

## CHAPTER IV

### CONCLUSION

Polyethylene glycol derivatives containing urea or thiourea moieties, **5a**, **5b** and **5c**, have been synthesized. In the first step, the nucleophilic substitution reaction of pyrocatechole with  $\text{CH}_3\text{I}$  in the presence of  $\text{K}_2\text{CO}_3$  yielded *o*-methoxy phenol **1a** in 85% yield. A nitration reaction of **1a** in  $\text{HNO}_3$  and  $\text{CH}_3\text{COOH}$  resulted in the major product 2-methoxy-4-nitrophenol **2b**, in 46% yield and the minor product, 2-methoxy-6-nitrophenol **2a**, in 8% yield. Then, a coupling reaction of **2a** with tetraethylene glycol ditosylate gave tetraetylenoxy derivative **3a** in 85% yield. The nitro substituents of **3a** were reduced by Raney Ni and  $\text{N}_2\text{H}_4 \cdot 2\text{H}_2\text{O}$  to obtain **4a** in quantitative yield. Subsequently, addition of hexylisocyanate, *p*-nitrothiocyanate, and phenylisocyanate resulted in **5a**, **5b**, and **5c** in 68%, 48%, and 90% yields, respectively.

$^1\text{H-NMR}$  titrations showed that **5a** were able to form complexes with  $\text{Na}^+$  and  $\text{K}^+$  ion in a 1:1 ratio. However, the ionic radius of  $\text{Na}^+$  is more suitable for the glyme-5 moiety of ligand **5a**. In the case of anion complexation studies, we found that the bis-urea unit of ligand **5a** selectively bound  $\text{H}_2\text{PO}_4^-$  via hydrogen bonding interactions. The anion binding trend of ligand **5a** for other anions was in the order of  $\text{AcO}^- > \text{NO}_3^- \sim \text{BzO}^- > \text{Cl}^- > \text{Br}^- > \text{I}^-$ . These can be rationalized based on anion geometry, multivalent sites of anion for hydrogen bonding interactions with the host molecule and also anion basicity. In complexation studies of ligand **5a** towards various anions in the presence of 2 equivalents of  $\text{NaClO}_4$ ,  $^1\text{H-NMR}$  titration plots of **5a**. $\text{Na}^+$  with  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{NO}_3^-$ ,  $\text{AcO}^-$  and  $\text{BzO}^-$  displayed a sigmoid curve. In addition, the anion binding constant in the case of  $\text{H}_2\text{PO}_4^-$  was less than expected. This evidence suggested that  $\text{Na}^+$  inhibited the anion affinity of **5a** by forming ion pair. However, in the case of  $\text{I}^-$ ,  $\text{Na}^+$  induced a rigid preorganized structure of the bis urea moieties of ligand **5a** for binding  $\text{I}^-$  and enhance the anion binding ability of ligand **5a** via cooperative electrostatic interactions. On the other hand,  $\text{Na}^+$  complexation affinities of ligand **5a** diminished in the presence of 1.2 equivalents of  $\text{Cl}^-$ ,  $\text{Br}^-$  and  $\text{I}^-$  and could not be determined in the presence of 1.2 equivalents of  $\text{BzO}^-$ ,  $\text{AcO}^-$  and  $\text{H}_2\text{PO}_4^-$ . Hence, the stronger the anion complexation, the smaller  $\text{Na}^+$  binding ability was obtained. This is probably due to the rigid structure of anion complexes, causing the

poly(oxyethylene) glycol moiety of ligand **5a** not flexible enough and unfavorable to arrange themselves for binding  $\text{Na}^+$ .

UV-vis titrations between ligand **5b** and metal ions in DMSO showed notable changes in spectra by addition of excess metal ions. These results suggested that the etheric moieties of ligand **5b** were in gauche conformation and not preorganized to capture and to detect cation. In the case of anion complexation abilities of ligand **5b**, the order of formation constants for 1:1 complexes is  $\text{NO}_3^- > \text{Br}^- \sim \text{Cl}^-$  and for 1:2 complexes is  $\text{BzO}^- > \text{H}_2\text{PO}_4^- \gg \text{I}^-$ . This agreed with results obtained by using  $^1\text{H-NMR}$  titrations. In addition, upon addition of  $\text{H}_2\text{PO}_4^-$ ,  $\text{BzO}^-$  and  $\text{AcO}^-$ , the characteristic absorption band of ligand **5b** at 361 nm decreased and moved to longer wavelength concomitant with the gradual increase of a new band around 459 nm and the solution color of ligand **5b** in DMSO changed from light yellow to deep-red orange. This can be detected by the naked eye and ligand **5b** may possibly be used as a naked eye anion sensor. On the other hand, anion binding abilities of ligand **5b** in the presence of alkali metal ion ( $\text{Na}^+$  or  $\text{K}^+$ ) were enhanced in cases of **5b**. $\text{K}^+/\text{NO}_3^-$ , **5b**. $\text{Na}^+/\text{NO}_3^-$  and **5b**. $\text{K}^+/\text{I}^-$  and decreased in cases of **5b**. $\text{Na}^+/\text{Cl}^-$ , **5b**. $\text{K}^+/\text{Cl}^-$ , **5b**. $\text{Na}^+/\text{Br}^-$ , **5b**. $\text{K}^+/\text{Br}^-$ , **5b**. $\text{Na}^+/\text{I}^-$ , **5b**. $\text{Na}^+/\text{BzO}^-$ , **5b**. $\text{K}^+/\text{BzO}^-$  and **5b**. $\text{Na}^+/\text{H}_2\text{PO}_4^-$ . These results can be attributed to the nature of the **5b**.alkali metal ion complexes and anions as well as ion pairing ability between alkali metal ions and anions. In alkali metal complexation studies of ligand **5b** in the presence of anions such as  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{I}^-$ ,  $\text{H}_2\text{PO}_4^-$ , the pseudocyclic ring of the poly(oxyethylene) glycol moiety is not organized for binding alkali metal ions. These anions probably departed from coordinated thiourea units inducing by added alkali metal ions resulting in ion pair formation that inhibited an alkali metal ion to coordinate oxyethylene glycol moieties of ligand **5b**. The remarkable case of **5b**. $\text{H}_2\text{PO}_4^-$ /alkali metal ions confirm that ion pairing occurred in these systems as the evidence of reversion of color and their spectra to those of free ligand **5b**. However, the alkali binding abilities increased in the cases of the strong and appropriate anion complexes such as  $\text{NO}_3^-$  and  $\text{BzO}^-$  that could diminish the ion pair effect and induce an alkali metal ion to coordinate and to stabilize by a secondary interaction.

Electrochemical studies using cyclic voltammetry and square wave voltammetry showed a new wave at -210 mV. However, the redox waves of original free ligand **5b** shift insignificantly. We suggested that  $\text{Na}^+$  did not probably bind the ethyleneoxy to form pseudocyclic crown ether ring but mainly interacted with the

reduced nitro groups of ligand **5b** and formed a more stable complex. This may be applied to the fabrication of a molecular device to recognize  $\text{Na}^+$ . In the case of anion complexation studies, voltammograms displayed negligible change upon addition of  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{I}^-$  and  $\text{NO}_3^-$ . However, a redox wave around -1418 mV shifted remarkably to a more positive potential upon addition of 2 equivalents of  $\text{H}_2\text{PO}_4^-$ ,  $\text{BzO}^-$  and  $\text{AcO}^-$  which suggested 1:2 complexes as observed in UV-vis titrations. The more cathodic shift suggested that nitrophenyl moieties of ligand **5b** were destabilized by the coulombic repulsion between strongly coordinated anionic guests by the thiourea units and reduced nitro moieties. In the complexation studies of bifunctional ligand **5b** in the presence of 2 equivalents of  $\text{NaClO}_4$  toward chosen anions such as  $\text{H}_2\text{PO}_4^-$ ,  $\text{BzO}^-$  and  $\text{AcO}^-$ , we obtained the two significant characteristics: i) the initial wave around -2000 mV, indicated interactions between  $\text{Na}^+$  and the reduced nitro residues, shifted cathodically and completely disappeared upon increasing amount of such anions that showed clearly in the case of **5b**. $\text{Na}^+/\text{H}_2\text{PO}_4^-$ . ii) The redox wave  $\text{Ic}$  in all cases exhibited drastic shifts to negative potential. This indicated the occurring of ion pairing between  $\text{Na}^+$  and anions and the high ability of anion complexation caused the nitro residues to be less reducible. Upon addition of  $\text{Na}^+$  to the electrochemical solution of **5b**.anion, the initial cathodic waves at 1586 mV, -1534 mV and -1628 mV, presenting in the interaction between the reduced nitro thiourea moieties and  $\text{H}_2\text{PO}_4^-$ ,  $\text{BzO}^-$  and  $\text{AcO}^-$  respectively, shifted reversely to the original potential of free ligand **5b**. Especially, the cathodic wave of **5b**. $\text{H}_2\text{PO}_4^-/\text{Na}^+$  completely changed to the original potential. Added  $\text{Na}^+$  may form ion pair with anions and diminish electron density from anions. Therefore, the presence of the ion pair makes the nitro aromatic residues be reduced more easily.

**Suggestion for future works**

From all obtained results and discussion, future works should be focused on;

1. X-ray crystal structures of ligands **5a** and **5b** and their complexes with various ionic guests should be obtained in order to understand the structure of the synthetic receptors and their coordination chemistry.
2. Use of other techniques such as fluorescence, calorimetric titrations and solvent extraction with various ionic guests should be investigated to obtain complexation constants and structural behaviors upon complexation.
3. Synthesize macrocyclic crown ether containing bis urea/thiourea that can reduce the ion-pair effect.
4. The possibility of using ligand **5b** as a molecular device should be explored.



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