Carbazole Based Anion Receptors

Presented by Vinay K. Mikkilineni

In partial fulfillment of the requirements for graduation with the
Dean's Scholars Honor's Degree in the Department of Chemistry and Biochemistry

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Department: Chemistry and Biochemistry

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Abstract

Anions are of great importance in the environment and health, thus it is no wonder that a great deal of research has been conducted to create synthetic receptors that can bind to various anions. In the past few decades, research and synthesis of novel receptors containing pyrrole, such as “expanded” porphyrins, has increased tremendously. These new synthetic molecules have been used as means for various applications including anion binding, sensing, transport and delivery. Previous work has shown some success in trying to use carbazole as a key component in combination with pyrrole for receptor synthesis. Carbazole has a large size, flourescent properties and a more acidic NH donor than the pyrrolic NH normally found in these analogues to bind ions. The synthesis and analysis of new carbazole-based receptors, “expanded” porphyrin macrocycles and amidopyrroles, is discussed with special attention paid to the modification of carbazole in an attempt to enhance binding and solubility of the receptors. Binding with various anions (chloride, benzoate, and dihydrogen phosphate) was studied and all molecules were shown to have an increased affinity for phosphate. However, there were notable differences in anion selectivity between the various receptors.

Introduction

Supramolecular chemistry is a study of intermolecular interactions.[1] Although this is inclusive of all types of noncovalent intermolecular bonds, hydrogen bonds probably hold the greatest importance, given their presence in significant associations such as between nucleotides in DNA. This chemistry is also very important when considering the interactions of ions and receptor molecules. Although cations have been

far more studied due to easier coordination, higher charge density and less diversity of species. Nonetheless, anion binding has become increasingly more important.

Anions are very significant in chemistry, specifically anions such as flouride, chloride, and phosphate play important roles in cells and various biological systems. Chloride is found in the nuerons and plays a role in signaling, and phosphate can be found throughout the body in the backbone of DNA and the biochemical energy molecule, ATP. Anions have also been shown to be a major contributing factor for various problems in the environment and the health of individuals. Increased fertiziler runoff has generated a concern for the presence of nitrates in our groundwater,[2] which has brought up health issues such as methemoglobinemia.[3] Many diseases involve anions such as the misregulation of chloride ions in cystic fibrosis[4] or the excess intake of fluoride in children for fluorosis.[5] With these issues in mind, the search for anion receptors is attractive to supramolecular chemists.[6-9]

Anion receptors can vary in their interaction with ions, from positively charged species or transition metals to hydrogen bond donors. Hydrogen bond donor receptors tend to be more selective than charged species due to the specific orientation of the donor groups. These donors include various amides, phenols, pyrroles, carbazole and indoles. Often synthetic receptors use combinations of these molecules.

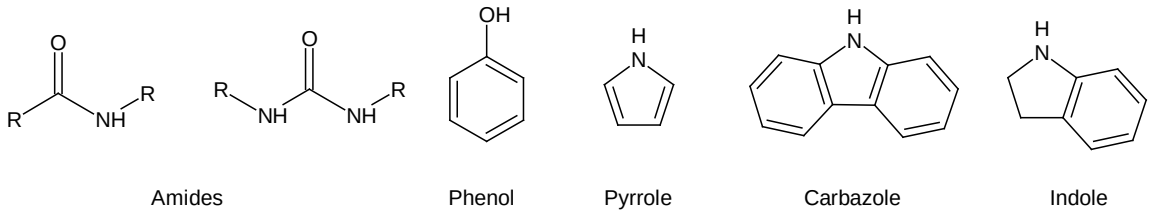


Figure 1: Some natural hydrogen bond donors

Pyrrole containing compounds have received attention in supramolecular chemistry due to their diverse function, properties, and presence, existing in natural roles of ion recognition, transport, and stabilization of larger biomolecules. Pyrrole is a heterocyclic aromatic ring with the formula C_4H_4NH with the nitrogen contributing its π electrons for conjugation. It has been found as a buiding block for many naturally important pigments and compounds. Pyrroles are also present in various alkaloids and also appear in amino acids like proline. They can be used in a range of conditions, being neither overly acidic or basic. The aromaticity allows for the generation of conjugated macrocyles having discrete absorptive and flourescent properties. Pyrroles show unique qualities in shape, size, structure, properties, and function making them ideal candidates for anion receptors.[10, 11]

Pyrrole was discovered by Runge as a specific fraction in coal tar and named in 1834. However, it was not characterized until 1858 by Anderson, after also being found in bone oil, with Bayer determining its constitution in 1870. [11] Although a derivative of pyrrole was originally found in coal tar and bone oil, pyrrole's role in biological systems cannot be overstated. Pyrroles naturally occur in various macrocyclic and acyclic molecules such as porphyrins and prodigisions, respectively. There have also been many classes of compounds synthesized anthropogenically for the sole purpose of taking advantage of the ion binding and sensing ability of pyrrole.[10] Included in these molecules are those of amidopyrroles, calixpyrroles, and analogues of porphyrins called "expanded" porphyrins.

Amidopyrroles have distinct advantages over other simple dihydrogen bond donors due the orientation of the donors. This provides an increased number of bonds

towards the same atom in an ion, thereby generating stronger ion-receptor interactions. Considerable effort has been devoted to the synthesis of new amidopyrrole receptors in recent years.[8, 12-16] Many of these, including several from our group,[17] have taken advantage of a basic strategy first pioneered by Crabtree[18, 19] and then exploited so effectively by a number of leaders in the anion recognition community.

As mentioned before, pyrrole occurs naturally in macrocycles. One of great importance, porphyrin has been the one of the most studied macrocycles, due to their key presence in biological systems, such as in the macrocyclic centers of heme and chlorophyll. This macrocycle's ligand properties can be seen with its ability to form complexes with numerous metals.

In the study of porphyrin, a range of analogues were created and studied to mimic the properties of this rich molecule. An unique class of analogues that has spawned a great deal of reasearch in the past 30 years are the "expanded" porphyrins.[20] These molecules originally discovered by accident in 1966 with the creation of sapphyrin. The synthesis of this molecule wasn't published until 1983, and research didn't really pick up in this area until 1990.[21-23] A definition of expanded porphyrins includes two basic points; the internal core of the macrocycle contains atleast 17 atoms (1 more than porphyrin), and the macrocycle contains at least one five membered hetercycle in its structure. The second point includes the discussion of the incorporation of molecules similar to pyrrole in the macrocycles.[22]

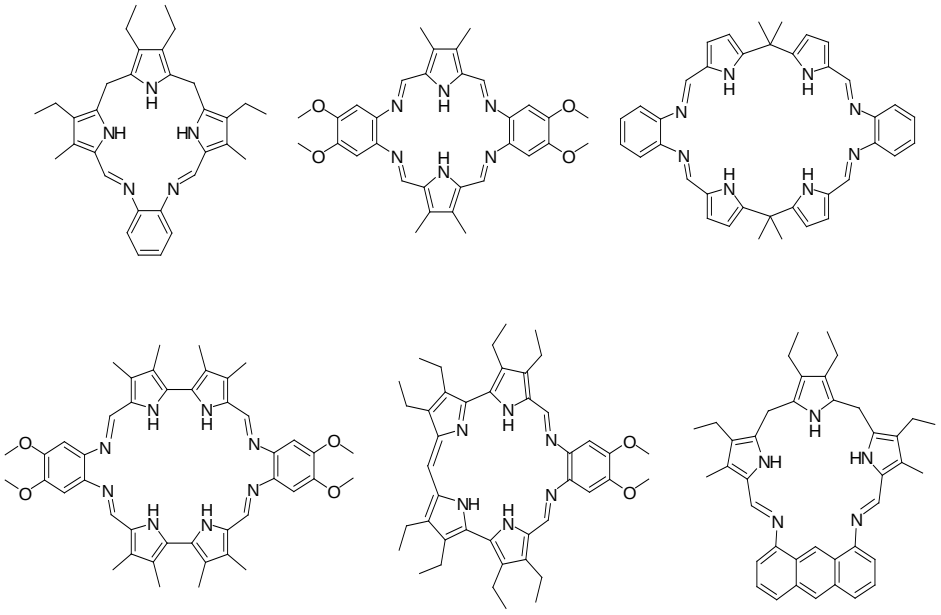


Figure 2: Examples of some expanded porphyrins

Research of these molecules has brought into light the study of some unique questions and properties of these molecules. Porphyrins are able to coordinate with many metals of the periodic table. Expanded porphyrins have an enlarged central core entrusting them with novel chelating properties. Some have been found to act as ligands to coordinate larger metals such as lanthanide and actinide species, notable is the discovery of texaphryin which was the first to show diverse metallation properties.[24] This property can be used in magnetic resonance imaging as a great contrast agent. Although the coordination chemistry of expanded porphyrins has been an area of great study, the unique property of these molecules to act as receptors for nuetral and anionic substrates is more relevant.

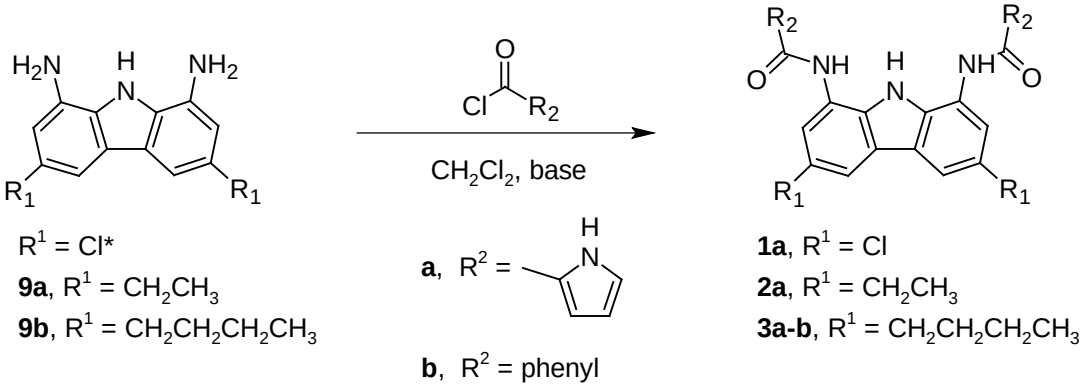
The increased conjugation of expanded porphyrins has been of increased study as a means to explore the limits of the Huckel definition of aromaticity and to answer what factors entail a fully conjugated molecule with characteristics that are either aromatic or antiaromatic. The increase of π-conjugation in these analogues has led to the presence of

absorbance bands that are more red-shifted than those of porphyrin. These properties have been of interest in various biomedical applications such as photodynamic therapy (PDT).[23]

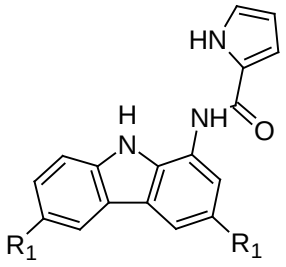
Many examples and classes of expanded porphyrins have been found over the years. Each class having its own unique properties and benefits. These molecules have been covered in various reviews throughout the years. [10, 21-23, 25, 26]

The idea of combining pyrrole amides with carbazole was inspired by the separate works of Gale and Jurczak.[27, 28] The Sessler group was the first to introduced carbazole into the literature[29] as a "pyrrole-like" binding motif, which has emerged recently as a fresh new scaffold for the construction of various new anion receptors. The size and rigidity of carbazole provide a macrocyclic system that is expanded relative to previous diamines. The fluorescent properties would be useful in detection of the binding event, and the greater acidity of the carbazole NH over the pyrrolic NH would hopefully lead to a stronger bond with the anionic guest. The group of Jurczak first introduced diaminocarbazole as a promising building block to prepare various diamide derivatives,[28] which were further elaborated to incoporate a diazo chromophore. Our current work incorporates the use of pyrrole amides along with carbazole to produce bis-pyrrole amidocarbazoles as new anion receptors with high carboxylate/halide selectivity. The 3,6 positions of the carbazole have been modified in an attempt to increase the binding of the amidocarbazole. The awareness of various interesting properties of expanded porphyrins has also led us to focus on the construction of new, rationally designed Schiff base oligopyrrole macrocycles (expanded porphyrins), with current

research involving the incorporation of carbazole as a key building block in the synthesis of the macrocycle.

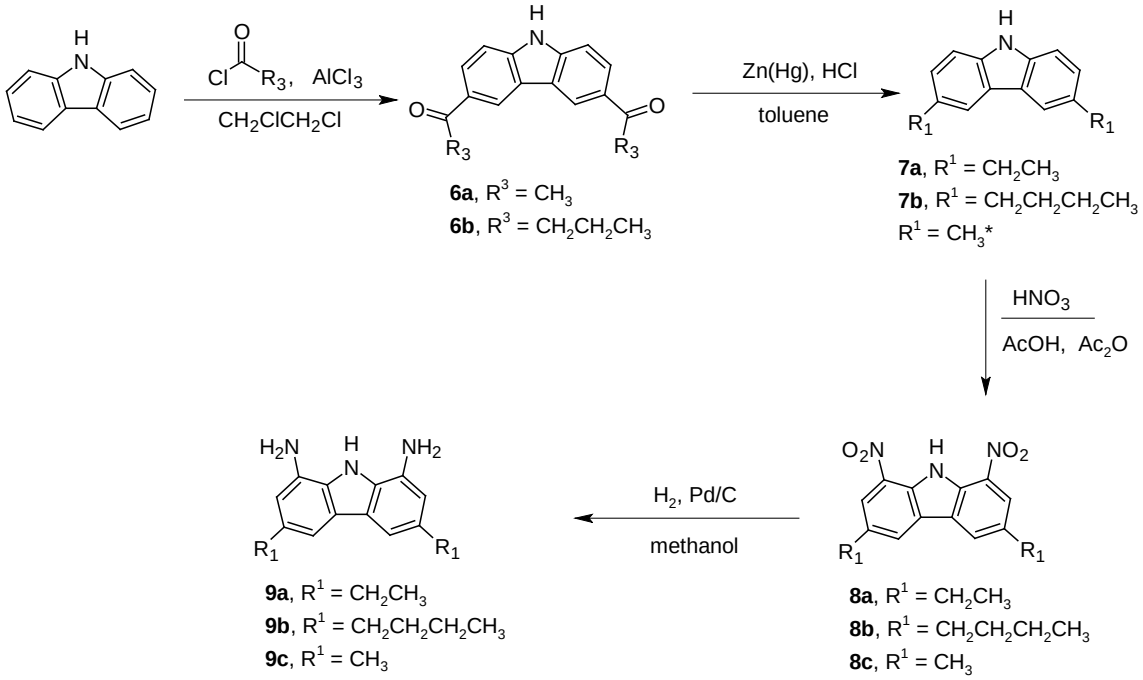


Amidocarbazole receptors **3a** and **3b** were synthesized via the reaction of the key precursor 1,8-diamino-3,6-dibutylcarbazole **9b** with excess pyrrolyl chloride and benzoyl chloride, respectively. Diamine **9b** was synthesized in four steps from carbazole. First di-acylation using butyryl chloride in dichloroethane afforded 3,6-dibutyrlcarbazole **6b** in 42% yield. Subsequent clemenson reduction yielded dibutylcarbazole **7b** in 50% yield. Nitration in acetic acid and acetic anhydride provided the dinitro compound **8b** and the mononitro derivative, which was able to be separated by column chromatography using CH_2Cl_2. Finally, palladium catalyzed hydrogenation of **8b** led to diamine **9b**. Alternatively, the mixture of mono- and dinitro products could be subjected to hydrogenation conditions to yield **8b** along with monoamine, which were isolated after column chromatography. The resulting diamine was then reacted with the appropriate acid chloride to yield receptors 1,8-di(pyrrolylamino)-3,6-dibutylcarbazole **3a** and 1,8-di(benzoylamino)-3,6-dibutylcarbazole **3b**.



4, $R^1 = CH_2CH_2CH_2CH_3$

Additionally, the isolated monoamine product was reacted with pyrrolyl chloride to yield 1-pyrrolylamino-3,6-dibutylcarbazole **4**. Similarly the amidocarbazole receptor **2a** was synthesized by the reaction of 1,8-diamino-3,6-diethylcarbazole with excess pyrrolyl chloride. The diamine was synthesized in the same manner as **9b** with di-acylation with ethyryl chloride, clemenson reduction, nitration, and palladium catalyzed hydrogenation. The 1,8-diamino-3,6-dichlorocarbazole from literature[28] was reacted with excess pyrrolyl chloride to generate the amidocarbazole receptor **1a**.



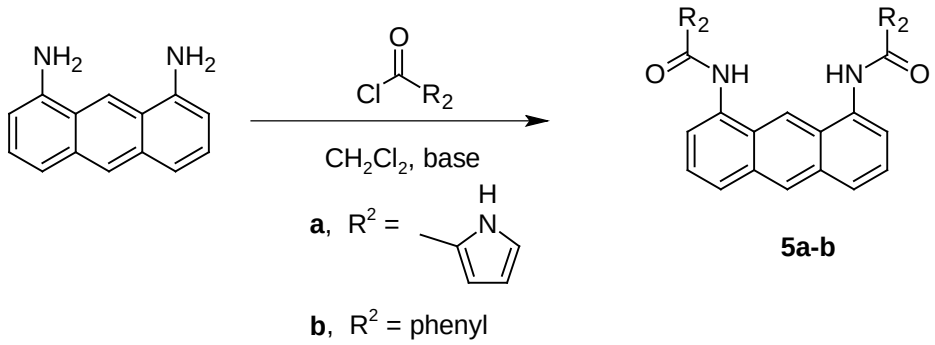
6a, $R^3 = CH_3$
6b, $R^3 = CH_2CH_2CH_3$

7a, $R^1 = CH_2CH_3$
7b, $R^1 = CH_2CH_2CH_2CH_3$
$R^1 = CH_3$*

8a, $R^1 = CH_2CH_3$
8b, $R^1 = CH_2CH_2CH_2CH_3$
8c, $R^1 = CH_3$

9a, $R^1 = CH_2CH_3$
9b, $R^1 = CH_2CH_2CH_2CH_3$
9c, $R^1 = CH_3$

Amidoanthracene receptors **5a** and **5b** were synthesized by the reaction of 1,9-diaminoanthracene with excess pyrrolyl chloride and benzoyl chloride, respectively. Synthesis for 1,9-diaminoanthracence can be found in prior literature.[30]



In the search for new Schiff base oligopyrrole macrocycles, we attempted to react the diaminocarbazoles with diformyltripyrrane (provided by Pharmacyclics). Additionally a new diamine was used with the R1 substituents as methyl groups. This molecule, 1,8-diamino-3,6-dimethylcarbazole **9c** was derived by bromination,[31] alkyl lithium substitution,[32] and then nitration (**8c**), and hyrdrogenation similar to **9a** and **9b**.

Experimental – Synthesis

3,6-diethyl-1,8-dinitrocarbazole (8a): 334 mg (1.5 mmol) of 3,6-diethylcarbazole was dissolved in 25mL of acetic anhydride and 10mL acetic acid. 0.57 mL (13.5 mmol) of nitric acid was added dropwise. The solution was then heated at 65ºC for 2hr, 75ºC for 1hr and 100ºC for 1hr. The solvent was evaporated under vacuum to yield 3,6-diethyl-1,8-dinitrocarbazole in >90% yield. ^{1}H NMR (400 MHz; $CDCl_3$) δ 11.22 (bs, 1H), 8.28 (s, 2H), 8.25 (s, 2H), 2.93 (q, J = 7.6 Hz, 4H), 1.40 (t, J = 7.4 Hz, 6H), ^{13}C NMR (100 MHz; $CDCl_3$) δ 137.2 (CH), 132.5 (CH), 132.2 (CH), 127.0 (CH), 125.9 (CH), 122.8 (CH), 28.5 (CH_2), 15.8 (CH_3). HRMS (ESI) calcd for $C_{16}H_{14}N_3O_4$ $[M-H]^-$: 312.0984, found: 312.0990.

1,8-diamino-3,6-diethylcarbazole (9a): To a solution of 3,6-dimethyl-1,8-dinitrocarbazole 250 mg (0.8 mmol) in acetonitrile (100 mL), a palladium catalyst in carbon was added. Gases from flask were removed by vacuum and the reaction was exposed to H2. The reaction was allowed to proceed overnight and the yellow solution turned black. The solution was filtered through celite and the solvent evaporated. The product was purified via column chromatography with 1% MeOH in CH_2Cl_2 (60% yield). ^{1}H NMR (600 MHz; DMSO-d_6) δ 10.1 (bs, 1H), 7.04 (d, J = 0.8, 2H), 6.46 (d, J = 0.8, 2H), 4.87 (bs, 4H), 2.62 (q, J = 7.6 Hz, 4H), 1.22 (t, J = 7.4 Hz, 6H), ^{13}C NMR (150 MHz; DMSO-d_6) δ 134.5 (CH), 133.0 (CH), 127.5 (CH), 123.5 (CH), 109.5 (CH), 107.4 (CH), 28.6 (CH_2), 16.5 (CH_3). HRMS (ESI) calcd for $C_{16}H_{20}N_3$ $[M+H]^+$: 254.1657, found: 254.1652.

1,8-dipyrrolamido-3,6-diethylcarbazole (2a): A solution of 1,8-diamino-3,6-diethylcarbazole (250 mg, 1 mmol) and pyrrolylchloride (300 mg, 2.31 mmol) in CH_2Cl_2 was stirred overnight. The solvent was evaporated and the product purified via column chromatography with 1% MeOH in CH_2Cl_2 (yield %). ^{1}H NMR (400 MHz; DMSO-d_6) δ 11.71 (bs, 2H), 10.20 (bs, 1H), 9.90 (bs, 2H), 7.78 (s, 2H), 7.45 (s, 2H), 7.13 (s, 2H), 6.99 (s, 2H), 6.20 (d, J = 3.2 Hz, 2H), 2.77 (q, J = 7.4 Hz, 4H), 1.30 (t, J = 7.0 Hz, 6H), ^{13}C NMR (100 MHz; DMSO-d_6) δ 159.4 (C=O), 134.4 (CH), 131. (CH), 126.0 (CH), 124.4 (CH), 122.6 (CH), 122.5 (CH), 120.4 (CH), 115.4 (CH), 111.8 (CH), 109.0 (CH), 28.4 (CH_2), 16.5 (CH_3). HRMS (ESI) calcd for $C_{26}H_{26}N_5O_2$ $[M+H]^+$: 440.2083, found: 440.2081; calcd for $C_{26}H_{25}N_5O_2Na$ $[M+Na]^+$: 462.1907, found: 462.1901.

3,6-dibutyrylcarbazole (6b): to a mixture of carbazole (30 g, 0.179 mol) and aluminum chloride (53 g) in 1,2-dichloroethane (500 mL) butyryl chloride (43 mL) was added

slowly. The reaction was then stirred at 65°C for 5 hrs, quenched with water and hcl solution, the organic solvents removed, and the remaining components redissolved in chloroform and subsequently crystallized from the solvent. To afford colorless crystals in 42 % yield. ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.79 (d, *J* = 1.6 Hz, 2H), 8.68 (bs, 1H), 8.15 (dd, J = 1.6 Hz, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 3.11 (t, J = 7.4 Hz, 4H), 1.86 (m, J = 7.4 Hz, 4H), 1.07 (t, J = 7.4 Hz, 6H), ^{13}C NMR (400 MHz; $CDCl_3$) δ 199.9 (C=O), 142.7 (CH), 130.1 (CH), 127.0 (CH), 123.3 (CH), 121.6 (CH), 110.8 (CH), 40.5 (CH_2), 18.2 (CH_2), 14.0 (CH_3). HRMS (ESI) calcd for $C_{20}H_{20}NO_2$ $[M-H]^-$: 306.1493, found: 306.1500.

3,6-dibutylcarbazole (7b): Zinc (200g) and mercuric chloride (20g) were added to 400 ml water containing concentrated hydrochloric acid (26 mL), after stirring for 20 minutes more concentrated hydrochloric acid was added slowly (400 mL) followed by 3,6-dibutyrylcarbazole (16 g, 52 mmol). Toluene (200 mL) was added to the reaction mixture, which was then refluxed for 96 hrs. The toluene layer was separated and all volatiles were evaporated. The light brown solid was purified by column chromatography in 2:1 hexanes/DCM to yield in 50%. ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.89 (s, 2H), 7.77 (bs, 1H), 7.28 (dd, J = 8 Hz and 0.4 Hz, 2H), 7.24 (dd, J = 8 Hz and 1.2 Hz), 2.81 (t, J = 7.8 Hz, 4H), 1.74 (m, J = 7.6 Hz, 4H), 1.44 (m, J = 7.5 Hz, 4H), 1.00 (t, J = 7.4 Hz, 6H), ^{13}C NMR (400 MHz; $CDCl_3$) δ 138.2 (CH), 133.7 (CH), 126.4 (CH), 123.3 (CH), 119.5 (CH), 110.2 (CH), 35.7 (CH_2), 34.5 (CH_2), 22.4 (CH_2), 14.0 (CH_3). HRMS (ESI) calcd for $C_{20}H_{24}N$ $[M-H]^-$: 278.1912, found: 278.1914.

3,6-dibutyl-1,8-dinitrocarbazole (8b): 3,6-dibutylcarbazole (204 mg, 0.7 mmol) was dissolved in acetic anhydride (25 mL) and acetic acid (10 mL). Nitric acid (0.19 mL, 4.5

mmol) was added dropwise. The solution was then heated at 65 ºC for 2 hr, 75 ºC for 1 hr and 100 ºC for 1 hr. The solvent was evaporated and product was purified via column chromatography with CH_2Cl_2 to yield 3,6-dibutyl-1,8-dinitrocarbazole in 55% yield. ^{1}H NMR (400 MHz; $CDCl_3$) δ 11.20 (bs, 1H), 8.24 (s, 2H), 8.22 (s, 2H), 2.88 (t, J = 7.6 Hz, 4H), 1.74 (m, J = 7.6 Hz, 4H), 1.43 (m, J = 7.5 Hz, 4H), 0.98 (t, J = 7.4 Hz, 6H), ^{13}C NMR (100 MHz; $CDCl_3$) δ 135.9 (CH), 132.5 (CH), 132.3 (CH), 127.5 (CH), 125.9 (CH), 123.3 (CH), 35.2 (CH_2), 33.9 (CH_2), 22.2 (CH_2), 13.9 (CH_3). HRMS (ESI) calcd for $C_{20}H_{22}N_3O_4$ $[M-H]^-$: 368.1609, found: 368.1616.

1,8-diamino-3,6-dibutylcarbazole (9b): To a solution of 3,6-dimethyl-1,8-dinitrocarbazole (200 mg, 0.54 mmol) in acetonitrile (200mL), 10 % palladium on carbon was added. The air in the flask was evacuated, and the reaction was exposed to H_2. The reaction was allowed to proceed overnight and the yellow solution turned black. The solution was filtered through celite and the solvent evaporated. The product was purified via column chromatography with 1-2% MeOH in CH_2Cl_2 to achieve a 79% yield (132 mg). ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.87 (bs, 1H), 7.33 (s, 2H), 6.13 (d,J = 1.2 Hz, 2H), 3.13 (bs, 4H), 2.69 (t, J = 7.6 Hz, 4H), 1.66 (m, J = 7.6 Hz, 4H), 1.38 (m, J = 7.5 Hz, 4H), 0.94 (t, J = 7.4 Hz, 6H), ^{13}C NMR (100 MHz; $CDCl_3$) δ 134.7 (CH), 130.1 (CH), 129.2 (CH), 124.7 (CH), 113.3 (CH), 111.67 (CH), 35.7 (CH_2), 34.4 (CH_2), 22.4 (CH_2), 14.0 (CH_3). HRMS (ESI) calcd for $C_{20}H_{28}N_3$ $[M+H]^+$: 310.2284, found: 310.2277.

1-amino-3,6-dibutylcarbazole: 1-nitro-3,6-dibutylcarbazole (side product from nitration of **7b**) was dissolved in acetonitrile and 10 % palladium on carbon was added. The air in the flask was evacuated, and the reaction was exposed to H_2. The reaction was allowed to proceed overnight and the yellow solution turned black. The solution was filtered through

celite and the solvent evaporated. ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.8 (s, 1H), 7.71 (bs, 1H), 7.39 (s, 1H), 7.30 (d, J = 8.4 Hz, 1H), 7.19 (dd, J = 8.0 Hz, J = 1.4 Hz, 1H), 6.63 (s, 1H), 3.16 (bs 2H), 2.76 (t, J = 7.6 Hz 2H), 7.69 (t, J = 7.6 Hz 2H), 1.68 (m, 4H), 1.40 (m, 4H), 0.95 (m, 6H) ^{13}C NMR (90 MHz; $CDCl_3$) δ 138.5 (CH), 135.0 (CH), 134.0 (CH), 129.9 (CH), 129.0 (CH), 126.3 (CH), 124.5 (CH), 124.3 (CH), 119.7 (CH), 113.6 (CH), 111.5 (CH), 110.7 (CH), 35.8 (CH_2), 35.7 (CH_2), 34.5 (CH_2), 34.4 (CH_2), 22.4 (CH_2), 22.4 (CH_2), 14.1 (CH_3), 14.1 (CH_3). HRMS (ESI) calcd for $C_{20}H_{27}N_2$ $[M+H]^+$: 295.2171, found: 295.2169.

1,8-diamidopyrrolyl-3,6-dibutylcarbazole (3a): A solution of 1,8-diamino-3,6-dibutylcarbazole (500 mg, 1.62 mmol) and pyrrolyl chloride (800 mg) in CH_2Cl_2 was stirred overnight. The solvent was evaporated and the product purified via column chromatography with 1% MeOH in CH_2Cl_2. The product was precipitated from CH_2Cl_2 with a 78 %. ^{1}H NMR (400 MHz; DMSO- d_6) δ 11.73 (bs, 2H), 10.20 (bs, 1H), 9.92 (bs, 2H), 7.77 (s, 2H), 7.44 (s, 2H), 7.15 (s, 2H), 7.00 (s, 2H), 6.22 (d, J = 3.2 Hz, 2H), 2.76 (t, J = 7.4 Hz, 4H), 1.68 (m, J = 7.2 Hz, 4H), 1.39 (m, J = 7.5 Hz, 4H), 0.95 (t, J = 7.0 Hz, 6H), ^{13}C NMR (150 MHz; DMSO-d_6) δ 158.3 (C=O), 132.8 (CH), 131.7 (CH), 126.0 (CH), 124.3 (CH), 122.46 (CH), 122.43 (CH), 120.7 (CH), 115.9 (CH), 111.7 (CH), 108.9 (CH), 34.9 (CH_2), 33.8 (CH_2), 21.8 (CH_2), 13.9 (CH_3). HRMS (ESI) calcd for $C_{30}H_{33}N_5O_2Na$ $[M+Na]^+$: 518.2538, found: 518.2527.

1-amidopyrrolyl-3,6-dibutylcarbazole(4): A solution of 1-amino-3,6-dibutylcarbazole (90 mg) and pyrrolyl chloride in CH_2Cl_2 was stirred overnight. The solvent was evaporated and the product purified via column chromatography with CH_2Cl_2 (yield 85%) ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.70 (bs, 1H), 9.24 (bs, 1H), 7.90 (s, 1H), 7.84 (s,

1H), 7.75 (s, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.22 (dd, J = 8.0 Hz, J = 1.6 Hz, 1H), 6.98 (m, 1H), 6.92 (d, J = 1.2 Hz, 1H), 6.80 (bs, 1H), 6.26 (m, 1H), 2.77 (q, J = 8.0 Hz, 4H), 1.69 (m, 4H), 1.41 (m, 4H), 0.96 (m, 6H). ^{13}C NMR (100 MHz; $CDCl_3$) δ 158.9 (CH), 138.9 (CH), 133.9 (CH), 133.8 (CH), 131.5 (CH), 126.9 (CH), 126.3 (CH), 125.4 (CH), 123.5 (CH), 122.7 (CH), 120.9 (CH), 119.5 (CH), 118.6 (CH), 117.2 (CH), 111.1 (CH), 110.5 (CH), 110.3 (CH), 35.7 (CH_2), 35.4 (CH_2), 34.5 (CH_2), 34.3 (CH_2), 22.4 (CH_2), 22.4 (CH_2), 14.0 (CH_3). HRMS (ESI) calcd for $C_{25}H_{28}N_3O$ $[M-H]^-$: 386.2234, found: 386.2238.

1,8-diphenylamido-3,6-dibutylcarbazole (3b). A solution of 1,8-diamino-3,6-dibutylcarbazole (90 mg, 0.3 mmol) and benzoyl chloride in CH_2Cl_2 was stirred overnight. The solvent was evaporated. ^{1}H NMR (400 MHz; DMSO-d_6) δ 10.32 (bs, 3H), 8.02 (d, J = 7.2, 4H), 7.79 (s, 2H), 7.61-7.51 (m, 8H), 2.74 (t, J = 7.4 Hz, 4H), 1.67 (m, J = 7.2 Hz, 4H), 1.37 (m, J = 7.5 Hz, 4H), 0.93 (t, J = 7.0 Hz, 6H), ^{13}C NMR (100 MHz; DMSO-d_6) δ 165.7 (CH), 134.8 (CH), 132.9 (CH), 132.0 (CH), 131.7 (CH), 128.4 (CH), 128.0 (CH), 124.4 (CH), 122.6 (CH), 121.2 (CH), 116.4 (CH), 35.0 (CH_2), 33.9 (CH_2), 21.9 (CH_2), 13.9 (CH_3). HRMS (ESI) calcd for $C_{34}H_{35}N_3O_2Na$ $[M+Na]^+$: 540.2634, found: 540.2622.

1,8-dipyrroloamido-3,6-dichlorocarbazole (1a): In CH_2Cl_2 (20 mL) 1,8-diamino-3,6-dichlorocarbazole (160 mg, 0.6 mmol) and pyrrole-2-carboxylic acid chloride (300 mg) were dissolved. The mixture was stirred for 15 hours then quenched with methanol (20 mL). All volatile solvents were removed under vacuum and the product was purified by column chromatography, ethyl acetate to afford a >90 % yield. ^{1}H NMR (400 MHz; DMSO- d_6) δ 11.80 (bs, 2H), 10.95 (bs, 1H), 10.02 (bs, 2H), 8.13 (s, 2H), 7.78 (s, 2H),

7.14 (s, 2H), 7.01 (s, 2H), 6.22 (d, J = 0.8 Hz, 2H). ^{13}C NMR (100 MHz; DMSO-d_6) δ 159.5 (C=O), 131.5 (CH), 125.5 (CH), 124.3 (CH), 124.2 (CH), 123.2 (CH), 123.1 (CH), 119.9 (CH), 116.4 (CH), 112.3 (CH), 109.1 (CH). HRMS (ESI) calcd for $C_{22}H_{14}N_5O_2Cl_2$ $[M-H]^-$: 450.0527, found: 450.0530.

1,9-dipyrroloamidoanthracene (5a). In CH_2Cl_2 (40 mL) 1,9-diaminoanthracene (710 mg, 3.4 mmol) and pyrrole-2-carboxylic acid chloride (1.4 g) were dissolved. The mixture was stirred for 15 hours then quenched with methanol (40 mL). All volatile solvents were removed under vacuum yielding a green solid. The solid was washed with consecutive aliquats of methanol and water to yield a light green solid, which was dried under vacuum to afford a 71 % yield. ^{1}H NMR (500 MHz; DMSO-d_6) δ 11.70 (bs, 2H), 10.04 (s, 2H), 9.00 (s, 1H), 8.64 (s, 1H), 7.96 (d, J = 6.8, 2H), 7.81 (d, J = 5.6, 2H), 7.56 (dd, J = 6.8 and J = 1.2, 2H), 7.21 (m, 2H), 6.99 (m, 2H), 6.19 (m, 2H). ^{13}C NMR (125 MHz; DMSO-d_6) δ 159.8 (C=O), 133.5 (CH), 131.8 (CH), 126.6 (CH), 126.4 (CH), 126.1 (CH), 125.5 (CH), 125.0 (CH), 122.4 (CH), 121.2 (CH), 117.1 (CH), 111.8 (CH), 108.9 (CH). HRMS (ESI) calcd for $C_{24}H_{19}N_4O_2$ $[M+H]^+$: 395.1509, found: 395.1503; calcd for $C_{24}H_{18}N_4O_2Na$ $[M+Na]^+$: 417.1327, found: 417.1322.

1,9-diphenylamidoanthracene (5b). In CH_2Cl_2 (25 mL) 1,9-diaminoanthracene (110 mg, 0.53 mmol), benzoyl chloride (350 uL), and pyridine (200 uL) were dissolved. The mixture was stirred for 15 hours then quenched with water (50 mL) causing a white precipitate. The precipitate was filtered and wash successively with water and methanol. The white solid was dried under vacuum to afford a 93 % yield. ^{1}H NMR (500 MHz; DMSO-d_6) δ 10.60 (bs, 2H), 8.92 (s, 1H), 8.70 (s, 1H), 8.06-8.01 (m, 6H), 7.70 (d, J = 6.8 Hz, 2H), 7.61-7.57 (m, 4H), 7.41 (t, J = 7.8 Hz, 4H). ^{13}C NMR (125 MHz; DMSO-d_6)

δ 166.3 (C=O), 134.8 (CH), 133.9 (CH), 131.8 (CH), 131.4 (CH), 128.3 (CH), 127.8 (CH), 127.3 (CH), 126.8 (CH), 126.2 (CH), 125.4 (CH), 122.9 (CH), 117.97 (CH). HRMS (ESI) calcd for $C_{28}H_{19}N_2O_2$ $[M-H]^-$: 415.1445, found: 415.1452.

3,6-Dimethyl-1,8-dinitrocarbazole (8c) 293 mg (1.5 mmol) dimethylcarbazole was dissolved with 25mL acetic anhydride and 10 mL of acetic acid. 200uL of >90% HNO3 was added to the solution. The reaction was stirred at 65ºC for 3 hr, at 75ºC for 1 hr, and at 100ºC fro 1 hr. The resulting mixture was quenched with 10mL in H2O. The solution was filtered and washed with H2O. The solution was dried over vacuum. The light yellow solid was dissolved in 50mL DCM. The resulting solution was filtered, dried with NaSO4, and filtered. The solvent was removed on a rotary evaporator.

1,8-Diamino-3,6-dimethylcarbazole (9c) 165 mg (0.58 mmol) of dimethyldinitrocarbazole was dissolved in 75mL of methanol. Air and gases were removed using argon and hydration was done using a Palladium catalyst and H2 gas. The reaction was stirred overnight and filter through celite and washed with methanol to remove the palladium. The solvent was removed using a rotary evaporator.

Discussion – Binding Studies

NMR titration studies were performed in DMSO, with 4-5 mM host concentrations, to be able to effectively evaluate and compare the phenyl and pyrrole derivatives as well as the differences between the carbazole and the anthracene scaffolds. All compounds show increased selectivity for higher order structures, but have notable differences in binding patterns.

Ka (M^{-1})	Guest						
Host	1a	2a	3a	3b	4	5a	5b
Chloride	68	>50	>50	>50	280	80	83
Benzoate	2500	770	1600	790	190	310	65
Phosphate	4700	1700	2000	1400	880	2600	160

Table 1: Association constants of amidic NH

Compound **5a** was found to bind to chloride weakly while the binding of oxoanions was greater. **5a** was most selective for phosphate with a Ka of 2600 M^{-1}, almost 10 times stronger than benzoate. However the addition of the of phenyl groups and the loss of the pyrrolic NH in **5b** reduced the binding affinity for both oxoanions. There was no difference between benzoate and chloride, which had a Ka in the 10s, while the binding for phosphate was reduced to 160 M^{-1}. The two coordinating NHs from the pyrrole are very important to stabilizing oxoanions.

Compounds **3a** and **3b** showed similar trends as seen with the anthracene compounds, however the binding was selective for oxoanions in general and the reduction was less when the pyrrole groups were replaced. **3a** showed less selectivity for the phosphate over benzoate. Both these oxoanions were bound as strongly as the pyrrolyl anthracence bound phosphate. When the pyrrole groups were replaced the binding of benzoate was reduced by a factor of 2 (1600 M^{-1} to 790 M^{-1}) and the phosphate only by a factor of ¼ (2000 M^{-1} to 1400 M^{-1}). The carbazole NH provides a advantage in binding with oxoanions as compared to the antracene moiety especially in the absence of the pyrrolic NH donors.

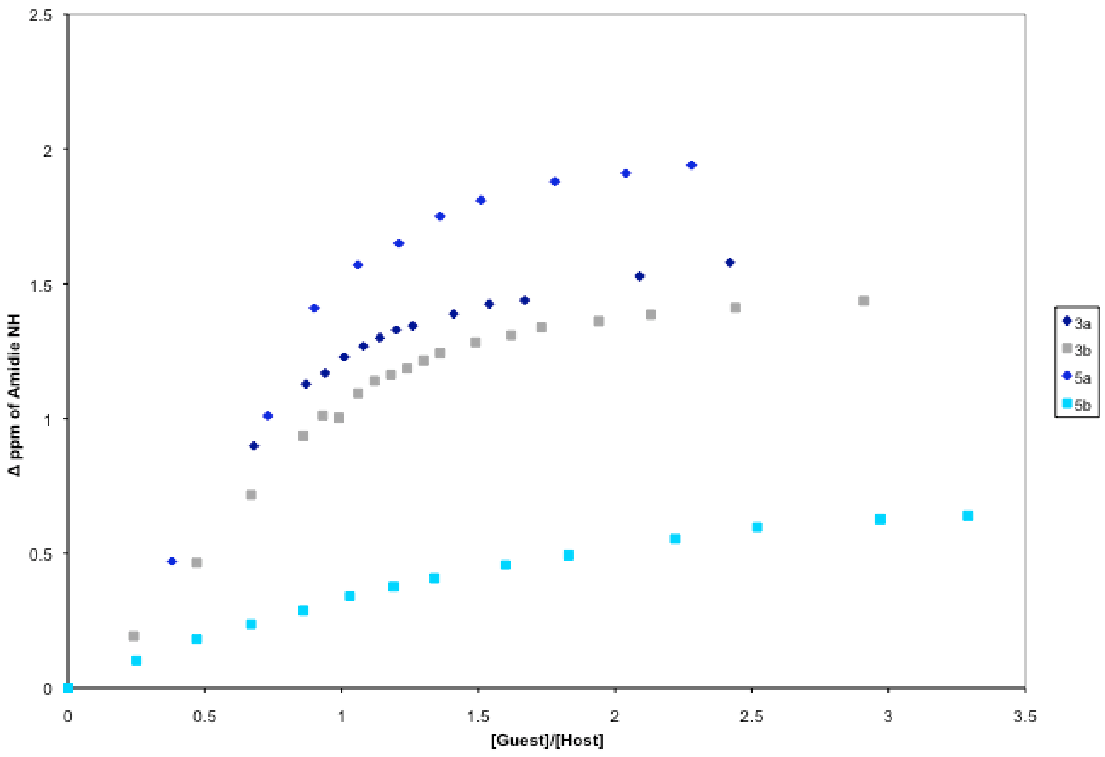


Figure 3: Comparison of binding between receptors 3 and 5 with phosphate

As both carbazole and anthracene are known for their flourescent properties, a qualitative study was done with a range of ions. This property of the receptor would allow for a visual confirmation of binding.

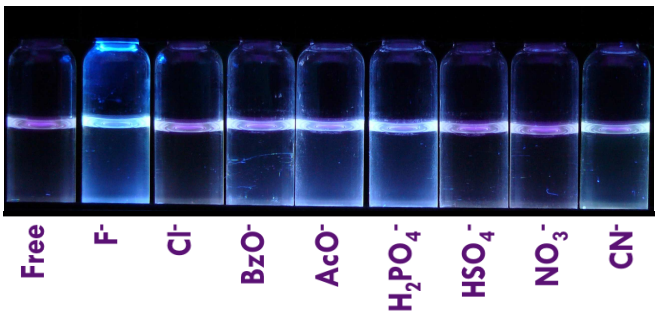


Figure 4: Fluorescence of 3a with various anions

In regards to the 3,6 positions of the carbazole, 3 molecules were compared, **1a**, **2a**, and **3a**. It seems that the chlorine substituents allow for the strongest binding with the

benzoate and phosphate (2500 M^{-1} and 4700 M^{-1} Ka respectively) and also shows the most selectivity. This might be attributed to the electronegativity of the chlorine pulling away from the macrocycle making the NH molecules more acidic. Butyl groups generate stronger bonds than ethyl groups but provide less specificity between benzoate and phosphate. In an attempt to further study the affect of the alkyl chain length on binding strenght and selectivity, we tried to synthesize the diaminocarbazole with octyl groups in the 3,6 positions. However, the large alkyl chains generated problems with solubility and created a difficult synthesis.

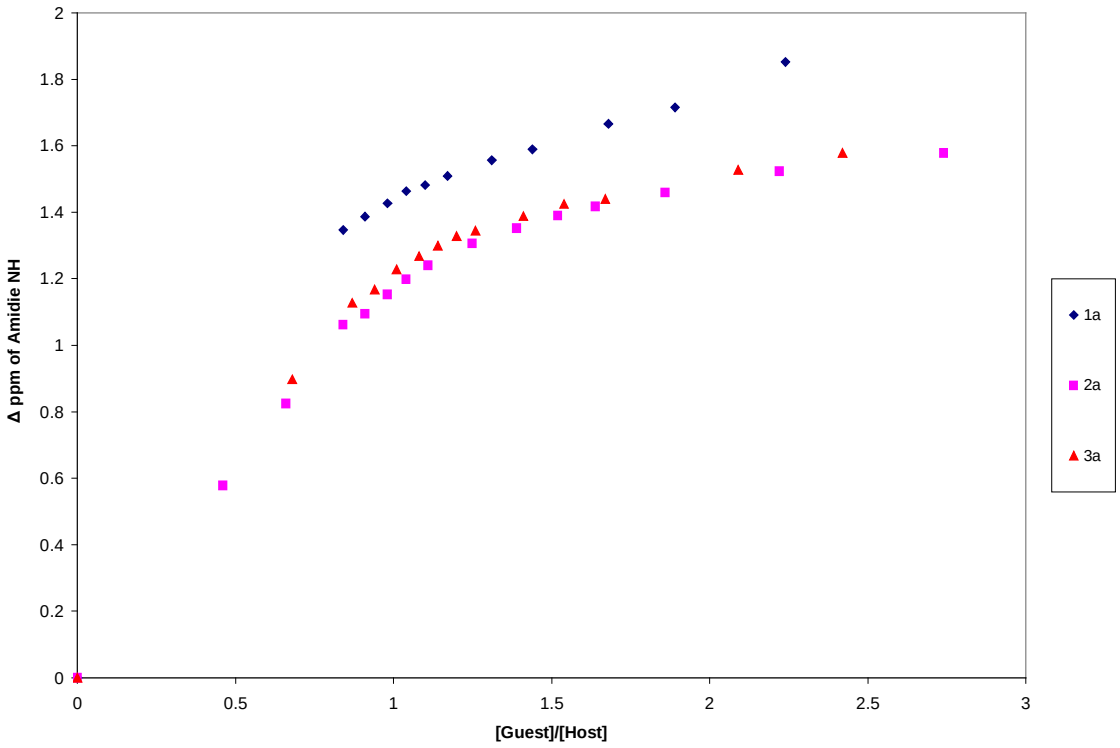


Figure 5: Comparison of binding of bisamidopyrrolyl carbazole receptors with phosphate

An interesting observation from the synthesis of the mono-amidopyrrolyl-3,6-dibutylcarbazole, revealed the importance of steric hinderance in selectivity of the anion.

An increase can noted in the binding of chloride by **3a** and a reduction in the binding of the other two anions as opposed to **4**.As noted the loss of a pyrrolic NH greatly reduced the binding affinity for all oxoanions as the ions can move easier. However, the opening of the structure allowed for the circular chloride ion to better fit into the groove increasing the receptors afinity for the ion.

X-Ray quality crystals of 3a and 3b were obtained by slow evaporation of ethyl acetate with the compounds. This shows proof the binding of the receptor in a solid state structure along with solution. However we do not believe this is a represenation of binding in solution as the amide NH are binding with nearby receptors in formation of the crystals.

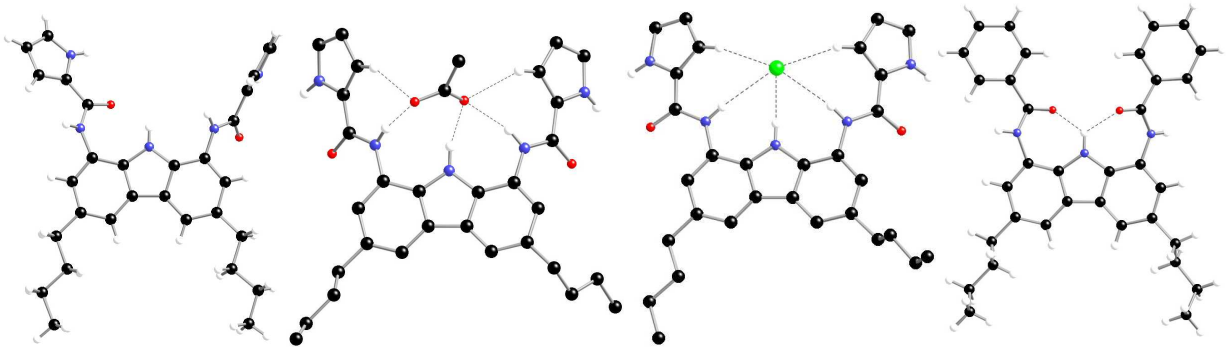


Figure 6: X-Ray crystal structures of 3a alone, with chloride, and acetate respectively

New “expanded” porphyrins were attempted to be constructed from the condensation of diaminocarbazoles **9** and diformyltripyrrane. Prior work in our lab has successfully shown the synthesis and characterization of the macrocycle created with 1,8-diamino-3,6-dichlorocarbazole. It also showed increased binding for oxoanions over single circular ions similar to the binding of the amidopyrroles. The macrocycle showed 10^4 M^{-1} Ka with oxoanions but either no change or very small change (Ka < 10) with chloride and other circular ions. Also the molecule could be readily oxidized to afford a

fully conjugated molecule that could be used to bind cations. However, the solubility of this molecule was an inconvenience, making it difficult to crystalize and work with. Thus the use of alkyl groups at 3,6 positions are being used in the hope of increasing solubility while maintaining comparable binding properties. Work is still being done in this area.

We were able to create novel amidopyrrole receptors to bind anions. These molecules have shown an increased affinity for oxoanions with many receptors binding phosphate over benzoate. The carbazole NH and the pyrrolic NHs are important in the binding of anions, however in the presence of the carbazole NH the loss of the pyrrolic NH's doesn't tremendously affect the binding to phosphate, actually making the receptor more selective. This provides an interesting characteristic as substituted phenyl groups might be used without affecting the binding of the receptor severely. This might allow for the creation of larger strucutres with the receptor included. Thus evidence shows the carbazole NH can provide a key advantage in anion binding.

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