Naphthalene Urea Derivatives for Anion Receptor: Effects of Substituents on Benzoate Binding

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Anions play an important role in a wide range of chemical and biological processes, and considerable attention has been focused on the design of host molecules that can recognize and sense anion species selectively through the naked eye, electrochemical, and optical responses. Recently it has been reported that the optical anion receptors could be developed with aromatic moieties such as anthracene, anthraquinone, pyridinium and naphthalene. Those chemosensors are constructed according to the receptor-chromophore general binomial, which involves the binding a specific anion substrate with receptor sites and a chromophore responsible for translating the receptor-anion association into an optical signal. This variation can be related to either structural or conformational changes in the receptor structure when a complex is formed or to the formation of a charge transfer complex. As one type of important receptors, urea groups have been suited as fluorescent and color change receptors of anion sensors based on the hydrogen-bonding mechanism.

By developing a relatively simple urea derivative from naphthalene moiety, the fluoride selective receptor for fluorescence has been reported in our group, which gave a unique fluorescence peak in the presence of fluoride ions. Also a following investigation have produced the several unique fluorescence peak in the presence of fluoride ions. From the nitration reaction of 1,8-diaminonaphthalene and the corresponding dinitronaphthalene urea derivative, which shows a characteristic singlets at around δ 8.9 ppm for the two different urea N-H protons and butyl urea (2) shows a triplet at δ 5.6 ppm for the N-H protons connecting to butyl group. From the nitration reaction of 2, two receptors (13 and 14) have been prepared. By controlling the amount of the KNO3/AlCl3 ligands such as that the phenyl urea ligands shows two characteristic singlets at around δ 8.9 ppm for the two different urea N-H protons and butyl urea (2) shows a triplet at δ 5.6 ppm for the N-H protons connecting to butyl group. From the nitration reaction of 2, two receptors (13 and 14) have been prepared. By controlling the amount of the KNO3/AlCl3 compound 13 and 14 were also obtained from treatment of 1,8-bis(N-butylureido)naphthalene with KNO3/AlCl3 in CHCl3.

Four urea protons in naphthalene urea derivatives have provided the positive dipole for the anion binding. In order to examine the anion binding properties in detail, fourteen naphthalene urea receptors have been synthesized and their anion binding properties were investigated from 1H NMR titration.

Results and Discussion

Anion binding sites in naphthalene urea derivatives are in the area of urea groups, which provide the positive dipole due to the N-H protons. Anions bind at the urea N-H protons by the ion-dipole interaction. The magnitude of the positive dipole primarily determined the anion binding strength. The electronic factor on urea N-H protons can be influenced from the R and X groups on receptor. Electronically R groups can affect H2 protons, on the other hand X group can influence the H1 protons more easily. By varying R groups 12 receptors (1-12) were prepared and two more receptors (13, 14) were synthesized by nitrating ligand 2.

Synthesis. Ligands 1 to 12 were synthesized from the reaction of 1,8-diaminonaphthalene and the corresponding isocyanates in high yield. The urea ligands can be easily confirmed the structure from 1H NMR spectrum of the ligands such as that the phenyl urea ligands shows two characteristic singlets at around δ 8.9 ppm for the two different urea N-H protons and butyl urea (2) shows a triplet at δ 5.6 ppm for the N-H protons connecting to butyl group. From the nitration reaction of 2, two receptors (13 and 14) have been prepared. By controlling the amount of the KNO3/AlCl3 compound 13 and 14 were also obtained from treatment of 1,8-bis(N-butylureido)naphthalene 2 with KNO3/AlCl3 in CHCl3. From the 1H NMR spectrum, 13 was identified as a dinitronaphthalene urea derivative, which shows a singlet and a triplet at δ 6.57 and 7.08 for the four urea N-H protons and two doublets at δ 8.36 and 8.18 for the four aromatic protons of naphthalene. In case of compound 14, 1H NMR spectrum shows two singlets at δ 9.78 and 8.58 for the two urea N-H protons connected to the naphthalene and two triplets at δ 7.14 and 6.58 for the two urea N-H protons connected to the butyl group. Also, aromatic proton peaks of naphthalene were appeared as four doublets and one triplet at δ 8.25 and 7.64 as expected from the mononitronaphthalene structure.

Binding Properties. 1H NMR titration method has been applied for the binding constant determination and benzoate ion was used as an anion comparison. Fluoride ions were bound with ligands selectively, but the binding constants were too high for comparison.

Chemical shifts of H1 and H2 of ligand 1 are δ 9.01 and 8.83 ppm in the absence of anions. Addition of benzoate cause the downfield shift dramatically and then saturated after 1 equivalent of benzoate as shown in Figure 1, suggesting that ligand 1 bind with benzoate 1:1 ratio. Chemical shift of NH2 changed from δ 9.01 to δ 10.33 ppm (Δδ 1.32 ppm) and δ 8.83 to δ 10.50 ppm (Δδ 1.67 ppm) for the NH2 upon addition of 10 equivalents of benzoate, indicating that NH2 protons contributed more strongly for the benzoate binding probably due to the steric factor.

Chemical shifts of H1 and H2 for ligand 2 are δ 8.78 and 6.70 ppm in the absence of anions. Addition of benzoate cause the downfield shift and then saturated after 1 equival-
ent of benzoate as shown in Figure 2, suggesting that ligand 2 bind with benzoate 1:1 ratio. Chemical shift of NH changed from $\delta 8.78$ to $\delta 10.40$ ppm ($\Delta\delta 1.62$ ppm) and $\delta 6.70$ to $\delta 7.74$ ppm ($\Delta\delta 1.04$ ppm) for the NH upon addition of 10 equivalents of benzoate, indicating that NH protons contributed more strongly for the benzoate binding probably due to the electronic factor in this case. As expected from the bulky structure, chemical shifts of $H_b$ and $H_b$ for ligand 3 are hardly changed at all ($\delta 10.080 \sim \delta 10.085$) upon addition of 10 equivalents of benzoate. Steric hindrance of t-butyl group inhibits the benzoate binding completely. From the same method all ligands were titrated and stability constants ($K_a$) were determined from the EQ NMR.$^{15}$

Electron withdrawing groups such as chloro, fluoro, nitro-phenyl strengthen the anion binding from the development of more positive charge on N-H protons by pulling electron to urea group. Binding constant increase from 4,070 for 1 to 22,090 for 4 as can be seen in Table 1. A similar increase was observed for the ligands 6, 10 and 11 as expected. Ligands 13 and 14 which possess the nitro groups in the naphthalene moiety could influence the N-H protons, thus expecting high binding constant, but unfortunately due to the bad solubility of the ligands, $K_a$ could not be available. A qualitative investigation of binding constants from UV

![Figure 1](image1.png)

**Figure 1.** Chemical shifts changes of urea $H_a$ and $H_b$ protons for ligand 1 in the presence of benzoate ions.

![Figure 2](image2.png)

**Figure 2.** Chemical shifts changes of urea $H_a$ and $H_b$ protons for ligand 2 in the presence of benzoate ions.
at this moment. Chemical shift of N-H protons which could be influenced directly from naphthalene ring is less effective for participating the anion binding due to the geometric reason.

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<th>Ligands</th>
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Table 1. Stability constants ($K_a$) of the ligands in DMSO for the benzoate ions

*aToo weak to measure. *b Due to the bad solubility, $K_a$ was not obtained for the ligands 13 and 14.

suggests a small increase in the anion binding indicating that the N-H protons which could be influenced directly from naphthalene ring is less effective for participating the anion binding due to the geometric reason.

On the other hand, electron donating groups such as butyl, methylphenyl and methoxyphenyl weaken the anion binding from the development of less positive charge on N-H protons by donating electron to urea group. Binding constant decreases from 4.070 for 1 to 2,870 for 2 as can be seen in Table 1. A similar decrease was observed for the ligands 9, 10, 11, and 12.

**Summary**

A simple reaction of 1,8-diaminonaphthalene and various isocyanates provides the important anion receptors. Electronic effect on the para position of the phenyl ring of the urea ligands do influence the anion binding significantly and nitration on naphthalene ring also influence the binding properties, but much less compared with the changes of other side of urea group due to the structural easiness of N-H protons for anion binding.

**Experimental**

1,8-Bis(N-phenylureido)naphthalene (1)

To a stirred solution 0.2 g (1.26 mmol) of 1,8-diaminonaphthalene in 30 mL of THF/DMF (2:1 ratio), 0.55 mL (5.20 mmol) of butyl isocyanate in THF 15 mL was added and the reaction mixture was refluxed for 24 hours under the nitrogen atmosphere. The precipitate was occurred in reaction mixture. The reaction mixture was cooled and filtered. The precipitate was washed with MeOH (100 mL) and filtered to give 0.35 g (78%) of 2. mp 195 °C, decomp.; $^1$H NMR (DMSO-d$_6$) $\delta$ 10.05 (s, 2H, NH), 7.21 (t, 2H, ArH, $J$ = 8.5 Hz), 7.10 (d, 2H, ArH, $J$ = 8.5 Hz), 6.51 (d, 2H, ArH, $J$ = 8.0 Hz), 5.69 (t, 2H, NH, $J$ = 3.3 Hz), 2.96 (m, 4H, -CH$_2$), 1.29 (m, 8H, -CH$_2$), 0.86 (t, 6H, -CH$_3$); FAB MS m/z 357 (M+1, Calcd 357). Anal. Calcd for C$_{20}$H$_{28}$N$_4$O$_2$: C, 67.42; H, 7.86; N, 15.73. Found: C, 67.40; H, 7.80; N, 15.68.

1,8-Bis(N-t-butylureido)naphthalene (2).

To a stirred solution 0.2 g (1.26 mmol) of 1,8-diaminonaphthalene in 30 mL of THF/DMF (2:1 ratio), 0.33 mL (2.93 mmol) of tert-butyl isocyanate in THF 15 mL was added and the reaction mixture was refluxed for 3 days under the nitrogen atmosphere. The precipitate was occurred in reaction mixture. The reaction mixture was cooled and filtered. The precipitate was washed with acetone (100 mL) and filtered to give 0.40 g (89%) of 3. mp 247 °C, decomp.; $^1$H NMR (DMSO-d$_6$) $\delta$ 10.07 (s, 2H, NH), 7.20 (t, 2H, ArH, $J$ = 8.4 Hz), 7.10 (d, 2H, ArH, $J$ = 7.5 Hz), 6.51 (d, 2H, ArH, $J$ = 7.2 Hz), 5.44 (s, 2H, NH), 1.18 (s, 18H, -C(CH$_3$)$_3$).

1,8-Bis(N-4-chlorophenylureido)naphthalene (4).

Following the procedure described for ligand 2, 0.2 g (1.26 mmol) of 1,8-diaminonaphthalene and 0.45 g (2.91 mmol) of 4-chlorophenyl isocyanate produced 0.52 g (89%) of 4. mp 293 °C, decomp.; $^1$H NMR (DMSO-d$_6$) $\delta$ 9.11 (s, 2H, NH), $\delta$ 8.79 (s, 2H, NH), $\delta$ 7.75 (d, 2H, ArH, $J$ = 7.8 Hz), $\delta$ 7.65 (t, 2H, ArH, $J$ = 7.8 Hz), $\delta$ 7.48 (t, 2H, ArH, $J$ = 7.8 Hz), $\delta$ 7.41 (d, 4H, ArH, $J$ = 9.0 Hz), $\delta$ 7.24 (d, 4H, ArH, $J$ = 8.7 Hz).

1,8-Bis(N-2-chlorophenylureido)naphthalene (5).

Following the procedure described for ligand 2, 0.2 g (1.26 mmol) of 1,8-diaminonaphthalene and 0.35 mL (2.91 mmol) of 2-chlorophenyl isocyanate gave 0.56 g (95%) of 5. mp 276 °C, decomp.; $^1$H NMR (DMSO-d$_6$) $\delta$ 9.28 (s, 2H, NH), 8.46 (s, 2H, NH), 8.14 (d, 2H, ArH, $J$ = 8.4 Hz), 7.75 (d, 2H, ArH, $J$ = 8.4 Hz), 7.62 (d, 2H, ArH, $J$ = 7.2 Hz), 7.48 (t, 2H, ArH, $J$ = 7.8 Hz), 7.34 (d, 2H, ArH, $J$ = 8.1 Hz), 7.31 (t, 2H, ArH, $J$ = 7.8 Hz), 6.93 (t, 2H, ArH, $J$ = 8.4 Hz); $^{13}$C NMR (DMSO-d$_6$) $\delta$ 152.9 (-CO), 136.4, 135.7, 133.4, 128.9, 127.2, 125.5, 125.4, 123.0, 122.7, 121.8, 121.3 (Ar).
1,8-Bis(N-4-fluorophenylureido)naphthalene (6). Following the procedure described for ligand 2, 0.2 g (1.26 mmol) of 1,8-diaminonaphthalene and 0.33 mL (2.91 mmol) of 4-fluorophenyl isocyanate gave 0.50 g (84%) of 4H, ArH), 7.04 (t, 4H, ArH), 271 °C, decomp.; 1H NMR (DMSO-d6) δ = 8.31 (d, 2H, ArH), 8.78 (s, 2H, NH), 7.72 (d, 2H, ArH, J = 8.1 Hz), 7.65 (d, 2H, ArH, J = 7.2 Hz), 7.46 (d, 2H, ArH, J = 7.8 Hz), 7.39 (m, 4H, ArH), 7.04 (t, 4H, ArH, J = 9.0 Hz).

1,8-Bis(N-2,4-difluorophenylureido)naphthalene (7). Following the procedure described for ligand 2, 0.2 g (1.26 mmol) of 1,8-diaminonaphthalene and 0.31 mL (2.91 mmol) of 2,4-difluorophenyl isocyanate gave 0.50 g (84%) of 7. mp 271 °C, decomp.; 1H NMR (DMSO-d6) δ = 8.31 (d, 2H, ArH), 8.72 (s, 2H, NH), 8.07 (m, 2H, ArH), 7.75 (d, 2H, ArH, J = 7.8 Hz), 7.60 (d, 2H, ArH, J = 7.8 Hz), 7.47 (t, 2H, ArH, J = 7.8 Hz), 7.18 (t, 2H, ArH, J = 9.3 Hz), 7.69 (t, 2H, ArH, J = 9.0 Hz).

1,8-Bis(N-4-methylphenylureido)naphthalene (8). Following the procedure described for ligand 2, 0.2 g (1.26 mmol) of 1,8-diaminonaphthalene and 0.37 mL (2.91 mmol) of 4-tolyl isocyanate gave 0.45 g (84%) of 8. mp 247 °C, decomp.; 1H NMR (DMSO-d6) δ = 8.82 (s, 2H, NH), 8.75 (s, 2H, NH), δ = 7.70 (d, 2H, ArH, J = 7.5 Hz), 7.65 (d, 2H, ArH, J = 8.1 Hz), 7.42 (t, 2H, ArH, J = 7.5 Hz), 7.29 (d, 4H, ArH, J = 8.1 Hz), 7.01 (d, 4H, ArH, J = 8.1 Hz), δ = 2.24 (s, 6H, -CH3).

1,8-Bis(N-4-methoxyphenylureido)naphthalene (9). Following the procedure described for ligand 2, 0.2 g (1.26 mmol) of 1,8-diaminonaphthalene and 0.38 mL (2.91 mmol) of 4-methoxyphenyl isocyanate gave 0.40 g (69%) of 9. mp 280 °C, decomp.; 1H NMR (DMSO-d6) δ = 8.76 (s, 2H, NH), 8.75 (s, 2H, NH), 7.70 (d, 2H, ArH, J = 7.8 Hz), 7.66 (d, 2H, ArH, J = 8.1 Hz), 7.42 (t, 2H, ArH, J = 7.8 Hz), 7.31 (d, 4H, ArH, J = 9.0 Hz), 6.79 (d, 4H, ArH, J = 9.0 Hz), 2.24 (s, 6H, -OCH3).

1,8-Bis(N-4-nitrophenylureido)naphthalene (10)12. A solution of 1,8-bis(N-butylureido)naphthalene 2 (0.10 g, 0.28 mmol) in dried CH2Cl2 20 mL was added potassium nitrate 0.34 g (3.36 mmol) and aluminium chloride 0.67 g (5.04 mmol) and the reaction mixture was stirred 2 hours in 0 °C and stirred at the room temperature for 24 hours. The residue was treated with 5% HCl 100 mL. The precipitate was filtered to give 0.08 g (64%) of 13. mp 195 °C, decomp.; 1H NMR (DMSO-d6) δ = 9.26 (s, 2H, NH), 8.36 (d, 2H, ArH, J = 9.0 Hz), 8.18 (d, 2H, ArH, J = 9.0 Hz), 7.08 (t, 2H, NH, J = 5.2 Hz), 3.12 (m, 4H, -CH2-), 1.35 (m, 8H, -CH2-CH2-), 0.91 (t, 6H, -CH3, J = 7.2 Hz).

1,8-Bis(N-butylureido)-4-nitronaphthalene (14). To a solution of 1,8-bis(N-butylureido)naphthalene 2 (0.20 g, 0.56 mmol) in dried CH2Cl2 20 mL was added potassium nitrate 0.20 g (1.68 mmol) and aluminium chloride 0.30 g (2.24 mmol) and the reaction mixture was stirred 2 hours in 0 °C and stirred at the room temperature for 24 hours. The residue was treated with 5% HCl 100 mL. The precipitate was washed with CHCl3 (100 mL) and filtered to give 0.15 g (66%) of 14. mp 195 °C, decomp.; 1H NMR (DMSO-d6) δ = 9.78 (s, 1H, NH), 8.58 (s, 1H, NH), 8.25 (three d, 3H, ArH), 7.64 (m, 2H, ArH), 7.15 (t, 1H, NH, J = 5.3 Hz), 6.62 (t, 1H, NH, J = 5.6 Hz), 3.10 (m, 4H, -CH2-), 1.41 (m, 8H, -CH2-CH2-), 0.91 (two t, 6H, -CH3).

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References