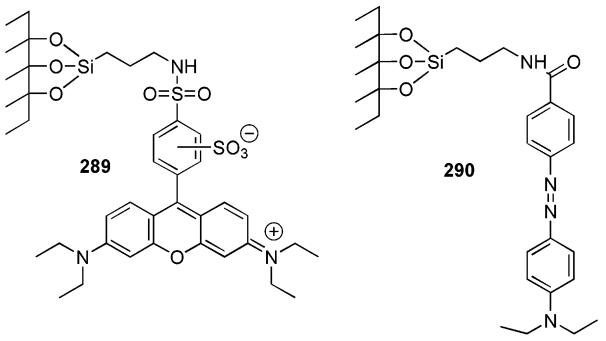
In an aqueous media (pH 3), a mixture of **288** and methylene blue gave no reaction and the solution was



288 **Methylene blue**

characterized by the blue color of the dye ($\lambda_{max} = 665$ nm).[248] Upon fluoride addition the oxidation potential of the redox active ferrocene derivative decreases (due to reaction of the fluoride anion with the boron atom in **288**) and under these conditions, the ferrocene group was able to reduce the dye. The 665 nm band disappeared allowing visual detection of fluoride. The absorbance maximum at 665 nm in a mixture of **288** and methylene blue was scarcely affected by addition of Cl^-, Br^-, SO_4^{2-}, HPO_4^{2-}, or SCN^-. This paper also described the detection of saccharides on a similar basis.

Another system to detect fluoride was based on the reaction of HF (in acetonitrile−water 7:3 v/v mixtures at pH 2.5) with the MCM-41 based solids **289** and **290**. These solids were obtained anchoring lissamine



rhodamine B sulfonyl chloride and 4-{2-[4-(dimethylamino)phenyl]diazanyl}benzoic acid to a mesoporous MCM-41 solid.[249] At pH 2.5, the fluoride anion was transformed into HF that attacked the siliceous support releasing the dyes into the solution. After filtration, the absorbance of the solutions at 566 nm for **289** and at 460 nm for **290** was measured and the results were proportional to the fluoride concentration in water.

5. Concluding Remarks

Since 1968, when Park and Simmons described the first synthetic receptor capable of encapsulating chloride anions, the field of synthetic abiotic receptors for anions has been growing in interest. A sister area that has been rising alongside since more than 10 years ago is that of optical chemosensing for the recognition of anions. The most classical approximation to the development of anion chemosensors, and the most widely used, follows the binding site−signaling subunit approach. This protocol relies today in the well-established area of anion coordination chemistry and in the choice of suitable signal mechanisms generation. Probably the most interesting feature of such approach is that following rational designs, it allows one to build a wide variety of molecular sensors. It also allows a rational study of the diverse sensing mechanisms (photoelectron transfer, energy transfer, CT processes, etc.). This approach has a clear intrinsic interest and will be surely of great importance in future research of selective molecular sensors for target anions. Interesting alternatives to this basic model are the displacement and the chemodosimeter approaches. They show several features that make them newly revived attractive schemes for the design of new chemosensing ensembles. As they are relatively new ideas in the chemosensing field, such approaches will surely be more and more used in the future. Whereas in the chemodosimeter approach the objective is to find specific reactivity, the goal in both the binding site−signaling unit and displacement protocols is selective coordination.

It is also important to point out that although many systems described outline attractive, imaginative, and suggestive approaches to anion sensing, there is a lack of systematic and rigorous analytical studies in order to evaluate the actual application in true mixtures and future efforts are necessary in this line. Some reported systems display poorly selective sensing properties in nonaqueous solvents, and despite their intrinsic and academic interest, they probably do not have actual applicability. In this sense, one interesting goal in the development of optical sensors for anions would deal with the synthesis of highly selective sensing systems for aqueous solvents (pure water or water−organic solvent mixtures). Another important point would be the use of dyes and fluorophores capable of absorbing and emitting in near-IR regions because in this region the number of colored interferences is usually very limited. A different, but also suggestive, recent approach will be the use of differential receptors using a series of rather unspecific sensors capable of giving suitable pattern recognition for anions. Advanced and complete photophysical and mechanistic studies will also be necessary. Of importance will also be efforts to develop new and more selective sensors for the chromogenic or fluorogenic detection of target medicinal, biological, and environmentally relevant anions such as nitrite, nitrate, cyanide, lactate, pertechnate, borate, and many others. To achieve all this, new and improved anion binding topologies, for instance mimicking active sites in biological receptors, coupled to suitable or advanced signaling processes would probably be necessary.

In conclusion, topical advances on anion coordination chemistry, supramolecular chemistry, environmental and biological processes and mechanisms, analytical chemistry, etc. have recently established the basis for the flowering of the anion chemosensing field. We are convinced that new upcoming advances, innovative points of view, and original ideas will seed the imagination of future research in order to meet the challenge of developing highly selective and specific sensing receptors for a number of target anions.

6. References

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