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Recognition of Carboxylate Anions and Carboxylic Acids by Selenium-Based New Chromogenic Fluorescent Sensor: A Remarkable Fluorescence Enhancement of Hindered Carboxylates

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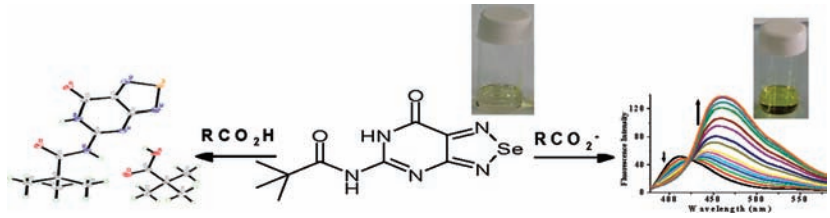
ABSTRACT



A selenium metal-based new fluorescence sensor 5-pivaloylamino-1,2,5-selenodiazolo[3,4-*d*]pyrimidin-7-(6*H*)-one (receptor 1) has been reported for the recognition of monocarboxylic acids and carboxylate anions both by UV−vis and fluorescence methods. Receptor 1 recognizes carboxylate anions more than monocarboxylic acids and it is a selective sensor for carboxylates with specially hindered carboxylate anions. The changes of fluorescence intensity are remarkably enhanced with red shift in presence of bulky carboxylate anions. The X-ray crystal structure of receptor 1 with pivalic acid has been reported.

Molecular recognition[1] involving noncovalent interactions between the functional groups of host−guest molecules is the main dynamic force for development of supramolecular chemistry and related disciplines.[2] Recognition of carboxylate anions and carboxylic acids by synthetic receptors is one of most important research sectors due to the biological importance and the huge application in pharmaceutical science.[3] In recent years, development of a sensor for recognition and sensing of a particular anion over broad range of anions and other guests has been an important molecular

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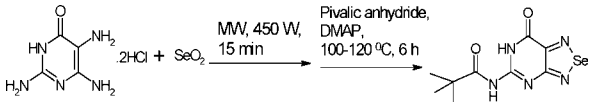
recognition research.[4] The recognition of anions is based on electrochemical changes in redox potential, chemical shift in ^{1}H NMR, fluorescence change, and change in color.[5,6]

Selenium-containing heterocyclic compounds have been widely synthesized[7] for their medicinal applications such as antiviral, antihypertensive, and fungicidal properties, and these are also potent cancer chemopreventive and chemotherapeutic agents.[8] Selenium is the trace element controlled by genes in the human body.[9]

Various metal complexes of 2,1,3-benzoselenadiazole (BS) have been synthesized, and these are an interesting area in recent coordination chemistry.[10] In this paper, we report the development of a new seleniumbased chromogenic fluorescent sensor 5-pivaloylamino-1,2,5-selenodiazolo[3,4-*d*]pyrimidin-7-(6*H*)-one (2-pivaloyamino-6-selenoguanine) having a bulky pivaloyl group in the binding site for studying the change in recognition behavior from monocarboxylic acids to carboxylate anions.

The receptor **1** was synthesized in the solid phase simply by irradiation of a mixture of 2,5,6-triamino-3*H*-pyrimidin-4-one dihydrochloride with selenium dioxide in a microwave oven. After pivaloylation with pivalic anhydride, receptor **1** has been obtained (Scheme 1) (Supporting Information). The

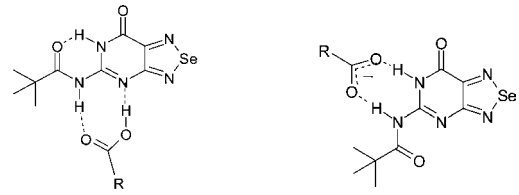
Scheme 1. Synthesis of Receptor **1**



compound was characterized by spectral analysis (Figures S1−S3, Supporting Information), and the single crystal X-ray structure of receptor **1** with pivalic acid has been reported.

The receptor **1** has one donor−acceptor array for binding monocarboxylic acid since receptor **1** mainly exists in the form **I** in which the lactam N*H* proton of pyrimidine moiety makes a strong intramolecular hydrogen bond with amide C═O (another donor−acceptor array), whereas in the presence of carboxylate guests the intramolecular hydrogen bonding has been destroyed and the flexible amide proton is available in the same direction with lactam N*H* for recognition of carboxylate (form **II**). This conformational change of receptor **1** has been observed by comparing the UV−vis and fluorescence behavior of both carboxylic acids and carboxylate anions (Scheme 2).

Scheme 2. Mode of Binding of Receptor **1** to (I) a Carboxylic Acid Moiety and (II) the Carboxylate Moiety



I **II**

The binding behavior of receptor **1** was observed both by UV−vis and fluorescence methods in chloroform solution.[11] The absorption spectra of receptor **1** (1.00×10^{-4} mL^{-1}) appeared at λ_{max} 356 nm. The absorption intensity decreases upon gradual addition of carboxylic acid solution ($\sim 10^{-3}$ mL^{-1}). However, during titration of receptor **1** with carboxylate anions the absorption intensity gradually decreases at 356 nm with concomitant increasing intensity at 304 and 396 nm (bathochromic shift by 40 nm) (Figure 1) (Figures S8 and S9, Supporting Information). The decrease in the absorption maxima is more in adamantane-1-carboxylate and pivalate rather than acetate and phenyl acetate (Figure 2). Two isosbestic points were observed at 320 and 326 nm which indicate that carboxylate anions strongly bind the two protons of receptor **1** by breaking the intramolecular hydrogen bonding between pivaloyl amide C═O and lactam N*H* (Scheme 2). The

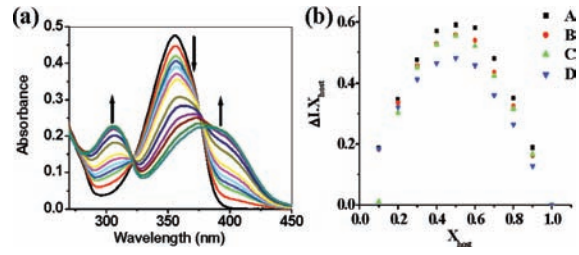


Figure 1. (a) Change of absorption spectra of receptor **1** upon addition of tetrabutylammonium pivalate in chloroform. (b) Job plots (absorbance at 356 nm) determined by UV−vis method: (A) adamantane-1-carboxylate; (B) pivalate; (C) acetate; (D) phenyl acetate.

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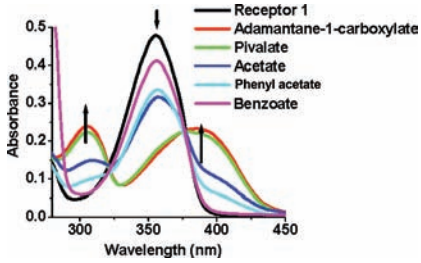

Figure 2. Change of absorption spectra of receptor **1** upon addition of different tetrabutylammonium carboxylate salts (8 equiv) in chloroform.

association constant of receptor is higher with carboxylate anions rather than monocarboxylic acid. Job plots indicate 1:1 complexation between host−guest since receptor and carboxylate complex concentration goes maxima where molar fraction of receptor is about 0.5 (Figure 1).

The red shift in absorption maxima upon addition of carboxylate anions toward visible region is also confirmed by the color change visible to the naked eye (Figure 3). The

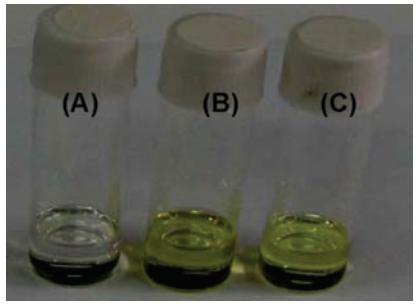

Figure 3. Change in color of receptor **1** (20 μM) (A) upon addition of 2 equiv of adamantane-1-carboxylate (B) and acetate (C) in chloroform.

receptor turns yellow in the presence of carboxylate anions. The intensity of the color is much lower for acetate and phenyl acetate, whereas the color becomes deeper in the case of pivalate and adamantane-1-carboxylate. The color change is not observed in the presence of guest acids or other anions.

Fluorescence titrations are performed to study the binding behavior and the sensing selectivity of receptor **1** with different guests. The fluorescence emission spectrum of receptor **1** (1.87×10^{-4} mL^{-1}) shows a broad peak at 412 nm when it is excited at 356 nm (excited slit width 14 nm, emission slit width 12 nm) (Figure S10, Supporting Information). The fluorescence intensity does not change upon gradual addition of monocarboxylic acids, although upon addition of carboxylate anions the fluorescence intensity gradually undergoes quenching at 412 nm with an increase in the emission maxima toward longer wavelength and making a bathochromic shift (about 47 nm) (Figure 4). The

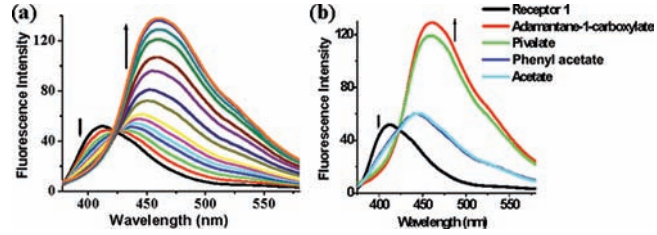

Figure 4. (a) Change of emission for receptor **1** in the presence of increasing amounts of adamantane-1-carboxylate in $CHCl_3$. (b) Change of fluorescence intensity of receptor **1** upon addition of different tetrabutylammonium carboxylates (8 equiv) with excitation at 356 nm.

enhancement of emission intensity observed at 459 nm is higher for adamantane-1-carboxylate and pivalate compared to acetate and phenyl acetate. We have also performed the fluorescence studies with other anions such as F^-, Cl^-, Br^-, and I^-, but in all these cases, the change of emission intensity is irregular and minor. The binding constants are determined both by UV−vis and fluorescence methods and summarized in Table 1. Hence, receptor **1** can be useful as a selective

Table 1. Binding Constant (K_a) Values of Receptor **1** with Guests

guests	K_a (M^{-1}) in UV−vis method	K_a (M^{-1}) in fluorescence method
acetic acid	$(8.87 \pm 0.9) \times 10^2$	[a]
pivalic acid	$(7.55 \pm 0.4) \times 10^2$	[a]
adamantane-1-carboxylic acid	$(1.22 \pm 0.3) \times 10^3$	[a]
phenylacetic acid	$(5.46 \pm 0.4) \times 10^2$	[a]
acetate	$(1.27 \pm 0.6) \times 10^3$	$(3.24 \pm 0.3) \times 10^3$
pivalate	$(1.56 \pm 0.1) \times 10^3$	$(4.35 \pm 0.2) \times 10^3$
adamantane-1-carboxylate	$(2.34 \pm 0.2) \times 10^3$	$(5.21 \pm 0.4) \times 10^3$
phenyl acetate	$(2.54 \pm 0.8) \times 10^2$	$(8.20 \pm 0.5) \times 10^2$
benzoate	$(1.25 \pm 0.7) \times 10^2$	[a]

[a] No change.

fluorescence sensor for detecting carboxylate anions over the wide range of other interfering anions and carboxylic acids.

To evaluate the binding behavior of receptor **1** with carboxylates and carboxylic acids, we carried out the ^{1}H NMR study adding with equivalent amounts of guests. In receptor **1**, the lactam N−H proton (12.03 ppm) makes a strong intramolecular hydrogen bonding with C═O of amide

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linkage, and this proton is shifted downfield ($\Delta\delta = 0.5$ ppm) in presence of guest acids. The amide N−H proton of receptor **1** itself appears at 8.54 ppm, and the downfield chemical shift of receptor **1** is $\Delta\delta = 1.59$ ppm in the presence of an equivalent amount of pivalic acid. The downfield chemical shift of amide proton in receptor **1** is $\Delta\delta = 1.47$ ppm on addition of an equivalent amount of acetic acid. Interestingly, the peaks of two amide protons of receptor **1** are not observed in NMR due to deprotonation in presence of an equivalent amount of tetrabutylammonium adamantane-1-carboxylate (Figures S4−S7, Supporting Information), which points out that carboxylate recognizes receptor **1** in form **II** binding mode (Scheme 2).

The recognition pattern of receptor **1** with pivalic acid is observed by growing single crystals and analysis of the X-ray crystal structure (CCDC No. 740531).[12] Although guest pivalic acid is liquid and hindered, the solid 1:1 complex is crystallized out in the space group *P*-1 (Tables 1 and 2, Supporting Information). The N2−C1and N3−C2 bond distances of receptor **1** are 1.3183(13) and 1.3137(12) Å, respectively, and show the double bond characters like N1−C4 bond [1.3093(12) Å]. The C1−C2 bond distance at 1.4419(12) Å exhibits almost single-bond character. The Se1−N2 and Se1−N3 bond distances are 1.8077(7) and 1.7969(9) Å, respectively (Figure 5).

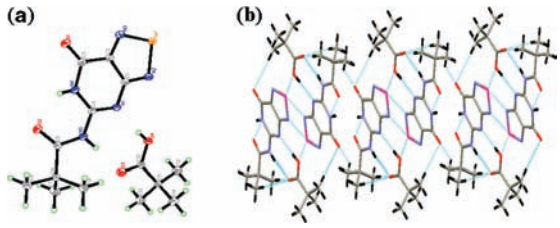

Figure 5. (a) ORTEP diagram (50% probability) of complex of receptor **1** with pivalic acid; (b) two-dimensional polymeric crystal structure viewed down crystallographic *a* axis. Hydrogen bonds are shown as dashed lines.

The receptor has multiple sites of donor−acceptor array. In the solid state, the 1:1 complex is formed by an eight-membered cyclic hydrogen-bonding network between host and guest [O4−H1···N1, 2.7257(11) Å; N5−H1···O3, 2.8966(11) Å].[13] The receptor itself makes a strong intramolecular six-membered hydrogen-bonding network [N4−H1···O2, 2.6313(11) Å]. The two asymmetric units make a chairlike supramolecular view by C−H···O interaction [C12−H12A···O1, 3.5175(14) Å] between the "H" atom of pivalyl methyl group of guest and the lactam "O" atom of receptor **1** (Figure S11, Supporting Information). The polymeric chain is elongated by another C−H···O secondary interactions [C9−H9A···O1, 3.3030(13) Å] to form a nice supramolecular architecture (Figure 5). Two receptor molecules are linked by two *anti* parallel Se−N intermolecular secondary nonbonding interactions (2.82 Å).[14]

Thus, it has been observed that the receptor **1** recognizes carboxylate anions more compared to carboxylic acids by changing its mode of binding sites. Both small and hindered carboxylate anions are recognized by this receptor, but the binding affinity is better toward hindered carboxylate anions. Receptor **1** thus developed as a successful fluorescence sensor for distinguished carboxylate anions from carboxylic acids and other anions due to its high selectivity toward hindered carboxylate anions. Also, interestingly, receptor **1** having hindered pivaloylamino group binds with hindered pivalic acid without fluorescence change in a different binding motif (I) as proved by the X-ray crystal structure of receptor with pivalic acid.

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Supporting Information Available: Synthetic procedures, spectroscopic data, supplementary spectral data, and crystal data. This material is available free of charge via the Internet at http://pubs.acs.org.

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