RSC Advances

Cite this: *RSC Advances*, 2012, **2**, 12594–12605

www.rsc.org/advances

REVIEW

Triazole: a new motif for anion recognition

V. Haridas,* Srikanta Sahu, P. P. Praveen Kumar and Appa Rao Sapala

Received 19th July 2012, Accepted 24th September 2012
DOI: 10.1039/c2ra21497k

Anion receptors have attracted growing interest because of their role in chemistry, the environment, biology and medicine. The mis-regulation of anion flux causes a variety of lethal human diseases. Recently, triazole has been found to be an excellent motif for molecular recognition. This review depicts an overall picture of developments in the design and synthesis of anion receptors along with an up-to-date emphasis on the triazole unit as a motif for anion recognition. The acidic CH of triazole is involved in binding with the anions, which makes these receptors different from other classes of receptors. The chemo- and regio-selectivity of the click reaction provides further impetus for future developments in this area.

Introduction

Molecular recognition has attracted considerable interest in recent years because it is integral in many scientific areas, such as biology, chemistry, and pharmacology.[1] Molecular recognition of cations,[2] anions,[3] and neutral molecules[4] are important in biology and chemistry. Although rigorous attention has been paid to the recognition of cations, recognition of anions has received less attention.[5] Anions are everywhere in living systems and are vital in carrying out many biochemical operations for sustaining life. Anions such as chloride, phosphate, and sulfate regulate the flux of key metabolites into and out of cells while maintaining osmotic balance.[6] Among all anions, anion receptors specific to chloride and fluoride have attracted growing interest because of their role in chemistry, biology and medicine.[7] The mis-regulation of chloride ion flux causes severe human diseases, such as cystic fibrosis,[8] myotonia,[9] and epilepsy.[10] Accumulation of excess fluoride ions in living organisms causes collagen breakdown, bone disorder, impact on the immune system and thyroid activity.[11] Oxalate, arsenate, and nitrite can produce chronic diseases.[12] Naturally occurring phosphate and sulfate can cause renal failure for patients, due to poor catabolic activity.[13]

In recent years, increasing attention has been devoted to the synthesis of receptors for recognition of anions. Serious efforts have been paid since the beginning of anion co-ordination chemistry in the late 1960s for the development of synthetic

Department of chemistry, Indian Institute of Technology (IIT), Hauz Khas, New Delhi, 110016. E-mail: h_haridas@hotmail.com; Tel: 01126591380

V. Haridas

Dr V. Haridas is an Associate Professor in the Department of Chemistry at the Indian Institute of Technology Delhi (IITD), India. He finished his PhD under the guidance of Prof. D. Ranganathan (National Institute for Interdisciplinary Science and Technology, India). He did his post doctoral studies with Prof. R. M. Ghadiri (The Scripps Research Institute, USA) and with Prof. Herbert Waldmann (Max Planck Institute, Germany). His research group at IIT Delhi is involved in the design and synthesis of dendrimers, and secondary structure mimetics. In addition to that the group is also working on various aspects of synthetic and bioorganic chemistry.

Srikanta Sahu

Srikanta Sahu was born in Karkachia (Mayurbhanj), Orissa, India. He received his BSc from the North Orissa University, Orissa, India, in 2002 and completed his MSc in Organic Chemistry in 2004, from Ravenshaw Autonomous College (Utkal University), Orissa, India, in 2004. He qualified the National Eligibility Test (NET), jointly conducted by CSIR & UGC (New Delhi, Govt. of India), the Graduate Aptitude Test Examination conducted by IITs, India, and continued his PhD under the supervision of Professor V. Haridas at Indian Institute of Technology Delhi (IITD), India.

receptors for recognition of anions. However, the major binding motifs that have been utilized until now are as follows: cationic polyammonium, quaternary ammonium, amide, urea, thiourea, guanidinium, pyrrole, imidazolium and boron containing receptors (Fig. 1).[14]

These motifs have been utilized for the construction of receptors for anions with varying selectivity. A preliminary discussion about these receptors is given below. The discovery of novel motifs for the recognition of anions is a rate limiting step in the area of anion recognition research. In the latter part of this review, we provide a brief history, detailed analysis of the origin of triazole as an anion recognition motif, and the recent developments in this area using triazole as an anion recognition motif. Most of the examples of the receptors presented here are designed for use in organic solvents.

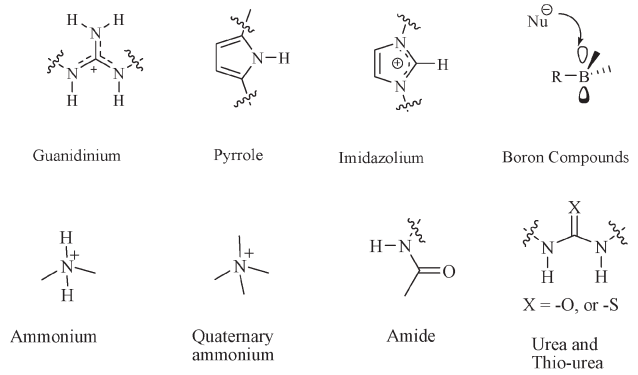

Fig. 1 Commonly used motifs for anion receptors.

1.1 Polyammonium-based receptors

The first synthetic anion receptor (Fig. 2) was reported by Park and Simons in 1968.[15] These macrocyclic compounds, consisting of two bridgehead ammonium units, showed binding behaviour towards halide ions. However, the [8.8.8] and [10.10.10]-bridged compounds **1** and **3** showed no appreciable binding behavior towards halide ions; while the analogous [9.9.9]-bridged compound **2** binds chloride ions with an affinity of 10^2 M^{-1}, with modest selectivity for chloride over bromide by a factor of eight.

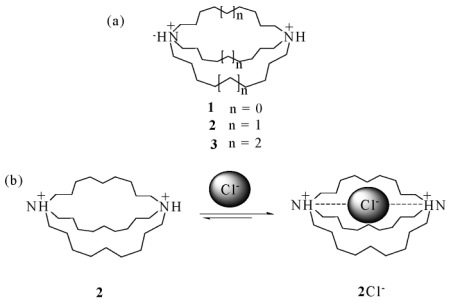

Fig. 2 (a) Ammonium receptors **1**, **2**, and **3** (b) complex of receptor **2** with Cl^- ion.

Bowman-James *et al.* synthesized various bicyclic azacryptands (Fig. 3) containing ammonium units, for binding of anions.[16] Crystal structure analysis of **4** showed the encapsulation of a single F^- ion with a water molecule inside the cavity. Whereas the bicyclic azacryptand **5**, having a bigger cavity than **4**, accommodated two F^-s with a water molecule inside the cavity. The water molecule acts as bridge between the two fluoride ions and thus generates an anion-based cascade complex.

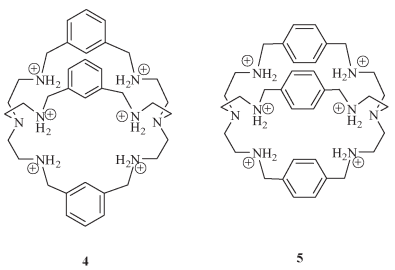

Fig. 3 Azacryptands **4** and **5** for F^-.

1.2 Quaternary ammonium-based receptors

Schmidtchen *et al.* first reported a series of quaternary ammonium-based receptors (Fig. 4) for the recognition of anions.[17] The most attractive feature in such receptors is the utilization of electrostatic interaction for the recognition of

Praveen Kumar P. P

Mr. Praveen Kumar P. P was born in 1987 in Kerala, India. He received his Masters degree in synthetic organic chemistry from Christ College affiliated to Calicut University, Kerala, in 2009. In the same year he was honoured with CSIR–JRF, and GATE. Presently he is a PhD student in the department of chemistry, IIT Delhi, under the guidance of Dr V. Haridas. He is working on the design and synthesis of molecular receptors for various anions and cations.

Appa Rao Sapala

Appa Rao Sapala was born in Rajahmundry, Andhra Pradesh, India (1984), received his bachelor's degree (2005) from the same place and MSc degree (2007) in Chemistry from Gitam College, Andhra University, Visakhapatnam. He had 3 years experience in G. V. K Bio Pvt. ltd, Hyderabad. He qualified CSIR–JRF and is currently pursuing his PhD degree at IIT Delhi under the guidance of Dr V. Haridas. His research interests are in the area of peptide design, synthesis and their applications.

anions. Receptor **6** contains four tetra-alkylammonium-bridged centres, which are connected through $(CH_2)_6$ alkyl linkers. Crystal structure analysis of this receptor with iodide shows that it encapsulates iodide into its tetrahedral cage by utilizing the electrostatic interactions. The receptor **7** binds to *p*-nitrophenolate as a result of having a higher cavity size than receptor **6**.

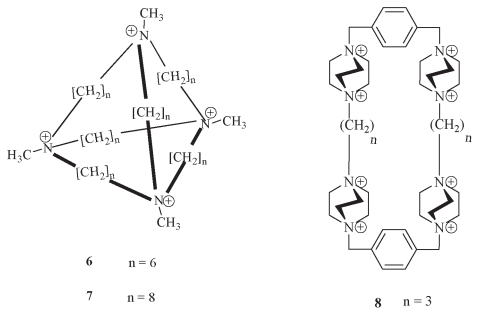

Fig. 4 Quaternary ammonium receptors **6** and **7** that bind I^- electrostatically. Quaternary ammonium receptor **8** for ATP.

Menger *et al.* designed and synthesized a new class of quaternary ammonium-based receptors (Fig. 4) for recognition of anions.[18] Receptor **8** showed binding with various anions: benzene sulphonate, naphthalene-2-sulfonate and naphthalene-2,7-disulphonate in aqueous solution. It also binds to ATP very strongly with an association constant of 13 300 M^{-1}.

1.3 Amide-based receptors

Pascal *et al.* first reported abiotic amide-based receptor (Fig. 5) for recognition of anions by utilizing amide –NHs as hydrogen-bonding donor groups.[19] The crystal structure analysis of cyclophane **9** offers a cylindrical cavity of approximately 4 Å in length and 3 Å in diameter, due to the presence of two facial aromatic rings that are connected through three bridging arms. The crystal structure revealed that three amide–NHs are inclined by 47, 54, and 68° to radii drawn from the central axis through the nitrogen atoms.

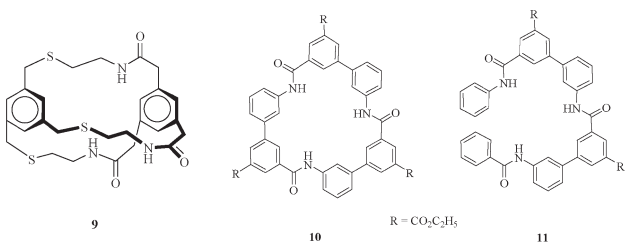

Fig. 5 Amide receptors **9–11**.

Choi and Hamilton reported a series of amide-containing rigid macrocycles and acyclic compounds (Fig. 5).[20] These compounds bind to various anions as follows: I^-, Cl^-, NO_3^-, pTsO$^-$, HSO_4^-, and $H_2PO_4^-$ with varying ability. Binding studies showed that macrocycle **10** is a better binder towards anions than the acyclic **11**. The receptor **10** showed 1 : 1 binding with a tosylate anion, whereas **11** binds to I^-, Cl^-, and NO_3^- in 2 : 1 stoichiometry.

Bowman-James *et al.* designed and synthesized a polyamide-based cryptand (Fig. 6) to investigate the binding behaviour for various anions.[21] The receptor **12** showed promising binding behaviour for the fluoride ion in DMSO-d_6 with a log K value of 5.0 followed by Cl^- (log K = 3.47), CH_3COO^- (log K = 3.38), $H_2PO_4^-$ (log K = 3.30), NO_3^- (log K = 1.93), HSO_4^- (log K = 1.83), and Br^- (log K = 1.6) with the formation of 1 : 1 complexes.

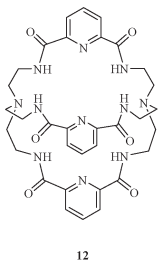

Fig. 6 Polyamide cryptand receptor **12** for F^-.

1.4 Urea and thiourea-based receptors

Wilcox *et al.* reported urea and thiourea-based synthetic receptors for recognition of various oxo-anions.[22] The binding behavior of receptor **13** (Fig. 7) with various oxo-anions **a–d** in chloroform was examined by UV/vis titration experiments. The thiourea-based receptor **14** is a better binder than **13** for oxo-anions **a–d**.

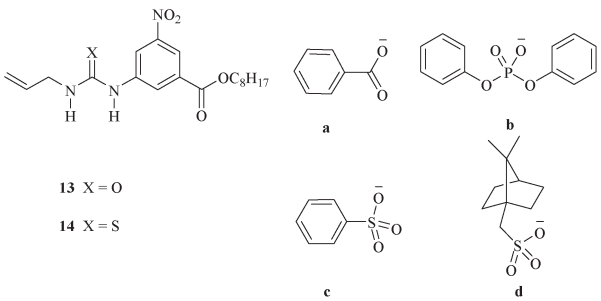

Fig. 7 Urea and thiourea-based receptors **13** and **14**.

Reinhoudt *et al.* designed and synthesized various urea- and thiourea-based molecules (Fig. 8) for recognizing anions.[23] The cleft-like acyclic urea-based receptor **15** binds to $H_2PO_4^-$, in a 2 : 1 stoichiometry with an association constant of 5×10^7 M^{-1}. It showed very poor binding affinity towards Cl^-, Br^-, NO_3^-, and HSO_4^-. The thiourea-based receptor **16** binds similarly to **15**. The rigid macrocycles **17** and **18** offered a 1 : 1 binding stoichiometry toward $H_2PO_4^-$ with association constants of 4×10^3 and 2.5×10^3 M^{-1}, respectively.

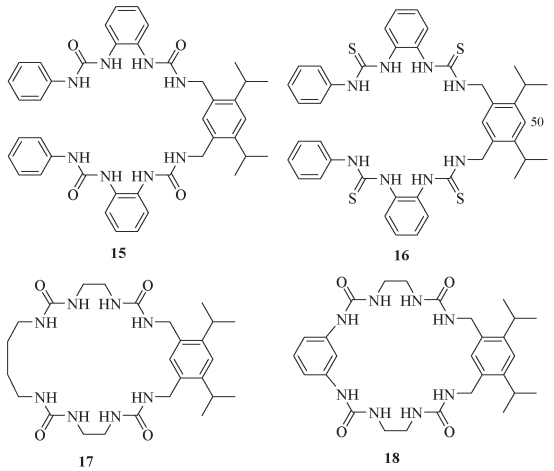

Fig. 8 Urea and thiourea-based receptors **15–18** for recognition of $H_2PO_4^-$.

Gale *et al.* proposed an acyclic, urea-based receptor **19** (Fig. 9) to acknowledge anions.[24] The bis-urea containing receptor **19** binds to the acetate ion more selectively with a binding constant of 3210 M^{-1} over Cl^-, Br^-, $H_2PO_4^-$, and HSO_4^-. The receptor **19** binds to acetate more strongly than receptors **20** and **21**.

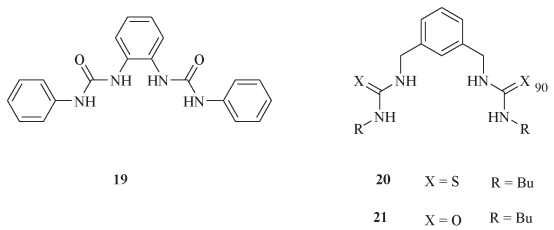

Fig. 9 Urea receptors **19–21** for acetate.

1.5 Guanidinium-based receptors

Since the beginning of anion co-ordination chemistry, the guanidinium moiety was used for design of anion receptors, as the guanidinium moiety has two key major features for the creation of abiotic anion receptors: (1) its high basic nature, which helps in sustaining a wide pH range; (2) its ability to donate two parallel hydrogens for hydrogen bond donors. Because of these unique features, guanidinium-based receptors show high affinities and selectivities for oxyanions. Taking advantage of this moiety, Lehn *et al.* reported a series of novel guanidinium-based cyclophanes (Fig. 10).[25] The binding studies of these macrocycles **22**, **23**, and **24** showed 1 : 1 binding with trianionic phosphate (PO_4^{3-}) in methanol–water (9 : 1) solution with log K_a = 3.1, 3.4, and 4.3 respectively.

Schmidtchen designed and synthesized a bis-guanidinium-based acyclic molecule (Fig. 11) for the binding of anions.[26] The two-guanidinium moieties in **25** converged in the presence of tetrahedral anions, such as thymidine-5′-phosphate (**e**) and thus provided a suitable geometry for binding. The NMR titration experiment showed a 1 : 1 complex of **25** with **e**, having a binding constant of 10^6 M^{-1} in water. The compound **25** displayed no binding for simple HPO_4^{2-} anions.

Lavigne and Anslyn reported on a guanidinium-based receptor (Fig. 11) for detecting tartrate anions.[27] The receptor **26**, containing two guanidinium moieties, provides a suitable geometry with the correct cavity size for binding of tartrate. It also responded to other analytes: ascorbate, L-malate, succinate, lactate, and sugars. It binds strongly to tartrate as compared to other analytes in 1 : 1 stoichiometry and with a binding constant of 5.5 × 10^4 M^{-1} towards tartrate.

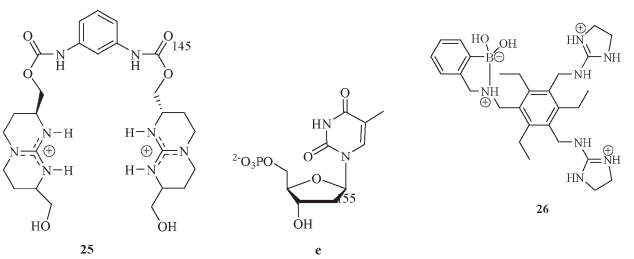

Fig. 11 Guanidinium receptor **25** for the selective recognition of thymidine-5′-phosphate **e**. **26** for the selective recognition of tartrate.

1.6 Pyrrole-based receptors

The first pentapyrrolic macrocyclic receptor (Fig. 12) was reported by Sessler *et al.* in the late 1990s.[28] The crystal structure analysis showed the complex as a diprotonated macrocycle with fluoride residing inside the cavity. Solution phase studies showed that the diprotonated sapphyrin (expanded porphyrin containing five pyrrole units) **27** binds to fluoride 10^3 fold more than chloride and bromide. This finding opened up a new direction for the exploration of anion co-ordination chemistry of pyrrole-containing systems.

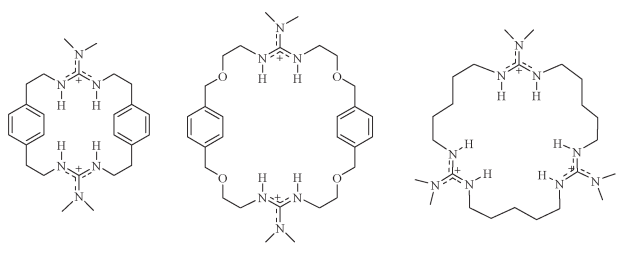

Fig. 10 Guanidinium receptors **22–24** for PO_4^{3-}.

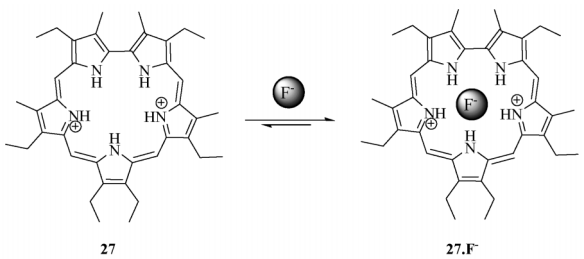

Fig. 12 Sapphyrin receptor **27** for F^-.

A new type of calixpyrrole (Fig. 13) was synthesized for binding towards anions.[29] The crystal structure analysis of **28** showed a wing-like architecture with a benzoate ion between the two wings. It showed a strong affinity for acetate in 1 : 1 stoichiometry with binding constant value of 229 000 M^{-1}.

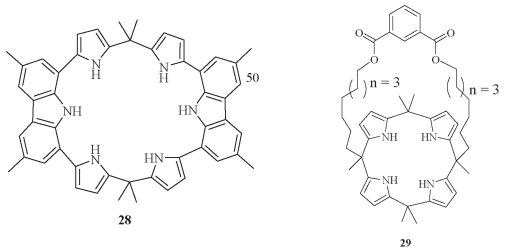

Fig. 13 Pyrrole-based receptor **28**, **29** with controlled cavity size for anions.

Lee *et al.* designed and synthesized a new class of calix[4]pyrrole containing a flexible strap on one side of the molecule (Fig. 13) for controlling the cavity for better selectivity and affinity toward various anions.[30] The receptor **29** showed significant binding behaviour for fluoride and chloride. It showed better binding ability for fluoride and chloride than the simple calix[4]pyrrole moiety. However, it does not show any appreciable binding ability with bromide, iodide, sulphate, and phosphate. The smaller cavity of these molecules disfavoured the accommodation of larger anions for binding.

1.7 Imidazolium-based receptors

Welton *et al.* designed and synthesized imidazolium-based (Fig. 14) compound **30**.[31] The ^{1}H NMR study of **30** with halide ions (Cl^-, Br^-, and I^-) showed significant interaction to the C2H group of imidazolium located between the two nitrogen atoms. This result demonstrated that the imidazolium –CH could be exploited for binding towards halides. Later, Sato *et al.* investigated the binding event of **31** with halide ions (Cl^-, Br^-, and I^-).[32] The binding constant values of **31** with chloride, bromide, and iodide ions were 78, 59, and 29 M^{-1}, respectively. Taking the structural benefits of the imidazolium moiety, Sato *et al.* designed and synthesized receptors **32–34**. These receptors showed better binding ability for halides than mono-imidazolium **31**.

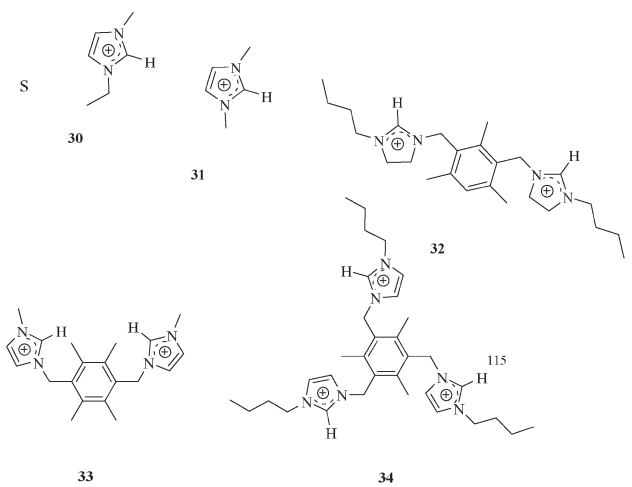

Fig. 14 Imidazolium-based receptors **30–34**.

Kim *et al.* reported a cyclic imidazolium receptor **35** (Fig. 15) and discussed its binding behaviour toward various anions.[33] ^{1}H NMR studies showed that receptor **35** binds to fluoride more strongly than to other anions, such as chloride, bromide, iodide, and hydrogen sulphate ions. Crystal structure analysis, as well as Job's plot, supported the formation of a 1 : 1 complex of **35** with a fluoride ion, whereas for other anions, it was a 1 : 2 binding stoichiometry. The binding constant value of **35** with the fluoride ion was found to be 28 900 M^{-1}.

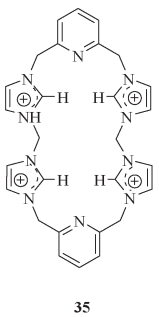

Fig. 15 Cyclic imidazolium-based receptor **35** for the selective recognition of F^-.

1.8 Boron-based receptors

Boron in the trisubstituted state with sp^2 hybridization has a vacant p orbital that can easily accommodate nucleophiles (Fig. 16) and therefore can act as good receptors for anions.[34]

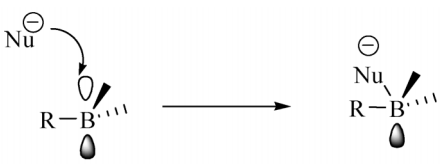

Fig. 16 Coordination of boron with nucleophiles.

In 1985, Katz studied the binding affinity of receptor **36** (Fig. 17) and utilizing ^{19}F–^{1}H, ^{19}F–^{13}C and ^{11}B NMR, and found that the B-B distance becomes shorter after binding with F^-.[35a]

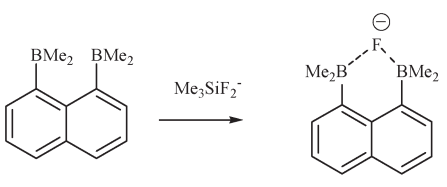

Fig. 17 Boron-based receptor for F^-.

A mixed Lewis system (Fig. 18) containing boron and silicon centers on an *o*-phenylene backbone showed stronger binding toward F^- than the monodentate boron analogues.[35b]

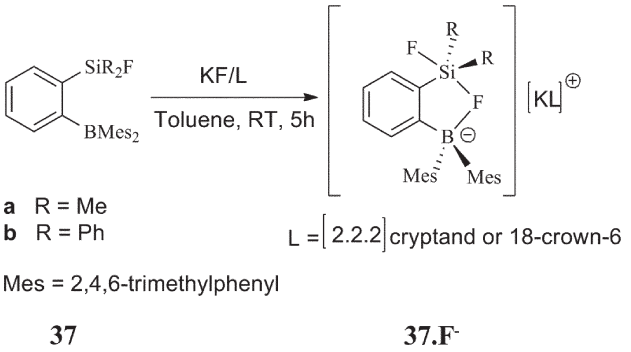

Fig. 18 Mixed Lewis system for F^- recognition.

1.9 Triazole-based receptors

The examples illustrated above delineate some of the developments in the anion receptor design. The majority of anion binding motifs make use of strong hydrogen bond donor groups like NH and OH. The proton transfer and strong binding affinity are attributes of such moieties. The untapped potential of the non-conventional hydrogen bonding interaction could be exploited in the receptor design, in order to craft a truly reversible system with good binding affinity and selectivity. Therefore, novel motifs utilizing a variety of less explored non-covalent interactions for binding to the guest are much sought after. Design and synthesis of neutral receptor molecules for the anion are more difficult, because they mainly make use of the hydrogen bond, which is weaker than the coulombic interaction utilized in charged anion receptors. The maximum use of hydrogen bond donor units and the preorganized cavity are the typical design criteria for neutral anion receptors. The triazole moiety is one of the recent examples that showed good promise for the design of various neutral receptors. The testimony to that is the fairly good number of receptors that appeared in the literature in a short period of time.

Why triazoles. The majority of the synthetic receptors designed have a strong binding affinity towards anions; therefore, the release of anions is a real issue. The CH···X interaction, though weaker than the conventional H-bond, could be utilized for binding to neutral as well as charged guests.

The H-bonding ability of triazole CH could be modulated by substituents (R_1 and R_2) and thereby provide an additional benefit for making truly reversible systems. The high yield and chemoselective nature of the click reaction makes the introduction of triazole an easier task, and thus this reaction[36] provides a better future for the design of receptors for neutral as well as charged guest molecules (Fig. 19).

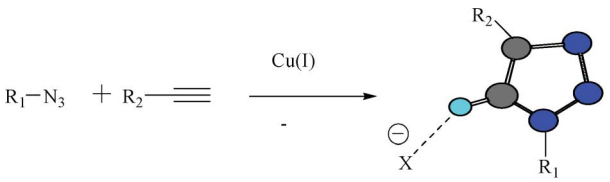

Fig. 19 Synthesis of a triazole moiety and the interaction of the CH of triazole with an anion.

In 2008, our group reported a neutral triazolophane that can bind to an acetonitrile molecule (Fig. 20).[37] Compound **38** showed a unique type of binding with acetonitrile because of non-classical hydrogen-bonding interactions. The only available hydrogen bond donor in **38** was the CH of triazole, and the macrocycle could bind the acetonitrile molecule by the non-classical hydrogen bonds and CH···π interactions.

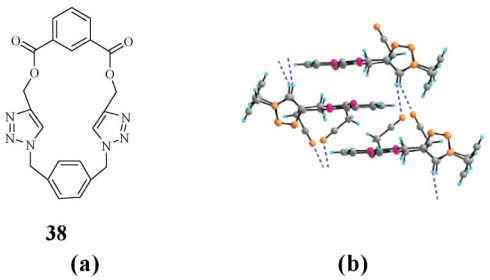

Fig. 20 Structural representation (a) and acetonitrile mediated assembly in the solid state of triazolophane **38** (b).

In the same year, Li and Flood designed and synthesized a series of shape-persistent preorganized triazolophanes (Fig. 21) by exploiting the click reaction for the recognition of anions.[38] Macrocycle **39** binds the chloride ion with a high affinity and selectivity over all halide ions. This is due to its ideal cavity size with cumulative binding effects of all the triazole CHs, and the endocyclic benzene CHs, which are oriented inwards in the cavity. The triazolophane **39** showed a very strong binding affinity value (K = 1.1 × 10^7 M^{-1}) with the chloride ion in dichloromethane.

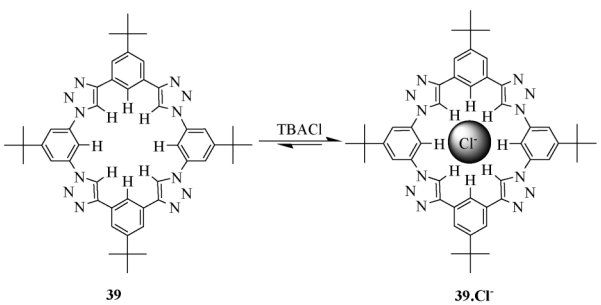

Fig. 21 Shape-persistent preorganised triazolophane **39** binds Cl^- selectively.

A new class of triazolophanes (**40** and **41**) containing pyridine rings (Fig. 22) were synthesized.[39] This generated a negative electrostatic potential due to the presence of a nitrogen lone pair in the pyridyl ring; thus, the cavity became oval, which favoured a 2 : 1 binding towards various halide ions. The receptor **40** showed the highest binding towards I^-, followed by Br^- and F^-. However, it shows a negative cooperative effect with the Cl^- ion. The receptor **40** showed relative values of K_1 and $<3200\ M^{-1}$ and $>32\ 000\ 000\ M^{-1}$, respectively, with the iodide ion. These results clearly indicate that the presence of pyridyl units in the ring destabilizes the formation of 1 : 1 triazolophane complexes due to $N\cdots X^-$ electron pair repulsion; rather, it favours 2 : 1 sandwich complexes.

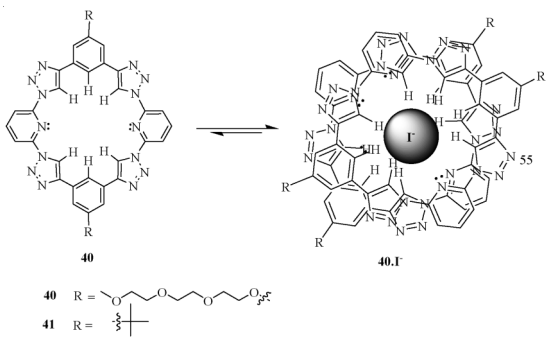

Fig. 22 Pyridyl-containing triazolophanes **40** and **41**.

The receptor **42**, which has two hydroxyl groups on the central phenylene ring, makes an intramolecular hydrogen bond with the N3 of the triazole ring, and thus brings about a preorganized structure (Fig. 23). Because of preorganisation, it binds the chloride ion with ~50 fold greater affinity compared to non-preorganized pentad receptor **43**.[40]

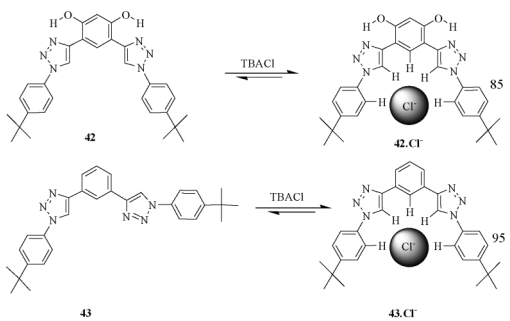

Fig. 23 Preorganised *vs.* non-preorganised receptors **42** and **43**.

In 2008, Craig *et al.* demonstrated the ideal manipulation of weak CH interactions for synthesizing anion assisted foldamers (Fig. 24).[41] The receptor **45**, which contains four triazole moieties, shows better binding ability for the chloride ion due to the involvement of more hydrogen bond donors, compared to receptor **44**. The result is the folding of **45** in the presence of the chloride ion and is confirmed by detailed 2D NOESY experiments. The titration of **45** with the chloride ion gives a binding constant of $1.7 \times 10^4\ M^{-1}$, which is higher than the receptor **44**.

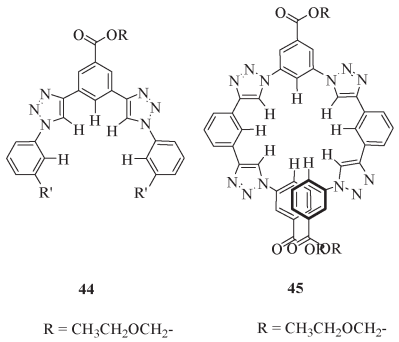

Fig. 24 Acyclic triazole-based receptors **44** and **45**.

In 2008, Meudtner and Hecht demonstrated the design and synthesis of a novel class of triazole-based clickamers (Fig. 25), *via* the click reaction, and their folding behavior under various conditions.[42] The clickamer **47**, which contains two complete turns with a number of π–π stacking units, showed very insignificant folding behavior in acetonitrile. The population of the helical conformation was observed upon the addition of substantial amounts of water. The helicity with addition of water is due to the intramolecular chirality transfer from the chiral side chains to the backbone, which is evidenced from temperature dependent circular dichroism (CD) as well as dynamic light-scattering (DLS) and UV/Vis absorption spectroscopy studies. The shorter oligomer **46** also exists in a helical conformation. The foldamer **47** showed very unusual folding behavior toward various halides. The size of the halide ion plays a major role in helix inversion by transforming intramolecular chirality from the chiral side chain to the backbone, thus establishing an equilibrium between left- and right-handed helices.

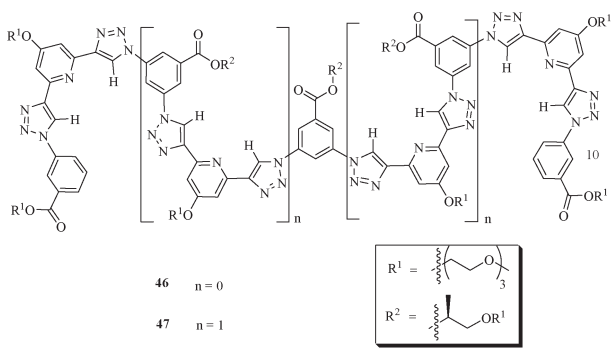

Fig. 25 Triazole-based foldamers **46** and **47**.

Sanotoyo-Gonzalez *et al.* synthesized various calixarene based cavitands (**48–50**) using the click reaction. Interestingly, compound **50** showed binding affinities towards various anions (Fig. 26).[43]

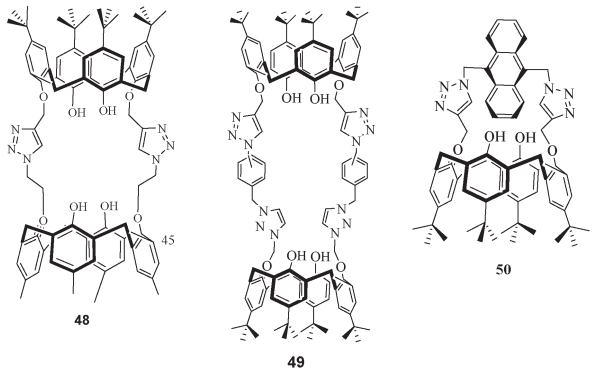

Fig. 26 Calixarene-based cavitands.

Molina *et al.* synthesized ferrocene-pyrene dyad **51** (Fig. 27) by coupling the terminal alkyne of pyrene with that of ferrocenyl azide *via* a click reaction.[44] The receptor **51** displays a highly selective binding event for trianionic $HP_2O_7^{3-}$ over various anions such as F^-, Cl^-, AcO^-, NO_3^-, HSO_4^-, and $H_2PO_4^-$. A fluorescence titration experiment of **51** with $HP_2O_7^{3-}$ shows a 2 : 1 complex formation.

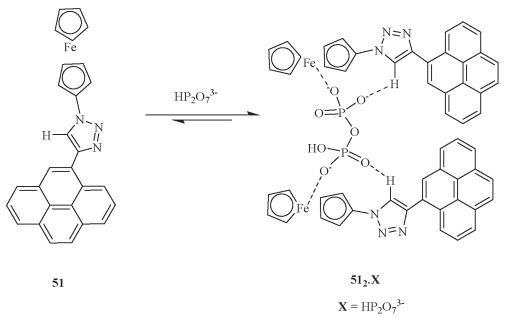

Fig. 27 Ferrocene–pyrene coupled triazole-based receptor **51** for $HP_2O_7^{3-}$.

Sessler *et al.* discussed a pyrrolyl-based triazolophane (Fig. 28), which displays highly selective binding affinity for the pyrophosphate anion, followed by HSO_4^-, $H_2PO_4^-$, Cl^- and Br^-.[45] The receptor **52** binds to trianionic pyrophosphate with a 10-fold greater affinity and selectivity as compared to hydrogen sulphate. However, the binding constant was found to be (2.30 $\pm$ 0.40) $\times$ 10^6 M^{-1} for pyrophosphate. The X-ray crystal structure analysis shows that all the pyrrole NH, triazole CH, and the endocyclic benzene CH protons are involved in stabilizing a pyrophosphate molecule in its cavity.

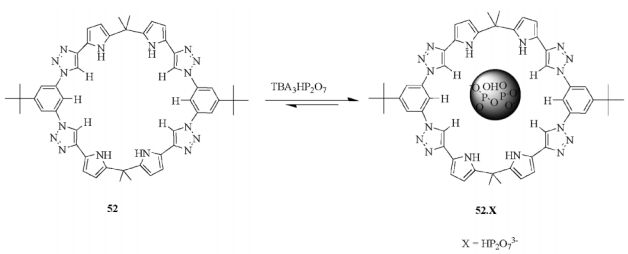

Fig. 28 Pyrrole-based triazolophane **52** for the recognition of pyrophosphate.

In 2012, Beer *et al.* synthesised Zn containing porphyrin-cages (Fig. 29) for the recognition of anions with the aid of click chemistry.[46] The ^1H NMR and UV/vis spectroscopic titration experiments showed that the receptor can bind with Cl^- with a binding constant of 10^4 M^{-1} in a 1 : 1 stoichiometry.

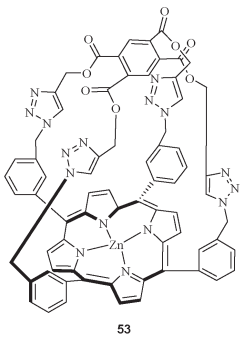

Fig. 29 Porphyrin cages for anions.

Jiang *et al.* demonstrated a light-induced triazole-based foldamer, containing a photoresponsive azo-benzene in between the two phenyl-triazole oligomer units (Fig. 30).[47] The compound **54** adopts two conformations, **54***trans* and **54***cis*, with respect to azo-linkage. The **54***cis* isomer predominates upon irradiation of UV light; however, it binds anions more strongly than the **54***trans* conformer. This behavior is expected due to its scissor-like conformation, which results in assembling all the binding sites ideally for the recognition of ions. The **54***trans* conformer predominantly exists in the presence of visible light, and it binds weakly as compared to **54***cis* to various anions, due to the extended conformation of the azo-benzene core. The receptor **54***cis* binds the chloride ion strongly with a binding constant of 290 M^{-1}, which is approximately a 4-fold excess compared to the **54***cis* conformer.

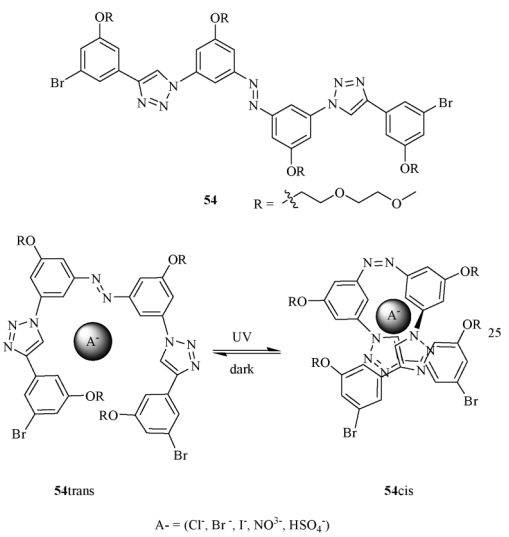

Fig. 30 Photoswitchable receptor **54**.

In 2011, Kim synthesised a neutral ferrocene appended aryl triazole receptor **55** that can bind strongly with phosphate (Fig. 31).[48] Ferrocene, being an electrochemical sensor, enabled detection of phosphate using cyclic voltammetry (CV) and

differential pulse voltammetry (DPV). All of the triazole CHs, phenyl CH, and ferrocene CH, take part in binding with phosphate. These interactions induce a large shift in CV and DPV and thus act as an electrochemical sensor.

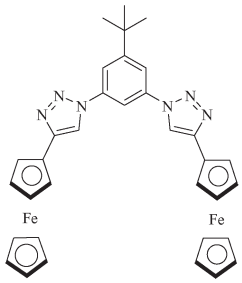

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Fig. 31 Ferrocene appended redox neutral receptor for $H_2PO_4^-$.

Hua and Flood addressed the photoisomerisation behavior leading to foldamer and its binding ability towards the chloride ion of a triazole-based azo-benzene molecule (Fig. 32).[49] The compound **56** exists in three isomeric forms: **56***trans–trans*, **56***cis–trans* and **56***cis–cis*. Among them, the **56***trans–trans* isomer prefers the helical form under visible light (436 nm) and is more preorganised for chloride binding. Owing to its ideal arrangement of H–bonding donor sites, the **56***trans–trans* isomer binds

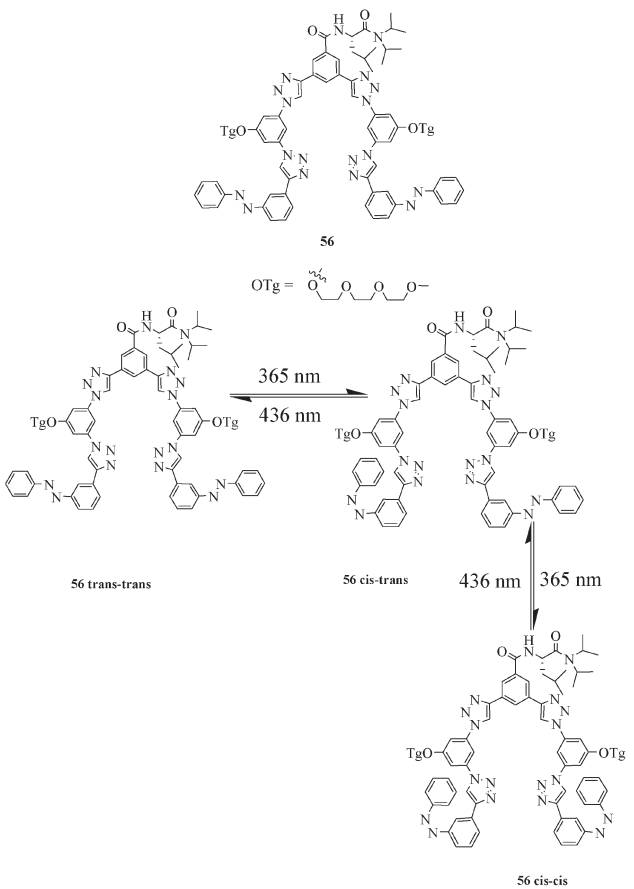

Fig. 32 Photoswitchable triazole-based receptor.

chloride more strongly than **56***cis–trans* and **56***cis–cis* isomers. The binding constant value of receptor **56***trans–trans* with the chloride ion under dark conditions was found to be 3000 M^{-1}.

Jiang *et al.* investigated the anion-induced folding behavior with binding properties of novel oligo(phenyl-amide-triazoles) (Fig. 33) in great detail.[50] The NMR titration experiments of chloride, bromide, and iodide ions (TBACl, TBABr and TBAI) with oligomer **57** showed a 1 : 1 binding stoichiometry, with association constants of 350, 80 and 15 M^{-1}, respectively. However, the longer oligomers **58** and **59** showed 1 : 2 complexes with both the chloride and bromide ions, and both of the oligomers bind to the chloride ion more strongly than to the bromide ion. Stepwise association constants for oligomer **57** with the chloride ion were found to be $K_1 = 4.9 \times 10^3$ M^{-1} and $K_2 = 13$ M^{-1}, indicating a negative cooperative effect for folding.

Similar results were observed for oligomer **59** in the presence of the chloride ion, but it showed a better binding ability than oligomer **58**.

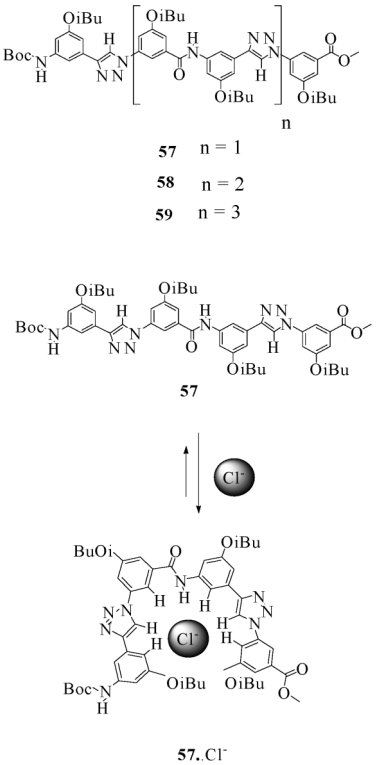

Fig. 33 Oligo(phenyl-amide-triazoles) **57–59** and the chloride assisted folding of **57**.

Sanchez *et al.* described the self-assembly behavior of aryl triazole molecules (Fig. 34), with their anion binding properties leading to disruption of the molecular self-assembly due to the conformational changes in the molecules.[51] Molecular self-assembly of aryl triazole **60** resulted in flat lamella-like architectures, while **61** was organized into spheres, which was confirmed by scanning electron microscopy (SEM) studies. NMR studies of **60** and **61** indicated the existence of "*anti*" conformations, which are switched over to "*syn*" conformations in the presence of bromide ions, resulting in disorder of the structural morphologies. The receptor **60** binds to bromide in 1 : 1 stoichiometry with a binding constant of 15 M^{-1}, which is higher than **61**.

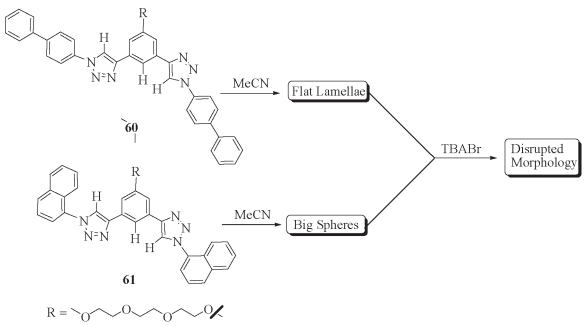

Fig. 34 Molecular self-assembly and binding behaviour of **60** and **61**.

Our group successfully used triazole in conjunction with an amide unit as a excellent moiety for anion recognition (Fig. 35). Various receptor systems (**63–67**) were synthesised and validated for anion binding. Since the triazole moiety can mimic an amide bond, the triazole with amide could be compared with two peptide linkages.[52]

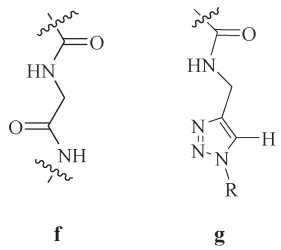

Fig. 35 Comparison of amide-triazole and peptide linkages.

Interestingly, the dialkyne precursor **62** showed less binding compared to the amide-triazole version, thus underscoring the usefulness of this moiety in anion recognition.[53]

Increasing the acidity of triazole CH is another way to modulate the binding affinity. The introduction of phenyl substituents on the triazole rings showed higher binding ability compared to the benzyl substituents. Receptor **65** binds F^- with a high binding constant ($K \sim 10^5\ M^{-1}$). Receptor **67** showed a color change from pale yellow to orange upon adding F^-.[52]

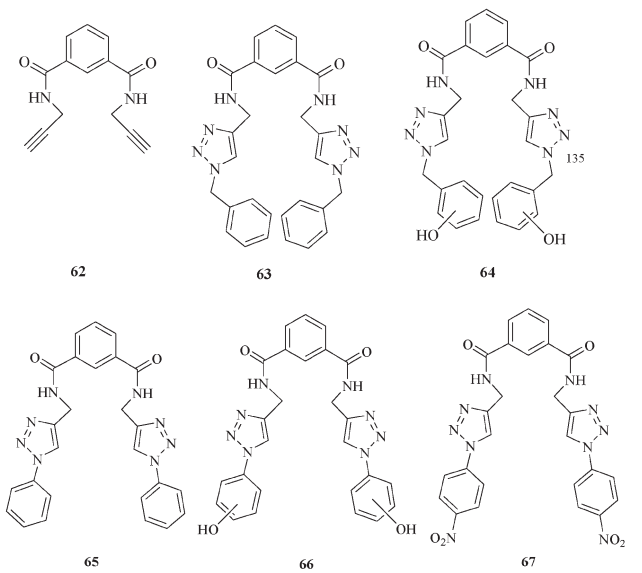

Fig. 36 The dialkyne precursor **62** and triazole receptors **63–67** for anion binding.

Various triazole based receptors (**64** and **66**) containing a phenolic group were designed and synthesized in order to provide extra binding sites for anions (Fig. 36). Interestingly, in most of the cases, proton exchange was observed between the F^- and the phenolic –OH. All other anions showed less binding to phenolic receptors. These results further emphasize the challenge in anion receptor design.

Li *et al.* replaced one of the amide NH of urea with a triazole to generate various receptors (Fig. 37).[54] The amide-triazole combines the characteristics of urea and triazole. The ease of synthesis, coupled with better solubility for the amide-triazole compounds compared to urea-based compounds, is a factor that enhances the utility of this moiety in the future.

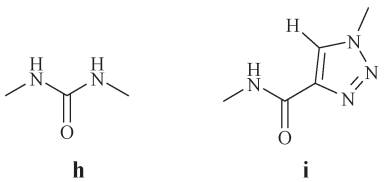

Fig. 37 Comparison of urea and the amide-triazole moieties.

Various acyclic receptors were synthesized and they showed good binding affinities for tetrahedral oxyanions (Fig. 38). Receptor **68**, containing OH, NH and CH motifs at the binding site, showed good colorimetric response in the presence of

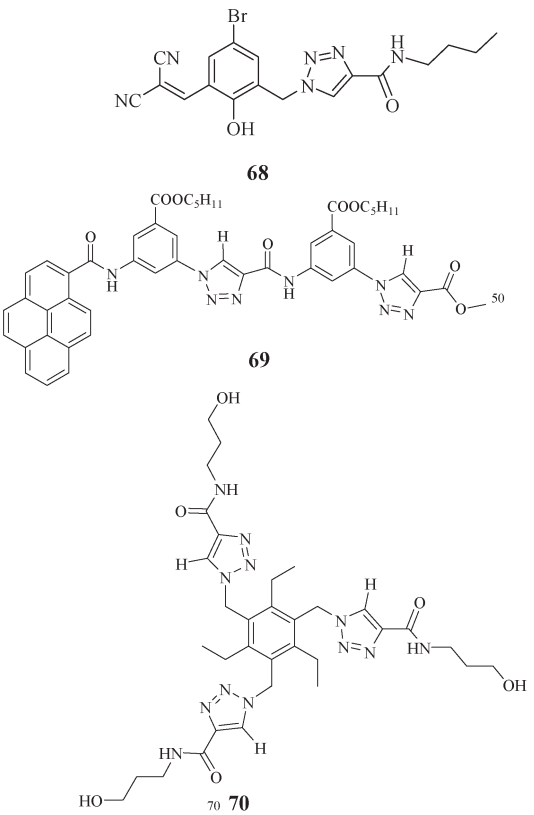

Fig. 38 Amide-triazoles for the selective recognition of oxyanions.

fluoride.[55] Various acyclic receptors, such as **69** and **70**, were synthesized, and they showed significant binding affinities for tetrahedral oxyanions.

Conclusion

The use of non-conventional hydrogen bonding makes the binding to anions weaker and more reversible and therefore useful for a variety of biological applications. The use of the $CH\cdots X^-$ interaction is relatively new and is not much exploited in the anion receptor design. The moderate binding ability of $CH\cdots X^-$ in isolation or in conjunction with other hydrogen bonding moieties will expand the repertoire of receptors. The last four years witnessed the utilization of the acidic –CH of triazole for non-conventional hydrogen bonding with guest molecules. Notably, many receptors were found to utilize non-conventional hydrogen bonding interactions that were unknown a few years back. The explosive developments in this area of molecular recognition using the triazole motif are expected to flourish further because of the clean and high yielding nature of this reaction, along with other attributes. A combination of conventional and non-conventional hydrogen bonding in the receptor design using this reaction will enhance the power of organic chemists in designing compounds with high binding and good release rates of guest molecules.

Most of the anion receptors are designed for binding in organic solvents. The design and synthesis of receptors for binding anions in the aqueous environment is an additional challenge to chemists. The chemoselective nature of the click reaction will be a useful attribute for the synthesis of water soluble receptors.

Acknowledgements

We thank the Department of Science and Technology (DST), New Delhi, for financial assistance.

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