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Amide-nitrophenyl based colorimetric receptors for selective sensing of fluoride ions

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Abstract—New chromogenic receptors containing 2-nitrophenyl or 3,5-dinitrophenyl groups appended to the amide or in secondary amine positions have been synthesized and characterized. Upon addition of fluoride to two of the receptors in acetonitrile, the solution acquired a yellow colour. The third receptor showed an intense purple colour with fluoride in acetonitrile and the appearance of the purple colour can be detected by the naked eye at parts per million level. The addition of chloride, bromide and iodide to the receptors did not induce any colour. Thus the receptors can act as fluoride ion sensors even in the presence of other halide ions.

The design and synthesis of sensitive chemosensors for anions is of growing interest, because the anions play an important role in a wide range of environmental and chemical processes.[1] The development of chromogenic receptors for anion sensing is a relatively new area of research.[2] Indeed, colorimetric anion sensing is particularly challenging since visual detection can give immediate qualitative information.[3] Colorimetric sensors have considerable advantages over other molecular sensors because they do not require the use of costly equipment such as spectrophotometers or cyclic voltameters.[4] Among the inorganic anions, fluoride ions have received significant interest due to their beneficial effects (e.g., prevention of dental caries) and detrimental (e.g., fluorosis) roles.[5] Chromogenic receptor systems generally consist of two parts. One is the anion binding part employing various combinations of pyrroles,[6] guanidiniums,[7] Lewis acids,[8] amides[9] and urea or thioureas.[10] The other is the chromophore part, which converts binding induced changes or recognition phenomena to optical signals. Previously we have reported a ferrocene-functionalized redox-active receptor that can sense only fluoride anions among halides.[11] In this letter, we report the synthesis, characterization and colorimetric sensing nature of the receptors **R1**, **R2** and **R3** containing nitroaromatic moieties. The receptor **R1** possesses amide and amine groups that serve as interaction sites whilst the receptors **R2** and **R3** contain only amide groups.

The receptor *N*,*N*′-bis{3-(2-nitrobenzyl)aminopropyl}-oxamide **R1** was obtained in one step from the condensation of 2-nitrobenzaldehyde in methanol with a solution of $oxpnH_2$ (*N*,*N*′-bis(3-aminopropyl)oxamide)[12] in methanol (20 ml) with subsequent reduction with excess $NaBH_4$. After basic work-up, the product was purified by column chromatography on neutral alumina ($CHCl_3$–CH_3OH, 99:1 v/v). The receptor **R1** was obtained as a crystalline powder (Scheme 1). Crystals of receptor **R1** were obtained from methanol:acetonitrile (1:1) mixture. The receptors **R2** (*N*,*N*′-bis{3-(2-nitrobenzoyl)aminopropyl}oxamide) and **R3** (*N*,*N*′-bis{3-(3,5-dinitrobenzoyl)aminopropyl}oxamide) were synthesized[13] by the reaction of either 2-nitro- or 3,5-dinitrobenzoic acid with $oxpnH_2$ in THF in the presence of *N*,*N*′-dicyclohexylcarbodiimide. The reaction mixture was stirred at room temperature for 4 h, and the resulting insoluble precipitate was removed by filtration. The solvent was evaporated and the resulting compound was dissolved in ethyl acetate (10 ml). Addition of hexane (25 ml) afforded the receptors **R2** and **R3** (Scheme 2),

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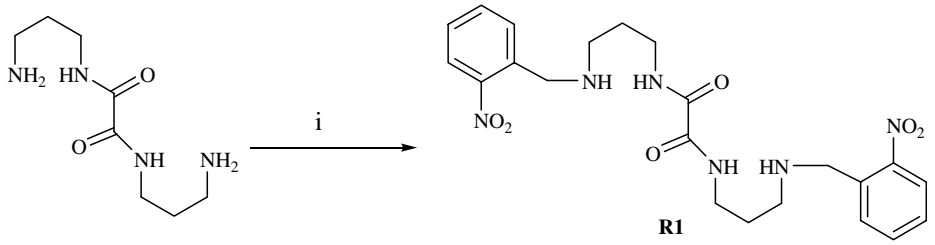
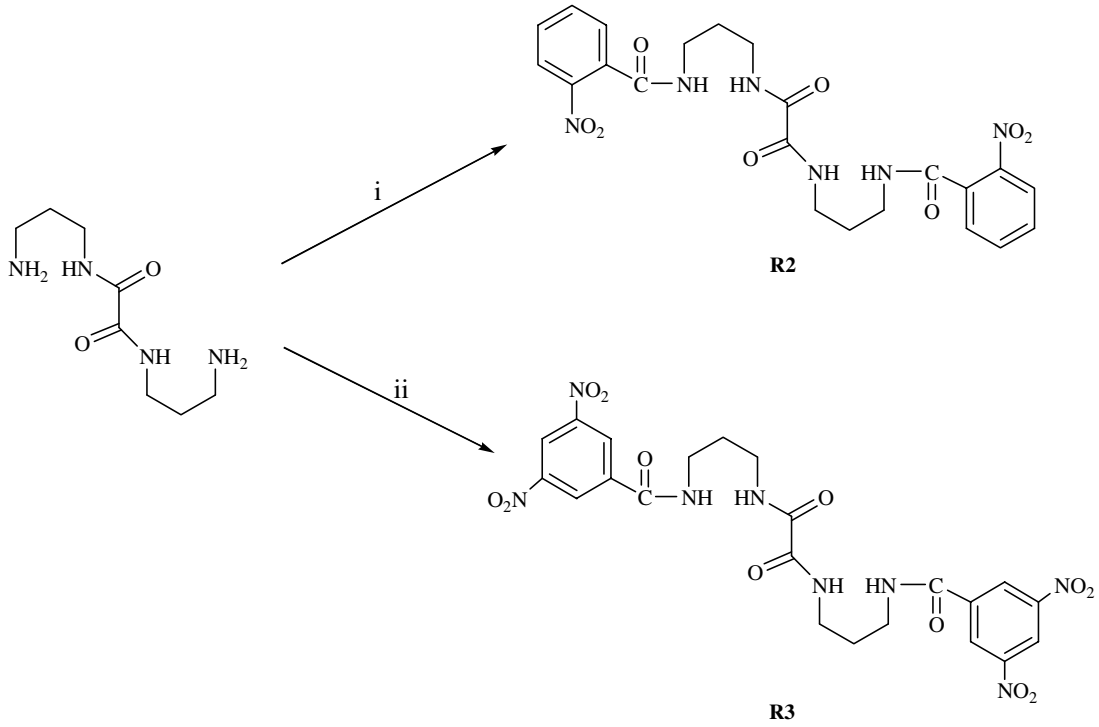


Scheme 1. Reagents and conditions: (i) 2-nitrobenzaldehyde, methanol, reflux, 6 h, then $NaBH_4$, rt, 1 h, 72%.



Scheme 2. Reagents and conditions: (i) 2-nitrobenzoic acid, *N*,*N*′-dicyclohexylcarbodiimide, THF, rt, 4 h, 68%; (ii) 3,5-dinitrobenzoic acid, *N*,*N*′-dicyclohexylcarbodiimide, THF, rt, 4 h, 70%.

which were purified by recrystallization from chloroform. Elemental and spectroscopic analysis were consistent with the proposed formulations of **R1**, **R2** and **R3**.[14] The receptor **R1** was characterized by XRD[15] and the ORTEP plot is shown in Figure 1.

The colorimetric sensing ability of the receptors **R1**–**R3** with anions (F^-, Cl^-, Br^- and I^-) in acetonitrile was monitored by UV–visible absorption and by 'naked eye' observations. The anions were added as tetrabutylammonium salts to the acetonitrile solutions (5×10^{-5}) of the receptors **R1**–**R3**.

The absorption spectra of the receptors **R1** and **R2** were characterized by the presence of single absorption maxima at 264 nm. Upon addition of fluoride, the intensity of the peak at 264 nm decreased while a new peak appeared at 427 nm along with an isosbestic point at

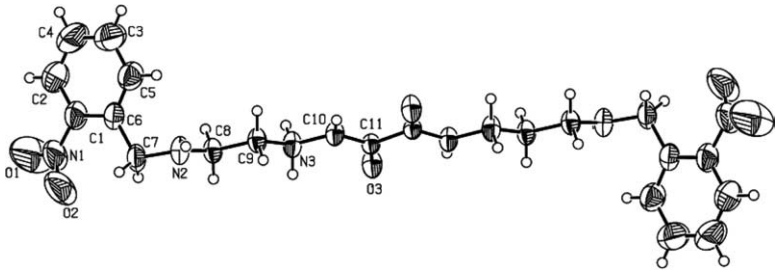


Figure 1. ORTEP plot of the crystal structure of **R1**.

334 nm whilst the colourless solution changed to yellow. The receptor **R3** displayed a single band at 230 nm. During titration with fluoride, two new bands appeared at 402 nm and at 529 nm for **R3** along with the appearance of a purple colour (Fig. 2). The intensity of the absorption band at 230 nm decreased in the absorption spectrum with an isosbestic point at 262 nm. Figure 3 shows the spectra of **R3** obtained during the titration with fluoride ions. On the other hand, addition of chloride, bromide and iodide (more than 100 equiv) to the receptors did not cause marginal spectral changes even marginal. This is due to the high electronegativity and the smaller size of the fluoride ion among the other halides. Moreover, the fluoride-induced colour changes remain the same even in the presence of other halide anions. Upon addition of less than 1 equiv of fluoride the colour of the solution changed from colourless to purple for **R3**. Hence, fluoride anions can be detected even at low concentrations (10^{-6} M). The colourless solutions of **R1** or **R2** changed to a yellow colour after the addition of 1 equivalent of fluoride ions. The receptor **R3** displayed a larger bathochromic shift in the presence of fluoride when compared to the receptors **R1** and **R2**. This may be due to the fact that receptors **R1** and **R2** contain one nitro group on each aromatic ring whereas **R3** contains two nitro groups on each aromatic ring. Colour changes are most probably due to formation of hydrogen bonds between the amide groups and fluoride ions. The formation of these hydrogen bonds affects the electronic properties of the chromophore, resulting in a colour change with a subsequent new charge-transfer interaction between the fluoride-bound amide and the electron deficient 2-nitrobenzene or 3,5-nitrobenzene group.[9,16] The binding constant for the fluoride complex was obtained from the variation in the absorbance at the appropriate wavelength [264 nm (**R1**); 264 nm (**R2**); 230 nm (**R3**)]. The binding constants (K_a) for **R1**, **R2** and **R3** with fluoride were determined to be 6.8×10^3, 8.1×10^3 and 1.9×10^4 M^{-1}, respectively. The higher fluoride binding ability of **R3** over **R1** and **R2** is due to the more acidic nature of the amide groups present in **R3**. The presence of two electron withdrawing nitro groups on each ring enhances the binding nature of the amide groups with the fluoride ions.[17]

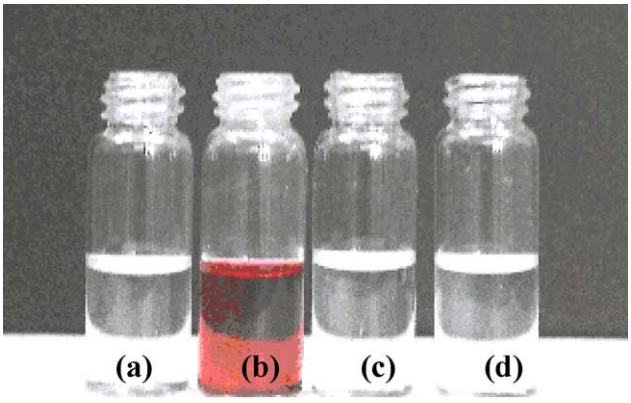


Figure 2. Colour changes of **R3** in CH_3CN [**R3**] = 5×10^{-5} M, [anion] = 5 equiv: (a) **R3** only, (b) F^-, (c) Cl^- and (d) Br^-.

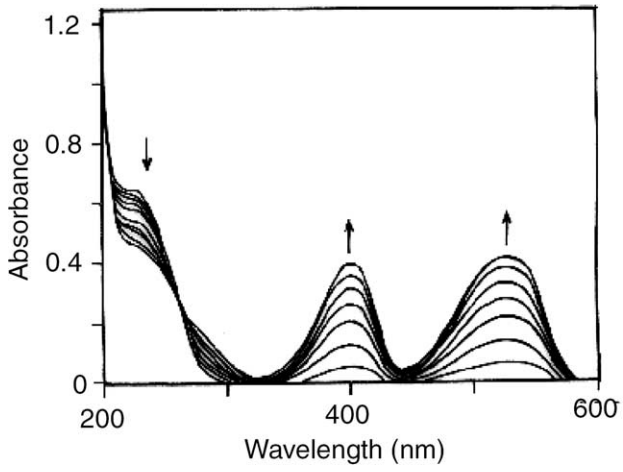


Figure 3. UV–visible spectral changes observed for **R3** upon addition of fluoride anions in CH_3CN. [**R3**] = 5×10^{-5} M; [F^-] = 0–2 equiv of **R3**.

In the case of acetate and phosphate anions, the receptors **R1** and **R2** developed the same yellow colour only upon addition of more than 10 equiv of each anion. Moreover, the addition of more than 3 equiv of acetate or phosphate to **R3** induced the purple colour change in acetonitrile. This selectivity can be understood on the basis of guest basicity and the structure of the complex. Fluoride ions having higher electronegativity and a smaller size compared to phosphate and acetate, binds strongly with the receptors.[3a,c]

In aprotic solvents, the receptors **R1**–**R3** induced a colour change with fluoride ions; upon addition of a few drops of protic solvents (water, methanol, etc.), the colour disappeared. This is because protic solvents compete with amide or amino groups for fluoride ions. This observation indicated that hydrogen bonding is involved between the receptors and fluoride ions.[18]

Among the chromogenic receptors **R1**–**R3**, the receptor **R3** developed an intense purple colour upon addition of fluoride ions, the appearance of which can be detected by the naked eye at parts per million level concentrations of fluoride ions. Hence, the receptor **R3** can be used as a selective colorimetric sensor for fluoride ions.

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14. Data for **R1**: Yield: 72%; mp 134 °C; ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ 1.73 (quint, 4H, $J = 6.2$ Hz, CH_2–CH_2–CH_2), 2.70 (t, 4H, $J = 6.2$ Hz, CO–NH–CH_2–), 3.40 (q, 4H, $J = 6.2$ Hz, –CH_2–NH–CH_2–), 4.03 (s, 4H, NH–CH_2–Ar), 7.40 (t, 2H, $J = 4.6$ Hz, Ar), 7.57 (t, 2H, $J = 4.4$ Hz, Ar), 7.65 (d, 2H, $J = 4.2$ Hz, Ar), 7.94 (d, 2H, $J = 4.6$ Hz, Ar), 8.12 (s, 2H, CO–N*H*–CH_2); ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 29.1 (–CH_2–*C*H_2–CH_2–), 38.7 (–CH_2–CH_2–*C*H_2–NH–Ar), 47.2 (CO–NH–*C*H_2–CH_2), 50.8 (–CH_2–Ar), 124.8, 128.1, 131.5, 133.3, 135.4 (aromatic), 160.1 (–*C*O–NH–); IR (cm^{-1}, KBr pellet): 3286 (N–H stretching), 1647 (CO stretching), 1519 (NH bending), 1461 (NO_2); EI MS (*m*/*z*): 472 (M^+), 65%; Analytical data for: $C_{22}H_{28}N_6O_6$: Calculated (%): C, 55.92; H, 5.97; N, 17.79; Found (%): C, 55.89; H, 5.95; N, 17.76. Data for **R2**: Yield: 68%; mp 174 °C (dec) ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ 1.22 (quint, 4H, $J = 7.1$ Hz, CH_2–CH_2–CH_2), 2.05 (t, 4H, $J = 7.1$ Hz, CO–NH–CH_2–), 3.70 (q, 4H, $J = 7.1$ Hz, –CH_2–NH–CH_2–), 6.16 (s, 2H, CO–N*H*–CH_2), 7.10–7.60 (m, 8H, Ar), 8.61 (br s, 2H, CO–N*H*–Ar); ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 16.1 (–CH_2–*C*H_2–CH_2–), 52.2 (–CH_2–CH_2–*C*H_2–NH–Ar), 59.2 (CO–NH-*C*H_2–CH_2), 126.6, 130.8, 136.2, 136.6, 148.4 (aromatic), 160.1 (–*C*O–NH–), 169.1 (–*C*O–NH–Ar); IR (cm^{-1}, KBr pellet): 3282 (N–H stretching), 1649 (CO stretching), 1523 (NH bending), 1434 (NO_2); FAB MS (*m*/*z*): 500 (M^+), 65%; Analytical data for: $C_{22}H_{24}N_6O_8$: Calculated (%): C, 52.80; H, 4.83; N, 16.79; Found (%): C, 52.78; H, 4. 82; N, 16.77. Data for **R3**: Yield: 70%; mp 194 °C (dec) ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ 1.93 (quint, 4H, $J = 7.6$ Hz, CH_2–CH_2–CH_2), 3.41 (t, 4H, $J = 7.6$ Hz, CO–NH–CH_2–), 4.20 (q, 4H,$J = 7.6$ Hz, –CH_2–NH–CH_2–), 6.21 (s, 2H, CO–N*H*–CH_2), 6.9–7.15 (m, 6H, Ar), 9.15 (br s, 2H, CO–N*H*–CH_2); ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 29.1 (–CH_2–*C*H_2–CH_2–), 38.4 (–CH_2–CH_2–*C*H_2–NH–Ar), 47.3 (CO–NH–*C*H_2–CH_2), 122.5, 123.2, 136.7, 137.3, 149.3, 149.5 (aromatic), 160.1 (–*C*O–NH–), 160.4 (–*C*O–NH–Ar); IR (cm^{-1}, KBr pellet): 3283 (N–H stretching), 1652 (CO stretching), 1518 (NH bending), 1455 (NO_2); FAB MS (*m*/*z*): 590 (M^+), 65%; Analytical data for: $C_{22}H_{22}N_8O_{12}$: Calculated (%): C, 44.75; H, 3.76; N, 18.98; Found (%): C, 44.71; H, 3.74; N, 18.95.
15. Crystal data for **R1**: CCDC No.: 272158. Light yellow prism, $C_{22}H_{28}N_6O_6$, $M_r = 472.5$, monoclinic, space group $P2_1/n$, $a = 6.762(1)$, $b = 5.062(3)$, $c = 35.356(4)$ Å, $\alpha = 90.00(3)$, $\beta = 92.70(2)$, $\gamma = 90.00(2)°$, $V = 1208.9(8)$ Å^3, $\rho_{calcd} = 1.298$ mg/m^3, $\mu = 0.096$ mm, $Z = 4$, reflections collected : 3556, independent collections: 3507 ($R_{int} = 0.0164$), Final R indices [$I > \sigma I$]: $R1 = 0.0698$, $wR2 = 0.2371$, R indices (all data): $R1 = 0.1294$, wR2 = 0.2883.
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