Synthesis of Indeno[2′,1′:5,6]pyrido[2,3-*d*]pyrimidine Derivatives and Their Recognition Properties as New Type Anion Receptors

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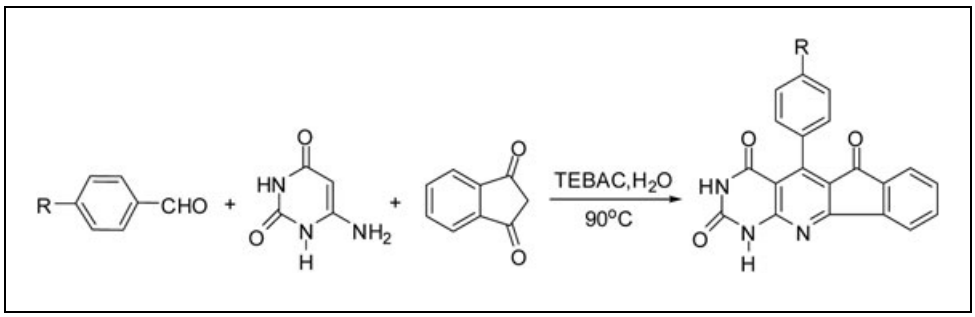

A new type anion receptors containing indeno[2′,1′:5,6]pyrido[2,3-*d*]pyrimidine have been synthesized *via* three-component reaction of aldehyde, 6-aminopyrimidine-2,4-dione, and 1,3-indanedione in aqueous media. The binding properties of the receptors with anions such as F^-, Cl^-, Br^-, AcO^-, HSO_4^-, and $H_2PO_4^-$ have been investigated by UV–vis spectroscopy methods. The results have shown that receptors have good selectivity to F^- and AcO^-, and a 1:1 stoichiometry complex has been formed between compounds and anions.

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INTRODUCTION

The recognition and sensing of anions have received considerable attention for their important roles in biological, industrial, and environmental process [1]. Selective colorimetric anion sensing is particularly challenging as visual detection can give immediate qualitative information, while absorption spectroscopy gives quantitative information [2]. Most of these sensors have the chromophore covalently attached to the anion recognition unit [3]. Hydrogen-bonding receptors with redox-active and/or fluorogenic units have also been reported for selective anion detection. By contrast, despite their considerable advantages over other modes of signal transduction, there are only a few reports that can recognize anions by a readily observable color change [4–6].

Among anions, F^-, the most electronegative atom, usually forms the strongest H-bond interaction with an NH or OH fragment of the artificial receptor, and further the interaction should likely arouse an advanced stage of the proton transfer reactions, which partially depend on the intrinsic acidity of the H-bond donor group of the artificial receptor [7–10].

Multicomponent reactions (MCRs) are a valuable approach to synthesize novel compounds [11]. The MCR strategy offers significant advantages over conventional liner-type synthesis, by which three or more simple and flexible molecules are brought together and structural complexity and diversity are build up rapidly [12]. As a part of our interest in the synthesis of heterocyclic compounds by MCRs [13], we wish to report the synthesis of indeno[2′,1′:5,6]pyrido[2,3-*d*] pyrimidine derivatives and their recognition properties as new type anion receptors.

RESULTS AND DISCUSSION

The synthesis of indeno[2′,1′:5,6]pyrido[2,3-*d*]pyrimidine derivatives **4a–d** is shown in Scheme 1. In a typical general experimental procedure, the three-components, that is, aldehydes (**1**), 6-aminopyrimidine-2,4(1*H*,3*H*)-dione (**2**), and 1,3-indanedione (**3**) were treated in water and stirred thoroughly at 90°C in the presence of triethylbenzylammonium chloride (TEBAC) as catalyst to afford the indeno[2′,1′:5,6]pyrido[2,3-*d*]pyrimidine derivatives **4a–d** in good to excellent yields.

UV–vis absorption spectra. The UV–vis spectroscopic titration experiment was taken to investigate the possible interaction between receptors and each anion. All titrations were carried out in acetonitrile solution.

Scheme 1. Synthesis of receptors **4a–d. a**. R = NO_2; **b**. R = Cl; **c**. R = CH_3; **d**. R = OCH_3.

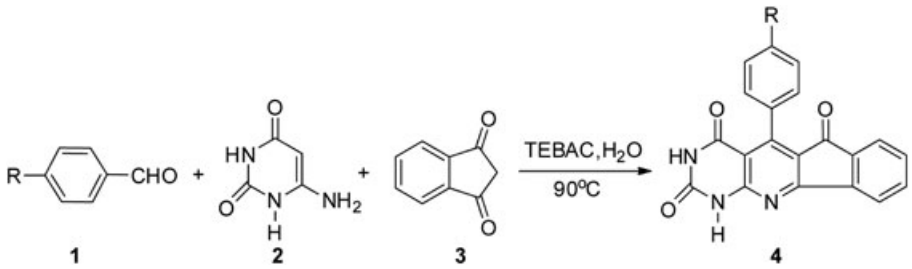

Figure 1 shows the absorption spectra of receptor **4a** in the presence of the anions. On addition of F^- and AcO^-, the intensity of the absorption maxima peak at 324 nm decreased while a new peak appeared at 399 nm. On the other hand, addition of HSO_4^-, Br^-, and Cl^- to the receptors did not cause even marginal spectral changes.

The absorption spectra of the receptors **4a** were characterized by the presence of single absorption maxima at 324 nm. On addition of fluoride, the intensity of the peak at 324 nm decreased while a new peak appeared at 399 nm along with four isosbestic points at 281, 311, 334, 365 nm while the yellow solution changed to pale red (Fig. 2). This is due to the high electronegativity and the smaller size of the F^- and AcO^- among the other anions. Moreover, the fluoride-induced color changes remain the same even in the presence of other anions. Color changes are most probably due to formation of hydrogen bonds between the NH and fluoride ions. 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 fluoride-bound NH and the electron-deficient 6-aminopymidine-2,4(1*H*,3*H*)-dione group [14].

In the case of AcO^-, the spectral changes were similar to F^-, and the receptor **4a** developed the same pale red color only gradually on addition of AcO^- (Fig. 3). This selectivity to F^- and AcO^- can be rationalized on the basis of the guest structure. The structural complementarity is an important factor for effective hydrogen bonding. Thus, receptor **4a** would preferably bind F^- of spherical geometry or AcO^- of planar geometry but not those of tetrahedral geometry ($H_2PO_4^-$ and HSO_4^-). Moreover, the fluoride-induced color changes remained the same even in the presence of other halide anions. Color changes are most probably due to the formation of hydrogen bonds between the aminopymidine dione NH groups of receptor **4a** and F^-. The formation of such hydrogen bonds affects the electronic properties of the chromophore, resulting in a color change with a subsequent new charge-transfer interaction between the fluoride-bound amide moiety and the electron-deficient NH group [15–17].

The Job plots of receptor **4a** with F^- and AcO^- at a total concentration of 0.2 mmol/L in acetonitrile are

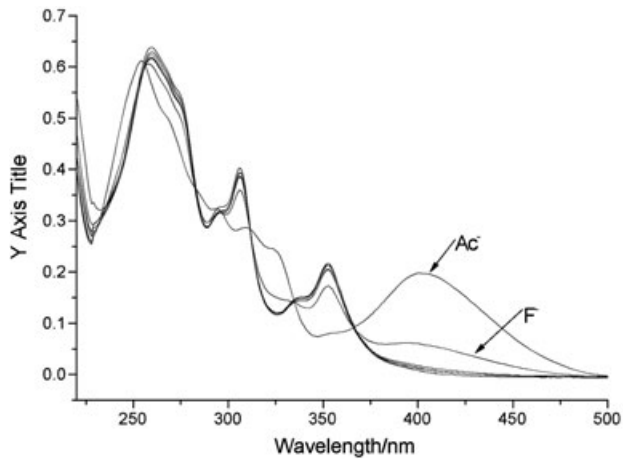

Figure 1. Absorption spectra of receptor **4a** ($2 \times 10^{-5}M$) on addition of tetrabutylammonium F^-, AcO^-, $H_2PO_4^-$, HSO_4^-, Br^-, and Cl^- ($2 \times 10^{-5}M$) in acetonitrile solution.

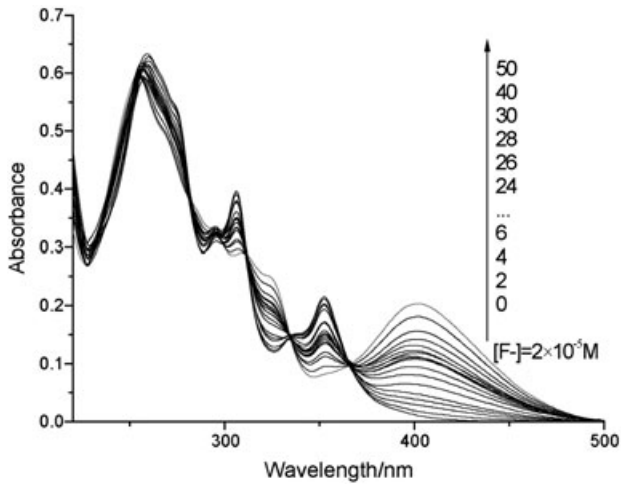

Figure 2. UV–visible spectral changes observed for **4a** on addition of F^- in acetonitrile solution. **4a** = $2 \times 10^{-5}M$; [F^-] = 0–50 equiv of **4a**.

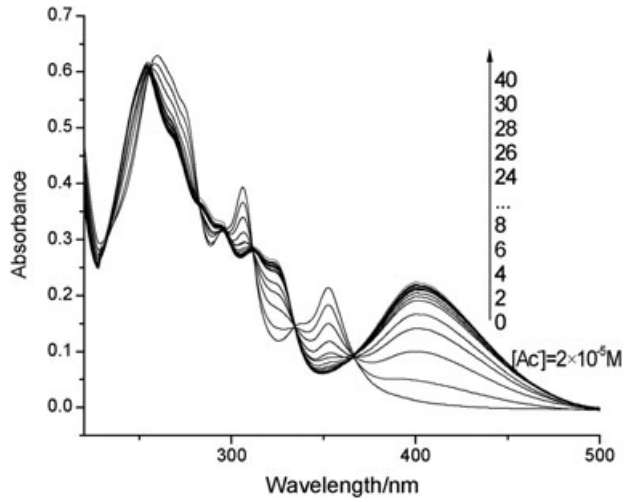

Figure 3. UV–visible spectral changes observed for **4a** on addition of AcO^- in acetonitrile solution. **4a** = $2 \times 10^{-5}M$; [AcO^-] = 0–40 equiv of **4a**.

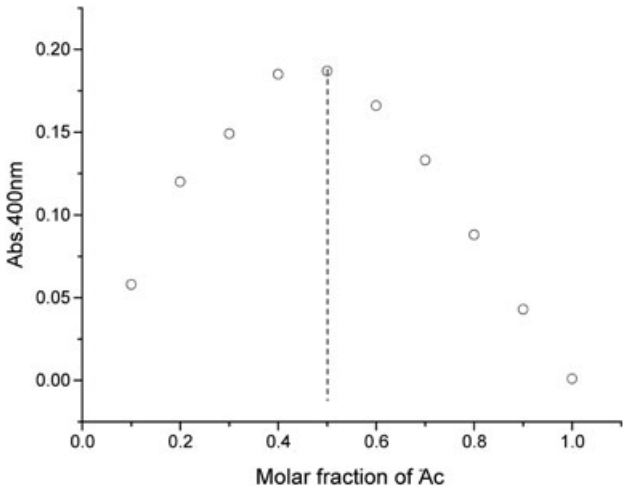

Figure 5. Job plot for receptor **4a** and AcO^-.

shown in Figs. 4 and 5. When the molar fraction of [F^-]/([**4a**] + [F^-]) and [AcO^-]/([**4a**] + [AcO^-]) was about 0.5, the absorption got to a maximum, which means that there is formation of 1:1 complexes between **4a** and F^- and AcO^-. Similarly, 1:1 complexes of the receptors **4b**, **4c**, **4d** with F^- and AcO^- were also formed.

For the complex of 1:1 stoichiometry, according to the following relation equation [18]:

$$A = A_0 + \frac{A_{\lim} - A_0}{2c_0} \times \left\{ c_0 + c_A + \frac{1}{K_a} - \left[\left(c_0 + c_A + \frac{1}{K_a} \right)^2 - 4c_0c_A \right]^{1/2} \right\}$$

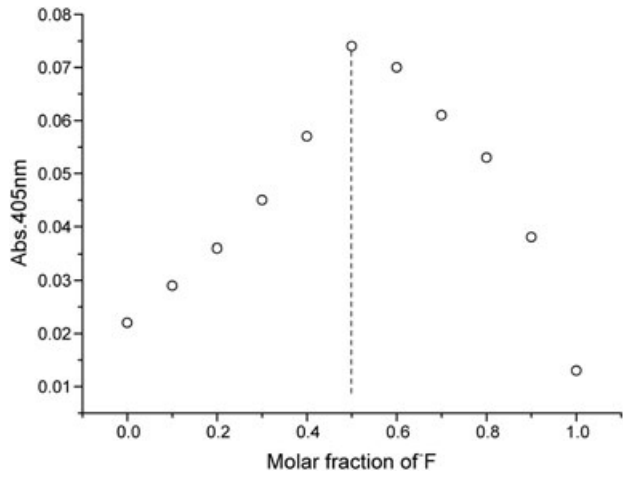

Figure 4. Job plot for receptor **4a** and F^-.

where A represented the absorption intensity of interaction of receptors **4a**, **4b**, **4c**, and **4d** with various concentrations of anion, and C_0 and C_A represented the corresponding concentration of host and guest anion. The association constants obtained by a satisfactory nonlinear least-square analysis of *A versus* is listed in Table 1, which proved the formation of 1:1 complexes between **4a**, **4b**, **4c**, **4d** with F^- and AcO^-.

In summary, the receptors (**4a**, **4b**, **4c**, and **4d**) could provide simple and efficient choromogenic-sensing molecule model by hydrogen bonding interactions. There were observable color changes by the naked eyes for **4a**, **4b**, **4c**, and **4d** with F^- and AcO^-, which shows that the receptors of pyrimidine derivatives might also be a promising candidate for various applications such as anion transports and/or electrochemical sensor.

EXPERIMENTAL

All anions were tetrabutylammonium salts that were obtained from Alfa-Aesar China (Beijing, China). All other commercially available reagents were of analytical purity and were used without

Table 1

Binding constants between receptors and F^-, AcO^- in acetonitrile solution.

	F^-		AcO^-	
Receptor	λ_{max} (nm)	K_a (mol/L)	λ_{max} (nm)	K_a (mol/L)
4a	400	0.23×10^5	400	0.95×10^5
4b	400	0.34×10^5	400	0.59×10^5
4c	400	0.18×10^5	400	0.52×10^5
4d	400	0.52×10^5	400	0.71×10^5

further purification. Acetonitrile was not dried and distilled before use. A 2501PC ultraviolet spectrophotometer (Shimadzu, Kyoto, Japan) was used and cell dimensions are $1 \times 1 \times 4$ cm^3. Infrared (IR) spectra were recorded on a Varian 1000 Fourier transform infrared (FTIR) spectrometer using KBr discs in the 4000–500 cm^{-1} region. ^{1}H NMR spectra were obtained on a Invoa-400 MHz superconductive nuclear magnetic resonance (NMR) spectrometer using dimethyl sulfoxide (DMSO)-d_6 as solvent and tetramethylsilance (TMS) as an internal standard. Melting point was measured using an XT-5 apparatus and is uncorrected. High-resolution mass spectra (HRMS) data were obtained using TOF-MS instrument.

General procedure for the synthesis of indeno[2′,1′:5,6] pyrido[2,3-*d*]pyrimidine derivatives 4. A 50 mL flask was charged with the aldehyde **1** (2 nmol), 6-aminopymidine-2,4 (1*H*,3*H*)-dione **2** (2 mmol), 1,3-indenedione **3** (2 nmol), TEBAC (0.10 g), and water (10 mL). The mixture was stirred at 90°C for 20 h. After completion of the reaction, the mixture was cooled to room temperature. The solid was filtered and recrystallized from ethanol to afford the pure product **4**.

5-(4-Nitrophenyl)-1*H*,3*H*-indeno[2′,1′:5,6]pyrido[2,3-*d*] pyrimidine-2,4,6-trione (4a). This compound was obtained as yellow needle crystal with mp>300°C; yield 89%; IR (KBr): 3136, 3054, 2815, 1715, 1567, 1343, 1288, 1175, 1133 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.57 (d, J = 8.8 Hz, 2*H*, ArH), 7.61–7.67 (m, 2H, ArH), 7.76–7.80 (m, 1H, ArH), 7.86 (d, J = 7.2 Hz, 1H, ArH), 8.27 (d, J = 8.4 Hz, 2H, ArH), 11.45 (s, 1H, NH), 12.37 (s, 1H, NH). HRMS Calculated for $C_{20}H_{10}N_4O_5$: 386.0651, found 386.0632.

5-(4-Chlorophenyl)-1*H*,3*H*-indeno[2′,1′:5,6]pyrido[2,3-*d*] pyrimidine-2,4,6-trione (4b). This compound was obtained as yellow powder with mp > 300°C; yield 95%; IR (KBr): 3480, 3168, 3056, 2829, 1717, 1597, 1574, 1561, 1530, 1492, 1446, 1397, 1370, 1288, 1180, 1157, 1134 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.30 (d, J = 8.0 Hz, 2H, ArH), 7.44 (d, J = 8.4 Hz, 2H, ArH), 7.61–7.66 (m, 2H, ArH), 7.78 (t, J = 7.2 Hz, 1H, ArH), 7.86 (d, J = 7.6 Hz, 1H, ArH), 11.36 (s, 1H, NH), 11.27 (s, 1H, NH). HRMS Calculated for $C_{20}H_{10}ClN_3O_3$: 375.0411, found 375.0428.

5-(4-Methylphenyl)-1*H*,3*H*-indeno[2′,1′:5,6]pyrido[2,3-*d*] pyrimidine-2,4,6-trione (4c). This compound was obtained as yellow powder with mp > 300°C; yield: 98%; IR (KBr): 3414, 3174, 2914, 1742, 1596, 1389, 1236, 1185 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.40 (s, 3H, CH_3), 7.14–7.19 (m, 4H, ArH), 7.59–7.66 (m, 2H, ArH), 7.77 (t, J = 7.2 Hz, 1H, ArH), 7.85 (d, J = 7.6 Hz, 1H, ArH), 11.29 (s, 1H, NH), 12.21(s, 1H, NH). HRMS Calculated for $C_{21}H_{13}N_3O_3$: 355.0957, found 355.0935.

5-(4-Methoxyphenyl)-1*H*,3*H*-indeno[2′,1′:5,6]pyrido[2,3-d] pyrimidine-2,4,6-trione (4d). This compound was obtained as yellow powder with mp > 300°C; yield: 85%; IR (KBr): 3521, 3463, 3172, 3057, 2841, 1708, 1556, 1370, 1285, 1176, 1022 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.81 (s, 3H, CH_3O), 6.92 (d, J = 8.8 Hz, 2H, ArH), 7.22 (d, J = 8.8 Hz, 2H, ArH), 7.60–7.65 (m, 2H, ArH), 7.74–7.78 (m, 1H, ArH), 7.84 (d, J = 7.6 Hz, 1H, ArH), 11.29 (s,1H, NH), 12.20 (s, 1H, NH). HRMS Calculated for $C_{21}H_{13}N_3O_4$: 371.0906, found 371.0902.

Binding studies. To a 10-mL tube, 1.0 mL of the derivatives of receptor indeno[2′,1′:5,6]pyrido[2,3-*d*]pyrimidine **4** (2.0×10^{-4} mol/L) in acetonitrile solution was added after adding the representative anions (2.0×10^{-4} mol/L) such as F^-, AcO^-, $H_2PO_4^-$, HSO_4^-, Br^-, and Cl^- (2.0×10^{-4} mol/L) in acetonitrile solution (to control ionic intensity) and mixing. The colorimetric sensing ability was monitored by UV–visible absorptions at 290 K and by "naked eye" observations.

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