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Synthesis of colorimetric receptors for dicarboxylate anions: a unique color change for malonate

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Abstract—Three new chromogenic receptors (**1**, **2**, and **3**) containing *p*-nitrophenyl or *p*-nitronaphthyl or methyl groups appended to the thiourea groups were synthesized and characterized. Upon addition of a series of dicarboxylate anions to receptor **1** in DMSO, only the appearance of the solution of receptor **1** with malonate showed a color change from blue to yellow which can be detected by the naked eye at parts per million. With the addition of the series of dicarboxylate anions to receptor **2**, the solutions showed an indistinct intense dark-red color. Whereas the addition of the same dicarboxylate anions to receptor **3**, the solutions did not induce any color change. Thus, for the unique color change, the receptor **1** can act as an optical chemosensor for the malonate anion even in the presence of other dicarboxylate anions.

The design and synthesis of sensitive chromogenic receptors for detecting biologically important anions and monitoring environmentally harmful anion pollutants have attracted considerable attention in the field of supramolecular chemistry.[1] Particularly, dicarboxylates play an important role in chemical and biological processes. Dicarboxylates are critical components of numerous metabolic processes including, for instance, the citric acid and glyoxylate cycles.[2] They also play an important role in the generation of high-energy phosphate bonds and in the biosynthesis of important intermediates.[3] To date, several receptors containing different functional groups for selective binding of dicarboxylate anions have been reported.[4,5] However, to our best knowledge, chromogenic sensors selecting recognizing dicarboxylate anions are still limited.[5] Herein, we report the synthesis and binding properties of three new chromogenic receptors (**1**, **2**, and **3**) containing *p*-nitrophenyl or *p*-nitronaphthyl or methyl groups appended to the thiourea groups. The anionic recognition of receptors has been investigated by UV–vis absorption and ^{1}H NMR spectroscopy.

The receptors **1**–**3** were synthesized by the reaction of *p*-nitrophenylisothiocyanate or *p*-nitronaphthylisothiocyanate or methylisothiocyanate with 1,4-di-(2-aminoethylamino)-anthraquinone (**4**) in high yields (Scheme 1).[6,7] All of these compounds were characterized by ^{1}H NMR, IR, and HRMS.

The colorimetric sensing ability of the receptors **1**–**3** with a series of dicarboxylate anions [$^-O_2C(CH_2)_nCO_2^-$] such as malonate, succinate, glutarate, adipate ($n = 1, 2, 3, 4$), terephthalate and isophthalate in DMSO was monitored by UV–vis absorption and by 'naked eye' observation. The anions were added as tetrabutylammonium salts to the DMSO solutions of the receptors **1**–**3** (5×10^{-5} M). Figure 1 shows that the UV–vis absorption spectra of a mixture of receptor **1** with different concentrations of malonate in DMSO. When increasing the concentration of malonate, a new absorption band at 480 nm was gradually enhanced, while the intensity of absorption at 362 nm was decreased correspondingly. The color of the solution of receptor **1** was changed from blue to yellow, which could be easily observed by the naked-eyes. A clear isobestic point was observed at 393 nm. This result demonstrates that a complex formation of **1** with malonate anion is taking place via hydrogen bonding electrostatic interactions. The formation of these hydrogen bonds affects the electronic properties of the chromophore, resulting in a color change with a subsequent new charge-transfer interaction between the malonate-bound thiourea and electron deficient 4-nitrophenyl group.[8] Judging from the titrations, the strong binding of malonate allowed the Job's plot method[9] (as shown in the inset of Fig. 1) to be used in the

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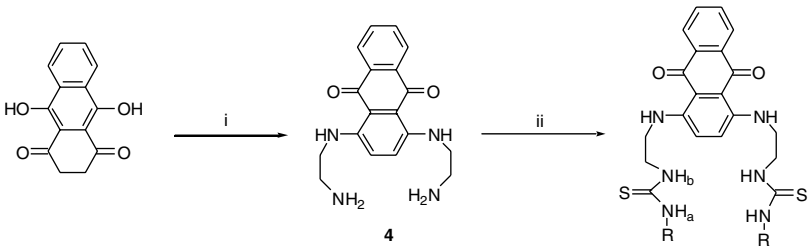

1. R = p-NO_2-phenyl (Yield : 81%)

2. R = p-NO_2-naphthyl (Yield : 91%)

3. R = methyl (Yield : 69%)

Scheme 1. Reagents and conditions: (i) ethylenediamine, THF, 50 °C, 2 h, 37.2%; (ii) *R*-isothiocyanate, THF, reflux, 18 h.

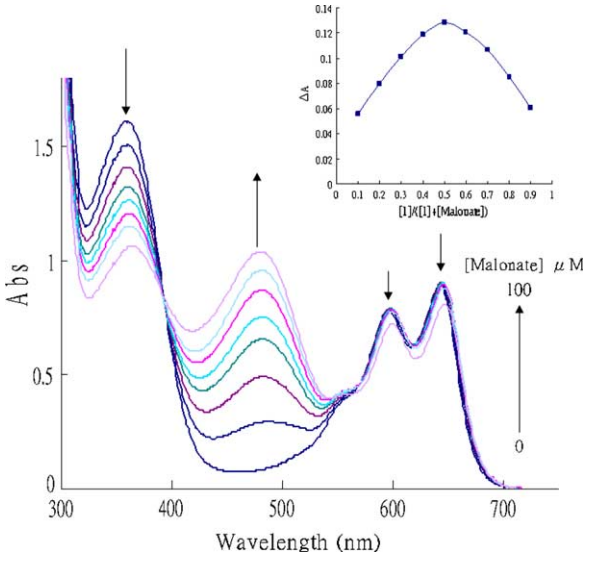

Figure 1. A family of spectra taken in the course of the titration of a 5×10^{-5} M DMSO solution in **1** with a standard solution of malonate at 25 °C titration profiles (insert) indicate the formation of a 1:1 complex.

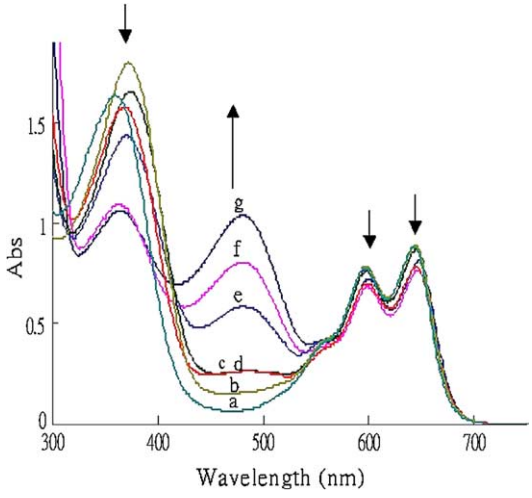

Figure 2. UV–vis changes of **1** operated in DMSO (5×10^{-5} M) after the addition of 2 equiv of anion: (a) **1** only, (b) **1** + isophthalate, (c) **1** + terephthalate, (d) **1** + adipate, (e) **1** + glutarate, (f) **1** + succinate, (g) **1** + malonate.

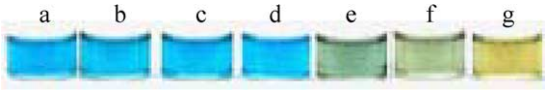

Figure 3. Effect of anions (as $(C_4H_9)N^+$ salt) on color changes of **1** in DMSO: (a) **1** only, (b) **1** + isophthalate, (c) **1** + terephthalate, (d) **1** + adipate, (e) **1** + glutarate, (f) **1** + succinate, (g) **1** + malonate.

determination of the binding stoichiometry, which was found to be a 1:1 host-to-anion complexation.

Parallel investigations were carried out with a series of other dicarboxylate anions (succinate, glutarate, adipate, terephthalate, and isophthalate). A similar phenomena of UV–vis absorptions are observed in Figure 2. Spectrum (a) was measured in the absence of anions where **1** has a UV–vis spectrum with λ_{max} at 396, 596, and 643 nm. As shown in spectrum (b)–(d), **1** exhibits negligible perturbations upon addition of 2 equiv of isophthalate, terephthalate, and adipate anions, respectively. By contrast, significant changes are observed in the presence of glutarate as well as other anions such as succinate and malonate anions. As shown in spectra (e)–(g), the CT absorption bands appear at 480 nm and the solution color changes from blue to yellow color (Fig. 3). Interestingly, the colors of (e) and (f) stay consistently even at higher concentrations of glutarate or succinate. It is apparent that **1** has a unique color change and higher selectivity for malonate anion than other anions. The selectivity of **1** for recognition of these anions can be rationalized on the basis of the chain length of the anionic species. The original blue color in the host solution might be ascribed to the chromophore of 1,4-diaminoanthraquinone moiety. The yellow color (new absorption peak at 480 nm) could be explained by the charge-transfer interactions between the electron-rich donor nitrogen of the thiourea units and the electron-deficient *p*-nitrophenyl moieties. The receptor bound anions, hydrogen bonds were constructed to form stable complexes, and the electron density in the

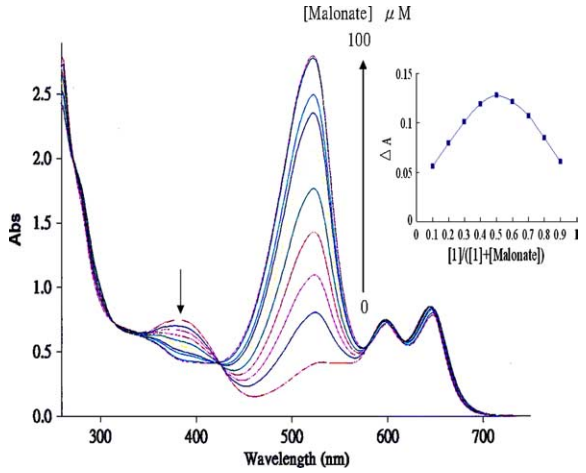

Figure 4. A family of spectra taken in the course of the titration of a 5×10^{-5} M DMSO solution in **2** with a standard solution of malonate at 25 °C titration profiles (insert) indicate the formation of a 1:1 complex.

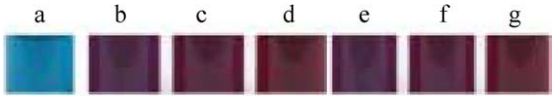

Figure 5. Effect of anions (as $(C_4H_9)N^+$ salt) on color changes of **2** in DMSO: (a) **2** only, (b) **2** + isophthalate, (c) **2** + terephthalate, (d) **2** + adipate, (e) **2** + glutarate, (f) **2** + succinate, (g) **2** + malonate.

supramolecular system was much increased to enhance the charge-transfer interactions between the electron-rich and electron-deficient moieties, which resulted in a visible color change.[10]

The UV–vis absorption spectral interactions of receptor **2** with malonate anion were studied by gradual addition of different concentrations of malonate anion to a solution of receptor **2** and results are shown as Figure 4. The initial absorption peak at 384 nm was gradually decreased and a new absorption band appeared with a maximum absorption at 523 nm. The color of the solution of receptor **2** with malonate was changed from blue to dark-red. The color change can be attributed to the appearance of a new long wavelength peak. This result demonstrates that the receptor **2** formed complex with malonate. Similarly, a dark-red color can be observed while adding other dicarboxylate anions into the solution of **2** in DMSO, but the color changes were not distinct (Fig. 5). Judging from the titrations, the Job's plot method (as shown in the inset of Fig. 4) proved the formation of a 1:1 stoichiometry complex of **2** with malonate. The association constants were calculated by the Benesi–Hildebrand equation[9] and listed in Table 1. The data showed that receptor **1** has higher selectivity for malonate than other dicarboxylate anions.

In order to gain a clear picture of how *p*-nitrophenyl or *p*-nitronaphthyl unit affects the chromogenic property of **1** or **2**, a UV–vis study was conducted on the control compound **3**. In contrast to both **1** and **2**, **3** showed two absorption bands at 596 and 643 nm in DMSO. Upon gradual increase of the concentration of malonate, the peaks at 596 and 643 nm were gradually decreased and no color change was observed. The Job's plot of malonate in DMSO showed a 1:1 binding stoichiometry, and the association constant was calculated as 1.54×10^3 M^{-1} which is smaller than that for receptor **1** or **2**. Based on the above results, the receptor **1** provides a suitable chromophore and a binding site for malonate anion.

^{1}H NMR spectroscopy is of immense value in the understanding of receptor–substrate interaction and is capable of providing a revealing picture of the details of the interaction between receptor and dicarboxylate anions. Addition of 1 equiv of the tetrabutylammonium salts of malonate to **1** or **2** in DMSO-d_6 caused remarkable downfield shifts of the NH resonances in the ^{1}H NMR. In the case of **1** with malonate, the proton chemical shifts of thiourea (H_a, H_b) changed from 10.26 to 11.00 ($\Delta\delta = 0.74$ ppm), 8.51 to 8.95 ($\Delta\delta = 0.44$ ppm), respectively (Fig. 6). These larger downfield shifts indicate the formation of two hydrogen bondings between H_a, H_b and malonate. These results show that receptor **1** and malonate form a 1:1 stoichiometry complex via

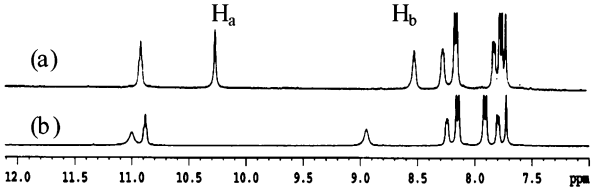

Figure 6. Partial ^{1}H NMR (400 MHz) spectra of sensor **1** (10 mM) in DMSO-d_6 at rt in: (a) sensor **1** only, (b) **1** + 1.0 equiv tetrabutylammonium malonate.

Table 1. Association constants K_a (M^{-1}) of receptors **1** and **2** with guest anions

Anion	Receptor **1** K (M^{-1})[a]	R[b]	Receptor **2** K (M^{-1})[a]	R[b]
Malonate[c]	$(1.39 \pm 0.03) \times 10^4$	0.9937	$(1.42 \pm 0.02) \times 10^4$	0.9967
Succinate[c]	$(1.00 \pm 0.03) \times 10^4$	0.9924	$(1.38 \pm 0.03) \times 10^4$	0.9904
Glutarate[c]	$(6.22 \pm 0.29) \times 10^3$	0.9957	$(1.20 \pm 0.02) \times 10^4$	0.9976
Adipate[c]	$(3.38 \pm 0.29) \times 10^3$	0.9961	$(1.02 \pm 0.01) \times 10^4$	0.9011
Terepthalate[c]	$(3.21 \pm 0.10) \times 10^3$	0.9967	$(1.17 \pm 0.03) \times 10^4$	0.9919
Isophthalate[c]	$(1.60 \pm 0.29) \times 10^3$	0.9901	$(1.13 \pm 0.01) \times 10^4$	0.9973

[a] The data were calculated from UV–vis titration in DMSO.
[b] The data values of R were obtained by the results of nonlinear curve fitting.
[c] The anions were used as their tetrabutylammonium salts.

hydrogen-bonding interaction between the thiourea with carboxyl groups.

In conclusion, the new colorimetric anion receptors **1**, **2**, and **3** were synthesized in high yields and can form 1:1 complex with dicarboxylate anions by multiple hydrogen bonding interactions. Among them, only the receptor **1** has higher selectivity for the malonate and there is a distinct color change that can be observed by the naked-eyes. Thus, the receptor **1** can act as an optical chemosensor for the malonate anion even in the presence of other dicarboxylate anions.

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2005.12.009.

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6. Data for **1**: Yield 81%. Mp 213–214 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.74–3.76 (m, 8H), 7.71 (s, 2H), 7.75–7.77 (m, 4H), 7.80–7.82 (m, 2H), 8.14–8.16 (m, 4H), 8.25–8.27 (m, 2H), 8.49 (br s, 2H), 10.24 (br s, 2H), 10.90 (br s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 40.6, 44.1, 109.0, 120.9, 124.7, 125.9, 132.6, 134.0, 142.1, 146.2, 146.3, 180.7, 181.1. IR (KBr): $\nu = 3329$, 3067, 2933, 2858, 2356, 2335, 1639, 1598, 1511, 1326 cm^{-1}. UV (DMSO): 362 nm ($\varepsilon = 3504$), 596 nm ($\varepsilon = 9370$), 643 nm ($\varepsilon = 8635$). HRMS (FAB): calcd for $C_{32}H_{28}N_8O_6S_2$ [M$^+$] 684.1576; found 684.1584. Compound **2**: Yield 91%. Mp 206–207 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.72–3.75 (m, 8H), 7.67–7.69 (m, 4H), 7.76–7.83 (m, 6H), 8.10 (d, $J = 8.4$ Hz, 2H), 8.26–8.31 (m, 6H), 8.41 (d, $J = 8.4$ Hz, 2H), 10.13 (br s, 2H), 10.92 (br s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 30.9, 40.8, 44.3, 108.9, 122.4, 122.9, 123.9, 124.8, 125.6, 125.9, 127.7, 129.5, 130.0, 132.7, 134.0, 141.0, 143.4, 146.4, 181.1, 182.2. IR (KBr): $\nu = 3293$, 3068, 2930, 2853, 2330, 1639, 1568, 1506, 1311, 1265, 1168, 1045, 1025, 830 cm^{-1}. UV (DMSO): 382 nm ($\varepsilon = 2510$), 532 nm ($\varepsilon = 7493$), 597 nm ($\varepsilon = 2662$), 644 nm ($\varepsilon = 1442$). HRMS(FAB): calcd for $C_{40}H_{32}N_8O_6S_2$ [M$^+$] 784.1890; found 784.1891. Compound **3**: Yield 69%. Mp 219–220 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.66–2.81 (m, 6H), 3.63 (s, 8H), 7.57–7.65 (m, 6H), 7.78–7.80 (m, 2H), 8.23–8.25 (m, 2H), 10.89 (br s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 41.3, 108.8, 124.9, 125.9, 132.6, 134.1, 146.4, 181.0. IR (KBr): $\nu = 3477$, 3313, 3067, 2934, 1634, 1567, 1501 cm^{-1}. UV (DMSO): 596 nm ($\varepsilon = 5400$), 644 nm ($\varepsilon = 3715$). HRMS(FAB): calcd for $C_{22}H_{26}N_6O_2S_2$ [M$^+$] 470.3396; found 470.1533.
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