ISSN: 2186-8476, ISSN: 2186-8468 Print
Vol. 1. No. 2. June 2012

SYNTHESES AND CHARACTERISATION OF MOLECULAR TWEESORS FOR THE RECOGNITION OF GUEST SUBSTRATES

R. C. Jagessar

Department of Chemistry, University of Guyana,
Turkeyen campus, Greater Georgetown,
SOUTH AMERICA
raymondjagessar@yahoo.com

ABSTRACT

Two novel amido anion receptors were synthesized from building block 3,3' methylene diamine and was characterized via the techniques of ^{1}H NMR, ^{13}C NMR, DEPT- 135 spectroscopy, ^{1}H-^{1}H COSY, HMQC and HMBC. Preliminary anion binding studies via $^{1}HNMR$ spectroscopy revealed complexation with phosphate anions in the highly competitive solvent, d_6-DMSO.

This paper focuses on the syntheses, characterization and preliminary anion binding studies of molecular clef type receptors (4) and (5) incorporating the amide, -HNCO- units. These receptors are built on the molecular scaffold of 3,3' methylene diamine and present convergent binding sites to anionic substrates.

Keywords: molecular scaffold, methylene, anionic substrates

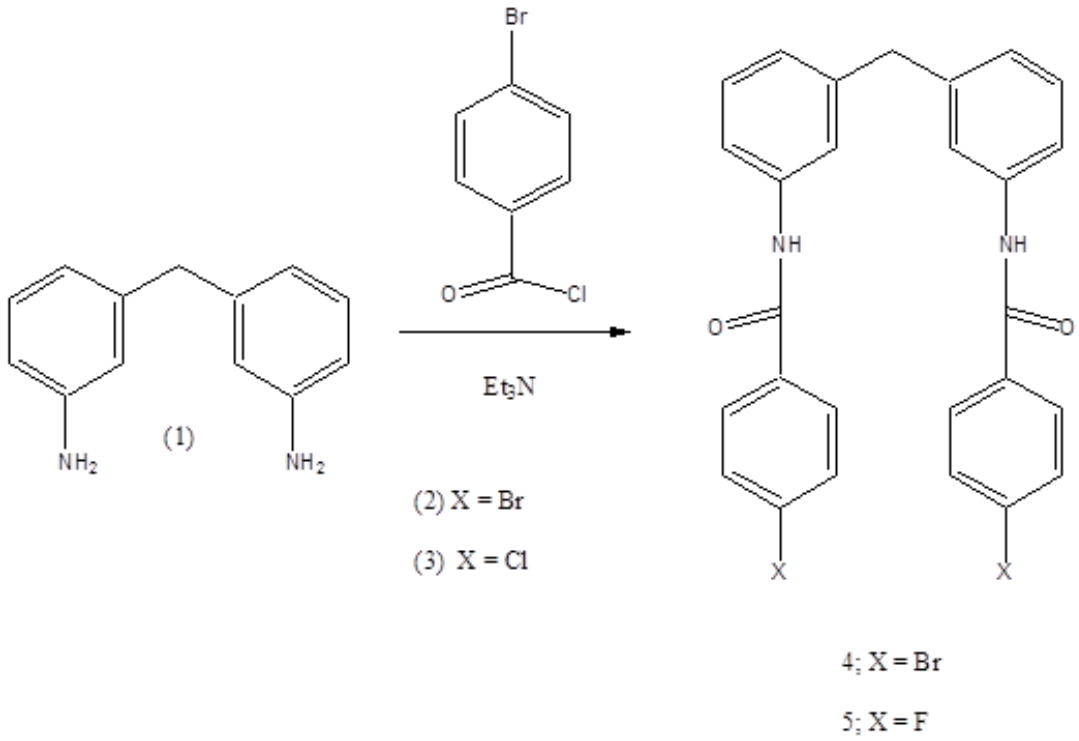
INTRODUCTION

The molecular recognition of anions is an active, and difficult area of Supramolecular chemistry, considering the properties of anions[1,2]. It's an area of current intense research considering the ubiquitious roles anion play in biological, environmental andSupramolecular sciences[1-24]. Of great interest is the design, syntheses and use of neutral receptors for selective binding of anions[6-19]. In designing an anionic host, charge and shape complementarity between the host and anionic guest are of paramount importance[1,5]. Neutral anion receptors, especially those of the amido type exploit hydrogen bonding interactions with anions and are found in biological systems. Neutral amides, depending on their spatial orientation (geometry) are expected to selectively complex guest substrates [12-14,20-24]. Neutral receptors of amides, urea and thiourea types are of significance because the transport of anions such as phosphate, PO_4^{3}- anion through cell membranes is regulated by neutral binding proteins[9-14]. Most anion receptors reported to date are macrocyclic in nature[5,6-24]

Apart from neutral amido receptors, anion receptors exploiting the neutral urea binding motif have been reported[15-19]. Significantly large association constants have been shown for compounds binding to anion in highly competitive solvents . For example a porphyrin urea anion receptors have been reported to selectively complex halides anions over phosphate with association constant of 1 x 10^5 M^{-1} in the highly competitive solvent d_6-DMSO [17-18]. Other anion receptors reported to date require the presence of the amide unit in close proximity to a Lewis acid /metal centre, metallocene, positively charged binding sites or electrochemically induced metallocenium unit[20-24]. The oxidation of the metallocene to the metallocenium ion in tandem

with the amide bonds have been shown to induced anion binding. The ligand's topology, acyclic vsmacrocyclicvsmacrobicyclic also has a profound influence on anion binding.

Compounds (4) and (5) present convergent amides hydrogen bonding moities for complexation of anions. Also, the presence of electronegative substituents (Fluoro and bromo) is expected to modulate the hydrogen bonding interactions of the amide protons, fostering stronger hydrogen bonding interactions with the anions and leading to an increase in association constants. Compounds (4) and (5) were synthesized via the condensation of one mole of the diamine (1) with two moles of bromobenzoyl and chlorobenzoyl acid chloride respectively in CH_2Cl_2 solvent, with Et_3N as the base under nitrogen and was obtained in significant yield after workup, Scheme 1.0. Each compound was characterized via the spectroscopic techniques of ^{1} HNMR, ^{13} CNMR, DEPT 135 NMR, ^{1}H-^{1}H COSY, HMQC and HMBC. These data are presented in the experimental section of this paper. A ^{1}H NMR profile of compound (1) is shown in Fig. 1.0 .



.

Scheme 1.0

DISCUSSION

Compounds (4) and (5), described as molecular tweezers, are built on the building block, 3,3' methylene diamine. Both compounds (4) and (5) spectroscopic profiles were established via^{1} H NMR, ^{13} C NMR, DEPT-135, ^{1} H-^{1}H COSY, HMQC and HMBC spectroscopic techniques. ^{1}H-^{1}H COSY shows protons – protons connectivity, HMQC shows the connectivity of individual protons to carbon and HMBC also shows the connectivity of protons to two or more carbon away. Using all these spectroscopic data, the structural integrity of these compounds was assigned as shown in Figure 1.0. A ^{1} HNMR profile of compound (4) is shown in Fig. 1.0.

Both compounds exhibit diagnostic ^{1}H NMR splitting pattern. Compound (4) and (5) show a singlet for the amide, H-6 proton and methylene, H-5 protons at (10.27, 3.94 ppm) and at 10.215, 3.943 ppm) respectively. Aromatic protons from rings A, B, C and D resonate in the region 8.037 ppm to 7.315 ppm.

For both compounds , H-7/H-8 and H-9/H-10 protons are magnetically and electronically equivalent and the splitting pattern which is of the AB type is reminiscent of that for a disubstituted benzene ring. In both cases, H-7 proton is split by H-8 proton yielding a doublet (J = 8.4Hz) and vice versa. Thus, two distinct doublets are seen and these appear at (7.872 , 7.740 ppm, J = 8.4Hz) and (8.018, 7.989 ppm, J = 5.7Hz) for compound (4) and (5) respectively. Likewise protons H-9 and H-10 are split by each other resulting in the typical AB doublet at 7.74, J = 8.4Hz) for compound (4) and (5) respectively. Protons on phenyl rings C and D are more downfield or deshielded than protons on rings A and B due to the electron withdrawing effect of the bromo and Fluoro substituent and this is supported by the ^{1}H NMR profile. The splitting confirms to proton with the AB Chemical shift and whose protons are strongly coupled.

Protons on ring A and B mostly exhibit the ABC splitting pattern. For example, H-1 proton is split by H-2 , resulting in a doublet (J = 7.8 Hz) which is then further split by H-3 resulting in a doublet of doublet. However, the chemical shift of these two doublet of doublets are close, resulting in a virtual triplet (J = 8.7Hz) . This resonate at 7.294 and 7.34 ppm for compound (4) and (5) respectively. For compound (5), this triplet is close in chemical shift with H-9/H-10 doublets and overlaps. The same analogy holds for H-2 and H-3 protons, resulting in a triplet at 7.62 ppm for both compounds. Protons H-4 is seen as a doublet at 7.03 ppm (7.5Hz) and 7.02 ppm (J=7.45 Hz) for compound (4) and (5) respectively. Methylene, H-5 equivalent protons resonate as a singlet at 3.94 and 3.94 ppm respectively. The fact that the methylene signal is a singlet suggest that there is no conformational rotation about the CH_2 unit of the 3,3' methylene dianiline scaffold. The labile amide proton is seen as a singlet at 10.27 and 10.25 ppm for compound (4) and (5) respectively.

^{1}H-^{1}H COSY experiments revealed ^{1}H-^{1}H connectivity. For example, H-1 proton couples with H-2 and H-3 protons i.e shows cross peaks which are in line with those for H-2 and H-3. H-7 couples with H-8 and H-9 couples with H-10. Methylene, H-5 protons shows no ^{1}H-^{1}H connectivity and thus resonate as a singlet.

Both molecules has fourteen different carbons and thus fourteen signals are seen in the ^{13}C NMR spectrum. Each molecule also has five ipso carbons and these resonate at 141.52 ppm, 164.52 ppm, 138.98 ppm, 133.93 ppm, 125.22 ppm and 138.93 ppm for compound (1) and at 165.05, 162.02, 141.51, 139.17 and 131.02 ppm for compound (2) respectively. A Dept^{13}C experiment (Distontionlessenchancement by Polarization Transfer experiments) is used to separate the signals arising from carbons in CH_3, CH_2 and CH groups. Usually with $Dept_{135}$ experiment ipso or quaternary carbon signals are not evident. Also, CH_2 protons point downwards and CH and CH_3 upwards. As anticipated the CH_2 signal for each compound points downward at 41.34 ppm. Aromatic carbons resonate in the region: 118.27 ppm to 141.52 ppm. The carbonyl carbon resonate at 164.0 and 165.65 ppm. For compound (2), CH proton resonances are seen at 130.25, 128.60, 124.23, 120.68, 118.23, 115.36 and 115.07 ppm.

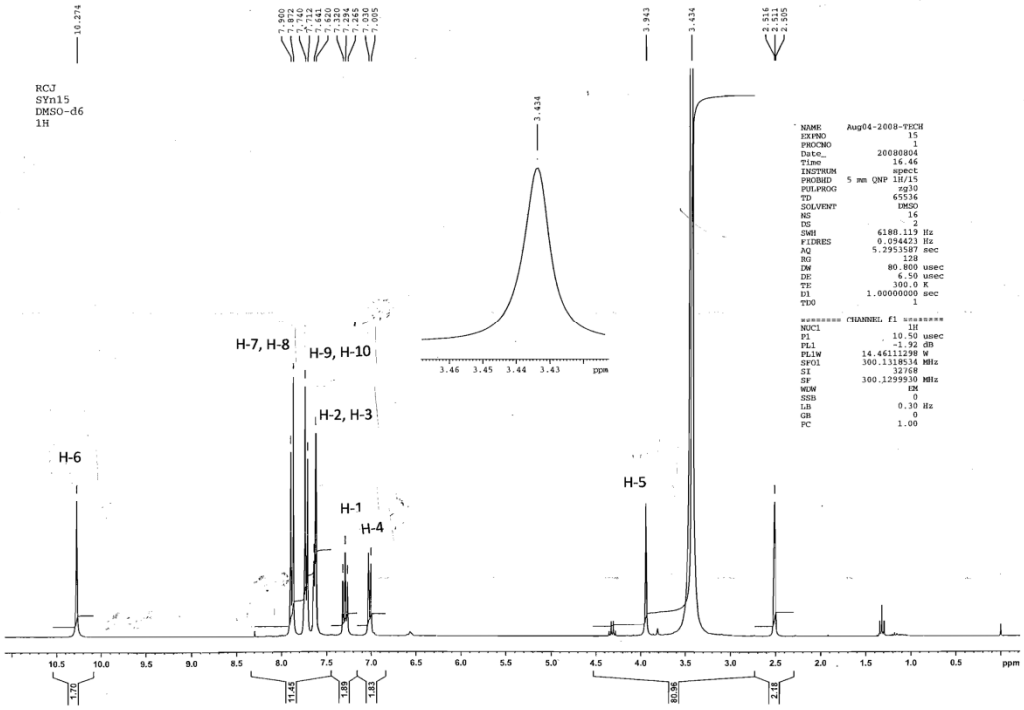
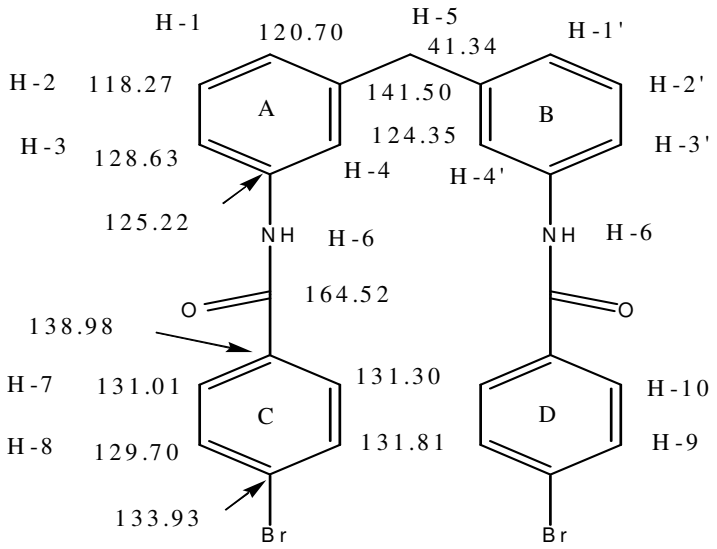
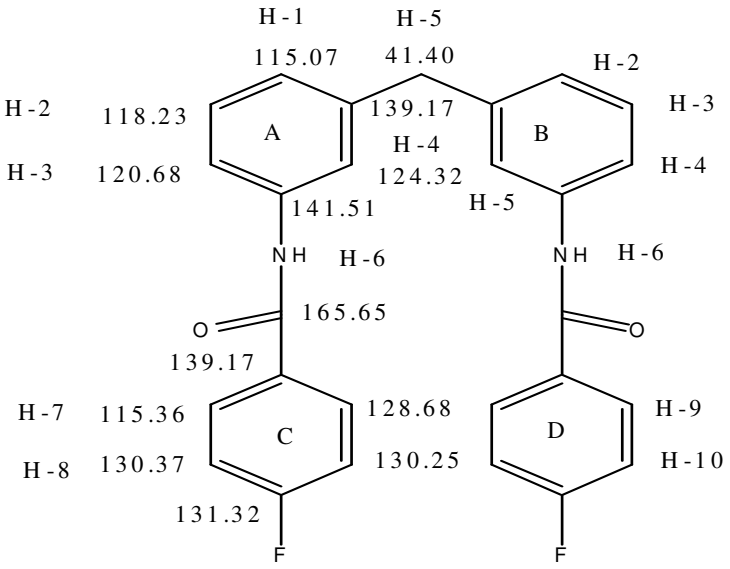


Figure 1.[1] H NMR spectrum of compound (4)



Compound 1



Compound (2)

Figure 2.Structural Assignments

Preliminary, ^{1}H NMR titration experiment was carried out via the addition of tetrabutylammonium phosphate to deuterated d_6-DMSO solution of receptor (4). Addition of the anion, induced distinct changes in the ^{1}H NMR profile of compound (4) and should do even better for compound (5) since, the latter protons are more acidic. There are distinct changes in the aromatic proton resonance of compound which definitely indicatescomplexation. Amide proton shifted downfield by 1.5 ppm in chemical shift, indicating significant -NHCO------Anion hydrogen bonding interactions

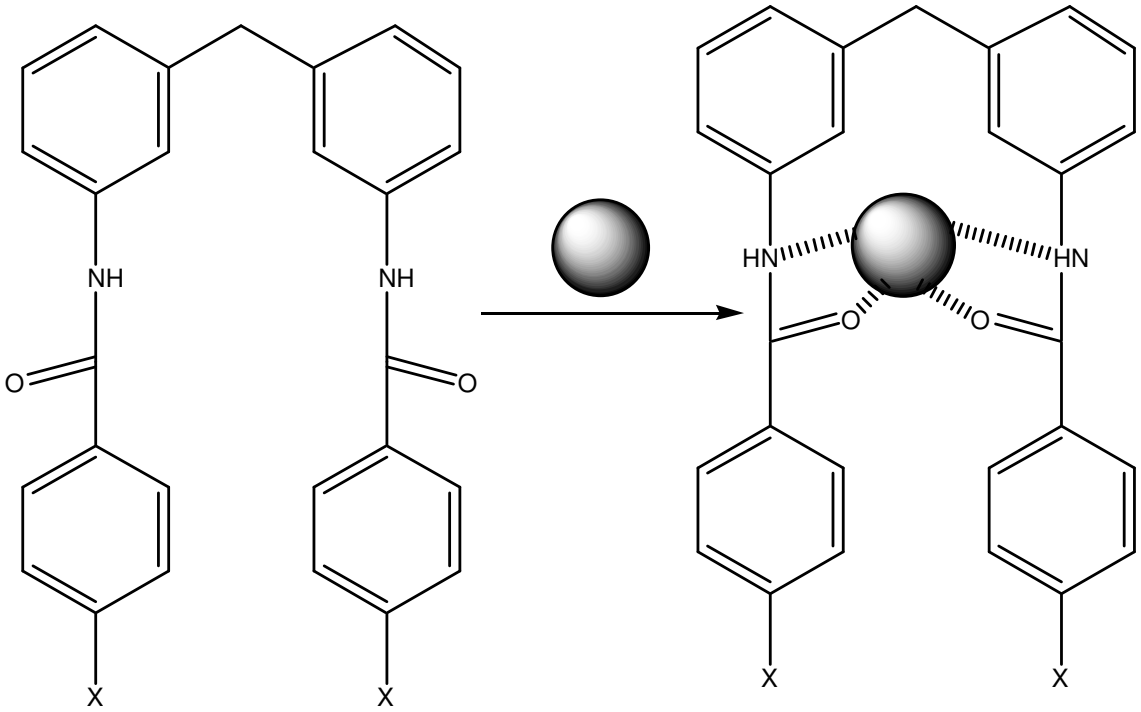


Fig. 3.Anion Encapsulation by compound (4)

In conclusion, two new amido anion receptors have been synthesized and fully characterized via spectroscopic techniques of ^{1}H NMR, ^{13} C NMR, DEPT- 135 spectroscopy, ^{1}H-^{1}H COSY, HMQC and HMBC. Preliminary studies reveal complexation with phosphate anions in d_6-DMSO.^{1} H NMR titration revealed complexation to the phosphate anion. Future work entails, the complexation of the receptor to other anions such as the halides and nitrates and the evaluation of complexation stability constants.

PROCEDURE

For a typical procedure, (0.33g, 1.66442 x 10^{-3}mol) of the dianiline, 3,3' methylene dianiline was dissolved in CH_2Cl_3 in a 100ml RB flask. To this solution was added triethylamine, ET_3N () under nitrogen. This was followed with the addition of 4-fluorobenzoyl chloride (0.63g, 3.972758 x 10^{-3}mol). A white precipitate was formed after one hour of stirring. The reaction was further stirred for 24 hours after which it was taken up in distilled water and extracted thrice with $CHCl_3$. Solvents were removed in *vacuo*from the extract to yield, a white solid (0.87g, 92.65%) which was found to be spectroscopically pure. The yield being (0.87g, 92.65%) and (0.71g, 96.41%) for compound (4) and (5) respectively.

Compound (1)

$C_{27}H_{20}N_2O_2Br_2$: ^{1} H NMR ($CDCl_3$, 300MHz):□□□□ppm□: 10.27 (-NHCO-), 7.872 (d; J = 8.4Hz , Ar-H), Phenyl), 7.74 (dd; J = 8.4Hz ; Ar-H), 7.62 (m, 4H; Ar-H), 7.29(t, J = 7.8Hz, 2H; Ar-H), 7.03 (d; J = 7.5Hz, 2H; Ar-H), 3.94 (s, -CH_2-); **^{13} C NMR ($CDCl_3$, 300MHz):** 164.00 , 141.52, 138.98, 133.93, 131.81, 131.30, 131.01, 129.7, 128.63, 125.22, 124.35, 120.70, 118.27,

41.34; **DEPT-135**: 131.30 (CH), 129.70 (CH), 128.64 (CH), 124.35 (CH), 120.69 (CH), 118.25 (CH), 131.81 (CH), 131.01 (CH), 41.34 (CH_2); **^{1}H-^{1}H COSY:** H-1/H-3, H-4; H-2/H-3; H-4/H-1; H-3/H-4, H-1, H-2; H-4/H-3, H-2, H-1; H-5/H-4, H-1, H-2; H-6/(-); H-7/H-8; H-9/H-10; **HMQC**: H-1/115.27; H-2/120.70; H-3/128.63; H-4/124.35; H-5/41.34; H-6/(-), H-7/H-8: 129.70, 131.01; H-9/H-10: 131.81,131.30; **HMBC**: H-1/H-2: 124.35; H-3: 138.98, 141.52; H-4: 118.27, H-5: 120.70, 124.35, 125.22, 141.52, H-6: 118.27, 120.70, 164.50; H-7/H-8: 124.35, 125.22, 129.70, 164.50, H-9/H-10: 124.35, 125.22, 131.01, 133.93, 164.50;

Compound (2)

$C_{27}H_{20}N_2O_2F_2$: ^{1} H NMR (300MHz, $CDCl_3$), □: 10.25 (s, NHCO), 8.007(d, J = 5.7Hz, 4H; ArH), 7.625 (d, J = 5.7 Hz; 4H; ArH), 7.315-7.375 (m, J = 9.0 Hz, 6H; Ar-H), 7.01 (d, J =5.9 Hz, 2H, ArH), 3.94 (s); **^{13}CNMR (300MHz, $CDCl_3$)**□: 165.65, 141.51, 139.17, 131.32, 130.37,130.25, 128.60, 124.32, 120.68, 118.23, 115.36, 115.07, 41.40; ^{1}H-^{1}H COSY: H-1/H-2, H-3, H-4; **DEPT 135**: 130.37 (CH), 130.25(CH), 128.60 (CH), 124.23 (CH), 120.68(CH), 118.23(CH), 115.36(CH), 115.07(CH), 41.39 (CH_2); **^{1}H-^{1}H COSY**: H-1/H-2, H-3, H-4; H-2/H-3: H-4, H-1, H-2; H-4: H-3,H-1, H-2; H-5: (-); H-6: (-); H-7, H-8/H-8,H-7; H-9/H-10/H-10/H-9; **HMQC**: H-1: 115.36,128.60, 124.23; H-2/H-3: 115.36, 118.23, 120.68, 128.60 ; H-4: 124.23; H-5: 41.39; H-7/H-8: 115.36, 131.32; H-9/H-10: 115.36, 124.23,128.60 ; **HMBC**: H-1: 115.36, 118.23,120.68,124.23,131.32; H-2/H-3: 41.40, 118.23,120.68,124.23,130.35,141.51; H-4: 115.36, 118.23, 120.68, 130.25, 130.37; H-5: 120.68, 124.23, 141.51 ; H-7/H-8: 115.36, 131.32, 162.35, H-9/H-10: 115.36, 118.28,120.68, 124.23, 131.32;

Acknowledgements

This research was financially supported by Dr. R. C. Jagessar

REFERENCES

1. Lehn, J.M. (1995). *Supramolecular Chemistry: Concepts and Perspectives*. (1st ed.). New York: Wiley-VCH, (Chapter 3)

2. *Supramolecular Chemistry of Anions*. New York:Wiley-VCH(1997).

3. Schmidtchen, F.P.. Berger, M. (1997). Artificial Organic Host Molecules for Anions: *Chem. Rev*. 97, 1609-1646.

4. Beer, P.D. (1998). Transition-Metal Receptor Systems for the Selective Recognition and Sensing of Anionic Guest Species**.,***Acc. Chem. Res*. 31 (2), 71-80.

5. Bowman-James, K. (2005). The Coordination Chemistry of Anions, *Acc. Chem. Res*. 38, 671-678.

6. Martinez-Manez, R., Sancenon, F. (2003). Fluorogenic and chromogenicchemosensors and reagents for anions, *Chem. Rev*., 103, 4419-4476.

7. Sancenon, F.,Descalze, A.B., Miranda, M.A., Sato, J.(2001).A colorimetric ATP sensor based on 1,3,5-triarylpent-2-en-1,5-diones*, Angew. Chem., Int. Ed*., 40, 2640.

8. Gunnlaugason,T., Davis, A.P., O'Brien, J.E., Glynn, M. (2002). Fluorescent sensing of Pyrophosphate and Bis-carboxylates with charge neutral PET chemosensors.,*Org. Lett.. 4*, 2449.

9. Hennrich, G., Sonnennachein, H., Reach-Genger, L. (2001). *Tetrahedron Lett*., 42, 2805.

10. Choi, K.; Hamilton, A.D.(2003). Macrocyclic anion receptors based on directed hydrogen bonding interaction ,*Coordination Chem. Rev*, 240, 101-110.

11. Wiskur, S.L., Ait-Hissou, H., Lavigne, J.J., Anslyn, E.V. (2001). Teaching Old Indicators New Tricks, *Acc. Chem. Res. 34*, 963-972.

12. Kuo. L.,Liao, J.H. , Chen, C.T., Huang, C.H., Chen, C.S., Fang, J.M. (2003). Two Arm Ferrocene Amide Compounds: Synclinal Conformations for Selective Sensing of DihydrogenPhosphate ion, *Organic Letters*, 5 (11), 1821-1824.

13. Kubic, S., Goddard, R., Kirchner, R., Nolting, D., Seidel. (2001). Recognition of Anions, *J. Angew. Chem. Int. Ed.*, 40, 2648.

14. Korendovych, I.V., Cho. M., Butler, L.P., Staples, J.R., Rybak-Akimova, E.V.R. (2006). Anion binding to monotopic and ditopicmacrocyclic amides, *Organic letters*. 8(15):3171-4.

15. Schearder, J., Engbersen, J.F.J., Casnati, A., Ungaro. R., Reinhoudt, D. N. (1995). Complexation of halide Anions and Tricarboxylate anions by Neutral Urea Derivatives, p-*tert*-butylcalix[6]arene, *J .Org. Chem.,* 60, 6448-6454.

16. Jagessar, R.C., Shang, M., Scheidt, W.R.,* Burns*, D. H.(1998). Neutral Ligands for selective Chloride Anion Complexation: □□□□□□□□) (Cis)-5,10,15,20 -*Tetrakis* (2-(arylurea) phenyl porphyrins: *J. Am.Chem.Soc.,* 120 (45), 11684-11692.

17. Jagessar, R.C.,Burns, D. H. (1997). (Cis)-5,10,15,20 -*Tetrakis* (2-(arylurea) phenyl porphyrins: Novel neutral ligands for remarkablely selective and exceptionally strong chloride anion complexation in $(CD_3)_2SO$, *J. Chem. Soc., Chem. Commun*., 1685 - 1686.

18. Amemiya, S.,Buhlmann, P.,Umezawa, Y.,Jagessar, R. C., Burns, D. H. (1999). An ion-selective electrode for acetate based on a urea-functionalized porphyrin as a hydrogen bonding ionophore, *Anal Chem*., 71(5), 1049 - 1054.

19. (1995): Complexation of Halide Anions and Tricarboxylate Anions by Neutral Urea-Derivatised p-tert-Butylcalix(6)arenes, *J.Org.Chem*., 60, 6448-6454.

20. Beer, Paul D., Graydon, Andrew R., Sutton, Liam.R. (1996). Luminescent anion recognition: selective induced emission by binding of dihydrogenphosphate. *Polyhedron*, 15 (14), 2457-2461.

21. Chen, Z, Graydon, A.R., Beer, P.D. (1996). Electrochemical response to anions in acetonitrile by neutral molecular receptors containing ferrocene, amide and amine moieties.,*J. Chem. Soc., Faraday Trans*. 92(1), 97-102.

22. Beer, P.D, Drew, M.G.B, Smith, D.K., (1997). Selective electrochemical recognition of bidentate anionic guests in competitive solvents using novel ferrocenylthiourea and guanidinium receptors. *J. Organomet. Chem*. 543 (1-2), 259-261

23. Beer, P.D.; Drew, M.G.B., Jagessar, R., (1997).Selective anion recognition by Novel 5, 10, 15, 20 - *tetrakis* (o-ferrocenylcarbonylaminophenyl - substituted) zinc metalloporphyrin receptors, *J. Chem. Soc., Dalton Trans., 881* - 886.

Beer, P.D.; Drew, M.G.B.; Hesek, D.; Jagessar, R., (1995). Spectral and Electrochemical Anion Sensing by a novel 5,10,15,20-tetrakis(R-substituted)Porphyrin Receptor(R=$C_6H_4NHC(O)C_5H_4CoC_5H_5^+PF_6^-$), *J. Chem. Soc.,Chem.Commun*., 1187-1189.