Alcoholic-OH in Anion Coordination Chemistry

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Abstract: Anion Recognition using synthetic receptors is one of the central areas of research in contemporary supramolecular chemistry. To date, numerous receptors have been reported for the recognition and sensing of anionic substrates. Among the several anion-binding moieties, the alcoholic hydroxyl groups C-O-H is an important functional group in molecular recognition. In this mini-review, we cover the use of this group in development of synthetic anion receptors.

Keywords — alcoholic-OH, anion recognition, hydrogen bonding, supramolecular chemistry.

I. INTRODUCTION

Design and synthesis of abiotic receptors for anionic substrates is of immense interest in the field of supramolecular chemistry. Anions play a major role in many biological processes and are involved in agricultural fertilizers as well as in food additives. For instance, fluoride ion is of particular interest because of its role in preventing dental caries, and treatment of osteoporosis [1]. However, an excess fluoride anion can lead to fluorosis, which is a type of fluoride toxicity [2]. On the other hand, chloride ion is related with cystic fibrosis [3], inherited kidney, stone diseases, myotonia, and epilepsy. In a similar way, iodide plays an important role in thyroid function. The iodide content of urine and milk is often required for nutritional, metabolic and epidemiological studies of thyroid disorder [4]. Carboxylates are also essentially important anions, involved in many biological processes together with pyrophosphate which itself is essential for energy formation as it is the product of the hydrolysis of ATP under cellular conditions. On the other hand dicarboxylates are found to play their considerable roles in numerous metabolic processes such as the generation of high-energy phosphate bonds and the biosynthesis of important intermediates [5]. In addition, enantioselective recognition of carboxylates has important implication in asymmetric synthesis and drug discovery [6]. On the other hand, pertechnatate is an oxonion of radioactive element Tc, can be used as nuclear medicine [7].

Although anions are important in biology and medicinal research they are also harmful to environment and causes environmental pollution [8]. On very different level, an ability to process or catabolize effectively xenobiotic anions, including chemically simple species as cyanide, oxalate, arsenate, or nitrite, can produce symptoms of chronic or acute toxicity. Poor processing of naturally occurring phosphate and sulphate is also a serious problem for patients with renal failure. For instance, eutrophication is considered as one type of environmental pollution. It is the process by which a body of water acquires a high concentration of nutrients, especially phosphates and nitrates. These typically promote excessive growth of algae. As the algae die and decompose, high levels of organic matter and the decomposing organisms deplete the water of available oxygen, causing the death of other organisms, such as fish. So it is necessary to remove these anionic species (phosphate, nitrates) from aqueous solution to make a defence against eutrophication to save water life.

Thus, the diversity of function, both beneficial and detrimental, necessitates the development of receptors capable of detecting the anions. In order to recognize and sense the anions, initially charged host molecule, such as protonated polyamines or azamacrocycles, guanidinium cation, transition metal or lanthanide ion based complexes were utilized [9]. Recently, imidazolium or benzimidazolium, pyridinium, etc are mentionable [10]. The disadvantage of charged host molecule lies on the fact that since such coulombic interactions (charge-charge) are non-directional, it is very difficult to achieve higher degree of selectivity. On the other hand, charge neutral receptors containing amide, urea /thiourea, carbamates, amidourea, pyrrole, indole or calixpyrrole with conventional hydrogen bond donors (N-H…..A, A = N, O.), have been widely used for recognition of anions [11].

Alcohol functionality (-OH) is an important motif in molecular recognition and it has been used in complexation of various guest molecules of interest. In contrast phenolic OH (pK_a = 10 for phenol) donor, alcoholic OH (pK_a = 15.5 for methanol) are less prone to deprotonation and thus acid-base reaction could be side passed during complexation. In this review we will focus on the selected examples of anionic hosts containing alipahatic C-O-H donors that interact with anion involving O-H---anion type hydrogen bond [12, 13].

II. ALCOHOL-BASED RECEPTORS FOR ANIONS

Davis and co-workers showed that the three H-bond donor groups in the α-face of the steroid nucleus (**1-3)** were pre-organised to accommodate tridentate anionic substrates such as sulfonates. Alkyl cholates **2** and **3** were shown to

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bind tridentate oxoanions such as sulfonate anion in hydrocarbon solvents in the mode as shown in structure **4** [14].

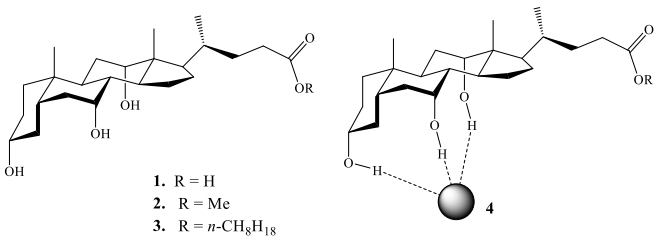

Figure 1. Structures of 1-3 and suggested binding mode of 1-3 with amino acids (4).

Maitra *et al.* reported that the cholaphane **5** was able to bind two F^- ions selectively utilizing the glycolate motif in chloroform [15]. This "inside-out" cyclodextrin analogue encapsulates F^- through O-H...F^- and C-H...F^- interactions.

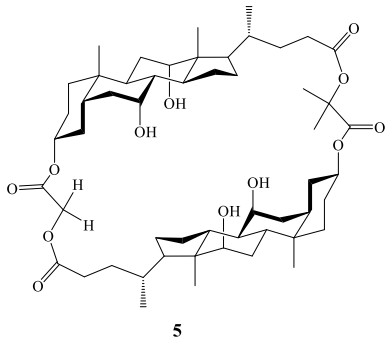

Figure 2. Structure of receptor 5.

Ungaro *et al.* designed and synthesized calix[4]arenes **6a**, **6b** and **7** with perfluorinated alcoholic functions at the upper rim for anions [16]. **6a** binds acetate anion (K_{ass} = 435 M^{-1}) more efficiently than the *meso* compound **6b** (K_{ass} = 200 M^{-1}).

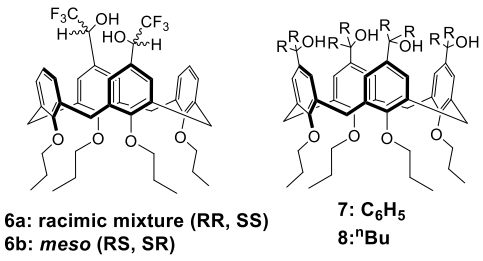

Figure 3. Structures of receptors 6-8.

Compound **6a** also showed a greater affinity towards chiral guest like the anion of *N*-lauroyl-L-phenylalanine compared to the *meso* compound **6b** due to presence of unfavourable steric interactions in the later. On the other hand, the tetrafunctionalized receptor **7** binds spherical anions such as bromide (K_{ass} = 480 M^{-1}) more efficiently than acetate anion (K_{ass} = 90 M^{-1}). Although these data may be negatively affected by the presence of intramolecular hydrogen bonding, a comparison with the data reported in the literature [17] for the interactions between anions and other hydrogen bonding donor groups seems to indicate that the strength of the interaction between the perfluorinated alcoholic functions and anions is smaller than that of the same anions with urea or sulphonamide groups, but comparable with carboxamides. The importance of the perfluorinated groups for anion binding is however indicated by the fact that compound **8** showed no interaction with either bromide or acetate anions under the same conditions.

Kondo *et al.* reported that the receptor **9** bearing disulfonamide and hydroxyl groups can bind anion in CH_3CN [18]. The hydroxyl groups of the receptor **9** act as hydrogen-bond donors in anion recognition and showed good selectivity for AcO^- compared with other anions. The anion-binding ability of receptor **9** are in the order of AcO^- >$H_2PO_4^-$ >Cl^- >Br^- ~ HSO_4^- >I^- >ClO_4^- and it was explained by considering both basicity and shape factors.

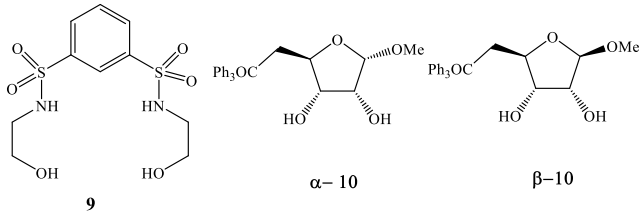

Figure 4. Structures of receptors 9-10.

The same group showed that between the receptors α- and β-**10**, receptor β-**10** showed effective binding with anions by cooperative hydrogen bonds of *cis*-diol [19]. The anomeric isomer α-**10** is a less effective anion receptor which has similar *cis*-diol as a recognition site, indicating that the stereo configuration of the anomeric position is of significant influence on the anion recognition ability. The anion-binding abilities of receptors **10** are in the order of AcO^- >$H_2PO_4^-$ >Cl^- >Br^- in both anomers.

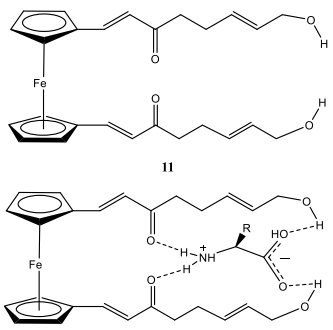

Figure 5. Structures of receptors 11 and suggested mode of binding with amino acid.

Roy and coworkers reported a ferrocene-based receptor **11** with two pendant hydroxyl group can recognize unprotected α-amino acids [20]. The binding behaviour was studied through UV-vis, fluorescence, CV, ITC, NMR, and ESI-MS. As shown figure 5, an encapsulative binding mode involving the α,β-unsaturated carbonyl residue (site

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for $–NH_3^+$ ion binding) and the terminal –OH groups (site for $-COO^-$ binding) was suggested.

Kondo *et al*. reported a series of silanol – based receptors **12** – **14** that have sufficient anion recognition ability by the cooperative hydrogen bonds of two or more silanol hydroxy groups present therein [21]. However, it is mentionable that the carbon analogues of gem-silanediol and 1, 3- disiloxane-1, 3-diol are not effective anion receptors because of the instability to form the corresponding ketone and intramolecular hydrogen bonds, respectively.

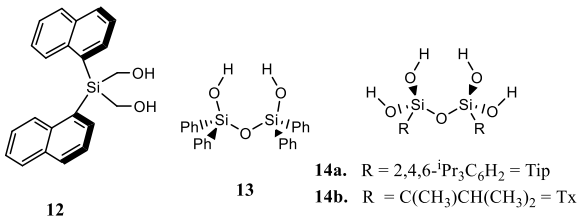

Figure 6. Structures of receptors 12-14.

The silane diol based receptor **12** bind selectively AcO^- and Cl^-, having higher affinity towards AcO^-, via two hydrogen bonds. The trend is in accordance with the basicity of the anions. On the other hand, the disiloxane-1,3-diol binds AcO^- and halides with higher affinity towards Cl^-. The lower affinity of **13** towards AcO^- was due the flexibility of Si–O–Si bond of disiloxane-1,3-diol skeleton. As expected, 1,3-disiloxane-1,1,3,3-tetraols **14a** and **14b** bind halides more effectively than both **12** and **13** due to cooperative hydrogen bonds of the four silanol –OH groups.

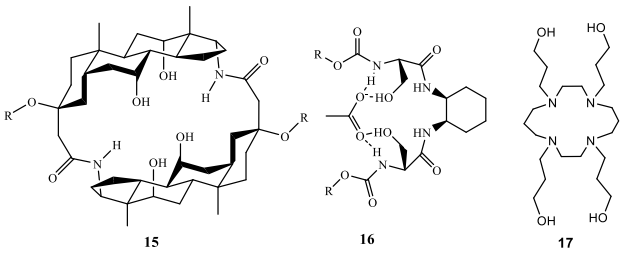

Figure 7: Structures of receptors 15-17.

Davis and coworkers designed a steroid – based cryptand **15** capable of recognizing halide anions. Cholic acid derived macrodilactam with four hydroxyl and amide groups provided a small – size cavity and a rigid framework that selectively recognized F^- ion over the other halides (K_a = 3220, 990 and 250 M^{-1} for F^-, Cl^- and Br-, respectively) [22]. Hamilton *et al*. developed a new family of receptors for carboxylates based on the multidentate recognition strategy of ristocetin [23]. The design employs four hydrogen bond donors from either urea or amino acid derivatives. Particularly strong binding is seen with receptors that employ hydroxyl binding sites, as in **16**.

Steed's group employed Cu(II) complex of hydroxypropyl chains appended cyclam-derivative **17** for binding anion binding. Based on FAB mass spectrometry experiments the authors suggested that one acetate anion remain bound to the $[Cu(\mathbf{17})]^{2+}$ cation in the gas phase. Although the quantitative anion binding studies in solution were not reported structure of the acetate complex was determined using single crystal X-ray analysis. Single crystals obtained as the mixed-anion material $[Cu(\mathbf{17})](OAc)_{1.3}(Cl)_{0.7}$ displayed two anion binding sites. One site was bound to aceate anion involving three O-H---anion type hydrogen bonds while the other site contains disordered chloride/acetate anion [24].

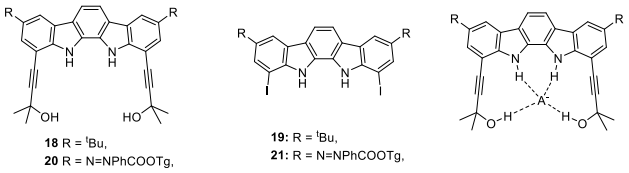

Figure 8. Structures of receptors 18-21.

Butynol appended indolocarbazoles are also found to effective in anion complexation. Jeong et all reported that indolocarbazole receptor **18** could anion and displayed high affinity (>10^6) for acetate anions in 99:1 CD_3CN:H_2O. The observation that compound **19** without O-H group displayed much lower affinity for anion was taken as evidence for involvement of the pendent O-H function in anion recopgnition. Crystal structures of $H_2PO_4^-$ and Cl^- complexes of **18** provided further evidence for the involvement of O-H anion coordination. However, diazobenzene appended indolocarbazole receptor **20** bearing butynol groups displayed weaker colorimetric response to anions than the receptor **21** that does not contain butynol groups. Such apparently contrasting results was explained in terms of OH---anion hydrogen that lower the effect of anion binding on the indolocarbazole and hence on the diazobenzene chromophore [25].

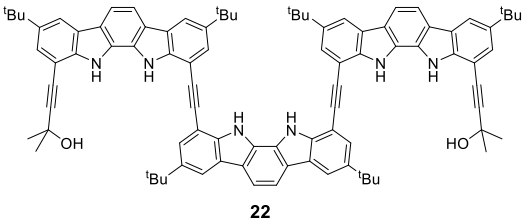

Figure 9: Structure of receptor 22.

A trimeric analogue of **18** was also prepared by Jeong et al,. The trimeric indolocarbazole **22** is able to fold around the anion to form a helix in which the six NH and two OH functionalities are suitable position to for hydrogen bonds with anion. The receptor displayed strong affinity for sulfate anion in CH_3CN:CH_3OH ((1:1, v/v) solution. The formation of helical structure was confirmed by 1D and 2D NMR as well as single crystal;l X-ray crystallography. The strong interaction between the O-H and sulfate anion, as

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inferred from significant shift in the O-H proton signal in the presence of sulfate anion, was proposed to be the key factor for the formation of coiled structure [26].

In addition to indolocarbazoles bearing butynol groups, Jeong et al also prepared a series of pheny urea receptors (for example, **23**, R = Cl)) containing butynol subunits. The association constants for the interaction of these receptors with chloride anions were found to be in the range of 5000-17000M^{-1} in $CD_3CN:H_2O$ (99:1, v/v) solution depending on the nature of substituent on phenyl ring. Additionally, these receptors were shown to transport anion across lipid bilayer [27].

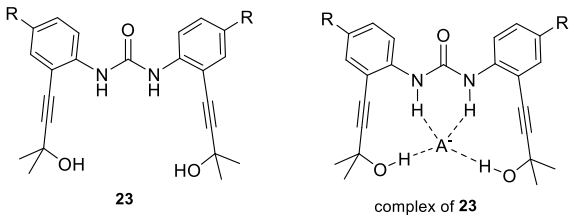

Figure 10: Structures of receptor 23 and suggested anion binding mode.

Wang and Kass et al studied anion binding properties of a range of aliphatic diols and polyols [28].Among the various receptors the insitol based receptor were found to be most efficient in anion binding. The receptor **24** having three O-H donar displayed strong affinity for chloride binding with an association constant value in the order of 10^6 M^{-1}. Only two of the three hydroxyl groups were found to form direct hydrogen bonds with anions while the third (though not directly involved in hydrogen bonding with anion) plays an important role to augment the anion binding strength of the first to two. It has been further shown that the anion binding affinity of **24** could also be enhanced significantly by judiciously chosen equatorial substituent [29].

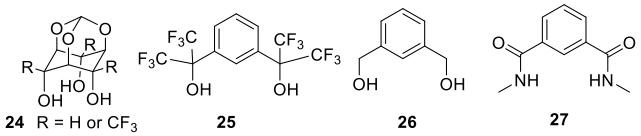

Figure 11: Structures of receptors 24-27.

Anion binding properties of fluorinated alcohol **25** was reported by Gale et al. The receptor **25** displayed higher affinities for acetate, benzoate, sulfate (K_a > 10^4 M^{-1}) in comparison to the non-fluorinated **26** (K_as: 290-1400 M^{-1}) and amide analogueand **27** (K_as: 790-830 M^{-1}) respectively [30].

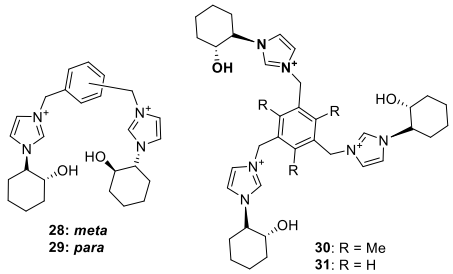

Figure 12: Structures of receptors 28-30.

Alfonso et al utilized chiral dipodal (**28** and **29**) and tripodal (**30** and **31**) imidazolium based receptors having cyclohexanol OH donors for the recognition of citrate, isocitrate and D and L malonate anions. Anion binding studies in 9:1 $CD_3CN:CD_3OD$ revealed tripodal receptors **30** and **31** are better than the dipodal receptors in anion binding and between the two tripodal receptors **30** having three methyl substituents at central benzene ring is more efficient than other. This finding was ascribed to cone-type conformation of the imidazolium receptors favored by the presence methyl substituents. Receptor **30** displayed higher affinities for malonate than citrate or isocitrate which was explained in terms of better fit of malonate within the cavity. However, little chiral discrimination was observed between D- and L-malonates [31].

III. Conclusion

Since the first report of O–H containing anion receptors in the mid-1990s, there has been significant progress in the past 20 or so years. Sophisticated molecular constructs have now been prepared that can achieve selective anion recognition, and a few of these can function in aqueous or semi aqueous. However, there is much space in the applications of O–H---anion interactions, specifically in the fields of anion transport, anion-templated assembly and anion binding catalysis.

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