Colorimetric Sensors Based on Hydrogen-bond-induced π-delocalization and/or Anion-triggered Deprotonation

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Abstract: Most receptors are designed to explore the anion-binding affinities for medical, biological, environmental relevant anions. Of the major types of receptors, sensors related to hydrogen bond have been studied widely by numerous researchers. Both hydrogen-bond-induced π-delocalization and anion-triggered deprotonation govern the signal transduction of the binding events in these systems. An overview of the inclusion of the (thio)urea and pyrrole groups within synthetic receptor molecules is presented in this article.

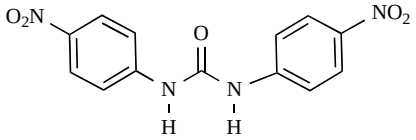
Keywords: Colorimetric sensors, hydrogen bond, hydrogen-bond-induced π-delocalation, anion-triggered deprotonation.

I. INTRODUCTION

During the past two decades, molecular recognition of anionic species has received much more attention in the supramolecular community [1-4], due to the realization of the vital roles that anions play in the biology [5], medicine [6], catalysis [7] as well as the environment [8, 9]. Chemical sensing is a compelling area of application for continuous monitoring of the presence of such anions. Furthermore, the utilization of (supra)molecular ground-state charge transfer is a more effective approach to signal transduction in anion sensing. Ideally, chemical sensors have become increasingly recognized in qualitative and quantitative analysis, which can provide certain continuous and intuitionistic information about a specific substrate. The relevant anion sensing involves two steps: one is to bind specific anionic species from its environment by suitable binding agents; the other is signal transduce of binding events. The corresponding chemosensors can be divided into three classes in consideration of the property to be determined as: electrical, fluorescent and optical chemical sensors. In contrast to fluorescent and electrochemical sensors, colorimetric chemosensors, named "naked-eye anion sensors", are especially attractive on the transduction of a modulated signal, because of their impressive detectability, experimental simplicity and low cost. They can distinguish qualitatively and quantitatively the related target by visual color changes without resorting to instruments. Nowadays, they have significant positions among the available sensors, which have applications in clinical, industrial, environmental and agricultural analysis.

Generally, colorimetric sensors have involved the design of receptors that can signal the presence of special subunit with color changes. These usually consist of anion-binding sites employing various combinations of anion receptor units and chromophores converting the binding events into detectable signal. The chromophores generally contain many conjugated bonds to form a large conjugated system. Many conjugated systems have HOMO to LUMO energy differences (namely, energy gap) which correspond to the color of a certain chromophore. Furthermore, it was well confirmed that a charge transfer band, corresponding to the charge transition and color change, can be observed upon excitation with light when conjugated bonds link electron donor (NH_2, OH, O^-, *etc*.) to electron acceptor (NO_2, CF_3, C=O, etc.) in a molecular. Similarly, for a given sensor containing chromophore, the coordination of anions to the binding sites makes the later more electron donor (due to the negative charge of bound anion), thus pumping more electrons to conjugated system and strengthening the conjugation, as well as producing spectra shift. In fact, the interaction between the anion and the anion-binding sites produces electron perturbation on the chromophore which would result in the color variation of the system.

For these sensors containing hydrogen-bond interaction sites, the addition of anionic species produces dramatic color changes with increase of the anion concentrations, especially for basic anions such as F^- and AcO^-. These beautiful color changes had been ascribed to the charge transfer from the hydrogen-binding assembly donor of binding-sites and anions to chromogenic acceptors, namely hydrogen-bond-induced π-delocalization [4, 10, 11] in the past. Such a characteristic phenomenon and the similar spectra changes have been observed for many sensors containing (thio)urea with different chromogenic groups [4, 10, 11]. For elucidating the nature of the color variations resulting from anion-receptor interaction, Fabbrizzi and co-workers deliberately designed receptor (**1**) and found that both hydrogen-bond-induced π-delocalization and deprotonation of hydrogen-bond donor were responsible for the aforementioned ones [12]. These results furthered the knowledge of anion-receptor interaction based on hydrogen-bond interaction and paved the way to construct new, high selective and sensitive colorimetric sensors.



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According to the view, "All hydrogen bonds can be considered as incipient proton-transfer reactions, and for strong hydrogen bonds, this reaction can be in a very advanced state." [13] A given sensor containing hydrogen-binding sites can be regarded as Brønsted acid and the anionic analyte can be considered as basicity. The recognition becomes the Brønsted acid-base reaction. The "reaction" equilibrium equations are illustrated in Scheme **1**. Original H-bond complex of receptor with the analytes formed, and then deprotonation of receptor occurred due to the interaction between the receptor and anionic species. Hydrogen bonding acts as "frozen" intermedia between pre-organization state of receptor to link analytes and the dissociation state after proton transfer occurred (Equation 3). For this kind of sensors, the deprotonation of binding sites after the addition of anionic substrates, increases the electron density of the hydrogen-binding sites apparently related to the original

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H-bond complex (due to the negative charge of the hydrogen-binding sites losing proton), thus conveys much more electrons to the conjugated system, and produces the new absorption band and the striking color variation.

$$LH + B^- \rightleftharpoons LH\cdots B^- \quad \text{Equation 1}$$

$$LH\cdots B^- + B^- \rightleftharpoons L^- + BHB^- \quad \text{Equation 2}$$

$$LH + B^- \rightleftharpoons LH\cdots B^- \rightleftharpoons L^- + BHB^- \quad \text{Equation 3}$$

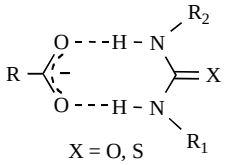
Scheme 1. Equation **1**: The formation of hydrogen bonding receptor:anion complex. Equation **2**: The classical stepwise deprotonation of receptors containing hydrogen binding sites by basic anions, *e.g.* F^- and AcO^-. Equation **3**: The role of H-bond complexes in the process of host:guest interaction.

Based on the analysis of the deprotonation, the anion-triggered deprotonation was commonly thought as the further development of hydrogen-bond-induced π-delocalization. And, under the same conditions, the former induced more striking spectrum shift compared with the later. Both these interactions resulted in the enhancement of the donor character of binding sites, and produced red-shift of charge-transfer band, as well as the color changes. In these processes, the chromophores, the acidity of the binding sites, the basicity of the analyte, and the corresponding stability of the conjugated base, as well as the selectivity of solvent, play important roles.

Hydrogen-bond-induced π-delocalization and anion-triggered deprotonation are good approaches for colorimetric sensing anions. These approaches are fundamental, and are comprehensively used in development of anion chemosensors, as can be seen in many anion chromogenic chemosensors [14]. In this review, the development of colorimetric sensors, consisting of anion-binding agents conjugatedly linking signal transducers, are described in detail in recent years. Furthermore, the specific attention is paid to the receptors containing hydrogen-bond sites that distinguish the analytes by hydrogen-bond-induced π-delocalization and/or anion-triggered deprotonation. And the paper is comprised of three sections according the type of hydrogen-bond donor.

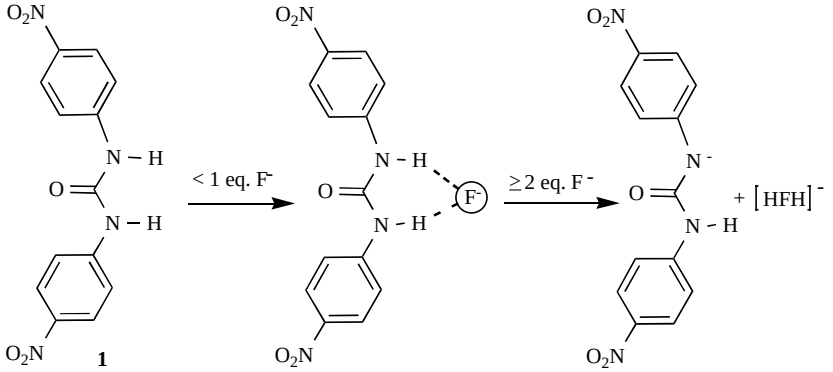
II. CHROMOGENIC SENSORS CONTAINING THIOUREA OR UREA

Thiourea and urea subunits as good hydrogen-bond donors, especially for Y-shape carboxylate groups (Scheme **2**) and spherical anions, have been widely used in anion receptors. Receptors, in which one or more urea or thiourea moieties were incorporated, were designed and synthesized by a number of groups following the independent pioneering work of Wilcox [15] and Hamilton [16] on these systems. At the same time, by covalent linking signal transducer, colorimetric sensors based on the thiourea or urea, developed extensively. The interaction between compound (**1**) and anions is a classic example of the above-mentioned mechanism [12]. P-nitrophenyl unit, appended to the hydrogen-bond donor by conjugated bond, was choosed as the signal transducer in consideration of the enhancement of the acidity of receptor due to the electron-withdrawing properties of chromophore. Upon addition of the oxoanions ($CH_3CO_2^-$, $PhCO_2^-$, $H_2PO_4^-$, NO_2^-, HSO_4^-, NO_3^-) to the receptor (**1**) in CH_3CN, the characteristic peak at 345 nm decreased and the new peak at ~ 370 nm appeared simultaneously, with a concomitantly color change to bright yellow, which resulted from the charge transfer from the urea unit linking oxoanion to the NO_2 group. ^1H NMR and UV-vis spectroscopic data suggested the formation of the 1:1 adduct by two hydrogen bonds involving the NH fragments of receptor (**1**) and oxygen atoms of oxoanions, and showed a trend in the association constants (logK, $CH_3CO_2^-$ > $PhCO_2^-$ > $H_2PO_4^-$ > NO_2^-> HSO_4^- > NO_3^-) for receptor (**1**). Specifically, a reasonably linear correlation was observed between logK and the average negative charge on oxygen atoms of oxoanions outlined above, suggesting that the electrostatic interaction between receptor (**1**) and the oxoanions, rather than geometric effect, played a vital role in the process of receptor determining selectively anions. Subsequently, the group thoroughly studied the interaction between compound (**1**) and F^-. Addition of F^- (< 1.0 equivalent) to the solution containing (**1**) induced similar spectral changes to those produced by oxoanions. However, when being close to 1.0 equivalent F^-, a new peak at 475 nm occurred and arrived at limiting value after addition of 2.0 equivalent F^- with an orange-red color. The distinct color change resulted from the deprotonation of NH of the urea group of the receptor (**1**), as confirmed by ^1H NMR. The occurrence of deprotonation of NH of urea (Scheme **3**) should be ascribed to two contributions: one was the intrinsic acidity of the urea group, that was strengthened by two adjacent electron-deficient nitrophenyl subunits; the other was the formation of particularly stable $[FHF]^-$ self-complex due to the higher electronegativity and basicity of F^-. So, an advanced stage of proton transfer [13] occurred. At the same time, the deprotonation of the receptor prevented further deprotonation of NH fragments of the urea unit due to the repulsion of the deprotonation formation of receptor for F^-.

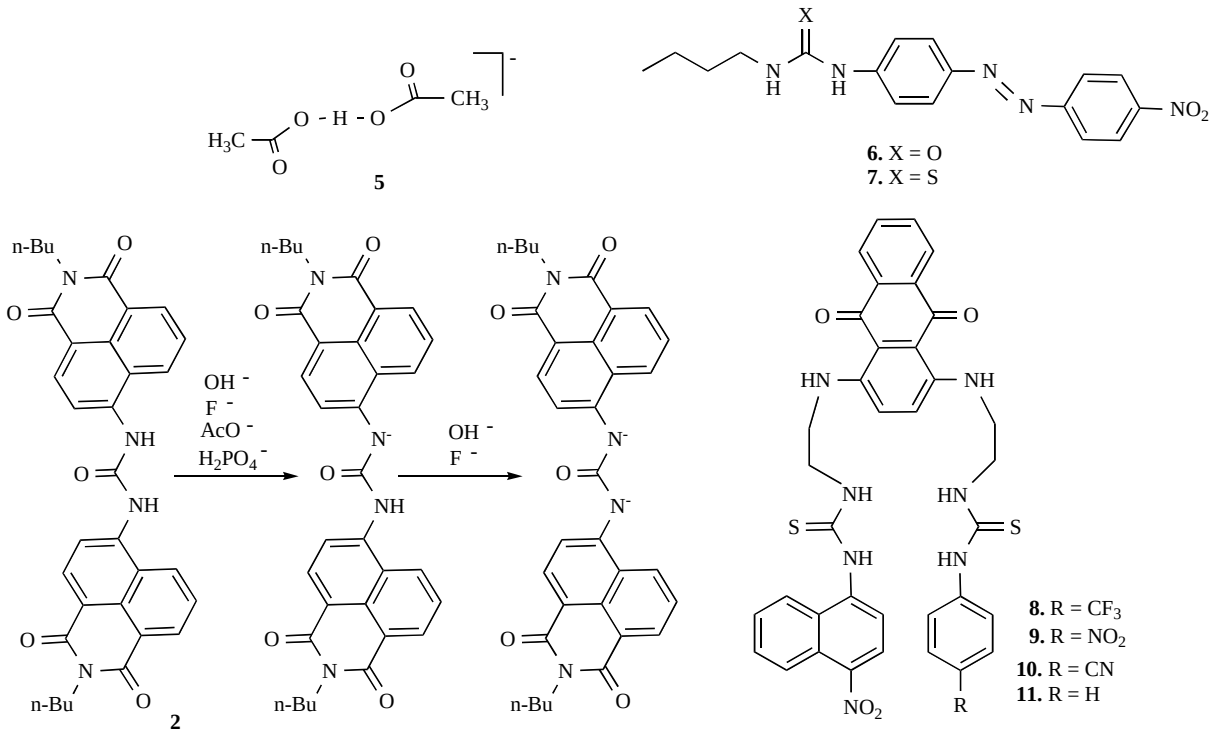


Scheme 2. The ideal interaction mode of (thio)urea with carboxylate anions.

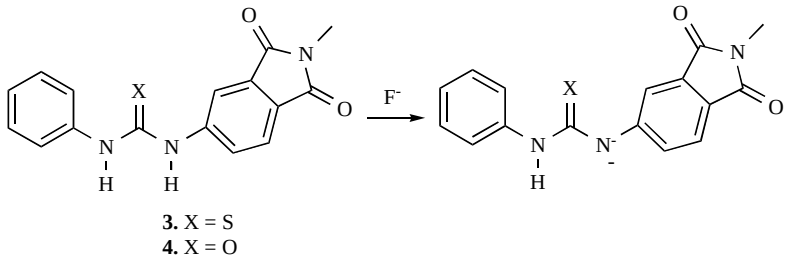
As an extension of their work, Fabbrizzi and his colleagues described the synthesis of receptor (**2**) [17] by incorporation of naphthalenimide onto urea. Binding studies carried out using ^1H NMR and UV-vis spectroscopy in DMSO revealed that less basic anions



Scheme 3. F^--induced deprotonation of receptor **1**.



Scheme 4. Anion-triggered deprotonation of receptor **2**.



Scheme 5. Deprotonation of receptor **3** and **4** induced by F^-.

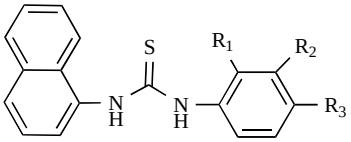
induced deprotonation of only one N-H and, hydroxide and F^- resulted in the double deprotonation of urea subunits (Scheme **4**). The differences between receptor (**1**) and (**2**) mainly derived from the electron-withdrawing properties of chromophores.

To explore the affinity of receptors based (thio)urea fragments, and anions for deprotonation, the same group designed and synthesized the receptor (**3**) and (**4**) [18]. For the sensor (**3**), the characteristic band at 360 nm (in DMSO) undergone red shift to 375 nm, corresponding to the formation of $[\mathbf{3}\cdots CH_3CO_2]^-$, and the new peak at 410 nm developed with further addition, that indicated the stable existence of deprotonation formation of receptor. On the other hand, results also displayed that $CH_3CO_2^-$ stabilized the formation of dimmer (**5**). ^{1}H NMR titration experiment also proved the point outlined above and suggested that deprotonation occurred at the NH fragment of thiourea subunit close to electron-withdrawing naphthalenimide substituent. Similar results were also found for F^- (Scheme **5**), $PhCO_2^-$ and (even less basic) $H_2PO_4^-$. However, Cl^-, even at higher concentration, failed to induce the deprotonation of receptor (**3**), maybe due to the unstabilization of $[ClHCl]^-$ self-aggregation. For receptor (**4**), the deprotonation formation existed only in case of F^-, that was ascribed to the less acidity of urea compared with thiourea [19].

A family of azo dyes containing hydrogen-bond sites, such as thiourea (**6**) and urea (**7**), were synthesized by Rurack and co-workers [20]. The responses of these compounds to anions of various shapes and sizes in CH_3CN were studied by UV-vis spectra and ^{1}H NMR spectra. Two different effects were distinguished: one was the red shift < 40 nm (from *ca*. 400 nm to *ca*. 440 nm) with color changes from yellow to pale orange, corresponding to the anion coordination; the other was distinctly more pronounced bathochromic shift ~200 nm (from *ca*. 400 nm to *ca*. 600 nm) with color variations from yellow to blue due to the deprotonation of hydrogen-binding sites by highly basic F^-. These features were ascribed to the delicate balances between the different binding sites and the proton affinities of anions, which were proved by the PM3 calculations and ^{1}H NMR studies. Subsequently, the solution containing thiourea (**6**) and TBAF was used to colorimetric determination CO_2 based on the reaction of deprotonated forms of (**6**) and traces of water and CO_2, accompanying the color shift from blue to yellow.

Following on from their earlier work [21, 22], Yao-ping *et al* synthesized compounds (**8-11**) [23] to discriminate important biological isomeric dicarboxylate anions. Addition of maleate to the DMSO of compound (**8**), the characteristic absorption peak at 385 nm gradually decreased, while the new peak at 521 nm appeared and reached its limiting value after addition of 2.0 equivalent maleate, at the same time the solution showed striking color shift from dark-blue to dark-red. ^{1}H NMR titration experiment carried out in DMSO-d_6 proved that the monodeprotonation of the thiourea

unit linking 4-nitronaphthyl chromophore resulted in color changes. At the same conditions, fumarate anions also induced the color change (from dark-blue to bright-yellow) of the solution containing (**8**) due to the twisting of the two thiourea units out of the plane of the 4-trifluoromethylphenyl and 4-nitronaphthyl moieties, respectively. Likewise, chromophore (**9**) was then used to discriminate maleate and fumarate. With progressive addition of maleate to chromophore (**9**), the characteristic absorption band at 360 nm decreased in intensity, and a new charge transfer band at 523 nm occurred and reached its limiting value after addition of 2.0 equivalent maleates. All these changes were ascribed to the hydrogen-bond-induced π-delocalization on the 4-nitrophenyl thiourea moiety, and then, the monodeprotonation of 4-nitronaphthyl thiourea moiety, as confirmed by ^{1}H NMR spectra and *ab* initio calculation. Whereas, addition of fumarates to the DMSO solution containing (**9**) produced unnoticeable color change, because the *trans* disposition of dicarboxylate moieties in fumarate induced no changes of the configuration structure of receptor (**9**). Moreover, it was also found that the substituent on the phenyl ring tuned the anion-binding properties of sensors with maleate. Stronger electron-withdrawing moieties are, more stable the complexes are. For receptor (**10**) and (**11**), fumarate failed to induce striking color change. At the same time, no distinct color shifts were observed when aromatic isomeric dicarboxylate anions (*ortho*/ *meta*/ *para*-phthate) were added to the solution of receptor (**8**-**11**).



12. R_1= NO_2, R_2 = R_3 = H

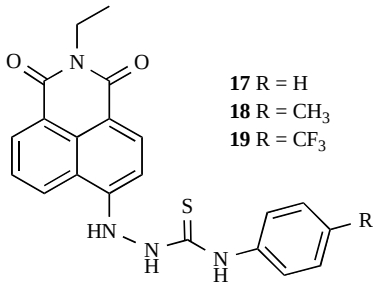
13. R_2= NO_2, R_4 = R_3 = H

14. R_3= NO_2, R_2 = R_4 = H

Das and co-workers have designed and synthesized three simple isomeric sensor molecules (**12**-**14**) based on urea to explore the effect of substituent on their aromatic rings of isomer on receptor-anion binding [24]. Solution (DMSO/CH_3CN, 1:9, v/v) of (**12**-**14**) changed from pale yellow to orange in presence of F^- (> 2.0 equivalent), which resulted from a new absorption band in the visible region. The formation of the new band was ascribed to the intramolecular charge transfer interaction between the mono-deprotonated urea groups and the electron-deficient nitrophenyl units. The selectivity trend observed in binding affinity was determined to be F^- > AcO^- > $H_2PO_4^-$ >> Cl^-. For these receptors, the anion-binding affinity decreased in the sequence of (**13**) < (**12**) < (**14**), established by the computer *ab* intio. Moreover, the results showed that the mono-deprotonation occurred at the NH close to the nitrophenyl for receptor (**14**), and to naphthalent for receptor (**12**) and (**13**), as confirmed by the time-resolved emission studies. Thereby, the positions of electron-withdrawing moieties played important roles in tuning anion-binding affinities of receptor.

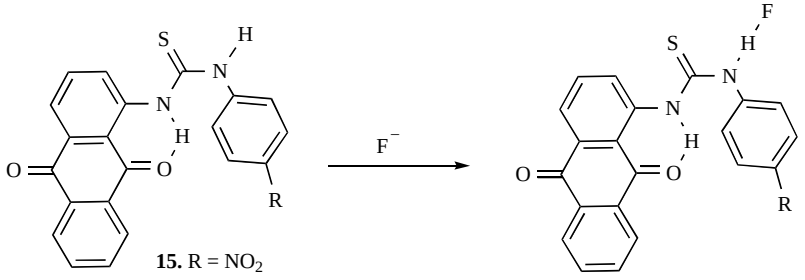
Compound (**15**) contains the thiourea moieties as binding sites conjugatedly connected to nitrophenyl and anthraquinone group [25]. DMSO solution of (**15**) exhibited striking color change from colorless (λ_{max} = 304 nm) to yellow (λ_{max} = 304, 427 nm) after addition of F^-, and the saturated yellow color of the system was observed with addition of 1.0 equivalent F^-. These changes were mainly attributed to the formation of hydrogen-bond complex between F^- and (**15**), that disturbed original charge transfer from thiourea to nitrophenyl. Addition of other anions such as Cl^-, AcO^-, $H_2PO_4^-$, HSO_4^- induced no detectable color shift, and led to the appearance of the new shoulder peak at ~ 360 nm. The anion association constants for receptor (**15**) were determined to be F^- >> $CH_3CO_2^-$ > $H_2PO_4^-$ > HSO_4^- >Cl^- >Br^-, which was not completely in agreement with the basicity of anions. It was reasoned the stronger hydrogen bonds of $F^-$and conformation conversion of receptor (**15**) (Scheme **6**), which was confirmed by AM1 calculations.

Gunnlaugsson and co-workers have continued their work on neutral urea-based receptors containing naphthalimide to act as chromophore [26, 27]. Compound (**16**), based on the introduction of amidourea based receptor into calix [4]arene scaffold, was prepared and showed highly symmetrical and pre-organized cavity for anion recognition through hydrogen bonding [28]. Anion-binding studies were investigated in DMSO using UV-vis spectroscopy and ^{1}H NMR in DMSO-d_6, it was confirmed that (**16**) formed 1:1 complex with pyrophosphate and $H_2PO_4^-$, and 1:2 complex with F^- and AcO^- at higher concentrations. Dramatic color change (to red) of the solution containing receptor (**16**) was ascribed to the formation of HF_2^-, which was formed the deprotonation of the urea group. In the case of AcO^- the occurrence of changes from colorless to light yellow was assigned to the new charge transfer from amidourea linking $AcO^-$to the p-nitrophenyl chromophore, which resulted in the redistribution of π-electron of the system.



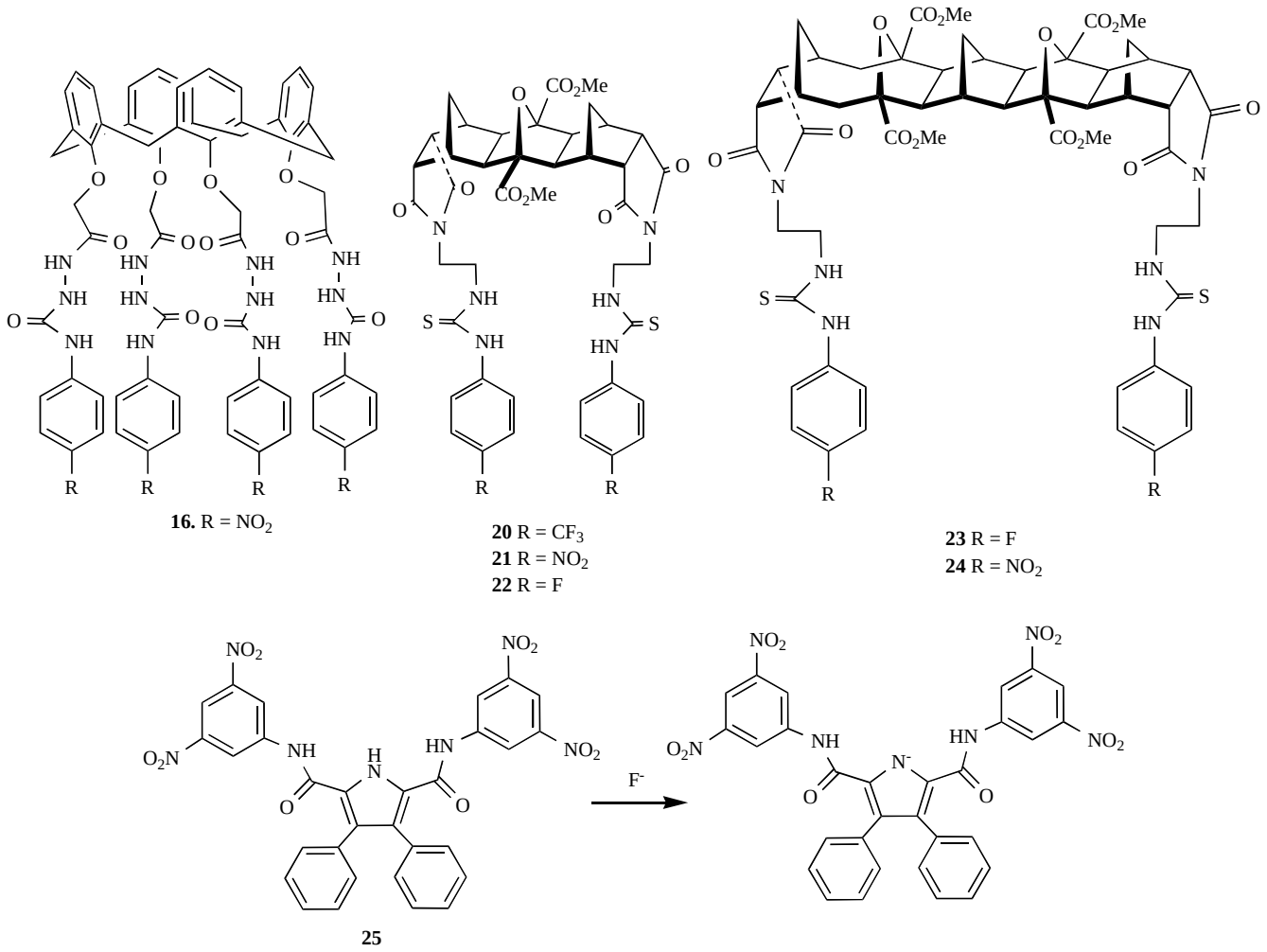
17 R = H
18 R = CH_3
19 R = CF_3

Recently, the same group described the synthesis and anion-binding properties of naphthalimide receptors (**17**-**19**) [29]. The colorimetric responses of these receptors to various anions were carried out in DMSO solution. A bright fluorescent color to blue and deep purple occurred upon addition of AcO^- and $H_2PO_4^-$, respectively. In the case of F^-, the purple color changes were observed at low guest concentration, and at high concentrations the initial color changed, via purple to pale orange. No color changes were observed for Cl^- and Br^-. The author concluded that color



15. R = NO_2

Scheme 6. Proposed hydrogen-bonding interaction between F^- and receptor **15**.



16. R = NO_2

20 R = CF_3
21 R = NO_2
22 R = F

23 R = F
24 R = NO_2

25

Scheme 7. Deprotonation of receptor **25** by F^-.

changes of the solution upon addition of AcO^- were attributed to the pure hydrogen bonding interaction that strengthened the charge transfer from the assembly of binding sites with anions to chromophore, and the changes observed upon addition of $F^-$and $H_2PO_4^-$ were due to the initial hydrogen bonding interaction, then followed by the full or partial deprotonation of amidourea.

Preffer and co-workers have synthesized four novel thiourea-functionalized polynoborane (**20**-**24**), which were easily prepared and functionalized and tunable size, and then studied their anion-binding abilities by ^{1}H NMR spectroscopic methods in DMSO-d_6 [30, 31]. Compound (**20**) and (**21**) displayed high affinities for $H_2PO_4^-$ and $H_2P_2O_7^-$, binding them in 1:1 and unusual 2:1 stoichiometry, respectively. In addition to binding urea, anions also formed hydrogen bond interaction with the non-polar C-H groups in the binding cavity of the framework deriving from the anion-mediated self-assembly of this complex species. In the case of F^-, 1:1 and 1:2 host-guest stoichiometry occurred, and obvious color changes from pale yellow to red observed in the NMR tube were attributed to the deprotonation of urea unit. The deprotonation of urea unit increased the electron density of the receptor and strengthened the internal charge transfer to electron-deficient chromophore. Receptor (**24**) can selectively bind terephthalate dianion based on the size complementary of the pre-organized binding cleft with the rigid dicarboxylate guest.

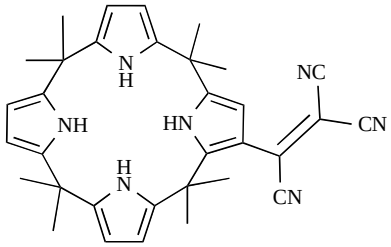
III. CHROMOGENIC HOST CONTAINING PYRROLE

Pyrrole subunits have been used as the binding sites in design of receptors based on hydrogen bond. These tunable hydrogen donors are easily functional and incorporation into acyclic, cyclic and polycyclic framework [32]. Therefore, receptors containing pyrrole have been paid much more attention in supramolecular community. By tuning the electronic characteristics through introducing different electron-rich or electron-deficient groups, many colorimetric sensors based on pyrrole [1, 4, 10, 11, 32-34], such as pyrrole amides, calix[4]pyrrole, and dipyrroylquinone have been developed.

By appending the electron-withdrawing 3,5-dinitrophenyl to the amide position, the first prototypical pyrrole-based colorimetric sensor (**25**) was constructed by Gale *et al.* [35]. The dramatic color changes (from colorless to deep blue in CH_3CN) resulted from the anion deprotonating pyrrole and a subsequent new charge transfer from N^- to the electron poor aromatic (Scheme **7**), as confirmed by the X-ray crystal analysis and the identical UV-vis spectrum of the tetrabutylammonium salts of (**25**) with the compound (**25**) in presence of F^-.

Anzenbacher and Dahaen *et al* designed many colorimetric sensors by the conjugated attachment of dye units to calix[4]pyrrole [36, 37]. The approach made colorless calix[4]pyrrole to chromogenic receptor, and produced obvious color variation after addition of anionic analytes. For instance, compounds (**26**) has tricyanoethylene, attached to calix[4]pyrrole skeleton [36]. As outlined above, addition of fluoride, acetate and phosphate made the solution containing sensors (**26**) change from original color to others, that was ascribed to the anion-binding induced charge transfer between the the pyrrole linking anionic species and chromophores, rather than deprotonation of acidic NH proton in the dye pyrrole confirmed by ^{1}H NMR. In addition, chloride, bromide, iodide, and

nitrate could not produce any color changes. Furthermore, sensor (**26**) was demonstrated to be used for detecting carboxylate anions in blood plasma.



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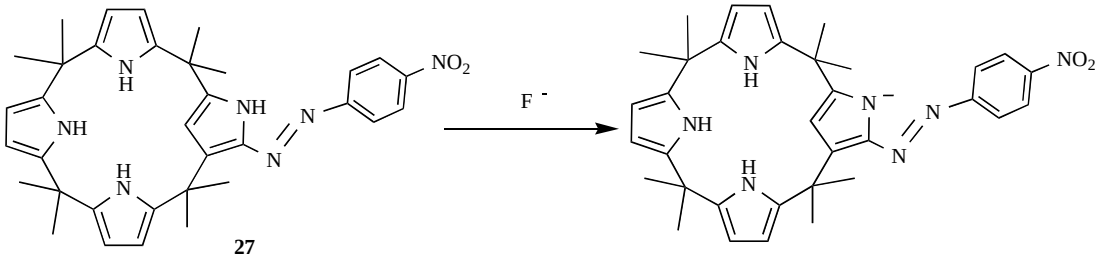
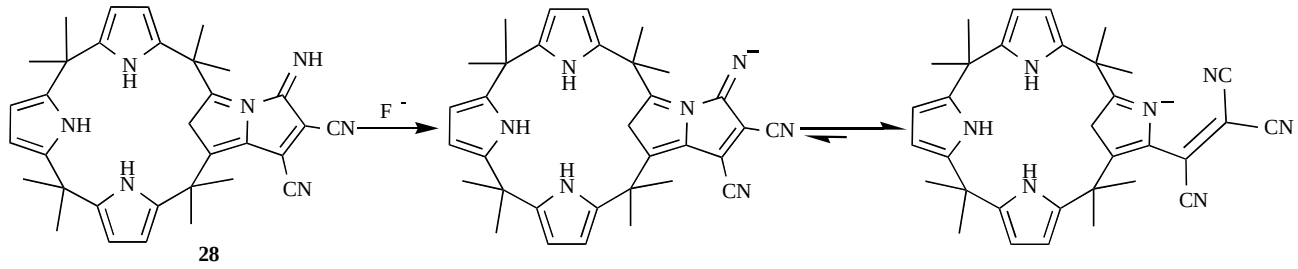
As an extension of their work, Anzenbacher and Dahaen *et al*. studied the anion-binding affinities of the N-confused octamethylcalix[4]pyrrole [38-40] such as (**27**) and (**28**). Addition of F^-, Cl^-, Br^- and $H_2PO_4^-$ to the CH_3CN solution of these compounds led to significant spectral changes. As an example, in presence of F^-, the maximum absorption band of (**27**) in CH_3CN displayed an obvious bathochromic shift from *ca*. 450 nm to *ca*. 600 nm, due to the anion-triggered deprotonation of inverted pyrrole NH (Scheme **8**). In case of receptor (**28**), an enhanced absorption in the 500 nm region was observed after addition of F^-, accompanying distinct pink-to-orange color change. These changes were assumed the deprotonation of imine moieties leading to the simultaneous opening of the pyrrolizine moieties to form (Scheme **9**), as confirmed by ^1H NMR and UV-vis spectra titration experiment [39, 40]. Furthermore, the energetics was responsible for the isomerization of the receptor induced by deprotonation. The B3LYP/LANL2DZ calculation indicated that the opening of pyrrolizine decreased the Gibbs free energy of the system compared with the pyrrolizine one [41]. Subsequently, the group investigated the anion-binding affinity of N-confused calix[4]pyrrole with anions such as Cl^-, Br^-, HSO_4^-, $H_2PO_4^-$, AcO^- and $PhCO_2^-$ in DMSO-d_6-0.5% water [40]. ^1H NMR titration experiments suggested that these compounds formed N-confused cone-like conformation to bind anion substrates by three NH groups of non-inverted pyrroles and the β-CH moiety of inverted pyrrole [40]. These compounds showed the anion association in the order of $AcO^- > PhCO_2^- > H_2PO_4^- > Cl^-$, which was in agreement with the basicity of these anionic analytes. Whereas, addition of SCN^-, I^-, HSO_4^- and NO_3^-(even at higher concentrations) to the solution of these receptors caused no any dramatic spectral changes, that indicated no or weak receptor-anion interaction between the receptor and anions.

Sun and his co-workers have synthesized series of molecular probes (e.g. **29** and **30**) integrating an amide and a pyrrole functionality for anion-recognition and -sensing [42]. These probes typically displayed a strong response to CN^- with striking color change. Changes were thought as the deprotonation of the amide group that perturbed the electron distribution of the system and altered the HOMO-LUMO gap. Anions usually formed hydrogen bonds with amide pyrrole groups of these probes these probes, followed by the deprotonation of the amide group at higher anion concentration. The weakest anions only formed hydrogen bonds with these probes. All these interaction modes depended on the basicity and nucleophilicity of the anions, and the electron deficiency of the acidic pyrrolecarboxyamide N-H.



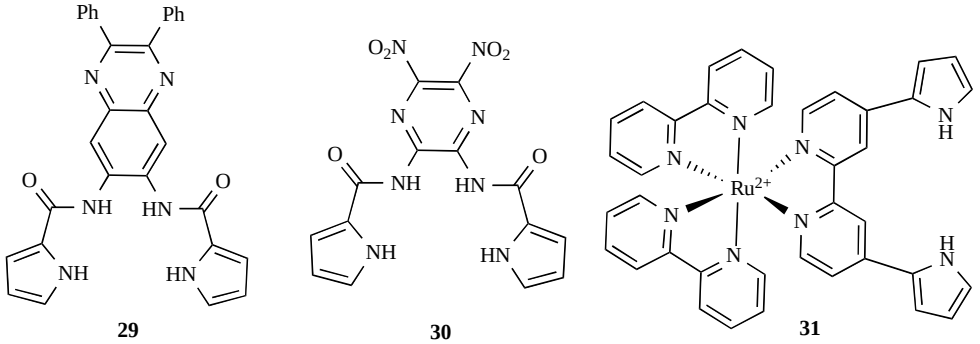
27

Scheme 8. Deprotonation of receptor **27** induced by F^-.

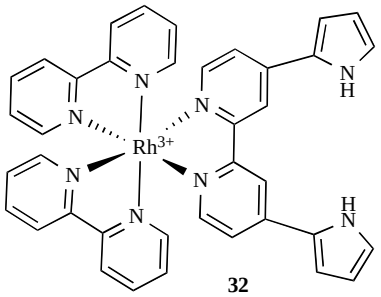


28

Scheme 9. Proposed anion-triggered deprotonation of receptor **28** and subsequently isomerization.



29 **30** **31**



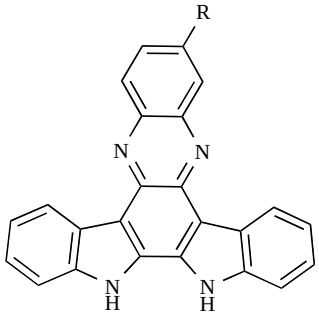
32

In a continuation of their early work [43, 44], Sessler and co-workers have described the synthesis and their anion-binding properties of chromogenic sensors (**31**) and (**32**) [45]. Chromogenic sensors (**31**) and (**32**) displayed stronger anion-triggered color changes and higher affinity with simple anions in comparison to the previously studied analogues of Ru^{II} and Rh^{III} dipyrrolyl quinoxalines, which resulted from the larger pyrrole-based anion-binding cavity size and the deprotonation of pyrrole NH.

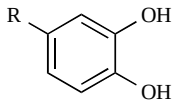
IV. MISCELLANEOUS

The novel conjugated bisindole (**33**), including hydrogen-donor unit and hydrogen acceptor moiety, was first synthesized and used for optical sensing of F^- and AcO^- in aprotic solution (*e.g.* CH_3CN and DMSO) and HSO_4^- in protic solution such as H_2O and MeOH [46]. CH_3CN solution of (**33**) was yellow with two strong absorption band at 277 nm and 423 nm and one less strong shoulder peak at 500 nm related to intramolecular hydrogen bond, as well as one weak band at 347 nm. When 0-0.5 equivalents of F^- were added to the solution of (**33**), the characteristic band at 423 nm gradually increased and reached the maximum, concomitantly, the band at 500 nm disappeared. These spectral changes indicated the formation of a F^- H-bond complex with (**33**) and the disturbance of the intramolecular hydrogen bond aggregation of receptor (**33**) itself. Further addition of F^- to receptor (**33**) caused the disappearance of band at 423 nm and the appearance of new peak at 517 nm which pertained to the deprotonated receptor (**33**) (Scheme **10**) and reached its limiting value after addition of 25 equivalents of F^-, as well as the corresponding color change to red. Similar but less noticeable spectral behaviors were found for AcO^-. Deprotonation of receptor (**33**) did not occur after addition of the other less basic anions such as Cl^-, Br^-, I^-, ClO_4^-, HSO_4^- and $H_2PO_4^-$ even at higher concentration. Most interestingly, addition of HSO_4^- to the receptor (**33**) in water-containing medium (CH_3CN/ H_2O, 4:1, v/v) induced the disappearance of characteristic band at 435 nm and appearance of the new band at 500 nm, with concomitant yellow-to-red color change. The spectral changes, as well as the color shifts, mainly derived from the protonation of the receptor (**33**) (Scheme **10**).

Recently, hydroxyl groups have been used to construct novel anion receptors [47] to stimulate important biological interaction between O···H and anions [48]. Smith and co-workers have studied the anion-binding properties of phenolic receptors (**34**) and (**35**) [49]. The stability constants of these receptors with halide anions

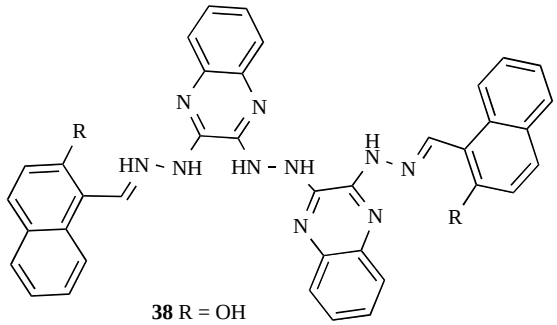


36 R = H
37 R = NO_2



34 R = H
35 R = NO_2

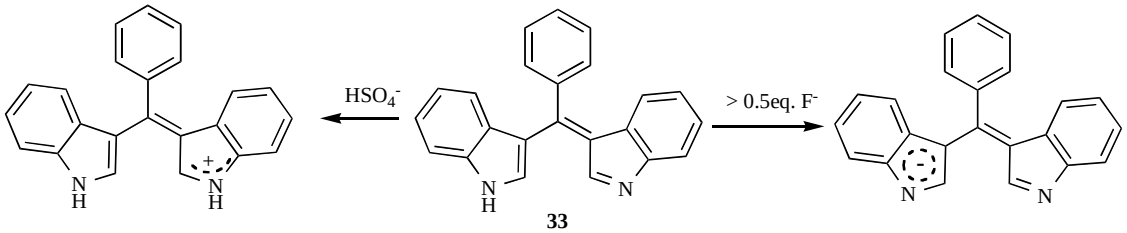
were determined by ^1H NMR in CD_3CN. Results indicated that the angle of the chelating hydrogen bonding groups of catechol played an important role in determining anions. Most interestingly, the binding events occurred even in competitive solvents (e.g. water). Moreover, receptor (**34**) and (**35**) allowed visual detection F^-, $H_2PO_4^-$ and HSO_4^-, due to the oxidative degradation of catechol and the corresponding proton-transfer (acid-base) processes.



38 R = OH
39 R = H

Yan and co-workers recently reported the synthesis and anion-binding properties of indolocarbazole-quinoxaline (**36**) and (**37**) with a large π system [50]. In presence of AcO^- and F^-, colorimetric responses observed in (**36**) and (**37**) were assigned to H-bond-induced π-delocalization. Moreover, receptor (**36**) and (**37**) displayed higher binding affinity and optical properties for AcO^- and F^- in comparison to the corresponding acyclic indole-based quinoxaline [51].

Sun and co-workers have synthesized a variety of chromogenic probes (**38**) and (**39**) including hydrazine, hydrazone and hydroxyl functionalities for potential hydrogen bond sites [52]. Anion-binding affinities were measured by UV-vis spectroscopic technique and ^1H NMR spectroscopy. Results indicated that both (**38**) and (**39**) had higher affinity and sensitivity for F^-, AcO^- and $H_2PO_4^-$ within the nine anions tested and the binding constants of (**38**) for anions were slightly higher compared to those displayed by (**39**) due to the involvement of hydroxyl groups in hydrogen bonding. A 1:2 binding stoichiometry was found for probe (**38**) with AcO^- and $H_2PO_4^-$ and probe (**39**) with F^-, AcO^- and $H_2PO_4^-$, and



33

Scheme 10. Deprotonation and protonation of receptor **33**.

1:1 probe (**38**) to F^- was determined. Noticeable color changes for F^- were observed due to a neat deprotonation process of the most acidic hydroxyl O-H to form the HF_2^- anion as confirmed by ^1H NMR spectra.

CONCLUSION

This review gives account of the work in optical chemosensing, based on hydrogen bond and/or anion-triggered proton transfer, for the medical, biological, environmental relevant anions. The basic mode to build anion chemosensors follows the hydrogen-binding site−signaling subunits approach. The process relates to the suitable choice of binding sites and signaling reporter. By rationally designing, it allows to construct wide varieties of 'naked-eye' chemosensors for anions based on the diverse sensing mechanisms. This approach is important and effective in the development of anion chemsensors, and would give rise to much more attention in the future. The further development to this classical approach relating to hydrogen bond is proton transfer. This approach is used comprehensively in anion chemosensing. At the same time, a new but suggestive pattern recognition approach for anions occurs, which uses a variety of receptors to give specific response for target anions. Whereas, many synthetic receptors have limit uses in aqueous solvents. Therefore, chromogenic sensors for anions need more investigations to develop diverse systems with high selectivity and use in practical. Anion chemosensing is destined for a bright future.

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REFERENCES

[1] Gale, P.A. Anion coordination and anion-directed assembly: highlights from 1997 and 1998. *Coord. Chem. Rev.*, **2000**, *199*(1), 181-233.

[2] Schug, K.A.; Linder, W. Noncovalent binding between guanidinium and anionic groups: focus on biological- and synthetic-based arginine/guanidinium interactions with phosph[on]ate and sulf[on]ate residues. *Chem. Rev*., **2005**, *105*(1), 67-114.

[3] Kruppa, M.; König, B. Reversible coordinative bonds in molecular recognition. *Chem. Rev*., **2006**, *106*(9), 3520-3560.

[4] Martínez-Máñez, R.; Sancenón, F. Fluorogenic and chromogenic chemosensors and reagents for anions. *Chem. Rev.*, **2003**, *103*(11), 4419-4476.

[5] Chakrabarti, P. Anion binding sites in protein structures. *J. Mol. Biol.*, **1993**, *234*(2), 463-482.

[6] Sessler, J.L.; Sansom, P.I.; Andrievsky, A.; Král, V. *Supramolecular Chemistry of Anions*. Wiley-VCH: New York, **1997**.

[7] Scheele, J.; Timmerman, P.; Reinhoudt, DNA significant effect of anion binding ureas on the product ratio in the palladium(II)-catalyzed hydrocarbonylation of alkenes. *Chem. Commun.*, **1998**, 2613-2614.

[8] Moss, B. A land awash with nutrients- the problem of eutrophication. *Chem. Ind*., **1996**, 407-411.

[9] Holloway, J.M.; Dahlgren, R.A.; Hansen, B.; Casey, W.H. Contribution of bedrock nitrogen to high nitrate concentrations in stream water. *Nature*, **1998**, *395*(6704), 785-788.

[10] Suksai, C.; Tuntulani, T. Chromogenic anion sensors. *Top. Curr. Chem.*, **2005**, *255*, 163-198.

[11] Suksai, C.; Tuntulani, T. Chromogenic anion sensors. *Chem. Soc. Rev.*, **2003**, *32*(4), 192-202.

[12] Boiocchi, M.; Boca, L.D.; Gómez, D.E.; Fabbrizzi, L.; Licchelli, M.; Monzani, E. Nature of urea−fluoride interaction: incipient and definitive proton transfer. *J. Am. Chem. Soc*., **2004**, *126*(50), 16507-16514.

[13] Steiner, T. The hydrogen bond in the solid state. *Angew. Chem., Int. Ed.*, **2002**, *41*(1), 48-76.

[14] Gunnlaugsson, T.; Glynn, M.; Tocci (née Hussey), G.M.; Kruger, P.E.; Pfeffer, F.M. Anion recognition and sensing in organic and aqueous media using luminescent and colorimetric sensors. *Coord. Chem. Rev*., **2006**, *250*(23-24), 3094-3117.

[15] Smith, P.J.; Reddington, M.V.; Wilcox, C.S. Ion pair binding by a urea in chloroform solution. *Tetrahedron Lett.*, **1992**, *33*(41), 6085-6088.

[16] Fan, E.; van Arman, S.A.; Kincaid, S.; Hamilton, A.D. Molecular recognition: hydrogen-bonding receptors that function in highly competitive solvents. *J. Am. Chem. Soc*., **1993**, *115*(1), 369-370.

[17] Gómez, D.E.; Fabbrizzi, L.; Licchelli, M. Why, on interaction of urea-based receptors with fluoride, beautiful colors develop. *J. Org. Chem*., **2005**, *70*(14), 5717-5720.

[18] Gómez, D.E.; Fabbrizzi, L.; Licchelli, M.; Monzani, E. Urea *vs*. thiourea in anion recognition. *Org. Biomol. Chem*., **2005**, *3*(8), 1495-1500.

[19] Bordwell, F.G. Equilibrium acidities in dimethyl sulfoxide solution. *Acc. Chem. Res.*, **1988**, *21*(12), 456-463.

[20] Ros-Lis, J.V.; Martínez-Máñez, R.; Sancenón, F.; Soto, J.; Rurack, K.; Weiβhoff, H. Signalling mechanisms in anion-responsive push-pull chromophores: the hydrogen-bonding, deprotonation and anion-exchange chemistry of functionalized azo dyes. *Eur. J. Org. Chem.*, **2007**, 2449-2458.

[21] Yen, Y.-P.; Ho, K.-W. Synthesis of colorimetric receptors for dicarboxylate anions: a unique color change for malonate. *Tetrahedron Lett.*, **2006**, *47*(7), 1193-1196.

[22] Yen, Y.-P.; Ho, K.-W. Development of colorimetric receptors for selective discrimination between isomeric dicarboxylate anions. *Tetrahedron Lett.*, **2006**, *47*(7), 7357-7361.

[23] Tseng, Y.-P.; Tu, G.-M.; Lin, C.-H.; Chang, C.-T.; Lin, C.-Y.; Yen, Y.-P. Synthesis of colorimetric sensors for isomeric dicarboxylate anions: selective discrimination between maleate and fumarate. *Org. Biomol. Chem*., **2007**, *5*(22), 3592-3598.

[24] Jose, D.A.; Kumar, D.K.; Kar, P.; Verma, S.; Ghosh, A.; Ganguly, B.; Ghosh, H.N.; Das, A. Role of positional isomers on receptor–anion binding and evidence for resonance energy transfer. *Tetrahedron*, **2007**, *63*(48), 12007-12014.

[25] Wu, F.-Y.; Hu, M.-H.; Wu, Y.-M.; Tan, X.-F.; Zhao, Y.-Q.; Ji, Z.-J. Fluoride-selective colorimetric sensor based on thiourea binding site and anthraquinone reporter. *Spectrochim. Acta Part A*, **2006**, *65*(3-4), 633-637.

[26] Gunnlaugsson, T.; Kruger, P.E.; Jensen, P.; Pfeffer, F.M.; Hussey, G.M. Simple naphthalimide based anion sensors: deprotonation induced colour changes and CO_2 fixation. *Tetrahedron Lett*., **2003**, *44*(49), 8909-8913.

[27] Gunnlaugsson, T.; Kruger, P.E.; Jensen, P.; Tierney, J.H.; Ali, D.P.; Hussey, G.M. Colorimetric "naked eye" sensing of anions in aqueous solution. *J. Org. Chem.*, **2005**, *70*(26), 10875-10878.

[28] Quinlan, E.; Matthews, S. E.; Gunnlaugsson, T. Colorimetric recognition of anions using preorganized tetra-amidourea derived calix[4]arene sensors. *J. Org. Chem.*, **2007**, *72*(20), 7497-7503.

[29] Ali, H.D.P.; Kruger, P.E.; Gunnlaugsson, T. Colorimetric 'naked-eye' and fluorescent sensors for anions based on amidourea functionalized 1,8-naphthalimide structures: anion recognition *via* either deprotonation or hydrogen bonding in DMSO. *New J. Chem.*, **2008**, *32*(7), 1153-1161.

[30] Pfeffer, F.M.; Kruger, P.E.; Gunnlaugsson, T. Anion recognition and anion-mediated self-assembly with thiourea-functionalised fused[3]polynorbornyl frameworks. *Org. Biomol. Chem.*, **2007**, *5*(12), 1894-1902.

[31] Lowe, A.J.; Pfeffer, F.M. Size matters-strong binding of the terephthalate dianion by thiourea functionalised fused [n]polynorbornane hosts. *Chem. Commun.*, **2008**, 1871-1873.

[32] Sessler, J.L.; Camiolo, S.; Gale, P.A. Pyrrolic and polypyrrolic anion binding agents. *Coord. Chem. Rev.*, **2003**, *240*(1-2), 17-55.

[33] Gale, P.A.; Anzenbacher Jr., P.; Sessler, J.L. Calixpyrroles II. *Coord. Chem. Rev.*, **2001**, *222*(1), 57-102.

[34] Anzenbacher Jr., P.; Nishiyabu, R.; Palacios, M.A. N-confusedcalix[4]pyrroles. *Coord. Chem. Rev.*, **2006**, *250*(23-24), 2929-1938.

[35] Camiolo, S.; Gale, P.A.; Hursthouse, M.B.; Light, M.E. Nitrophenyl derivatives of pyrrole 2,5-diamides: structural behaviour, anion binding and colour change signalled deprotonation. *Org. Biomol. Chem.*, **2003**, *1*(4), 741-744.

[36] Nishiyabu, R.; Anzenbacher Jr., P. Sensing of antipyretic carboxylates by simple chromogenic calix[4]pyrroles. *J. Am. Chem. Soc.*, **2005**, *127*(23), 8270-8271.

[37] Nishiyabu, R.; Anzenbacher Jr., P. 1,3-Indane-based chromogenic calixpyrroles with push−pull chromophores: synthesis and anion sensing. *Org. Lett.*, **2006**, *8*(3), 359-362.

[38] Gu, R.; Depraetere, S.; Kotek, J.; Budka, J.; Wagner-Wysiecka, E. J.; Biernat, F.; Dehaen, W. Anion recognition by α-arylazo-N-confused calix[4]pyrroles. *Org. Biomol. Chem.*, **2005**, *3*(16), 2921-2923.

[39] Nishiyabu, R.; Palacios, M.A.; Dehaen, W.; Anzenbacher Jr., P. Synthesis, Structure, Anion binding, and sensing by calix[4]pyrrole isomers. *J. Am. Chem. Soc*., **2006**, *128*(35), 11496-11504.

[40] Dehaen, W.; Gale, P.A.; García-Garrido, S.E.; Kostermans, M.; Light, M.E. Anion recognition by N-confused calix[4]pyrrole-alpha-carbaldehyde and its Knoevenagel reaction derivatives. *New J. Chem.*, **2007**, *31*(5), 691-696.

[41] Collange, E.; Flamini, A.; Poli, R. Stopped-Flow and DFT Studies of Proton Transfer and Isomerization of 5-Amino-3-imino-1,2,6,7-tetracyano-3H-pyrrolizine and Its Related Base 2-(5-Amino-3,4-dicyano-2H-pyrrol-2-ylidene)-1,1,2-tricyanoe- thanide in Water: A Completely Sorted out Square Scheme. *J. Phys. Chem. A.*, **2002**, *106*(1), 200-208.

[42] Chen, C.-L.; Lin, T.-P.; Chen, Y.-S.; Sun, S.-S. Probing receptor-anion interactions by ratiometric chemosensors containing pyrrolecarboxamide interacting sites. *Eur. J. Org. Chem.*, **2007**, *2007*(24), 3999-4010.

[43] Mizuno, T.; Wei, W.-H.; Eller, L.R.; Sessler, J.L. Phenanthroline complexes bearing fused dipyrrolylquinoxaline anion recognition sites: efficient fluoride anion receptors. *J. Am. Chem. Soc*., **2002**, *124*(7), 1134-1135.

[44] Anzenbacher Jr., P.; Tyson, D.S.; Jursikova, K.; Castellano, F.N. Luminescence lifetime-based sensor for cyanide and related anions. *J. Am. Chem. Soc.*, **2002**, *124*(22), 6232-6233.

[45] Plitt, P.; Gross, D. E.; Lynch, V.M.; Sessler, J.L. Dipyrrolyl-functionalized bipyridine-based anion receptors for emission-based selective detection of dihydrogen phosphate. *Chem. Eur. J.*, **2007**, *13*(5), 1374-1381.

[46] He, X.; Hu, S.; Liu, K.; Guo, Y.; Xu, J.; Shao, S. Oxidized bis(indolyl)methane: a simple and efficient chromogenic-sensing molecule based on the proton transfer signaling mode. *Org. Lett.*, **2006**, *8*(2), 333-336.

[47] Guo, L.; Wang, Q.-L.; Jiang, Q.-Q.; Jiang, Q.-J.; Jiang, Y.-B. Anion-triggered substituent-dependent conformational switching of salicylanilides. New hints for understanding the inhibitory mechanism of salicylanilides. *J. Org. Chem.*, **2007**, *72*(26), 9947-9953.

[48] Lindsell, P. Relationship between anion binding and anion permeability revealed by mutagenesis within the cystic fibrosis transmembrane conductance regulator chloride channel pore. *J. Physiol.*, **2001**, *531 (1)*, 51-66.

[49] Winstanley, K.J.; Smith, D.K. Ortho-substituted catechol derivatives: the effect of intramolecular hydrogen-bonding pathways on chloride anion recognition. *J. Org. Chem.*, **2007**, *72*(8), 2803-2815.

[50] Wang, T.; Bai, Y.; Ma, L.; Yan, X.-P. Synthesis and characterization of indolocarbazole-quinoxalines with flat rigid structure for sensing fluoride and acetate anions. *Org. Biomol. Chem.*, **2008**, *6*(10), 1751-1755.

[51] Sessler, J.L.; Cho, D.-G.; Lynch, V. Diindolylquinoxalines: effective indole-based receptors for phosphate anion. *J. Am. Chem. Soc.*, **2006**, *128*(51), 16518-16519.

[52] Chen, C.-Y.; Lin, T.-P.; Chen, C.-K.; Lin, S.-C.; Tseng, M.-C.; Wen, Y.-S.; Sun, S.-S. New chromogenic and fluorescent probes for anion detection: formation of a [2+2] supramolecular complex on addition of fluoride with positive homotropic cooperativity. *J. Org. Chem.*, **2008**, *73*(3), 900-911.

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