Anion coordination chemistry using O–H groups†

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This review covers significant advances in the use of O–H groups in anion coordination chemistry. The review focuses on the use of these groups in synthetic anion receptors, as well as more recent developments in transport, self–assembly and catalysis.

Introduction

Anions are of crucial importance in a range of biological, environmental and industrial processes. Motivated by potential applications in these fields, as well as to achieve a greater understanding of host–guest interactions, a plethora of synthetic receptors for anions have been reported in the last few decades.[1-4]

A range of interactions have been used to interact with anions including interactions with Lewis acids such as transition metal cations,[5,6] hydrogen bonding, and more recently halogen bonding[7-9] and other σ-hole interactions such as chalcogen bonding.[10] Within the realm of hydrogen bonding, the majority of systems contain N–H hydrogen bond donors[11-13] while within the last decade C–H hydrogen bond donors have received increasing attention.[14] While it is well-established that O–H···anion hydrogen bonds are important in biological anion recognition processes (*e.g.* chloride channels, Fig. 1),[15-18] use of these interactions in synthetic systems has received relatively little attention.

Nonetheless, a number of notable results have been reported: as has been common in anion supramolecular chemistry,[19] attention initially focused on O–H containing anion receptors, while in the last decade more varied applications of O–H···anion coordination have been realised. This review aims to highlight key work within this field starting from the initial discoveries that cyclodextrins can interact with anions, through to recent reports of hydroxy-containing anion receptors that can function in aqueous media, conduct anion-binding catalysis and transport charged species across membranes. We survey the field to November 2018 and primarily focus on systems where there is clear evidence for O–H···anion hydrogen bonding during anion recognition. This review is not intended to be a comprehensive survey of the field but rather to focus on systems that were significant in the development of the field or suggest avenues for its future progress.

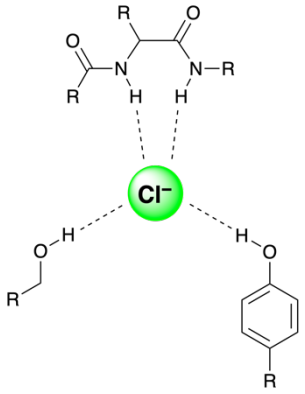

Fig. 1 Diagram showing the chloride anion binding site of ClC chloride channels, as determined by X-ray crystallography (R = protein chain).[15]

Advantages of O–H groups

Alcohol groups have several advantages that make them ideal candidates for use in anion coordination chemistry: perhaps most importantly having a "sweet spot" in term of acidity. The pK_a of phenol is 10.0 and methanol is 15.5,[20,21] meaning that alcohol groups are strong enough acids to be potent hydrogen bond donors, but in most cases not so strong that they are prone to deprotonation. This is perhaps best illustrated by the fact that simple phenols can bind anions, including in the polar organic solvent, acetonitrile.[22-24] An additional bonus is that hydroxy-containing receptors are often easy to synthesize: alcohol compounds with numerous additional substituents are commercially-available; these additional substituents may be used to build up more complex polyfunctional host systems, or to tune binding properties. Furthermore, protecting group methodology is well-established for alcohol groups if required.[25]

Receptors from the 20th century

As long ago as 1961, Schlenk and Sand noted that α-cyclodextrin could interact with iodide anions in water while other halides interacted less strongly.[26] Subsequent studies confirmed that a range of anions could weakly bind to both α-cyclodextrin (**1**) and β-cyclodextrin (**2**) in water, with large lipophilic anions such as ClO_4^- binding much more strongly than Br^- and NO_3^-.[27,28] Binding was attributed to both the hydrophobic cavity and the hydrophilic hydrogen bonding "plane" of O–H groups present in the cyclodextrin macrocycle (Fig. 2),[27] although the significance of the hydrophobic effects in these kinds of interactions is a matter of some debate, as is the location of anion binding (inside or outside the macrocycle).[29-32]

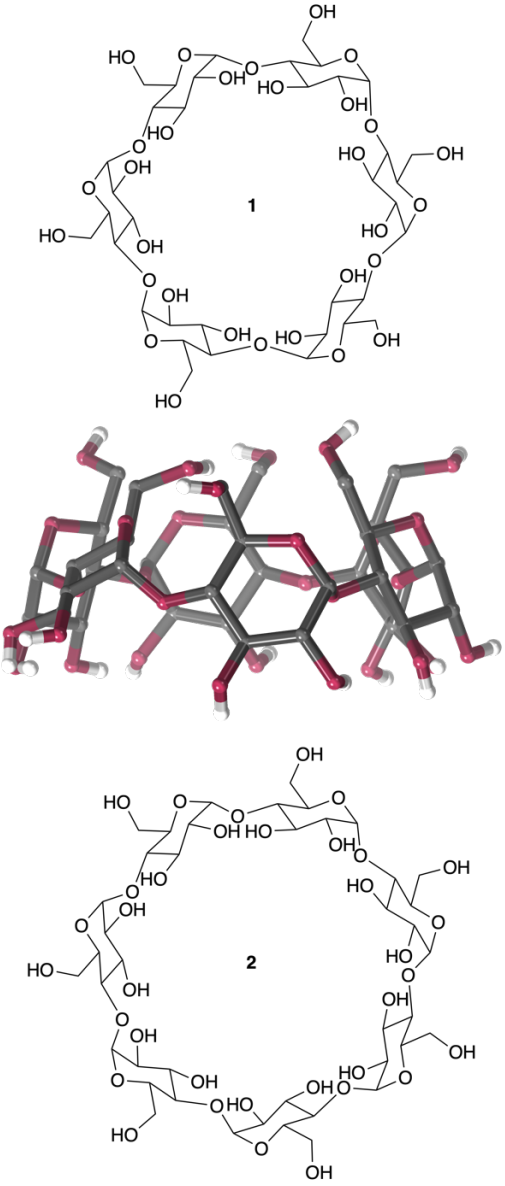

Fig. 2 Structures of **1** and **2** and X-ray crystal structure of **1** (CCDC: 1124602, solvent molecules and most hydrogen atoms omitted for clarity).

Generally, the binding of inorganic anions to cyclodextrins and their derivatives is weak (K_a < 30 M^{-1} for ClO_4^-), while the binding strength of organic anions such as carboxylates is determined more by the hydrophobicity of the substituent group than the carboxylate moiety. Indeed, in many cases, carboxylate anions bind *less strongly* than their conjugate acids.[33,34‡]

After the initial forays with cyclodextrins, there was something of a lull in the field of O–H···anion chemistry until the 1990s. In 1993, reported a family of analogues of the antibiotic ristocetin, which is known to complex the carboxylate termini of amino acids. A family of receptors were prepared, and it was shown that receptor **3** (Fig. 3), containing hydroxy groups bound acetate strongly in CD_3CN (K_a > 10^5 M^{-1}). Importantly, this association constant was three orders of magnitude greater than that recorded for receptor **4**, which does not contain any O–H groups, showing the importance of these moieties for guest recognition. [35]

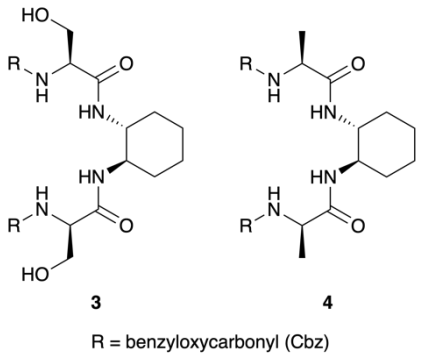

Fig. 3 Ristocetin analogues prepared by Hamilton.

Two years later, Beer demonstrated that the ammonium and potassium salts of a calixarene-based ditopic receptor **5** containing two benzo-15-crown-5 macrocycles could bind anions strongly in CD_3CN (Fig. 4).[36] The host was selective for $H_2PO_4^-$, which was bound too strongly for an association constant to be determined by NMR techniques (> 10^4 M^{-1}); this was attributed to the pseudo-tetrahedral cavity afforded by the two amide and two hydroxy protons. The following year, the same group described a ruthenium tris(bipyridine) complex functionalised with amide groups with or without phenol motifs (Fig. 4).[37] Receptors **6** and **7** containing *para* or *meta* phenol groups bound halide anions much more strongly than receptor **8** containing *ortho* phenol groups, or receptor **9** containing a phenyl ring. Interestingly *tert*-butylphenyl-substituted receptor **10** displays stronger anion recognition than any of **6**–**9**, suggesting a more complex mechanism than simple hydrogen bond donor arrangement.

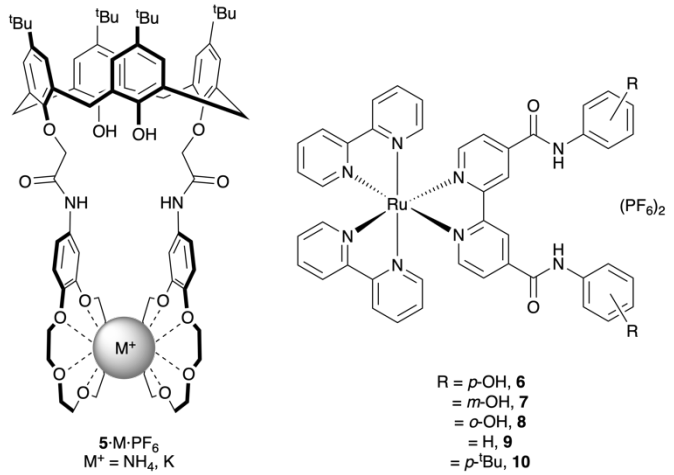

Fig. 4 Early anion receptors using O–H functionality reported by the Beer group.

In 1996 Schneider reported an investigation into the binding of anions by substituted sugar molecules as well as simpler alcohols in $CDCl_3$. Benzyl alcohol, isopropanol, and cyclohexanol displayed very weak anion recognition in this non-polar solvent, but alkyl-substituted sugars **11** and **12** (Fig. 5) displayed moderately strong binding with association constants up to 1067 M^{-1}, with anion binding affinities following basicity trends.[38] This work built upon studies by Hamilton, who showed that receptors containing anionic phosphonate groups could bind alkyl glycosides.[39§] A year after Schneider's study, Dondoni reported calixarene derivatives bearing sugar molecules at the upper rim;[40] one of these, **13**, showed weak binding of $H_2PO_4^-$ in highly polar d_6-DMSO. Interestingly, evidence of binding to *cationic* glucosamine hydrochloride was also observed with the same receptor.

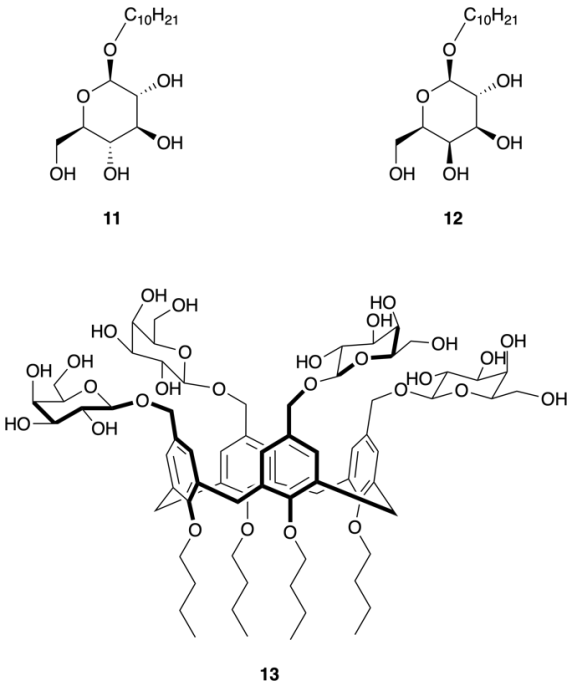

Fig. 5 Structures of sugar-based receptors **11**, **12** and **13**.

The Davis group studied derivatives of the steroid, cholic acid, for use in anion recognition.[41] They prepared cryptand **14** containing four hydroxy groups and two amide donors (Fig. 6). The cryptand bound halide anions, with strong binding of fluoride in $CDCl_3$ and weaker binding of chloride and bromide. Molecular modelling studies suggested that halide anions were complexed by the four hydroxy groups and only one of the two amides, with minimal rearrangement required for guest binding. Later, the same group investigated the anion recognition properties of the simplified acyclic system **15**.[42] This displayed notably weaker binding, functioning only in hydrocarbon solvents. Subsequently, Kolehmainen used a porphyrin scaffold to prepare highly-charged 4^+ systems incorporating four quaternary ammonium-derivatised cholic acid motifs; these receptors displayed little selectivity but were able to bind AMP, ADP and ATP in methanol:aqueous buffer mixtures.[43]

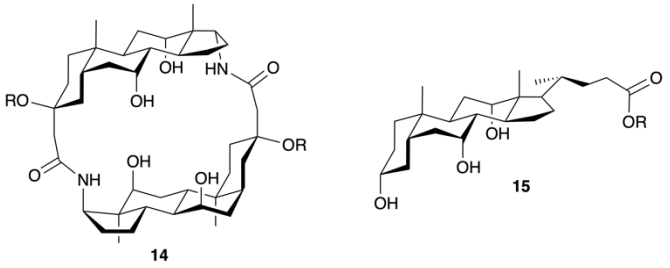

Fig. 6 Structures of Davis' receptors based on cholic acid (R = alkyl chain).

In 1998 important work by Odashima and Umezawa revealed that phenol and simple substituted phenols could bind anions in benzene.[22] Remarkably, this study revealed chloride binding constants as high as 2×10^5 M^{-1} for 4-nitrophenol. The paper is quite a contrast from Davis' elegant cryptand systems but represents a powerful demonstration of the potency of O–H hydrogen bond donors, admittedly in a non-polar solvent.

In the same year, Ungaro reported a new family of calixarene-based receptors containing either two or four fluorinated alcohol groups (Fig. 7).[44] In the case of the difunctionalised receptor **16**, the anion recognition motif is inherently chiral and the authors were able to separate the racemic mixture of homochiral receptors (*rac*-**16**) from the *meso* compound (*meso*-**16**). Interestingly, *rac*-**16** was able to bind both the achiral acetate anion and the chiral anion of *N*-lauroyl-L-phenylalanine more strongly than *meso*-**16** in $CDCl_3$. Both anions were bound more strongly than halide anions, while the tetrafunctionalised host **17** bound bromide more efficiently than acetate in the same solvent. Notably, receptor **18** containing non-fluorinated alcohols did not bind bromide or acetate.

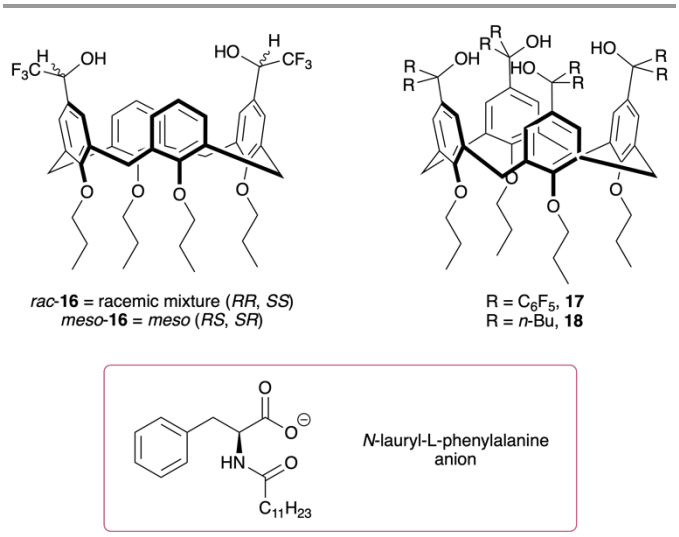

Fig. 7 Structures of Ungaro's fluoroalcohol-based host systems, and chiral carboxylate anion bound by **16**.

Receptors from this century

This century has seen a much larger number of O–H containing anion receptors than the previous, and so for ease of reading this section has been split into three subsections: receptors containing phenolic O–H groups, receptors containing aliphatic O–H groups and receptors containing heteroatom–O–H groups.

O–H anion receptors containing phenolic O–H groups

Another calixarene-based host was reported by Pocchini, who prepared the ion pair receptor **19** (Fig. 8).[45] This system bound tetramethylammonium (TMA) salts in CD_3CN, as determined by ^1H NMR titration experiments. A combination of NMR and computational techniques provided evidence that the TMA cation bound within the host cavity, while the anion associated externally forming hydrogen bonds to the O–H groups. Binding affinities followed anion basicity trends, with acetate and tosylate anions binding particularly strongly.

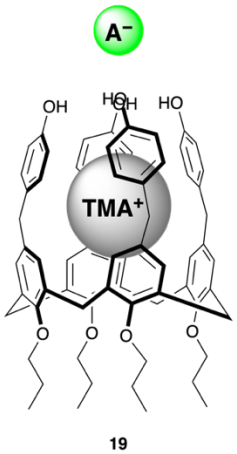

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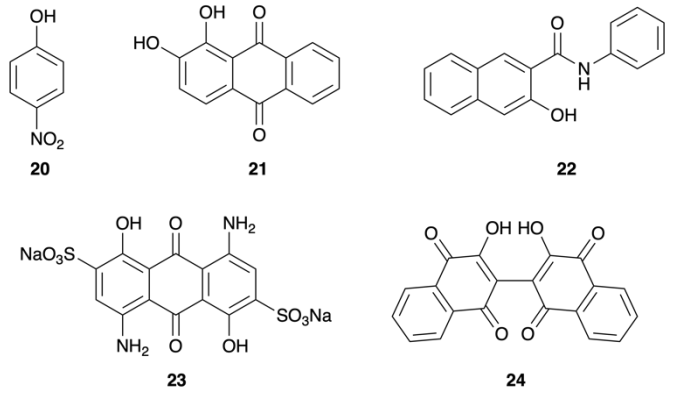
Fig. 8 Binding of TMA salts as ion pairs in a calixarene-based ditopic receptor reported by Pocchini.

In 2001, Sessler screened a series of commercially available compounds that contained chromophores and hydrogen bonding groups to see if they could colourimetrically sense anions in CH_2Cl_2.[23] While no quantitative studies were conducted nor binding modes elucidated, several O–H containing molecules were found to sense anions (**20**–**24**), apparently through O–H···anion interactions (Fig. 9). Remarkably, compound **24** could extract chloride into CH_2Cl_2 from aqueous solutions (including seawater) in the presence of a crown ether phase transfer agent.



20 **21** **22**

23 **24**

Fig. 9 Commercially-available anion sensors containing O–H groups identified by Sessler.

Continuing the theme of simple compounds that can be potent anion hosts, in 2003 Smith used a high throughput NMR screening process to identify simple compounds that could function as anion receptors.[24] This methodology, which was developed within his group to identify cation receptors,[46] uses a reference compound of known binding strength, and studies the ability of other hosts to remove a guest from this compound. The advantage of this approach is that only one spectrum needs to be run per compound to be screened allowing a wide range of data to be obtained quickly. Importantly, the work showed that phenols containing *ortho*-methyl substituents did not bind chloride in CD_3CN (*e.g.* **25**), while phenol (**26**) bound weakly and *p*-nitrophenol (**20**) displayed moderately strong binding (Fig. 10 shows the K_a values for these receptors). Commercially-available catechol (**27**) displayed even stronger binding with an association constant greater than 10^3 M^{-1}.

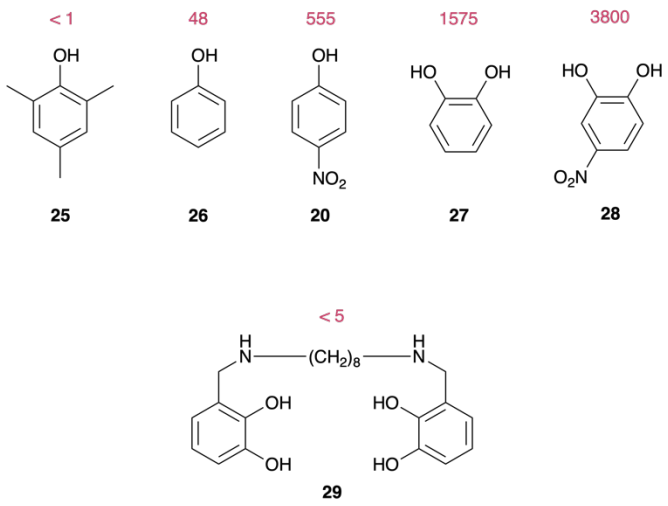


Fig. 10 Simple anion binding compounds containing O–H groups identified by Smith. Binding affinities for chloride anion in CD_3CN are provided above each receptor (K_a in M^{-1}).

A later paper by the same group revealed that 4-nitrocatechol (**28**) is an even stronger anion host than catechol and could even bind anions in CH_3CN containing 0.5% H_2O.[47] A sensing response was also observed for this compound due to a reduction of the intensity of a UV-Vis absorbance band upon addition of anions. The same paper also demonstrated that catechols could sense anions electrochemically by inducing an anodic shift in the catechol oxidation potential. Attempts to incorporate catechol motifs into more complex receptors were hampered as functional groups *ortho* to the catechol motif often favour intramolecular hydrogen bonding that weakens anion recognition (*e.g.* receptors **29**–**31**, which display negligible chloride binding in acetonitrile, Figs. 10 and 11). A similar phenomenon was observed soon after by Jiang, who observed that dihydrogenphosphate anion binding to salicylanilides (**32**) was impeded by formation of intramolecular hydrogen bonds.[48]

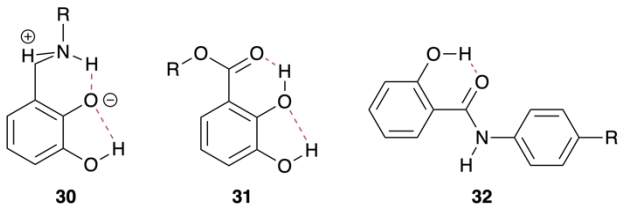


Fig. 11 Diagram showing unfavourable intramolecular hydrogen bonding in receptors reported by Smith and Jiang, resulting in weak anion binding.

When fluoride was added to catechol in CD_3CN, Smith observed deprotonation and a dramatic colour change to deep blue. After detailed studies, the authors were able to assign the colour as arising from products of oxidative degradation of catechol that is initiated by deprotonation of one of the O–H groups.[47] Deprotonation of a phenolic receptor was also observed in 2000 by Hiratani who showed that receptor **33** gave dramatic fluorescence responses to the basic anions fluoride and acetate as well as to dihydrogenphosphate (Fig. 12).[49] ^{19}F NMR spectroscopy indicated that HF_2^- was formed upon fluoride addition, and the fluorescence responses produced by fluoride and acetate could be reproduced by addition of hydroxide as anion, clearly showing that these responses are due to a deprotonation event. Since Hiratani's report, numerous other O–H containing sensors have been described that show dramatic colour/fluorescence changes on addition of basic anions in aprotic solvents. This seems to be particularly common when the phenolic O–H group is *ortho* to an amide or imine functionality, presumably due to increased acidity of the O–H group due to conjugation (*e.g.* **34**).[50] Given these colour/fluorescence changes appear to be largely/exclusively down to deprotonation instead of O–H···anion H-bonding (even if this has not always been commented on by the authors), they will not be discussed further.[§§]

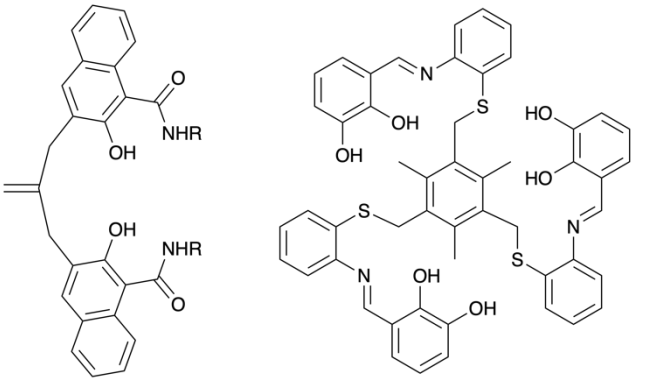


Fig. 12 Representative structures of anion receptors that give sensing response to fluoride caused by deprotonation.

It is however possible to prepare fluoride-selective systems that do not deprotonate, by taking advantage of the fact that basic fluoride forms stronger hydrogen bonds with anions than less-basic guests. Scott prepared metal salphen complexes containing four phenol donors (**35** and **36**, Fig. 13) and showed that these metallohosts could selectively bind fluoride in DMSO with association constants > 10^5 M^{-1} and a colourimetric response to the anion.[51] Detailed ^1H and ^{19}F NMR studies were used to show that deprotonation was not occurring. A crystal structure of the fluoride complex of the nickel(II)-containing receptor was obtained and shows very short O–H···F^- hydrogen bonds. Another metal-containing system was reported the following year by Ganguly, Ghosh and Das: this system contained a ruthenium(II) tris(bipyridine) system functionalised with either phenol or catechol.[52] Anion binding to fluoride was observed at low fluoride concentrations, followed by deprotonation with higher amounts of guest.

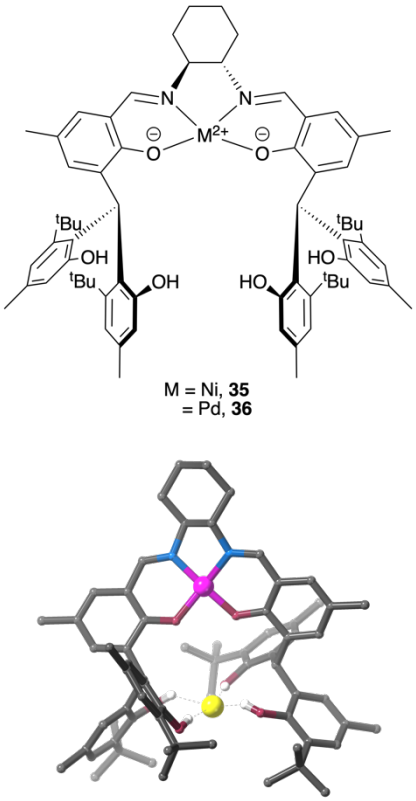


Fig. 13 Structure of Scott's fluoride-selective hosts and crystal structure of the fluoride complex of **35** (CCDC: 296136; TBA cation, solvent molecules and most hydrogen atoms omitted for clarity).

Shinmyozu used a stilbene derivative to prepare the switchable anion receptor **37** based on BINOL anion recognition motifs (Fig. 14).[53] Light-controlled isomerisation of the stilbene allowed switching between the *cis* and *trans* arrangement. While this was an innovative attempt to prepare a stimuli-responsive anion host, unfortunately similar binding strengths were observed for the two isomers of the receptor. Yu also used the BINOL scaffold to prepare anion receptors (**38** and **39**).[54] These systems showed some discrimination between the anions of L- and D-BOC-amino acids in CH_3CN and also gave a fluorescent response to acetate and fluoride (presumably caused by deprotonation).

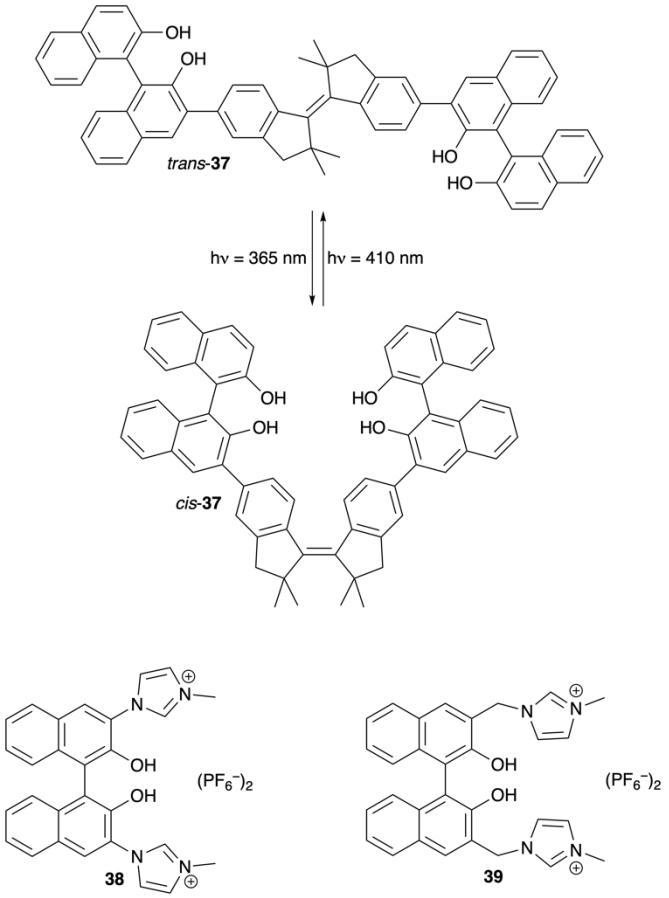


Fig. 14 BINOL-based receptors for anions.

In 2012, Wang and Kass reported the tris(phenol) compound **40**.[55] This molecule exists as a separable mixture of rotamers at room temperature, with the *syn* rotamer having all hydroxy groups on one face of the central benzene ring, while the *anti* rotamer has two hydroxy groups on one face and the other on the opposite face. The *syn* rotamer shows remarkably strong chloride anion binding in acetonitrile (> 10^5 M^{-1}), which was attributed to the three O–H groups binding convergently to the anion as shown in Fig. 15. Almost concurrently, Ito reported a family of similar tripodal receptors (**41**), which show strong anion binding in chloroform.[56] Association constants were slightly smaller than those reported for **40** in CD_3CN, although given the different solvents used and the well-known tendency of the TBA·anion salts used in these studies to ion-pair in chlorinated solvents,[57,58] it is difficult to draw any firm conclusions about relative binding strengths.

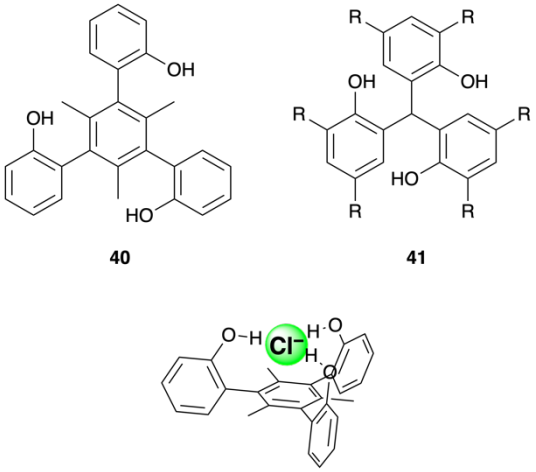


Fig. 15 Tripodal anion receptors reported by Wang and Kass, and Ito, and proposed binding mode for Wang and Kass' system.

O–H anion receptors containing aliphatic O–H groups

In 2002, Kondo reported receptor **42** containing sulfonamide and aliphatic O–H groups (Fig. 16).[59] This receptor showed very strong acetate binding in CD_3CN (K_a > 10^4 M^{-1}) and moderate chloride binding in the same solvent (K_a = 930 M^{-1}). Importantly, binding was much stronger than an analogous receptor that did not contain hydroxy groups. A follow-up paper showed that receptor **43** containing aromatic O–H groups displayed even stronger anion recognition, with chloride now bound with a K_a > 10^4 M^{-1}.[60]

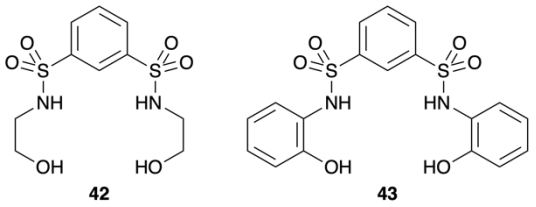


Fig. 16 Sulfonamide receptors reported by Kondo.

Steed's group prepared Cu(II) and Ni(II) complexes of the cyclam-derived ligand **44** (Fig. 17).[61] Single crystals were obtained of the mixed-anion material $[Cu(\mathbf{44})](OAc)_{1.3}(Cl)_{0.7}$, which contains two anion sites – one of which is a disordered chloride/acetate anion, while the other site is an acetate anion, which is held in place by short O–H···anion hydrogen bonds from three O–H groups from the hydroxypropyl chains of the ligand, one of which is also coordinated to the Cu(II) centre. While no quantitative solution anion binding studies were reported, FAB mass spectrometry experiments suggested that one acetate anion remains bound to the $[Cu(\mathbf{44})]^{2+}$ cation in the gas phase.

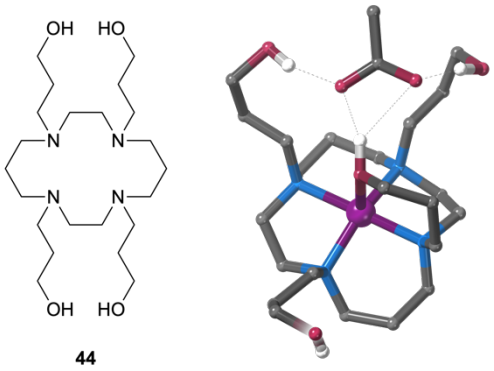


Fig. 17 Structure of cyclam-derived ligand **44**, and X-ray crystal structure of $[Cu(\mathbf{44})](OAc)_{1.3}(Cl)_{0.7}$ (CCDC: 267670; most hydrogen atoms, disordered anion position and solvents omitted for clarity).

Yang and Wong also utilised metal cations to assist with anion recognition, and prepared a terbium-containing metal organic framework composed of mucicate ligands (**45**), $[Tb(\mathbf{45})_{1.5}(H_2O)_2]_n$ (Fig. 18).[62] This ligand presents a number of hydroxy groups into the channels of the porous framework and the authors showed that the materials could sense a range of anions (CO_3^{2-}, CN^-, I^-, Br^-, Cl^-, F^-) in water through enhancement of the terbium-centred luminescence intensity. While little selectivity was observed, and the strongest-binding anion bound relatively weakly (K_a ~ 350 M^{-1}), the ability to sense anions in water is a significant achievement. Unlike most systems documented in this review, this system functions heterogeneously. Since this work, several more coordination polymers have been reported that show anion binding/sensing behaviour attributed to O–H···anion interactions,[63-65] although quantitative anion recognition experiments have rarely been conducted.

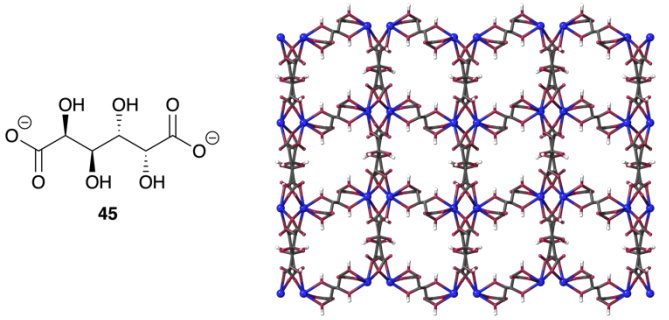


Fig. 18 Structure of mucicate ligand **45** used to prepare an anion-sensing terbium organic framework, and crystal structure of the framework (CCDC: 295441; water molecules coordinated to terbium cations, solvent molecules and some hydrogen atoms omitted for clarity).

In 2008, Jeong prepared indolocarbazole receptor **46** containing unusual butynol O–H donors (Fig. 19), and demonstrated that this host could bind anions in 99:1 CD_3CN:H_2O.[66] Remarkably, an association constant > 10^6 M^{-1} was recorded for acetate in this highly competitive aqueous solvent medium. Anion binding affinities generally followed anion basicities, and **46** bound anions much more

strongly than an analogous receptor (**47**) that did not contain the O–H donors. Crystal structures of the $H_2PO_4^-$ and Cl^- complexes of **46** were obtained and clearly showed the role of the O–H groups. Interestingly when diazobenzene chromophores were appended to the indolocarbazole aromatic system (**48**), this receptor displayed a weaker colourimetric response to anions than a control system without the butynol groups (**49**).[67] The authors attributed this to the O–H···anion hydrogen bonds lessening the impact that anion coordination has on the indolocarbazole motif, and thus the chromophore reporter groups.

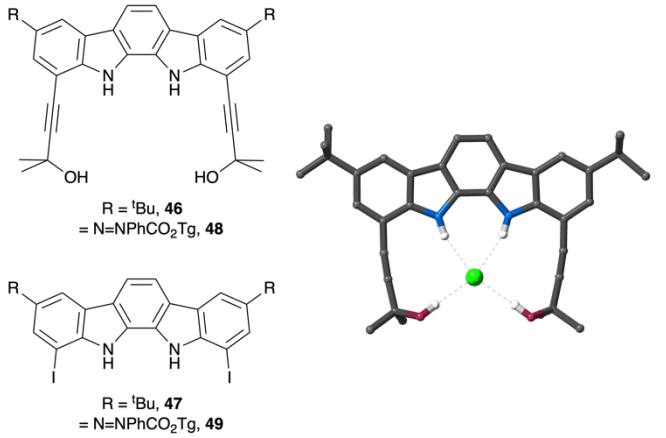


Fig. 19 Structure Jeong's indolocarbazole based receptors, and crystal structure of the chloride complex of **46** (CCDC: 674972; TBA cation and most hydrogen atoms omitted for clarity).

In an elegant extension of this work, a trimeric analogue of **46** was also synthesised (**50**), which displays strong sulfate binding in competitive 9:1 CH_3CN:CH_3OH (Fig. 20).[68] This strong binding was attributed to the ability of **50** to coil around the anion to form a helix and encapsulate it through six N–H and two O–H hydrogen bond donors. The formation of this coiled arrangement was confirmed using 1D and 2D NMR spectroscopy, and X-ray crystallography. Interestingly, a dramatic shift in the O–H proton resonance (~2 ppm) was observed on addition of sulfate anion, but no change was observed when halides were added leading the authors to implicate O–H···sulfate hydrogen bonds as key for formation of the helical architecture. A later foldamer incorporating pyridine groups showed different behaviour, where the structure was coiled in the absence of a guest but switched to a fluorescent non-coiled structure on addition of anion (due to repulsion between the pyridine nitrogen lone pair and the anion).[69]

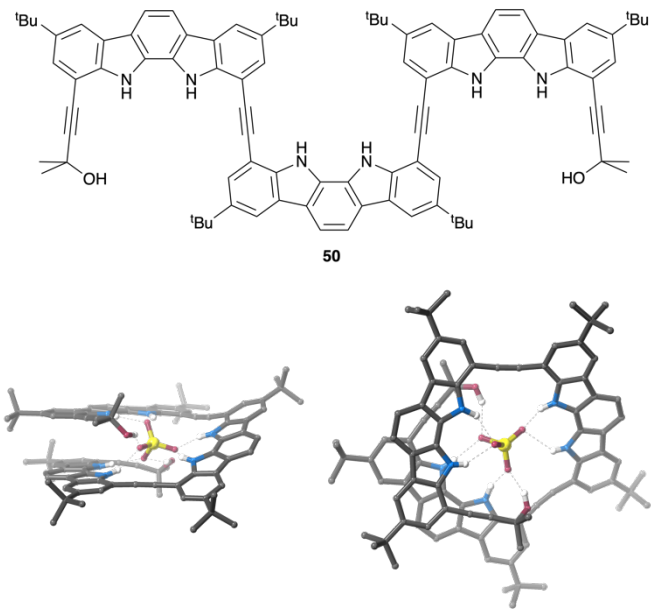


Fig. 20 Structure of **50** and two views of the crystal structure of its sulfate complex (CCDC: 727661; crystallographic disorder, solvent molecules, TBA cations and most hydrogen atoms omitted for clarity.

Jeong then prepared a family of phenyl urea receptors with butynol O–H donors, and varying substituents on the phenyl groups (*e.g.* Cl, alkyl, esters; an example, **51**, where R = Cl is given in Fig. 21).[70] These receptors are notable as they have a very similar hydrogen bonding arrangement to that seen in the ClC channel (Fig. 1). Depending on the nature of the R substituent, association constants for chloride anion ranged from 5,000–17,000 M^{-1} in competitive 99:1 CD_3CN:H_2O. Additionally the authors also demonstrated the utility of these compounds as anion transporters (*vide infra*). Subsequently, phenyl urea receptors containing butynol groups were incorporated into foldamers (**52**–**54**), and these were shown to bind sulfate strongly in highly competitive 2:3 CD_3OH:d_6-DMSO.[71] Interestingly no increase in chloride anion binding strength was observed on increasing the number of urea motifs past three (**52**), while sulfate binding continued to get stronger with up to five urea groups (**54**). Modification of **52** to include aza-crown macrocycles also allowed the synthesis of contact ion pair receptors (**55** and **56**), which displayed impressive salt binding in CD_3OH/CD_3CN mixtures, and also acted as salt transporters (*vide infra*).[72]

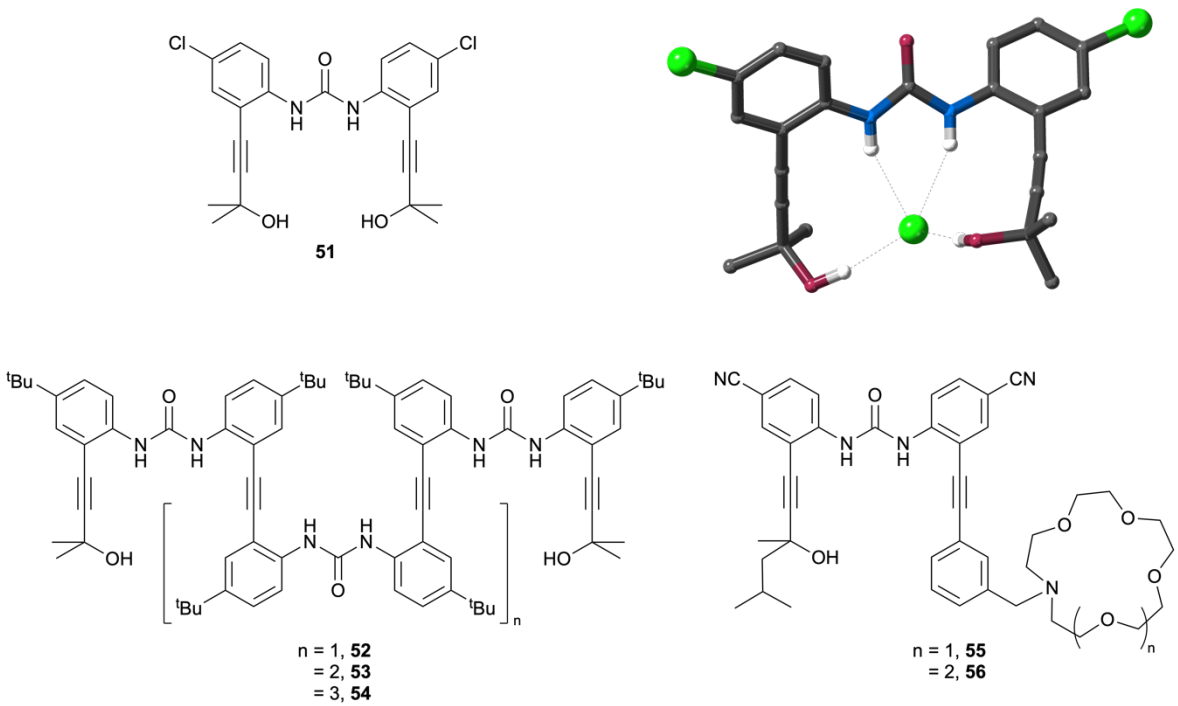


Fig. 21 Butynol urea receptor **51**, phenyl urea foldamers **52**–**54** and ion pair receptors **55** and **56**, and crystal structure of the chloride complex of **51** (CCDC: 875574; TBA cation and most hydrogen atoms omitted for clarity).

Since 2012, the Wang and Kass groups have published a significant body of work investigating aliphatic O–H anion receptors. Initially, they investigated simple diols and polyols such as those shown in Fig. 22. Having shown that these could be potent acids (attributed to stabilisation of the conjugate base),[73] subsequent studies showed that heptaol **57** could complex chloride anions in CD_3CN with an association constant of 360 M^{-1}, and that binding was both enthalpically and entropically favourable.[74] §§§ A later paper revealed that the fluorinated alcohols **58** and **59** showed even stronger chloride binding with association constants of 3,300 and 6,700 M^{-1}, respectively (in CD_3CN).[75]

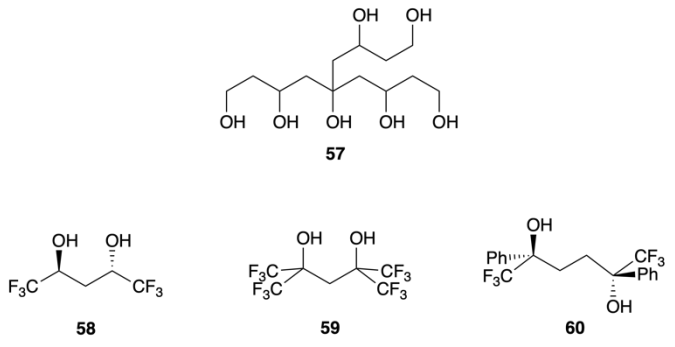


Fig. 22 Structure of Wang and Kass' aliphatic diol and heptaol chloride receptors.

Kass subsequently investigated the effect of solvent on the anion recognition properties of **58** and **60**, studying the binding affinities in $CDCl_3$, CD_3CN, and mixtures of the two.[76] In work reminiscent of Hunter's seminal studies of the H-bonding interaction between a fluorinated alcohol and phosphine oxide in $CDCl_3/d_8$-THF mixtures,[77] Kass showed that binding in mixtures of $CDCl_3$:CD_3CN was orders of magnitude weaker than in either solvent alone (Table 1). A similar effect was seen when mixtures of CD_3CN and other non-polar solvents were studied.

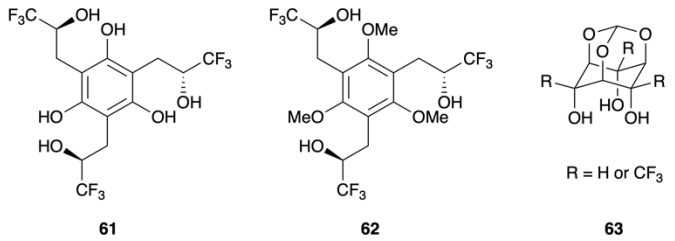
Table 1. Chloride[a] association constants for **58** in mixtures of $CDCl_3$ and CD_3CN.

Solvent mixture	K_a (M^{-1})
$CDCl_3$	4000
9:1 $CDCl_3$:CD_3CN	870
3:1 $CDCl_3$:CD_3CN	270
1:1 $CDCl_3$:CD_3CN	190
1:3 $CDCl_3$:CD_3CN	160
1:9 $CDCl_3$:CD_3CN	460
CD_3CN	3300

[a]Chloride added as TBA salt.

Building on their work with fluorinated aliphatic alcohol groups, Wang and Kass prepared tripodal systems containing three of these motifs and then either three phenolic O–H groups (**61**) or three methoxy groups (**62**, Fig. 23).[78] Interestingly, **62** binds anions significantly more strongly than **61** despite containing fewer potential donor groups, which was attributed to the additional O–H groups in **61** organising the system into an arrangement that is less favourable for guest binding. Strong anion binding to **62** was observed in a range of solvents with association constants > 10^5 M^{-1} for chloride and acetate anions in d_6-acetone. When using inositol-based systems (**63**), even

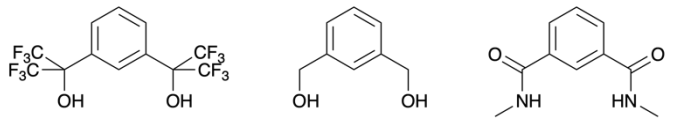
stronger chloride anion recognition was observed in CD_3CN (K_as as large as 10^6 M^{-1}). In this system, it was demonstrated that only two of the three O–H groups interact directly with the anion, while the third enhances the anion binding strength of the first two.[79] A later study showed that binding affinity could also be enhanced by careful use of equatorial substituents in these types of compounds.[80]



61 62 63

Fig. 23 Structure of tripodal and inositol-based anion hosts **61**–**63**.

Gale investigated the anion binding of fluorinated alcohol host **64** in CD_3CN and compared this to both the non-fluorinated analogue **65** and to isophthalamide derivative **66** (Fig. 24).[81] Very strong binding of the oxoanions acetate, benzoate and sulfate to **64** was observed (K_a > 10^4 M^{-1}) and these association constants were much stronger than those recorded for **65** (K_as: 290–1400 M^{-1}) or **66** (K_as: 790–830 M^{-1}). When carbonate or fluoride was added to **64**, deprotonation was observed showing the high acidity of these hydroxy protons.



64 65 66

Fig. 24 Gale's fluorinated hydroxy-containing anion host and model compounds used for comparisons.

Alfonso prepared chiral imidazolium hosts containing cyclohexanol O–H donors (Fig. 25).[82] Bipodal (**67** and **68**) and tripodal receptors (**69** and **70**) were synthesized and the binding of citrate, isocitrate and malonate studied in 9:1 CD_3CN:CD_3OD. Generally the tripodal receptors were stronger anion binders than the bipodal hosts and **69** bound guests more strongly than **70**, which was attributed to the methyl substituents favouring a cone-type conformation of the imidazolium groups. While little chiral discrimination was observed between L- and D-malonate by any of the receptors, **69** showed an interesting selectivity preference where 2^- malonate was bound preferentially over 3^- citrate and isocitrate, due to its better fit in the host cavity.

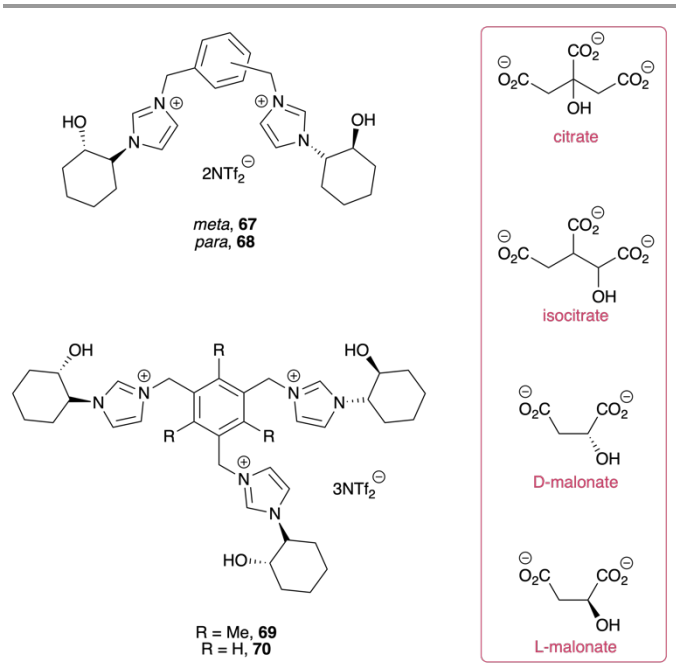
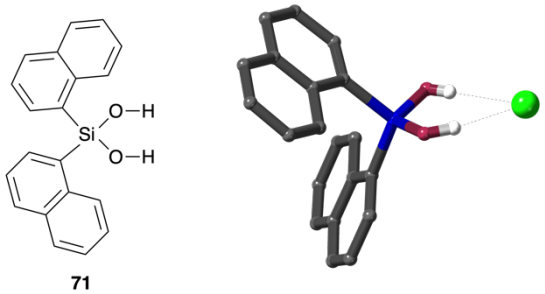


Fig. 25 Alfonso's hosts for malonate, citrate and isocitrate.

O–H anion receptors containing heteroatom–O–H groups

While alcoholic hydroxy groups (C–OH) have proven to be very useful anion recognition motifs, these are by no means the only possible hydroxy group. Silanols (Si–OH) are also potent anion binders, particularly if silanediols are used (the analogous carbon functionalities, geminal carbon diols spontaneously decompose). In 2006, Kondo and Unno reported that silanediol **71** could bind halide anions and acetate in $CDCl_3$, with both O–H groups participating in hydrogen bonding to the anion (Fig. 26).[83]



71

Fig. 26 Structure of **71** and crystal structure of its complex with chloride anion (CCDC: 627429; TBA cation, solvent molecules and most hydrogen atoms omitted for clarity).

Subsequent work by the same authors showed that the expanded receptor **72** (Fig. 27) containing two silicon atoms and two hydroxy groups was able to bind anions in $CDCl_3$ and CD_3CN, and the disiloxane tetrols **73** and **74** showed high binding affinities in CD_3CN (K_a > 10^3 M^{-1}).[84,85] A downside of receptors **72**–**74** is that they are susceptible to base-induced condensation to form polysiloxanes, so binding of acetate could not be determined. Subsequently, Kondo reported an anion sensor **75**, which contains two pyrene motifs attached to a silanediol core.[86] This receptor

was able to sense acetate and dihydrogenphosphate in acetonitrile, with the sensing response attributed to a change in the pyrene–Si–pyrene bond angle upon formation of a hydrogen bond to the anion. Cuadrado further extended the use of silanols in anion sensing by synthesizing ferrocene-silanol hosts **76** and **77**.[87] While binding of chloride anion was relatively weak (K_a < 50 M^{-1} in $CDCl_3$), these hosts could detect chloride and acetate electrochemically in 1:1 CH_2Cl_2:CH_3CN.

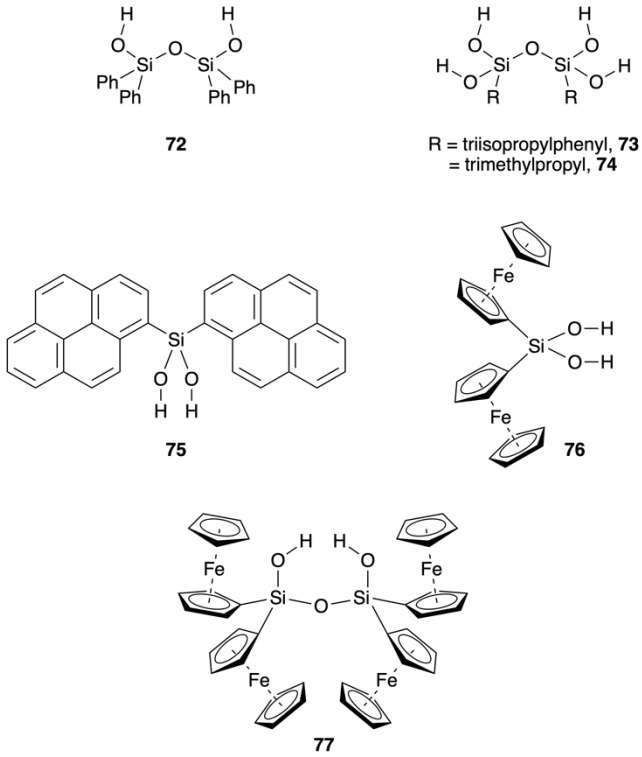


Fig. 27 Structures of silicon-containing receptors **72–77**.

In 2008 James implicated a B–O–H···Cl^- hydrogen bonding interaction in the response of receptor **78** to chloride anions (Fig. 28).[88] Interest in this type of hydrogen bonding was reinvigorated a few years ago when Yatsimirsky conducted a detailed study of the interactions between arylboronic acids (**79**) and anions.[89] This study showed that halide anions, acetate and hydrogensulfate bound to these species through hydrogen bonding interactions, with the boronic acid acting as a Brønsted acid. Conversely, fluoride and dihydrogenphosphate bound through covalent B–F and B–O bonds, *i.e.* a Lewis acid mechanism. Remarkably, the boronic acids displayed association constants up to 6,200 M^{-1} with acetate, even in the very polar solvent DMSO, and these association constants are significantly higher than those recorded for classical anion receptors such as diphenyl isophthalamide (K_a for acetate = 110 M^{-1} in d_6-DMSO[90]).

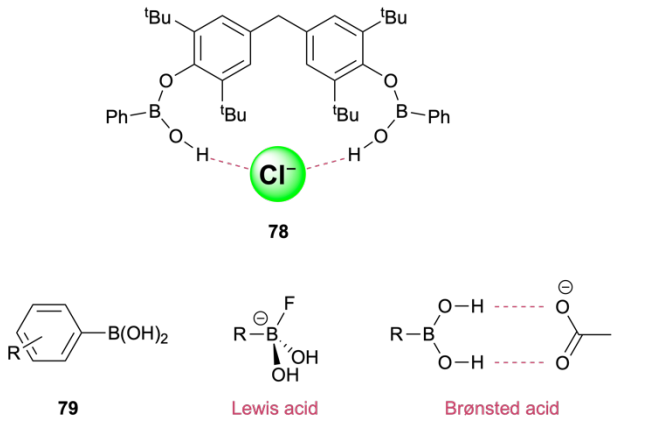


Fig. 28 Proposed chloride binding mode of **78**, and different binding modes of **79**.

Very recently, Gabbaï reported a receptor that combined both Lewis acid and Brønsted acid activity at boron.[91] Receptor **80** (Fig. 29), which contains two boron atoms in close proximity forms a covalent B–F^- bond as well as a short B–O–H···F^- hydrogen bond from a borinic acid group (H···F = 1.79 Å, 67% of the sum of the van der Waals radii[92] of H and F). This favourable arrangement allowed for very strong fluoride binding (> 10^4 M^{-1}), even in highly competitive 4:1 THF:H_2O. The remarkable binding exhibited by this host, and the strong binding observed by even simple boronic acids suggest that anion receptors based on boronic and borinic acids have great potential for use in potent anion host systems.

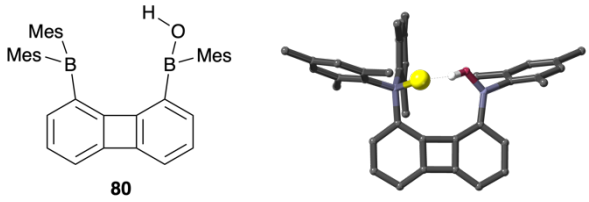


Fig. 29 Structure of Gabbaï's receptor **80** and X-ray crystal structure of its fluoride complex [CCDC: 1573890; tris(dimethylamino)sulfonium cation and most hydrogen atoms omitted for clarity].

Beyond anion recognition

Within the last decade, applications of O–H···anion recognition have started to become apparent. These can largely be divided into three main fields: anion transport, anion-templated self–assembly and anion binding catalysis, which will be discussed in the following subsections.

Anion transporters

The transport of ions across biological membranes is an important process, which maintains ions and pH homeostasis in cells. Incorrectly functioning ion transport channels are responsible for a range of diseases including cystic fibrosis.[93,94] The development of supramolecular systems for transmembrane ion transport has been partially driven by potential applications of these systems

for the treatment of diseases caused by dysregulated anion transport.[95] Given that natural chloride channels contain hydroxy H-bond donors,[15] it is perhaps unsurprising that synthetic transporters incorporating these groups have also been developed.

Building on Smith's seminal work showing that catechols are effective anion receptors,[24,47] the Davis group reported a series of dipodal catechol ligands containing both NH and OH groups (Fig. 30).[96] The anion membrane transport activity of the tren-based bis-catechols **81**–**86** was studied and it was determined that **82** was the most effective anion transporter. It was proposed that the medium length alkyl chain of **82** allowed the compound to partition into the membrane efficiently. Compounds with short or long alkyl chains were less effective, while compounds **85** and **86** which do not contain the 2,3-dihydroxy motif were inactive. It is interesting to note that Smith has shown that the 2,3-dihydroxybenzamide motif present in **81–84** shows very weak anion recognition properties in polar organic solvents as the hydroxy groups are "tied up" forming intramolecular hydrogen bonds.[97] This suggests that a different recognition mechanism may be present when the compounds are located in membranes.

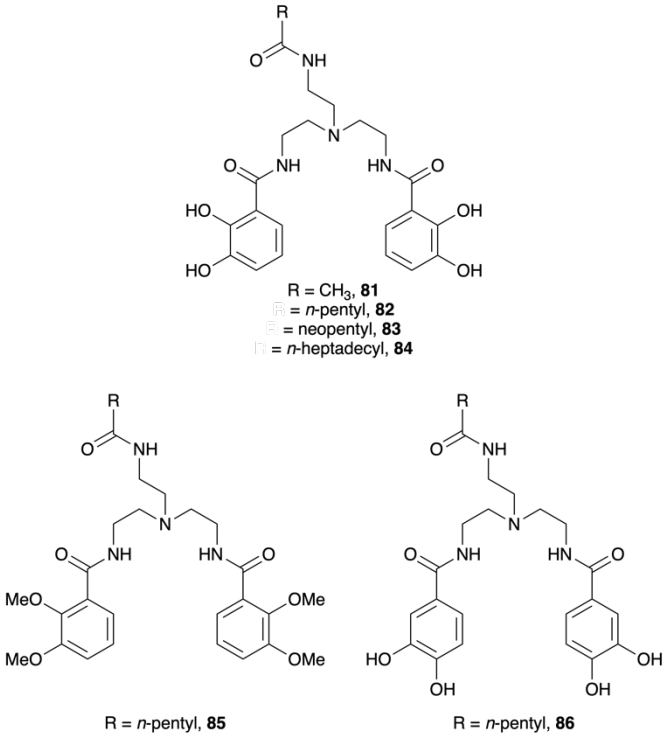


Fig. 30 Potential anion transporters studied by Davis.

The Davis group subsequently investigated the transmembrane transport of Cl^- and HCO_3^- by the sphingolipid ceramide, **87** as well as derivative **88**, which contains no O–H groups (Fig. 31).[98] Unsurprisingly, compound **87** shows much stronger chloride anion binding than **88**, and importantly this also resulted in **87** acting as an effective chloride and bicarbonate transporter, while **88** was inactive. Two years later, the same group showed that another natural product (**89**) could also act as an effective anion transporter, with the 1,2-diol being integral for these transport properties.[99] Modification of **89** by inclusion of an amide group and perfluorination of the alkyl chain to prepare transporters such as **90** gave further improvement of the anion transport properties.

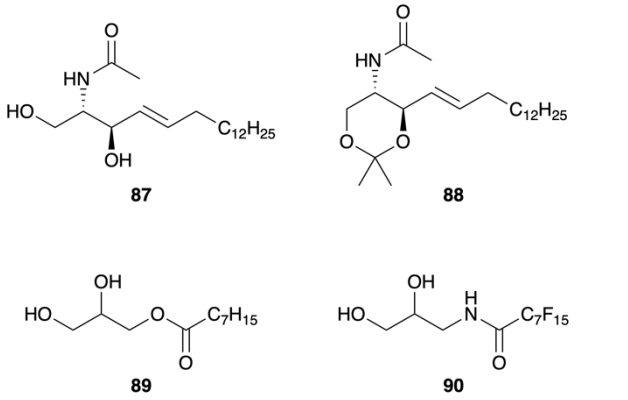


Fig. 31 Anion transporters based on natural products reported by the Davis group.

Jeong has investigated the ability of butynol functionalised ureas such as compound **51** (Fig. 21) to transport chloride across a lipid bilayer.[70] It was found that derivatives containing more lipophilic substituents increased the anion transport rate, and that transport occurred through a Cl^-/NO_3^- exchange mechanism. Related ion pair receptors (**55** and **56**, Fig. 21) were able to transport sodium chloride or potassium chloride across membranes with the transport selectivity determined by the size of the crown ether macrocycle.[72]

In 2016 the Wang group reported a series of ten oxacalix[2]arene[2]triazine derivatives and investigated their use as transmembrane ion pair transporters.[100] The group had previously demonstrated that this class of macrocycles can bind anions through anion–π interactions with the electron-deficient triazine ring,[101] however this work showed that incorporation of the hydroxy groups was essential for anion transport activity. The incorporation of lipophilic substituents to the triazine rings was also crucial as compounds without this substituent (*e.g.* **91**, Fig. 32) showed little activity. Additionally, a transporter containing an electron-withdrawing lipophilic substituent (*e.g.* **92**) was more active than those containing an electron-donating substituent (*e.g.* **93**).

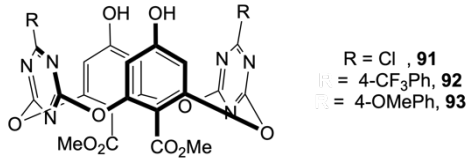


Fig. 32 Structures of some of the oxacalix[2]arene[2]triazine anion transporters reported by Wang.

In natural ion transport, the ions are generally transferred through membranes by ion channels or ion pumps instead of by encapsulation within a transporter molecule,[102] and

the Talukdar group have reported two studies into synthetic chloride ion channels using hydroxy containing compounds.[103,104] §§§§ The first study used diketal-protected mannitols containing hydroxy groups which form a polar face and cyclohexylidene or isopropylidine groups forming a non-polar face, **94** and **95** (Fig. 33).[103] The hydroxy groups allowed the molecules to form a nanotube lined with polar groups, while the hydrophobic face stabilised the nanotube within the membrane wall. It was observed that **95** was inactive to ion transportation, while **94** showed effective chloride transportation, which was attributed to the balance of hydrophilic and hydrophobic character favouring incorporation of the ion channel into membranes. Subsequently the compounds **96**–**99** were prepared (Fig. 33):[104] these also formed ion channels, and were effective at inducing significant cell death through chloride transport, suggesting similar compounds may provide a route to potential therapeutics in the future.

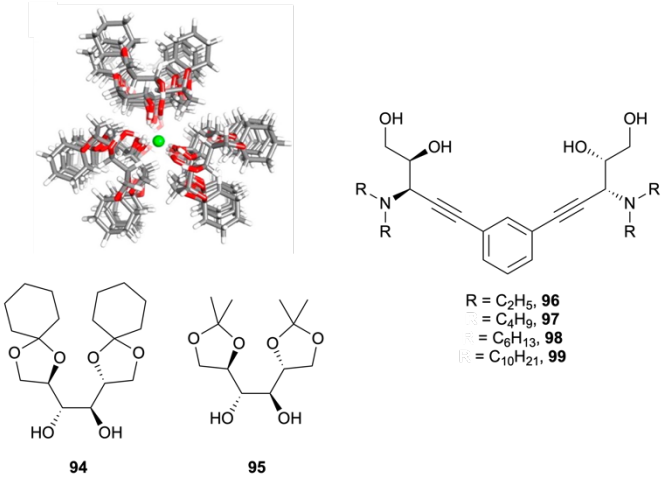


Fig. 33 Structures of compounds investigated by Talukdar as potential ion channel formers, and modelled structure of ion channel formed by **94**. Modelled structure reprinted from Saha *et al.*, *J. Am. Chem. Soc.* 2014**, 136**, 14128–14135. Copyright 2014 American Chemical Society.

Self–assembled structures

The interactions between anions and hydroxy groups can also be utilised to template the formation of supramolecular architectures. The earliest example of anion-templated self–assembly using O–H groups was reported as long ago as the mid-1980s. In two papers, Khan crystallised catechol with tetraalkylammonium halide salts and observed that tetrabutylammonium (TBA) chloride and bromide formed discrete 1:1 halide:catechol complexes in which the two O-H groups point towards each other, in order to both bind to the same anion (Fig. 34).[105] When crystallised with tetraethylammonium (TEA) chloride and bromide, dimeric structures were isolated, while TMA chloride and tetrapropylammonium (TPA) bromide gave 1D polymeric structures.[106]

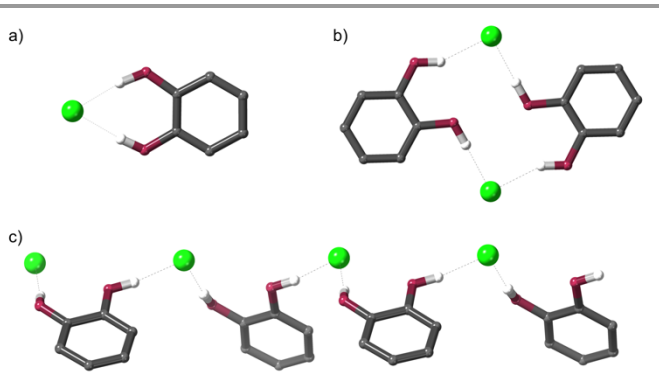


Fig. 34 Crystal structures of catechol complexes with tetraalkylammonium chloride salts: a) monomeric catechol·TBA·Cl (CCDC: 1139483); b) dimeric catechol·TEA·Cl (CCDC: 1155711); c) polymeric catechol·TMA·Cl (CCDC: 1155710, cations and most hydrogen atoms omitted from all structure for clarity).

Following Khan's pioneering work there was a significant lull in this area. In 2015, MacLachlan reported the self–assembly of a bis-pyrogallol compound **100** with halide, nitrate and hydrogensulfate anions.[107] The same structure was formed in each case, with **100** and the anion forming a [2+2] macrocycle in the solid state (Fig. 35), with these macrocycles then assembling into 2D sheets through hydrogen bonding between alcohol groups of **100**. These sheets alternated with layers made up of TBA cations and solvent molecules.

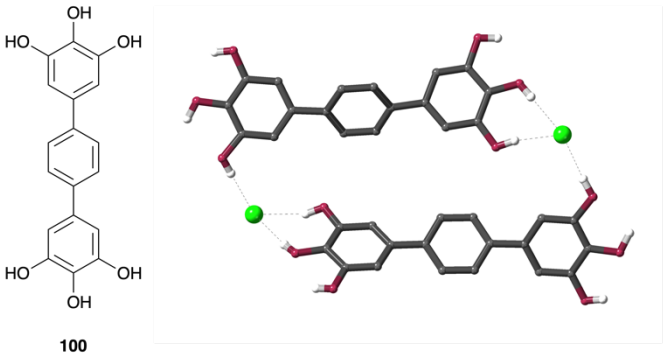


Fig. 35 Structure of **100** and its assembly into [2+2] macrocycles with chloride anion (CCDC: 1043470; TBA cations, solvent molecules and most hydrogen atoms omitted for clarity).

MacLachlan then used the triptycene derivative **101** containing two catechol moieties to prepare hexagonal nanotubes assembled through O–H···Br^- hydrogen bonds (Fig. 36).[108] Despite bromide forming relatively weak hydrogen bonds to catechol, these nanotubes were stable to heat, vacuum and water. When the hexahydroxytriptycene ligand **102** was used instead of **101**, nanotubes also formed but this time containing **103**, the spontaneously oxidised triptycene compound. Subsequent work showed that varying either the anion or tetraalkylammonium cation led to different products: TPA·Br gave a discrete complex, while TEA·Br gave a 2D network structure. When terephthalate was used, the authors isolated 1D polymeric structures.[109]

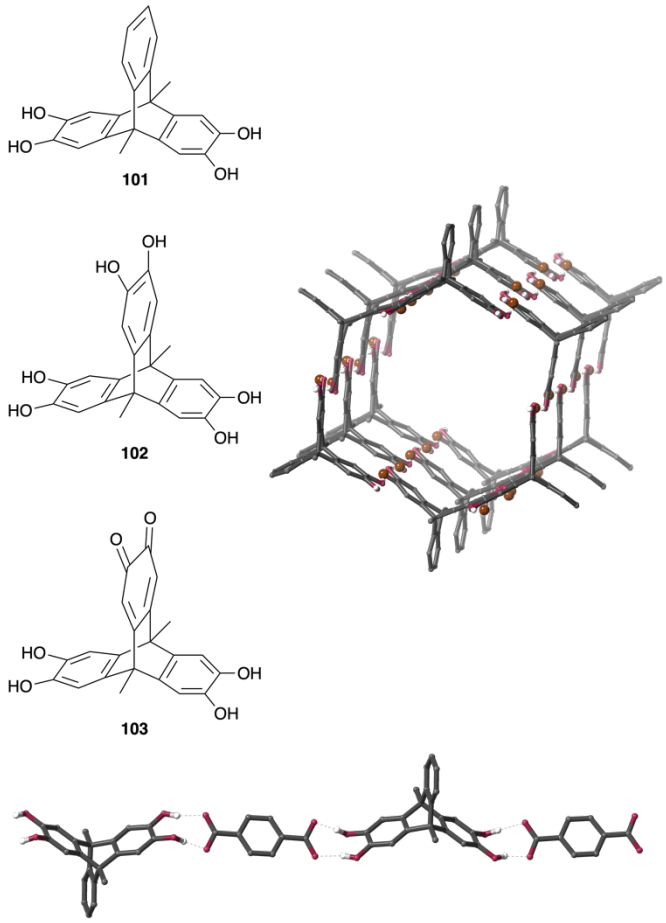


Fig. 36 Structures of **101**–**103** and crystal structures of hexagonal nanotubes formed from **101** and bromide (CCDC: 1400481), and 1D polymeric structures prepared from **101** and terephthalate (CCDC: 1418007; TBA cations, solvent molecules and most hydrogen atoms omitted from both structures for clarity).

In 2016, White crystallised planar hexahydroxytriphenylene (**104**) with halide and oxoanions and observed structures assembled by O–H···anion hydrogen bonding.[110] As with MacLachlan's work with **100**, 2D sheet-like structures were observed, with alternating sheets made up of TBA cations and solvent molecules (Fig. 37). The following year, Mak used the related tris(catechol) molecule **105** to prepare a diverse range of structures with the product dependent on both the anion and tetraalkylammonium cation used.[111] As well as 2D layered structures similar to those prepared by MacLachlan[107] and White,[110] the authors were also able to prepare channel and cage structures – an impressive array of architectures from one relatively simple organic molecule.

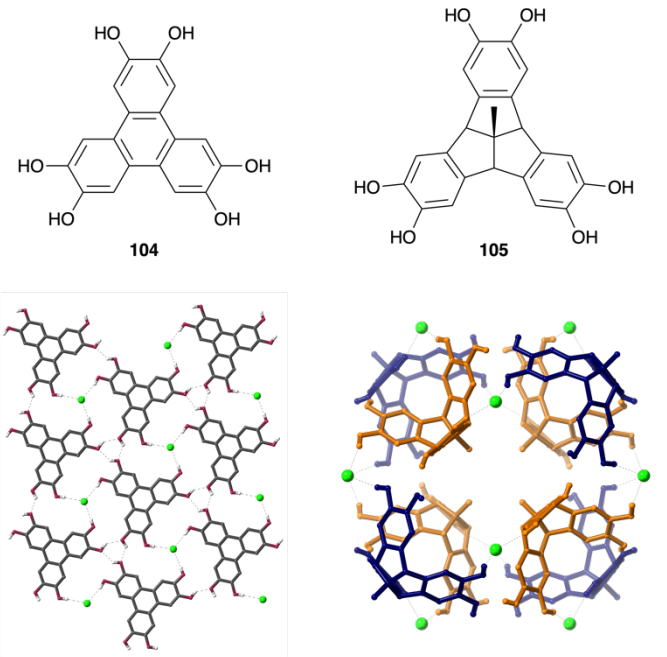


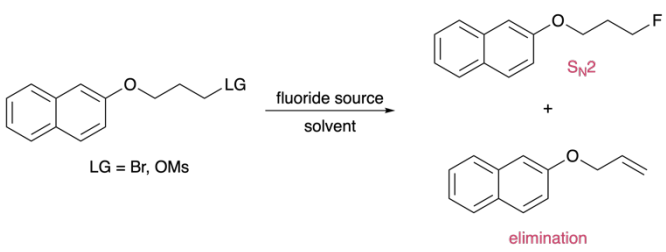
Fig. 37 Structures of **104** and **105** and crystal structure of 2D sheets prepared from **104** (CCDC: 1451578), and cage compound prepared from **105** (CCDC: 1527027; TBA cations, solvent molecules and most hydrogen atoms omitted from both structures for clarity).

While to date self–assembled structures prepared using O–H···anion coordination have only been observed in the solid state, it seems probable that solution–stable self–assembled architectures could also be realised given the strength of these interactions.

Catalysis and reactivity

In the last decade or so, the utility of supramolecular anion receptors to catalyse organic reactions has become apparent.[19] While many of these organocatalysts have used N–H donors such as ureas and thioureas,[112] the use of O–H···anion interactions to control reactivity and potentially act as catalysts has received a limited amount of attention. Given the line between hydrogen bonding catalysis and anion binding catalysis is understandably blurry, this section will highlight a few examples of O–H receptors being used for anion binding catalysis, where there is clear evidence of an interaction between the catalyst and an anion.

Nucleophilic fluorination is an important transformation particularly given the importance of organofluorines in pharmaceuticals and the use of ^{18}F tracers for positron emission tomography.[113] Reactions such as those shown in Scheme 1 are of interest as a method for late-stage installation of fluorine groups, although such reactions are prone to several side reactions, most notably elimination caused by basic fluoride. Some work has investigated methods to control the reactivity of fluoride using hydrogen bonding.



Scheme 1 Prototypical nucleophilic fluorination reaction studied by several groups.

In 2008, Kim reported that TBA·F·(^{t}BuOH)$_4$ is a far more selective fluoride source for nucleophilic fluorination reactions such as that shown in Scheme 1 than TBA·F.[114] The crystal structure of this compound (Fig. 38) shows that fluoride is held by four short O–H···F$^-$ hydrogen bonds (H···F$^-$ = 1.83 Å, ~69% of the sum of the vdW radii[92]), and kinetic studies suggested that these hydrogen bonds persist in solution (at least to some extent). The authors attributed the favourable reactivity of this compound to the shielding effect of the hydrogen bonded alcohol molecules giving a "flexible" fluoride anion that is less basic due to the absence of water present in highly hygroscopic TBA·F.

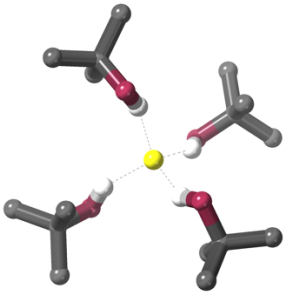


Fig. 38 Crystal structure of TBA·F·(^{t}BuOH)$_4$ (CCDC: 779205; TBA cation, disorder, and most hydrogen atoms omitted for clarity).

It had previously been shown that using alcohols as solvent could increase the rate of similar fluorination reactions with alkali metal fluorides,[115] although quantum chemical studies suggested this is due to the alcohols solvating the cation and thus decreasing ion-pairing in the metal fluoride rather than significant hydrogen bonding interactions.[116] A later paper showed that dihydroxypolyethers such as tetraethyleneglycol were more effective promoters of this reaction, with calculations showing that the ether groups could solvate the alkali metal cation while one of the hydroxy groups could hydrogen bond to the fluoride anion potentially helping control its reactivity (Fig. 39).[117]

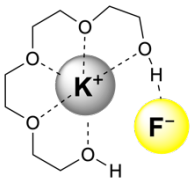


Fig. 39 Proposed mechanism of action of tetraethyleneglycol for promoting nucleophilic fluorination with KF.

In 2015, to help understand the superior fluorination properties of TBA·F·(^{t}BuOH)$_4$, the Gouverneur group studied the solid state structures of fluoride···alcohol complexes by crystallising TBA·F in the presence of alcohols to give a range of crystalline complexes of the form TBA·(ROH)$_n$·F.[118] Between two and four O–H···F$^-$ hydrogen bonds were present in the complexes depending on the steric bulk of the alcohol used (Fig. 40), with the hydrogen bonds shorter in complexes containing fewer hydrogen bonds. Generally, complexes with a coordination number of two reacted more rapidly than those with a coordination number of four, although increased reaction rate was correlated with a decrease in selectivity for the S$_N$2 fluorination reaction *vs.* elimination.

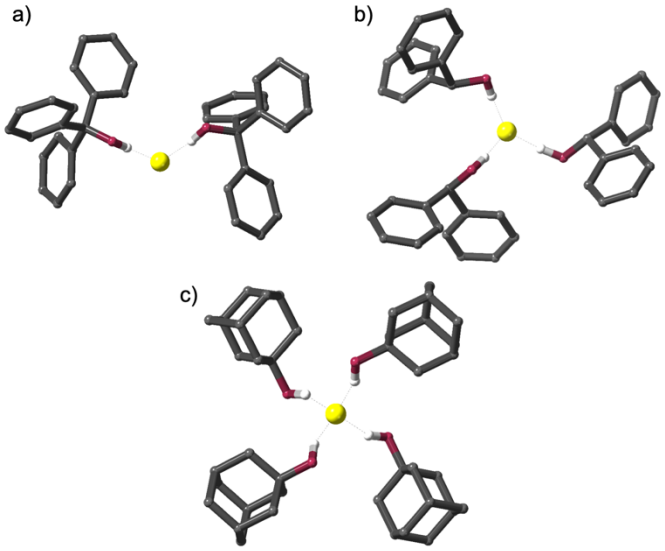


Fig. 40 Varying coordination numbers in crystal structures of alcohol–fluoride complexes reported by Gouverneur a) TBA·F·(trityl alcohol)$_2$ (CCDC: 1401776); b) TBA·F·(diphenylmethanol)$_3$ (CCDC: 1401775); c) TBA·F·(adamantol)$_4$ (CCDC: 1401765); TBA cations, most hydrogen atoms and solvent molecules omitted for clarity from all structures).

Recently, Shinde reported that tri-alcohol **106** (Fig. 41) could promote nucleophilic fluorination using CsF as the fluoride source.[119] The reaction could be conducted in acetonitrile on a wide variety of substrates with little elimination observed. Subsequent quantum chemical calculations suggested that **106** complexed the fluoride ion through three O–H···F$^-$ hydrogen bonds during the fluorination reaction, but intriguingly this did not decrease the reactivity of the coordinated anion.[120]

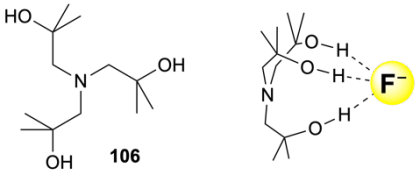


Fig. 41 Structure of **106** and structure of calculated pre-reaction complex.

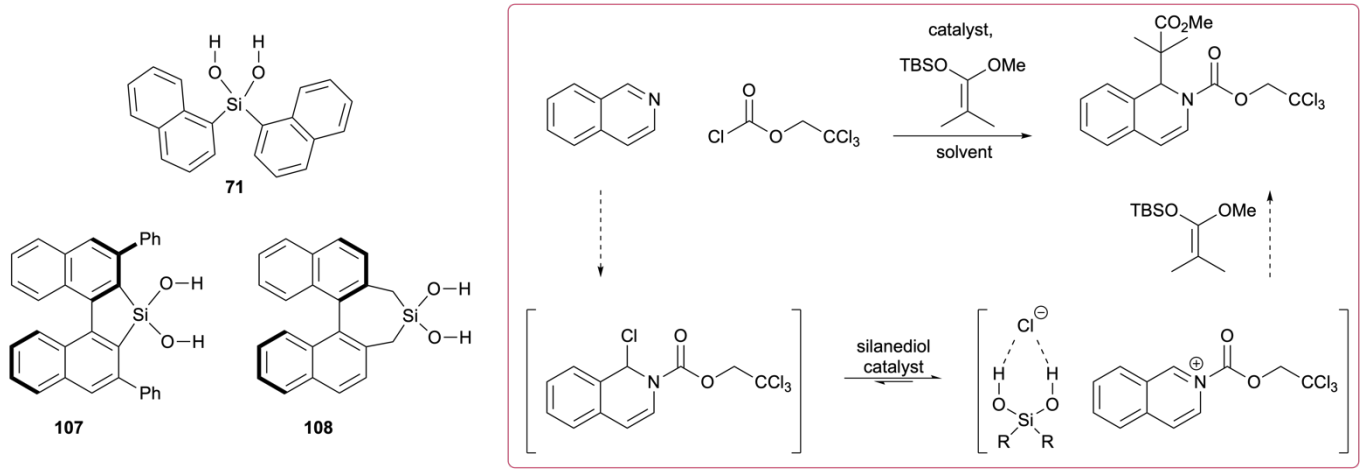


Fig. 42 Demonstration of chloride binding catalysis in *N*-Acyl Mannich reactions, and structures of some catalysts.

The anion binding affinity of silanediols has been utilised to design a range of chiral silanediols for enantioselective anion-binding catalysis. In 2013, Mattson reported that hydrogen bonding of silanediols **71**, **107** and **108** to chloride promotes the reaction of silyl ketene acetals with *N*-acylisoquinolines in good yield with 20% catalyst loading (the *N*-acyl Mannich reaction, Fig. 42).[121] NMR binding studies showed that these molecules bound chloride in solution, and by using enantiopure BINOL-derived silanediols such as **107** and **108**, modest enantioselectivities could be obtained. A subsequent paper showed that substitution of the BINOL scaffold in **108** with phenyl rings could improve the yield and enantioselectivities of the reaction.[122]

Mattson also showed that these chiral silanediols could hydrogen bond to the triflate anion with surprisingly high affinities for what is typically considered[123] a non-coordinating anion (K_a ~ 2300 M^{-1} in $CHCl_3$).[124] Binding to chiral silanediols (*e.g.* **108**, **109**) was then used to induce a chiral environment around a benzopyrylium ion intermediate to facilitate somewhat enantioselective addition of carbonyl nucleophiles to chromones (Fig. 43). While enantioselectivities were modest (up to 56% ee), the use of anion binding catalysis at a relatively non-coordinating anion is remarkable. In related work, the same group have recently reported that silane diols can activate copper(II) triflate as a catalyst, with the mechanism believed to involve the diol abstracting one of the triflate ligands from the copper, making it more catalytically active.[125]

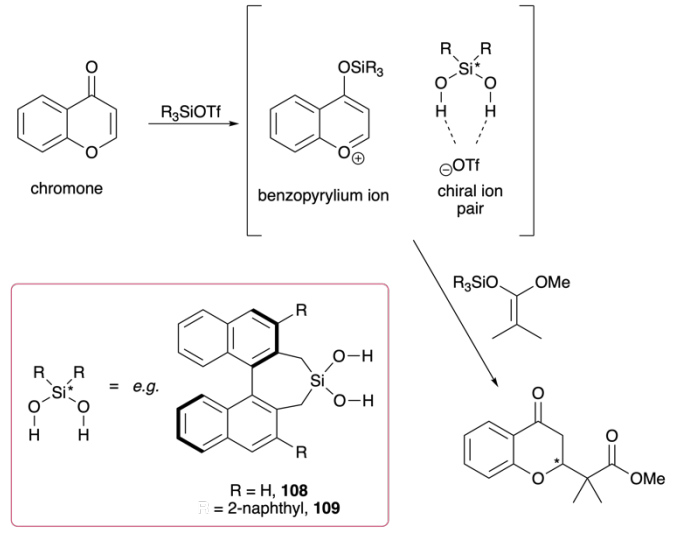
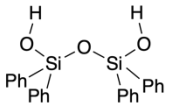
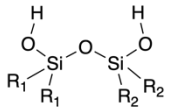


Fig. 43 Triflate binding catalysis mediated by silanediol catalysts.

In 2016 the Franz group reported the synthesis and anion-binding catalysis of a series of 1,3-disiloxanediols (Fig. 44).[126] The anion binding catalytic activity of these compounds was demonstrated with the same *N*-acyl Mannich reaction of isoquinoline as was used to investigate **107** and **108** also with a 20 mol% catalyst loading, achieving up to 78% yield. Interestingly, while the chloride binding properties of receptors **72**, **110** and **111** vary considerably (K_as range from 340 to 4600 M^{-1} in $CDCl_3$), no correlation was observed with catalytic efficiency with all three receptors giving similar yields for the tested reaction (78–84%). The weakest chloride binder gave an almost identical association constant to that measured for *N,N'*-diphenylthiourea, showing the potency of these compounds for anion recognition.



72



110, $R_1 = R_2$ = naphthyl
111, R_1 = ^{i}Pr, R_2 = 4-fluoronaphthyl

Receptor	K_a, Cl^- in $CDCl_3$ (M^{-1})	Reaction yield[b]
72	340	83%
110	1000	84%
111	4600[c]	78%

Fig. 44 Disiloxanediols studied by Franz and their anion recognition and catalysis properties. [a]Binding measured by ^{1}H NMR spectroscopy using TBA·Cl; b) yield for reaction shown in Fig. 42 using 20 mol. % catalyst at –50 °C and 25 mM in toluene; c) average of two K_as calculated using two chemically distinct O–H resonances in **111**.

While the development of anion binding catalysts containing O–H donors is still in its infancy, it is clear that this field has considerable promise. To date, the systems used have been simple and relatively weak anion binders: it will be interesting to see how this field progresses over the coming years.

Conclusions and future perspectives

From the first synthetic O–H containing anion receptors in the mid-1990s, there has been considerable development in the last 20 or so years. Sophisticated receptors have now been prepared that can achieve selective anion recognition, and a few of these can function in solvent media containing a significant amount of water. Additionally, more applications of O–H···anion interactions are beginning to emerge, specifically in the fields of anion transport, anion–templated assembly and anion binding catalysis.

Several questions remain to be addressed as this area matures and we suggest the following are particularly pertinent:

1) Can selective anion receptors that function in pure water through O–H hydrogen bonding be prepared? While anion recognition in water is a major challenge, progress has been made recently in this regard. The majority of O–H containing anion receptors are neutral molecules, and it may be that cationic receptors can help make the jump to water. Care will need to be taken to ensure that cationic O–H receptors are not so acidic that deprotonation by basic anions becomes a problem.
2) Can a wide range of synthetic anion channels be prepared? Are these more or less effective than molecular transporters? As O–H groups can act as both hydrogen bond donors and acceptors, O–H containing molecules appear to be ideal candidates for self–assembling into channels that still maintain the ability to hydrogen bond to anions.
3) Can solution stable self–assembled architectures based on O–H···anion interactions be prepared? A range of complex structures (*e.g.* cages, nanotubes) have been isolated in the solid state – can this be extended to solution? As with Question 1, it may be that the use of cationic systems containing O–H groups are of use here, both to increase the strength of the interaction and to remove the need for non-coordinating cations.
4) How general is anion binding catalysis using O–H groups? To date, only a small number of reactions have been studied using receptors that are not particularly strong anion binders. Do more strongly binding receptors give better catalysis, or does this limit turnover number? As yet, reaction yields and enantioselectivities do not compete with those obtained using thiourea catalysts[127] – can O–H containing catalysts become competitive as their design is optimised?

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

‡ Similarly, Stoddart's cyclodextrin-based frameworks that complex potassium tetrachloroaurate and tetrabromoaurate do not seem to show hydrogen bonding interactions between the cyclodextrin O–H groups and the anion: Z. Liu, M. Frasconi, J. Lei, Z. J. Brown, Z. Zhu, D. Cao, J. Iehl, G. Liu, A. C. Fahrenbach, Y. Y. Botros, O. K. Farha, J. T. Hupp, C. A. Mirkin and J. F. Stoddart, *Nat. Commun.* 2013, **4**, 1855.
§ In related work, the groups of Aoyama and Koga showed that pyridine-functionalised resorcinol derivatives could bind substituted phosphoric and phosphonic acids as the mono-anions following proton transfer: (a) T. Motomura and Y. Aoyama, *J. Org. Chem.* 1991, **56**, 7224–7228; (b) K. Manabe, K. Okamura, T. Date and K. Koga, *J. Am. Chem. Soc.* 1992, **114**, 6940–6941.
§§ Interestingly, in the late 1990s Remington reported that certain fluorescent proteins were able to sense halide and nitrate anions, as these species induced changes in the pK_a of a tyrosine O–H group. The anions destabilise the anionic phenolate form of the protein, which is fluorescent, and thus the protein acts as a turn-off sensor. It is not clear whether an O–H···anion hydrogen bond is present in these systems or whether this is purely due to electrostatic (de)stabilisation: (a) R. M. Wachter and S. J. Remington, *Curr. Biol.* 1999, **9**, 628–629; (b) R. M. Wachter, D. Yarbrough, K. Kallio and S. J.

Remington, *J. Mol. Biol.* 2000, **301**, 157–171.
§§§ It should be noted that complexation for these types of polyol is not always entropically favoured, see A. Shokri, X.-B. Wang, Y. Wang, G. A. O'Doherty and S. R. Kass, *J. Phys. Chem. A*, 2016, **120**, 1661–1668.
§§§§ In the 1990s, Matile prepared somewhat related rigid polyol compounds, which functioned as ion transporters. While these were predominantly viewed as cation transporters (and showed cation selectivity), the authors noticed that there was evidence for polyol-mediated anion transport: (a) N. Sakai, K. C. Brennan, L. A. Weiss and S. Matile, *J. Am. Chem. Soc.* 1997, **119**, 8726–8727; (b) L. A. Weiss, N. Sakai, B. Ghebremariam, C. Ni and S. Matile, *J. Am. Chem. Soc.* 1997, **119**, 12142–12149.

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