Anion receptors based on organic frameworks: highlights from 2005 and 2006

Philip A. Gale,* Sergio E. García-Garrido and Joachim Garric

Received 12th October 2007
First published as an Advance Article on the web 14th November 2007
DOI: 10.1039/b715825d

This *critical review* covers advances in anion complexation chemistry related to receptors based on organic frameworks in the years 2005–2006. The review covers anion receptors that employ amides and thioamides, pyrroles and indoles, ureas and thioureas, ammonium, guanidinium, imidazolium, and receptors containing hydroxyl groups. There is a discussion of anion templated assembly, followed by a short section outlining modelling studies of these systems. (226 references.)

Introduction

Anion receptor chemistry continues to be a very vigorous area of research.[1–4] Anions play many positive roles in biological systems but can also have deleterious effects, for example as pollutants in the environment. Much effort is currently being directed towards the use of anion receptors as membrane transport agents for chloride in biological systems, as ion-pair receptors, as sensors for the detection of biologically important anionic species and in a variety of other applications. This *critical review* covers developments in the years 2005 and 2006 and focuses on the design of receptors based on organic frameworks. Receptors containing metals are not included.

Amide based anion receptors

Secondary amides have been widely employed as hydrogen bond donor groups in anion receptors.[5] Receptors containing isophthalamide or pyridine-2,6-dicarboxamide have been synthesised by a number of groups following the independent pioneering work of Crabtree *et al.*[6,7] and B. D. Smith and Hughes[8] on these systems in 1997.

Kondo and co-workers have reported the synthesis of receptors **1** and **2a**–**c** composed of three parts: an isophthalamide core, an α-amino acid spacer, and terminal amide groups appended with either a phenyl or pyridine group.[9] The four amide NH groups form a complex with Y-shaped anions such as acetate and phosphate. The complexation studies demonstrate the selectivity of compound **2c** toward $H_2PO_4^-$ ($K_{11}(H_2PO_4^-)/K_{11}(AcO^-) > 59.9$ in 0.5% DMSO–MeCN (v/v)) illustrating the importance of the terminal pyridyl groups which are presumably accepting hydrogen bonds from the dihydrogen phosphate anion (Scheme 1).

Gale and co-workers have previously shown that functionalised isophthalamides can form a '2 + 2' double helical complex with fluoride.[10] In more recent work, this group has deliberately designed receptors to form higher order complexes with anions. Specifically they have employed steric interactions in 1,3-dicarboxamidoanthraquinones **3** to 'twist' the isophthalamide-like anion binding site.[11] Steric interactions between the amide in the 1-position and the adjacent oxygen atom force this group to twist out of plane, giving a divergent hydrogen

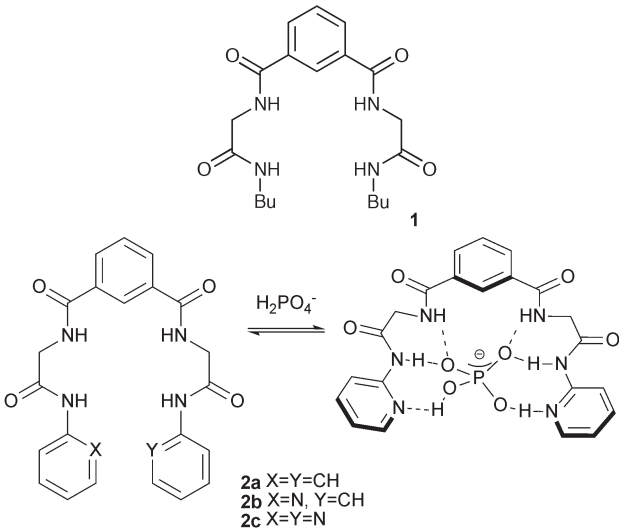
School of Chemistry, University of Southampton, Southampton, UK, SO17 1BJ. E-mail: philip.gale@soton.ac.uk; Fax: +44 23 8059 6805; Tel: +44 23 8059 3332

Sergio E. García-Garrido, Philip A. Gale and Joachim Garric

Phil Gale received his DPhil (Oxon) (1995) under the supervision of Paul Beer before moving to Jonathan Sessler's group in Austin as a Fulbright Postdoctoral Fellow. He returned to Oxford in 1997 as a Royal Society University Research Fellow, moving to the University of Southampton in 1999 where he is now Professor of Supramolecular Chemistry. A major focus of his research is the supramolecular chemistry of anionic species. He has won a number of awards including a 2005 Corday-Morgan medal and prize from the Royal Society of Chemistry.

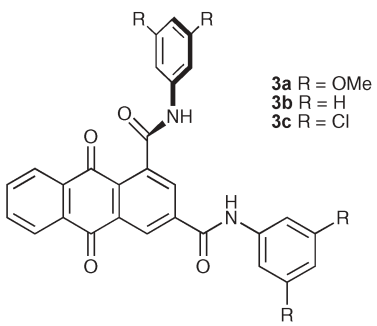
Sergio E. García-Garrido studied chemistry at the University of Oviedo and received his PhD in 2005 under the supervision of Prof. J. Gimeno and Dr V. Cadierno working in the synthesis and catalytic applications of Ru(II) and Ru(IV) complexes. He then joined the group of Prof. Gale with a two-year postdoctoral fellowship.

Joachim Garric studied chemistry at the University Bordeaux I where he received his PhD in 2005 under the guidance of Dr Ivan Huc, working on the synthesis of helicoidal capsules similar to the shape of the skin of an apple peeled in a helical fashion. He has currently a postdoctoral position with Prof. Gale.

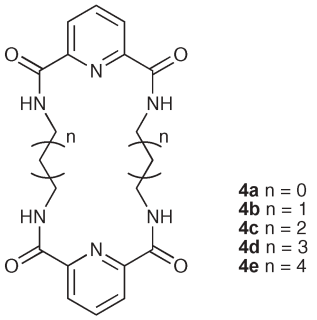


Scheme 1 Dihydrogen phosphate complexation by receptor **2c**.

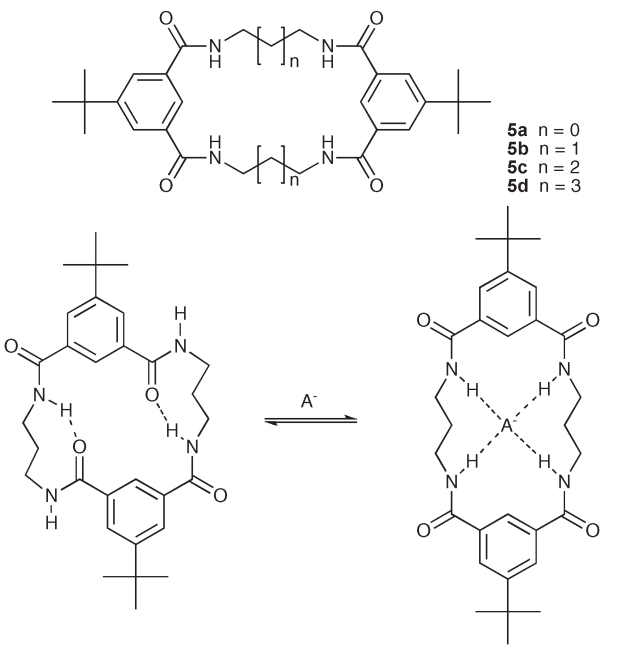
bonding array. It was shown that receptor **3c** forms a '2 + 2' complex with fluoride in the solid state. This family of compounds also gives a colorimetric response to the presence of anions in solution. It has also been shown that the electrochemistry of the anthraquinone redox system dramatically changes when an appropriate ion (for example fluoride) is added to the receptor in DMSO solution. In the presence of a competitive anion, intramolecular hydrogen bonds between the amides and the semiquinone and dianion species are broken, dramatically changing the electrochemistry of this system.[12]



Chmielewski and Jurczak have continued their work on neutral macrocyclic tetraamides containing two 2,6-dicarboxamidopyridine or isophthalamide groups linked *via* short aliphatic chains.[13,14] 2,6-Dicarboxamidopyridines **4a**–**e** were prepared[15,16] and anion binding studies in DMSO-d_6 solution revealed that the size of the receptor has a significant effect on anion affinity. Size complementarity between the putative anionic guest and the receptor cavity was found to play only a secondary role in determining selectivity, as receptor **4b** was found to have the highest affinity for all the anions studied from this series of receptors (binding chloride with a stability constant of 1930 M^{-1} *vs.* 65 M^{-1} for compound **4a**). The authors postulate that this receptor has the optimal balance of preorganisation and adaptability from this series of compounds, resulting in high affinity for a variety of anionic guests.



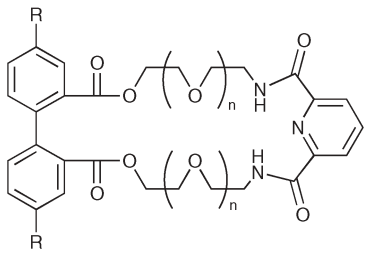
Recently, the same group has described the synthesis and anion binding properties of macrocyclic isophthalamide receptors **5a**–**d**.[17] The stability constants of these receptors with various anions were determined by ^{1}H NMR titrations in DMSO-d_6 and, contrary to the authors' initial assumptions, the isophthalamides turned out to be weaker anionophores than their 2,6-dicarboxamidopyridine counterparts. Combined theoretical and experimental structural studies demonstrate that this unexpectedly low anion binding ability of the isophthalic acid-based receptors is due to the self-complementary nature of the isophthalic bis-amide fragments: when two such moieties are present within a sufficiently flexible macrocycle, they adopt *syn–anti* conformations and bind to each other by two strong intramolecular hydrogen bonds that close the macrocyclic cavity. Nevertheless, anion binding is able to break these hydrogen bonds and switch a macrocycle into a convergent all-*syn* conformation (Scheme 2). In a further study, a hybrid macrocycle containing both 2,6-dicarboxamidopyridine and isophthalamide anion binding sites linked *via* a three carbon chain was shown to have a higher affinity for anions than either of its homoaromatic congeners.[18] The authors attribute this to the *syn–syn* conformation adopted by the 2,6-dicarboxamidopyridine



Scheme 2 Anion complexation results in a conformational change in receptor **5b**.

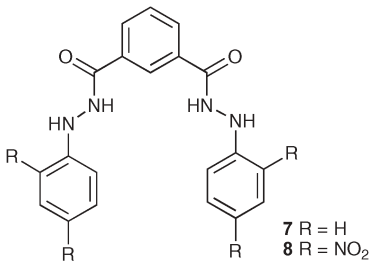
enforcing the same conformation in the isophthalamide. Thus these systems do not contain intramolecular hydrogen bonding interactions as seen in compound **5**.

Costero and co-workers have studied macrocycles **6a**–**d** as part of a colorimetric displacement assay for sensing inorganic anions such as F^-, AcO^- and $H_2PO_4^-$.[19] Complexation of nitrophenolate (log K = 4.55 ± 0.03, 3.22 ± 0.22 and 4.09 ± 0.02 M^{-1} by compounds **6a**, **6b** and **6c** respectively in CH_3CN at 25 °C) results in a partially discoloured complex. Addition of competitive anions displaces the nitrophenolate anion and restores the yellow colour. Competition studies have been performed using UV-vis spectroscopic techniques, revealing that the most basic anions (F^-, AcO^- and $H_2PO_4^-$) displace the nitrophenolate anion whilst other halides had little effect on the nitrophenolate complex.



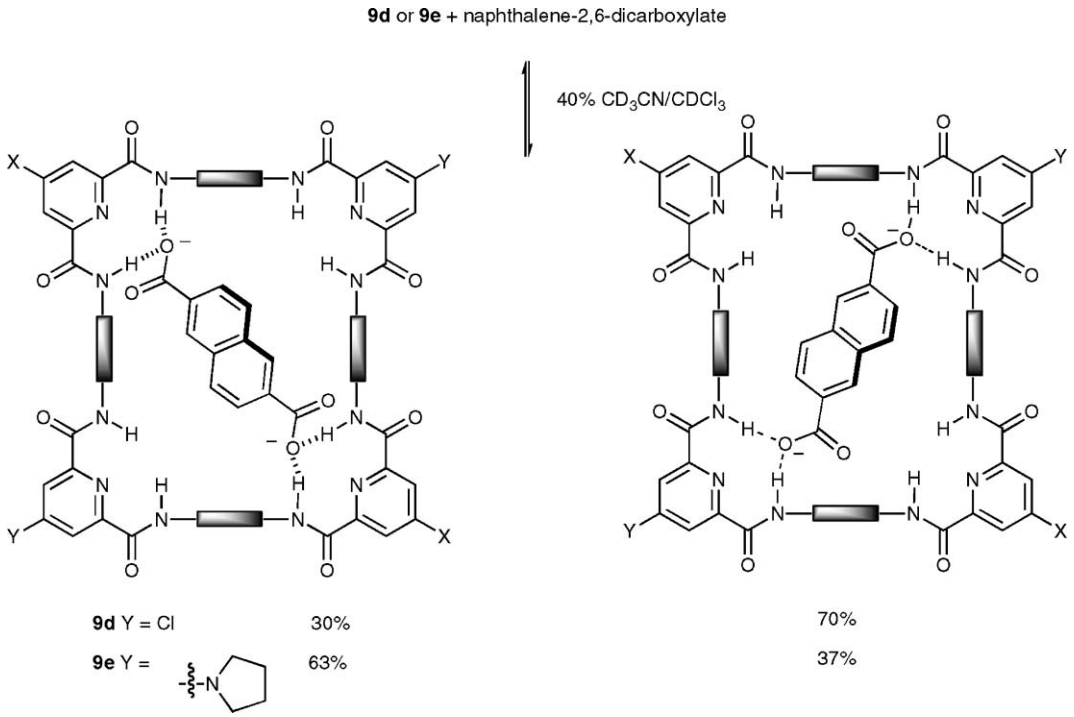
6a R = NO_2, n = 0
6b R = $N(CH_3)_2$, n = 0
6c R = NO_2, n = 1
6d R = $N(CH_3)_2$, n = 1

Gupta and co-workers have synthesised two novel isophthalamide-based receptors *N*,*N*′-bis(phenyl)isophthalohydrazide (**7**) and *N*,*N*′-bis(2,4-dinitrophenyl)isophthalohydrazide (**8**) and studied their anion binding abilities by UV-vis spectroscopic methods in acetonitrile solution.[20] These two compounds displayed selectivity for carbonate ($CO_3^{2-} \gg HPO_4^{2-} > F^- > Cl^- > SO_4^{2-}$). As a consequence of this selectivity, PVC based membranes containing these receptors have been prepared and investigated as carbonate selective ion selective electrodes (ISEs), which showed a selective response to the presence of other lipophilic anions such as salicylate, ClO_4^- and SCN^-. Thus, these sensors can be used for the selective determination of carbonate. The analytical utility of these ISEs has been demonstrated by measuring the total inorganic carbon (TCO_2) in water samples.

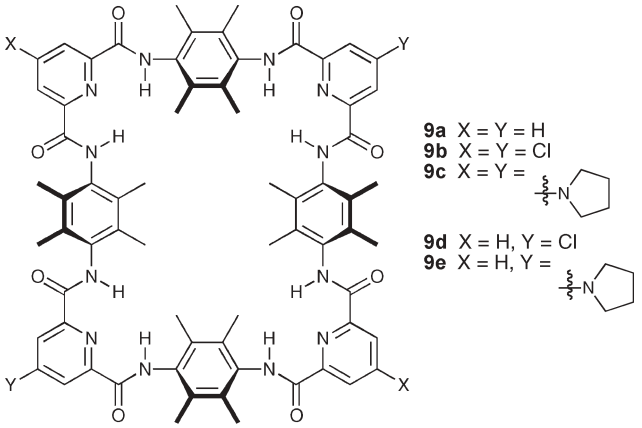


7 R = H
8 R = NO_2

Jeong and co-workers have synthesised a series of large 44-membered macrocycles **9a**–**e** which can display two different diagonal binding modes.[21] The unsubstituted macrocycle **9a** binds naphthalene-2,6-dicarboxylate strongly through hydrogen bonds (K_a = 4500 M^{-1}) in 40% (v/v) CD_3CN–$CDCl_3$. Introduction of an electron-withdrawing substituent (Cl) at all four corners increases the binding affinity (22000 M^{-1} for **9b**), while that of an electron-donating substituent (pyrrolidinyl) greatly decreases it (150 M^{-1} for **9c**). The same propensity has been observed by the authors with macrocycles **9d** and **9e**, bearing different substituents at two diagonal corners, with NMR experiments showing the anion favouring binding to the most electron deficient corners in these cases (Scheme 3).

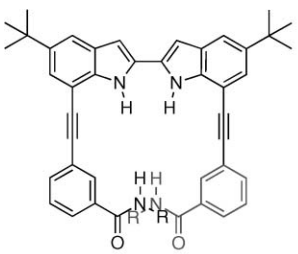


Scheme 3 Relative populations of two different binding modes of complexes between macrocycles **9d** and **9e**, and naphthalene-2,6-dicarboxylate in 40% CD_3CN–$CDCl_3$ at 24 ± 1 °C.

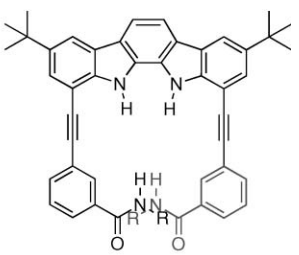


9a X = Y = H
9b X = Y = Cl
9c X = Y =
9d X = H, Y = Cl
9e X = H, Y =

The same research group has also studied the anion binding properties of new molecular clefts based on a 2,2′-biindolyl scaffold (**10a**,**b** and **11a**,**b**) that contain both indole and amide hydrogen bond donor groups.[22] The binding properties of the compounds were evaluated in CH_3CN solution by UV-vis spectroscopy, showing a dramatic increase in the association constants of up to 40-fold when the biindolyl was rigidified (for example, stability constants with bromide in CH_3CN at 22 °C were found to be 2.1×10^2 M^{-1} with **10a** and 8.7×10^3 M^{-1} with **11a**). Stability constants were also found to be higher for the phenyl amides *vs.* the methyl amides, presumably due to electronic effects.

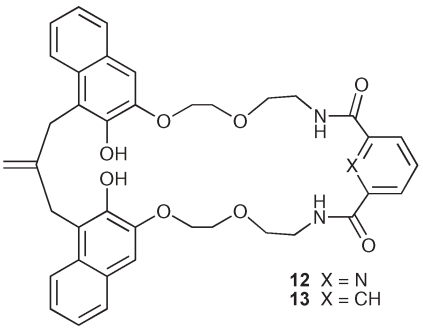


10a R = CH_3
10b R = Ph

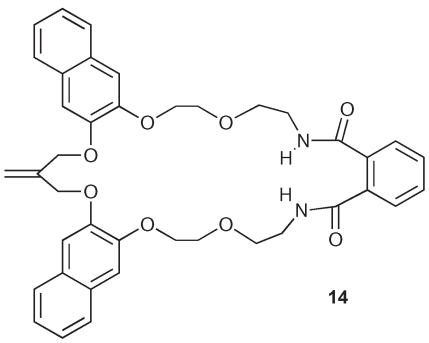


11a R = CH_3
11b R = Ph

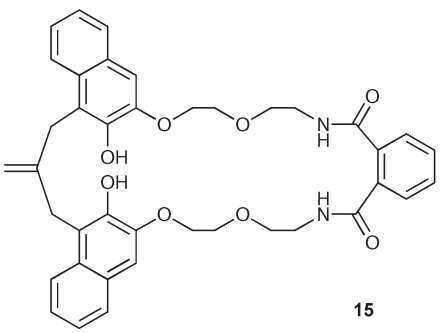
Hiratani and co-workers have investigated the molecular recognition properties of a series of crownophanes containing two hydroxy groups and two amide groups (**12**–**13** and **15**) and model compound **14** with anions such as halides, dihydrogen phosphate and acetate.[23] The anion coordination ability of these species was measured by ^1H NMR techniques in $CDCl_3$ solution, and it was found that amidocrownophanes **12** and **13** bind anions with moderate affinity with the following order of selectivity: $H_2PO_4^- > F^- > CH_3COO^- > Cl^- \gg Br^-$ and I^- (*e.g.* compound **12** binds $H_2PO_4^-$ with a stability constant of 4.42×10^2 M^{-1} under these conditions), whilst compounds **14**, which possesses no hydroxyl groups, and **15** had no affinity for anions under these conditions. This lack of affinity must presumably be due to intramolecular hydrogen bonding interactions in the phthalamide derivatives **14** and **15** that are not present in the isophthalamide derivatives **12** and **13**.



12 X = N
13 X = CH



14



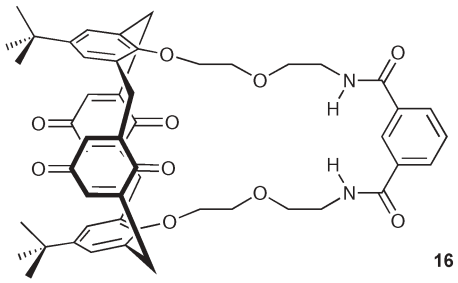
15

Beer and co-workers continued their work on calix[4]diquinone systems[24,25] and have described the synthesis and binding properties of a novel heteroditopic calix[4]diquinone receptor **16**.[26] This compound demonstrates a dramatic enhancement of anion binding in the presence of a co-bound cation (Table 1) and, in some cases, strong binding with associated ion pairs where no affinity for the free ions is observed. This is the first example of a receptor where the compound displays no discernible affinity for either one of the free ions, but which binds the associated ion pair species strongly. A possible reason for this phenomenon could be the self-inhibition of the cation and anion binding sites of the molecule by intramolecular hydrogen bonding of the quinone unit by the isophthalamide, which is disrupted only by a suitable ion-pair.

Table 1 Switching on chloride binding in compound **16** by coordinating cations

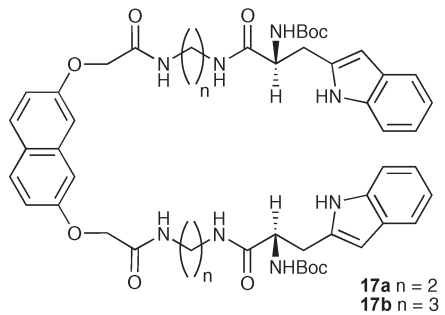
Cation	TBA^+	NMe_4^+	Li^+	Na^+	K^+	NH_4^+
NH $\Delta\delta^a$	0.057	0.101	0.881	~0.99	~1.51	1.106
log K_{Cl}	—[b]	—[b]	3.79[c]	>4	>4	>4

[a] Change in amide chemical shift (ppm) on addition of 1 equivalent of chloride anion. [b] No binding observed. [c] Error < 10%.



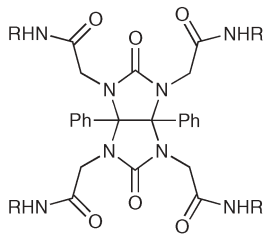
16

He and co-workers have reported the synthesis of two fluorescent chiral receptors **17a**,**b** containing amide units and L-tryptophan.[27] Proton NMR and fluorescence studies have shown that the compounds exhibit enantioselective recognition properties with D- and L-bis(tetrabutylammonium) dibenzoyl tartrate, forming a 1 : 1 complex between host and guest. For example, compound **17a** was found to bind D-dibenzoyl tartrate in DMSO with a stability constant of (7.93 ± 0.04) × 10^4 M^{-1} *vs.* (1.28 ± 0.02) × 10^4 M^{-1} for L-dibenzoyl tartrate. Most interestingly, compound **17b** bound the D-enantiomer with a stability constant of (2.61 ± 0.05) × 10^5 M^{-1} whilst the stability constant of the complex formed with the L-enantiomer was too small to calculate.



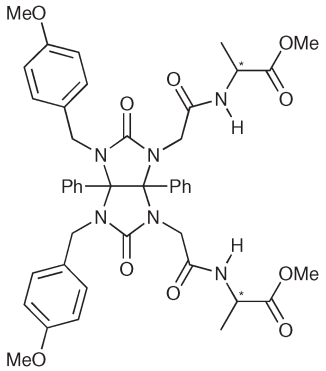
17a n = 2
17b n = 3

Kang and Kim have followed their previous work on diphenyl glycoluril scaffolds[28,29] producing receptor **18** that contains four pendant naphthyl groups.[30] This host shows selectivity for bromide, binding this anion more strongly than the other halides ($Br^- > Cl^- > F^- > I^-$) with a stability constant 1.2 × 10^5 ± 1.4 × 10^4 M^{-1} in acetonitrile. The authors suggest this selectivity is due to the complementarity of size between the receptor and bromide anion.



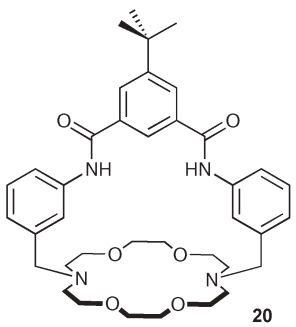
18 R = 2-naphthyl

The same group has described the synthesis of a new enantioselective receptor **19** by incorporation of chiral building blocks onto a glycoluril core.[31] Binding studies carried out using ^{1}H NMR spectroscopy in CD_3CN revealed that the receptor **19** possesses moderate enantioselectivity with a general preference for D-amino acids. The highest enantioselectivity was observed with the D- and L-enantiomers of *N*-Boc–$LeuCO_2^-$ amongst the amino acids investigated (8.9 × 10^2 M^{-1} for the D-enantiomer *vs.* 2.5 × 10^2 M^{-1} for the L-).



19

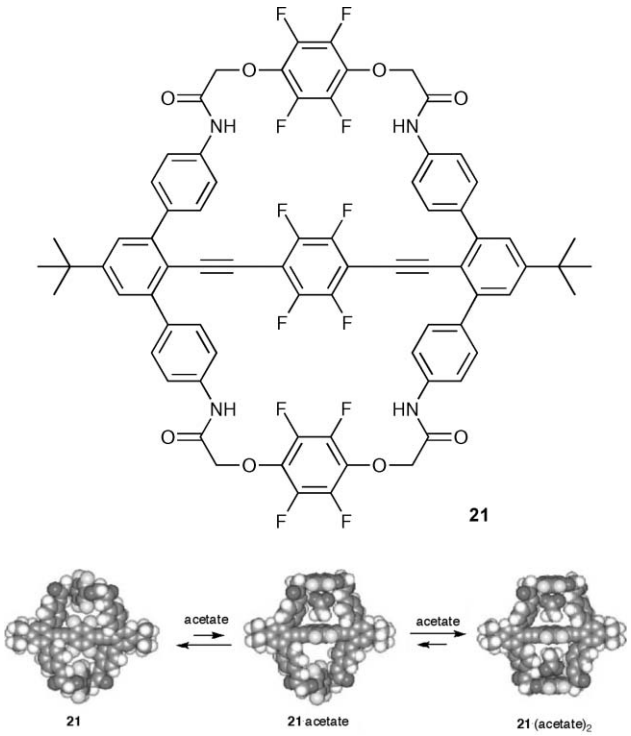
B. D. Smith and co-workers have continued their work on ion-pair receptor systems[32,33] with a detailed study of nitrate inclusion by receptor **20**.[34] Detailed X-ray analysis of a series of nitrate salts bound in the receptor together with solution NMR binding data in $CDCl_3$ suggests that anisotropy in the nitrate anion may act to shield NH protons bound to it in certain geometries (when binding nitrate salts, upfield shifts of the amide NH resonances of between 0.05–0.22 ppm were observed). The authors calculated the shielding surface around nitrate and found that it is deshielding around the peripheral plane of the anion and shielding in a region above the central nitrogen.



20

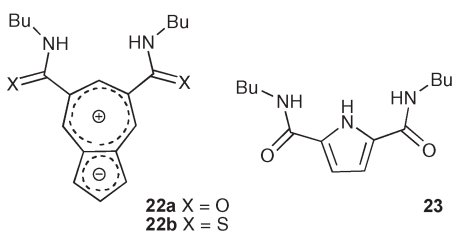
Shinkai and co-workers have described a new dynamic bicyclic receptor **21** which has a diethynyl tetrafluorophenyl axis.[35] This host displays allosteric binding, controlled by the central tetrafluorophenyl platform which functions as a molecular 'turnstile'. Initially, the receptor adopts a closed state with the central ring in the plane of the rest of the receptor preventing the approach of guest anions. However, should one acetate bind to the interior of the receptor this forces the central ring to be perpendicular to the receptor so opening up the second binding site (Scheme 4). For example, in THF-d_8–DMSO-d_6 (5 : 1, v/v) solution acetate is bound with K_1 = 144 ± 2 M^{-1} and K_2 = 66 ± 3 M^{-1} with a Hill parameter *n* of 1.4, indicating cooperative binding.

Bis-amide **22a** and thioamide **22b**, derivatives of azulene-5,7-dicarboxylic acid, were synthesised by Jurczak and co-workers.[36] The seven-membered azulene ring gives access to a new geometry for 'Crabtree-type isophthalamide' analogues in *syn–syn* conformations. Thioamide **22b** was found to bind anions about twice as strongly as the amide analogue **22a** with the



Scheme 4 Cooperative acetate binding to **21** with the energy-minimised structures of free **21**, **21**·acetate 1 : 1 complex and **21**·(acetate)$_2$ 1 : 2 complex. Reproduced with permission from ref. 35. Copyright © 2005 Royal Society of Chemistry.

same selectivity (Table 2). The anion affinities of the two azulene derivatives were compared to Jurczak's dicarboxamidopyrrole **23**[37] which showed that the azulenes generally had a lower affinity for anions than compound **23** (excepting chloride).



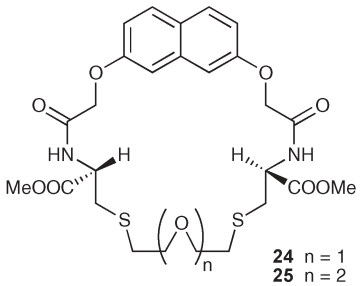
He and co-workers have synthesised two chiral fluorescent macrocycles **24** and **25** containing naphthalene and amino acid units.[38] The enantioselective recognition properties of these

Table 2 The binding constants (M^{-1}) for the formation of 1 : 1 complexes of **22a**, **22b** and **23** with various anions in DMSO-d_6–0.5% H_2O at 298 K[a]

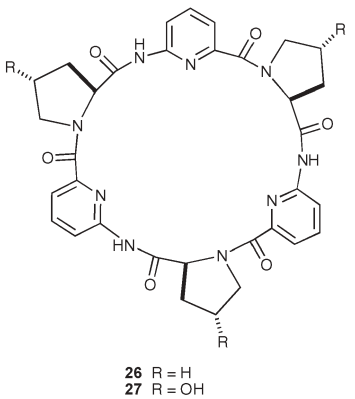
Anion	Receptor **22a**	Receptor **22b**	Receptor **23**[37]
$H_2PO_4^-$	27	104	150
$PhCOO^-$	13	46	49
Cl^-	6.1	13.3	1.7
Br^-	—[b]	—[b]	—[b]

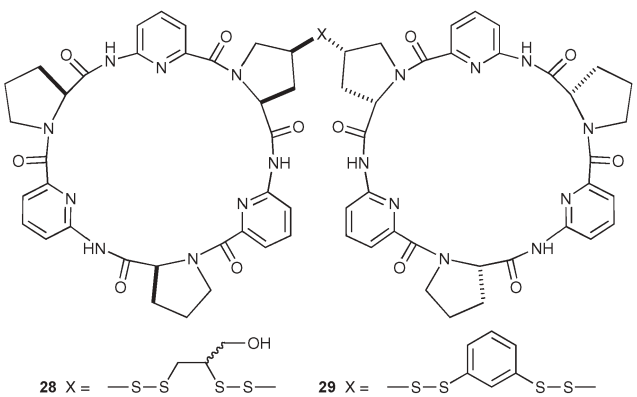
[a] Determined by ^{1}H NMR titration techniques. Errors estimated to be <10%. Tetrabutylammonium salts were used as anion sources. [b] Interaction too weak to be measured.

macrocycles for amino acid anions were explored using fluorescence and ^{1}H NMR spectrometry in DMSO and DMSO-d_6, respectively, indicating good enantioselectivity of compound **24**. For example, **24** binds N-protected phenylalanine anions with a ratio $K_{(D\text{-Phe})}/K_{(L\text{-Phe})} = 4.94$.



Following on from their earlier work,[39] Kubik, Otto and co-workers have presented structural and thermodynamic data on the binding properties of anion receptors composed of cyclopeptides **26**–**29** that complex sulfate and iodide anions with micromolar affinity in aqueous solution.[40] Specifically, they showed how hydrophobic interactions between two covalently linked peptide rings that do not directly involve the guest contribute to the complexation of iodide and sulfate by two synthetic bis-cyclopeptide-based anion receptors **28** and **29**. Evidence comes from X-ray structure data, the solvent dependence of the anion affinity and previous observations of the binding behaviour of structurally related monomeric cyclopeptides.[39]





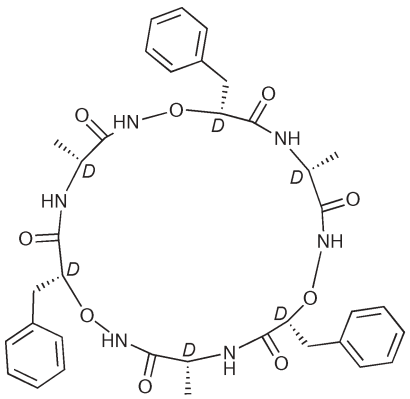
Yang, Wu and co-workers have synthesised cyclic hexapeptide **30** which contains alternating D-α-amino and D-α-aminoxy acids.[41] In dichloromethane solution, this macrocycle

Table 3 Stability constants for the binding of **30** with anions[a] in CD_2Cl_2 at 298 K

Anion	K_a/M^{-1}[b]	$\Delta\delta_{max}$(O–NH)[c]	$\Delta\delta_{max}$(NH)[c]
Cl^-	15000 ± 1500	2.39	−1.39
Br^-	910 ± 43	1.70	−1.07
I^-	51 ± 3	[d]	[d]
NO_3^-	440 ± 42	1.43	−0.55

[a] Anions were added as concentrated CD_2Cl_2 solutions of Ph_4PCl, Ph_4PBr, Bu_4NI, or Bu_4NNO_3. To account for dilution effects, these anion solutions also contained receptor **30** at its initial concentration (2–4 mM). [b] Determined by following the changes that occurred to the resonances of the aminoxy amide NH protons. [c] Estimated maximum change in chemical shift (ppm). [d] Cannot be estimated from the titration curve.

displays a high selectivity for chloride anions amongst the anions studied (Table 3).



30

Chen, Huang and co-workers have synthesised the novel upper-rim anthracene bridged calix[4]arene **31**.[42] The close proximity of the anthracene group to the anion binding site effectively couples the fluorescence of this system to its guest binding properties. It was found that the fluorescence of the anthracene group was quenched upon addition of basic anions such as AcO^- and F^- in acetonitrile solution (Fig. 1). Stability

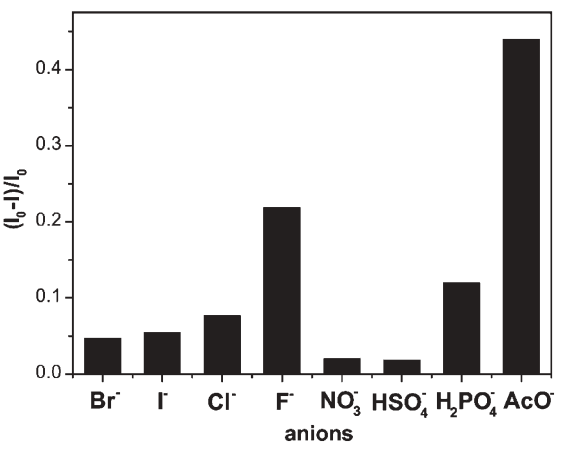
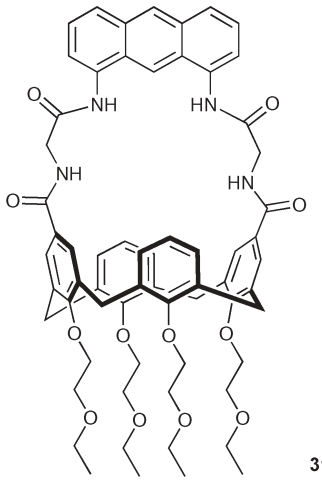


Fig. 1 Fluorescence quenching ratio $(I_o - I)/I_o$ of compound **31** with various anions (added as tetrabutylammonium salts) in CH_3CN (0.4% v/v $CHCl_3$) at λ_{ex} = 370 nm. Reproduced with permission from ref. 42. © 2005 Elsevier.

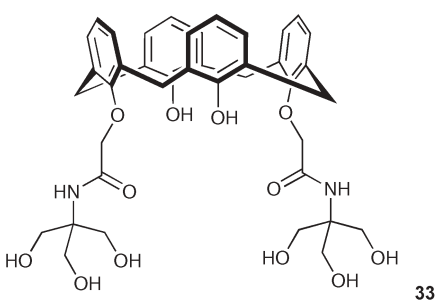
constants were found to be 3200 M^{-1} and 800 M^{-1} for AcO^- and F^-, respectively.



31

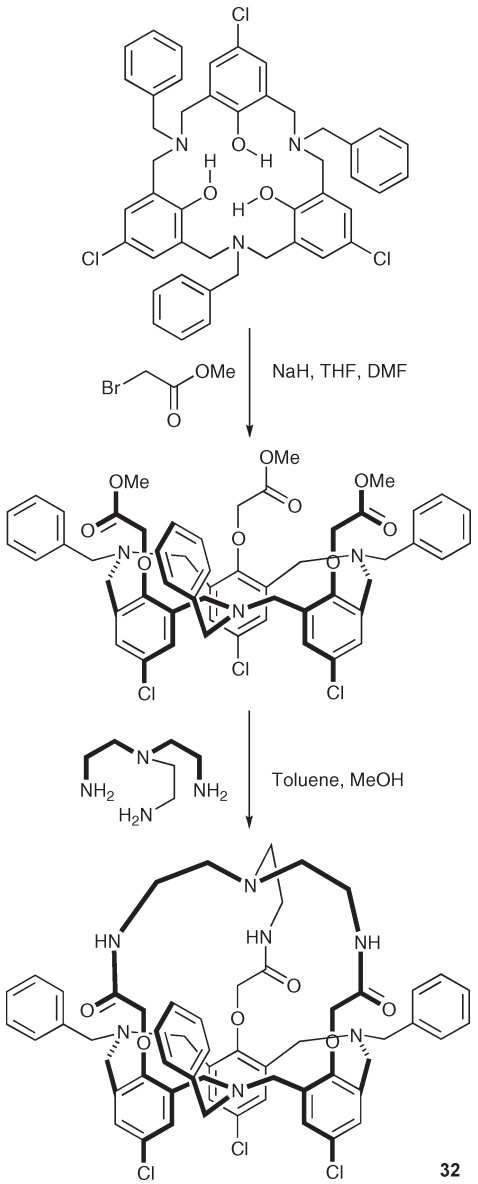
Receptors based on tris(2-aminoethyl)amine (tren) have been explored by a number of groups since Reinhoudt *et al.*'s seminal paper on these systems in 1993.[43] A novel C_{3v}-symmetrical N_7-hexahomotriazacalix[3]cryptand (**32**) has recently been reported by Pulpoka and co-workers (Scheme 5).[44] The binding abilities of **32** were evaluated by ^1H NMR spectroscopy and UV-vis spectrometry in $CDCl_3$ and DMSO solutions, respectively, showing that the receptor selectively binds halide anions ($Cl^- > Br^-$) over CH_3COO^-, $PhCOO^-$, NO_3^-, PF_6^-, and ClO_4^-, forming complexes with 1 : 1 stoichiometry with all the anions except carboxylates (see Table 4). Presumably access to the interior of this capsule is restricted in this case, diminishing the affinity of the receptor for the more basic yet larger carboxylates. The anion complexation ability of a zinc complex of **32** was also studied by the authors.

De Namor and co-workers have studied the complexation ability of a partially lower-rim substituted calix[4]arene hydroxyamide derivative, 25,27-bis[*N*-(2-hydroxy-1,1-bishydroxymethylethyl)aminocarbonylmethoxy]calix[4]arene-26,28-diol (**33**) for cations and anions through ^1H NMR spectroscopy, conductometry, spectrophotometry, and calorimetry in dipolar aprotic media.[45] These studies suggest that this receptor is able to interact with divalent cations through the carbonyl, the phenolic, and the hydroxyl oxygens of the pendant arms and with inorganic anions (fluoride, dihydrogen phosphate, and pyrophosphate) through hydrogen bond formation to the amide groups.



33

Continuing their seminal work on amide based cryptand hosts for anionic species,[46] Bowman-James and co-workers have synthesised a tricyclic receptor **34** consisting of two



Scheme 5 Synthesis of compound **32**.

monocyclic macrocycles joined by two bridging ethylene linkages.[47] Binding studies of **34** with anions by using ^{1}H NMR techniques revealed remarkably selective binding and

Table 4 Stability constants (log β)[a] of N_7-azacalix[3]cryptand (**32**) complexes with anions in DMSO by UV-vis titration methods (25 °C, I = 0.01 M Bu_4NPF_6)

Anion	log β/M^{-1}[a]
F^-	2.78 (0.01)
Cl^-	4.55 (0.03)
Br^-	3.97 (0.01)
I^-	2.72 (0.01)
NO_3^-	1.77 (0.01)
ClO_4^-	Undetermined
CH_3COO^-	β_1 = 2.92 (0.01), β_2 = 6.06 (0.01)
$PhCOO^-$	β_1 = 2.36 (0.06), β_2 = 6.26 (0.01)

[a] Mean values of $n \geqslant 3$ independent determinations, with standard deviation σ_{n-1} on the mean in parentheses.

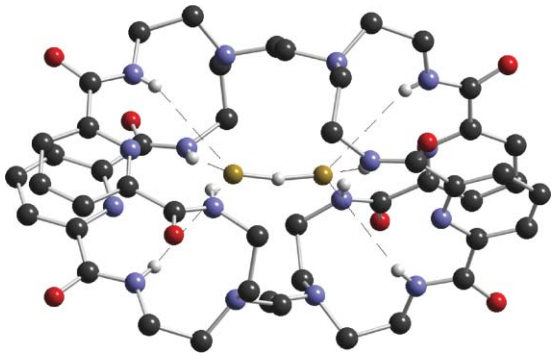
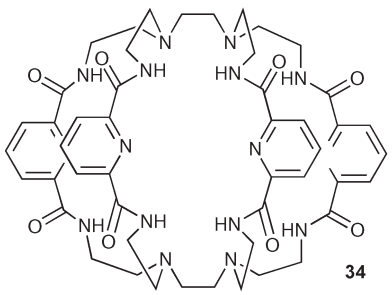


Fig. 2 The X-ray crystal structure of the bifluoride complex of **34**.

high affinity for the bifluoride FHF^- ion (K_a = 5500 M^{-1}) followed by $H_2PO_4^-$ (K_a = 740 M^{-1}), N_3^- (K_a = 340 M^{-1}) and CH_3COO^- (K_a = 100 M^{-1}), with negligible binding for HSO_4^-, Cl^-, Br^-, I^-, NO_3^- and ClO_4^- ions in DMSO-d_6. The crystal structure of the bifluoride complex (nBu$_4$N[**1**(FHF)]·3H$_2$O) was also elucidated (Fig. 2), and shows that the FHF^- anion is encapsulated within the receptor in the solid state, bound by four amide NH groups.



Beer and co-workers have continued their work on anion templated assembly and with a detailed study of the effect of anion template, strength of ion-pair thread association and macrocyclic ring size on pseudorotaxane formation (Fig. 3). A series of different threads and macrocycles were studied, including macrocycles containing isophthalamide groups

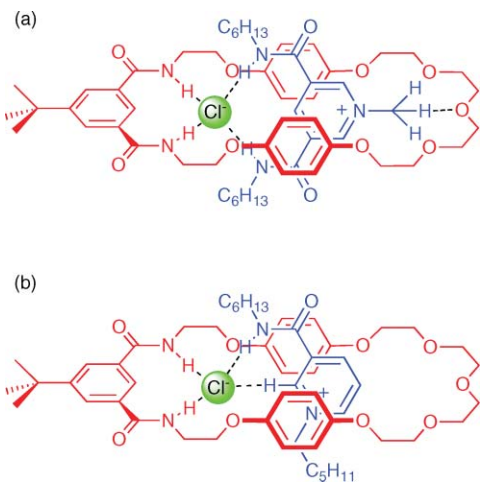
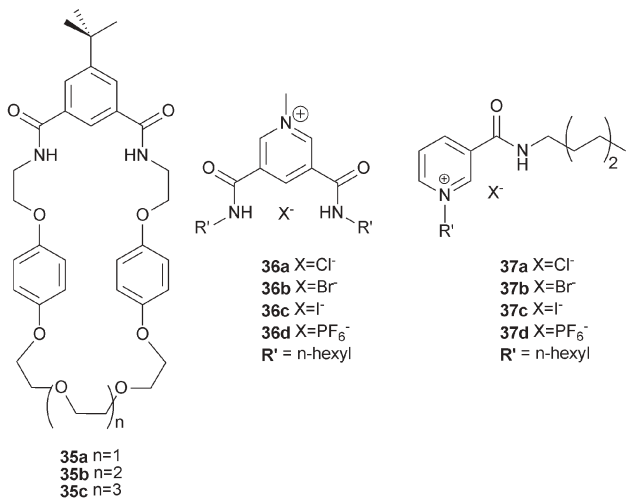


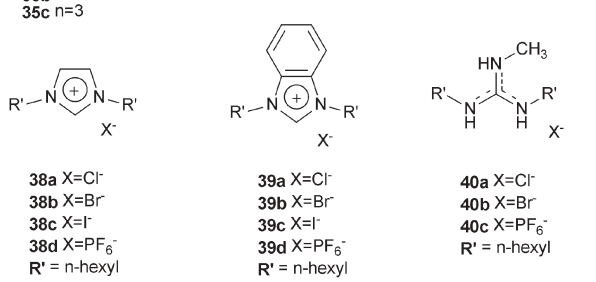
Fig. 3 (a) 3,5-Dicarboxamidopyridinium-based pseudorotaxane assembly. (b) Nicotinamide pseudorotaxane assembly.

Table 5 Stability constants (K_a/M^{-1}) for threads **36a–c** and **37a–c** with macrocycles **35a**,**b** and **c** as determined by ^{1}H NMR titrations in acetone-d_6 at 293 K (errors less than 10%)

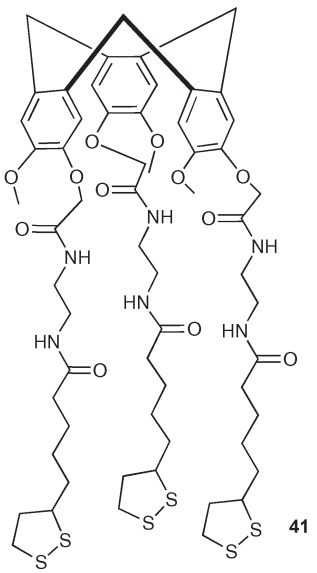
	Macrocycle		
Thread	**35a**	**35b**	**35c**
36a	9500	2400	980
37a	1900	950	320
36b	610	700	120
37b	200	240	180
36c	<50	65	<50
37c	65	<50	50

35a–c and threads **36–40**.[48] Proton NMR studies have demonstrated that the penetration of the ion pair into the macrocycle and the stability of the pseudorotaxane depends critically on the nature of the halide anion template (chloride was the optimum template), π–π stacking interactions between macrocycle and thread, CH hydrogen bonding, size effects and also, importantly, on the strength of the ion-pairing between the anion template and the cationic thread. For example, the association of macrocycles **35a**, **35b** and **35c** with threads **36** and **37** have been measured with the results shown in Table 5. A variety of crystal structures confirmed pseudorotaxane formation in the solid state in a number of cases. Further examples of anion templated assembly are discussed later in this review.

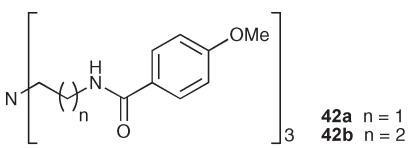




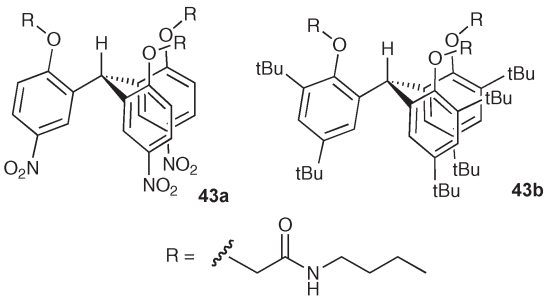
Zhang and Echegoyen have immobilised a tris-amide receptor functionalised cyclotriveratrylene on a gold surface forming a self-assembled monolayer.[49] Proton NMR titrations and UV-vis spectroscopy showed that the receptor is selective for acetate from amongst the anions studied (Cl^-, Br^-, NO_3^-, HSO_4^-, $H_2PO_4^-$) in $CDCl_3$. The cyclotriveratrylene thioctic ester **41** was immobilised on a gold support and impedance spectroscopy used to study anion complexation using $Fe(CN)_6^{3-/4-}$ as a redox probe. Impedance responses employing both negatively and positively charged redox couples have confirmed acetate was bound selectively on the modified surface in aqueous media.



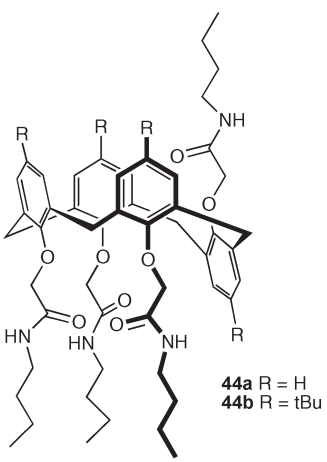
Tucker and co-workers have synthesised two tripodal receptors **42a** and **42b** and evaluated their anion binding properties with phosphate and vanadate anions in different organic solvents.[50] They found that in CD_3CN solution vanadate was bound by receptor **42a** in a similar fashion to its interaction with dihydrogen phosphate. However, receptor **42b** in CD_3CN–CD_2Cl_2 produced a very different response with vanadate by ^{1}H NMR titration, with an upfield shift of the amide NH protons observed. The authors suggest that this is indicative of the formation of a N–V bond between the receptor and anion.



The application of receptors as membrane transport agents for anions with potential future application in the treatment of channelopathies such as cystic fibrosis (CF) is attracting increasing interest.[51] J. T. Davis and co-workers have continued their studies on the transport of anions across lipid bilayer membranes; studies with tripodal amides **43a** and **43b** in egg yolk phosphatidylcholine (EYPC) liposomes showed that receptor **43a** selectively transports NO_3^- over Cl^- in a H^+–NO_3^- cotransport process (for examples of H^+–Cl^- cotransport please see below).[52] This is the first example of a synthetic transporter displaying such selectivity and in the future will allow a new approach to inducing pH changes in cells containing NO_3^-/Cl^- gradients.



J. T. Davis and co-workers have also continued their work on calixarene and oligophenoxyacetamide-based[53,54] membrane transport agents for chloride and HCl. Previous work had shown that tetraamide calix[4]arenes in the 1,3-alternate conformation form channels across liposomal membranes that allow chloride to pass through. Tetraamide functionalised calixarenes **44a** and **44b** were synthesised in the partial cone conformation.[55] Both compounds were shown to bind chloride in $CDCl_3$ solution, albeit with low stability constants (K_a = 10–20 M^{-1}). However, studies in dipalmitoyl phosphatidylcholine (DPPC) liposomes at 43 °C showed that only compound **44a** transports chloride anions. By lowering the temperature to 37 °C the lipid undergoes a phase change to a gel phase, conditions under which compound **44a** shows a non-linear dependence of chloride transport activity with concentration, a result consistent with the formation of membrane active aggregates. Solid state evidence shows that 'inverted' amide NH in **44a** forms an intramolecular hydrogen bond with the ether oxygen atom in the same chain whilst in **44b** the equivalent amide NH forms intermolecular hydrogen bonds giving a significantly more staggered arrangement of calixarenes in the solid state. The authors hypothesise that the dramatically different packing arrangement is also reflected in aggregate formation by these species in membranes. Interestingly, it was found that chloride transport by **44a** was inhibited upon addition of **44b**.

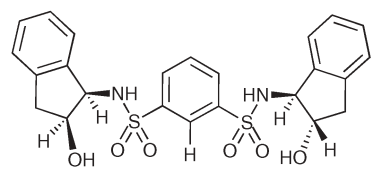


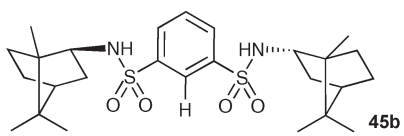
Gokel and co-workers have pioneered the application of chloride transport by synthetic molecules in lipid bilayer membranes. In a series of recent papers[56–59] this group has shown that amphiphilic peptide chains of general structure $(R^1)_2NCOCH_2OCH_2CO–(Gly)_3Pro(Gly)_3–OR$ can render lipid bilayer membranes permeable to chloride. In important recent work, this group has studied the effects of these compounds on epithelial cells.[60] Specifically, the biological activity of $(H_{37}C_{18})_2NCOCH_2OCH_2CO–(Gly)_3Pro(Gly)_3–OCH_2Ph$[57] was compared with that of model compound $(H_{37}C_{18})_2$-$NCOCH_2OCH_2CO–(Gly)_3Leu(Gly)_3–OCH_2Ph$ (used as a control as it is six times less effective as a chloride transporter than the proline containing analogue). Studies showed that the proline containing peptide functioned as a chloride transporter in the epithelial cells whereas the model compound did not, demonstrating that synthetic compounds have real potential in the treatment of diseases such as CF.

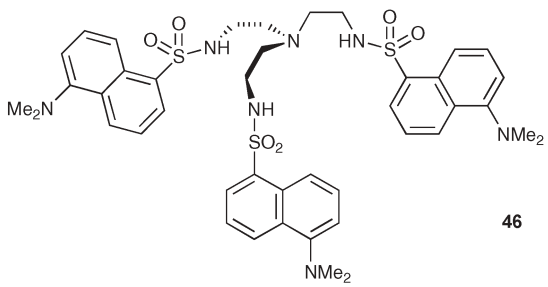
Sulfonamide based anion receptors

Sulfonamides have also been widely employed as anion binding groups in hydrogen bond donor organic based receptors. These groups are more acidic than the analogous secondary amides and hence are expected to form more stable complexes with anions.

Atmospheric pressure chemical ionisation mass spectrometry (APCI-MS) was employed by Kavallieratos and co-workers to identify anion complexes ($M–Cl^-$, $M–Br^-$, $M–I^-$, $M–NO_3^-$) formed by sulfonamide receptors **45a**, **45b** and **46** in dichloromethane.[61] This method offers the advantage that multiply charged species are not detected. Additionally, larger supramolecular ions are generally not detected meaning that species that are detected by this method are generally the more stable supramolecular complexes. Kavallieratos showed that complexes with the above anions could easily be detected using this technique.







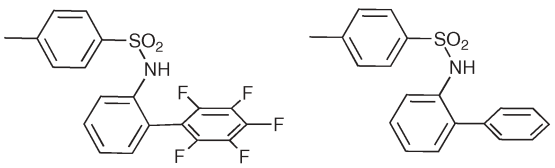
Berryman, Johnson and co-workers have designed and synthesised a pair of sulfonamide-based receptors **47a** and **47b** that differ only by the substituents on their aromatic rings.[62] Proton NMR spectroscopic data obtained from each receptor with an array of halides (Table 6) show a trend in stability

Table 6 Stability constants (K_a/M^{-1}) of receptors **47a** and **47b** with selected halides[a]

Halide	Receptor **47a**[b]	Receptor **47b**[b]
Cl^-	30 ± 3	<1[c]
Br^-	20 ± 2	<1[c]
I^-	34 ± 6	<1[c]

[a] The NEt_4^+ salts of each halide were used. [b] Initial receptor concentrations fall in the range of 9–25 mM. [c] Stability constants for receptor **47b** were too small to be determined by ^1H NMR titration experiments.

constant strength for receptor **47a** and the halides chloride, bromide and iodide that cannot solely be explained by the strength of the hydrogen bond with each anion, suggesting that there is an attractive interaction between the electron deficient aromatic ring in receptor **47a** and the anionic guests underscoring the hypothesis that electron deficient aromatics can be used as a component of a design strategy to target anions in solution.



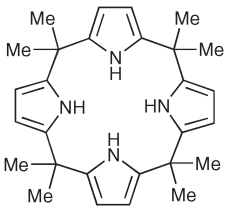
47a **47b**

Pyrrole and indole based anion receptors

Amongst neutral hydrogen bond donor groups used to bind anions, pyrroles and indoles differ from the amides and sulfonamides discussed above and the urea derivatives discussed below as they do not contain a hydrogen bond acceptor group.

Arguably the simplest pyrrole based anion receptor is *meso*-octamethylcalix[4]pyrrole **48** which can be synthesised in one step by the acid catalysed condensation of pyrrole with acetone. In 1996, Sessler and co-workers demonstrated that this macrocycle binds fluoride anions selectively in CD_2Cl_2 solution.[63] More recently, evidence began to emerge that the selectivity of calix[4]pyrrole for anions was very dependent on the nature of the solvent[64] and that fluoride selectivity could be lost under certain conditions. A detailed study by Sessler, Schmidtchen, Gale *et al*. with several chloride salts in solution by isothermal titration calorimetry (ITC) and ^1H NMR spectroscopic titrations and in the solid state by X-ray crystallography[65] showed no dependence of stability constant on method of measurement. However, the resulting stability constants were found to be highly dependent on the choice of solvent with K_as ranging from 10^2–10^5 M^{-1}. When dichloromethane was used as solvent, a strong dependence on the countercation was also seen, with the K_as for the interaction with chloride ranging from 10^2–10^4 M^{-1}, demonstrating that the choice of countercation can be significant.

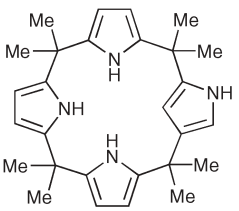
Direct evidence for anion pair complexation by compound **48** came from solution state and solid state studies of compound **48** with a variety of caesium and imidazolium



48

salts. Moyer, Sessler, Gale *et al*. demonstrated[66] that anion complexes of **48** can include large charge diffuse cations such as caesium and imidazolium in the anion-induced calix[4]pyrrole cup. Shielding of the imidazolium CH hydrogen atoms in CD_2Cl_2 solution in the presence of calixpyrrole and an anion which binds to calixpyrrole was presented as evidence of solution complexation of ion pairs. This work was extended to show that *N*-ethylpyridinium cations also bind within the calix[4]pyrrole cavity in anion complexes (Fig. 4).[67]

N-Confused calix[4]pyrrole **49** is formed in moderate yield during the acid catalysed condensation of pyrrole and acetone to form compound **48**. The first crystal structures of imidazolium chloride complexes of **49** show that compound **49** employs three NH groups to bind chloride in the solid state (Fig. 5).[68] Solution state studies by Anzenbacher and co-workers show that the β-CH on the inverted pyrrole ring is involved in hydrogen bonding to bound anion guests in solution.[69,70]



49

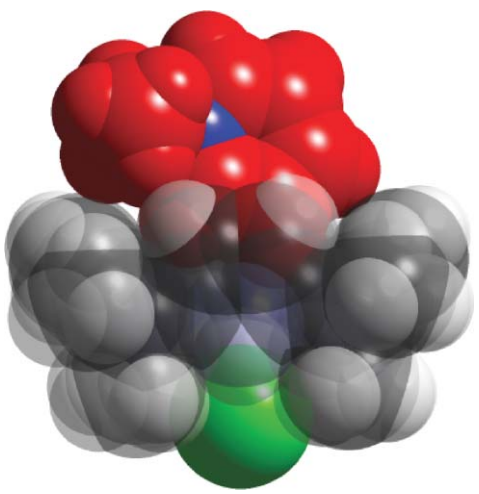


Fig. 4 *N*-Ethylpyridinium chloride–*meso*-octamethylcalix[4]pyrrole complex (solvent omitted for clarity). The macrocycle is rendered transparent and the pyridinium carbons and hydrogens in red to illustrate the degree of penetration of the cation into the calixpyrrole cup shaped cavity. Reproduced with permission from ref. 67 (Fig. 2). Copyright © 2006 The Royal Society of Chemistry.

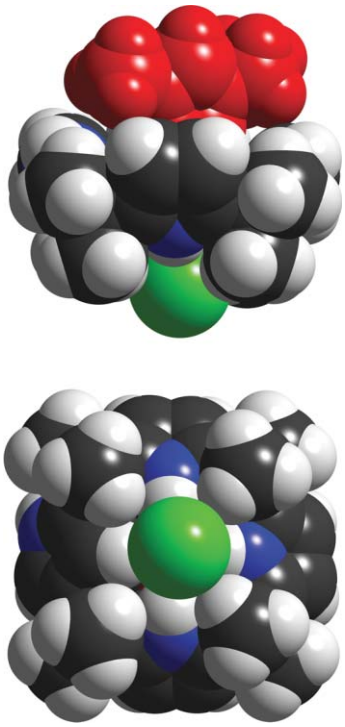
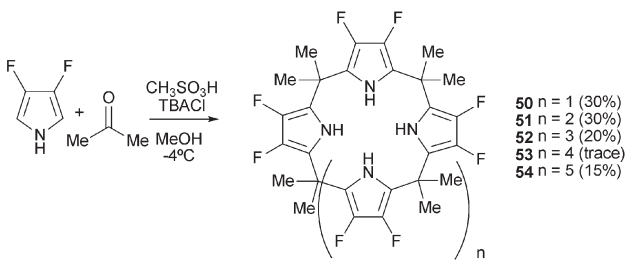


Fig. 5 Space filling representations of the side and bottom views of the ethylmethylimidazolium chloride complex of compound **49**. The bottom view of the complex illustrates the displacement of chloride towards the NH groups. Reproduced with permission from ref. 68 (Fig. 2). Copyright © 2006 The Royal Society of Chemistry.



Scheme 6 The synthesis of fluorinated calixpyrroles.

Sessler and co-workers have continued their work on fluorinated calixpyrroles. The use of 3,4-difluoropyrrole in the condensation reaction allows access to kinetic products with calix[4–8]pyrroles being isolated in the yields shown in Scheme 6.[71]

Detailed binding studies by ITC in CH_3CN and DMSO show size effects play a major role in the selectivity of this set of compounds (Table 7).

An alternative approach to the synthesis of expanded calix[4]pyrroles is to construct them from bipyrrole.[74] Recently, Sessler has shown that macrocycle **56** has a particularly high affinity for chloride (K_a = 2900000 M^{-1} in acetonitrile).[75] Solid state evidence shows that this macrocycle can adopt a V-shaped conformation when binding this anion, so employing all eight hydrogen bond donor NH groups (Fig. 6), which is presumably the reason for the high affinity in

Table 7 Stability constants (K_a/M^{-1}) for anion binding by fluorinated calixpyrroles **50**–**52** and by receptor **48** in CH_3CN or DMSO as determined by ITC analysis at 30 °C, using the corresponding tetrabutylammonium salts as the anion source[a]

Anion	Solvent	**48**	**50**	**51**	**52**
Cl^-	CH_3CN	140000	530000[72]	41000	280000
	DMSO	1300[72]	1500[72]		
Br^-	CH_3CN	3400[72]	8500[72]	4500	110000
I^-	CH_3CN	[b]	[b]	[b]	610
$CH_3CO_2^-$	CH_3CN	290000[73]	1900000	[c]	[c]
	CH_3CN[d]	350000	2400000	520000	1000000
	DMSO	6100	48000		
$C_6H_5CO_2^-$	CH_3CN	120000[73]	1200000	52000	[c]
	CH_3CN[d]	170000	1400000	83000	580000
$H_2PO_4^-$	DMSO	5100	17000	9600	15000
$H_2PO_2^-$	DMSO	[b]	3300	13000	35000

[a] The host (macrocycle) solution was titrated with the guest (anion) solution unless otherwise indicated. [b] Stability constant too low to be determined by ITC. [c] A good fit of the data to a 1 : 1 binding profile could not be made. [d] The guest solution was titrated with the host solution (reverse titration).

solution. The calix[3]bipyrrole analogue of this receptor (**55**) has a lower affinity for chloride (K_a = 110000 M^{-1} in acetonitrile). In addition to this work, this group has also synthesised calixpyrrole analogues containing other heterocyclic rings.[76]

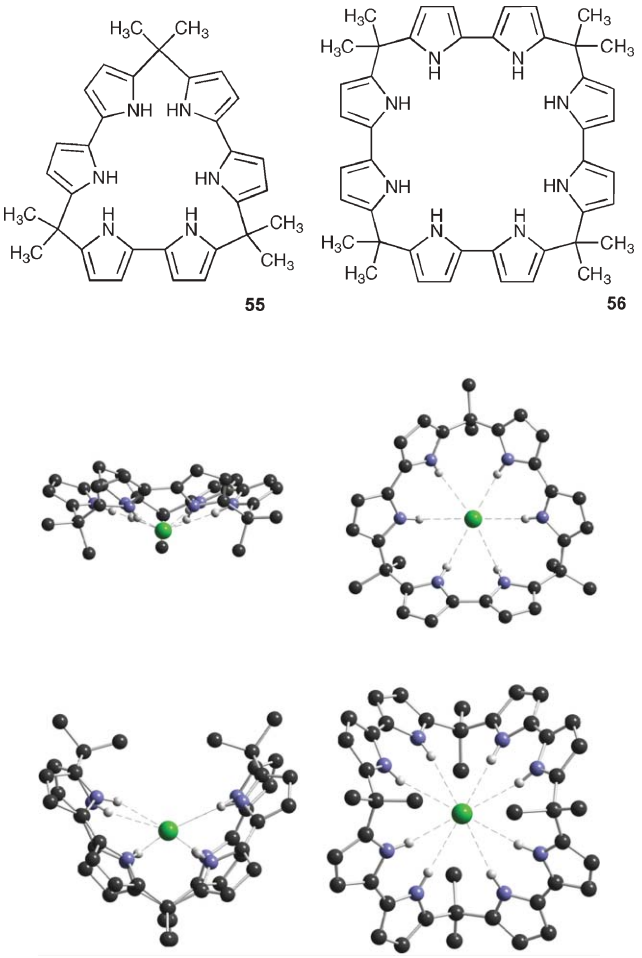
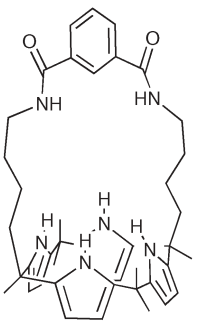


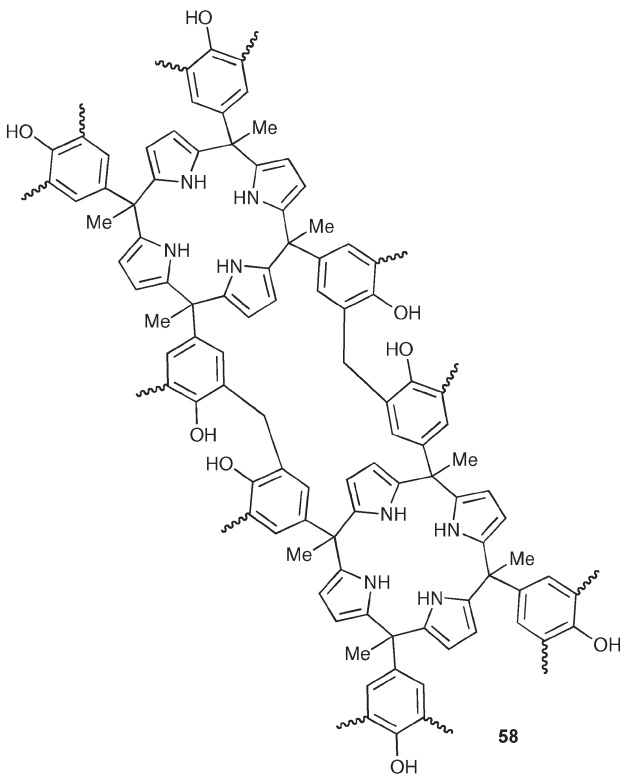
Fig. 6 Side and top views of the X-ray crystal structures of the chloride complexes of **55** (top) and **56** (bottom).

Lee, Sessler and co-workers have synthesised a variety of 'strapped' calixpyrroles including the isophthalamide strapped system **57**.[77] This bridge was found to increase the binding affinity for halide anions in acetonitrile solution but failed to show an appreciable size-based selectivity amongst the anions (Br^-, Cl^- and I^-) due to the tilt of the strap to one side of the receptor, allowing the formation of 2 : 1 (receptor : anion) complexes. Fluorescent analogues of this strapped system have been synthesised that contain coumarin and function as fluorescent sensors for anionic guests.[78]



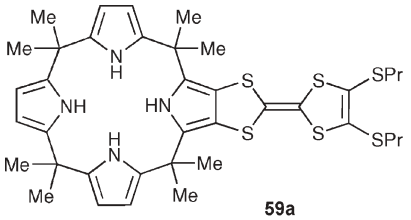
57

Kałedkowski and Trochimczuk have synthesised a number of calixpyrrole based resins including resin **58**, prepared by reacting the calix[4]pyrrole prepared from 4-hydroxyphenylmethylketone and pyrrole[79] as a mixture of isomers with formaldehyde and sodium hydroxide.[80] This material was shown to selectively extract fluoride anions from dry acetonitrile solution, complexing up to 96.5% of fluorides from 10^{-3} M solutions.

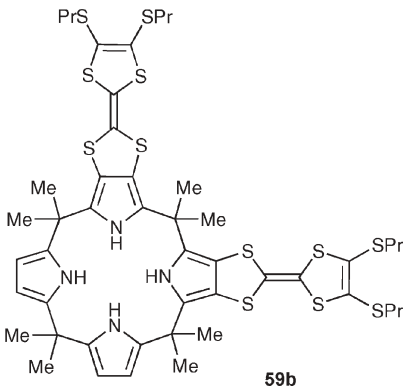


58

Continuing on from earlier work,[81] Sessler, Jeppesen and co-workers have described the synthesis of two new tetrathiafulvalene (TTF)-calix[4]pyrroles, namely monotetrathiafulvalene-calix[4]pyrrole **59a** and bis(tetrathiafulvalene)-calix[4]pyrrole **59b**, as well as their anion binding properties using ^{1}H NMR spectroscopic and ITC techniques in CD_2Cl_2, acetone-d_6 and CD_3CN.[82] These studies provide support for the notion that the incorporation of one or more electron rich TTF subunits into the calix[4]pyrrole backbone improves the anion binding abilities of the receptors, while also affecting their selectivity. Halide anion complexation was also monitored by cyclic voltammetry studies in 1,2-dichloroethane, which provided evidence of an anion-dependent electrochemical response with Cl^- and Br^- ions.



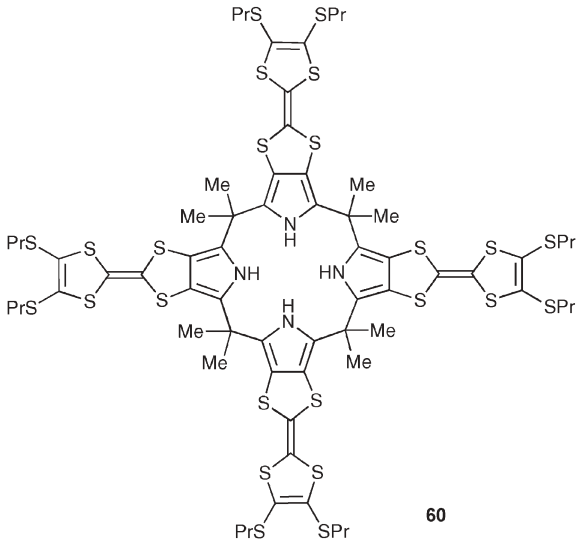
59a



59b

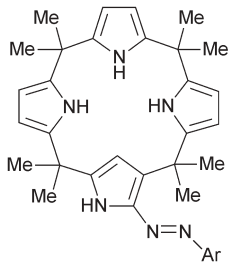
The same researchers have studied the treatment of a solution of a tetrathiafulvalene-functionalised calixpyrrole (**60**) with chloride anions in dichloromethane, affording a bowl-like receptor that is able to encapsulate C_{60} in a 2 : 1 (calixpyrrole–chloride : C_{60}) barrel-like manner.[83] As was observed with cation inclusion in the calixpyrrole cup, initial anion binding in the present ensemble serves as a ''trigger'' for the crucial reorganisation of the calix[4]pyrrole receptor needed to produce a ''cone'' conformation, wherein multiple TTF units are appropriately arranged to allow for fullerene binding. The binding constants were determined by UV-vis and fluorescence titration experiments in dichloromethane as solvent, leading to the formation of the putative 2 : 1 complex between **60**·Cl^- and C_{60} with $K_1 = 2.3 \times 10^3$ M^{-1} and $K_2 = 1.3 \times 10^4$ M^{-1} reflecting the formation of $C_{60}\subset$**60**·Cl^- and $C_{60}\subset$(**60**·Cl^-)$_2$, respectively. Moreover, the dramatic colour change that accompanies the C_{60} binding event allows the recognition process to be followed easily, and thus the presence of this fullerene to be readily ''sensed''.

Dehaen and co-workers have reported the first example of substitution reaction in the free α-position of *N*-confused calix[4]pyrroles **61a**–**e**[84] by azo-coupling with various arenediazonium salts. The stabilities of anion complexes formed



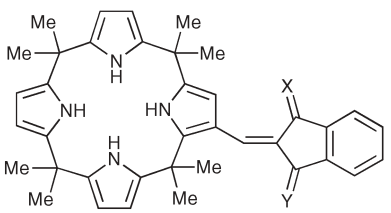
60

with α-arylazo-*N*-confused calix[4]pyrroles were found to be slightly higher than those of unsubstituted *N*-confused calix[4]pyrrole.



61a Ar = C_6H_5
61b Ar = *p*-C_6H_4-OMe
61c Ar = *p*-C_6H_4-Br
61d Ar = *p*-C_6H_4-NO_2
61e Ar = C_6F_5

Knoevenagel condensations of 2-formyl-octamethylcalix[4]-pyrrole with selected 1,3-indanedione derivatives to yield calix[4]pyrrole anion sensors (**62a**–**d**) with push–pull chromophores displaying strong intramolecular charge transfer have been performed by Anzenbacher and Nishiyabu.[85] Visual inspection of solutions of these sensors in CH_2Cl_2 or DMSO with 0.5% water, before and after the addition of anion salts, showed a dramatic change in colour in the case of fluoride, acetate and, to a lesser extent, dihydrogen phosphate, suggesting strong binding, whereas the addition of chloride, bromide, or nitrate resulted in weak or no changes in colour. The ^{1}H NMR titrations in DMSO-d_6 with 0.5% water show that the sensors within the series show increasing affinity for anions and dramatically enhanced selectivity for acetate *vs.* chloride (see Table 8).



62a X = H_2, Y = $C(CN)_2$
62b X = Y = O
62c X = O, Y = $C(CN)_2$
62d X = Y = $C(CN)_2$

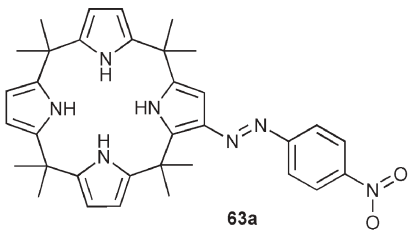
In a continuation of their earlier work,[86] Anzenbacher and co-workers have described the synthesis and anion binding properties of chromogenic octamethylcalix[4]-pyrroles **63a** and **64a** (OMCPs) as well as their *N*-confused

Table 8 Affinity constants (K_a/M^{-1})[a] for **62b**–**d** and anionic substrates in DMSO (50 μM, 0.5% water at 22 °C)

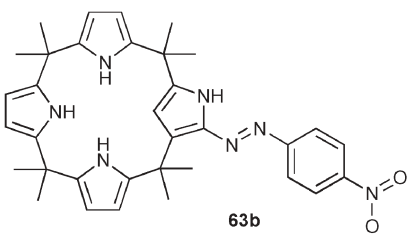
Anion	**62b**	**62c**	**62d**
F^-	$>10^6$	$>10^6$	$>10^6$
Cl^-	574	652	2840
AcO^-	15700	125000	$>10^6$
$H_2PO_4^-$	4560	8050	160000
K_{AcO^-}/K_{Cl^-}	27	191	>350
$K_{AcO^-}/K_{H_2PO_4^-}$	3.4	15.5	>35

[a] Determined from absorption spectroscopic titrations. Errors are <15%. 1 : 1 stoichiometry determined by Job plots.

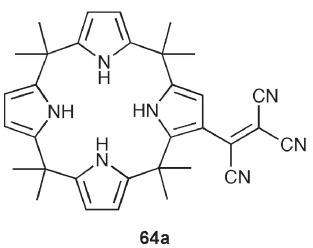
octamethylcalix[4]pyrrole isomers **63b** and **64b** (NC–OMCPs).[69] The chromogenic NC–OMCPs showed significantly stronger anion-induced colour changes compared to the corresponding chromogenic OMCPs, and the absorption spectroscopy titrations in DMSO indicated that chromogenic OMCPs ($F^- > HP_2O_7^{3-} > AcO^- > H_2PO_4^- > Cl^-$) and NC–OMCPs ($AcO^- > F^- > HP_2O_7^{3-} > H_2PO_4^- > Cl^-$) also possess different anion binding selectivity (see Table 9). Moreover, preliminary colorimetric microassays using chromogenic calixpyrroles embedded in partially hydrophilic polyurethane matrices allow for observation of analyte-specific changes in colour when the anions are administered in the form of their aqueous solutions and in the presence of weakly competing anions.



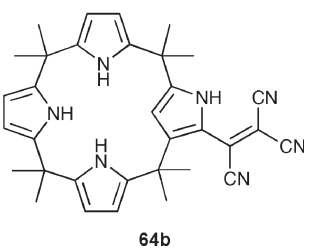
63a



63b



64a



64b

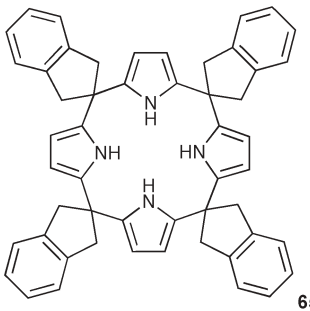
Black, Colbran and co-workers have synthesised two new *meso*-indanyl-substituted calix[4]pyrrole receptors **65** and **66**[87] in order to study the effect of *meso*-substitution on anion affinity. In CD_3CN (0.04% w/w H_2O), **65** has shown a higher affinity for chloride ion than **48** (K_a respectively 5.2 (± 0.8) × 10^4 M^{-1} and 2.6 (± 1.4) × 10^5 M^{-1}). Interestingly, the authors found mass spectroscopic evidence from negative ion

Table 9 Stability constants for **63**–**64a**,**b** and anions in DMSO at 22 °C determined by absorption spectroscopy titrations

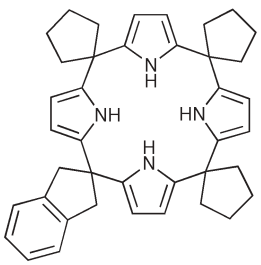
Anion[a]	**63a**	**63b**	**64a**	**64b**
F^-	$>10^6$	7240	$>10^6$	$>10^6$
Cl^-	741	<50	1370	319
AcO^-	8540	16600	242000	$>10^6$
$H_2PO_4^-$	3330	430	5230	810000
$HP_2O_7^{3-}$[b]	92200	5650	584000	N. D.
K_{AcO^-}/K_{Cl^-}	12	330	176	>10000
$K_{AcO^-}/K_{H_2PO_4^-}$	3	39	46	25

[a] Anions were used in the form of their Bu_4N^+ (TBA) salts. The errors in all fits are <15%. [b] Association constants were calculated on the assumption that pyrophosphate forms a dimer in DMSO.

ESI-FTICR experiments that compound **65** may be deprotonated by fluoride.

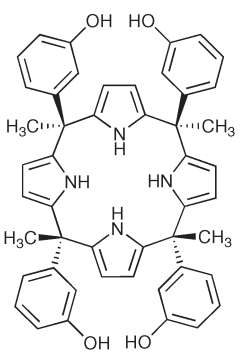


65

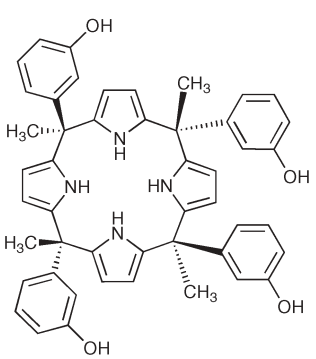


66

De Namor and co-workers have described the synthesis of two isomeric *meso*-tetramethyltetrakis(3-hydroxyphenyl)calix[4]pyrroles, **67**-αααββ and **68**-αβαβ and have investigated their anion binding properties by ^{1}H NMR and conductometric titrations in acetonitrile and *N*,*N*-dimethylformamide solutions.[88] These investigations revealed that **67**-αααββ shows selectivity for $H_2PO_4^-$ in acetonitrile while its isomer **68**-αβαβ is selective for fluoride. Moreover, using thermodynamic, conductometric and calorimetric data this paper demonstrates that the enthalpy parameter may be a suitable reporter of the number of hydrogen bonds formed when calix[4]pyrrole and its derivatives interact with the dihydrogen phosphate anion in acetonitrile, and highlight the importance of the medium effect on the stability of the complex reflecting the inherent nature of the solvent and its highly significant involvement in the complexation process.



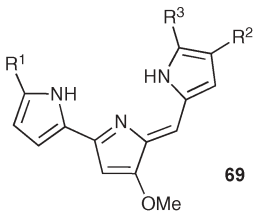
67-αααββ



68-αβαβ

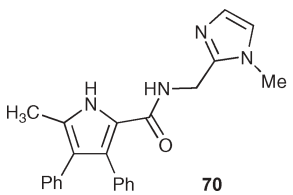
Acyclic pyrrole-based anion receptors have also been the subject of intense interest recently,[89,90] as these systems may have potential application in the transport of chloride across lipid bilayers. The prodigiosins are a family of naturally occurring pyrrole alkaloids[91] produced by organisms such as *Streptomyces* and *Serratia*.[92,93] They have the general structure **69** and show a range of useful biological activities including induction of tumour cell apoptosis and toxicity against fungi, bacteria and the malaria parasite. There is evidence that these species promote the co-transport of HCl across lipid bilayer membranes[94]—however, it is not clear whether this ability is the cause of their biological activity. This has prompted a number of groups to study the chloride transport ability of the prodigiosins and their analogues.

In a very interesting recent study, J. T. Davis and Seganish have shown that prodigiosin **69** (R^1 = H, R^2 = C_5H_{11}, R^3 = Me) can also transport chloride *via* an antiport mechanism, *i.e.* exchanging anions across a lipid bilayer, in addition to functioning as an H^+/Cl^- symporter.[95]

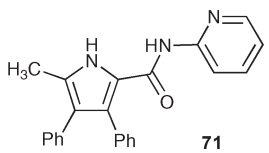


69

Gale, B. D. Smith and co-workers recently reported the synthesis of amidopyrroles **70** and **71**.[96] Like the prodigiosins, these compounds contain two hydrogen bond donor groups and a basic site that may be protonated. The crystal structure of the HCl complex of compound **70** shows that the receptor forms a "2 + 2" complex with HCl with two chloride anions bound, each by three NH hydrogen bonds, one each from the imidazolium ring of one receptor and the amide and pyrrole NH groups of the other receptor in the dimer (Fig. 7).



70



71

Transport studies, conducted using POPC (1-palmitoyl-2-oleoyl-*sn*-glycero-3-phosphocholine)/cholesterol vesicles showed that, in the presence of a pH gradient with low pH (high HCl concentration) inside the vesicle, receptor **70** can complex, cotransport across the vesicle membrane and release HCl much more efficiently than pyridyl analogue **71** (Scheme 7). A chloride selective electrode was used to monitor chloride release whilst release of protons from the vesicle was confirmed by the use of a pH sensitive dye (Oregon Green). Presumably the difference in transport ability between **70** and **71** is due to a combination of pK_a and geometry effects. Interestingly, in the absence of a pH gradient, compound **70** could still release chloride from the vesicles, although at a slower rate than in the presence of a pH gradient.

Sessler and co-workers have investigated the propensity of linear bi- and tripyrrolic fragments to complex and transport chloride.[97] Dipyrromethenes **72** and **73** were compared with prodigiosins **74**, **75** and **76**.

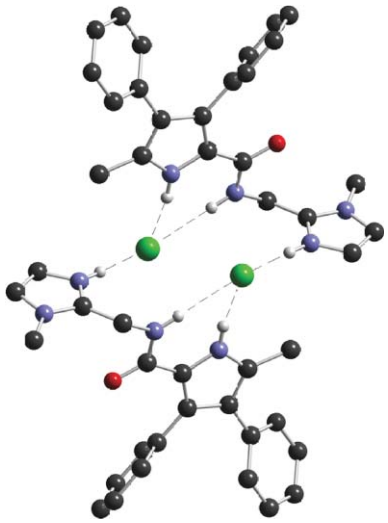
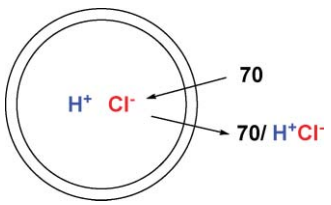
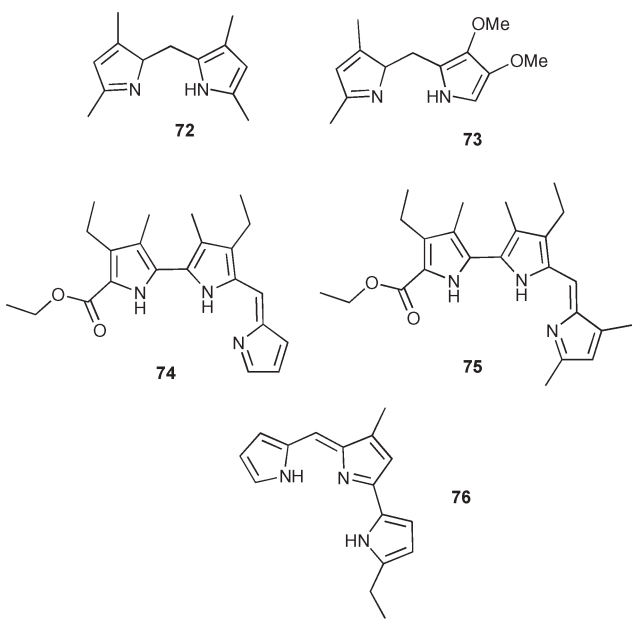


Fig. 7 Crystal structure of the HCl complex of **70** showing the formation of a '2 + 2' hydrogen bonded dimer in the solid state.



Scheme 7



The X-ray crystal structure of the protonated chloride complex of prodigiosin **75** revealed that the protonated species binds chloride with three hydrogen bonds (Fig. 8).

Experiments in POPC/POPS (1-palmitoyl-2-oleoyl-*sn*-glycero-3-phospho-L-serine) liposomes were conducted monitoring chloride efflux triggered by these receptors as a function of time (Fig. 9). The anticancer properties of the receptors were measured using a cell proliferation assay. pH changes

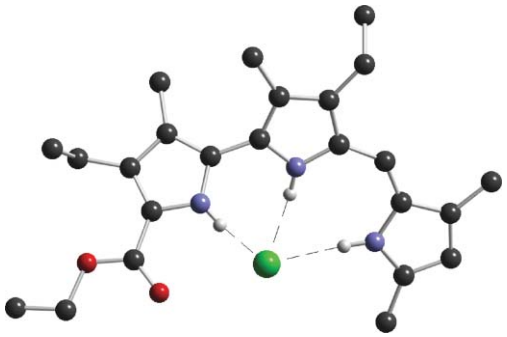


Fig. 8 The X-ray crystal structure of the complex formed between monoprotonated prodigiosin **75** and chloride.

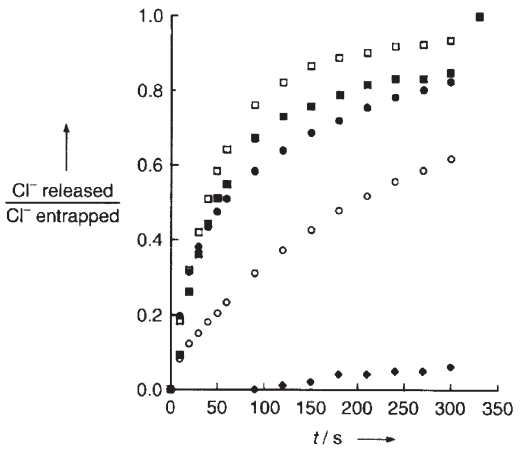
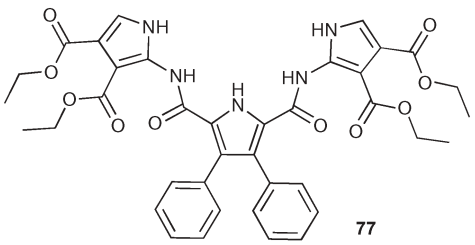


Fig. 9 Time dependent efflux of chloride ion from 200 nm vesicles loaded with a solution of NaCl (500 mM) and suspended in a solution of $NaNO_3$ (500 mM) and triethylsilane (5 mM) adjusted to pH 7.4. Prodigiosins are indicated by filled markers (● **76**; ■ **74**; ◆ **75**); dipyrromethenes are indicated by open markers (□ **72**; ○ **73**). Reproduced with permission from ref. 97. Copyright © Wiley-VCH 2005.

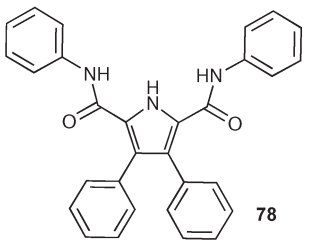
demonstrated that the receptors were functioning as H^+/Cl^- symporters whilst the cell assays showed that compounds **72**, **73**, **74** and **76** all exhibited significant cytotoxic activity with 100% cancer cells killed at a concentration of 40 μM in the cell lines studied.

A new bis(pyrrol-2-yl)-2,5-diamidopyrrole (**77**) has been synthesised by Sessler, Gale and co-workers, and its binding abilities studied by ^{1}H NMR titration techniques in DMSO-d_6 solution.[98] The authors found that receptor **77** showed a significantly higher affinity for oxo-anions such as acetate (K_a = 10300 M^{-1}) than previous generation 2,5-dicarboxamidopyrroles (**78**; K_a = 560 M^{-1} measured in DMSO-d_6–0.5% water),[99] results that can be rationalised by the presence of the two new pyrrole rings in **77** and hence a beneficial increase in the number of hydrogen bond donor sites as compared to 'parent' compound **78**.

Following on from their earlier work,[100] Sun and co-workers have reported the synthesis of compounds **79** and **80** featuring the dipyrrole carboxamide moiety for anion recognition.[101] The ability of **79** and **80** to complex anions was explored with UV-vis absorption and fluorescence spectrometry using a CH_3CN–H_2O mixture (90 : 10, v/v) as solvent,

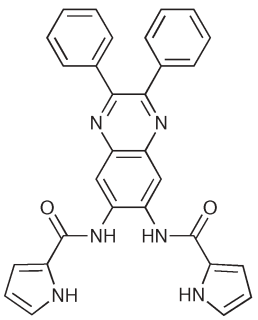


77

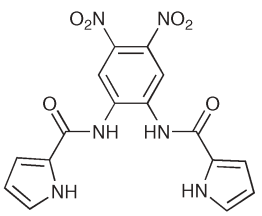


78

showing that both **79** and **80** responded to only cyanide anion resulting in a colour change from colourless to yellow and the fluorescence change for compound **79** from blue to green.



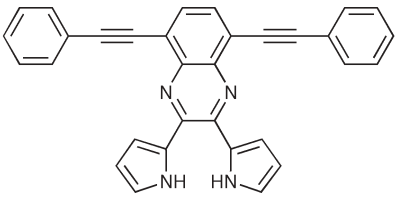
79



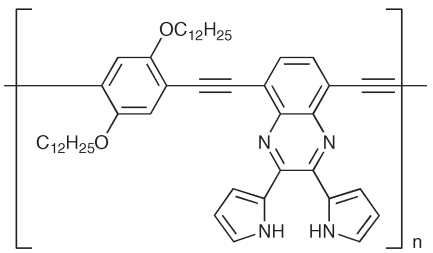
80

Sun and co-workers have synthesised a series of dipyrrolylquinoxaline (DPQ)-containing monomer (**81a**) and polymers (**81b** and **81c**) which were employed as chromogenic and fluorescent chemosensors for inorganic anions.[102] Anion binding studies were conducted using UV-vis, fluorescence and ^{1}H NMR spectroscopic techniques in CH_2Cl_2 and DMSO-d_6 solution, respectively, and the following binding affinity order for all the compounds examined was found: $F^- > HP_2O_7^{-3} > CN^- > AcO^- > H_2PO_4^- \approx Cl^- \approx Br^- \approx I^- \approx NO_3^-$. The sensitivity of the DPQ-based chemosensor was found to display a 34-fold enhancement by incorporation into the conjugated polymer. However, in the presence of fluoride or pyrophosphate, the colorimetric responses and fluorescence quenching observed in chemosensors **81a–c** were found to be due to deprotonation of the N–H proton of the pyrrole units, so the anion selectivity is primarily determined by the relative basicity of the anions.

Anzenbacher and co-workers have synthesised DPQ analogues **82a** and **82b**[103] containing quinone groups which combine colorimetric and electrochemical responses to anionic guests into single receptors. As each receptor has effectively two output channels, comparison of the colorimetric and electrochemical data can be used to determine the nature of the anionic substrate present, as opposed to systems with a single

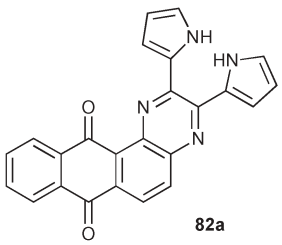


81a

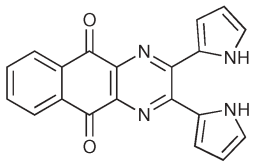


81b n = 7
81c n = 110

output channel which may not provide a unique response to each anionic guest.

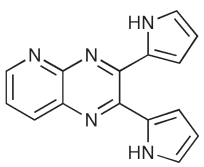


82a



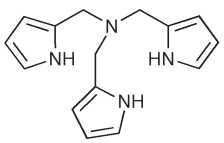
82b

The synthesis, characterisation and ion binding studies of 2,3-di(1*H*-2-pyrrolyl)pyrido[2,3-*b*]pyrazine (**83**) have been described by Samanta and co-workers.[104] Titration studies of compound **83** with different cations and anions were carried out in CH_3CN using UV-vis spectroscopic techniques, revealing a binding constant for fluoride of 4.9×10^3 M^{-1}. Fluoride also triggers a colour change in acetonitrile solutions of **83** from yellowish green to red.



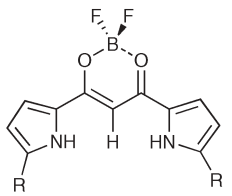
83

Cheng and co-workers have synthesised a new pyrrole-based tripodal anion receptor **84** and studied its anion binding properties by X-ray crystallography, ^{1}H NMR spectroscopy, and ESI-MS, revealing a selectivity for the more basic $H_2PO_4^-$ and F^- ions.[105]



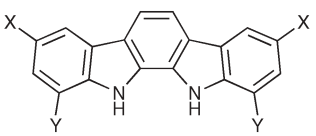
84

Maeda and Kusunose have synthesised a variety of receptors based upon dipyrrolylketone difluoroboron complexes (**85a** and **85b**).[106] These receptors employ both NH and CH interactions[107] to bind anionic guests. Stability constants of compound **85b** in CH_2Cl_2 at room temperature determined by UV-vis titration techniques with tetrabutylammonium anion salts revealed a selectivity for acetate,[108] with this anion bound with a stability constant of 110000 M^{-1} *vs.* 81000 M^{-1} for fluoride, 13000 M^{-1} for $H_2PO_4^-$ and 2000 M^{-1} for chloride. Analogues containing 3,4-difluoropyrrole units were shown to have enhanced anion affinities.



85a R = H
85b R = neopentyl

Beer and co-workers have synthesised a series of simple preorganised indolo[2,3-*a*]carbazole derivatives **86a–d**.[109] Proton NMR titrations in acetone with these receptors show that all the compounds are selective for benzoate followed by $H_2PO_4^- > F^- > Cl^- > HSO_4^-$. In acetone solution, a significant fluorescence enhancement was observed upon addition of fluoride, chloride and dihydrogen phosphate. The crystal structure of the fluoride complex of **86b** is shown in Fig. 10 showing the formation of an unusual 2 : 1 receptor : anion stoichiometry complex in the solid state.



86a X = H, Y = H
86b X = CH_3, Y = H
86c X = H, Y = Br
86d X = Br, Y = H

Jeong and co-workers have employed indoles and indolocarbazoles in the very rigid alkyne linked macrocyclic receptors **87a** and **87b**.[110] Anion affinity was measured by UV-vis titration techniques in acetonitrile. The results, shown in Table 10, reveal that both **87a** and **87b** have a high affinity for anions, binding fluoride selectively under these conditions.

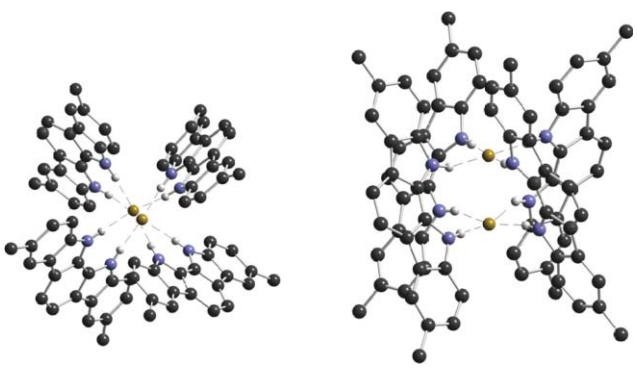


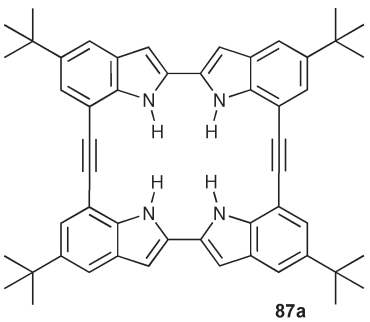
Fig. 10 Top (left) and side (right) views of the crystal structure of the 2 : 1 complex of TBAF with receptor **86b**. Countercation and non-acidic hydrogen atoms omitted for clarity.

Table 10 Stability constants (M^{-1}) of receptors **87a** and **87b** with a variety of inorganic anionic guests in CD_3CN

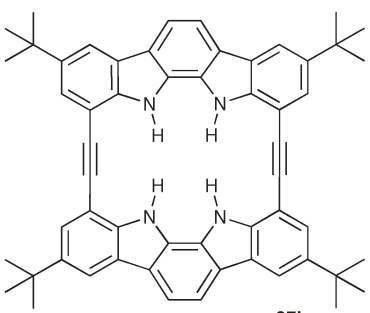
	Stability constant (K_a)/M^{-1}	
Anion	Receptor **87a**	Receptor **87b**
F^{-a}	2.0×10^8	5.6×10^8
AcO^-	5.9×10^6	6.5×10^6
$H_2PO_4^-$	2.1×10^6	3.2×10^6
Cl^-	1.5×10^6	2.1×10^6
N_3^-	8.8×10^5	9.1×10^5
HSO_4^-	6.5×10^5	6.8×10^5
NO_3^-	3.9×10^5	3.9×10^5
CN^-	6.5×10^4	7.5×10^4
Br^-	$K_1 = 1.9 \times 10^3$	$K_1 = 1.9 \times 10^3$
	$K_2 = 10$	$K_2 = 14$
I^-	$K_1 = 3.1 \times 10^2$	$K_1 = 3.0 \times 10^2$
	$K_2 = 6$	$K_2 = 5$

[a] The stability constants between the macrocycles and fluoride anions were determined by competition experiments with chloride.

The crystal structure of the chloride complex of **87b** (Fig. 11) shows chloride perched above the plane of the macrocyclic ring. Presumably, the smaller fluoride anion can fit more snugly in the macrocyclic cavity and hence is bound with higher affinity. Interestingly, in CD_3CN solution, slow exchange was observed on the NMR timescale at ambient temperature upon addition of all the putative anionic guests, including the weakly bound Br^- and I^- anions.



87a



87b

Kwon and Jeong have prepared a dihydrogen phosphate receptor **88** containing both hydrogen bond donors and acceptors by incorporating two pyridyl units into a preorganised biindole scaffold.[111] Receptor **88** strongly and selectively binds dihydrogen phosphate *via* multiple hydrogen bonds with an association constant of 1.1×10^5 M^{-1} in CH_3CN as determined by UV-vis spectroscopy. The high selectivity toward the target anion over other anions is presumably due

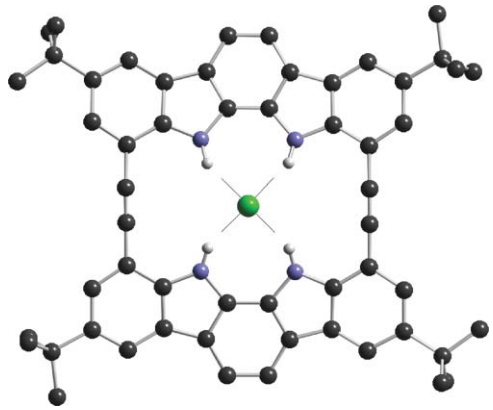
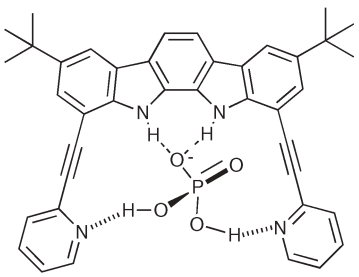


Fig. 11 The crystal structure of the chloride complex of receptor **87b**. Non-acidic hydrogen atoms and countercation omitted for clarity.

to two additional hydrogen bonds between the phosphate hydroxyl groups and the pyridyl nitrogens that can be formed when binding this diprotic anion.



88 - $H_2PO_4^-$

Sessler and co-workers have reported the synthesis of a new series of 2,3-diindol-3′-yl quinoxalines (**89a**,**b**) and studied their anion recognition properties by UV-vis absorption titrations in dichloromethane solution.[112] These new indole-based receptors proved to have a particular affinity for dihydrogen phosphate, binding this anion selectively with stability constants of 6800 and 20000 M^{-1}, for compounds **89a** and **89b**, respectively. Moreover, receptor **89b** allows for the visual detection of this anion *via* an anion-triggered colour change (Fig. 12).

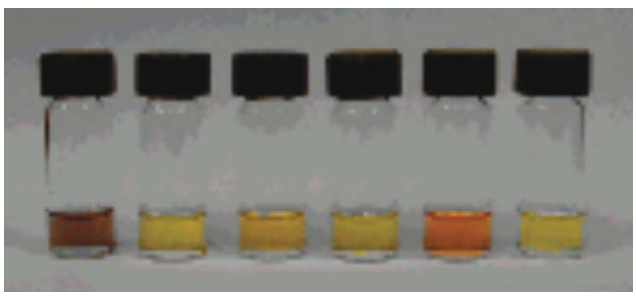
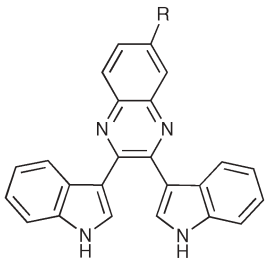


Fig. 12 Colour changes observed upon the addition of anions (10 equiv.) to otherwise identical solutions of receptor **89b** (4.34×10^{-5} M in dichloromethane. From left to right: F^- + **89**, Cl^- + **89**, BzO^- + **89**, HSO_4^- + **89**, $H_2PO_4^-$ + **89**, **89**. Reproduced with permission from ref. 112. Copyright © 2006 ACS.

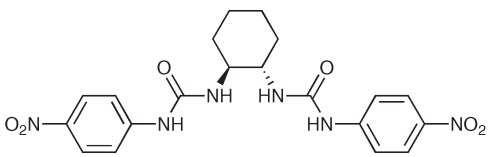


89a R = H
89b R = NO_2

Urea and thiourea based anion receptors

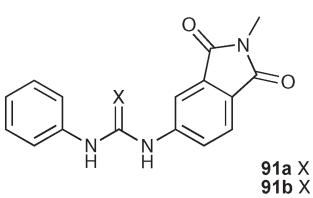
Ureas and thiourea groups are excellent receptors for oxoanions such as carboxylates and phosphates to which they can donate two hydrogen bonds. Their synthetic accessibility has allowed their inclusion in a wide variety of anion receptors with much effort still devoted to the synthesis and study of these effective receptor systems.[5]

Fabbrizzi and co-workers have synthesised two chiral receptors using the *R*,*R* or *S*,*S* enantiomeric forms of *trans*-1,2-cyclohexane by reaction with 4-nitrophenylisocyanate.[113] The *S*,*S* enantiomer **90** forms a hydrogen-bonded complex with the biologically important D-2,3-diphosphoglycerate anion, with a stability constant twice that formed with the *R*,*R* enantiomer in DMSO-d_6.



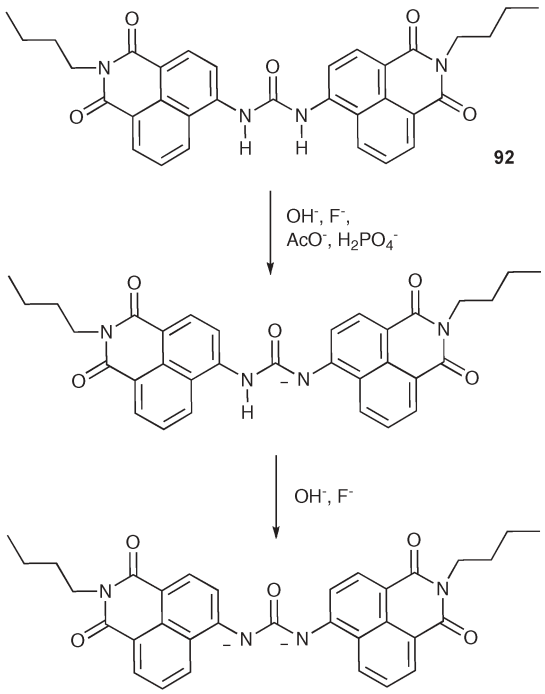
90

Fabbrizzi and co-workers have also conducted a number of studies on anion triggered deprotonation of ureas and thioureas. In organic solution, basic anions such as fluoride and acetate have been shown to deprotonate a variety of neutral hydrogen bond donor receptor systems.[89,114,115] Deprotonation processes are often driven by the formation of a particularly stable species such as HF_2^-. Fabbrizzi and co-workers have compared the anion complexation properties of urea **91a** and thiourea **91b**.[116] Thiourea **91b** is more acidic than urea **91a** and deprotonates in the presence of anions such as fluoride, carboxylates and dihydrogen phosphate whereas the less acidic receptor **91a** is deprotonated only by the most basic anion studied, fluoride in DMSO solution.



91a X = O
91b X = S

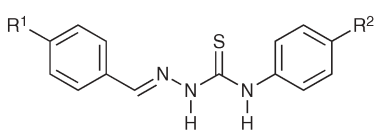
Deprotonation processes can be used to colorimetrically sense anions.[117,118] Fabbrizzi and co-workers have synthesised chemosensor **92** containing a urea group substituted with two



Scheme 8 Stepwise deprotonation of compound **92** in DMSO.

chromophoric electron-withdrawing naphthalenimide subunits.[119,120] In DMSO, anions such as acetate and dihydrogen phosphate were found to induce a single deprotonation of the receptor (Scheme 8), whilst more basic fluoride and hydroxide induced double deprotonation. The deprotonated species were shown to be red (LH^-) and blue (L^{2-}) respectively (Fig. 13).

Similar studies with (benzylideneamino)thiourea receptors **93a**–**g** in acetonitrile showed fluoride triggered monodeprotonation whilst oxo-anions such as acetate formed 1 : 1 complexes with the receptors.[121]

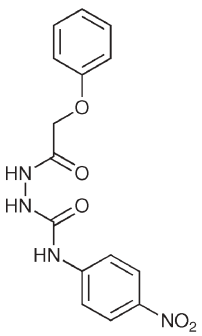


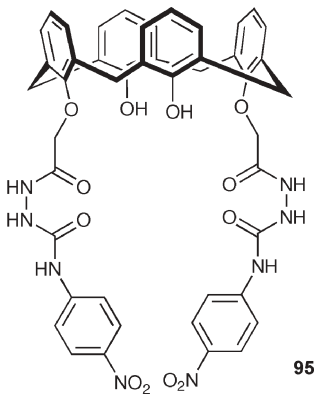
93a $R^1 = R^2 = H$
93b $R^1 = H$, $R^2 = OCH_3$
93c $R^1 = NO_2$, $R^2 = H$
93d $R^1 = NO_2$, $R^2 = OCH_3$
93e $R^1 = CF_3$, $R^2 = H$
93f $R^1 = CF_3$, $R^2 = OCH_3$
93g $R^1 = F$, $R^2 = H$

Matthews, Gunnlaugsson and Quinlan have reported the synthesis of amidourea-based colorimetric anion sensors **94**

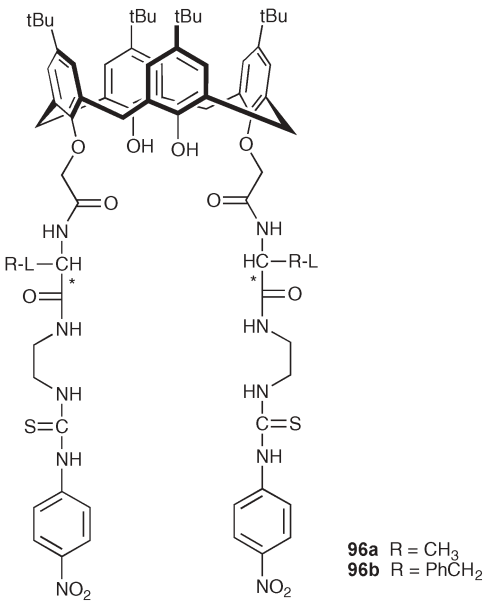
Fig. 13 Colour changes observed upon addition of TBAF to a DMSO solution of receptor **92** (= LH_2). Left to right: free receptor (dominant species LH_2); plus 5 equiv. TBAF (dominant species LH^-); plus 40 equiv. TBAF (dominant species L^{2-}) Reproduced with permission from ref. 119. Copyright © 2005 ACS.

and **95**.[122] The evaluation of these compounds as colorimetric sensors was studied using UV-vis spectroscopy with anions such as acetate, fluoride, dihydrogen phosphate and hydrogen pyrophosphate ($HP_2O_7^{3-}$) in DMSO. Whilst both sensors gave rise to red shifts in their absorption spectra in the presence of anions, addition of F^- or $HP_2O_7^{3-}$ gave rise to significant changes in the UV-vis spectra of the receptors with concomitant colour changes from yellow to purple, which were visible to the naked eye. The authors attribute the colour changes to a combination of anion complexation and deprotonation.





He and co-workers have reported the synthesis of two calix[4]arene-based chiral chromogenic receptors (**96a** and **96b**) which contain both thiourea and amino acid binding units.[123] Their chiral anion-binding abilities have been evaluated by UV-vis absorption and ^1H NMR spectroscopy in DMSO and $CDCl_3$, respectively. Table 11 shows that receptor **96a** has a higher degree of enantioselective discrimination relative to **96b**, with the most significant difference being obtained with enantiomers of α-phenylglycine anions (**96a**: $K_{(L)}/K_{(D)} = 4.76$; **96b**: $K_{(D)}/K_{(L)} = 2.84$).



96a R = CH_3
96b R = $PhCH_2$

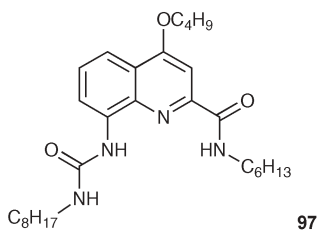
Albrecht, and co-workers have synthesised fluorescent receptor **97** consisting of a quinoline substituted with an amide in the 2-position and a urea group in the 8-position.[124]

Table 11 Association constants (K) for complexes formed between receptors **96a** and **96b** and anion guests in DMSO

Anion[a]	Receptor **96a** $K_{ass}/M^{-1b,c}$	Receptor **96b** $K_{ass}/M^{-1b,c}$
L-α-Phenylglycine	$(2.34 \pm 0.03) \times 10^5$	$(2.95 \pm 0.01) \times 10^3$
D-α-Phenylglycine	$(4.91 \pm 0.02) \times 10^4$	$(8.40 \pm 0.02) \times 10^3$
L-Mandelate	413.64 ± 2.70	194.16 ± 1.81
D-Mandelate	166.94 ± 2.53	337.51 ± 3.04
Dibenzoyl L-tartrate	1560.27 ± 5.52	1104.47 ± 4.41
Dibenzoyl D-tartrate	1654.36 ± 4.87	501.94 ± 3.91

[a] Anions were used as their tetrabutylammonium salts. [b] Values of K_{ass} were calculated from UV-vis titrations in DMSO. [c] All error values were obtained by non-linear curve fitting.

This system may be regarded as a semi-rigid version of a 2,6-dicarboxamidopyridine. As with the pyridine systems, two hydrogen bonds (between the quinoline nitrogen and the amide NH and adjacent urea NH) preorganise the binding site into a *syn–syn* conformation. NMR and fluorescence titration experiments in chloroform at 296 K revealed that the receptor has a high affinity for small halides; the highest affinity was observed for F^- (K_a = 14400 M^{-1} determined by fluorescence titration). Fluoride binding was accompanied by a strong fluorescence enhancement (Fig. 14).



97

There have been a number of recent accounts of amidourea compounds functioning as colorimetric anion sensors.[125] In order to investigate the interactions of this family of compounds with anions, Gale, Quesada and co-workers synthesised a series of pyrrolylamidothiourea derivatives **98a–d**[126] and **99a–c**[127] with a range of NH acidities. The anion binding abilities of these new receptors were studied by means

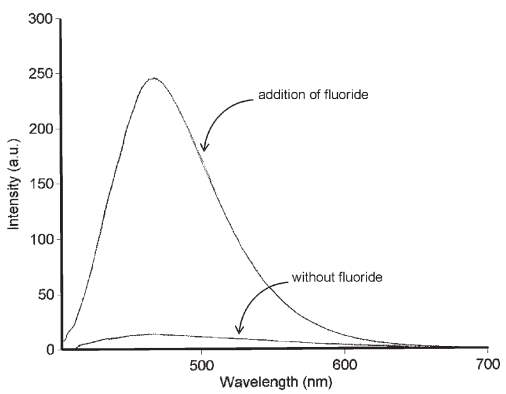


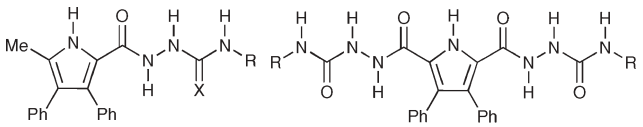
Fig. 14 Emission spectrum of **97** (1 μM) in chloroform at 296 K in the absence and presence of excess fluoride ions (excitation at λ = 403 nm). Figure reproduced with permission from ref. 124. Copyright © 2005 Georg Thieme.

Table 12 Stability constants (K_a/M^{-1}) for receptors **98b** and **99a–c** with different anions (added as tetrabutylammonium salts) at 298 K in DMSO[a] as determined by UV-vis titration techniques

Anion	**98b**	**99a**	**99b**	**99c**
F^-	3010	3890	8590	15300
$C_6H_5COO^-$	1440	5000	9630	16600
CH_3COO^-	5880	3610	6830	13800
$H_2PO_4^-$	1060	4010	8220	13000

[a] Errors estimated to be no more than ±10%.

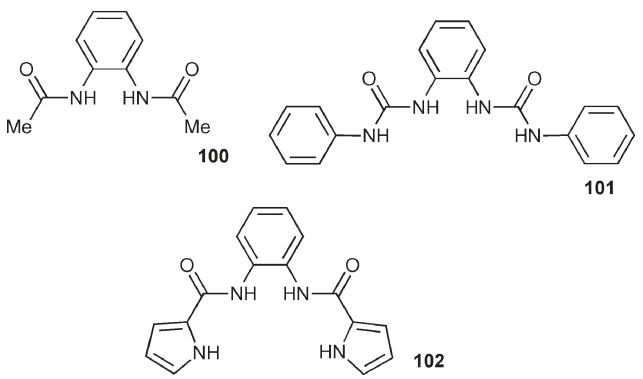
of UV-vis and ^1H NMR titration experiments using DMSO and DMSO-d_6 as solvent, respectively, revealing that compound **98b** and **99a–c** are capable of binding anions, however, with little selectivity (Table 12). However, interestingly, the more acidic derivatives **98c** and **98d** deprotonate upon addition of only one equivalent of anion (*e.g.* benzoate, acetate, dihydrogen phosphate or fluoride), a process accompanied by a distinctive colour change from yellow to red in DMSO. In the case of compound **98d** an X-ray crystal structure that was obtained using a synchrotron X-ray source confirmed deprotonation at the urea NH adjacent to the amide group.



98a X = O, R = phenyl
98b X = O, R = 4-nitrophenyl
98c X = S, R = phenyl
98d X = S, R = 4-nitrophenyl

99a R = phenyl
99b R = 4-nitrophenyl
99c R = 3,5-dinitrophenyl

Gale and co-workers have also synthesised a series of anion receptors **100–102** based upon an *ortho*-phenylenediamine core.[128] Compound **102** had previously been synthesised by Cheng and co-workers and its anion binding properties studied with a variety of anions excluding carboxylates.[129] Gale *et al.* found that the most effective receptor in this series is the bis-urea **101**, which shows selectivity for carboxylates (Table 13). In the solid state, an X-ray crystal structure revealed that the receptor forms four hydrogen bonds to a bound benzoate anion (Fig. 15).



100 **101** **102**

By attaching electron-withdrawing groups to this bis-urea skeleton (*e.g.* compounds **103** and **104**), Gale and co-workers have increased the affinity of this class of receptor for anions in DMSO-d_6–0.5% water solution.[130] In particular compound for example receptor **103** binds acetate with a stability constant of

Table 13 Stability constants (M^{-1}) of compounds **100**–**102** with a variety of putative anionic guests (added as tetrabutylammonium salts) at 298 K in DMSO-d_6–0.5% water.[a] In all cases 1 : 1 (receptor : anion) stoichiometry was observed

Anion	**100**	**101**	**102**
Cl^-	13	43	12
Br^-	—	<10	—
CH_3COO^-	98	3210	251
$C_6H_5COO^-$	43	1330	113
$H_2PO_4^-$	149	732	295
HSO_4^-	—	10	—

[a] Errors estimated to be no more than 10%.

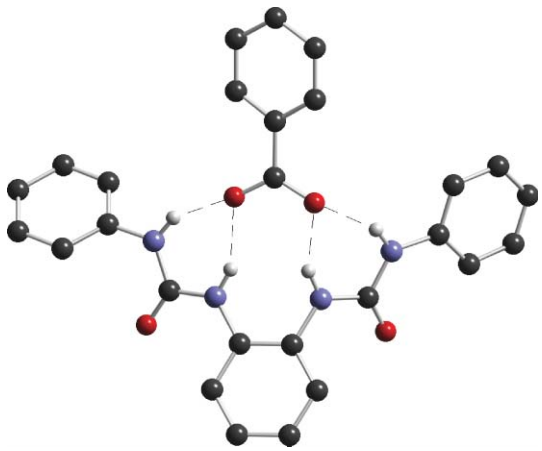
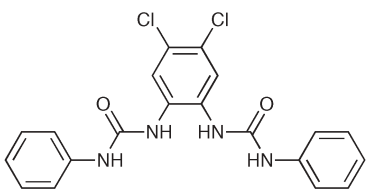
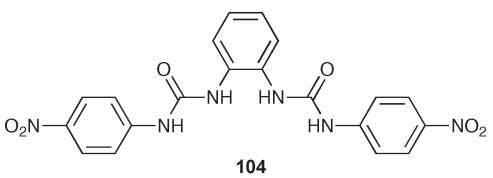


Fig. 15 The X-ray crystal structure of the benzoate complex of receptor **101**. Non-acidic hydrogen atoms and tetrabutylammonium countercation have been omitted for clarity.

8080 M^{-1} under the same conditions. Moreover, carboxylate/dihydrogen phosphate selectivity can be tuned by functionalising the bis-urea skeleton or by converting the urea groups to thioureas.

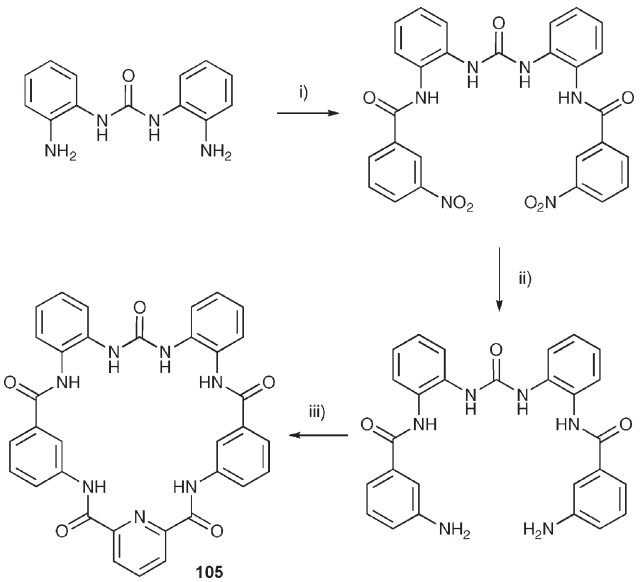


103



104

The same research group has also studied the anion binding properties of a new hybrid amide–urea macrocycle **105** (Scheme 9) with a variety of putative anionic guests.[131] This compound shows a high selectivity for carboxylate anions over dihydrogen phosphate and chloride, binding acetate approximately 100 times more strongly than dihydrogen phosphate both in DMSO-d_6–0.5% water and in DMSO-d_6–5% water solution (Table 14). Interestingly, crystals of **105** were grown



Scheme 9 The synthesis of macrocycle **105**. (i) 3-Nitrobenzoic acid, benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate (PyBOP), Et_3N, 1-hydroxybenzotriazole (HOBt), DMF (anhydrous). (ii) $NH_2NH_2{\cdot}H_2O$, Pd/C 10% cat., EtOH. (iii) 2,6-pyridine dicarbonylchloride, tetrabutylammonium acetate, Et_3N, DMAP, CH_2Cl_2.

by slow evaporation of a solution of the receptor in DMSO in the presence of tetrabutylammonium fluoride. Rather than a fluoride complex, a mixed carbonate, fluoride complex was obtained with carbonate (presumably arising from CO_2 fixation by the fluoride solution) bound within the macrocycle and hydrated fluoride bound outside the macrocyclic cavity. The crystal structure of the carbonate complex is shown in Fig. 16.

Gunnlaugsson and co-workers have described a family of fluorescent photoinduced electron transfer (PET) chemosensors **106a**–**c** for bis-anions.[132] The general structure for these sensors is based on the motif: receptor–spacer–fluorophore–spacer–receptor. This family of receptors is able to bind and

Table 14 Stability constants (M^{-1}) of compound **105** with a variety of anionic guests added as tetrabutylammonium salts as determined by ^1H NMR titration techniques performed in DMSO-d_6–0.5% water and in DMSO-d_6–5% water at 298 K. Errors <15%

	Stability constants/M^{-1}	
Anion	DMSO-d_6–0.5% water	DMSO-d_6–5% water
Cl^-	194	42
Br^-	10	—
HSO_4^-	115	—
$H_2PO_4^-$	142[a]	51
NO_3^-	<10	—
$CH_3CO_2^-$	16500[b]	5170
$C_6H_5CO_2^-$	6430	1830
Selectivity		
$K_{(CH_3CO_2^-)}/K_{(H_2PO_4^-)}$	116	101

[a] Due to NH broadening titration was conducted by following the shift of an ArH proton. [b] This value is greater than 10^4 M^{-1}. As such the stability constant is at the upper limit that can be determined by this technique and should be treated with caution.

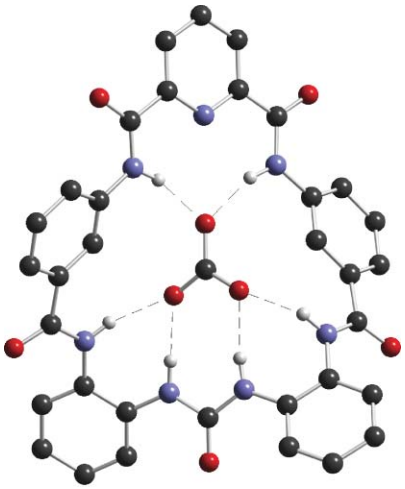
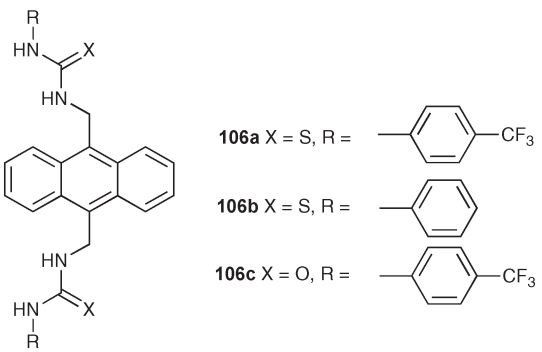


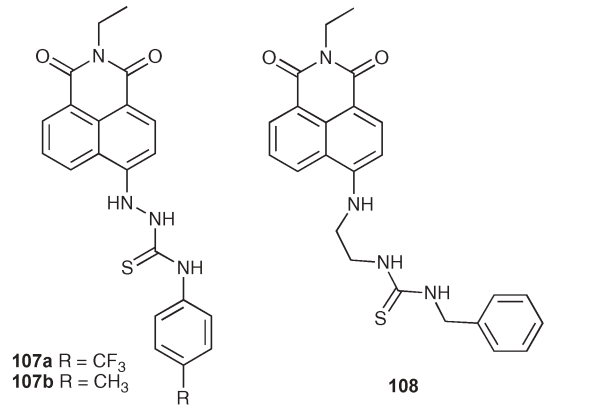
Fig. 16 The X-ray crystal structure of carbonate included within macrocycle **105**. Other components of the structure and non-acidic hydrogen atoms in the structure have been omitted for clarity.

sense simple inorganic anions such as F^-, AcO^- and $H_2PO_4^-$, but the most interesting result is with bis-anions such as dicarboxylates. In this case, they have observed the formation of a 1 : 1 or a 1 : 2 (receptor : anion) complex depending on the length of the spacer separating the two carboxylate moieties and the nature of the receptor. A variety of other thiourea containing fluorescent receptors have been synthesised by Ghosh and Adhikari,[133] Swamy, Yoon and co-workers,[134] and Kondo and Sato.[135]

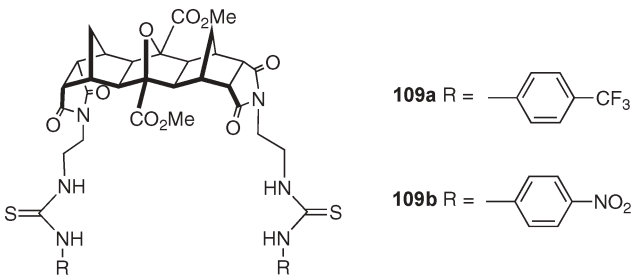


Gunnlaugsson, Kruger and co-workers have also developed thiourea-based sensors **107a** and **b** containing naphthalimide groups.[136] Receptor **107a** proved to be capable of sensing anions in 1 : 1 EtOH–H_2O imidazole–HBr buffered solutions at pH 7.15. Significant colour changes were observed upon addition of acetate or dihydrogen phosphate with NMR and UV-vis experiments providing evidence of a binding rather than a deprotonation process.[136] Pfeffer and co-workers have described the synthesis of receptor **108**. This receptor employs the naphthalimide NH group when binding dihydrogen phosphate in DMSO-d_6 but not when binding acetate, an interaction that should allow for future selective sensing of this anion.[137]

Pfeffer, Gunnlaugsson, Kruger and co-workers have described the use of a polynorbornane scaffold in the construction of anion receptors **109a** and **109b**.[138] Most interestingly, these systems form 2 : 1 receptor : anion



complexes with pyrophosphate ($H_2P_2O_7^{2-}$) anions in DMSO-d_6 opening up the prospect of using these systems as precursors to anion templated catenane systems.



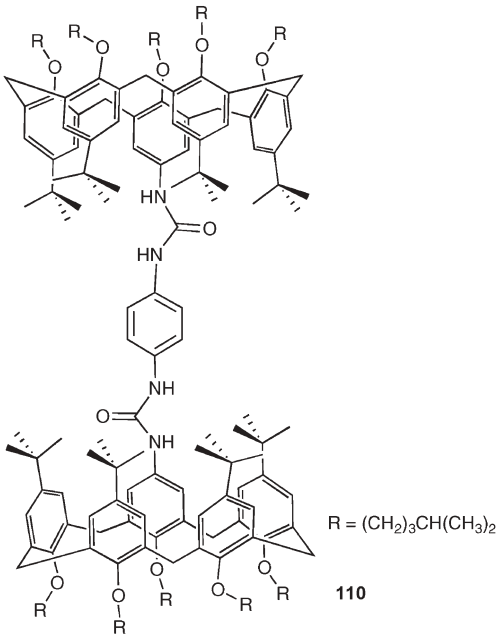
Pappalardo, Parisi and co-workers have reported the synthesis of the heterotetratopic receptor **110** composed of two calix[5]arene units (cation binding sites) linked *via* the upper rim by a 1,4-bis(ureido)phenylene spacer.[139] This compound has been shown to bind α,ω-alkanediammonium salts in the calixarene cups whilst binding the counteranions (chloride or acetate) to the urea groups. Depending on the length of carbon chain in the bis-ammonium salt, the receptor either encapsulates both ammonium groups (longer carbon chains) or only a single ammonium group from each cation (for shorter salts with carbon chains containing less than 10 carbon atoms).

Lang, Lhotak and co-workers have synthesised a series of calix[4]arenes substituted at the upper rim with 4-nitrophenylurea groups. 1,3-, 1,2- And monosubstituted derivatives were prepared (compounds **111a**–**c** respectively).[140] Interestingly, it was found that while the 1,3- and monosubstituted derivatives form 1 : 1 complexes with a variety of anionic guests in dichloromethane solution, the 1,2-substituted derivative forms 2 : 1 receptor : anion complexes with a variety of anionic guests (Table 15), forming 1 : 1 complexes at high anion

Table 15 Binding constants (K_{11}/M^{-1}) in CH_2Cl_2 at 298 K

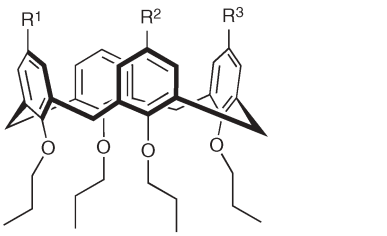
Anion[a]	**111a**	**111b**[b]	**111c**
Cl^-	$>10^6$	$\geqslant 10^5$, $\beta_{21} \geqslant 10^{11}$	5.3×10^4
Br^-	$>10^6$	$\beta_{21} \geqslant 10^{10}$	1.2×10^4
I^-	1.7×10^5	5×10^3, $\beta_{21} = 5 \times 10^9$	1.2×10^3
NO_3^-	4.1×10^5	1×10^4, $\beta_{21} \geqslant 10^{10}$	6.9×10^3
BzO^-	$>10^6$	1×10^5, $\beta_{21} \geqslant 10^{10}$	6.2×10^5
AcO^-	$>10^6$	$\beta_{21} \geqslant 10^9$	4.3×10^5

[a] Anions were used as tetrabutylammonium salts. Estimated error is 15%. [b] In all cases the Job plots indicate the stoichiometry of 2 : 1.



110

concentrations. The authors have also studied the anion binding properties of urea appended thiacalixarenes.[141]

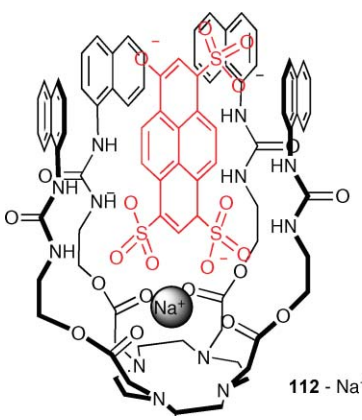


111a R^2 = H, R^1 = R^3 =

111b R^1 = H, R^2 = R^3 =

111c R^1 = R^2 = H, R^3 =

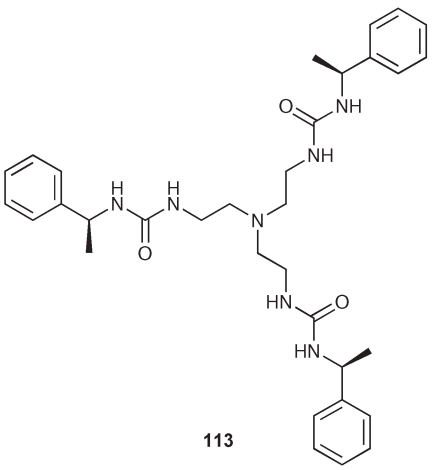
The cyclen receptor **112** has been designed by Sidorov and co-workers to bind anionic pyranine dyes (sulfonated pyrene derivatives) and functions under near physiological conditions.[142] The base of the receptor is a cyclen tetraester that is able to bind physiologically abundant Na^+ cations. Four thiourea groups are connected to this platform that can bind the pyrazine sulfonates. The terminal naphthalenes can



112 - Na^+ -pyranine dye

interact and stabilise the pyranine's aromatic core by π-stacking. This cyclen receptor shows a high affinity for pyranine and is finding application as a new membrane leakage assay.

Steed and co-workers have reported an enantiomerically pure tris-urea **113** which is able to act as a low molecular weight gelator (LMWG) in addition to binding chloride anions (with a stability constant of 1154 M^{-1} in DMSO-d_6 solution with 1 : 1 stoichiometry).[143] The self-association and anion interactions are in competition with the formation of the helical gel fibres partially inhibited by addition of chloride anions (a process which triggers full crystallisation of **113**).



113

Continuing their work on tripodal receptors for anions, Steed and co-workers have also reported the synthesis of two tripodal tris-urea pyridinium containing receptors **114a**,**b** with *p*-tolyl or octyl substituents, respectively. In a very elegant report the association behaviour with anionic guests has been studied using several methods including solid-state, solution and computational studies.[144,145] The studies reveal that the most stable conformation for the chloride complex of **114a** is an up, up, up conformation wherein the anion is encapsulated within the three arms of the receptor, whilst for **114b**, the most stable conformation is a 2-up, 1-down arrangement with the anion bound by two urea groups (Fig. 17). This group has also synthesised amidopyridinium calix[4]arenes and studied the interaction of these related species with anionic guests.[146]

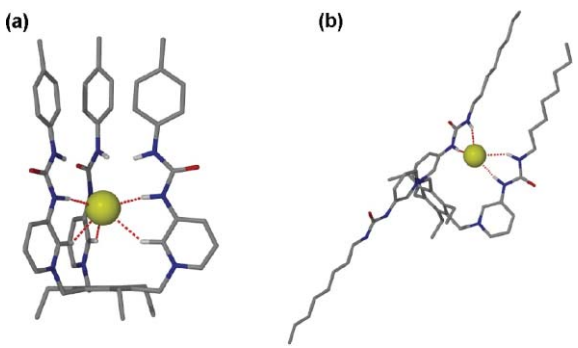
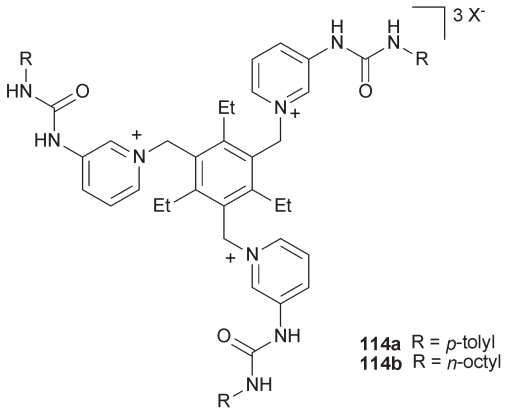
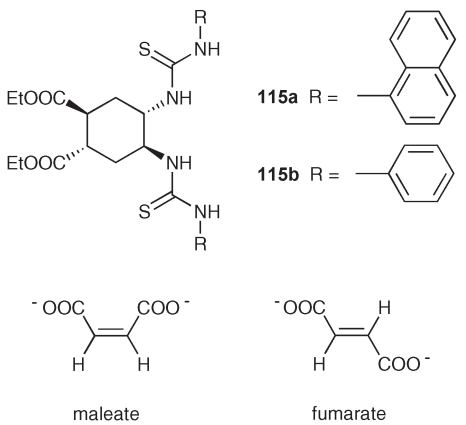


Fig. 17 (a) DFT-minimised structure of the **114a**–Cl^- complex showing the manner in which the anion is bound. (b) DFT-minimised structure of the 2-up, 1-down structure of **114b**–Cl^-. Reproduced with permission from ref. 144. Copyright © 2006 ACS.



114a R = *p*-tolyl
114b R = *n*-octyl

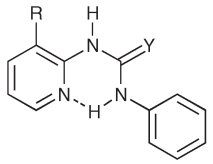
Following on from their earlier work,[147,148] Costero and co-workers have reported the preparation of two new cyclohexane based ligands **115a**,**b**, both as racemic mixtures, and their utility in the selective recognition of maleate *vs.* fumarate anions.[149] Compound **115a** can act as a selective fluorescent sensor for maleate *vs.* fumarate in DMSO even in the presence of 5% water. The selectivity is due to a conformational change from chair to boat in the cyclohexane moiety induced by the 1 : 1 complexation with maleate (both carboxylate groups can then be bound by the receptor). Fumarate, with a *trans* configuration, is able to be complexed by the ligand but the complexation does not cause a conformational change.



115a R =
115b R =

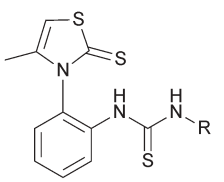
maleate fumarate

The synthesis of the simple pyridyl thioureas **116a**–**c** and their anion binding properties has been investigated by Kilburn and co-workers.[150] An intramolecular hydrogen bond between the urea NH group and pyridine nitrogen atom decreases the affinity of these receptors for anions. However, protonation of the pyridine nitrogen releases the urea or thiourea group, allowing more efficient anion complexation. They found that the neutral thioureas bind acetate, but not the more weakly basic chloride or bromide, whereas the protonated thioureas bind strongly to chloride or bromide (Fig. 18), but are deprotonated by acetate in CD_3CN solution. Chloride : receptor 2 : 1 complexation occurs at higher chloride concentrations due to a second anion binding to the protonated pyridine NH.



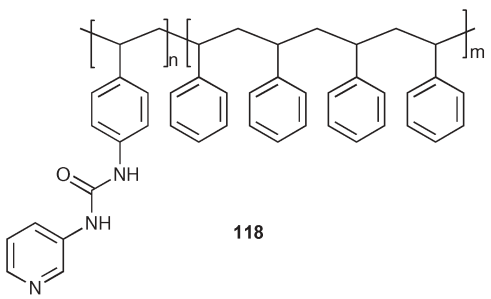
116a R = H, Y = S
116b R = CH_3, Y = S
116c R = CH_3, Y = O

Roussel and co-workers have described the synthesis of a limited series of non-racemic atropisomeric 1-(2-(4-methyl-2-thioxothiazol-3(2*H*)-yl)phenyl)-3-(hetero)aryl-(thio)ureas **117a**–**h** which present two (or more) hydrogen bond accepting sites and two (or more) hydrogen bond donating sites.[151] The binding constants for some of these optically pure (thio)ureas with the enantiomers of N-protected amino acid tetrabutylammonium salts of *N*-Ac–Phe–COO^-, *N*-Ac–Val–COO^-, *N*-Ac–Leu–COO^-, *N*-Ac–Trp–COO^- and naproxenate were determined in CD_3CN using ^{1}H NMR titration experiments, showing moderate binding affinities (K_{ass} = 330–3900 M^{-1}) and discrimination. Contrary to what was expected on the basis of the NH acidity of the thiourea *vs.* urea group, the stability constants were lower with the thiourea than with the corresponding urea (*i.e.* **117a** *vs*. **117i**).



117a R = phenyl
117b R = *o*-pyridinyl
117c R = *m*-pyridinyl
117d R = *o*-hydroxyphenyl
117e R = 3,5-dimethylphenyl
117f R = *o*-methoxyphenyl
117g R = *m*-CF_3-phenyl
117h R = 3,5-bis(CF_3)phenyl
117i Urea analog of **117a**

A polymer-supported ureidopyridyl ligand (**118**), capable of simultaneous anion and cation binding, has been reported by Steed and co-workers.[152] Exposure of this polymer to increasing concentrations of $CuCl_2$, $Cu(NO_3)_2$, $Co(NO_3)_2$ and $Cr(NO_3)_3$ results in the polymer taking on the characteristic colour of the metal ion (green for Cu(II), pink for Co(II) and yellowish brown for Cr(III)). The maximum uptake, determined by elemental analysis of the isolated products, corresponded to a ratio of 0.5 metal ions to pyridyl units for $Cu(NO_3)_2$ and 0.65 for $CuCl_2$.



118

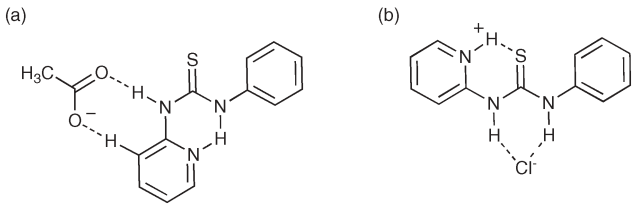
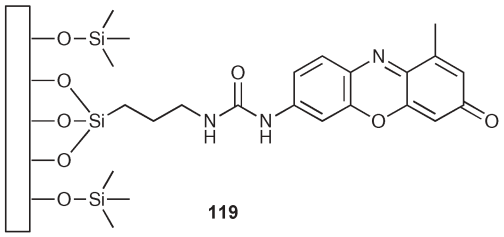


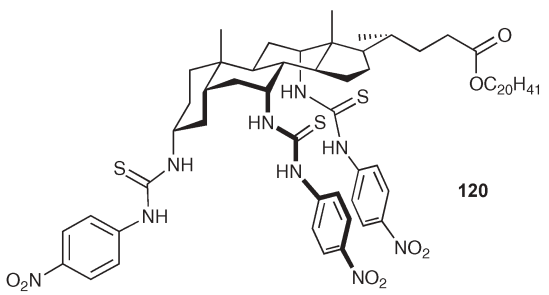
Fig. 18 Acetate binding to compound **116a** and chloride complexation by **116**–H^+

Rurack, Martínez-Mañez and co-workers have designed an optical sensor material for the selective recognition of long-chain carboxylates in water.[153] A spacer substituted 7-urea-phenoxazin-3-one was employed as a signalling unit and was bound to a mesoporous trimethylsilylated UVM-7 (MCM-41 type) solid support material to afford **119**. The hydrophobic nature of the surface allowed this material to selectively sense long chain carboxylates over short chain analogues and to function in water.



119

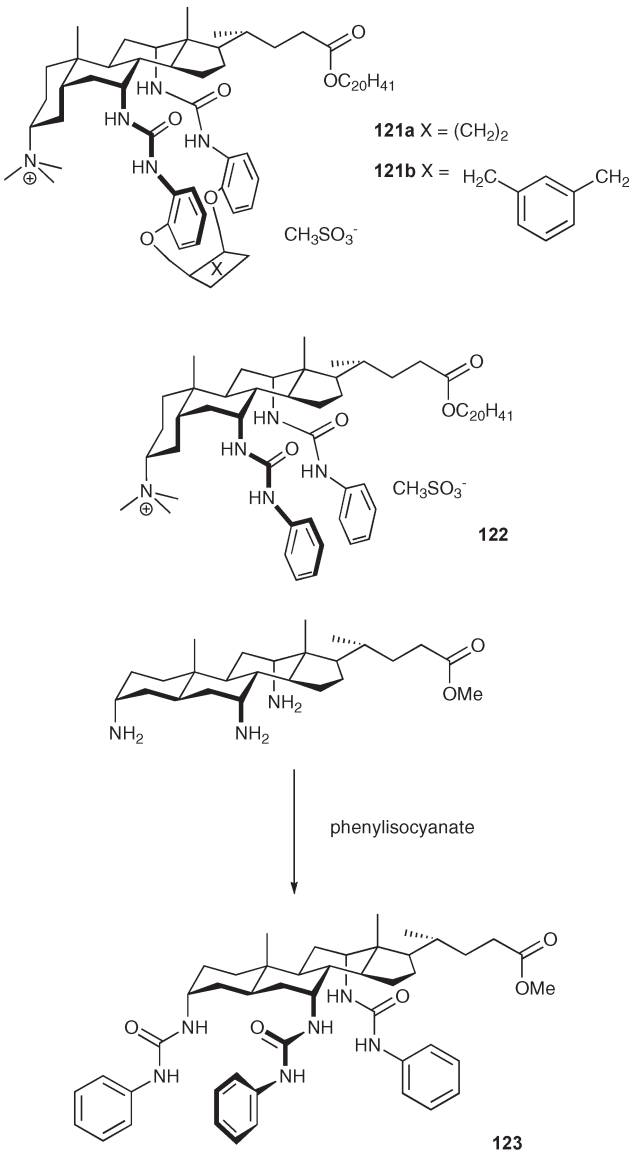
Receptors that employ a steroid backbone have been pioneered by A. P. Davis and co-workers and have found application as very high affinity chloride receptors and transport agents.[154] Davis coined the term 'cholapod' to describe this class of anion receptor as they are derived from cholic acid. Davis, B. D. Smith *et al.* have recently published an extensive study of geometric effects in these systems.[155] They studied a wide variety of different systems with different types and numbers of hydrogen bond donors and with a range of anion affinities and found that the more powerful receptors also have the widest range of binding free energies with different anions and hence a higher degree of selectivity. For example, compound **120** was found to bind chloride (as the tetraethylammonium salt) in water saturated chloroform with a stability constant of 1.8×10^{11} M^{-1} and bromide with a stability constant of 4.3×10^{10} M^{-1}.



120

Davis and co-workers have recently prepared macrocycles **121a**,**b** that contain a quaternary ammonium centre at C3.[156] The receptors were used in anion phase transfer experiments, comparing their anion extraction ability from water to chloroform to the previously reported[157] non-macrocyclic receptor **122**. It was found that receptor **121b** overcomes Hofmeister bias to a remarkable degree with an order of extractabilities of $Br^- > I^- \approx Cl^- > NO_3^- > PF_6^- > AcO^- \approx EtSO_3^-$.

Davis and co-workers have prepared the tris-urea **123** as the first example of an "allocholapod" anion receptor *i.e.* the steroid has a '5-α' skeleton rather than the more common '5-β' configuration.[158] Tris-urea **123** was synthesised in a single step



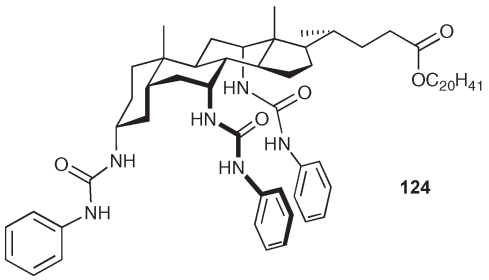
Scheme 10 The synthesis of compound **123** in THF.

from a "triaza-analogue" of an allocholic acid derivative through treatment with phenyl isocyanate (Scheme 10). The tris-amine described has the potential to be derivatised to form a whole new family of steroid based anion receptors. The anion complexation ability of compound **123** was measured in water saturated chloroform by extraction of salts and compared to the 5-β analogue **124** (Table 16).

Table 16 Binding constants (K_a/M^{-1}) for $Et_4N^+X^-$ to tris-urea receptors **123** and **124** in water saturated chloroform[a]

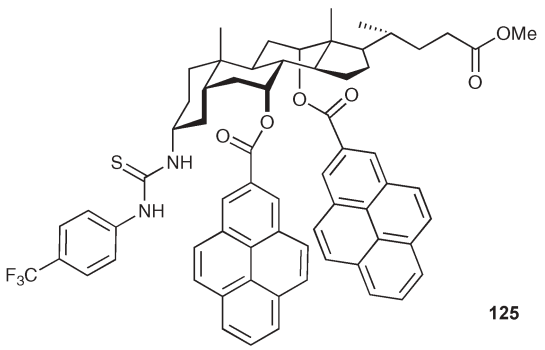
X^-	**123**	**124**	Ratio **123**/**124**
AcO^-	7.5×10^8	1.4×10^8	5.4
$EtSO_3^-$	5.5×10^8	2.2×10^8	2.5
Cl^-	8.0×10^8	2.7×10^8	3.0
Br^-	3.1×10^8	1.4×10^8	2.2
NO_3^-	3.2×10^8	1.6×10^8	2.0
I^-	9.4×10^7	2.2×10^7	4.3
ClO_4^-	2.3×10^7	6.0×10^6	3.8

[a] Measured by extraction of the salts from water into $CHCl_3$.



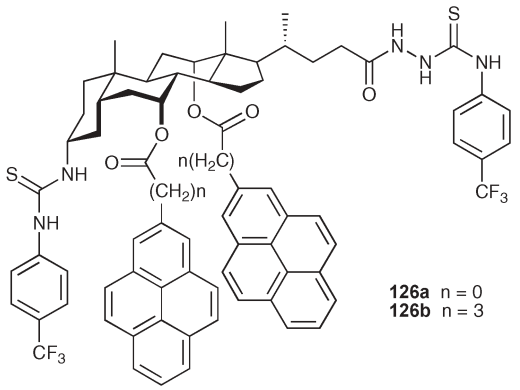
124

Chan and co-workers have reported a number of fluorescent steroid based anion sensors containing urea or thiourea groups.[159,160] For example chiral fluorescent receptor **125** based on cholic acid was designed and synthesised by Chan and co-workers.[161] The enantioselective recognition ability of this receptor for mandelate anion was studied by fluorescence and ^{1}H NMR spectroscopy in CH_3CN and DMSO-d_6, respectively, indicating that **125** exhibited a good enantioselectivity for the (*S*)-mandelate anion ($K_a = 3.43 \times 10^3$ M^{-1}) *vs.* (*R*)-mandelate anion (K_a too small to determine) in CH_3CN.



125

The same research group has reported the synthesis of two similar charge neutral fluorescent sensors **126a** and **b** bearing two pyrene signalling subunits at C7 and C12 and two binding groups at C3 and C24 of cholic acid, respectively.[162] The binding abilities of these compounds to dicarboxylates were determined using fluorescence, UV-vis and ^{1}H NMR spectroscopic techniques in acetonitrile. Compound **126a** and **b** were shown to exhibit a highly sensitive response to long-chain dicarboxylates (Table 17), with very strong binding between host and guest rendering the detection of dicarboxylates possible even at the concentration of 10^{-8} M.

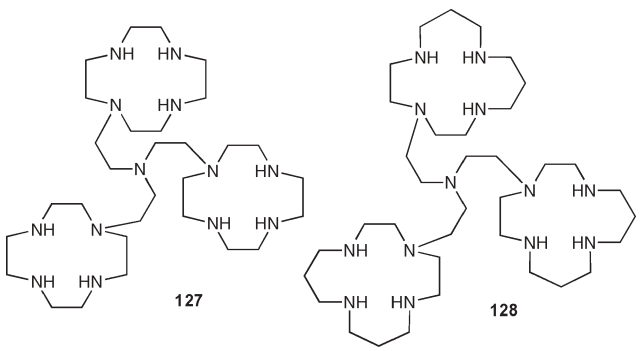


126a n = 0
126b n = 3

Ammonium based anion receptors

The earliest synthetic anion receptor systems were comprised of ammonium based cryptand-like receptors capable of encapsulating halide anions.[163] Today, research in anion complexation by ammonium based receptors continues—reflecting the ability of these species to function as anion receptors in aqueous solution.

Two tren-based macrocyclic receptors containing three [12]aneN$_4$ (**127**) or [14]aneN$_4$ (**128**) have been synthesised by Bencini and co-workers and their binding properties with benzene tricarboxylate isomers studied in detail.[164] These receptors have a large bowl-shaped cavity in which it is possible to control the degree of protonation of the cyclic amines. The stability constants of **127** and **128** in various protonation states with the tricarboxylates are shown in Table 18. Whilst these data are complex, it is possible to see that both systems bind the symmetrical 1,3,5-benzene tricarboxylate selectively over the pH range studied.



127 128

Table 17 The association constants (M^{-1}) of **126a**,**b** with dicarboxylates (1 : 1 binding mode) in CH_3CN

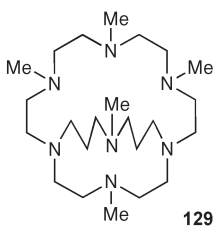
	126a		**126b**	
Anion[c]	K_a[a]	K_a[b]	K_a[a]	K_a[b]
Glutarate	$(8.22 \pm 1.51) \times 10^5$	$(1.08 \pm 0.09) \times 10^6$	$(1.68 \pm 0.17) \times 10^6$	$(1.60 \pm 0.11) \times 10^5$
Adipate	$(1.27 \pm 0.12) \times 10^6$	$(1.29 \pm 0.14) \times 10^6$	$(5.56 \pm 0.42) \times 10^6$	$(1.87 \pm 0.14) \times 10^7$
Suberate	$(1.64 \pm 0.14) \times 10^6$	$(1.03 \pm 0.06) \times 10^6$	$(2.10 \pm 0.19) \times 10^7$	$(3.19 \pm 0.10) \times 10^7$
Sebacate	$(2.27 \pm 0.23) \times 10^7$	$(2.30 \pm 0.23) \times 10^7$	$>10^{8d}$	$>10^{8d}$
L-Glutamate	$(1.18 \pm 0.13) \times 10^6$	$(2.21 \pm 0.13) \times 10^6$	$(2.35 \pm 0.11) \times 10^6$	$(2.03 \pm 0.22) \times 10^6$
D-Glutamate	$(1.81 \pm 0.11) \times 10^6$	$(1.81 \pm 0.19) \times 10^6$	$(4.21 \pm 0.23) \times 10^6$	$(5.23 \pm 0.11) \times 10^6$
N-Acetyl-L-glutamate	$(1.29 \pm 0.19) \times 10^6$	$(1.09 \pm 0.10) \times 10^6$	$(1.63 \pm 0.21) \times 10^6$	$(8.35 \pm 1.30) \times 10^5$

[a] The values were calculated from the change of the fluorescence spectra. [b] The values were calculated from the change of the UV-vis spectra. [c] Anions were used as their tetrabutylammonium salts. [d] The value is too large to calculate.

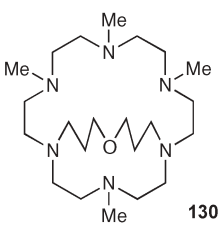
Table 18 Formation constants of the ligands (L) **127** and **128** with 1,2,3-BTC, 1,2,4-BTC, and 1,3,5-BTC (NMe_4Cl 0.1 M, 298.1 K)

	Log *K*					
	127			**128**		
Reaction	1,2,3-BTC	1,2,4-BTC	1,3,5-BTC	1,2,3-BTC	1,2,4-BTC	1,3,5-BTC
$H_2L^{2+} + A^{3-} \rightleftharpoons H_2LA^-$	3.18(5)	3.12(6)	4.51(6)			4.20(5)
$H_3L^{3+} + A^{3-} \rightleftharpoons H_3LA$	3.35(6)	3.30(7)	5.02(3)	2.83(4)	3.70(5)	4.34(9)
$H_4L^{4+} + A^{3-} \rightleftharpoons H_4LA^+$	4.27(6)	4.02(5)	5.90(5)	2.85(9)	3.75(9)	4.89(6)
$H_5L^{5+} + A^{3-} \rightleftharpoons H_5LA^{2+}$	3.80(8)	4.05(9)	5.85(5)	3.08(7)	4.08(9)	5.28(9)
$H_6L^{6+} + A^{3-} \rightleftharpoons H_6LA^{3+}$	4.47(5)	4.11(4)	6.23(5)	3.54(4)	4.15(9)	5.64(7)
$H_7L^{7+} + A^{3-} \rightleftharpoons H_7LA^{4+}$	6.28(5)	5.24(5)	7.73(5)	4.21(5)	4.85(8)	6.28(8)
$H_7L^{7+} + HA^{2-} \rightleftharpoons H_8LA^{5+}$	6.27(7)	5.00(3)	7.70(6)			
$H_8L^{7+} + A^{3-} \rightleftharpoons H_8LA^{5+}$				5.19(2)	5.42(7)	6.72(7)
$H_8L^{8+} + HA^{2-} \rightleftharpoons H_9LA^{6+}$	5.91(9)	4.62(6)	7.52(6)			
$H_9L^{9+} + A^{3-} \rightleftharpoons H_9LA^{6+}$				5.50(3)	5.71(9)	7.02(9)
$H_8L^{8+} + H_2A^- \rightleftharpoons H_{10}LA^{7+}$	5.48(7)	4.09(7)	7.26(6)			
$H_{10}L^{10+} + A^{3-} \rightleftharpoons H_{10}LA^{7+}$				6.00(2)	6.41(6)	7.40(7)
$H_8L^{8+} + H_3A \rightleftharpoons H_{11}LA^{8+}$	5.17(8)	3.61(9)	6.65(5)			
$H_{10}L^{10+} + HA^{2-} \rightleftharpoons H_{11}LA^{8+}$				5.57(2)	6.10(7)	7.54(7)
$H_{11}L^{11+} + HA^{2-} \rightleftharpoons H_{12}LA^{9+}$				4.87(2)	5.48(8)	7.08(8)
$H_{11}L^{11+} + H_2A^- \rightleftharpoons H_{13}LA^{10+}$					5.24(8)	6.95(7)
$H_{11}L^{11+} + H_3A \rightleftharpoons H_{14}LA^{11+}$					4.88(9)	6.37(8)

Continuing their studies of ammonium based receptors,[165–167] Bianchi and co-workers have described the binding properties of two macrobicyclic polyamines **129** and **130**, which contain N_7 and N_6O donor set of atoms respectively, towards halide anions by means of potentiometric titrations in aqueous media.[168] Interestingly, while compound **129** forms complexes with halides in various states of protonation $[\mathbf{129}H_nX]^{n-1}$ (n = 2–5 for F^- and Cl^-, n = 1–5 for Br^-) only $[\mathbf{130}H_4X]^{3+}$ ($X = F^-$, Cl^-, Br^-) complexes are formed by **130**. Molecular modelling studies were used to rationalise binding selectivities.



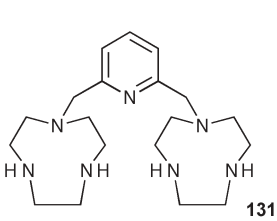
129



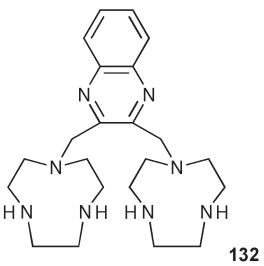
130

The same research group has also studied[169] the synthesis and characterisation of a new bis([9]aneN_3) ligand **131** containing two [9]aneN_3 macrocyclic moieties separated by a 2,6-dimethylenepyridine unit.[170] The coordination properties of these receptors toward Cu(II), Zn(II), Cd(II) and Pb(II) were studied by means of potentiometric and UV spectrophotometric measurements. Moreover, a potentiometric and ^1H NMR study of the coordination of halide anions by **131** and its structural analogue **132**,[169] in aqueous solution at different pH values and at ambient temperature, shows that bromide is selectively recognised by **131**, while chloride is selectively bound by **132**.

Delgado, Félix and co-workers have studied the molecular recognition ability of the ditopic receptor $(H_6Me_2[30]pbz_2N_6)^{6+}$ (**133**) towards a variety of aliphatic and aromatic carboxylate anions, which differ in size, shape, rigidity and electronic properties.[171] The binding studies were carried out by potentiometry and ^1H NMR spectroscopy in aqueous (or D_2O) solution.

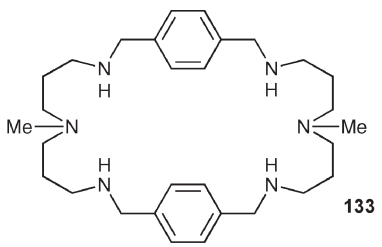


131

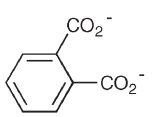


132

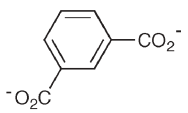
The molecular recognition processes in water of the receptor **133** with the three aromatic anions, phthalate (ph^{2-}), isophthalate (iph^{2-}), and terephthalate (tph^{2-}), were theoretically evaluated by MD simulations. The NMR and the theoretical studies suggest that the receptor has a clear preference for the tph^{2-} anion forming an inclusion supermolecule, while for the remaining anions the binding occurs outside of the macrocyclic cavity.



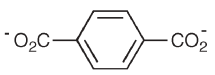
133



phthalate



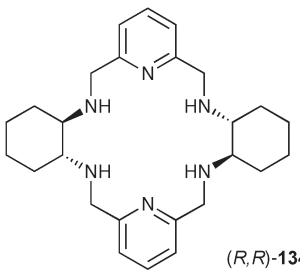
isophthalate



terephthalate

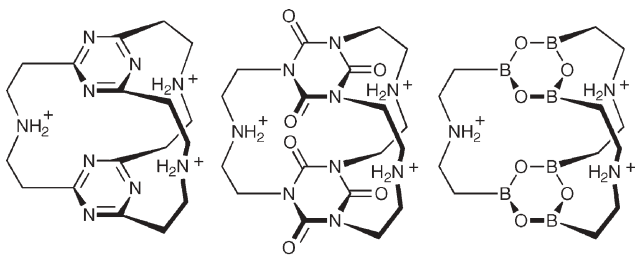
A highly enantioselective molecular recognition of the malate dianion by the synthetic receptor (*R*,*R*)-**134** in aqueous solution has been studied by Alfonso, Gotor, and co-workers using potentiometric titrations, mass spectrometry (ESI-MS), diffusion measurements (PGSE NMR) and molecular

modelling.[172] This combination of techniques revealed that the receptor (*R*,*R*)-**134** forms more stable complexes with (*S*)-malate than with the *R* enantiomer ($K_S > K_R$). This selectivity persists over the pH range tested, being very high at basic pH (pH = 10, K_S/K_R = 11.50) but lower when the pH was decreased (pH = 2, K_S/K_R = 3.89). Interestingly, at neutral pH the interaction is also highly enantioselective (pH = 6.5, K_S/K_R = 6.76). Thus significant enantioselective molecular recognition occurs with malate enantiomers under physiological conditions.



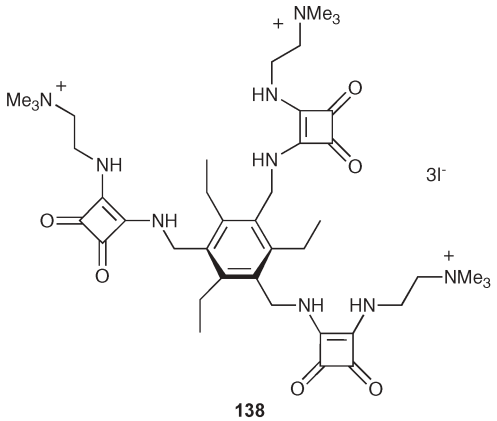
(*R*,*R*)-**134**

A detailed theoretical study of the association of triazine cage (**135**) and its cyanuric acid (**136**) and boroxine (**137**) analogues with the fluoride and chloride ions has been performed by Mascal.[173] Using the density functional B3LYP method, the author proposed that these novel receptors take advantage of the high conformational stability of the cylindrophane framework, which effectively discriminates guests by size. Based on these electron-deficient *s*-triazine, cyanuric acid, and boroxine ring systems, the theoretical analysis of the binding energies of chloride and fluoride ions in macrocycles **135**–**137** suggests a high level of selectivity for fluoride both in the gas phase and in a water solvent model.

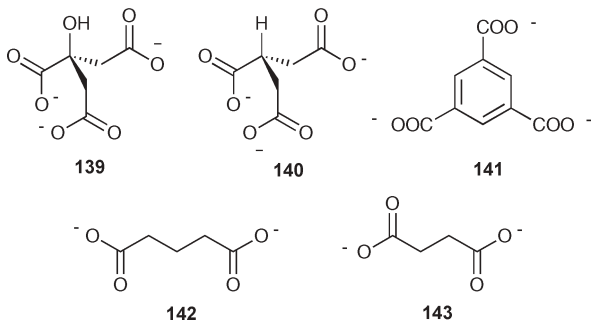


135 **136** **137**

Using DFT and *ab initio* calculations Frontera, Morey, Anslyn and co-workers have designed a quaternary ammonium containing squaramido functionalised tripodal receptor **138** (synthesised using "green chemistry") that is able to form stable complexes with tricarboxylate anions.[174] The anion complexation properties of this receptor have been determined with several mono-, di-, and tricarboxylate salts (**139**–**143**) using microcalorimetry experiments in very highly competitive media (H_2O–EtOH (1 : 3)). Stability constants in the range 10^4–10^5 M^{-1} were obtained with **139**–**141** whilst guest **143** was bound with a stability constant of 2.8×10^2 M^{-1}. Receptor **138** was used as part of a displacement assay with fluorescein to determine the citrate concentration in commercial toothpaste.



138



139 **140** **141**

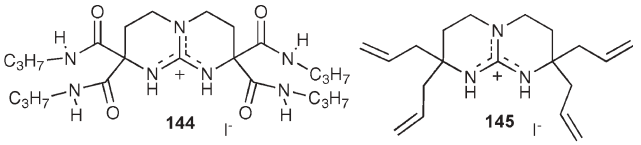
142 **143**

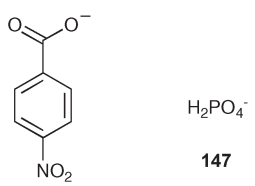
Guanidinium based anion receptors

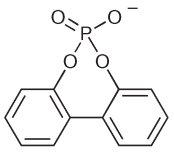
The combination of a positive charge and two hydrogen bond donor groups in bicyclic guanidinium species makes this group a particularly effective receptor for carboxylates and phosphates.[175]

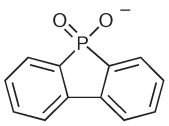
Continuing their detailed thermodynamic studies of the interactions of anion receptors with guests, Jadhav and Schmidtchen have studied the interaction of receptors **144** and **145** with guests **146**–**151** as tetrabutylammonium salts using isothermal calorimetry in acetonitrile. The authors found large entropy differences between the two receptors and the set of guests which were attributed to variations in the 'stiffness' and number of mutual binding modes rather than from desolvation processes. Binding studies show compound **144** has a higher affinity for anions than **145** due to a lower degree of 'structural definition' present in complexes with **145** resulting in a more favourable entropic component to binding rather than being due to the presence of extra hydrogen bond donor groups.[176]

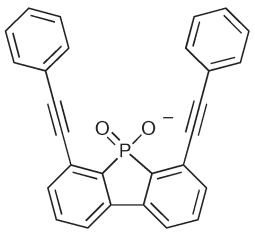
Following on from their earlier work,[177] Jadhav and Schmidtchen have synthesised the macrocycle **152** containing two chiral guanidinium anchor groups linked *via* four urea groups in an effort to address the order–disorder distinction in the diastereomeric complexes formed from a chiral macrocyclic host and enantiomeric carboxylates.[178] The complexation characteristics of the bis-guanidinium macrocycle **152** with a series of simple chiral carboxylates of varying dimensions were evaluated by isothermal titration calorimetry in acetonitrile solutions and at ambient temperature. Significant differences were found in the entropy of binding between enantiomers in the case of tartrate with a smaller difference observed upon aspartate binding.

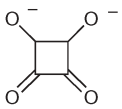


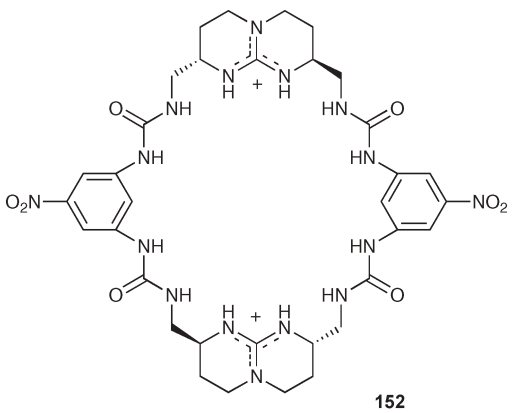






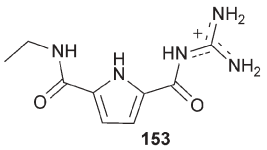


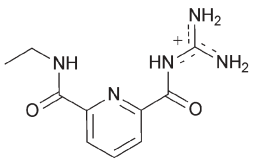


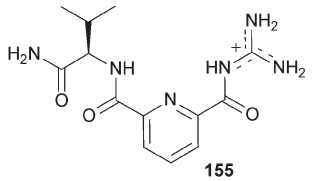


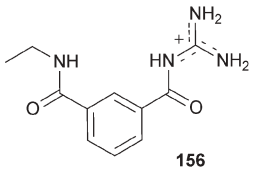
Over the last few years Schmuck and co-workers have demonstrated that guanidiniocarbonylpyrroles *e.g.* **153** are highly effective carboxylate receptors.[179] Recently, Schmuck and Machon have compared the binding ability of these types of receptor with guanidiniocarbonylpyridine (**154** and **155**) and benzene analogues (**156**).[180] They found that complexes formed by the pyridine receptors with amino acid carboxylates in aqueous DMSO were generally weaker than complexes formed by the analogous pyrrole containing receptor (or benzene analogue) presumably due to repulsion between the pyridine lone pair and the guest species. For example, Ac–L-Phe–O^- is bound with a stability constant of 1200 M^{-1} in water–DMSO-d_6 (40% v/v) at 25 °C by receptor **153** and 230 M^{-1} by receptor **154**. Similar studies with **156** showed anion affinities lying between those of the pyrrole and pyridine analogues.

Continuing this work on analogues of these receptors, Schmuck and Machon have synthesised a series of cationic 2-(guanidiniocarbonyl)furans **157**–**160** and studied their anion binding properties by UV-vis spectroscopy in water–DMSO (1 : 1).[181] The high acidity of the (guanidiniocarbonyl)furans **157**–**160** ($pK_a \approx 5.5$) means that these receptors can bind only weakly basic anions such as hydrogen sulfate (K_a = 600 M^{-1}). Hence anion complexation can only occur in acidic solutions

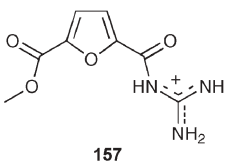


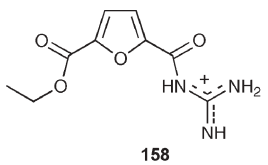


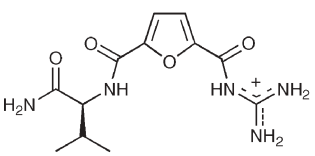


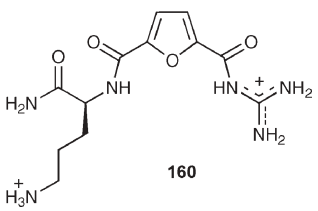


below pH 5, ruling out complexation of more basic anions such as carboxylates.

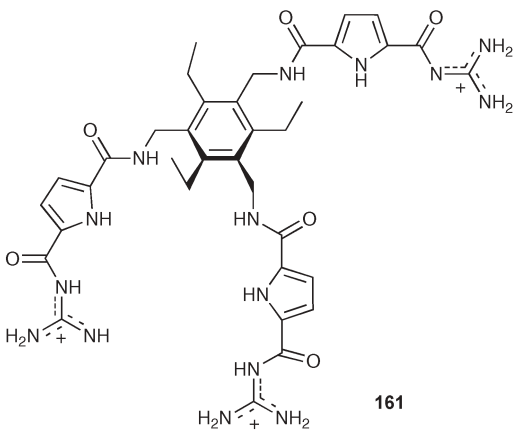








Schmuck and Schwegmann employed the guanidiniocarbonylpyrrole motif in tripodal receptor **161** that was employed as an Anslyn-type[182] displacement assay with carboxyfluorescein.[183,184] This system allowed remarkably selective, naked eye detection of citrate with respect to other substrates such as malate or tartrate in water.



Continuing their earlier work,[185] Schmuck and Heil have probed the substrate selectivity of the 'one-armed' receptor

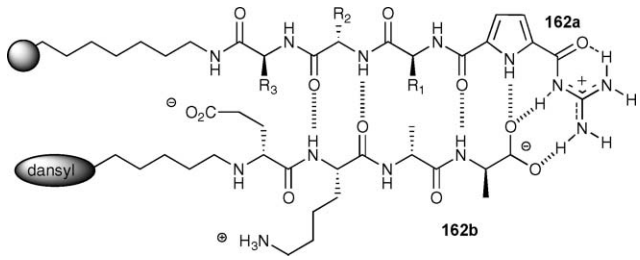
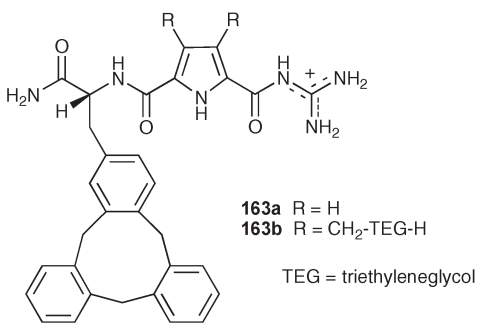


Fig. 19 Schematic representation of complex formation between the receptor library **162a** and the dansylated tetrapeptide substrate **162b**.

162a for binding the polar tetrapeptide *N*-Ac–D-Ala–D-Ala–L-Lys–D-Glu–OH (AAKE) **162b** in buffered water (Fig. 19).[186] This substrate is efficiently bound by the library of receptors **162a**, with $K_a \approx 6000\ M^{-1}$ by the library members with highest affinity, as determined both by a quantitative on-bead binding assays and by ^1H NMR, UV-vis and fluorescence binding studies in water solution. However, tetrapeptide **162b** is in general bound two or three times less efficiently than its inverse *N*-Ac–D-Glu–L-Lys–D-Ala–D-Ala–OH (EKAA) ($K_a \approx 17000\ M^{-1}$),[185] even though the complexation mainly involves long-range electrostatic interactions and both the receptor and substrate are flexible. Molecular modelling and *ab initio* calculations were used to rationalise the selectivity and analyse the binding interactions in the complexes.

Subsequently, Schmuck and Wich have also reported that receptor **162a** shows not only significant substrate selectivity but also a remarkable sequence dependent stereoselectivity in the binding of polar tetrapeptides in water.[187]

Following on from an earlier work,[188] Schmuck and co-workers have also synthesised receptors **163a** and **163b**, which contain hydrophobic cavities and are specifically designed to bind alanine-containing dipeptide carboxylates, and have evaluated their complexation properties using UV-vis and fluorescence titration studies.[189] They observed that these receptors are able to bind the deprotonated dipeptide Ac–D-Ala–D-Ala–OH in buffered water with K_a = 33100 M^{-1}, whilst dipeptides such as Ac–Gly–Gly–OH or Ac–D-Val–D-Val–OH had significantly lower affinities (K_a < 3000 M^{-1}). Molecular modelling studies revealed that this efficient binding and the pronounced sequence selectivity are the result of a combination of strong electrostatic contacts and size-discriminating hydrophobic interactions.



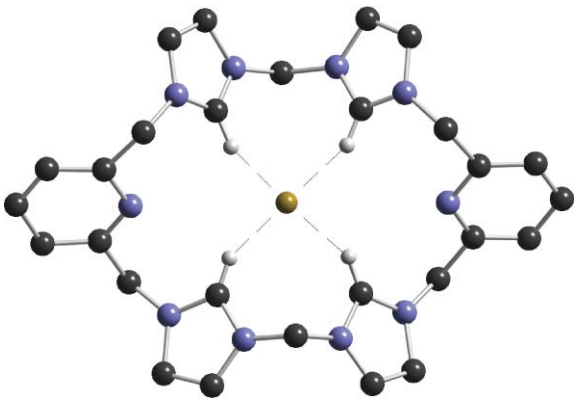
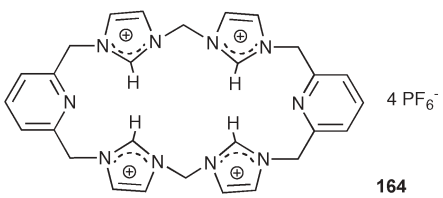


Fig. 20 The fluoride complex of receptor **164**. Countercations and non-acidic hydrogen atoms have been omitted for clarity.

Imidazolium based anion receptors

Imidazolium groups provide both a positive charge and relatively acidic CH group with which to bind anionic species. The use of these groups in anion complexation chemistry was pioneered by Alcalde *et al.* in a number of important papers over the past decade.[190,191] A number of groups are now exploring the molecular recognition properties of receptors containing this group.[192]

Hwang, Kim and co-workers have reported the simple and elegant synthesis and binding properties of a calix[4]imidazolium[2]pyridine.[193] The receptor **164** contains an array of positively charged imidazolium groups and was found to form a 1 : 1 complex with fluoride in solution and in the solid state (Fig. 20) and 1 : 2 (receptor : anion) complexes with Cl^-, Br^-, CH_3COO^- and HSO_4^-, binding the anions *via* CH···A^- hydrogen bonding interactions. In DMSO-d_6, this positively charged macrocycle shows the highest affinity with F^- as shown in Table 19.



Beer and co-workers have synthesised tetrakis(imidazolium) (**165**) and benzimidazolium (**166a–c**) macrocyclic receptors.[194]

Table 19 Association constants for **164** and anions in DMSO[a]

	K_a/M^{-1} (DMSO-d_6)	
Anion	K_1	K_2
F^-	28900	—
Cl^-	2030	2790
Br^-	100	10700
I^-	130	3330
AcO^-	5040	1940
HSO_4^-	40	1120

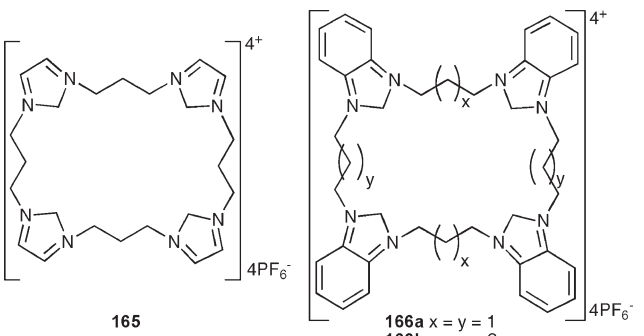
[a] The stability constants (K_a/M^{-1}) were measured using ^1H NMR spectroscopic titrations (25 °C). Errors estimated to be <10%. The anions were used as their tetrabutylammonium salts.

Table 20 Stability constants (K/M^{-1}) for tetrakis(imidazolium) macrocycles with a range of anions[a]

Anion	**165**	**166a**	**166b**	**166c**
F^-	[b]	$>10^4$	[c]	$>10^4$
Cl^-	[b]	1100	[c]	710
Br^-	[b]	1050	[c]	500
I^-	370	560	900	470
BzO^-[d]	K_1 1800	K_1 1070	K_1 1700	K_1 2700
	K_2 470	K_2 1000	K_2 940	K_2 600

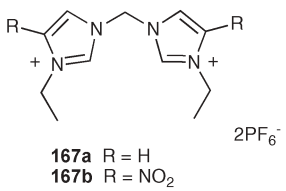
[a] Solvent = CD_3CN–H_2O 9 : 1, temperature = 295 K and errors are $\pm$10%. [b] Mixed host–guest binding stoichiometry prevented the calculation of a sensible stability constant value. [c] Precipitation occurred during titration. [d] The stoichiometry of receptor–benzoate binding is 1 : 2. K_1 and K_2 are quoted in the table.

In a competitive solvent mixture (9 : 1 CD_3CN–H_2O), macrocycles **166a** and **166c** show a marked selectivity for fluoride, binding this anion in a 1 : 1 stoichiometry (Table 20) as measured by ^{1}H NMR titration techniques. In the case of benzoate, a 1 : 2 complex (receptor : anion) was observed with the four macrocycles **165** and **166a**–**c**. A size effect was clearly shown with iodide; the strongest complex was obtained with the largest macrocycle **166b**.

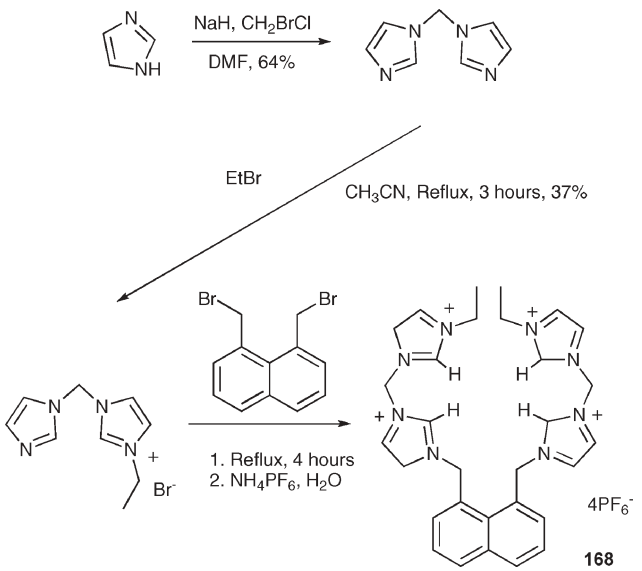


Kang and co-workers have synthesised a wide variety of imidazolium containing anion receptor species.

Kang and In have synthesised the methylene-bridged bis-imidazolium receptors **167a** and **b**.[195] Anion binding studies for these compounds were carried out using ^{1}H NMR spectroscopy in 10% DMSO-d_6 in CD_3CN and revealed that they displayed high affinities for acetate, with the more acidic derivative showing the higher affinity (K_a(**167a**) = 1.6 $\times$ 10^3 M^{-1}; K_a(**167b**) = 2.6 $\times$ 10^4 M^{-1}), and bound spherical halide anions only weakly.



Receptor **168**, which contains four imidazolium groups appended to a naphthalene scaffold, was synthesised by Kang and Kim as shown in Scheme 11.[196] Receptor **168** was found to bind iodide selectively over bromide by ^{1}H NMR titration techniques in 10% DMSO-d_6 in CD_3CN solution, with a



Scheme 11 Synthesis of receptor **168**.

stability constant of 1600 $\pm$ 220 M^{-1} found for iodide *vs.* 140 $\pm$ 7.0 M^{-1} found for bromide. Addition of iodide was also found to quench the fluorescence of the receptor. Kang and co-workers have also synthesised a number of other imidazolium containing anion receptors including systems appended to a glycouril scaffold,[197] and systems based on 1,3-functionalised phenyl scaffolds.[198,199]

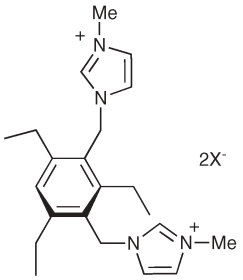
Schatz and co-workers have prepared a series of supramolecular imidazolium salts based on benzene (**169a**,**b** and **170a**–**d**) and calix[4]arenes (**171a**–**d**) that are easily accessible and efficient receptor molecules for small inorganic anions ($H_2PO_4^-$, HSO_4^-, Cl^- and Br^-).[200] Receptors **169b** and **171d** showed selective dihydrogen phosphate binding whilst the other receptors did not show a high degree of selectivity amongst the anions studied (Table 21).

Following on from their earlier work,[201,202] Kim, Yoon and co-workers have prepared two new fluorescent anion receptors (**172** and **173**) bearing two imidazolium groups at the 9,10-positions of anthracene and 2,2′-positions of the binaphthyl ring, respectively.[203] These receptors form strong $(C–H)^+\cdots X$ hydrogen bonds with anions and, as theoretical calculations predict, selectively recognise pyrophosphate and phosphate over other halides in acetonitrile. Binding can be monitored through ^{1}H NMR titration experiments and also *via*

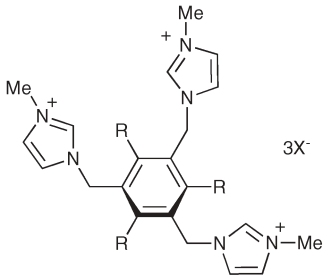
Table 21 Stability constants for the complexation of anions with the PF_6^- receptor salts **169b**, **170b**, **170d**, **171b** and **171d** in DMSO-d_6 at 298 K[a]

	K_a/M^{-1}			
Host	$H_2PO_4^-$	HSO_4^-	Cl^-	Br^-
169b	1520	<10	740	<10
170b	2080	1100	1100	180
170d	1950	1210	1020	760
171b	1910	1110	950	850
171d	1980	200	900	200

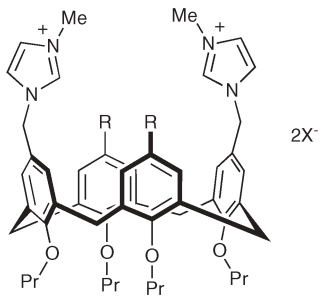
[a] Anions were used as their tetrabutylammonium salts. Estimated errors *ca.* 10%.

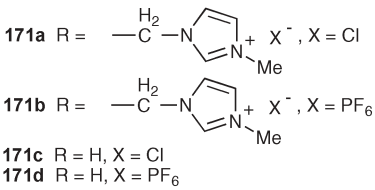


169a X = Br
169b X = PF_6



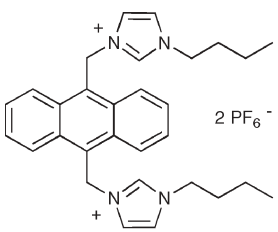
170a R = Me, X = Br
170b R = Me, X = PF_6
170c R = H, X = Br
170d R = H, X = PF_6



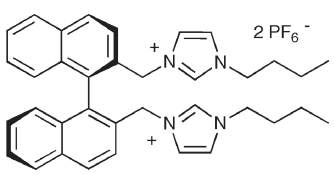


171a R = $-CH_2-N$ (imidazolium) X^-, X = Cl
171b R = $-CH_2-N$ (imidazolium) X^-, X = PF_6
171c R = H, X = Cl
171d R = H, X = PF_6

fluorescence quenching of the anthracene moiety. Using this method, association constants were found to be 3.58×10^6 M^{-1} ($HP_2O_7^{3-}$) and 6.31×10^5 M^{-1} ($H_2PO_4^-$) for **172** and 6.76×10^6 M^{-1} ($HP_2O_7^{3-}$) and 4.21×10^5 M^{-1} ($H_2PO_4^-$) for **173**.

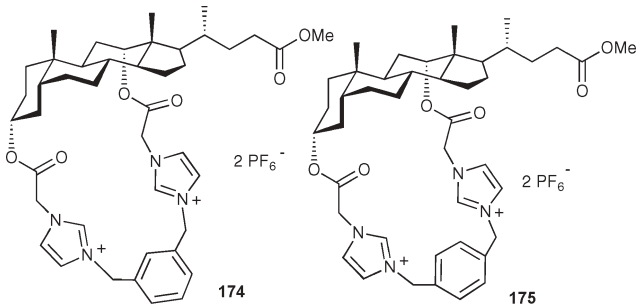


172



(S)-**173**

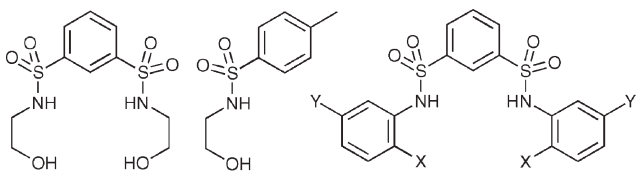
Novel deoxycholic acid-based cyclic receptors, **174** and **175**, containing two imidazolium groups and *m*-xylene and *p*-xylene as spacers have been synthesised by Pandey and co-workers.[204] The anion binding properties of these compounds were studied using standard ^1H NMR methods in $CDCl_3$ solutions, and revealed that the receptor with *m*-xylene shows a moderate selectivity for fluoride ion (K_a = 2400 M^{-1}) whereas the receptor with *p*-xylene, and hence a larger spacing between the imidazolium groups, exhibits high affinity and selectivity towards chloride (K_a = 12000 M^{-1}).



174 **175**

Receptors containing hydroxyl groups

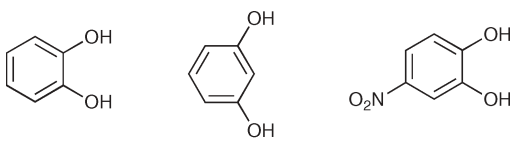
Hydroxyl groups have rarely been used in synthetic anion receptor systems. This may be because of their propensity to deprotonate in the presence of basic anions in organic solution. However, recently a number of groups have begun to explore the use of this moiety in anion complexation.[205] A series of sulfonamide receptors (**176**–**178b**) with pendant hydroxy groups were prepared by Kondo and co-workers.[206] Anion binding studies were limited to chloride, bromide and iodide in acetonitrile, which showed that compounds **178a** and **178b** had a particularly high affinity for chloride (Table 22).[207]



176 **177**

178a X = OH, Y= H
178b X = OH, Y= Cl
178c X = H, Y= H

D. K. Smith and co-workers have reported how some simple and commercial available dihydroxybenzenes such as **179**–**181** can exhibit relatively high degrees of tuneable anion selectivity using several methods including ^1H NMR spectroscopy and UV-vis spectrometry and electrochemical studies.[208]



179 **180** **181**

Stability constants in CD_3CN solution were determined for compounds **179** and **180** with halide anions. It was found that

Table 22 Stability constants of receptors with halide anions in MeCN-d_3

	K_{11}/M^{-1a}		
Receptor	Cl^-	Br^-	I^-
176	928	236	3
177	2000	140	25
178a	14000 (44)[b]	600	30
178b	32100 (26)[b]	800 (34)[b]	60
178c	490	130	30

[a] Determined by 500 MHz ^1H NMR spectroscopy in MeCN-d_3 at 298 K. [Receptor] = 5.0×10^{-3} mol dm^{-3}. [b] K_{12}/dm^3 mol^{-1}.

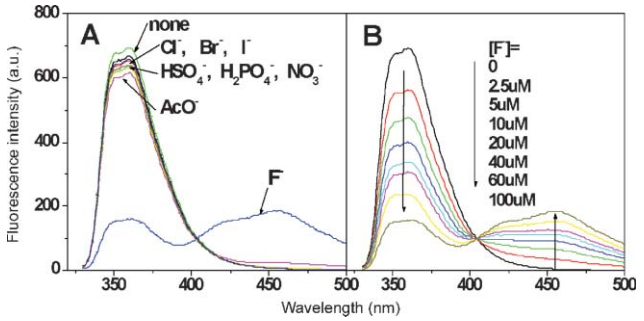
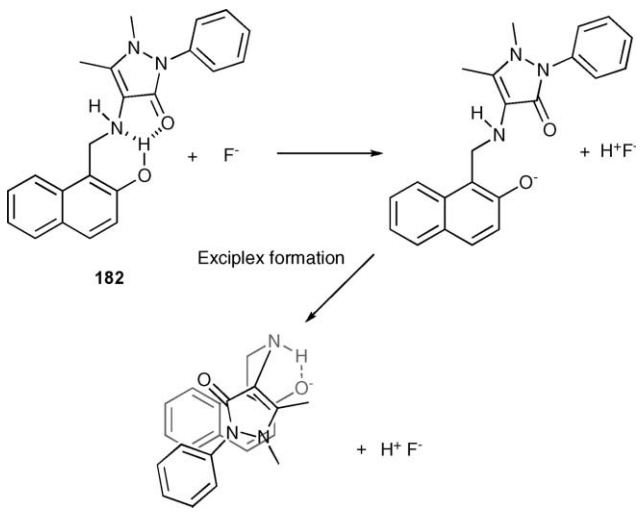


Fig. 21 Fluorescence spectra of compound **182** (10 μM) in acetonitrile upon addition of (A) different anions (F^-, $H_2PO_4^-$, AcO^-, HSO_4^-, NO_3^-, Cl^-, Br^-, I^-) (100 μM) and (B) different concentrations of F^-. Excitation wavelength: 320 nm Reproduced with permission from ref. 210 (Fig. 2). Copyright © 2005 ACS.

catechol **179** forms the strongest complex, with a stability constant of 1570 M^{-1}, with chloride *vs.* 110 M^{-1} for the chloride complex of compound **180**. Basic anions such as dihydrogen phosphate were found to deprotonate receptor **181**, whilst fluoride was found to selectively deprotonate catechol **179** in acetonitrile solution giving rise to a blue coloration due to deprotonation followed by oxidative degradation of the receptor. Linked catechol groups have also been shown to have appreciable anion affinity.[209]

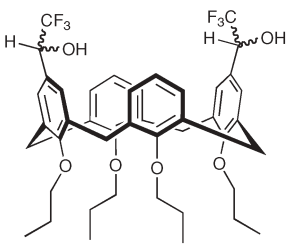
The fluorescent chemosensor **182**, prepared by Zhang, Wu and co-workers, employs anion triggered deprotonation as a novel sensing mechanism.[210] The fluorescence of the receptor was studied in the presence of different anions (F^-, $H_2PO_4^-$, AcO^-, HSO_4^-, NO_3^-, Cl^-, Br^-, and I^-) in acetonitrile solution and shows a fluoride selective response. The fluorescence intensity of compound **182** at 360 nm decreases dramatically and a new broad emission band peaked at 455 nm emerges with increasing intensity upon addition of fluoride (Fig. 21). The authors propose that the aminonaphthol hydroxyl OH group is involved in intramolecular hydrogen bonding that holds the receptor in a rigid conformation (Scheme 12), however in the presence of fluoride this hydrogen



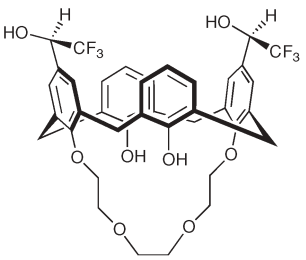
Scheme 12 Fluoride triggered deprotonation and conformational rearrangement by receptor **182**.

bond is removed as the OH group deprotonates, allowing the molecule to fold up into a conformation allowing exciplex formation.

A series of di- and tetrafunctionalised calixarenes have been prepared by Casnati and co-workers with pendant 2,2,2-trifluoroethanol binding groups at the upper rim.[211] The tetrapropoxy bis-trifluoroethanol calix[4]arenes **183a** (*R*,*R*+*S*,*S*) and **183b** (*R*,*S*) show selectivity for carboxylates and $H_2PO_4^-$ over HSO_4^-, Br^- and CN^- anions in chloroform solution, whereas calixarene **184**, bearing a crown ether at the lower rim and trifluoroethanol groups at the upper rim, behaves as a ditopic receptor, simultaneously binding the cation and the anion counterparts of ion pairs. Moreover, this calixcrown-4 derivative **184** shows a five-fold increase in the binding of acetate anion when a sodium ion is complexed in the polyether bridge.



183a (RR+SS) + **183b** (meso)



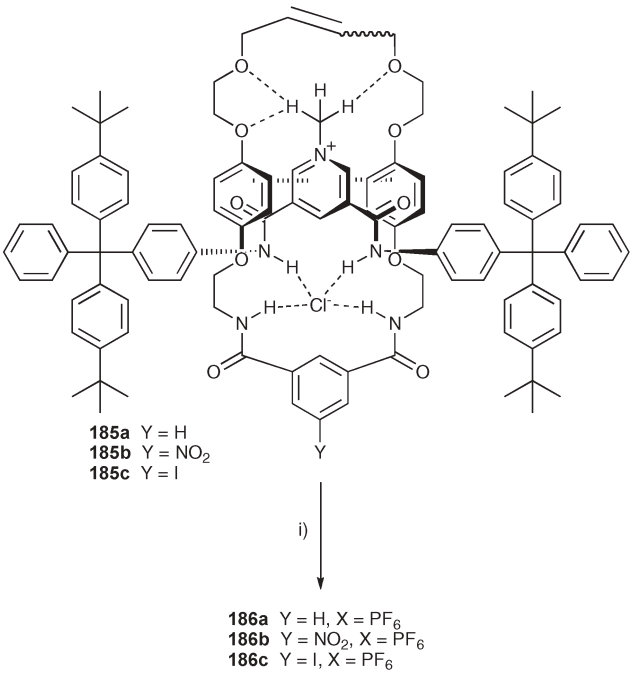
184

Anion templation and anion-directed assembly

Examples of anions directing the formation of molecular architectures were, until a few years ago, difficult to find. However, this situation has now changed, and reports of the templating influence of anions are now becoming widespread.[212,213]

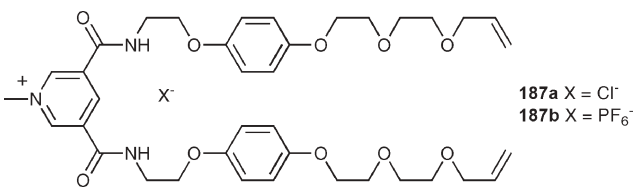
Following on from their earlier work,[214] Beer and co-workers have described the anion templated synthesis of three new [2]rotaxanes containing positively charged pyridinium axles and neutral isophthalamide macrocyclic components **185a**–**c**.[215] Removal of the chloride anion template from the cavity of the [2]rotaxanes using silver hexafluorophosphate yielded the corresponding hexafluorophosphate [2]rotaxane salts **186a**–**c** (Scheme 13). Simple modification of just one component can improve both rotaxane assembly yields and anion binding strengths significantly. In this instance the incorporation of electron-withdrawing substituents, such as a nitro group, into the 5-position of an isophthalamide anion binding motif increases the acidity of the amide protons, which leads to impressive yields of up to 60% for [2]rotaxane formation, concomitant with the rotaxane binding domain both augmenting thermodynamic stability and conserving selectivity for chloride, the templating anion, as indicated the ^{1}H NMR titration studies of compounds **186a**–**c** in a mixture of CD_3OD–$CDCl_3$ (1 : 1).

Beer and co-workers have also described the first example of an anion directed interweaving of two identical acyclic positively charged anion binding receptors. Mixing one equivalent of **187a** and one equivalent of **187b** resulted in the formation of an orthogonal assembled structure around the



Scheme 13 [2]Rotaxane synthesis. (i) $AgPF_6$, CH_2Cl_2.

single chloride anion which, upon a subsequent double cyclisation using ring closing metathesis methods, produces a novel [2]catenane **188**(Cl^-)(PF_6^-) in 78% yield.[216] Proton NMR spectroscopy, electrospray mass spectrometry and single crystal X-ray analysis (see Fig. 22) all provide evidence for the formation of this catenane. After anion exchange, the anion binding properties of the catenane **188**(PF_6^-)$_2$ with TBA salts of F^-, Cl^-, Br^-, $H_2PO_4^-$ and OAc^- in $CDCl_3$–acetone-d_6 1 : 1 were investigated, revealing that the catenane binds chloride much more strongly (K_{11} = 9240 M^{-1} K_{12} = 160 M^{-1}) than acetate (K_{11} = 420 M^{-1} K_{12} = 40 M^{-1}) or bromide (K_{11} = 790 M^{-1} K_{12} = 40 M^{-1}).



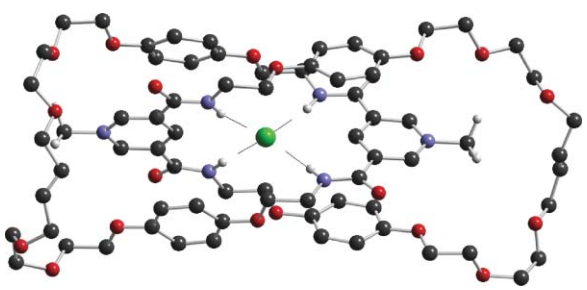
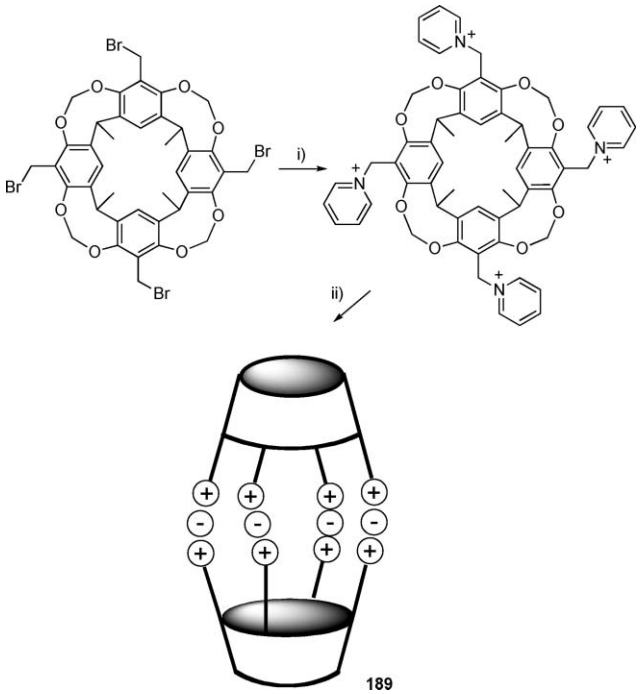


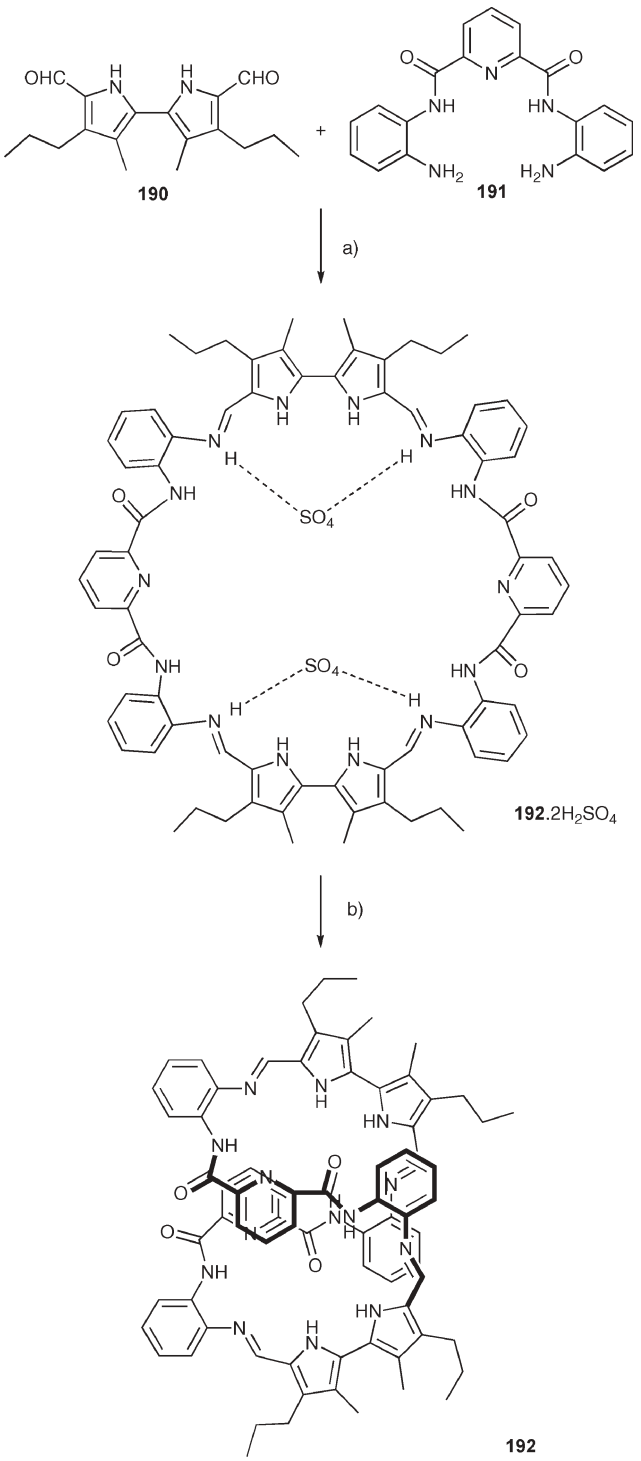
Fig. 22 The crystal structure of the [2]catenane **188** (Cl^-)(PF_6^-) with a chloride ion in the binding cavity. Hydrogen atoms have been omitted except for those involved in hydrogen bonding.



Scheme 14 Synthesis of cavitands **189**. (i) Pyridine, $CHCl_3$–MeOH, rt. (ii) Dowex X column.

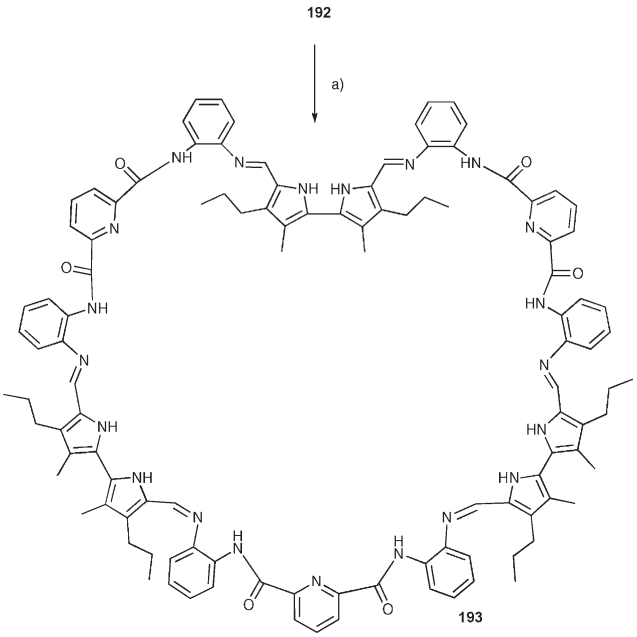
Verboom and co-workers have described the first example of the use of triple-ion interactions for the construction of novel [2 + 4] cavitand-containing capsules **189** in methanol and water.[217] The capsules employ four monovalent anions (bromide, nitrate, acetate or tosylate) to bring together two tetrakis(pyridiniummethyl)tetramethyl cavitands by pyridinium–anion–pyridinium interactions (Scheme 14). This work has been followed by work on [2 + 3] systems[218] and capsule formation with tetracationic and tetraanionic cavitands.[219]

Sessler and co-workers have reported the anion-induced synthesis of a new class of 2,6-diamidopyridine-bipyrrole macrocyclic receptor.[220] The macrocycles were obtained by reaction of diformylbipyrrole **190** and diamine **191** in methanol under acidic conditions. The choice of the acid used (HCl, HBr, CH_3CO_2H, CF_3CO_2H, H_3PO_4, H_2SO_4, HNO_3) was shown to play a critical role in defining the distribution of products from this condensation reaction. HCl and HBr afford the formation of oligomers with high molecular weights ($m/z >$ 3000) and a small amount of the unstable [1 + 1] macrocycle. The use of CH_3CO_2H, CF_3CO_2H and H_3PO_4 led to the formation of the [2 + 2] macrocycle **192** contaminated by uncharacterised oligomers. HNO_3 affords only oligomeric species with high molecular weights. The use of H_2SO_4 led to the formation of the kinetic product **192**·$2H_2SO_4$ under stirring with the free macrocycle being liberated by suspension of the H_2SO_4 complex in dichloroethane and treatment with triethylamine (Scheme 15). Macrocycle **192** interacts strongly with tetrahedral anions HSO_4^- (1 : 1; K_a = 63500 ± 3000 M^{-1}) and $H_2PO_4^-$ (2 : 1; K_{a1} = 191000 ± 15400 M^{-1}; K_{a2} = 60200 ± 6000 M^{-1}), less strongly with acetate (1 : 1, K_a = 26000 ± 2400 M^{-1}), and not at all with the Cl^-, Br^- and NO_3^-.



Scheme 15 (a) Conc. H_2SO_4 (2.2 equiv.), 48 h, rt; (b) dichloroethane, Et_3N (excess), MeOH–CH_2Cl_2.

If compound **192** was dissolved in acetonitrile and allowed to stand for 5 days in the presence of $TBAHSO_4$ or $TBAH_2PO_4$, it was found to rearrange to give the [3 + 3] analogue **193** (Scheme 16). However, if the reaction mixture was subject to stirring, the [3 + 3] macrocyclic product was formed only in trace amounts and instead the [2 + 2] macrocycle **192** was formed as the H_2SO_4 complex. Thus it



Scheme 16 (a) $TBAHSO_4$, MeCN, 5 days, room temperature without stirring followed by Et_3N; or $TBAH_2PO_4$, MeCN, 5 days, room temperature without stirring.

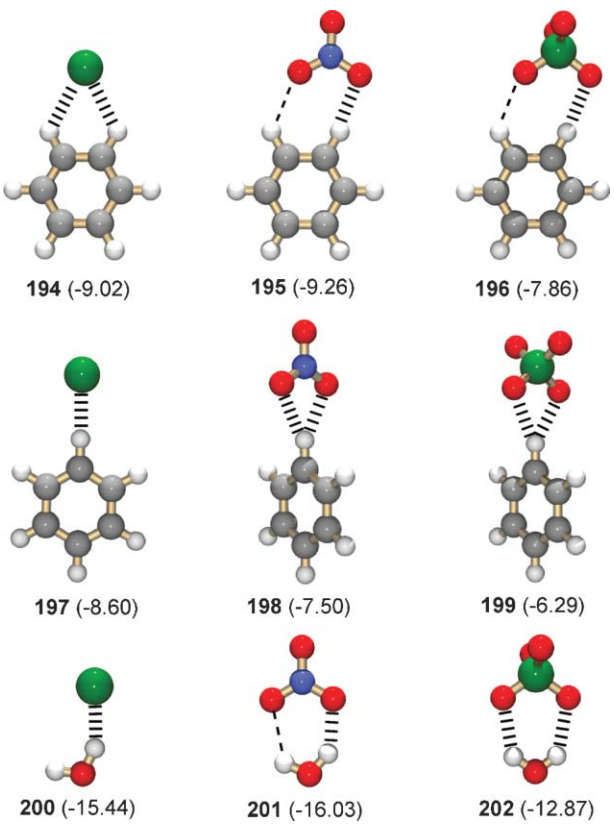


Fig. 23 Structures and ΔE values (kcal mol^{-1}) obtained after geometry optimisation at the MP2/aug-cc-pVTZ level of theory. When the two hydrogen bonds are not equivalent, **195**, **196**, **201**, the weaker interaction is indicated by the thinner dashed line. Reproduced with permission from ref. 221. Copyright © 2005 ACS.

seems that in this case the kinetics and thermodynamics of this reaction are in fine balance and depend on subtle changes in reaction conditions. Under stirring, the H_2SO_4 complex of **192** forms quickly and precipitates. In the absence of stirring the precipitation process is slow allowing isolation of **193** as the thermodynamic product.

Modelling studies

Hay and co-workers have continued their work on theoretical insights into anion complexation and anion receptor design. Bryantsev and Hay have combined theoretical calculations, an examination of the Cambridge Crystallographic Database and experimental results for binding energies to analyse whether C–H groups are significant hydrogen bond donor groups in anion receptors.[221] They studied in detail complexes of benzene with chloride, nitrate and perchlorate at the MP2/aug-cc-pVTZ level of theory with benzene interacting with these anions in several different binding geometries (Fig. 23). The authors found that even in the absence of electron-withdrawing groups, simple arenes can form hydrogen bonds that exceed 50% of the strength of those formed by OH or NH hydrogen bond donor groups. In another publication, the influence of substituents on the aromatic ring on hydrogen bond strength was evaluated.[222] Hay and co-workers have also conducted an extensive modelling study in order to find the optimal arrangement of urea groups to bind Cl^-, NO_3^- and ClO_4^- [223] and with Johnson and co-workers, in a seminal contribution dated 2007 but published in late 2006, a detailed study of the interaction of halides with electron-deficient arenes,[224] an area attracting much current interest.[225]

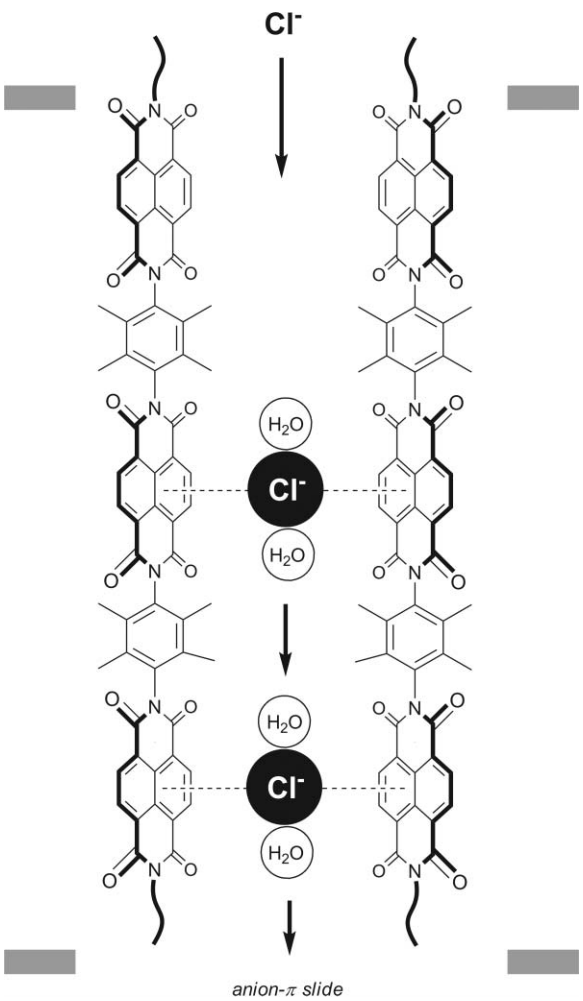


Fig. 24 An anion–π slide rendering a lipid bilayer permeable to chloride.

Conclusions

The years 2005 and 2006 saw continuing interest and effort devoted to the production of new anion receptors. The development of imidazolium based receptors continues apace whilst the first examples of synthetic indole containing receptors have been reported. Applications of receptors as lipid-bilayer membrane transport agents for chloride or HCl are attracting growing interest. Synthetic molecular shuttles and channels have been developed which show effective chloride transport ability in model systems and in the case of Gokel's peptide based transport agents in epithelial cells. New approaches to chloride transport are also being developed, including revolutionary systems such as Matile's anion–π slides[226] (Fig. 24) based on electron deficient oligo(*p*-phenylene)-*N*,*N*-naphthalenediimide (O-NDI) rods. Potential application of these systems as future treatments for cystic fibrosis and other channelopathies continue to drive this research forward.

Acknowledgements

We would like to thank the EPSRC for a postdoctoral fellowship (JG). SEGG would like to thank the Ministerio de Educacion y Ciencia of Spain for the award of a Postdoctoral grant.

References

1 J. L. Sessler, P. A. Gale and W.-S. Cho, *Anion Receptor Chemistry*, Royal Society of Chemistry, Cambridge, 2006.
2 R. Quesada and P. A. Gale, *Coord. Chem. Rev.*, 2006, **250**, 3219.
3 *Supramolecular Chemistry of Anions*, ed. A. Bianchi, K. Bowman-James and E. García-España, Wiley-VCH, New York, 1997.
4 P. D. Beer and P. A. Gale, *Angew. Chem., Int. Ed.*, 2001, **40**, 486.
5 P. A. Gale, in *The Encyclopedia of Supramolecular Chemistry*, ed. J. L. Atwood and J. W. Steed, Dekker, New York, 2004, p. 31.
6 K. Kavallieratos, S. R. de Gala, D. J. Austin and R. H. Crabtree, *J. Am. Chem. Soc.*, 1997, **119**, 2325.
7 K. Kavallieratos, C. M. Bertao and R. H. Crabtree, *J. Org. Chem.*, 1999, **64**, 1675.
8 B. D. Smith and M. P. Hughes, *J. Org. Chem.*, 1997, **62**, 4492.
9 S.-I. Kondo, Y. Hiraoka, N. Kurumatani and Y. Yano, *Chem. Commun.*, 2005, 1720.
10 S. J. Coles, J. G. Frey, P. A. Gale, M. B. Hursthouse, M. E. Light, K. Navakhun and G. L. Thomas, *Chem. Commun.*, 2003, 568.
11 S. J. Brooks, L. S. Evans, P. A. Gale, M. B. Hursthouse and M. E. Light, *Chem. Commun.*, 2005, 734.
12 S. J. Brooks, P. R. Birkin and P. A. Gale, *Electrochem. Commun.*, 2005, **7**, 1351.
13 M. J. Chmielewski and J. Jurczak, *Tetrahedron Lett.*, 2004, **45**, 6007.
14 M. J. Chmielewski, A. Szumna and J. Jurczak, *Tetrahedron Lett.*, 2004, **45**, 8699.
15 M. J. Chmielewski and J. Jurczak, *Chem.–Eur. J.*, 2005, **11**, 6080.
16 M. J. Chmielewski, L. Dobrzycki, J. Jurczak and K. Wozniak, *Cryst. Growth Des.*, 2005, **5**, 1339.

17 M. J. Chmielewski and J. Jurczak, *Chem.–Eur. J.*, 2006, **12**, 7652.
18 M. J. Chmielewski and J. Jurczak, *Tetrahedron Lett.*, 2005, **46**, 3085.
19 A. M. Costero, M. J. Banuls, M. J. Aurell and M. C. R. De Arellano, *J. Inclusion Phenom. Macrocyclic Chem.*, 2006, **54**, 61.
20 A. K. Jain, V. K. Gupta and J. R. Raisoni, *Electrochim. Acta*, 2006, **52**, 951.
21 M. K. Chae, G.-Y. Cha and K.-S. Jeong, *Tetrahedron Lett.*, 2006, **47**, 8217.
22 K.-J. Chang, M. K. Chae, C. Lee, J.-Y. Lee and K.-S. Jeong, *Tetrahedron Lett.*, 2006, **47**, 6385.
23 S. Naher, K. Hiratani and S. Ito, *J. Inclusion Phenom. Macrocyclic Chem.*, 2006, **55**, 151.
24 P. D. Beer, Z. Chen, M. G. B. Drew and P. A. Gale, *Chem. Commun.*, 2004, 2207.
25 P. D. Beer, P. A. Gale, Z. Chen, M. G. B. Drew, J. A. Heath, M. I. Ogden and H. R. Powell, *Inorg. Chem.*, 1997, **36**, 5880.
26 M. D. Lankshear, A. R. Cowley and P. D. Beer, *Chem. Commun.*, 2006, 612.
27 K.-X. Xu, Y.-B. He, H.-J. Qin, G.-Y. Qing and S.-Y. Liu, *Tetrahedron: Asymmetry*, 2005, **16**, 3042.
28 J. Kang, H.-K. Ju and J.-H. Jo, *Supramol. Chem.*, 2004, **16**, 175.
29 J. Kang, J.-H. Jo and S. In, *Tetrahedron Lett.*, 2004, **45**, 5225.
30 J. Kang and J. Kim, *Tetrahedron Lett.*, 2005, **46**, 1759.
31 H. Kim and J. Kang, *Bull. Korean Chem. Soc.*, 2006, **27**, 1791.
32 J. M. Mahoney, A. M. Beatty and B. D. Smith, *J. Am. Chem. Soc.*, 2001, **123**, 5847.
33 M. J. Deetz, M. Shang and B. D. Smith, *J. Am. Chem. Soc.*, 2000, **122**, 6201.
34 J. M. Mahoney, K. A. Stucker, H. Jiang, I. Carmichael, N. R. Brinkmann, A. M. Beatty, B. C. Noll and B. D. Smith, *J. Am. Chem. Soc.*, 2005, **127**, 2922.
35 O. Hirata, M. Takeuchi and S. Shinkai, *Chem. Commun.*, 2005, 3805.
36 T. Zieliński, M. Kędziorek and J. Jurczak, *Tetrahedron Lett.*, 2005, **46**, 6231.
37 T. Zieliński and J. Jurczak, *Tetrahedron*, 2005, **61**, 4081.
38 H. Qin, Y. He, G. Qing, C. Hu and X. Yang, *Tetrahedron: Asymmetry*, 2006, **17**, 2143.
39 S. Otto and S. Kubik, *J. Am. Chem. Soc.*, 2003, **125**, 7804.
40 Z. Rodriguez-Docampo, S. I. Pascu, S. Kubik and S. Otto, *J. Am. Chem. Soc.*, 2006, **128**, 11206.
41 D. Yang, X. Li, Y. Sha and Y.-D. Wu, *Chem.–Eur. J.*, 2005, **11**, 3005.
42 R. Miao, Q.-Y. Zheng, C.-F. Chen and Z.-T. Huang, *Tetrahedron Lett.*, 2005, **46**, 2155.
43 S. Valiyayeettil, J. F. J. Engbersen, W. Verboom and D. N. Reinhoudt, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 900.
44 C. Kaewtong, S. Fuangswasdi, N. Muangsin, N. Chaichit, J. Vicens and B. Pulpoka, *Org. Lett.*, 2006, **8**, 1561.
45 A. F. D. de Namor, J. K. Chaaban and I. Abbas, *J. Phys. Chem. A*, 2006, **110**, 9575.
46 K. Bowman-James, *Acc. Chem. Res.*, 2005, **38**, 671.
47 S. O. Kang, D. Powell, V. W. Day and K. Bowman-James, *Angew. Chem., Int. Ed.*, 2006, **45**, 1921.
48 M. R. Sambrook, P. D. Beer, J. A. Wisner, R. L. Paul, A. R. Cowley, F. Szemes and M. G. B. Drew, *J. Am. Chem. Soc.*, 2005, **127**, 2292.
49 S. Zhang and L. Echegoyen, *J. Am. Chem. Soc.*, 2005, **127**, 2006.
50 S. Tapper, J. A. Littlechild, Y. Molard, I. Prokes and J. H. R. Tucker, *Supramol. Chem.*, 2006, **18**, 55.
51 W. E. Allen and J. L. Sessler, *CHEMTECH*, 1999, **29**, 16.
52 P. V. Santacroce, O. A. Okunola, P. Y. Zavalij and J. T. Davis, *Chem. Commun.*, 2006, 3246.
53 V. Sidorov, F. W. Kotch, G. Abdrakhmanova, R. Mizani, J. C. Fettinger and J. T. Davis, *J. Am. Chem. Soc.*, 2002, **124**, 2267.
54 V. Sidorov, F. W. Kotch, J. L. Kuebler, Y.-F. Lam and J. T. Davis, *J. Am. Chem. Soc.*, 2003, **125**, 2840.
55 J. L. Seganish, P. V. Santacroce, K. J. Salimian, J. C. Fettinger, P. Zavalij and J. T. Davis, *Angew. Chem., Int. Ed.*, 2006, **45**, 3334.
56 P. H. Schlesinger, R. Ferdani, J. Liu, J. Pajewska, R. Pajewski, M. Saito, H. Shabany and G. W. Gokel, *J. Am. Chem. Soc.*, 2002, **124**, 1848.
57 P. H. Schlesinger, R. Ferdani, J. Pajewska, R. Pajewski and G. W. Gokel, *New J. Chem.*, 2003, **27**, 60.
58 N. Djedovič, R. Ferdani, E. Harder, J. Pajewska, R. Pajewski, M. E. Weber, P. H. Schlesinger and G. W. Gokel, *New J. Chem.*, 2005, **29**, 291.
59 R. Pajewski, R. Ferdani, J. Pajewska, N. Djedovič, P. H. Schlesinger and G. W. Gokel, *Org. Biomol. Chem.*, 2005, **3**, 619.
60 R. Pajewski, R. Garcia-Medina, S. L. Brody, W. M. Leevy, P. H. Schlesinger and G. W. Gokel, *Chem. Commun.*, 2006, 329.
61 K. Kavallieratos, A. J. Sabucedo, A. T. Pau and J. M. Rodriguez, *J. Am. Soc. Mass Spectrom.*, 2005, **16**, 1377.
62 O. B. Berryman, F. Hof, M. J. Hynes and D. W. Johnson, *Chem. Commun.*, 2006, 506.
63 P.A. Gale, J.L. Sessler, V. Král and V. Lynch, *J. Am. Chem. Soc.*, 1996, **118**, 5140.
64 S. Camiolo and P. A. Gale, *Chem. Commun.*, 2000, 1129; F. P. Schmidtchen, *Org. Lett.*, 2002, **4**, 431.
65 J. L. Sessler, D. E. Gross, W.-S. Cho, V. M. Lynch, F. P. Schmidtchen, G. W. Bates, M. E. Light and P. A. Gale, *J. Am. Chem. Soc.*, 2006, **128**, 12281.
66 R. Custelcean, L. H. Delmau, B. A. Moyer, J. L. Sessler, W.-S. Cho, D. Gross, G. W. Bates, S. J. Brooks, M. E. Light and P. A. Gale, *Angew. Chem., Int. Ed.*, 2005, **44**, 2537.
67 G. W. Bates, P. A. Gale and M. E. Light, *CrystEngComm*, 2006, **8**, 300.
68 G. W. Bates, M. Kostermans, W. Dehaen, P. A. Gale and M. E. Light, *CrystEngComm*, 2006, **8**, 444.
69 R. Nishiyabu, M. A. Palacios, W. Dehaen and P. Anzenbacher, Jr., *J. Am. Chem. Soc.*, 2006, **128**, 11496.
70 P. Anzenbacher, Jr., R. Nishiyabu and M. A. Palacious, *Coord. Chem. Rev.*, 2006, **250**, 2929.
71 J. L. Sessler, W.-S. Cho, D. E. Gross, J. A. Shriver, V. M. Lynch and M. Marquez, *J. Org. Chem.*, 2005, **70**, 5982.
72 C. H. Lee, H.-K. Na, D.-W. Yoon, H. Miyagi, W.-S. Cho, V. M. Lynch, S. V. Shevchuk and J. L. Sessler, *J. Am. Chem. Soc.*, 2003, **125**, 7301.
73 J. L. Sessler, D. An, W.-S. Cho and V. Lynch, *J. Am. Chem. Soc.*, 2003, **125**, 13646.
74 J. L. Sessler, D. An, W.-S. Cho and V. Lynch, *Angew. Chem., Int. Ed.*, 2003, **42**, 2278.
75 J. L. Sessler, D. An, W.-S. Cho, V. Lynch and M. Marquez, *Chem. Commun.*, 2005, 540.
76 J. L. Sessler, D. An, W.-S. Cho, V. Lynch, D.-W. Yoon, S.-J. Hong and C.-H. Lee, *J. Org. Chem.*, 2005, **70**, 1511.
77 C.-H. Lee, J.-S. Lee, H.-K. Na, D.-W. Yoon, H. Miyaji, W.-S. Cho and J. L. Sessler, *J. Org. Chem.*, 2005, **70**, 2067.
78 H. Miyaji, H.-K. Kim, E.-K. Sim, C.-K. Lee, W.-S. Cho, J. L. Sessler and C.-H. Lee, *J. Am. Chem. Soc.*, 2005, **127**, 12510.
79 P. Anzenbacher, Jr., K. Jursíkova, V. M. Lynch, P. A. Gale and J. L. Sessler, *J. Am. Chem. Soc.*, 1999, **121**, 11020.
80 A. Kałedkowski and A. W. Trochimczuk, *React. Funct. Polym.*, 2006, **66**, 740.
81 K. A. Nielsen, W.-S. Cho, J. O. Jeppesen, V. M. Lynch, J. Becher and J. L. Sessler, *J. Am. Chem. Soc.*, 2004, **126**, 16296.
82 K. A. Nielsen, W.-S. Cho, J. Lyskawa, E. Levillain, V. M. Lynch, J. L. Sessler and J. O. Jeppesen, *J. Am. Chem. Soc.*, 2006, **128**, 2444.
83 K. A. Nielsen, W.-S. Cho, G. H. Sarova, B. M. Petersen, A. D. Bond, J. Becher, F. Jensen, D. M. Guldi, J. L. Sessler and J. O. Jeppesen, *Angew. Chem., Int. Ed.*, 2006, **45**, 6848.
84 R. Gu, S. Depraetere, J. Kotek, J. Budka, E. Wagner-Wysiecka, J. F. Biernat and W. Dehaen, *Org. Biomol. Chem.*, 2005, **3**, 2921.
85 R. Nishiyabu and P. Anzenbacher, Jr., *Org. Lett.*, 2006, **8**, 359.
86 R. Nishiyabu and P. Anzenbacher, Jr., *J. Am. Chem. Soc.*, 2005, **127**, 8270.
87 X. K. Ji, D. S. Black, S. B. Colbran, D. C. Craig, K. M. Edbey, J. B. Harper and G. D. Willett, *Tetrahedron*, 2005, **61**, 10705.
88 A. F. D. de Namor, M. Shehab, I. Abbas, M. V. Withams and J. Zvietcovich-Guerra, *J. Phys. Chem. B*, 2006, **110**, 12653.
89 P. A. Gale, *Acc. Chem. Res.*, 2006, **39**, 467.
90 P. A. Gale, *Chem. Commun.*, 2005, 3761.
91 A. Fürstner, *Angew. Chem., Int. Ed.*, 2003, **42**, 3582.
92 N. N. Gerber, *Crit. Rev. Microbiol.*, 1974, **3**, 469.
93 J. W. Bennett and R. Bentley, *Adv. Appl. Microbiol.*, 2000, **47**, 1.

94 S. Ohkuma, T. Sato, M. Okamoto, K. Matsuya, K. Arai, T. Kataoka, K. Nagai and H. H. Wasserman, *Biochem. J.*, 1998, **334**, 731.
95 J. L. Seganish and J. T. Davis, *Chem. Commun.*, 2005, 5781.
96 P. A. Gale, M. E. Light, B. McNally, K. Navakhun, K. E. Sliwinski and B. D. Smith, *Chem. Commun.*, 2005, 3773.
97 J. L. Sessler, L. R. Eller, W.-S. Cho, S. Nicolaou, A. Aguilar, J. T. Lee, V. M. Lynch and D. J. Magda, *Angew. Chem., Int. Ed.*, 2005, **44**, 5989.
98 J. L. Sessler, G. D. Pantos, P. A. Gale and M. E. Light, *Org. Lett.*, 2006, **8**, 1593.
99 P. A. Gale, S. Camiolo, G. J. Tizzard, C. P. Chapman, M. E. Light, S. J. Coles and M. E. Hursthouse, *J. Org. Chem.*, 2001, **66**, 7849.
100 Z. Yin, Z. Li, A. Yu, J. He and J.-P. Cheng, *Tetrahedron Lett.*, 2004, **45**, 6803.
101 C.-L. Chen, Y.-H. Chen, C.-Y. Chen and S.-S. Sun, *Org. Lett.*, 2006, **8**, 5053.
102 C.-Y. Wu, M.-S. Chen, C.-A. Lin, S.-C. Lin and S.-S. Sun, *Chem.–Eur. J.*, 2006, **12**, 2263.
103 P. Anzenbacher, Jr., M. A. Palacios, K. Jursíkova and M. Marquez, *Org. Lett.*, 2005, **7**, 5027.
104 T. Ghosh, B. G. Maiya and A. Samanta, *Dalton Trans.*, 2006, 795.
105 Z. Yin, Y. Zhang, J. He and J.-P. Cheng, *Tetrahedron*, 2006, **62**, 765.
106 H. Maeda and Y. Kusunose, *Chem.–Eur. J.*, 2005, **11**, 5661.
107 C. Fujimoto, Y. Kusunose and H. Maeda, *J. Org. Chem.*, 2006, **71**, 2389.
108 H. Maeda and Y. Ito, *Inorg. Chem.*, 2006, **45**, 8205.
109 D. Curiel, A. Cowley and P. D. Beer, *Chem. Commun.*, 2005, 236.
110 K.-J. Chang, D. Moon, M. S. Lah and K.-S. Jeong, *Angew. Chem., Int. Ed.*, 2005, **44**, 7926.
111 T. H. Kwon and K.-S. Jeong, *Tetrahedron Lett.*, 2006, **47**, 8539.
112 J. L. Sessler, D.-G. Cho and V. Lynch, *J. Am. Chem. Soc.*, 2006, **128**, 16518.
113 V. Amendola, M. Boiocchi, D. Esteban-Gómez, L. Fabbrizzi and E. Monzani, *Org. Biomol. Chem.*, 2005, **3**, 2632.
114 T. Gunnlaugsson, P. E. Kruger, P. Jensen, F. M. Pfeffer and G. M. Hussey, *Tetrahedron Lett.*, 2003, **44**, 8909.
115 V. Amendola, D. Esteban-Gómez, L. Fabbrizzi and M. Licchelli, *Acc. Chem. Res.*, 2006, **39**, 343.
116 D. E. Gómez, L. Fabbrizzi, M. Licchelli and E. Monzani, *Org. Biomol. Chem.*, 2005, **3**, 1495.
117 S. Camiolo, P. A. Gale, M. B. Hursthouse and M. E. Light, *Org. Biomol. Chem.*, 2003, **1**, 741.
118 X. He, S. Hu, K. Liu, Y. Guo, J. Xu and S. Shao, *Org. Lett.*, 2006, **8**, 333.
119 D. Esteban-Gómez, L. Fabbrizzi and M. Licchelli, *J. Org. Chem.*, 2005, **70**, 5717.
120 D. Esteban-Gómez, L. Fabbrizzi, M. Licchelli and D. Sacchi, *J. Mater. Chem.*, 2005, **15**, 2670.
121 M. Bonizzoni, L. Fabbrizzi, A. Taglietti and F. Tiengo, *Eur. J. Org. Chem.*, 2006, 3567.
122 E. Quinlan, S. E. Matthews and T. Gunnlaugsson, *Tetrahedron Lett.*, 2006, **47**, 9333.
123 G.-Y. Qing, Y.-B. He, Y. Zhao, C.-G. Hu, S.-Y. Liu and X. Yang, *Eur. J. Org. Chem.*, 2006, 1574.
124 M. Albrecht, Triyanti, M. de Groot, M. Bahr and E. Weinhold, *Synlett*, 2005, 2095.
125 F.-Y. Wu, Z. Li, L. Guo, X. Wang, M.-H. Lin, Y.-F. Zhao and Y.-B. Jiang, *Org. Biomol. Chem.*, 2006, **4**, 624.
126 L. S. Evans, P. A. Gale, M. E. Light and R. Quesada, *Chem. Commun.*, 2006, 965.
127 L. S. Evans, P. A. Gale, M. E. Light and R. Quesada, *New J. Chem.*, 2006, **30**, 1019.
128 S. J. Brooks, P. A. Gale and M. E. Light, *Chem. Commun.*, 2005, 4696.
129 Z. Yin, Z. Li, A. Yu, J. He and J. P. Cheng, *Tetrahedron Lett.*, 2004, **45**, 6803.
130 S. J. Brooks, P. R. Edwards, P. A. Gale and M. E. Light, *New J. Chem.*, 2006, **30**, 65.
131 S. J. Brooks, P. A. Gale and M. E. Light, *Chem. Commun.*, 2006, 4344.
132 T. Gunnlaugsson, A. P. Davis, J. E. O'Brien and M. Glynn, *Org. Biomol. Chem.*, 2005, **3**, 48.
133 K. Ghosh and S. Adhikari, *Tetrahedron Lett.*, 2006, **47**, 8165.
134 E. J. Jun, K. M. K. Swamy, H. Bang, S.-J. Kim and J. Yoon, *Tetrahedron Lett.*, 2006, **47**, 3103.
135 S.-i. Kondo and M. Sato, *Tetrahedron*, 2006, **62**, 4844.
136 T. Gunnlaugsson, P. E. Kruger, P. Jensen, J. Tierney, H. D. P. Ali and G. M. Hussey, *J. Org. Chem.*, 2005, **70**, 10875.
137 F. M. Pfeffer, A. M. Buschgens, N. W. Barnett, T. Gunnlaugsson and P. E. Kruger, *Tetrahedron Lett.*, 2005, **46**, 6579.
138 F. M. Pfeffer, T. Gunnlaugsson, P. Jensen and P. E. Kruger, *Org. Lett.*, 2005, **7**, 5357.
139 D. Garozzo, G. Gattuso, A. Notti, A. Pappalardo, S. Pappalardo, M. F. Parisi, M. Perez and I. Pisagatti, *Angew. Chem., Int. Ed.*, 2005, **44**, 4892.
140 K. Lang, P. Cuřínová, M. Dudič, P. Prošková, I. Stibor, V. Šťastný and P. Lhoták, *Tetrahedron Lett.*, 2005, **46**, 4469.
141 P. Lhoták, J. Svoboda and I. Stibor, *Tetrahedron*, 2006, **62**, 1253.
142 C. A. Winschel, A. Kalidindi, I. Zgani, J. L. Magruder and V. Sidorov, *J. Am. Chem. Soc.*, 2005, **127**, 14704.
143 C. E. Stanley, N. Clarke, K. M. Anderson, J. A. Elder, J. T. Lenthall and J. W. Steed, *Chem. Commun.*, 2006, 3199.
144 D. R. Turner, M. J. Paterson and J. W. Steed, *J. Org. Chem.*, 2006, **71**, 1598.
145 J. W. Steed, *Chem. Commun.*, 2006, 2637.
146 M. H. Filby, T. D. Humphries, D. R. Turner, R. Kataky, J. Kruusma and J. W. Steed, *Chem. Commun.*, 2006, 156.
147 A. M. Costero, J. P. Villarroya, S. Gil, M. J. Aurell and C. Ramirez de Arellano, *Tetrahedron*, 2002, **58**, 6729.
148 A. M. Costero, J. P. Villarroya, S. Gil, P. Gaviña and C. Ramírez de Arellano, *Supramol. Chem.*, 2003, **15**, 403.
149 A. M. Costero, M. Colera, P. Gaviña and S. Gil, *Chem. Commun.*, 2006, 761.
150 S. Rashdan, M. E. Light and J. D. Kilburn, *Chem. Commun.*, 2006, 4578.
151 C. Roussel, M. Roman, F. Andreoli, A. Del Rio, R. Faure and N. Vanthuyne, *Chirality*, 2006, **18**, 762.
152 J. M. Russell, A. D. M. Parker, I. Radosavljevic-Evans, J. A. K. Howard and J. W. Steed, *Chem. Commun.*, 2006, 269.
153 A. B. Descalzo, K. Rurack, H. Weisshoff, R. Martínez-Mañez, M. D. Marcos, P. Amorós, K. Hoffmann and J. Soto, *J. Am. Chem. Soc.*, 2005, **127**, 184.
154 A. P. Davis, *Coord. Chem. Rev.*, 2006, **250**, 2939.
155 J. P. Clare, A. J. Ayling, J.-B. Joos, A. L. Sisson, G. Magro, M. N. Pérez-Payán, T. N. Lambert, R. Shukla, B. D. Smith and A. P. Davis, *J. Am. Chem. Soc.*, 2005, **127**, 10739.
156 A. L. Sisson, J. P. Clare and A. P. Davis, *Chem. Commun.*, 2005, 5263.
157 A. L. Sisson, J. P. Clare, L. H. Taylor, J. P. H. Charmant and A. P. Davis, *Chem. Commun.*, 2003, 2246.
158 K. M. Bhattarai, V. del Amo, G. Magro, A. L. Sisson, J.-B. Joos, J. P. H. Charmant, A. Kantacha and A. P. Davis, *Chem. Commun.*, 2006, 2335.
159 S.-Y. Liu, L. Fang, Y.-B. He, W.-H. Chan, K.-T. Yeung, Y.-K. Cheng and R.-H. Yang, *Org. Lett.*, 2005, **7**, 5825.
160 L. Fang, W.-H. Chan, Y.-B. He, D. W. J. Kwong and A. W. M. Lee, *J. Org. Chem.*, 2005, **70**, 7640.
161 S. Y. Liu, K. Y. Law, Y. B. He and W. H. Chan, *Tetrahedron Lett.*, 2006, **47**, 7857.
162 S.-Y. Liu, Y.-B. He, W. H. Chan and A. W. M. Lee, *Tetrahedron*, 2006, **62**, 11687.
163 C. H. Park and H. E. Simmons, *J. Am. Chem. Soc.*, 1968, **90**, 2431.
164 C. Bazzicalupi, A. Bencini, A. Bianchi, L. Borsari, C. Giorgi, B. Valtancoli, C. Anda and A. Llobet, *J. Org. Chem.*, 2005, **70**, 4257.
165 C. Bazzicalupi, A. Bencini, A. Bianchi, V. Fusi, P. Paoletti and B. Valtancoli, *J. Chem. Soc., Chem. Commun.*, 1994, 881.
166 A. Bencini, A. Bianchi, P. Dapporto, V. Fusi, E. Garcia-España, M. Micheloni, P. Paoletti, P. Paoli, A. Rodriguez and B. Valtancoli, *Inorg. Chem.*, 1993, **32**, 2753.
167 A. Bencini, A. Bianchi, E. Garcia-España, V. Fusi, M. Micheloni, P. Paoletti, J. A. Ramirez, A. Rodriguez and B. Valtancoli, *J. Chem. Soc., Perkin Trans. 2*, 1992, 1059.
168 C. Bazzicalupi, A. Bencini, A. Bianchi, A. Danesi, C. Giorgi, M. A. Martinez Lorente and B. Valtancoli, *New J. Chem.*, 2006, **30**, 959.

169 M. Arca, A. Bencini, E. Berni, C. Caltagirone, F. A. Devillanova, F. Isaia, A. Garau, C. Giorgi, V. Lippolis, A. Perra, L. Tei and B. Valtancoli, *Inorg. Chem.*, 2003, **42**, 6929.
170 C. Bazzicalupi, A. Bencini, E. Faggi, A. Garau, C. Giorgi, V. Lippolis, A. Perra and B. Valtancoli, *Dalton Trans.*, 2006, 1409.
171 S. Carvalho, R. Delgado, N. Fonseca and V. Félix, *New J. Chem.*, 2006, **30**, 247.
172 A. González-Álvarez, I. Alfonso, P. Díaz, E. García-España and V. Gotor, *Chem. Commun.*, 2006, 1227.
173 M. Mascal, *Angew. Chem., Int. Ed.*, 2006, **45**, 2890.
174 A. Frontera, J. Morey, A. Oliver, M. N. Piña, D. Quiñonero, A. Costa, P. Ballester, P. M. Deyà and E. V. Anslyn, *J. Org. Chem.*, 2006, **71**, 7185.
175 P. Blondeau, M. Segura, R. Pérez-Fernández and J. de Mendoza, *Chem. Soc. Rev.*, 2007, **36**, 198.
176 V. D. Jadhav and F. P. Schmidtchen, *Org. Lett.*, 2005, **7**, 3311.
177 A. Gleich, F. P. Schmidtchen, P. Mikulcik and G. Müller, *J. Chem. Soc., Chem. Commun.*, 1990, 55.
178 V. D. Jadhav and F. P. Schmidtchen, *Org. Lett.*, 2006, **8**, 2329.
179 C. Schmuck, *Coord. Chem. Rev.*, 2006, **250**, 3053.
180 C. Schmuck and U. Machon, *Chem.–Eur. J.*, 2005, **11**, 1109.
181 C. Schmuck and U. Machon, *Eur. J. Org. Chem.*, 2006, 4385.
182 S. L. Wiskur, H. Ait-Haddou, J. J. Lavigne and E. V. Anslyn, *Acc. Chem. Res.*, 2001, **34**, 963.
183 C. Schmuck and M. Schwegmann, *J. Am. Chem. Soc.*, 2005, **127**, 3373.
184 C. Schmuck and M. Schwegmann, *Org. Biomol. Chem.*, 2006, **4**, 836.
185 C. Schmuck, M. Heil, J. Scheiber and K. Baumann, *Angew. Chem., Int. Ed.*, 2005, **44**, 7208.
186 C. Schmuck and M. Heil, *Chem.–Eur. J.*, 2006, **12**, 1339.
187 C. Schmuck and P. Wich, *Angew. Chem., Int. Ed.*, 2006, **45**, 4277.
188 C. Schmuck and L. Geiger, *J. Am. Chem. Soc.*, 2004, **126**, 8898.
189 C. Schmuck, D. Rupprecht and W. Wienand, *Chem.–Eur. J.*, 2006, **12**, 9186.
190 E. Alcalde, N. Mesquida, L. Pérez-García, C. Alvarez-Rúa, S. García-Granda and E. García-Rodriguez, *Chem. Commun.*, 1999, 295.
191 E. Alcalde, S. Ramos and L. Pérez-García, *Org. Lett.*, 1999, **1**, 1035.
192 J. Yoon, S. K. Kim, N. J. Singh and K. S. Kim, *Chem. Soc. Rev.*, 2006, **35**, 355.
193 K. Chellappan, N. J. Singh, I.-C. Hwang, J. W. Lee and K. S. Kim, *Angew. Chem., Int. Ed.*, 2005, **44**, 2899.
194 W. W. H. Wong, M. S. Vickers, A. R. Cowley, R. L. Paul and P. D. Beer, *Org. Biomol. Chem.*, 2005, **3**, 4201.
195 S. In and J. Kang, *J. Inclusion Phenom. Macrocyclic Chem.*, 2006, **54**, 129.
196 H. Kim and J. Kang, *Tetrahedron Lett.*, 2005, **46**, 5443.
197 S. In and J. Kang, *Tetrahedron Lett.*, 2005, **46**, 7165.
198 S. In, S. J. Cho and J. Kang, *Supramol. Chem.*, 2005, **17**, 443.
199 S. In, S. J. Cho, K. H. Lee and J. Kang, *Org. Lett.*, 2005, **7**, 3993.
200 T. Fahlbusch, M. Frank, J. Schatz and H. Schmaderer, *Eur. J. Org. Chem.*, 2006, 1899.
201 S. K. Kim, N. J. Singh, S. J. Kim, H. G. Kim, J. K. Kim, J. W. Lee, K. S. Kim and J. Yoon, *Org. Lett.*, 2003, **5**, 2083.
202 J. Yoon, S. K. Kim, N. J. Singh, J. W. Lee, Y. J. Yang, K. Chellappan and K. S. Kim, *J. Org. Chem.*, 2004, **69**, 581.
203 S. K. Kim, N. J. Singh, J. Kwon, I.-C. Hwang, S. J. Park, K. S. Kim and J. Yoon, *Tetrahedron*, 2006, **62**, 6065.
204 V. K. Khatri, S. Upreti and P. S. Pandey, *Org. Lett.*, 2006, **8**, 1755.
205 H. Miyaji and J. L. Sessler, *Angew. Chem., Int. Ed.*, 2001, **40**, 154.
206 S.-i. Kondo, T. Suzuki, T. Toyama and Y. Yano, *Bull. Chem. Soc. Jpn.*, 2005, **78**, 1348.
207 S. Kondo, T. Suzuki and Y. Yano, *Tetrahedron Lett.*, 2002, **43**, 7059.
208 K. J. Winstanley, A. M. Sayer and D. K. Smith, *Org. Biomol. Chem.*, 2006, **4**, 1760.
209 K. Ito, M. Nishiki and Y. Ohba, *Chem. Pharm. Bull.*, 2005, **53**, 1352.
210 J.-S. Wu, J.-H. Zhou, P.-F. Wang, X.-H. Zhang and S.-K. Wu, *Org. Lett.*, 2005, **7**, 2133.
211 A. Casnati, A. Sartori, L. Pirondini, F. Bonetti, N. Pelizzi, F. Sansone, F. Ugozzoli and R. Ungaro, *Supramol. Chem.*, 2006, **18**, 199.
212 M. S. Vickers and P. D. Beer, *Chem. Soc. Rev.*, 2007, **36**, 211.
213 P. D. Beer, M. R. Sambrook and D. Curiel, *Chem. Commun.*, 2006, 2105.
214 J. A. Wisner, P. D. Beer, M. G. B. Drew and M. R. Sambrook, *J. Am. Chem. Soc.*, 2002, **124**, 12469.
215 M. R. Sambrook, P. D. Beer, M. D. Lankshear, R. F. Ludlow and J. A. Wisner, *Org. Biomol. Chem.*, 2006, **4**, 1529.
216 K.-Y. Ng, A. R. Cowley and P. D. Beer, *Chem. Commun.*, 2006, 3676.
217 G. V. Oshovsky, D. N. Reinhoudt and W. Verboom, *J. Am. Chem. Soc.*, 2006, **128**, 5270.
218 G. V. Oshovsky, D. N. Reinhoudt and W. Verboom, *J. Org. Chem.*, 2006, **71**, 7441.
219 G. V. Oshovsky, D. N. Reinhoudt and W. Verboom, *Eur. J. Org. Chem.*, 2006, 2810.
220 E. A. Katayev, G. D. Pantos, M. D. Reshetova, V. N. Khrustalev, V. M. Lynch, Y. A. Ustynyuk and J. L. Sessler, *Angew. Chem., Int. Ed.*, 2005, **44**, 7386.
221 V. S. Bryantsev and B. P. Hay, *J. Am. Chem. Soc.*, 2005, **127**, 8282.
222 V. S. Bryantsev and B. P. Hay, *Org. Lett.*, 2005, **7**, 5031.
223 B. P. Hay, T. K. Firman and B. A. Moyer, *J. Am. Chem. Soc.*, 2005, **127**, 1810.
224 O. B. Berryman, V. S. Bryantsev, D. P. Stay, D. W. Johnson and B. P. Hay, *J. Am. Chem. Soc.*, 2007, **129**, 48.
225 C. Garau, D. Quinonero, A. Frontera, P. Ballester, A. Costa and P. M. Deya, *J. Phys. Chem. A*, 2005, **109**, 9341.
226 V. Gorteau, G. Bollot, J. Mareda, A. Perez-Velasco and S. Matile, *J. Am. Chem. Soc.*, 2006, **128**, 14788.

