

# Chromogenic Anion Sensors

Chomchai Suksai · Thawatchai Tuntulani (✉)

Department of Chemistry, Supramolecular Chemistry Research Unit, Faculty of Science,  
Chulalongkorn University, Bangkok 10330, Thailand  
*thawatac@chula.ac.th*

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**Abstract** Chromogenic sensors for anions generally consist of two parts: anion receptors and chromophores. In this review, six types of chromogenic anion sensors are described, namely, NH-based hydrogen bonding, Lewis acid, metal-ion template, transition metal complexes, chromogenic guest displacement, and chromoreactands. The first four types possess anion receptors attached directly to the chromophores, while the guest displacement techniques employ indicators that are replaced by specific anions. The last type has emerged recently and uses specific reactions between chromogenic hosts or indicators and particular anions to cause dramatic color changes.

**Keywords** Chromogenic anion sensor · Colorimetric anion sensor

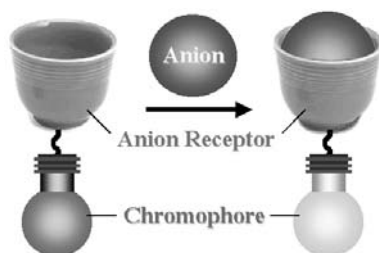
**Abbreviations**

AcO <sup>-</sup>	Acetate anion
ATP	Adenosine triphosphate
ADP	Adenosine diphosphate
A <sup>-</sup>	Anion
DMSO-d <sub>6</sub>	Deuterated dimethyl sulfoxide
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
EDOT	Ethylenedioxythiophene
EDTA <sup>4-</sup>	Ethylenediaminetetraacetate
GMP	Guanosine monophosphate
h	Hour(s)
<sup>1</sup> H NMR	Proton nuclear magnetic resonance spectroscopy
H-bpmp	2,6-Bis[[bis(2-pyridylmethyl)amino]methyl]-4-methylphenol
HEPES	2-[4-(2-Hydroxyethyl)-1-piperazinyl]ethanesulfonic acid
K <sub>a</sub>	Association constant
M <sup>-1</sup>	Per mole
M <sup>+</sup>	Metal ion
Me	Methyl
MeOH	Methanol
MLCT	Metal-to-ligand charge transfer
mV	Millivolt
nm	Nanometer
Ph	Phenyl
SEM	Monotrimethylsilylethoxymethyl
SHE	Standard hydrogen electrode
TCNQ	Tetracyanoquinodimethane
THF	Tetrahydrofuran
UV-vis	UV-visible spectroscopy
v/v	Volume by volume
λ <sub>max</sub>	Maximum absorption wavelength
λ <sub>em</sub>	Emission wavelength
λ <sub>ex</sub>	Excitation wavelength

**1****Introduction**

In the field of supramolecular chemistry, the progress in synthetic receptors for anions [1–5] has attracted considerable attention in recent decades due to the fact that a large number of biological processes involve molecular recognition of anionic species. It is thus important to develop techniques for quantifying or sensing such anions. Nowadays, the development of colorimetric anion sensing [6–11] is particularly challenging, since visual detection can give immediate qualitative information and is becoming increasingly appreciated in terms of quantitative analysis.

One approach to reach an effective anion sensor for biological anions involves the construction of optical anion sensors. Such a system generally



**Fig. 1** Operating principle of chromogenic anion sensors

consists of two parts. One part is an anion binding site employing various combinations of anion receptor units. Anion receptors can be mainly divided into two categories: neutral anion receptors and positive-charge anion receptors. Neutral anion receptors employed hydrogen bonding NH-based donors such as pyrroles, amides, and urea/thioureas or Lewis acids. Positive-charge anion receptors use ammonium derivatives or guanidinium centers for binding negative-charge anions. The other is the chromophore part, which converts the binding events or recognition phenomena to optical signals. These two parts can be either covalently attached or intermolecularly linked to each other.

The concept of chromogenic anion sensors is illustrated in Fig. 1. The crystal in the figure can be compared to analytes such as anions, and the cup acts like a receptor that is connected to a light bulb. When the crystal goes into the cup that fits its shape, the electronic part of the light bulb is perturbed, and the light bulb will give a different color.

Chromogenic anion sensors can be divided into two main categories: metal and nonmetal chromogenic hosts. For metal-involved chromogenic hosts, the changing color comes from the color of metals or metal complexes, especially transition metal ions, as their electronic properties are perturbed upon coordination to anions. The other way to generate a chromogenic sensor is to displace the coordinated chromophore by specific anions. Besides coordination aspects, the color changes can stem from reactions between chromogenic hosts or indicators and anions. This type of chromogenic anion sensor can be called a “chromoreactand”. When the reaction occurs, the conformed host will definitely change its electronic properties. This, therefore, results in an observable color change.

## 2

### NH-Based Hydrogen Bonding Chromogenic Hosts

These hosts include simple anion sensor systems containing urea, thiourea, amine, amide, alcohol, and pyrrole groups linked to chromophores. Chromophores used in this type of chromogenic anion sensors are mainly organic dyes such as azobenzene, nitrobenzene, indoaniline, and anthraquinone or

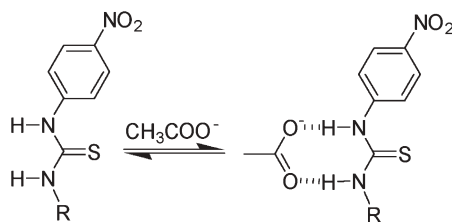
extensively conjugated aromatic compounds such as quinoxaline, oxadiazole, and porphyrin. The color change occurs upon binding of anion guests that affect the electronic properties of the chromophores.

Sessler and Miyaji [12] have investigated a number of commercially available compounds such as 1,2-diaminoanthraquinone, 1,8-diaminoanthraquinone, 4-nitroaniline, 4-nitro-1,2-phenylenediamine, L-leucine-4-nitroanilide, 1-(4-nitrophenyl)-2-thiourea, 4-nitrophenol, alizarin, 2,2'-bis(3-hydroxy-1,4-naphthoquinone), acid blue 45, naphthol AS, 9(10*H*)-acridone, and Direct Yellow 50 as anion sensors in organic solvents such as dichloromethane. These compounds contain hydrogen bond donors such as amine, amide, alcohol, and urea as anion binding sites. The compounds also contained chromophore subunits (acting as an electron acceptor) whose electronic properties were modified as a result of interactions with a bound anionic substrate (acting as an electron donor). The NH-based hydrogen bonding chromogenic hosts can be classified as follows.

## 2.1

### Chromogenic Hosts Containing Nitrophenyl Units

Thiourea is an especially good hydrogen bond donor and is an excellent anion receptor for carboxylate anions. Teramae and coworkers [13] prepared thiourea-based chromophores with *p*-nitrophenyl units, **1** and **2**. As a result, compounds **1** and **2** were found to be more highly selective for AcO<sup>-</sup> than other anions in 1% water:MeCN. The binding properties of **1** and **2** with AcO<sup>-</sup> showed that increasing the concentration of AcO<sup>-</sup> produced a significant bathochromic shift in the UV-vis spectra. The stability constant of the AcO<sup>-</sup> complex of **1** was  $5.6 \times 10^3 \text{ M}^{-1}$ , much weaker than that of **2** ( $K_a = 3.5 \times 10^5 \text{ M}^{-1}$ ). It was evident that introducing a *p*-nitrophenyl group into the (*p*-nitrophenyl)thiourea moiety enhanced the hydrogen bonding ability. Likewise, chromophore **2** was then applied to the colorimetric determination of acetic acid in commercially available brands of vinegar. The results agreed well with the specification provided by the suppliers.

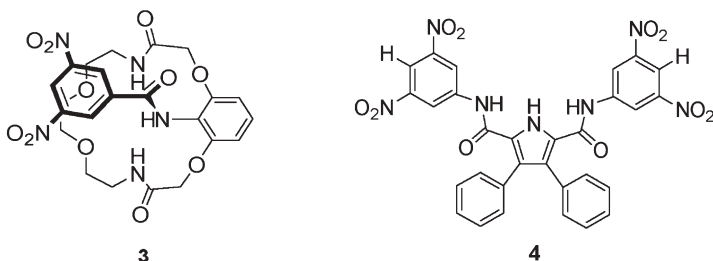


- 1.** R = CH<sub>3</sub>  
**2.** R = *p*-nitrophenyl

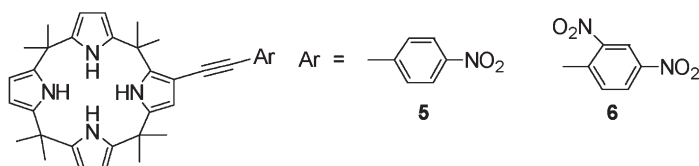
Besides urea and thiourea, amide groups can also form effective chromogenic anion sensors. Jurczak and coworkers [14] have demonstrated the use of amide groups containing nitrophenyl-macrocycle **3** as a selective colori-

metric sensor for  $F^-$ . A DMSO solution of compound **3** showed dramatic color changes upon addition of  $F^-$ ,  $AcO^-$ , and  $H_2PO_4^-$  ions. It was found that a colorless solution of **3** turned dark blue ( $\lambda=593, 708\text{ nm}$ ), yellow ( $\lambda_{\max}=375\text{ nm}$ ), and yellow ( $\lambda_{\max}=384\text{ nm}$ ) when exposed to  $F^-$ ,  $H_2PO_4^-$ , and  $AcO^-$ , respectively. However, compound **3** formed a substantially stable 2:1 anion-to-ligand ratio with  $F^-$  in DMSO- $d_6$  and  $CD_3CN$  with  $K_a$  values of  $7.8\times 10^6$  and  $7.5\times 10^6\text{ M}^{-1}$ , respectively.

The 3,5-dinitrophenyl derivatives of pyrrole 2,5-diamide **4** [15] acted as a selective naked-eye sensor for  $F^-$  in MeCN solution, which gives rise to a deep blue color ( $\lambda_{\max}=598\text{ nm}$ ). This color change was due to a deprotonation process caused by  $F^-$  acting as a base and subsequent charge-transfer interactions between the deprotonated pyrrole and the nitroaromatic groups.



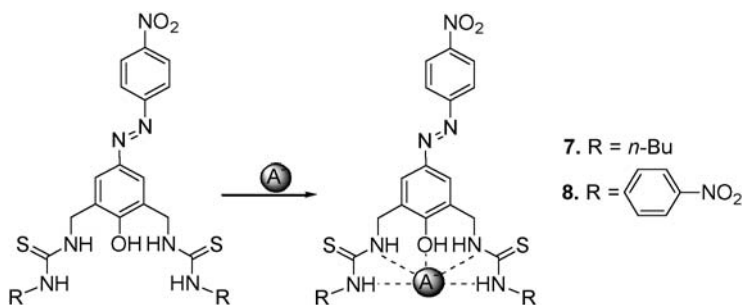
The calix[4]pyrroles functionalized with nitrobenzenes **5** and **6** [16] can act as  $F^-$  sensors. These systems bear an appended chromophore directly linked to the calix[4]pyrrole skeleton through a conjugated  $C\equiv C$  triple bond. Upon addition of tetrabutylammonium  $F^-$ , solutions of **5** and **6** in  $CH_2Cl_2$  turned from pale yellow ( $\lambda_{\max}=391\text{ nm}$ ) to intense yellow ( $\lambda_{\max}=433\text{ nm}$ ) for **5** and from yellow ( $\lambda_{\max}=441\text{ nm}$ ) to red ( $\lambda_{\max}=498\text{ nm}$ ) for **6**. In addition, the color changed from yellow ( $\lambda_{\max}=441\text{ nm}$ ) to orange when  $Cl^-$  ( $\lambda_{\max}=483\text{ nm}$ ) and  $H_2PO_4^-$  ( $\lambda_{\max}=478\text{ nm}$ ) were added to a solution of **6**.



## 2.2

### Chromogenic Hosts Containing Azo Dye Units

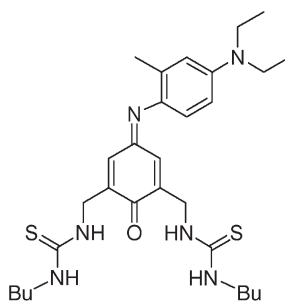
Hong and coworkers [17] have recently reported anion coordination with a nitro-azophenol thiourea-based sensor, compound **7**. Association constants for anion binding were determined by  $^1H$  NMR and UV-vis titrations in  $CDCl_3$ .  $H_2PO_4^-$  ( $K_a=2.6\times 10^4\text{ M}^{-1}$ ) and  $AcO^-$  ( $K_a=1.9\times 10^4\text{ M}^{-1}$ ) gave stronger complexes



with 7 than other anions due to their high basicity. Moreover,  $\text{H}_2\text{PO}_4^-$  with four oxygens makes the strongest complexes via multitopic hydrogen-bonding interactions and these results agreed with those obtained by  $^1\text{H}$  NMR. The large downfield shifts of thiourea NH resonances ( $>2.5$  ppm) were detected upon complexation with  $\text{H}_2\text{PO}_4^-$  and  $\text{AcO}^-$ . Broadening of the phenol OH resonance was also observed, indicating its participation in hydrogen-bonding interactions with anions.

In the absence of anions, the UV-vis absorption spectrum of 7 showed an absorption  $\lambda_{\text{max}}=376$  nm. Upon addition of  $\text{H}_2\text{PO}_4^-$ , the peak at 376 nm decreased while a new peak appeared at 529 nm, concomitant with a solution color change from light yellow to deep red. This may be due to electronic excitation through charge transfer from the oxygen donor of the phenol to an acceptor substituent ( $-\text{NO}_2$ ) of the chromophore. The excited state would be more stabilized by anion binding, resulting in a bathochromic shift in the absorption maxima as well as a color change. Changing the substituent at the thiourea moiety of 7 from butyl groups to nitrobenzene groups in compound 8 [18] allowed the easy colorimetric differentiation of  $\text{F}^-$ ,  $\text{H}_2\text{PO}_4^-$ , and  $\text{AcO}^-$  which have similar basicity. The degree of red shift for 8 was determined to be  $\text{H}_2\text{PO}_4^- \gg \text{AcO}^- \approx \text{F}^- > \text{Br}^- \approx \text{Cl}^- > \text{HSO}_4^- \approx \text{I}^-$  in  $\text{CHCl}_3$ . The maximum red-shift value ( $\lambda_{\text{max}}=538$  nm) for  $\text{H}_2\text{PO}_4^-$  can be understood on the basis of the guest basicity and the structure of the complex.

Later, Hong and coworkers changed the signaling unit in compound 7 from nitroazobenzene to indoaniline [19]. The compound 9, a new chromogenic indoaniline-thiourea-based sensor, showed significant color and UV-vis spectral changes upon binding anions. Upon the addition of  $\text{H}_2\text{PO}_4^-$  or  $\text{HSO}_4^-$ , the color of the  $\text{CHCl}_3$  solution changed from blue-green ( $\lambda_{\text{max}}=678$  nm) to deep blue ( $\lambda_{\text{max}}=632$  nm). The association constants obtained from UV-vis titrations for complexes of 9 with  $\text{H}_2\text{PO}_4^-$  and  $\text{HSO}_4^-$  in  $\text{CHCl}_3$  are  $1.1 \times 10^4$  and  $2.5 \times 10^4$   $\text{M}^{-1}$ , respectively. However, addition of  $\text{AcO}^-$  or  $\text{F}^-$ , which are more basic anions, caused a less intense color change. In addition, in the case of  $\text{Cl}^-$ ,  $\text{Br}^-$ , and  $\text{I}^-$ , no detectable color changes were observed. In the same manner as in compound 7, compound 9 possesses four NH urea moieties and allows the selective colorimetric detection of tetrahedral oxoanions such as  $\text{HSO}_4^-$  and  $\text{H}_2\text{PO}_4^-$ .

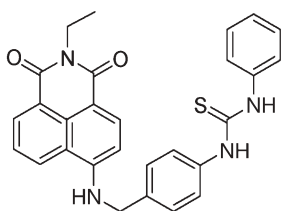


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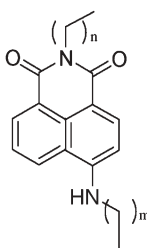
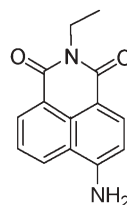
## 2.3

### Chromogenic Hosts Containing Naphthalimide Units

The receptors **10**–**13**, which contain naphthalimide groups, can act as chromophores and show recognition of anion especially  $F^-$  in DMSO. Upon addition of  $F^-$  to the solution of **10** [20], a 1:2 complex was found concomitant with the color change from light yellow to deep purple, while receptors **11**–**13** [21] showed color changes from green to purple. These results can be attributed to strong hydrogen-bonding interactions between the 4-amino moiety of the naphthalimide group and  $F^-$ , or more likely a complete deprotonation. Surprisingly, color changes of receptors **11**–**13** reversed gradually with time due to the fixation of  $CO_2$  (as  $HCO_3^-$ ) by the receptors as 1:1 adducts. This was confirmed by X-ray crystallography.



10

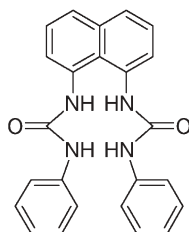
11.  $n = 1, m = 3$ 12.  $n = m = 3$ 

13

## 2.4

### Chromogenic Hosts Containing Naphthalene Units

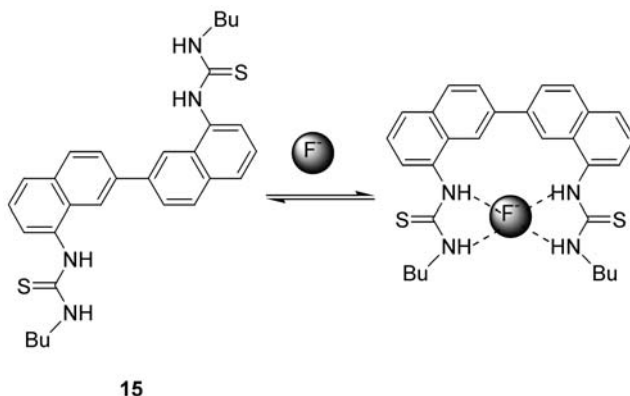
The fluoride-selective chromogenic and fluorescent sensor **14** containing naphthalene ureas was synthesized by Lee and coworkers [22]. From UV-visible studies, the sensor **14** showed a characteristic band at 325 nm. Upon addition of  $F^-$ , a new peak at 379 nm occurred in MeCN:DMSO (9:1 v/v). Furthermore,  $\lambda_{em}$  of **14** at 379 nm was shifted to 445 nm upon addition of  $F^-$  ( $K_a = 14,200 M^{-1}$ ).



14

Addition of other anions showed the same  $\lambda_{em}$  as free **14**.  $^1\text{H}$  NMR results suggested that  $\text{F}^-$  bound four urea NH protons via hydrogen-bonding interactions, which resulted in the downfield shift of the NH proton signals.

The other dual-sensing receptor based on binaphthalene skeleton **15** [23] bearing two thiourea groups showed sensing abilities toward  $\text{F}^-$ ,  $\text{AcO}^-$ , and  $\text{H}_2\text{PO}_4^-$  in MeCN. A bathochromic shift with unique isosbestic points was observed upon addition of these anions. From fluorescence titrations, the intensity of  $\lambda_{em}$  of **15** at 459 nm decreased and a weak broad emission band around 650 nm occurred upon addition of  $\text{F}^-$  ( $K_a=2.1\times 10^6 \text{ M}^{-1}$ ),  $\text{AcO}^-$  ( $K_a=1.1\times 10^5 \text{ M}^{-1}$ ), and  $\text{H}_2\text{PO}_4^-$  ( $K_a=5.5\times 10^4 \text{ M}^{-1}$ ). X-ray crystallography showed that two naphthyl rings are placed in the same plane and two thiourea groups are located in the *anti* position. The thiourea groups are in the *syn-anti* conformation due to formation of intermolecular hydrogen bonds in the solid state. In the solution state, two naphthyl rings of **15** can freely rotate. The complexation with anions then induced the rotation of naphthyl rings to form a planar conformer as shown in Fig. 2, which caused the emission spectrum to move to a longer wavelength.



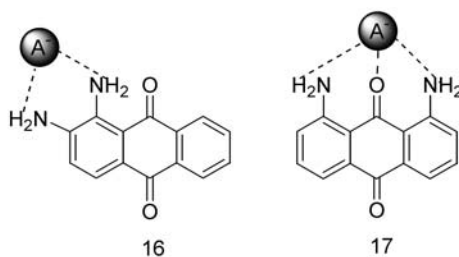
**Fig. 2** Proposed hydrogen-bonding interactions between fluoride and receptor **15**



## 2.5

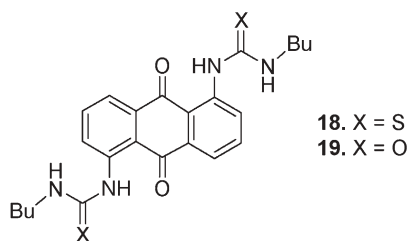
### Chromogenic Hosts Containing Anthraquinone Units

Anthraquinone derivatives **16** and **17** showed potential as off-the-shelf anion sensors [12]. It was found that **16** had a more dramatic color change than **17** upon addition of anions. The solution of **16** in  $\text{CH}_2\text{Cl}_2$  changed from yellow ( $\lambda_{\text{max}}=478$  nm) to dark purple ( $\lambda_{\text{max}}=555$  nm), red ( $\lambda_{\text{max}}=519$  nm), reddish orange ( $\lambda_{\text{max}}=513$  nm), orange ( $\lambda_{\text{max}}=499$  nm), purple ( $\lambda_{\text{max}}=548$  nm), and orange ( $\lambda_{\text{max}}=493$  nm) when exposed to  $\text{F}^-$ ,  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{I}^-$ ,  $\text{H}_2\text{PO}_4^-$ , and  $\text{HSO}_4^-$ , respectively. Proposed binding modes of sensors **16** and **17** with anions are presented in Fig. 3.



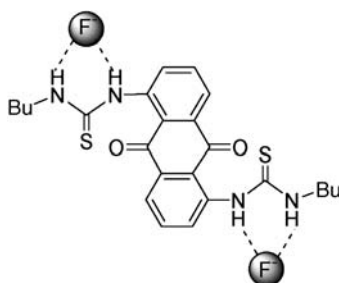
**Fig. 3** Proposed binding modes of an anion for sensors **16** and **17**

Jiménez et al. [24] have synthesized receptors 1,5-bis-*N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)-*N'*-butylthiourea **18** and its urea analogue, 1,5-bis-*N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)-*N'*-butylurea **19**, by condensation of 1,5-diaminoanthraquinone with butyl isothiocyanate and butyl isocyanate, respectively.

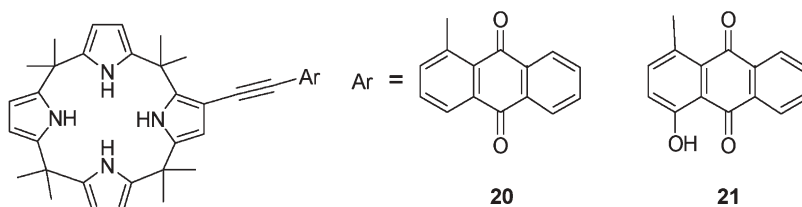


Compound **18** showed a remarkable color change from orange to brown ( $\lambda_{\text{max}}=670$  nm) in DMSO upon adding  $\text{F}^-$ . Color changes are most probably due to a charge-transfer process and electron-rich formation of hydrogen bonds between thiourea-bound  $\text{F}^-$  and the electron-deficient anthraquinone moiety. The anion was believed to form a 2:1 anion-to-ligand ratio as shown in Fig. 4.

Similar to compounds **5** and **6**, anthraquinone-functionalized calix[4]pyrroles **20** and **21** can act as  $\text{F}^-$  sensors [25]. Upon adding  $\text{F}^-$  to solutions of **20** and **21** in  $\text{CH}_2\text{Cl}_2$ , the color of **20** changed from yellow ( $\lambda_{\text{max}}=467$  nm) to red ( $\lambda_{\text{max}}=518$  nm),



**Fig. 4** Proposed hydrogen bond formation between fluoride and sensor 18

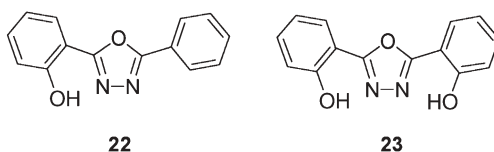


while **21** turned from red ( $\lambda_{\max}=526$  nm) to blue ( $\lambda_{\max}=613$  nm). The dramatic color changes were tentatively ascribed to charge-transfer interactions between electron-rich calix[4]pyrrole-bound anions and electron-deficient anthraquinone moieties.

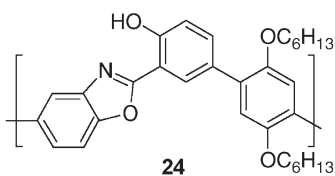
## 2.6

### Chromogenic Hosts Containing Oxadiazole and Benzoxazole Units

Wang and colleagues [26] have synthesized two derivatives of oxadiazole **22** and **23** that were used as anion-fluorescent and -colorimetric sensors. The two compounds showed high selectivity for  $\text{H}_2\text{PO}_4^-$  and  $\text{F}^-$  over  $\text{Cl}^-$  in DMF. It was found that compounds **22** and **23** changed their color from colorless ( $\lambda_{\max}=376$  nm) to yellow ( $\lambda_{\max}=400$  nm) upon addition of  $\text{F}^-$  and  $\text{H}_2\text{PO}_4^-$  in DMF. Association constants of **22** with  $\text{F}^-$  and  $\text{H}_2\text{PO}_4^-$  are  $8.6 \times 10^4$  and  $7.9 \times 10^5$   $\text{M}^{-1}$ , respectively. Furthermore, compound **23** showed high selectivity toward  $\text{H}_2\text{PO}_4^-$  with  $K_a=1.8 \times 10^6$   $\text{M}^{-1}$ .



In DMF solution, the hydroxybenzoxazole-based polymer **24** showed selective colorimetric sensing ability for  $\text{F}^-$  over  $\text{H}_2\text{PO}_4^-$ ,  $\text{Cl}^-$ , and  $\text{HSO}_3^-$  [27]. Upon ad-

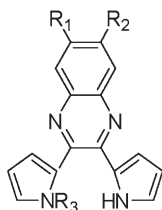


dition of  $F^-$  to the solution of **24**, the color changed from colorless ( $\lambda_{\max}=333$  nm) to yellow ( $\lambda_{\max}=420$  nm) due to the binding of  $F^-$  to this polymer. Therefore, compound **24** can act as a naked-eye detector for  $F^-$  anion.

## 2.7

### Chromogenic Hosts Containing Dipyrrylquinoxaline Units

Sessler and coworkers have recently investigated 2,3-dipyrrol-2'-ylquinoxaline derivatives **25**–**27** [28] as potential anion receptors and sensors. The electronic influence of the functional groups present in the receptor played a crucial role in its recognition and sensing ability. It was found that receptor **26** had a higher affinity for  $F^-$  ( $K_a=1.2\times 10^5$   $M^{-1}$ ) than **25** ( $K_a=2\times 10^4$   $M^{-1}$ ) in  $CH_2Cl_2$ . The solution of **26** underwent a dramatic color change from yellow to purple in the presence of  $F^-$ . Furthermore, receptor **27** showed the lack of a complete NH hydrogen bond donor. It then displayed a slight change in the optical spectrum.

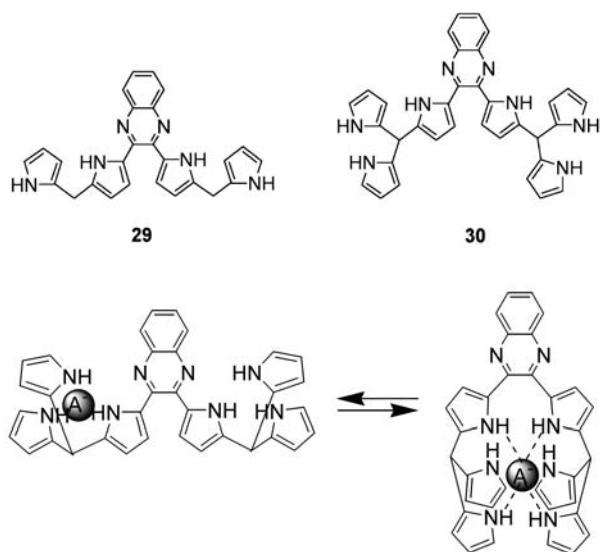


- 25.**  $R_1 = R_2 = R_3 = H$   
**26.**  $R_1 = R_3 = H, R_2 = NO_2$   
**27.**  $R_1 = R_2 = H, R_3 = SEM$

The fluorinated dipyrrylquinoxaline **28** [29] underwent a sharp yellow to orange color change in the presence of both  $F^-$  ( $K_a=61,600$   $M^{-1}$ ) and  $H_2PO_4^-$  ( $K_a=17,300$   $M^{-1}$ ) anions in  $CH_2Cl_2$ . No changes in color were observed upon addition of  $Cl^-$  ( $K_a=180$   $M^{-1}$ ).



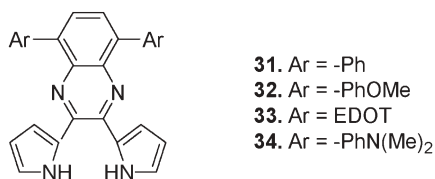
**28**



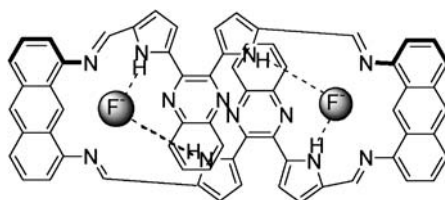
**Fig. 5** Proposed anion binding modes of receptor **30**

Sessler et al. [30] synthesized two novel quinoxaline derivatives bearing dipyrromethane **29** and tripyrromethane **30**. Both compounds were found to be much better anion receptors not only for  $F^-$  ( $K_a=32,000\text{ M}^{-1}$  for **29** and  $>1,000,000\text{ M}^{-1}$  for **30**), but also for  $H_2PO_4^-$  ( $K_a=4,300\text{ M}^{-1}$  for **29** and  $300,000\text{ M}^{-1}$  for **30**) in  $CH_2Cl_2$ . The substantial increase in affinities seen in the case of  $H_2PO_4^-$  was ascribed to the greater number of pyrrole NH donors required to bind a larger anion. In addition,  $^1H$  NMR results showed that compound **29** was able to bind anions using two modes of structure as shown in Fig. 5.

Extended dipyrrolyl quinoxalines **31–34** were synthesized by Anzenbacher et al. [31] and displayed strong selectivity for  $F^-$  and pyrophosphate anions ( $HP_2O_7^{3-}$ ). Addition of these anions to the solutions of **31–34** in  $CH_2Cl_2$  in all cases resulted in the decrease of absorptions at 400–450 nm concurrent with the appearance of strong bands around 500–550 nm.

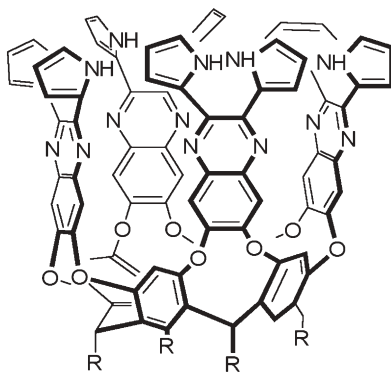


Recently, Sessler and coworkers [32] have synthesized a quinoxaline-bridged porphyrinoid **35** that can be used as a naked-eye sensor for  $F^-$ . Upon addition of  $F^-$  to a 10% DMSO: $CH_2Cl_2$  solution of compound **35**, the color of the solution changed from pale orange ( $\lambda_{max}=427\text{ nm}$ ) to red ( $\lambda_{max}=480\text{ nm}$ ) with

35.2F<sup>-</sup>

$\log K_{a1}=11$  and  $\log K_{a2}=2.2$ . The binding of the first fluoride anion makes the binding of the second somewhat more facile. The change in color is not observed upon addition of  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{NO}_3^-$ , or  $\text{HSO}_4^-$ .

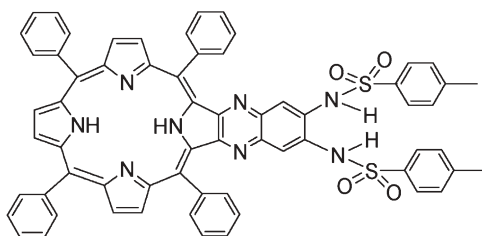
One example of the cavitand-based anion sensor, an open-ended host molecule with a vase-shaped cavity, was synthesized by Rebek and coworkers [33]. In this study, cavitand-based dipyrrolyl quinoxaline compound **36**, featuring four anion-detecting walls, was synthesized and showed a selective binding for  $\text{F}^-$  and  $\text{AcO}^-$  in toluene:acetone (4:1 v/v). A dramatic color change from yellow to dark red was observed. A band at  $\lambda_{\text{max}}=420$  nm disappeared and two new bands at  $\lambda=350$  and  $490$  nm emerged in the UV-vis spectrum.

36. R =  $(\text{CH}_2)_{10}\text{CH}_3$ 

## 2.8

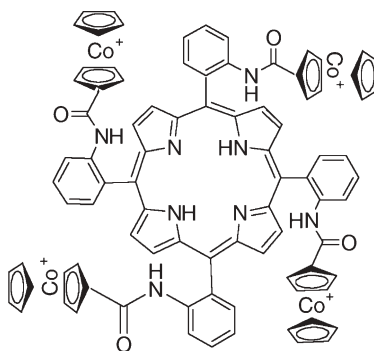
### Chromogenic Hosts Containing Porphyrin Units

Starnes et al. [34] synthesized a disulfonamide porphyrin receptor **37**. Anion binding was detected by the perturbations of the porphyrin Soret and Q bands. The Soret band of **37** at  $422$  nm showed a red shift upon addition of anions in  $\text{CH}_2\text{Cl}_2$  and isosbestic points were observed. Compound **37** was able to bind  $\text{F}^-$  via hydrogen bonding from sulfonamide NH protons in a 2:1 anion-to-ligand ratio with  $K_{a1}=255,000 \text{ M}^{-1}$  and  $K_{a2}=1,700 \text{ M}^{-1}$ .



37

In MeCN solutions, the Soret band of receptor **38** [35] at 425 nm significantly bathochromically shifted upon addition of H<sub>2</sub>PO<sub>4</sub><sup>-</sup> and hypsochromically shifted upon addition of Cl<sup>-</sup>, and split into two bands at 430 and 440 nm upon addition of HSO<sub>4</sub><sup>-</sup>. Anions formed 1:1 complexes with **38** via favorable amide hydrogen-bonding interactions and electrostatic interactions with four cobaltocenium moieties.

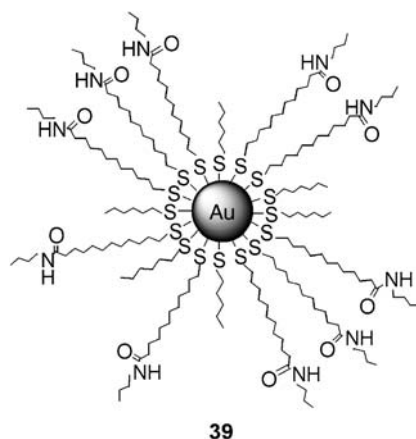


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## 2.9

### Nanoparticles Containing NH-Based Hydrogen Bonding Chromogenic Hosts

Nowadays, fabrication of chromophore-functionalized gold nanoparticles has emerged as one of the most exiting research areas, and their possible applications as anion sensors were also presented by Kamat et al. [36] The amide-functionalized gold nanoparticle **39** [37] was used for optical sensing of H<sub>2</sub>PO<sub>4</sub><sup>-</sup>, HSO<sub>4</sub><sup>-</sup>, AcO<sup>-</sup>, NO<sub>3</sub><sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup>, and I<sup>-</sup>. In CH<sub>2</sub>Cl<sub>2</sub>, nanoparticle **39** showed a red wine color with a characteristic plasmon band centered at 520 nm. When 0–0.5 equivalents of the anions were added to the solution of **39**, the plasmon band decreased in intensity with a slight red shift in wavelength. This marked decrease in the intensity of the band was ascribed to an anion-induced aggregation of **39** through hydrogen bond formation between anions and the interparticle amide groups. Further addition of anions to **39** solutions caused

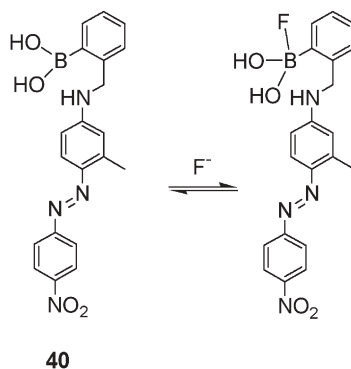


an increase in intensity of this plasmon band, which reflected the desegregation of the nanoparticle built by **39** and the corresponding anions. This nanoparticle was capable of optically sensing changes in anion concentration at a level of  $10^{-6}$  M.

### 3 Lewis Acid Chromogenic Hosts

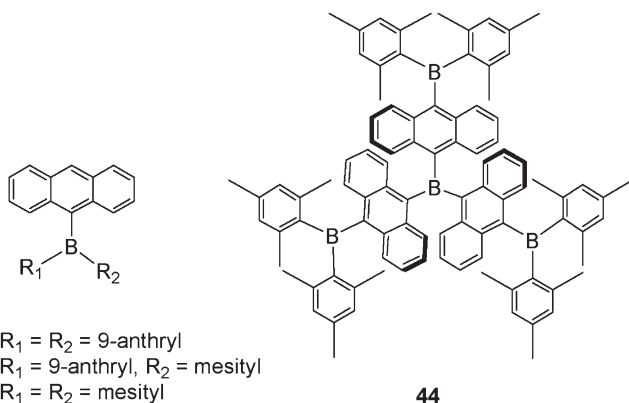
This section involves a type of receptor that requires the incorporation of a defined number and type of Lewis acids, such as B, Zn(II), and Hg(II), into a molecular skeleton with their electron-deficient sites exposed for interaction with the lone electron pair of anions.

James and coworkers [38] have synthesized an azo dye molecule with boronic acid, receptor **40**, which can act as a colorimetric sensor for detection



**Fig. 6** Proposed binding mode of fluoride with **40**

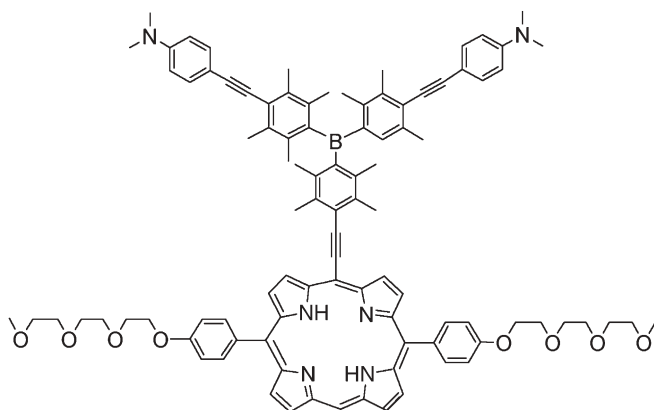
of  $F^-$ . Upon addition of KCl, KBr, and KI in MeOH solution of **40** the orange absorbance at 450 nm increased in intensity, while KF caused a dramatic color change from orange ( $\lambda_{\max}=450$  nm) to claret ( $\lambda_{\max}=563$  nm) with  $K_a=130$   $M^{-1}$ . The color change is due to the hybridization change from  $sp^2$  to  $sp^3$  when boron binds  $F^-$ , as shown in Fig. 6. Tamao and coworkers [39] reported a new type of multistage sensing of  $F^-$  anion based on boron-containing  $\pi$ -conjugating systems **41–44**. The boron atoms in this type of compound possess a unique LUMO in which  $\pi$ -conjugation is divergently extended through the vacant p-orbital of the boron atom. Complexation of the boron  $\pi$ -electron systems with anions would interrupt the  $\pi$ -conjugation extended through the boron atom, resulting in a dramatic color change. The complexation studies of compounds **41–43** and  $F^-$  were carried out using UV-vis spectrophotometry and showed  $K_a>2.6\times 10^5$   $M^{-1}$  in all cases. When  $F^-$  anion was added to a THF solution of each boron-containing compound, a dramatic color change occurred from colorless to orange for **41** and from yellow to colorless for compounds **42** and **43**.



The more extended  $\pi$ -electron system **44** has four boron atoms in two different environments. When the concentration of  $F^-$  increased, the absorption at 524 nm decreased, a new band at 474 nm emerged together with a broad shoulder band around 570 nm, and the color of the solution changed from red to orange. The UV-vis analysis implied that compound **44** was able to bind three  $F^-$  ions. The three stepwise binding constants in THF solutions are  $6.9\times 10^4$ ,  $9.0\times 10^2$ , and  $2.1\times 10^2$   $M^{-1}$ , respectively. The results suggest that the complexation of  $F^-$  in **44** may occur not with the internal boron atom but with the three peripheral boron atoms instead.

The triarylborane-porphyrin conjugate receptor **45** [40] can bind a  $F^-$  ion concurrent with the change from  $sp^2$  to  $sp^3$  hybridization of the boron atom. The change in the hybridization interrupts both the electronic communication and the dipolar interaction between the triarylborane and porphyrin unit as well as the internal charge transfer in the presence of  $F^-$ . Bathochromic shifts

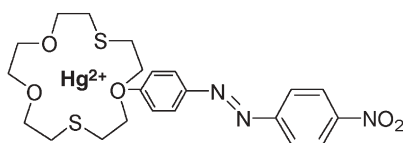




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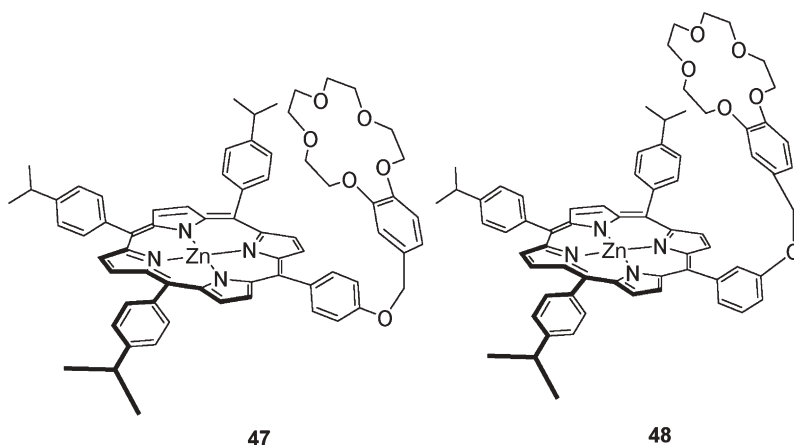
of the Soret and Q bands were observed upon addition of  $F^-$ . No changes in color were observed upon exposure of **45** to  $Cl^-$ ,  $Br^-$ ,  $I^-$ ,  $AcO^-$ , or  $OH^-$ .

Martínez-Máñez and coworkers [41] showed the complex of Hg(II) with aza-oxa-thia macrocycle **46** can be used for the specific chromogenic sensing of  $NO_3^-$  anion. Addition of  $NO_3^-$  to the MeCN solution of **46** resulted in a shift of the 540 nm band to 490 nm, with a concomitant change in color from red to yellow. UV-vis titrations of **46** with  $NO_3^-$  in  $CH_2Cl_2$  gave a stability constant of  $\log K=6.2$ . NMR studies of a **46**/ $NO_3^-$  system showed a slight shift of signals assigned to the protons *ortho* to the azo group. This shift could be related to the presence of  $\pi$ -stacking interactions between the nitrate ion and the *p*-nitrophenylazobenzene group. The selective sensing of nitrate by **46** has found application in  $NO_3^-$  determination in water.

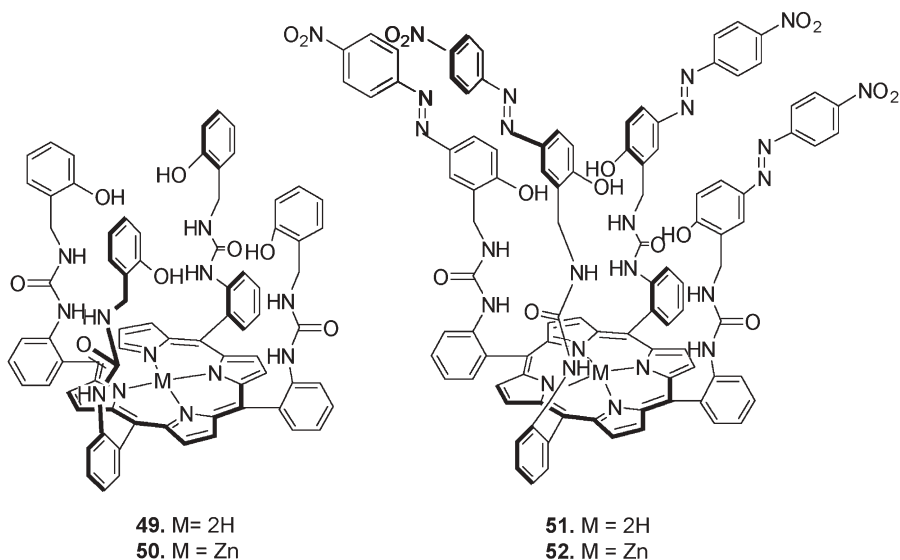


46

Ditopic neutral receptors composed of both a Lewis acid binding site (zinc porphyrin unit) and a Lewis base binding unit (crown ether moiety) **47** and **48** were reported by Kim and Hong [42]. Such receptors bound only NaCN in a ditopic fashion. UV-visible titrations between the receptors **47** and **48** with NaCN in  $CH_2Cl_2$  resulted in a red shift of the Soret band of the zinc porphyrin units, which were the origin of the color change from red to green in all cases. The association constants of **47** and **48** complexes with NaCN in DMSO:water (9:1 v/v) are  $5.7 \times 10^4$  and  $5.1 \times 10^4 M^{-1}$ , respectively.



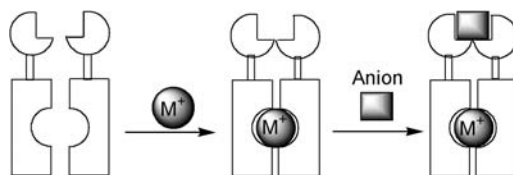
New azophenolurea-containing porphyrin compounds **49–52** for the colorimetric sensing of anions were reported by Hong and coworkers [43]. These compounds contained both Lewis acid centers and urea anion binding sites. Receptors **49** and **50** show high selectivity for  $\text{AcO}^-$  and  $\text{H}_2\text{PO}_4^-$  in DMSO. The Soret band at 433 nm shifted to 438 nm when  $\text{H}_2\text{PO}_4^-$  was added to the solution of **50**, indicating that a 1:1 complexation occurred with  $K_a=2\times 10^4 \text{ M}^{-1}$ . Compounds **51** and **52** showed dramatic color changes in  $\text{CH}_3\text{CN}$  upon addition of  $\text{F}^-$  due to an increased interaction with a nitrophenylazo phenolic OH group. Furthermore, upon addition of  $\text{H}_2\text{PO}_4^-$  to the solution of **51**, the intensity of the Soret band decreased concurrent with the appearance of a new band at about 600 nm.



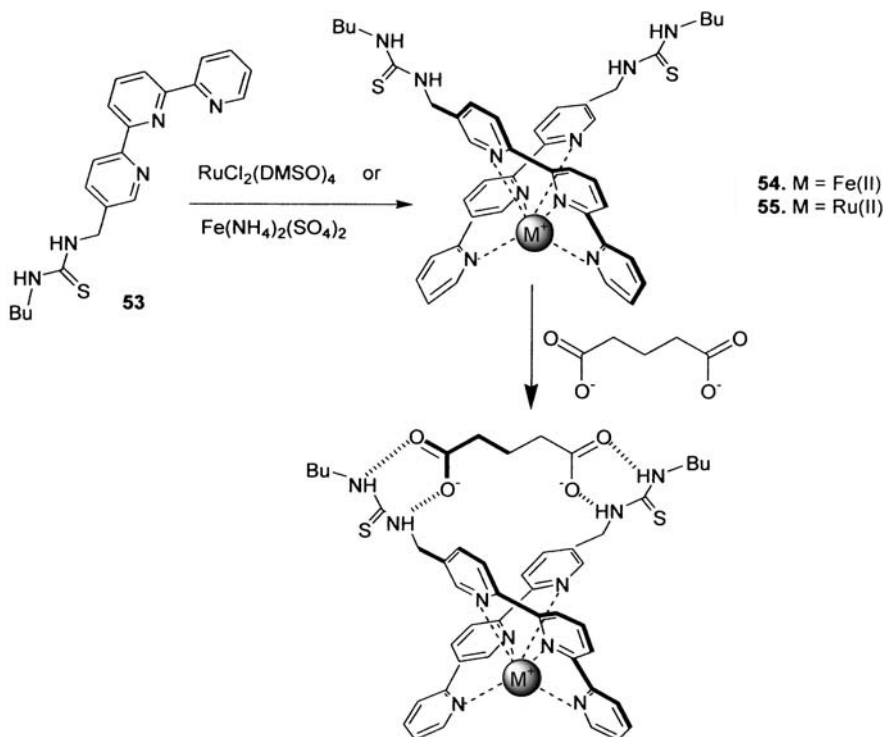
## 4 Metal-Ion-Templated Chromogenic Hosts

The intramolecular enrollment of different binding groups can be readily achieved by a metal template. The basic concept shown in Fig. 7 requires that individual subunits contain both a metal binding region and an anion binding site. Addition of a metal ion will cause the coordination of metal binding regions and the organization of the binding site for anions [44].

Hamilton and coworkers have synthesized bipyridine-bisthiourea subunit **53** in the presence of Fe(II) or Ru(II) ions [45]. These resulted in the forma-



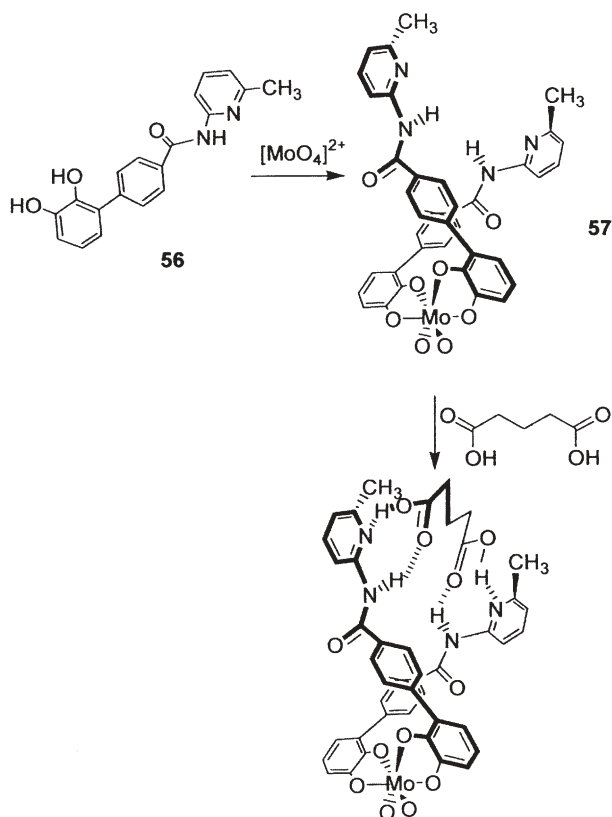
**Fig. 7** Schematic of binding site organization by metal template effects



**Fig. 8** Proposed binding mode of **54** and **55** with dicarboxylates

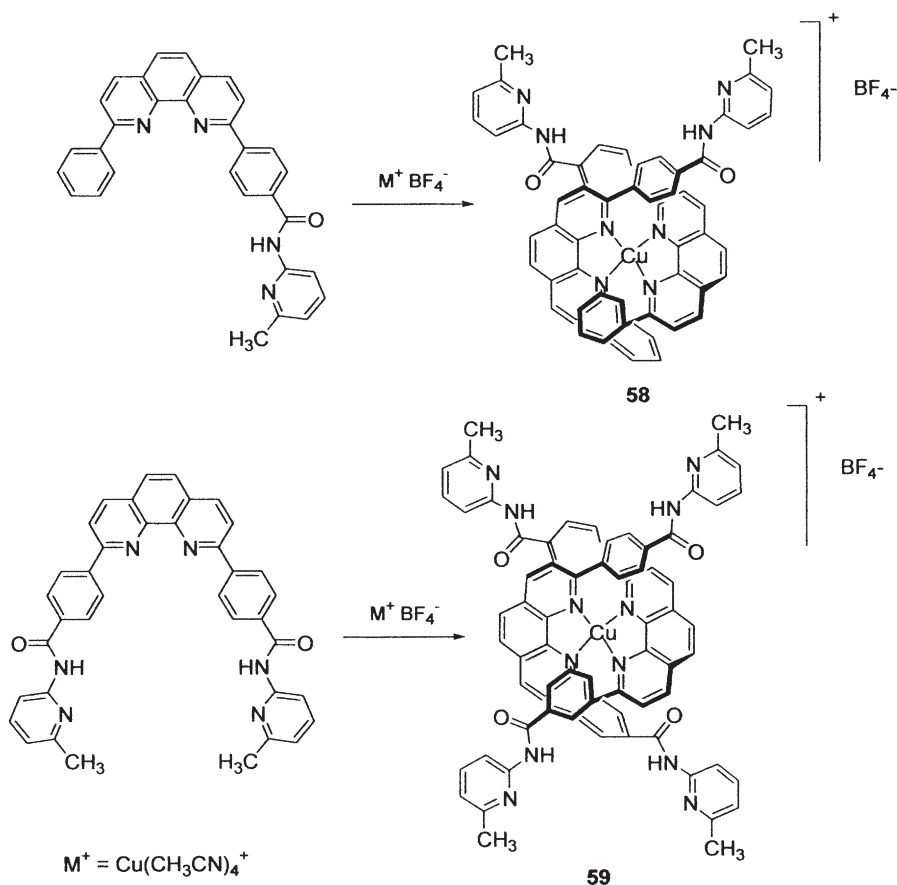
tion of bithiourea binding regions of complexes **54** and **55** for binding anions, as presented in Fig. 8. Preliminary results showed that complex **55** participated in binding with dicarboxylate anions such as glutarate ( $K_a=8.3 \times 10^3 \text{ M}^{-1}$ ), adipate ( $K_a=2.9 \times 10^3 \text{ M}^{-1}$ ), and pimelate ( $K_a=6.0 \times 10^3 \text{ M}^{-1}$ ) to different extents.

Weiss and coworkers [46] have reported a new receptor for dicarboxylic acids, related guests to dicarboxylate anions, based on the self-assembly of functionalized *meta*-catechol **56** around *cis*-[MoO<sub>2</sub>]<sup>2+</sup>. UV-vis studies for dicarboxylic acid binding showed a 1:1 stoichiometry for the complex formation (Fig. 9). Receptor **57** displayed selectivity for C<sub>4</sub> and C<sub>5</sub> dicarboxylic acids. The stability constants (log *K* values) of the complex **57** with C<sub>4</sub> and C<sub>5</sub> dicarboxylic acids in CH<sub>3</sub>CN are 6.1 and 4.3, respectively. This should be explained by the free rotation of the CO-phenyl bond enabling the receptor to adapt to the length of the diacid carbon chain. Furthermore, this receptor exhibited enantioselective recognition of D and L-*N*-Cbz-glutamic acid via directed multiple hydrogen bonding and lipophilic interactions with topographical control achieved by the *cis*-[MoO<sub>2</sub>]<sup>2+</sup> core.



**Fig. 9** Proposed binding mode of **57** with dicarboxylic acid

Furthermore, Hamilton and coworkers [47] synthesized the dicarboxylic acid receptors **58** and **59**. These two receptors consist of a 2,9-disubstituted phenanthroline bearing one or two acylamino pyridine binding sites, which can coordinate to a Cu(I) ion. This arrangement was ideally suited to the strong hydrogen bonding complexation of dicarboxylic acids (Fig. 10), and large downfield shifts of the NH resonances were observed in an NMR study. Significant changes in the UV absorption of **58** and **59** in  $\text{CHCl}_3$  also took place on addition of glutaric acid, with the color of solution changing from red-orange to orange-red for **58** and orange to red for **59**. The Job's plot showed 1:1 and 1:2 stoichiometries of complex formation between **58** or **59** and dicarboxylic acids, respectively. Binding constants for the complexes of **58** with glutaric acid and pimelic acid measured by  $^1\text{H}$  NMR in  $\text{CDCl}_3$  are  $4.3 \times 10^4$  and  $1.6 \times 10^4 \text{ M}^{-1}$ , respectively. The chromogenic effect presumably came from a change in the conjugation of the (benzoylaminopyridyl) side arm of the phenanthroline-metal system due to conformational changes on guest binding.



**Fig. 10** Proposed binding modes of **58** and **59** with dicarboxylates

## 5

## Transition Metal Complexes as Chromogenic Hosts

This type of chromogenic sensor utilizes the coordination chemistry of transition metal complexes, which have vacant binding sites to bind specific anions or have pendant arms containing anion receptor units. Transition metal complexes already have their own specific colors due to their different electronic structures. Coordinating directly to anions or binding of anions by the pendant arms results in perturbations of their electronic structures and causes color changes.

The dicopper(II) complex **60** [48] was capable of sensing imidazolate anion over others at pH 9 with  $\log K=4.7$  (Fig. 11). Upon addition of imidazolate, the pale blue color of **60** ( $\lambda_{\max}=640$  nm) turned to a more intense blue concurrent with the absorption band being shifted to 690 nm. In addition, these results suggest that **60** can detect L-histidine which contains an imidazole moiety giving intense blue color ( $\log K=5.5$ ).

Fabbrizzi and coworkers reported the synthesis of dicopper(II) complexes of bis-tren cryptands **61**–**63**. The metal center was coordinated by a tren subunit oriented to a trigonal bipyramidal geometry which had an available binding site for anions at a vacant axial position. The complex **61** [49] showed the highest

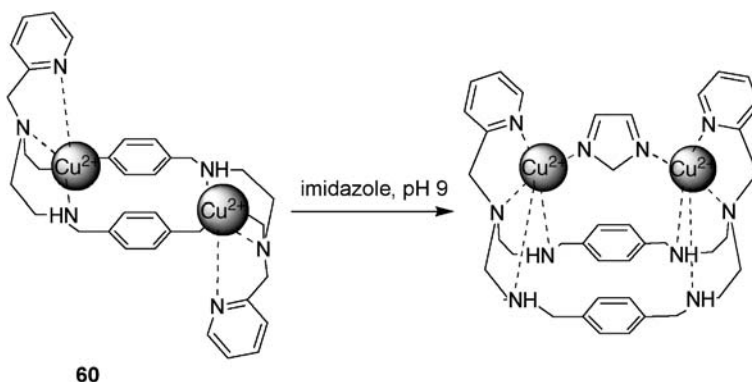
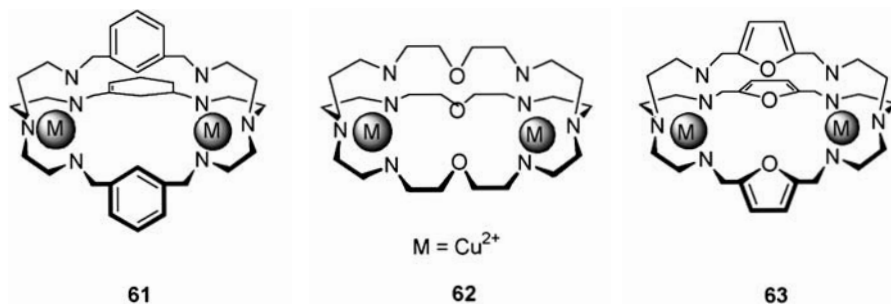
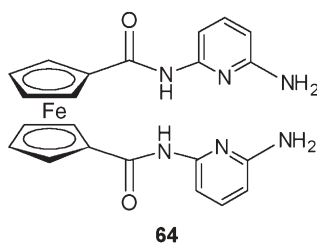


Fig. 11 Proposed binding mode of **60** with imidazolate

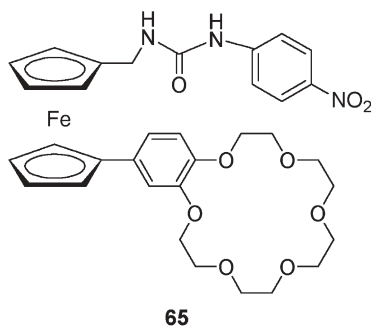


selectivity for  $\text{N}_3^-$  anion with  $\log K=4.78$  at pH 8 in a 1:1 complex stoichiometry, with a color change from blue to bright green ( $\lambda_{\text{max}}=400$  nm). Receptors **62** and **63** [50] displayed a special affinity for halide ions in a 1:1 stoichiometry. Halide inclusions could be detected visually by the appearance of an intense bright yellow color above 400 nm in the spectrum ( $\text{Cl}^-$ ,  $\lambda_{\text{max}}=410$  nm;  $\text{Br}^-$ , 430 nm, and  $\text{I}^-$ , 440 nm). Compound **63** was not only able to include halide ions but also linear triatomic anions such as  $\text{N}_3^-$  ( $\log K=4.7$ ) and  $\text{NCS}^-$  ( $\log K=4.28$ ). The aqueous solution turned pale blue to intense olive green ( $\lambda_{\text{max}}=386$  nm). This was due to the  $\text{NH}-\text{CH}_2-\text{C}-\text{O}$  torsion angles along the chain arm of 2,5-dimethylfuran behaving as a spring, which controlled the length of the intermetallic cavity.

Beer and coworkers [51] have combined ferrocene and mixed amide-amine moieties for a new anion sensor. The receptor **64** showed a spectacular UV-vis response to the addition of  $\text{H}_2\text{PO}_4^-$  in  $\text{CH}_3\text{CN}$ , which resulted in hydrogen bonding to the amide units near the ferrocene and caused a large UV perturbation. The d-d band at 443 nm showed a hypsochromic shift and a hyperchromic effect. This change was visible to the naked eye with the solution becoming brighter in color.

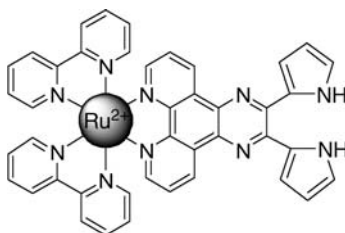


Recently, Miyaji and coworkers [52] reported the chromogenic molecular switch **65** as a new ditopic ferrocene receptor for anions in the presence of cations. Upon addition of  $\text{F}^-$  to a solution of **65** in  $\text{CH}_3\text{CN}$ , a new absorbance appeared at 472 nm ( $K_a=9,340 \text{ M}^{-1}$ ). Addition of  $\text{K}^+$  to the solution of  $\text{65}\cdot\text{F}^-$  caused a reverse behavior and the solution turned colorless. This implied that the color change was controlled by  $\text{F}^-$  “switches on” and  $\text{K}^+$  “switches off”. This result was

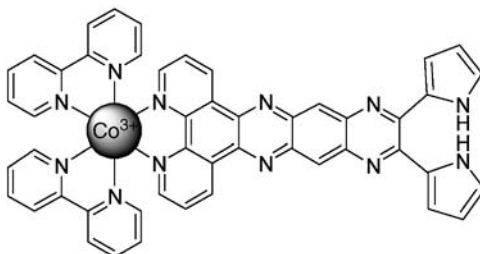


confirmed by NMR studies in  $\text{CD}_3\text{CN}$ . When  $\text{K}^+$  was added to the solution of  $65\cdot\text{F}^-$ , large upfield shifts of the proton of the urea-NH occurred and shifted to the position of the free receptor. The results from  $^1\text{H}$  NMR and UV-vis studies, therefore, supported the assumption that it was the presence of  $\text{K}^+$  in close proximity to the fluoride binding center of **65** that caused the color quenching process. This receptor may thus be applied as an optical device at the molecular level.

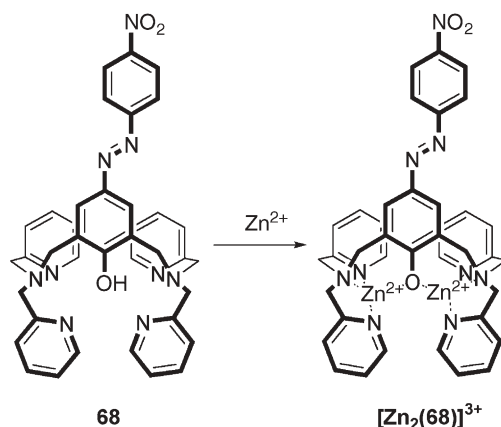
A luminescent Ru(II) metal complex with 2,3-di(1*H*-2-pyrrolyl)quinoxaline receptor **66** was reported by Castellano and colleagues [53] to undergo a red shift in the UV-vis spectrum upon addition of  $\text{CN}^-$  in 98%  $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$  solution ( $K_a=428,000\text{ M}^{-1}$ ). The low-lying MLCT absorption ( $\lambda_{\text{max}}=465\text{ nm}$ ) and the high-energy  $\pi-\pi^*$  ligand-based absorptions decreased monotonically throughout the addition. These absorption features signified that  $\text{CN}^-$  anion bound to the metal complex through the dipyrrolylquinoxaline receptor.

**66**

The receptor **67** [54] shows the sensing of  $\text{F}^-$  in DMSO. Upon addition of  $\text{F}^-$  to the solution of receptor **67** two bands at 323 and 525 nm decreased and a new band at 652 nm appeared. Furthermore, the color of the solution changed from red-pink to pale purple. These spectral changes were ascribed to the formation of a 1:1 adduct between the metal complex and  $\text{F}^-$  anion, in which  $\text{F}^-$  anion bound two dipyrrolylquinoxaline units ( $K_a=54,000\text{ M}^{-1}$ ). Receptor **67** was also studied electrochemically by cyclic voltammetry. A clearly reversible redox signal was observed at 160 mV (vs SHE), which was assigned to the  $\text{Co(III)}/\text{Co(II)}$  reduction. The addition of  $\text{F}^-$  led to a complete disappearance

**67**



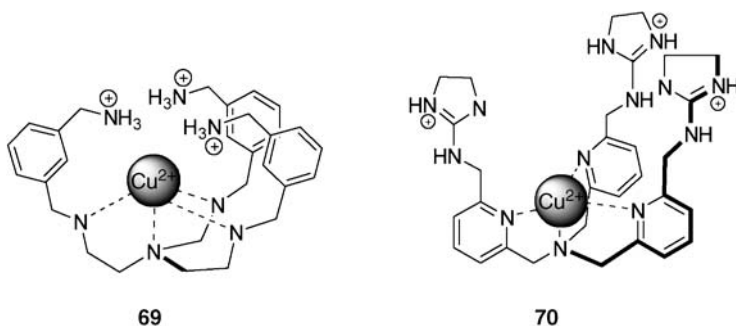


**Fig. 12** Formation of  $[Zn_2(68)]^{3+}$  complex

of the Co(III)/Co(II) reduction signal due to the formation of a redox-inactive complex.

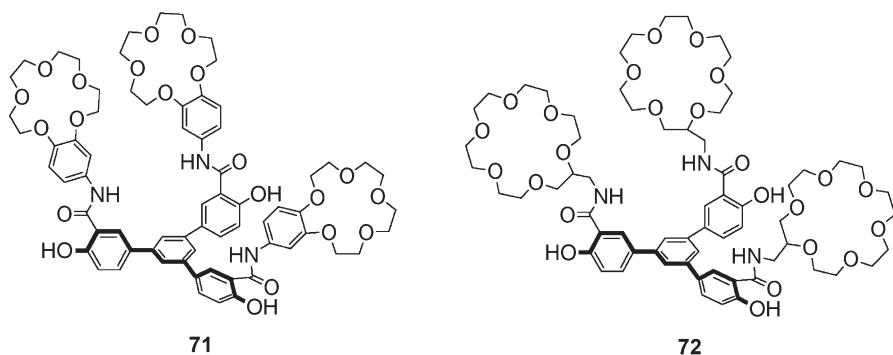
The complex of Zn(II) with **68** [55], in which both  $Zn^{2+}$  atoms coordinated to pyridine-nitrogen donors and a phenolate oxygen donor (Fig. 12), displayed a yellow color at  $\lambda_{max}=417$  nm in aqueous solution at pH 7.4. Addition of  $H_2PO_4^-$ ,  $AcO^-$ ,  $F^-$ ,  $HCO_3^-$ ,  $Cl^-$ ,  $HPO_4^{2-}$ , and citrate to the solution of  $[Zn_2(68)]^{3+}$  did not induce spectral changes. However, addition of pyrophosphate causes a bathochromic shift from 417 to 463 nm and a color change from yellow to red. The result showed that a 1:1 adduct was formed between the complex and pyrophosphate anion. Pyrophosphate reacts with  $[Zn_2(68)]^{3+}$  via oxygen to give two hexacoordinate  $Zn^{2+}$  ions. The red shift occurs by the weakening of the bond between the phenolate oxygen and  $Zn^{2+}$  atoms. This increases the negative charge character of the phenolate oxygen giving a bathochromic shift in the visible region.

Anslyn and coworkers [56, 57] synthesized receptors containing Cu(II) binding sites with appended ammonium **69** and guanidinium **70** groups. These receptors showed high affinities for tetrahedral anions such as  $HPO_4^{2-}$  and



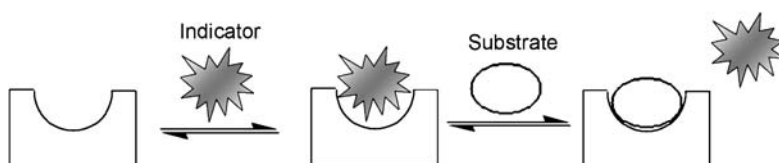
$\text{HAsO}_4^{2-}$  in aqueous solution at pH 7.4. Binding constants of **69** with these guests had the same value ( $K_a = 2.5 \times 10^4 \text{ M}^{-1}$ ). However, compound **70** was found to bind  $\text{HPO}_4^{2-}$  and  $\text{HAsO}_4^{2-}$  with binding constants of  $K_a = 1.5 \times 10^4$  and  $1.7 \times 10^4 \text{ M}^{-1}$ , respectively. Furthermore, the binding of host and guest is proposed through ion-pairing interactions between the charges of functional groups and between  $\text{Cu}^{2+}$  and guest reactions.

1,3,5-Triarylbenzoamido-crown ethers **71** and **72** [58] showed abilities as naked-eye sensors for  $\text{F}^-$ ,  $\text{H}_2\text{PO}_4^-$ ,  $\text{AcO}^-$ , citrate, trimesate, and isophthalate in the presence of potassium picrate in DMSO: $\text{H}_2\text{O}$  (1:1 v/v). Upon addition of the aforementioned anions to a solution of  $\text{71} \cdot \text{K}^+$  or  $\text{72} \cdot \text{K}^+$  picrate, the color of the solution changed from yellow to green.



## 6 Displacement of Chromogenic Guests

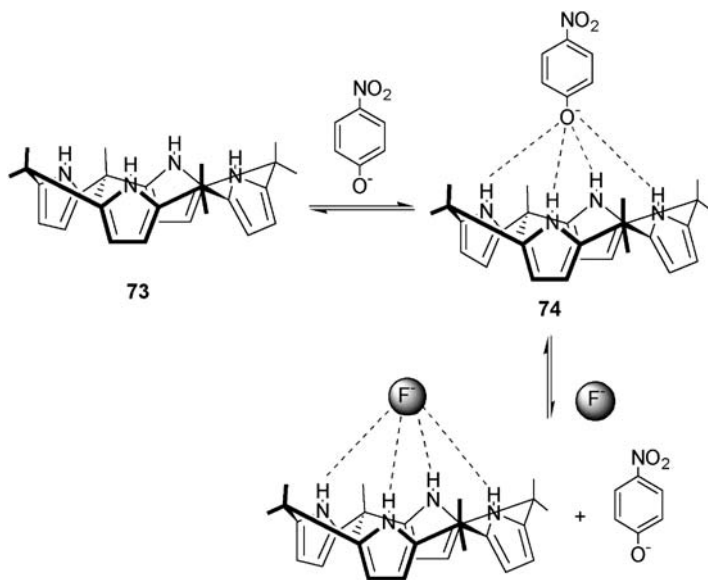
An alternative method to a covalently attached chromophore is a competition between the indicator and the analyte in the receptor unit. An indicator is displaced from the binding site upon addition of an analyte, causing a signal modulation (Fig. 13). In order to create a sensitive sensing strategy, an indicator must give a large absorption change upon addition to the receptor, since the subsequent addition of an analyte must lead to a large change in the opposite direction. The advancement of this method has been described in detail by Anslyn and his colleagues [59]. Therefore, the work included in Anslyn's excellent accounts are not restated.



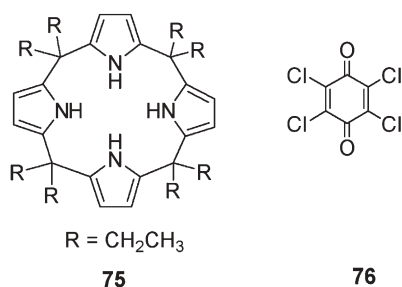
**Fig. 13** Schematic operation of displacement method for a chromogenic sensor

Gale and coworkers [60] have discovered a very simple displacement method for a calix[4]pyrrole-based anion receptor. Addition of calix[4]pyrrole **73** to a solution of tetrabutylammonium 4-nitrophenolate in  $\text{CH}_2\text{Cl}_2$  caused a decrease in intensity of a UV band at 432 nm, and calix[4]pyrrole-4-nitrophenolate complex **74** was formed. Upon addition of  $\text{F}^-$ , 4-nitrophenolate was displaced from the complex, and the color of the solution changed from colorless to yellow due to the presence of the free nitrophenolate anion (Fig. 14).

Shao and coworkers [61] have demonstrated that a noncovalent charge-transfer complex of calix[4]pyrrole-chloranil can be used as a chromogenic sensor for  $\text{F}^-$  and  $\text{H}_2\text{PO}_4^-$ . Upon addition of calix[4]pyrrole **75** to the solution of chloranil **76** in chloroform, the color changed from pale yellow to blue. This indicated the formation of a charge-transfer complex between calix[4]pyrrole and chloranil in chloroform. The Job's plot analysis showed a 1:1 complex with

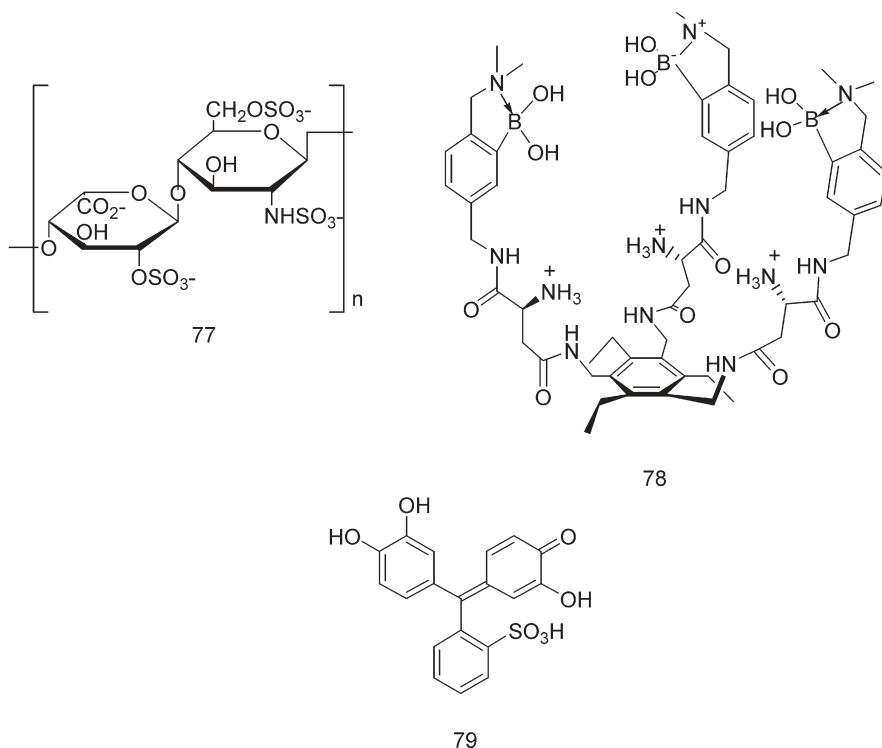


**Fig. 14** The displacement mode for detection of  $\text{F}^-$  with **73**

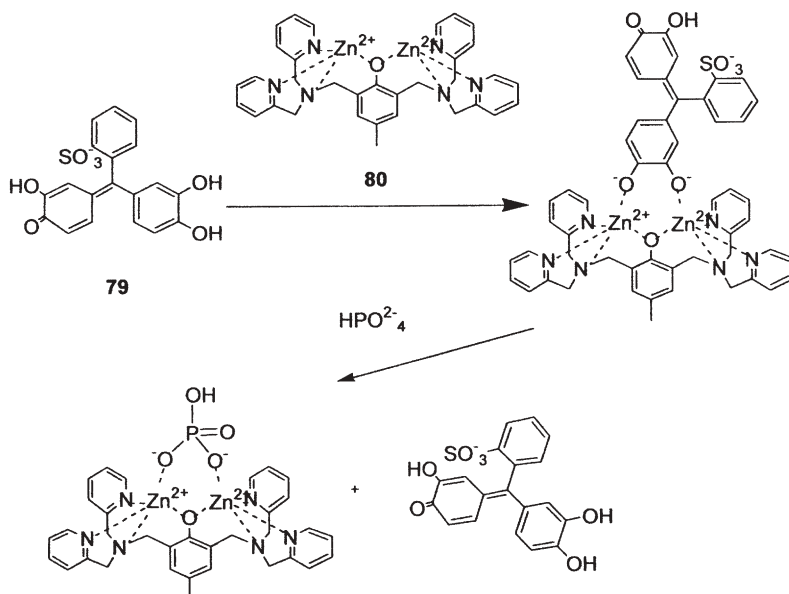


$K_a=5.8 \times 10^{-2} \text{ M}^{-1}$ . In the presence of  $\text{F}^-$  and  $\text{H}_2\text{PO}_4^-$ , the charge-transfer band,  $\lambda_{\text{max}}=622 \text{ nm}$ , of the complex **75**·**76** disappeared, while a new absorption band appeared around 400–500 nm and the color of the solution turned from blue to orange-yellow.

Heparin **77**, an anticoagulation reagent, is used during cardiopulmonary bypass surgery. During surgery, heparin is commonly monitored by determining the activated clotting time (ACT). Zhong and Anslyn [62] have recently reported a new designed receptor and sensor for heparin possessing a novel amino acid with a boronic acid side chain, **78**. This new receptor showed strong binding to heparin with good selectivity. Pyrocatechol violet **79** was used as an indicator for the colorimetric sensing of heparin. The binding of **79** to the receptor **78** in MeOH/water caused a color change from yellow ( $\lambda_{\text{max}}=430 \text{ nm}$ ) to grayish purple ( $\lambda_{\text{max}}=526 \text{ nm}$ ) with  $K_a=7.1 \times 10^3 \text{ M}^{-1}$ . When heparin replaced **79** and was bound in the cavity of the receptor **78**, the color of the solution turned to yellow ( $K_a=3.8 \times 10^4 \text{ M}^{-1}$ ).



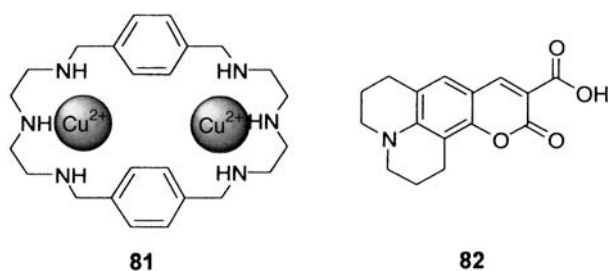
The detection of anions such as  $\text{HPO}_4^{2-}$  in water is a challenging task due to the competing solvation effect between water and anions. Han and Kim [63] have recently reported a colorimetric sensor that can detect  $\text{HPO}_4^{2-}$  in aqueous solution at neutral pH. The dinuclear Zn(II) complex of 2,6-bis{[bis(2-pyridylmethyl)amino]methyl}-4-methylphenol (H-bpmp) **80** was synthesized.



**Fig. 15** Schematic representation of the displacement of 79 from 80 by  $\text{HPO}_4^{2-}$

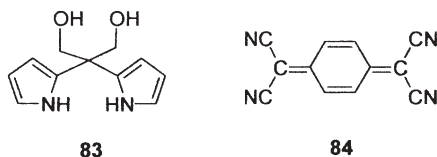
The Zn(II) H-bpmp is colorless and has good water solubility. In addition, it can bind  $\text{HPO}_4^{2-}$  very strongly. The authors used pyrocatechol violet 79, a catechol-type pH-sensitive dye, as a chromogenic indicator for the sensor. When the solution of complex 80 was titrated into the solution of the indicator, the color changed from yellow ( $\lambda_{\text{max}}=444$  nm) to blue ( $\lambda_{\text{max}}=624$  nm) signifying the binding of 79 to the zinc complex. The addition of  $\text{HPO}_4^{2-}$  to the aqueous solution of the ensemble resulted in a change of the color from blue to yellow, indicating free pyrocatechol violet that was replaced by the anion (Fig. 15). Moreover, other anions failed to cause the color change.

A similar system for detecting pyrophosphate optically in water was created by Fabbrizzi et al. [64]. The researchers used the Cu(II) complex of the bisdiene macrocycle 3,6,9,16,19,22-hexaazatricyclo[22.2.2.2(11.14)]-triaconta(1(26),-11(12),13,24,27,29)-hexaene 81 as a receptor for binding anions, dyes such as



coumarin 343, **82**, and pyrophosphate in their system. The displacement of the dye from the Cu(II) complex by pyrophosphate gave a naked-eye detectable change. The detection of carbonate in water was also developed by the same researchers.

Recently, Guo et al. [65] synthesized selective colorimetric detectors for  $\text{PO}_4^{3-}$  and  $\text{CO}_3^{2-}$  based on the assembly of dihydroxymethyl-di-(2-pyrrolyl)methane **83** and tetracyanoquinodimethane (TCNQ) **84** in  $\text{MeCN}:\text{H}_2\text{O}$  (1:1 v/v). Upon addition of **83** to the solution of **84**, an absorption peak at 397 nm evidently shifted to 317 nm concurrent with a new absorption band appearing at 627 nm. This indicated the formation of a 1:1 charge-transfer complex between **83** and **84** with  $K_a=463.4 \text{ M}^{-1}$ . Upon addition of  $\text{PO}_4^{3-}$  to the solution of **83**·**84**, the charge-transfer absorption band at 627 nm markedly decreased and the color changed from blue to orange. Similarly, the addition of  $\text{CO}_3^{2-}$  to the solution of **83**·**84** induced the color change from blue to pale purple ( $\lambda_{\text{max}}=550 \text{ nm}$ ) and finally to orange-yellow after 20 h. These results were caused by the break-up of the charge-transfer assembly **83**·**84**.

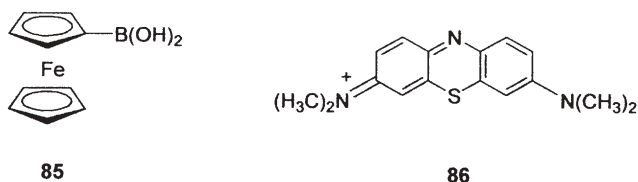


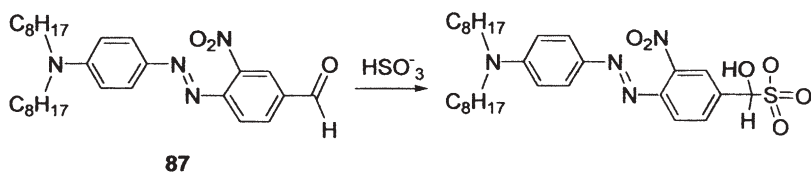
## 7

### Chromoreactands: Concurrent Recognition and Reaction

Besides the covalent attachment of the chromophore to the receptor units or displacement of a chromogenic guest, one can employ the advantages of the selective reactivity between a particular anion and chromogenic hosts, which will display dramatic color changes. There have been at least nine examples of these chromoreactands published recently.

The mixture of **85** and methylene blue **86** [66] at pH 3 showed the characteristic blue color ( $\lambda_{\text{max}}=665 \text{ nm}$ ) of the dye. Upon addition of  $\text{F}^-$ , the oxidation potential of the redox-active ferrocene unit decreased. Under these conditions, the ferrocene group was able to reduce the dye as detected by the disappearance of the band at 665 nm. Other anions had no effect on the ferrocene and dye units. Therefore, this system can be used as a colorimetric detector for fluoride.

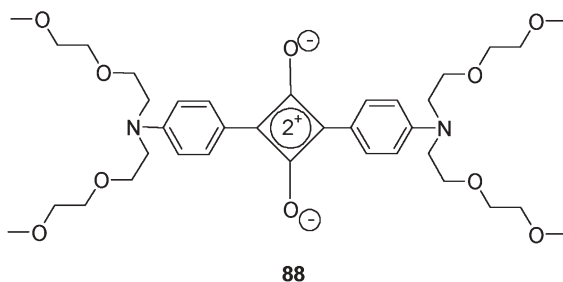




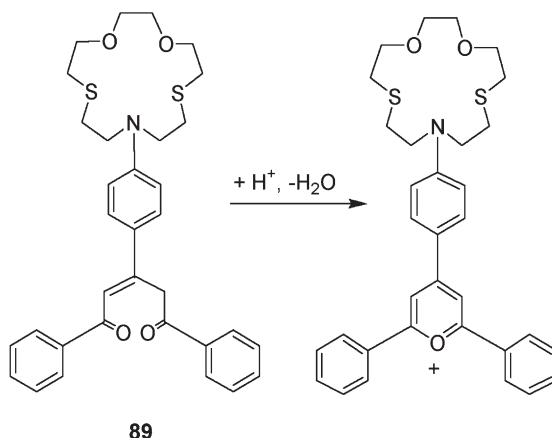
**Fig. 16** The chemical structure of receptor **87** and the corresponding bisulfite adduct

Mohr has used 4-*N,N*-dioctylamino-4'-formyl-2'-nitroazobenzene **87** as a chromoreactand for selective sensing of hydrogen sulfite ( $\text{HSO}_3^-$ ) [67]. The aldehyde moiety in **87** is known to interact with hydrogen sulfite by forming a bisulfite adduct, as shown in Fig. 16. The conversion of the aldehyde into the bisulfite adduct can bring about a change in the electron acceptor strength. Consequently, a color change of the formyl dye upon interaction with hydrogen sulfite can be noticed. The investigator has demonstrated that in a sensor layer composed of the chromoreactand and dioctadecylmethylamine in PVC plasticized by 2-nitrophenyloctyl ether, first with plain buffer of pH 4.9 and then with buffer containing 30 mM hydrogen sulfite, a shift in absorbance maximum from 524 to 484 nm was observed.

Ros-Lis et al. [68] have taken advantage of the selective reactivity toward a particular reaction that certain anions display. The nucleophilic characteristics of  $\text{CN}^-$  allow a reaction with a squaraine dye derivative **88** that results in a distinct color change. The chromogenic sensing ability of **88** was studied in acetonitrile in the presence of various anions:  $\text{F}^-$ ,  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{I}^-$ ,  $\text{NO}_3^-$ ,  $\text{H}_2\text{PO}_4^-$ ,  $\text{HSO}_4^-$ ,  $\text{AcO}^-$ ,  $\text{BzO}^-$ ,  $\text{CN}^-$ , and  $\text{SCN}^-$ . Only  $\text{CN}^-$  was able to decolorize **88**.  $^1\text{H}$  NMR data for **88** in  $\text{CD}_3\text{CN}$  upon  $\text{CN}^-$  addition were consistent with  $\text{CN}^-$  attack on a carbon of the four-atom squaraine ring next to the phenyl group. This caused the rupture of the electronic decolorization with the consequent disappearance of the 641-nm charge-transfer band.



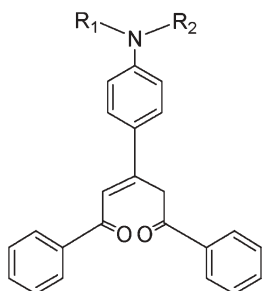
The transformation of a reactant to another form by changing the pH of the solution can be used as a chromogenic sensor. The 1,3,5-triaryl-1,5-pentanedione derivative **89** [69] can be readily transformed into the corresponding pyrylium ion, as shown in Fig. 17. Addition of nitric acid to a solution of **89** in



**Fig. 17** Transformation of receptor **89** into the pyrylium cation

1,4-dioxane/water caused a dramatic change in color from yellow to magenta. The changes in absorption spectrum of **89** at neutral pH upon adding anions such as chloride, bromide, sulfate, phosphate, ATP, ADP, and GMP have also been studied. However, the most remarkable effect was observed in the presence of ATP, whereby a bright magenta color was fully developed. Therefore, **89** is a selective chromogenic reagent for sensing ATP.

Sancenón et al. [70] have synthesized a number of colorimetric probes to discriminate isomeric dicarboxylate anions. A dioxane/water (70:30 v/v) solution of compound **90** at ca. pH 6 using 0.01 M HEPES buffer is yellow. Upon addition of oxalate and malonate anions, solutions of compound **90** turned to red-magenta. Other dicarboxylate anions such as succinate, glutarate, adipate, pimelate, and suberate did not change the color of the solutions, which remained yellow. The remarkable color change was a result of the anion-induced selective cyclization of **90** to give the colored 2,4,6-triphenylpyrylium cation similar to the one shown in Fig. 17. The solution of **91** in the same solvent and buffer was yellow in the presence of fumarate (a *trans* isomer), but turned to magenta in the presence of maleate (a *cis* isomer). Specific color change occurred because



**90.**  $R_1 = \text{CH}_2\text{CH}_2\text{OH}$ ,  $R_2 = (\text{CH}_2\text{CH}_2\text{O})_4\text{CH}_2\text{CH}_2\text{OH}$

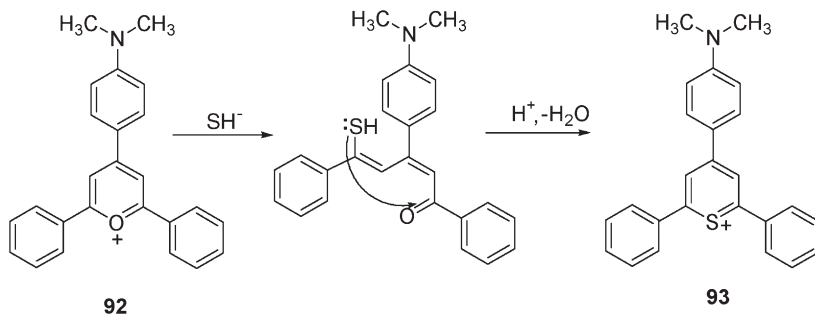
**91.**  $R_1 = R_2 = \text{CH}_3$



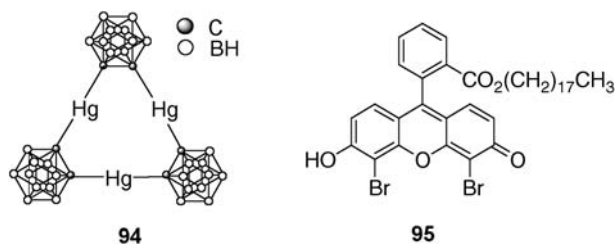
the tweezer-like diacid (*cis* isomer and oxalate) was able to act as a chelating ligand toward the hydroxyl group whereas other diacids did not. This shape-induced recognition enhanced the ease of cyclization to the magenta pyrylium cation.

A sensor containing a pyrylium–aniline backbone, **92** [71], reacted toward  $\text{SH}^-$  to give the pyrylium cycle (Fig. 18). Further addition of an acid induced cyclization and resulted in the corresponding anilinthiopyrylium derivative **93**. This transformation induced a charge-transfer color change from magenta ( $\lambda_{\text{max}}=540\text{ nm}$ ) to blue ( $\lambda_{\text{max}}=580\text{ nm}$ ) in water–MeCN (1:1 v/v) that allowed visual recognition of  $\text{SH}^-$ .

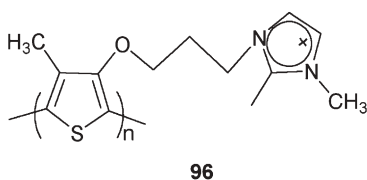
Bachas and coworkers [72] have reported a highly selective optical sensor for chloride in blood, based on the multidentate Lewis acid ionophore [9]mercuracarborand-3, **94**. This compound incorporates three electron-deficient mercury centers within a macrocyclic cavity and, therefore, is selective for chloride by such a preorganized cavity. In addition, the compound is chemically stable and hydrophilic and, thus, suitable for using as a sensor for  $\text{Cl}^-$  in blood. This sensor was constructed by embedding the mercuracarborand, a suitable acidic lipophilic dye **95**, and lipophilic cationic sites in a plasticized polymeric membrane film. The sensing mechanism was based on anion binding by **94**, followed by a concomitant protonation of the acid dye to ensure electroneutrality. Such protonation of the proton chromoionophore led to a large change in the absorbance of the optical film.



**Fig. 18** Transformation of receptor **92** into the thiopyrylium form in the presence of  $\text{SH}^-$



Leclerc et al. [73] have demonstrated that a cationic polymer which consists of polythiophene derivatives can be a colorimetric sensor for iodide. In aqueous solutions, polymer **96** is yellow ( $\lambda_{\text{max}}=406$  nm) due to a random coil conformation of the polythiophene derivative that leads to a decrease in effective conjugation through the polythiophene chain. Addition of  $\text{F}^-$ ,  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{SO}_4^{2-}$ ,  $\text{CO}_3^{2-}$ ,  $\text{HCO}_3^-$ ,  $\text{H}_2\text{PO}_4^-$ ,  $\text{HPO}_4^{2-}$ ,  $\text{EDTA}^{4-}$ ,  $(\text{C}_6\text{H}_5)\text{B}^-$ , and  $\text{AcO}^-$  induced negligible changes in the UV–visible spectrum of **96**. However, addition of  $\text{I}^-$  gave a red shift of the band centered at 406 to 543 nm (yellow to red-violet). This color variation was ascribed to iodide promoting the aggregation and planarization of polymer **96**. Furthermore, fluorimetric detection of iodide anion was also possible because the fluorescence spectrum of **96** in the yellow random coil form ( $\lambda_{\text{ex}}=420$  nm,  $\lambda_{\text{em}}=550$  nm) was quenched in the planar aggregated form.



## 8 Conclusion

We have summarized six types of chromogenic anion sensors. Many anion receptors containing different anion binding sites and a plethora of chromophores have been described. Each type has its own advantages and drawbacks. The NH-based hydrogen bonding-type and Lewis acid-type sensors are simple and easy to use, but they have a limited use in some media such as water. The metal ion template type can be alternatively employed as a switchable “on” or “off” sensor utilizing a metal ion as a switch. The transition metal complex chromogenic hosts are still waiting for new discoveries. The indicator displacement method is a powerful approach in terms of analytical aspects, but it is sometimes complicated to use. Therefore, this type of chromogenic sensor, in particular, needs more development. There should be a lot of space to fill in this area. The chromoreactant has only recently emerged and definitely needs more investigation. Overall, chromogenic anion sensing is still a young field waiting for new disclosures. It is yet a long way to bring these synthetic sensors or systems to practical use. We optimistically believe that there is a way to combine the aforementioned approaches to fabricate an ultimate chromogenic sensor for a particular anion.

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