Role of amide and urea moieties in molecular recognition

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The amide and urea moieties due to their unique stereoelectronic character interact with electron deficient centres through carbonyl group and with electron rich centers through N-H units. This dual character has been successfully used for the design of urea/amide based receptors for recognizing variety of guests. This review discusses the salient examples of such receptors to bring out the unique scope of urea and amide units in designing receptors for recognition of cations, anions and neutral molecules.

Molecular recognition is quite essential to most of the biological and chemical processes. Enzymes, antibodies, membranes, and other receptors; carriers, and channels all involve molecular recognition as a key step in their biochemical functioning. Molecular recognition in general involves multimolecular assemblies, called supramolecular complexes, formed between two or more topologically complementary chemical entities which are held together by non-covalent forces. For a deep insight into the basis of noncovalent interactions and biological functions of receptors and to emulate the basic principles of nature, the investigations on complementarity of various host guest interactions in structurally simpler model receptors have been carried out. In fact the concept of molecular recognition grew out of such studies in the mid-sixties from the observations of selective recognition of alkali metal cations by ionophoric antibiotics and synthetic macro(poly)cyclic polyethers.

Molecular recognition character of a receptor is governed by its overall structural topology where primarily the constituent functionalities trigger and influence the nature of its bindings. Amongst various functional groups such as ethers, thioethers, sulphides, disulphides, imines, amines, ureas and amides etc. used in the design of model receptors, amide and urea moieties enjoy a pre-eminent position because of their unique stereoelectronic character. As depicted below amides elaborate electron rich O, N centres and electron deficient N–H units, and thus can bind with both electron deficient guests (at O, N) and electron rich guests through hydrogen bonding (at N–H unit). Resonance assists amides to attain more negative charge than any other neutral oxygen functionality and also provides desirable rigid spatial geometry. The spatial orientation of the amide could be effectively controlled by the bulk and nature of substituents on the amide nitrogen.

Urea moiety also owes its importance to somewhat similar electronic character as the amide. Additional electron donation by the second nitrogen atom in the case of urea further increases the negative charge on the oxygen atom and provides rigidity to the geometry.

Nature has quite generously used amides in evolving receptors such as valinomycin, baeyericin, westelliamide etc. and many other molecules of biological importance. Importance of urea moiety in biological systems is quite evident from the fact that out of the five nucleobases, all three pyrimidine bases i.e. cytosine, thymine and uracil have urea moiety in their structure, which efficiently participates in double helix formation (H-bonds) and co-ordinates with metal ions.

In this article, the unique role of amide and urea moieties in molecular recognition of both electron rich and electron deficient guests in synthetic receptors has been highlighted. The presentation is categorized into cationic, anionic and neutral recognition and in each category the receptors in order of podands, coronands, cryptands, cyclophanes and calixarenes etc. are arranged.

1Dedicated to Professor S. M. Mukherji.
I: Cationic recognition

A pioneering effort to develop open chain amide based podands of utility in the development of ion selective electrodes was initiated by Simon and co-workers in Zürich and as early as 1972, Ca$^{2+}$ selective carrier 1\(^9\) was reported.

Numerous other ligands such as 2-5 were developed. From amongst a series of $N,N,N',N'$-tetrasubstituted diamides, the ionophores 3c and 5a-c showed a high Li$^+$ selectivity with 5b showing highest Li$^+$ selectivity over alkali (>1000 times) and alkaline earth (>100 times) cations. The ionophores 5b and 5c have been used for Li$^+$ assay determination\(^{10-12}\).

Amongst podands 6-8, 6b co-ordinates with Li$^+$ through four amide oxygens in a 2 : 1 (Ligand : Li$^+$) complex. Li$^+$ selective electrodes based on ionophores 6h, 8a, 8b, 8d have also been reported\(^{13}\).

Amongst 3-oxapentanediamides 9-11, the compound 9d forms an ideal co-ordination sphere of nine atoms in 3 : 1 ligand-Ca$^{2+}$ complex for the uptake of Ca$^{2+}$ and induces a selectivity in membranes for Ca$^{2+}$ over Mg$^{2+}$,
Na\(^+\), and K\(^+\) by a factor of 10\(^4\), 10\(^7\) and 10\(^8\) respectively\(^1^7\). The IR monitored solubilization studies on complexes of a series of N-bridged benzimidazolones 12 with alkali and alkaline earth metal cations exhibit significant selectivity in complexation and transportation of Ca\(^{2+}\) in preference to the other cations\(^1^8\).

\[
\begin{array}{ll}
a & R_1-R_2 = \text{CH}_2\text{CH}_2\text{CH}_3 \\
b & R_1-R_2 = \text{isopropyl} \\
c & R_1 = \text{CH}_3, R_2 = n-\text{C}_9\text{H}_{15} \\
d & R_1-R_2 = \text{C}_6\text{H}_{11} \\
e & R_1-R_2 = \text{morpholyl} \\
f & R_1-R_2 = \text{Bn} \\
g & R_1-R_2 = \text{Ph} \\
h & R_1 = \text{CH}_3, R_2 = p-\text{C}_6\text{H}_4\text{CH}=\text{CH}_2 \\
i & R_1-R_2 = \text{morpholinyl} \\
j & R_1-R_2 = \text{inn} \\
k & R_1-R_2 = \text{p-phenylene}
\end{array}
\]

The N,N-Di(8-quinolyl)malonamide derivative 13 selectively extracts Cu\(^{2+}\) amongst the transition metal ions from the aqueous phase. However, 14 hardly extracts any metal ion but effectively transports Cu\(^{2+}\) with high selectivity through liquid membranes\(^1^9\), whereas 13 exhibits poor transport character probably due to high binding ability. The N-benzyloxamidine derivatives 15 and 16 selectively formed complexes with Hg\(^{2+}\). Podand 15 can be used as ionophore for ion selective electrodes to detect Hg\(^{2+}\) with good reproducibility\(^2^0,2^1\). Podand 16 formed stable complexes accompanied by deprotonation of the amide groups only when Hg\(^{2+}\) was added.

Amongst the amide functionalised macrocyclic tweezer shaped coronands, the receptor 17a displays significant selectivity for Li\(^+\) over Na\(^+\) in polymeric membranes\(^2^2\). The optically active macrocycles 18 incorporating both ester and amide functionalities have been synthesized to mimic the highly selective binding character of natural ionophores\(^2^3\). Thus the 24-membered 18 \((n = 1, m = 3)\) mimics valinomycin in its ability to transport K\(^+\) and Na\(^+\) ions. Meso 18 \((n = 1, m = 3)\) is more efficient than \((\pm)\) 18 \((n = 1, m = 3)\) for the transport of alkali metal cations \((\text{Na}^+, \text{K}^+, \text{Rb}^+, \text{Cs}^+)\) but both exhibit negligible transport of alkaline earth \((\text{Ba}^{2+}, \text{Sr}^{2+}, \text{Mg}^{2+} \text{and Ca}^{2+})\) picrates.
For similar lipophilicity but smaller ring size, \(19\) extracts alkaline earth metal picrates better than the more flexible \(20\) in the order \(\text{Ba}^{2+} - \text{Sr}^{2+} > \text{Ca}^{2+}\) but \(20\) shows higher selectivity in extraction for \(\text{Ba}^{2+}\) ions. Both \(20a\) and \(20b\) furnish 1 : 1 complexes with \(\text{Ba}^{2+}\) picate. However, the increase in the ring size in \(21a, 21b\) over that of \(20a\) reveals order \(\text{Ca}^{2+} - \text{Sr}^{2+} > \text{Ba}^{2+}\) but \(21c\) is selective for \(\text{Ba}^{2+}\) over \(\text{Ca}^{2+}\) and \(\text{Sr}^{2+}\) ions.

Ferrocene containing unsymmetrical cryptand \(22 (n \geq 1)\) employs carbonyl oxygens in binding to divalent metal ions. The \(22a (n = 2)\) gives 2 : 1 (host-guest) complex with an yttrium cation. The ferrocenophane \(22b\) containing a pyridine unit, forms complexes with a series of guest cations (\(\text{Na}^+, \text{Cu}^{2+}, \text{Ba}^{2+}\) or \(\text{Y}^{3+}\)).

Macrocycles \(23\) and \(24\) with amine-amide combination undergo deprotonation at amide NH with divalent transition metal ions to form neutral complexes.

The ionophore \(23\) acts as a carrier for proton coupled transport of \(\text{Cu}^{2+}\) against concentration gradient. Ligand \(24\) (\(X = \text{NH}, \text{O}\)) transports \(\text{Pb}^{2+}\) and \(\text{Ag}^+\) picrates rejecting alkali metal picrates.

Ligand \(25(\text{E})\) having photosensitive azobenzene cap shows selective binding to \(\text{Na}^+\) while \(25(\text{Z})\) formed by photomerization, encapsulates \(\text{K}^+\) more strongly suggesting the expansion of the \(\text{N}_2\text{O}_4\) ring photoinduced by \((\text{E})\) to \((\text{Z})\) isomerization. The ligand \(26\) in which azobenzene cap is replaced by pyridine unit, strongly binds to heavy metal cations particularly \(\text{Cu}^{2+}\) and no such binding is encountered in \(26(\text{Z})\).

Amide functionalized appendages to the macrocyclic backbone also influence the binding character. Among the series of chiral mono- and di-substituted 14-crown-4 derivatives, the macrocycles \(27a\) and \(27b\) with amides as appendages induce the best \(\text{Li}^+\) to \(\text{Na}^+\) selectivity (630 : 1) in liquid membrane electrodes.
extracts $\text{Ag}^+$ picrate with remarkable selectivity over alkali, alkaline earth, $\text{Tl}^+$ and $\text{Pb}^{2+}$ picrates\textsuperscript{35}. groups complexes with $\text{Ni}^{2+}$, $\text{Cu}^{2+}$ and $\text{Zn}^{2+}$ \textsuperscript{39}.

Octamides \textsuperscript{32} of $p$-alkoxy-calix[8]arenes extract alkaline earth metal picrates from water to dichloromethane, and the corresponding nitrates from acidic water solution simulating radioactive waste to 2-nitrophenyl hexyl ether (NPHE)\textsuperscript{36}. In case of simulated waste solutions, the distribution coefficients for strontium removal by octamides are much higher than the corresponding value found for dicyclohexyl-18-crown-6 (DC\textsubscript{18}C\textsubscript{6}). Amongst various heterocalix[6]arenes with different number of uracil and benzimidazolone units and three aryl units, the heterocalix[6]arene \textsuperscript{33} exhibits \textit{t}-BuNH\textsubscript{3}+/K\textsuperscript{+} selectivity\textsuperscript{37}.

Tetraamide \textsuperscript{34} in its partial cone conformation forms a 1:1 complex with lanthanum picrate\textsuperscript{38} through three amide and two ethereal oxygens co-ordination. The cyclophane \textsuperscript{35} with amine, carboxylate and amide as three electron donor

A cyclic pseudo-peptide receptor \textsuperscript{36} has been isolated from a combinatorial library which shows a binding towards $N$-methylammonium salts\textsuperscript{40}.

Carboxamido nitrogens may be used in the synthesis of different receptors for binding $\text{Fe}^{3+}$ ion. Thus the compounds \textsuperscript{37-42} are used for the synthesis of the $\text{Fe}^{III}$ complexes\textsuperscript{41}.
More recently, receptors have been appended with appropriate fluorescent moieties and the change in fluorescence during complexation provides direct means of both qualitative and quantitative estimation of guest species. The solution of 43 and 42 in acetonitrile-water at pH 7.1 adjusted with 2,6-lutidine shows fluorescence quenching on addition of Cu^{2+} whereas no decrease in fluorescence is observed with Ni^{2+}, Mn^{2+} and Co^{2+} cations.

The chiral diaza-9-crown-3 derivative 44 displays "off-on" switching of fluorescence when treated with various lithium salts in organic solvents such as CH_{3}CN and discriminates against a variety of group I and group II metal ions.

The optically active cyclic hexapeptides 45a and 45b exhibit intense pyrene monomer emission at 375-418 nm and an additional pyrene excimer band at 487 nm (intramolecular) in 45a and 481 nm (intermolecular) in 45b. The addition of Ca^{2+}/Ba^{2+} perchlorate to a solution of cyclic peptide 45a causes a considerable increase of the excimer to monomer emission ratio \(I_{e}/I_{m}\) which is more pronounced in case of Ca^{2+}. Mg^{2+} does not affect the emission of 45a. Peptide 45b shows analogous fluorescence characteristics but \(I_{e}/I_{m}\) ratio is much lower in comparison to that observed in 45a.

Ureylene crown ether 46 binds with 2 equivalent of Li^{+} co-operatively and selectively \([K = 3 \times 10^{7} \text{ dm}^{3} \text{ mol}^{-1}]\) over other alkali metal ions such as Na^{+}, K^{+} and Cs^{+}.

The calix[4]arene 47 shows fluorescence enhancement with Zn^{2+} but fluorescence quenching with Ni^{2+}.

II. Anionic recognition

Anions are larger in size than isoelectronic cations (Table I) and therefore have a lower charge to radius ratio. This causes lower electrostatic binding interactions and lower
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"1__')
CNII liN)
O~NH

binding in case of anion receptors than observed for the cation receptors.

Table 1. A comparison of the radii (r) of isoelectronic cations and anions in octahedral environment

| Cation | r (Å) | Anion | r (Å) |
|--------|-------|-------|-------|
| Na⁺    | 1.16  | F⁻    | 1.19  |
| K⁺     | 1.52  | Cl⁻   | 1.67  |
| Rb⁺    | 1.66  | Br⁻   | 1.82  |
| Cs⁺    | 1.81  | I⁻    | 2.06  |

Additionally, anions are more sensitive to the pH (becoming protonated at lower pH), and therefore receptors must function within the pH range of the target anion. Anionic species have wide range of geometries and therefore a higher degree of design may be required to make receptors complementary to their anionic guest. Anionic receptors involving varied non-covalent interactions viz. electrostatic interactions, hydrogen bonding, hydrophilicity, co-ordination to a metal ion, and combination of these interactions have been developed. Receptors which use the amide moiety for binding anions, make use of the hydrogen bonds. Being directional in nature, hydrogen bonds allow the designing of receptors with specific shapes capable of differentiating anionic guests with different geometries.

Receptors 49-55 are all C3-symmetric and are consequently organized to bind tetrahedral anions. Anslyn and co-workers have reported the synthesis of a cage like molecule 56. Since the amide NH groups in 56 are arranged in a trigonal prismatic array, they are able to co-ordinate to the π-electron system of planar anions such as carboxylates and nitrate.

Ureas and thioureas are particularly good hydrogen bond donors and are excellent receptors for Y-shaped anions such as carboxylates through the formation of two hydrogen bonds. The urea based receptor 57 forms highly stable complexes with bidentate ligands.

The acyclic cleft molecules 52, 58 and 59 bind anions very strongly with stability constants up to 19500 M⁻¹ for receptor 59 and H₂PO₄⁻ ions in [D6]DMSO. The selectivity for H₂PO₄⁻ ions can be attributed to the complementary hydro-
gen bonding array present in these clefts that can form four hydrogen bonds to each H$_2$PO$_4^-$ ion.

Ferrocene units appended with secondary amides have also been used for anion recognition$^{53,54}$. For example, 60-63 were capable of detecting H$_2$PO$_4^-$ ions in the presence of a ten-fold excess of HSO$_4^-$ and Cl$^-$ ions in acetonitrile as shown by large cathodic shifts of up to 240 mV.

In evolving amide based anion receptors tris(2,2'-bipyridyl)ruthenium(II) ([Ru(bpy)$_3$]$^{2+}$), because of its chemical stability, redox properties, excited-state reactivity, and luminescent emission$^{55}$ had been one of the most extensively investigated platforms. Beer and co-workers have incorporated this moiety into acyclic, macrocyclic, and calix[4]arene structural frameworks to produce new class of anion receptors 64-68 capable of optical and electorchemical sensing$^{56-58}$.

Watanabe et al. has produced imidazole-functionalized ruthenium-bipyridyl complexes such as 69 which recognizes anionic and neutral phosphodiesters with luminescent signal enhancement observed for anionic phosphodiesters in acetone$^{59}$. Similar complexes have been proposed to be...

Ruthenium(II-) and rhenium(I)-bipyridylcalix[4] diquinone receptors 70 and 71 selectively bind and sense acetate ion through remarkable retrieval effects of luminescent emission intensity$^{60}$.
Diamides 72 are readily synthesized and are found to bind strongly to the acetate and halides in organic solvents. A structurally designed strategy for improving the binding ability of neutral urea and amide based receptors had been described. A series of boronate ureas 73 and a related bis(boronate-amide), 74 were prepared. Their enhanced binding towards carboxylate anions is explained due to the co-operative polarization effect which is induced by intramolecular co-ordination of urea or amide carbonyl to a Lewis acidic boronate group.

Beer and co-workers have synthesized some tripodal trisamidic receptors 75-77. Tripodal ligand 76 binds chloride, iodide, and perrenate anions via co-bound crown ether and efficiently extracts and transports the perrenate (ReO₄⁻) anion from simulated aqueous nuclear waste solution via co-operative ion-pair binding effect.

Different 2,2'-biimidazoles 79a-f with various amide groups at the position 4- and 4'- exhibit quenching in emission intensity in the presence of H₂PO₄⁻ and Cl⁻. The binding constants for 1:1 biimidazole-anion complexation are 10 M⁻¹ for H₂PO₄⁻ and Cl⁻.

Simple 2,5-diamidopyrroles such as 80 and 81 function as oxo-anion selective receptors in acetonitrile-d₃ and DMSO-d₆ 0.5% H₂O solutions.

Amongst different amine, ammonium, and amide pendant arm diamidopyrroles 82-84, the receptor 82 binds...
strongly with HSO₄⁻. This strong binding is attributed to the protonation of the receptor by the anion. Evidence to this fact is given by the fact that 84 has a lower affinity constant for HSO₄⁻, as protonation is not possible in this case. Receptor 83 shows enhanced binding with halide ions in comparison to 82 reflecting the extra electrostatic component to the binding interactions⁶⁷.

III. Neutral molecular recognition

The interactions between a neutral (usually organic) molecular guest and the host framework may vary from very limited (e.g. van der Waals interactions) to significant stability (e.g. hydrogen bonds). Unlike charged species, neutral molecules are neither bound by strong permanent electrostatic forces, nor do they undergo well-defined co-ordination interactions, and hence their bindings are weaker. Also the sizes of the neutral guests are larger than metal cations or simple anions. Despite these features, the importance of this phenomenon in biological systems has lead to an enormous diversity of hosts or lattice compounds, which can bind neutral molecules through H-bonding⁷⁰⁻⁷⁶.

Hydrogen bonds are simulated in molecular mechanics as attraction between the bridge-forming proton and the donor and acceptor hetero element bearing negative partial charges. Many supramolecular systems have been devised which are based essentially on the simultaneous action of properly arranged hydrogen bond donors and acceptors. Amides because of facility of their modification and lipophilicity have been widely used as H-bond donors.

In combination with pyridine group, receptor 87 prepared by Hamilton and co-workers⁷⁷ complexes glutaric acid with $K = 6.4 \times 10^2$ M⁻¹ in THF-CDCl₃ in an enthalpy driven process.

C₃ symmetric macrocyclic anion receptor 86 binds tetrahedral anions such as sulphate and phosphate with high affinity. Titration of 86 with tosylate anion as its tetra-n-butylammonium salt gave 1 : 1 binding isotherms for amide and aryl protons of 86⁶⁹.

Cyclic hexaamides 88 where the skeleton is stiffened by three $p$-phenylene spacer units and cavity diameter approaches that of small cyclodextrins, showed affinity to haloforms and some other molecules in organic solvents⁷⁸.
Systems 89 possessing six-basic heteroarenes are tailor-made for encapsulating sterically and functionally complementary trihydroxybenzene. Such hosts are sensitive to the introduction of methyl or ammonium groups into the guest molecules as 2,4,6-trihydroxytoluene or 2,4,6-trihydroxytoluene hydrochloride are not complexed. The more strongly acidic nitrophloroglucinol simply forms, like picric acid, 1 : 3 complexe.

In contrast to the tris(bipyridine) hosts, the macrobicyclic ligand 90 has pronounced proton donor character, due to six hydroxyl groups of the catechol units. As a consequence, it complexes organic molecules with basic functional groups as long as the $pK_a$ and $pK_B$ values are mutually compatible. Strongly basic triamines, form salt like aggregates by an acid-base reaction. Purine, pyrimidine and other less basic compounds are solubilised by 90 in dichloromethane in which they are otherwise sparingly soluble.

The macromonocyclic bis(catechol) host 91 constitutes a hydrogen bond receptor for piperazine-type guest molecules in organic solution and association for guests 92 (piperazine) and 93 (1,4-diazacycloheptane) are around $10^2$ M$^{-1}$. Extraction and transport studies show that host 91 is quite efficient in binding nucleic bases too.

The basket shaped molecule 94 in CDCl$_3$ solubilizes ammonium p-nitrophenolate by the formation of the complex.

The macrobicyclic hosts 95 and 96 employ multiple hydrogen bonds to bind organic guests with donor and acceptor functionalities arranged in a manner complementary to the cyclourea units and amide groups of the molecular cavities. Binding energy for the complex of 4-pyridone and 95 is approximately $-21$ kJ mol$^{-1}$. Potential guests such as pyridine or $N$-substituted imidazoles are discriminated,
since they do not possess proton donor properties.

\[
\begin{align*}
95 & \quad Z = CH_2, R = H \\
96 & \quad Z = m\text{-phenylene}, R = Bn
\end{align*}
\]

The water soluble macrobicyclic compound 97 (R = Me) constitutes a ditopic host for zwitterionic amino acid and binds \(\gamma\)-aminobutyric acid (GABA) with an association constant of \(3.2 \times 10^3\) M\(^{-1}\) (D\(_2\)O). Glycine, which is too small, and 6-aminocaproic acid, which is too large, are only weakly bound.

Macrobicyclic host 98\(^{86}\) complexes flat, disk shaped aromatic guest pyrene in aqueous phase\(^{87}\). Several macrocyclic hosts such as 99-103 have been prepared\(^{88}\) as domains for binding quinone, which play a key role in the photosynthetic energy conversion. Complexation of \(p\)-benzoquinone by the macrocycles was investigated using \(^1\)H NMR titrations. The limiting change in chemical shift observed for the 1 : 1 complexes support the structure shown in the Fig. 3. The signals due to amide protons show \(-1\) ppm downfield shifts characteristic of hydrogen bonding and the signals due to the quinone protons show \(-2.5\) ppm upfield shifts, which indicate that they lie over the host side walls.

A lipophilic glucose derivative is known to form a multiple hydrogen bonded 1 : 1 inclusion complex with a cholaphane host 104 having a significantly large internal cavity.\(^{89}\).
Aliphatic mono(poly)ols and even hydrocarbon adamantane can be bound as guests to well designed cyclophane hosts in water as trans-1,4-cyclohexanediol, trans-1,4-cyclohexanedicarboxylic acid, and adamantancarboxylic acid bind to host \( \text{105} \).

\[
\begin{align*}
\text{105} & \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad 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for flavins 119 as depicted in Fig. 595. In these synthetic hosts, systematic variation of the spatially remote substituents on the 6-aryl ring alters the hydrogen bond-donating abilities of the amide functionality and the hydrogen bonding accepting properties of the triazine-N.

three different ruthenium complexes with an attached barbituric acid and barbital moieties 121-123 has been studied in chlorinated solvents by NMR and fluorescence titrations96. Significant binding was only observed between 120 and 122 series while steric hinderance significantly diminished binding between 120 and 121 or 123.
Synthetic receptor 124 has been found via fluorescence titration to compete effectively with cytochrome c peroxidase for binding cytochrome c forming 1:1 complex. Chiral imidazole cyclophane receptors 125 exhibit good chiral recognition toward the enantiomers of L- and D-amino acid derivatives in chloroform.

Encapsulation of guests in self-assembled tetraurea calix[4]arene 126 and 127 dimers in organic solvents has been probed by PGSE NMR technique.

New polypyridine-macrocyclic receptors 128-130 for glucopyranoside recognition were designed and synthesized. The receptors possess a terpyridine skeleton as a hydrogen-bonding site and a flexible polyoxethylene chain as a bridge for the macrocyclic structure, in which the cavity of the receptor is large enough to incorporate pyranosides. The receptors showed high affinities for n-octyl-β-(D)-glucopyranoside, and selective binding of the receptors was observed between epimeric pyranosides.

A new rationally designed receptor molecule 131 binds adrenaline derivatives in water. Its binding pattern imitates the interplay of non-covalent interactions operating in the nature. High shape selectivity is achieved for the slim dopamine skeleton, and leads to the rejection of substrates with an α-substituent, such as amino acid derivatives.

Conclusion
Thus, the pre-eminent role of amide and urea moieties in recognition of both electron-rich (anions and neutral molecules) and electron deficient (cations and neutral molecules) guest species exemplified here points to the scope of exploration of abiotic receptors of these categories for evolving sensors and new models for recognition.

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