# The Anion Binding Properties Bearing Neutral Cycle Amine Recognition Sites
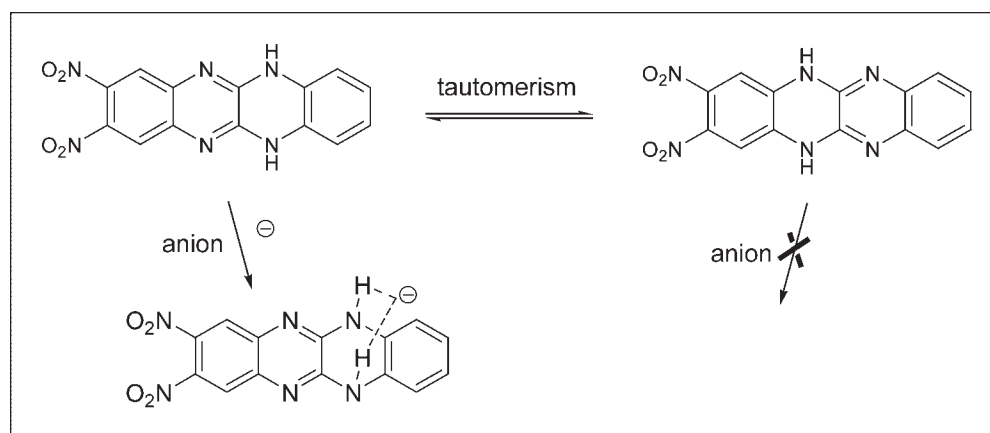
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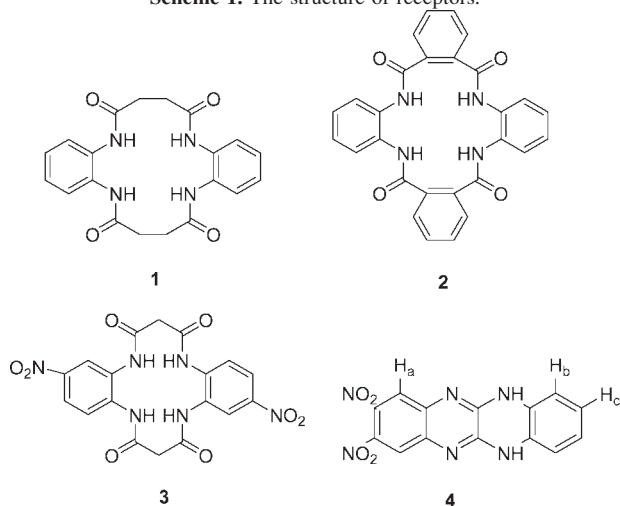*E-mail: xuefangshang@126.com

*O*-phenylene-diamine derivative containing colorimetric dinitroquinoxaline has been synthesized. Its UV-vis spectroscopy and ^{1}H NMR investigation reveal that the receptor shows the strong binding ability for AcO$^-$, F$^-$, and H$_2$PO$_4^-$, moderate binding abilities for OH$^-$ and almost no binding abilities for Cl$^-$, Br$^-$, and I$^-$. The interaction of the receptor with studied anions achieving the recognition of anions is proposed to come from the N—H...F and potential C—H...F hydrogen bonding in its neutral form. The results indicate that it is well suitable for the anion complexation, which is presumably contributed to its ring topology possessing a rigidity conjugation system. Moreover, the molecular orbital level of this receptor and its tautomer were further determined by means of theoretical investigations.

## INTRODUCTION

Host-guest systems for recognition of anionic guest species play an important role in the development of supramolecular chemistry [1]. The molecular recognition of anionic guests by synthetic hosts is an area of ever increasing research activity [2]. Study of anion receptors has special potential applications in the synthesis of anion sensors [3], membrane transmit carriers [4], and mimic enzyme catalysts, etc. [5,6]. Particularly there is a current interest in the synthesis of colorimetric neutral chemosensors for detection of anions. Synthetic nitrogen-based receptors designed for the selective binding of anions are usually either the positively charged ammonium salts, i.e., protonated polyamines and/or quaternary ammonium salts, or some of the neutral species, such as, amides, sulfonamides, pyrroles, ureas, and thioureas [7–9]. For example, in 1968, Park and Simmons [10] synthesized a series of dicyclopolyamines compounds and the results indicated that it is the protonated polyamines that interacted with anions. Lehn and co-workers [11–16] reported that during the interaction of

polyamines with anions, the polyamines were in the form of protonated polyamines too. However, the neutral amine receptors which can interact with various anions have not yet been reported, and even more for achieving the possibility of the naked-eye detection about the bonding of anions. In the previous work, we studied the recognition property of 16-membered or 14-membered amide macrocycle (Scheme 1, **1–3**) with various anions [17,18]. In this article, we synthesized and studied the anion binding abilities of six-membered cycle, a neutral diamine receptor containing dinitroquinoxaline (Scheme 1, **4**) in order to find the difference of anion binding ability between macro and microcycle. The anion recognition properties of receptor **4** with different anions (F$^-$, Cl$^-$, Br$^-$, I$^-$, AcO$^-$, H$_2$PO$_4^-$, and OH$^-$) has been studied by UV-vis and ^{1}H NMR experiment and the results indicate that the receptor shows higher binding abilities for AcO$^-$, F$^-$, and H$_2$PO$_4^-$ and the interaction of receptor **4** with various anions is in the form of a neutral diamine. This work is one of the progressive steps in pushing the development of an anion recognition method based upon the neutral amine recognition sites.

**Scheme 1.** The structure of receptors.



**Figure 1.** UV-vis spectrum of receptor **4** changes upon the addition of fluoride anion; [**4**] = $4.0 \times 10^{-5}$ mol/L, [F$^-$] = $0$–$160 \times 10^{-5}$ mol/L. Arrows indicate the direction of increasing anion concentration.

## RESULTS AND DISCUSSION

The interaction of receptor **4** with anions was investigated through the spectrophotometric titration by the addition of a standard dimethyl sulfoxide (DMSO) solution of the tetrabutyl ammonium salt (TBA) of the investigated anion to a DMSO solution of **4**.
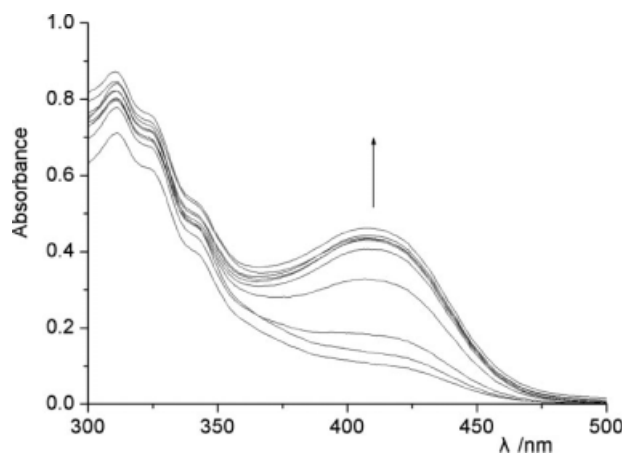
Figure 1 shows the changes in the absorption spectrum of receptor **4** observed upon the addition of fluoride anion. In the absence of anion, the spectrum of receptor **4** is characterized by the presence of one peak at 315 nm. The addition of fluoride anion results in the development of a new band at 409 nm, changing the
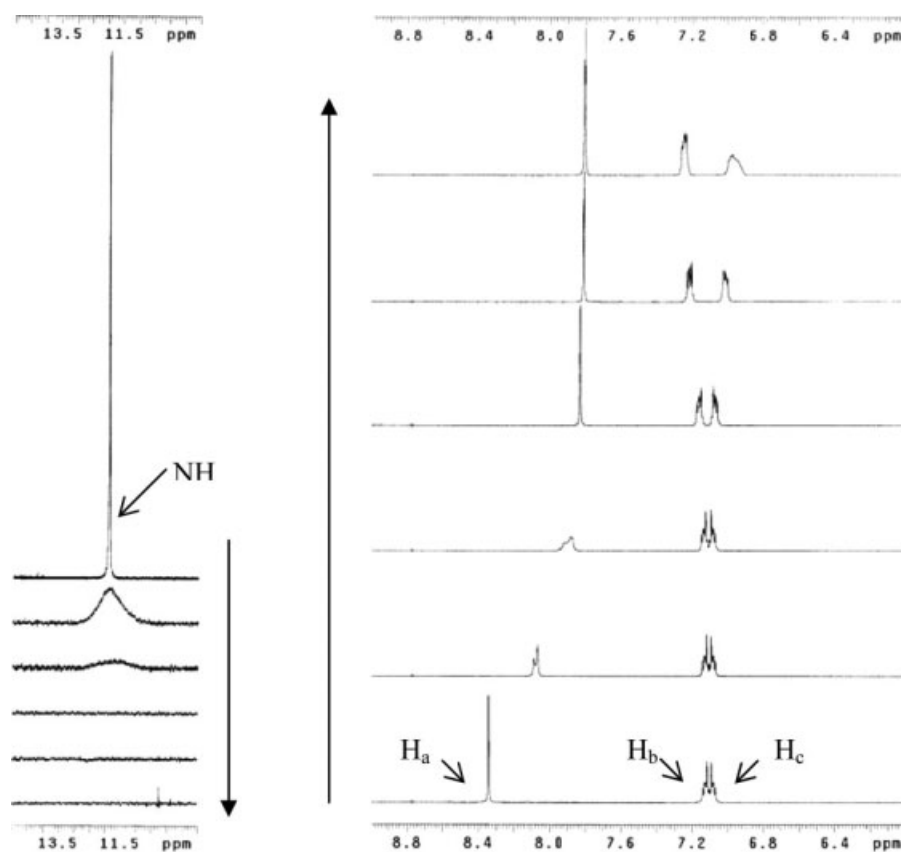


**Figure 2.** Plots of $^1$H NMR spectra of receptor **4** in DMSO-$d_6$ upon the addition of various quantities of Bu$_4$NF. The arrows' direction represent the additions of Bu$_4$NF are 0, 0.5, 1, 2, 5, 10 equiv., respectively.

**Table 1**

Affinity constants of receptor **4** with various anions.

| Anion | $K_s$ (M$^{-1}$) |
|---|---|
| AcO$^-$ | $(3.20 \pm 0.35) \times 10^4$ |
| F$^-$ | $(1.32 \pm 0.33) \times 10^4$ |
| H$_2$PO$_4^-$ | $(1.12 \pm 0.12) \times 10^4$ |
| OH$^-$ | $(2.99 \pm 0.41) \times 10^3$ |

color of the solution from colorless to pale-yellow. The addition of AcO$^-$, H$_2$PO$_4^-$, and OH$^-$, respectively, induces a similar color change. On the other hand, exposure to Cl$^-$, Br$^-$ or I$^-$, i.e., species that do not bind to receptor **4** appreciably, do not lead to any noticeable change in the solution color. This phenomenon makes this system an effective anion sensor under these solution conditions.

Very recently, a number of fluorogenic and/or chromogenic anion sensors comprising recognition moieties, such as, urea, thiourea, or amide have been reported to undergo an anion-induced deprotonation [19–21]. According to these reports, there appears one new triplet resonance at 16.1 ppm, the characteristic resonance of bifluoride (F—H—F) and the chemical shifts of noninteracted sites' proton signals occur up-field. To look into the anion binding properties of receptor for fluoride on anion recognition, $^1$H NMR titration experiments in DMSO-$d_6$ were performed (Fig. 2). From Figure 2, different patterns are observed in the titration ranges of 0–1 and 1–2 equiv. ranges. The NH signal (11.9 ppm) becomes broadened and the chemical shift of the phenyl signal $H_a$ upfield after the addition of 1 quantities of TBAF. During this process, the chemical shifts of $H_b$ and $H_c$ do not change. After the addition of 2 equiv of TBAF, the NH signal completely disappears and the shift of $H_a$ is stopped, only peak-shape change occur (from broad to sharp). The state of affairs can be accounted by hypothesizing that the first added fluoride anion establishes H-bonding interaction with the NH of receptor **4**. Due to the strong electron-withdrawing effect of NO$_2$, the shielding effect induced by H-bonding is more sensitive to $H_a$ than $H_b$ and $H_c$. Therefore, the signal of $H_a$ upfield and the signal of $H_b$, $H_c$ almost occurs no changes. On addition of 2 equiv. fluoride

anion, detailed analysis reveals the significant upfield shifts of $H_c$, except $H_b$, which exhibits a downfield shift from 7.1 to 7.3 ppm, indicating the formation of potential C—H…F H-bonding during the titration [22].

Job plots for receptor **4** at 298 K with anions as guest in DMSO solution show the maxima at a mole fraction of 0.5, which signifies that the host binds the anionic guest in a 1:1 ratio. Affinity constants of receptor **4** for anionic species are calculated according to the eq. (1), 1:1 host-guest complexation [23–25].

$$X = X_0 + 0.5\Delta\varepsilon\{c_H + c_G + 1/K_s \\ - [(c_H + c_G + 1/K_s)^2 - 4c_H c_G]^{1/2}\} \quad (1)$$

where $c_G$ and $c_H$ are the concentration of guest and host, respectively. $X$ is the intensity of absorbance at certain concentration of host and guest. $X_0$ is the intensity of absorbance of host when the anion is not added. $K_s$ is the affinity constant of host-guest complexation. $\Delta\varepsilon$ is the change in molar extinction coefficient.

Affinity constants of receptor **4** for anionic species are summarized in Table 1. The affinity constants of receptor with Cl$^-$, Br$^-$, and I$^-$ cannot be determined because the anions almost have no binding abilities with receptor. From Table 1, the anion affinity of receptor **4** is decreased in the order of AcO$^-$ > F$^-$ > H$_2$PO$_4^-$ > OH$^-$ >> Cl$^-$, Br$^-$, and I$^-$. Among the anions investigated, the highest affinity is observed with acetate. The reason may be that only the acetate matches perfectly with receptor **4** geometrically and thus has the highest affinity with receptor **4**.

As is well-known, neutral amines almost have no binding ability with anions. However, receptor **4** we synthesized has high affinity with some anions. We speculate that the electron density of diamine moieties is decreased due to the very strong electron-withdrawing effect of NO$_2$. Theoretical investigation on molecular orbital level using density functional theory at B3LYP/3-21G level with Gaussion03 program [26] can prove this (Fig. 3). In receptor **4**, the charges of the nitrogen atoms interacted with anion (N11, N12) are $-0.569624$ and $-0.569623$, respectively. The charges of N11 and N12 interacted with anions in non-containing NO$_2$



receptor 4                              5                              tautomerize
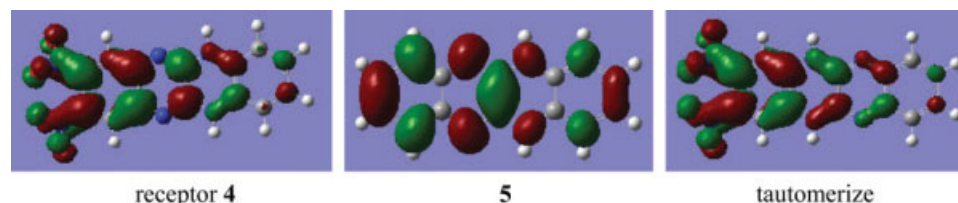
**Figure 3.** Molecular orbital level of receptor **4**, its tautomer and compound **5**. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]
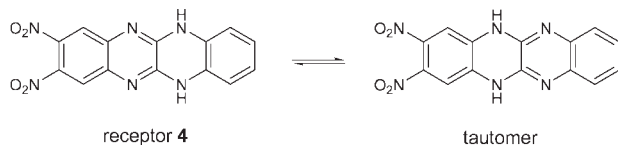
**Figure 4.** The structure of receptor **4** and tautomer.



**Scheme 2.** The synthesis route of **4**.

compound (**5**) are both −0.581427. The stronger the binding ability, the smaller the charge of N11 and N12. Thus, the ability of forming the hydrogen bond between diamine and anion is appeared in receptor **4**. In addition, receptor **4** exists as tautomer (Fig. 4). Whether does receptor **4** or its tautomer interact with various anions? The molecular orbital level of its tautomer was optimized (Fig. 3). The charges of N11 and N12 in tautomer are both −0.655013. Therefore, receptor **4** may interact with anions rather than its tautomer.

These results enable us to assume that the binding of anion with diamine moieties will induce a spectral change in the complex (Fig. 5). From Figure 5, the difference in spacer units are responsible for the anion selectivity. Fluoride anion, a spherical ion, interacts with diamines through the H-bonding. Both of the two oxygen atoms of acetate anion, forming a ''Y'' configuration, probably interact with diamines through two H-bonding. The affinity constant of acetate anion is higher than that of fluoride anion due to the ''Y'' configuration, acetate anion, is better matched with receptor than spherical configuration, fluoride anion in space. Therefore, the affinity constant is related on the matched degree between receptor and anion. Here, it should be pointed out that the proposed binding mode in Figure 5 as drown is planar structure and does not present its geometry. According to optimized results, the geometry of receptor **4** is planar. It may change under the inducement of anions, especially the NH ring may distort [27].

However, the selectivity between AcO⁻ and F⁻ is unfortunately not large enough for any practical application purpose. The selectivity is probably also influenced by the size complementarity between anions and cavity.
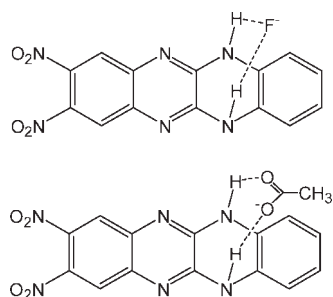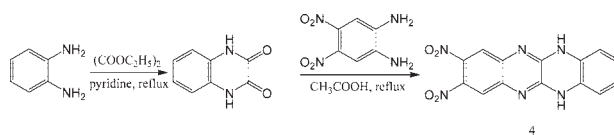
In previous papers, 16-membered and 14-membered amide macrocycle (receptor **1**-**3**) show high selectivity for certain anion. So, we may be further modify the receptor by tuning the size of the ring in receptor **4** (for example, altered to a 16-membered or a 18-membered ring, etc.) in order to find a receptor containing amine recognition site that fits well for AcO⁻, F⁻, or other anions geometrically.

## CONCLUSION

In summary, we have synthesized a neutral cyclic diamine containing phenyl ring and colorimetric dinitroquinoxaline. The UV-vis titration and ^{1}H NMR experiments indicate that receptor **4** shows the strong affinity for AcO⁻, F⁻, and $H_2PO_4^-$, moderate affinities for OH⁻, and almost no affinities for Cl⁻, Br⁻, and I⁻. Moreover, the interaction of the synthetic receptor with F⁻, AcO⁻, $H_2PO_4^-$, and OH⁻ results in a visible change of color, and the receptor can thus be used as a colorimetric sensor. Receptor **4** interacts with various anions in the form of a neutral diamine, not protonated polyamines. In addition, we found that the selectivity of six-membered amine cycle (**4**) is not better than that of 16- or 14-membered amide cycle (**1**–**3**). In addition, theoretical investigations show that receptor **4** may interact with anions rather than its tautomer.

This work is one of the progressive steps in pushing the development of an anion recognition method based upon the neutral amine recognition site. Further studies on this line are in progress.



**Figure 5.** A proposed hydrogen bond configuration formed between receptor **4** and anions.

## EXPERIMENTAL

Most of the starting materials were obtained commercially and all reagents and solvents used were of analytical grade. All anions, in the form of TBAs, were purchased from Sigma-Aldrich Chemical Co., stored in a desiccator under vacuum containing self-indicating silica, and used without any further purification. DMSO was distilled *in vacuo* after dried with $CaH_2$. Tetra-*n*-butylammonium salts (such as (*n*-$C_4H_9$)₄NF, (*n*-$C_4H_9$)₄NCl, (*n*-$C_4H_9$)₄NBr, (*n*-$C_4H_9$)₄NI, (*n*-$C_4H_9$)₄NAcO, (*n*-$C_4H_9$)₄NH₂PO₄, and (*n*-$C_4H_9$)₄NOH) were dried for 24 h in vacuum with $P_2O_5$ at 333 K before use. C, H, and N elemental analyses were made on Vanio-EL. ^{1}H NMR spectra were recorded on a Varian UNITY Plus-400 MHz Spectrometer. FAB-MS was made on VG ZAB-HS. UV-vis spectroscopy titrations were made on Shimadzu UV2450 spectrophotometer.

*N,N′*-(*o*-phenylene)-6,7-dinitro-2,3-diamino-quinoxaline (**4**) was synthesized according to the route shown in Scheme 2.

**1,4-Quinoxaline-2,3-dione [28].** *o*-diaminebenzene (10.8 g, 0.1 mol), diethyl oxalate (13.5 mL, 0.1 mol), and pyridine (200 mL) were added in 250 mL three-neck. The mixture refluxed with $N_2$ for 72 h. After cooled, the mixture was filtrated and we obtained colorless solid. The solid was washed with ethanol, ether, and dried in vacuum. Yield 61.3%. ^{1}H NMR (400 MHz DMSO-$d_6$) δ 11.9 (s, 2H), 7.1 (m, 4H). Anal. Calcd. for $C_8H_6N_2O_2$: C, 59.26; H, 3.73; N, 17.28; Found: C, 59.73; H 3.58; N, 17.67. FAB-MS (*m/z*): 163 $(M + H)^+$.

**N,N′-(*o*-Phenylene)-6,7-dinitro-2,3-diamino-quinoxaline (4).** 1,4-quinoxaline-2,3-dione (2.5 mmol, 0.81 g), 4,5-dinitro-*o*-diaminebenzene (2.5 mmol, 0.49 g), and acetic acid (100 mL) were refluxed for 12 h. After cooled, the mixture was filtrated and we obtained brown solid. The solid was washed with water, ethanol, and recrystallized, respectively, from acetic acid and dried in vacuum. Yield 84.8%. ^{1}H NMR (400 MHz DMSO-$d_6$) δ 11.9 (s, 2H), 8.3 (s, 2H), 7.1 (m, 4H). Anal. Calcd. for $C_{28}H_{16}N_{12}O_8$·$2CH_3COOH$: C, 50.01; H, 3.15; N, 21.87; Found: C, 49.73; H, 3.58; N, 21.77.

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