HETERODITOPIC RECEPTORS

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Abstract – The review outlines the recent advances in the field of coordination chemistry, and is focusing on the function-oriented design of heterotopic co-receptors. Comparative analysis of receptor ability for various classes of organic compounds toward two different substrates, ion pairs or zwitterionic species is presented.

Introduction
Conclusion

INTRODUCTION

Molecular recognition of both ion pair and bipolar organic molecules such amino acids is a rapidly growing area of research. Last decades have seen the burst-type growth of the number of publication devoted to the design of polyfunctional ligands called heteroditopic receptors[1] capable of binding both cation and anion. The interest in these compounds is due to their potential application as sensors for monitoring of biological systems and the environment, as selective extractants, and for the transfer of salts through lipophilic membranes.[2,3]

The idea of creation of heteroditopic receptors is to syntheses of compounds containing several complexing parts of different nature. Fragments capable of either hydrogen bonding with negatively charged species or ion-dipole interaction are suitable for anion acceptors. These sites include polyamines, urea derivatives and moieties containing amide groups and pyrrole units. The complexation with positively charged fragments is accomplished by using compounds that have already proved to be selective cation receptors such as crown ethers, calixarenes and compounds, modified by oligopyridyl groups.[4]

This review surveys the synthetic approaches to the development of heteroditopic receptors and data of their complexating properties.

1.   DESIGN OF HETERODITOPIC RECEPTORS FOR SALTS OF ALKALINE AND ALKALINE-EARTH METALS

Crown ethers and calixarenes are well-known selective extractants for alkaline metals, so such fragments are frequently apply for the design of heteroditopic receptors for salts of alkaline and alkaline-earth metals as cation-binding site.

1.1.   CROWN-CONTAINING LIGANDS

Crown ether **1** containing free hydroxyl group is among the first example of the heteroditopic receptors, based on macrocyclic matrix. This compound as a suspension in THF simultaneously binds a Li$^+$ cation and a thiocyanate anion.[5] The cation is retained by macrocyclic cavity, while the thiocyanate is coordinated to the hydroxyl group due to the formation of intermolecular H-bond.


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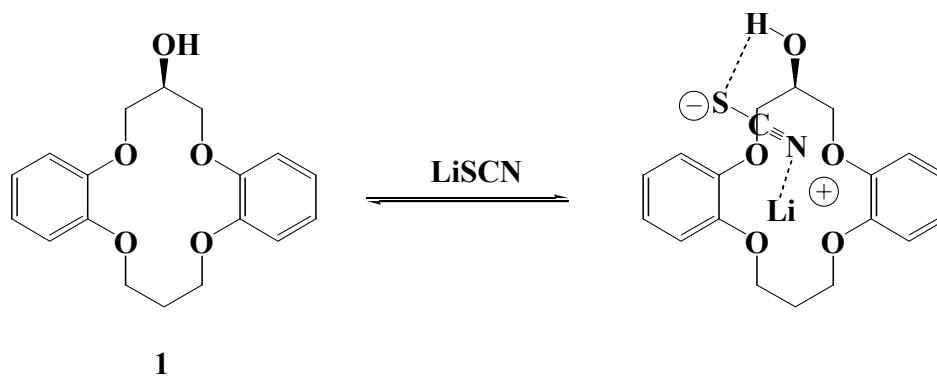
Crown ethers with Lewis acid fragments by covalent bond represent another example of heteroditopic receptor. It has been found that the oxygen atoms of the crown ether ring in compound **2** coordinate the potassium cation, the fluoride anion being bond simultaneously by the boron atom.

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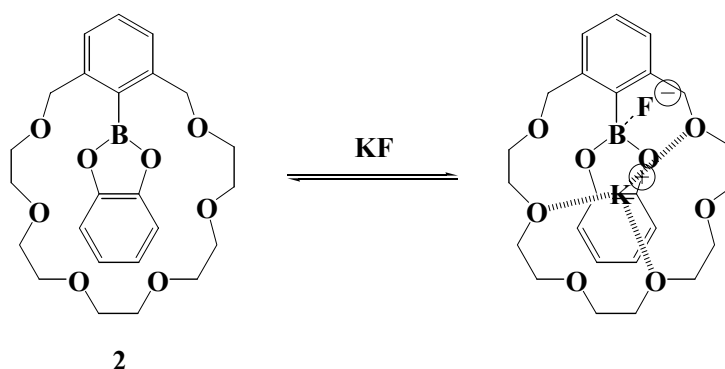
However, in attempt to trap KCl or KBr in the same way, compound **2** acts only as cation receptor. Related compound, obtained by the reaction of corresponding alcohol with Me_3Al forms with lithium chloride both in solution and in the suspension in THF.[6-9]

The introduction of urea fragments or amide groups, which tend to bind anion, in crown ether molecules, allow one to apply these compounds as bifunctional receptors.

A study of binding of benzo-15-crown-5, modified by a thiourea moiety toward a series of anion has shown that upon addition of 2 equivalents of $NaBPh_4$, ligand **3** simultaneously captures NO_3^- ($K_{ass} = 60$ M^{-1}), Br$^-$ ($K_{ass} = 260$ M^{-1}), I$^-$ ($K_{ass} = 20$ M^{-1}) anions by H-bond formation and Na$^+$ cation by interaction with oxygen atoms of crown ether ring.[10] Replacement of thiourea fragment into phenylurea moiety makes it possible to obtain ditopic receptor **4** for NaCl, $NaNO_3$, NaF, CF_3SO_3Na, Na_2ATP.[11,12]

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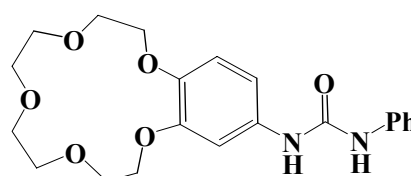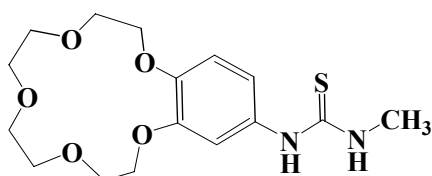
Ability of nitrogen atom to form nonrotative bonds is frequently used to the design of ditopic receptors. A tripodal tris(amidobenzo-15-crown-5) ligand **5** simultaneously binds chloride, iodide and perrhenate anion *via* co-bound crown ether complexed sodium cations and efficiently extracts and transports the pertechnitate anion waste solution via cooperative ion-pair binding effect.[13] Similar receptor **6** can be used for selective extraction of NaI.[14]

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6
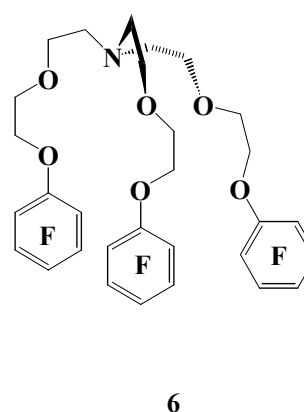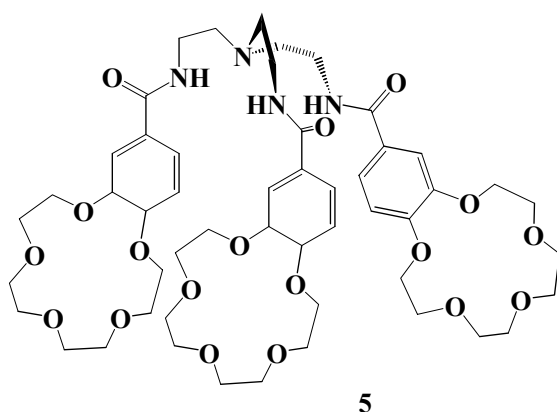
Introduction of fluorophore into the same tripodal molecules makes it possible to design of ditopic receptors with greater practical utility. Addition of potassium fluoride "switches on" the fluorescence of sensor **7** while potassium chloride and potassium bromide cause no fluorescence change. The fluorescence can be "switched off" the potassium cation from the crown ether cavity.[15]
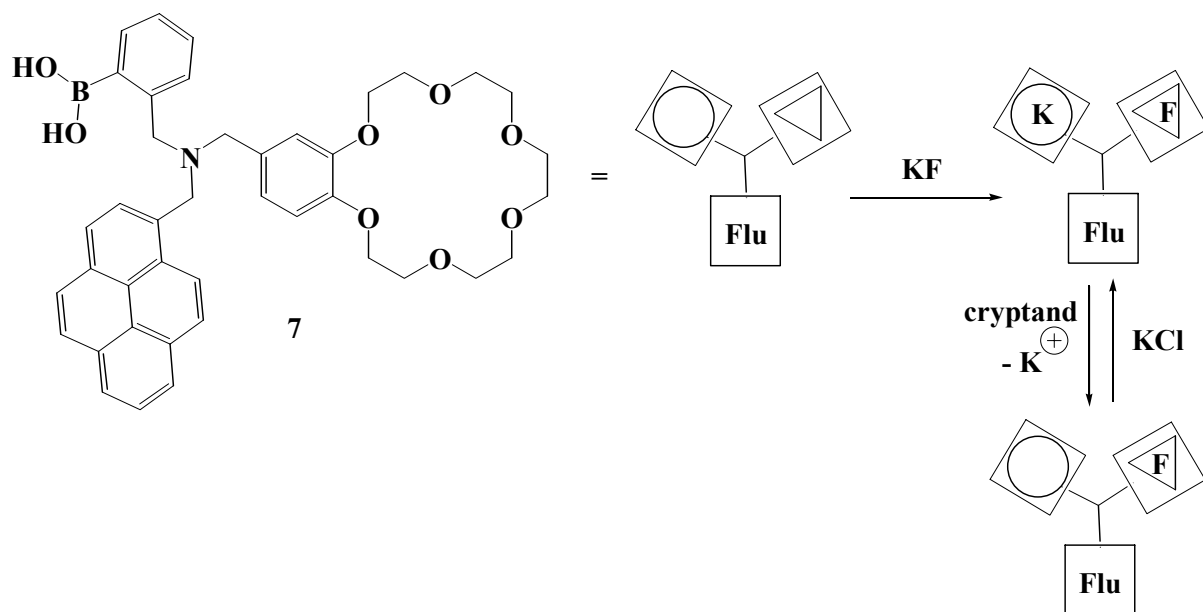
Charged sensor **8** shows the simultaneous presence of sodium and phosphate with an increased fluorescence signal in the manner of photoionic AND logic gate.[16]
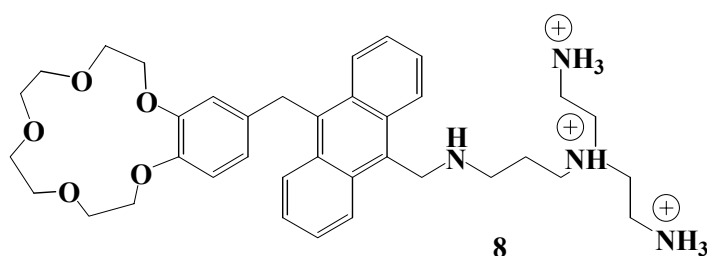
The presence in the molecule of two complexating centers is necessary but no sufficient antecedent for creation of heteroditopic receptor. It has been found that for spontaneous binding a cation and an anion the molecule requires an addition modification by the fragment that would fix the complexation centers in space. Ferrocene proved to be the most appropriate spacer; this was used for the synthesis of selective receptor for potassium fluoride **9**. A ferrocene-base receptor containing a urea and a crown ether fragments shows a remarkable color switching (*ON-and-OFF*) function induced by cation and anion recognition.[17]
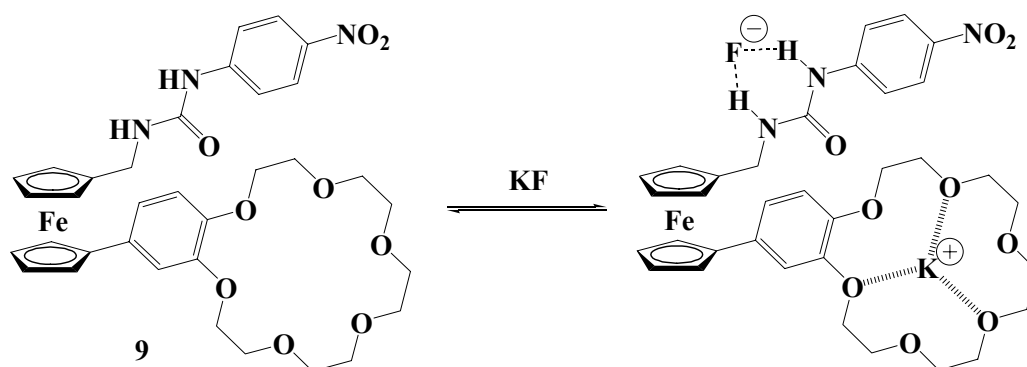
It has been shown that this system can be effectively used for the development of optical devices.[18]
Ferrocene-linked receptor **10** containing two crown ether units demonstrates that potassium cations can be electrochemically detected only in the presence of hydrophosphate anion.[19]
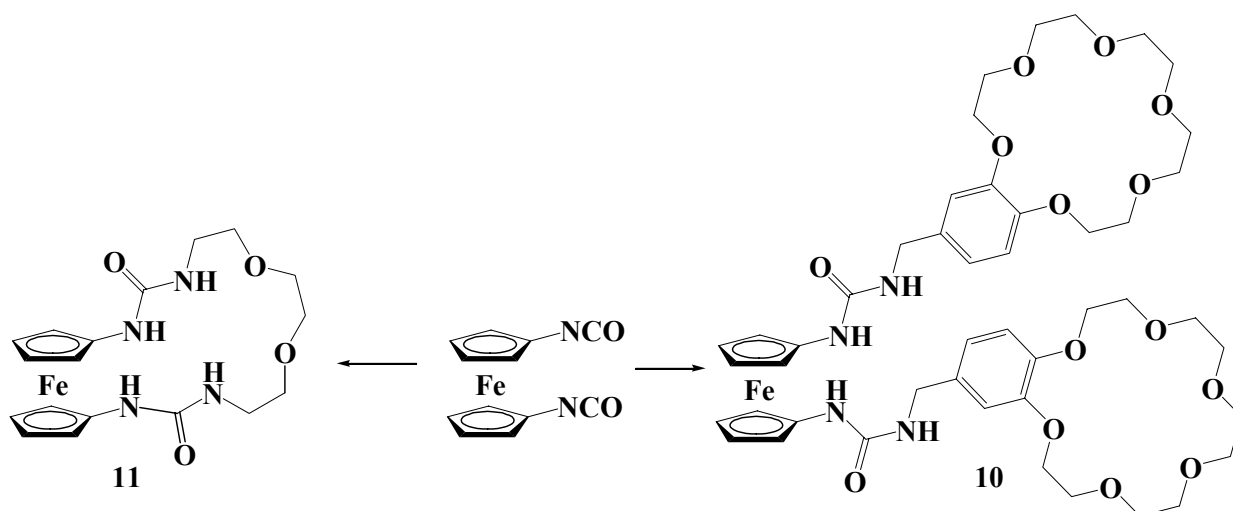

A similar ferrocene containing ligand **11**, in which the two urea groups are part of macrocyclic framework, is a selective electrochemical sensor for lithium cation in the presence of another alkaline metal cation. In this case association constant decreasing in the sequence: $H_2PO_4^-$ (K_{ass} = $3.7 \cdot 10^5$ M^{-1}) > AcO^- (K_{ass} = $1.3 \cdot 10^5$ M^{-1}) > F^- (K_{ass} = $3.9 \cdot 10^3$ M^{-1}).[19]

The heteroditopic receptor containing a crown ether and ferrocence-amide groups in the presence of Na^+ shows positive co-operative binding towards Br^- with the binding affinity K_{ass} = 16,096 M^{-1}. It should be noted that this ligand demonstrates a switched-on binding for Br^- in the presence of Na^+ and a switched-off binding in the absence of Na^+.[20]

Ligand **12** is able to interact with alkaline metal cations to bind two sodium cations or form sandwich-type complex with potassium cation. However, in attempt to trap anions in the presence of potassium cation, this compound acts only as cation receptor. But in the presence of sodium cation receptor **12** acts as heteroditopic.[21]

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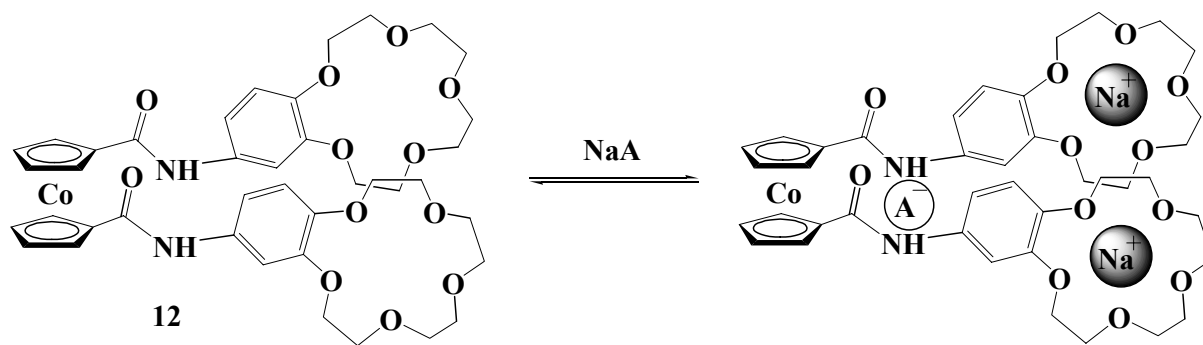
Another way to fixation of cation and anion-binding sites in space is introduction of ruthenium (II)- and rhenium(I)-bipyridyl fragments in the molecule. Heterotopic ruthenium (II)- and rhenium(I)-bipyridyl-bis(benzocrown ether) receptors **13** and **14** selectively bind KH_2PO_4 (K_{ass} = 205 M^{-1}) in the presence of chloride anion (K_{ass} = 55 M^{-1}).[22]

**13**   **14**
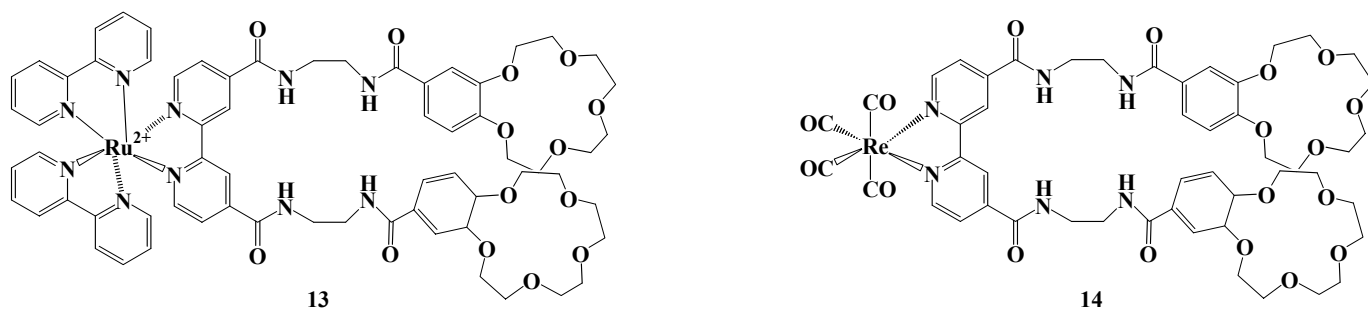
Binding of NaH_2PO_4 and KH_2PO_4 by crown-linked receptors, containing UO_2, has been described.[23,24] In these cases ditopic receptor **15** binds the potassium cation between the crown ethers substituents while amido center can coordinate with dihydrophosphate anion.


15
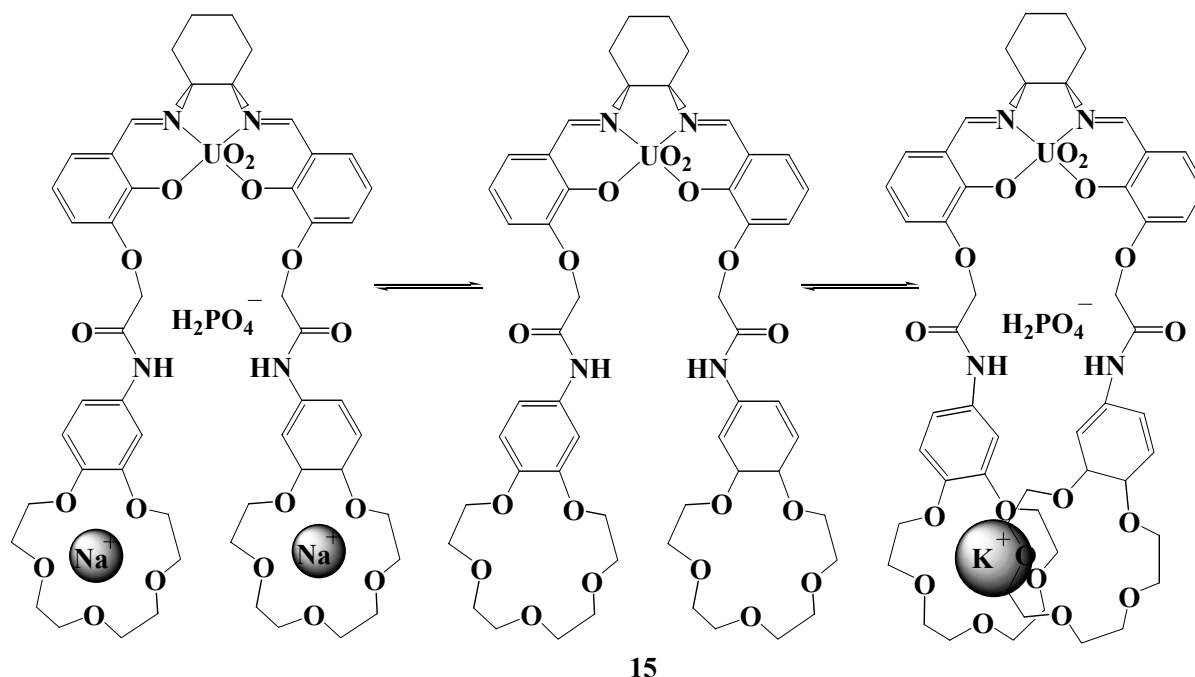
It should be noted that CsF can be bound by the same ligand, not containing crown ether fragments.[25] In this case recognition of anion ensured by strong binding to the Lewis acidic uranyl center in the equatorial plane of the uranium, whereas cation-π interactions are established between the aromatic sidearms and the cation partner of the ion pair.

A bicyclic receptor consisting of a dibenzo-18-crown-6 and a bridging 1,3-phenyldicarboxamide **16** is a straightforward heteroditopic receptor for recognizing and extraction of ion pairs of various alkali halides in organic solution.[26,27] This transport system exhibit ion selectivity: that is for the constant anion, the cation selectivity order is K^+ ($K_{ass} = 470$ M^{-1}) > Na^+ ($K_{ass} = 410$ M^{-1}) > Li^+ ($K_{ass} = 120$ M^{-1}) > Cs^+, and for a constant cation, the anion transport selectivity order is I^- > Br^- > Cl^-.[28-30] In the presence of trigonal oxyanions such as AcO^- and NO_3^- receptor ability toward anions order is $AcO^- \approx NO_3^-$ > Cl^- > Br^- > I^-.[31,32]
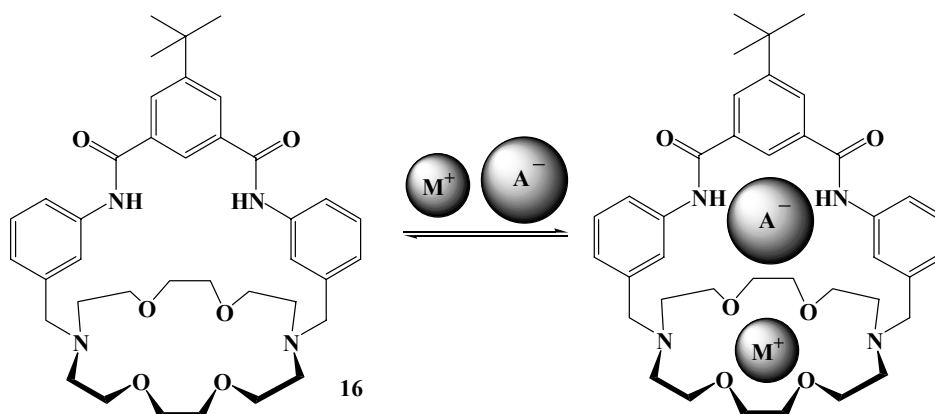
Coupling in on molecule two macrocyclic subunits, which are capable to chelate of different ions, yields increasing receptor ability. Thus, upper-rim functionalized calix[4]arene, containing amide linked bis-(benzo-15crown-5)ether in the presence on potassium cation selectively binds a benzoate anion forming 1:1 potassium cation sandwich complex **17** favoring anion complexation. It should be noted that complex with two sodium cations **18** is unable to cooperatively bind an anion.[33]
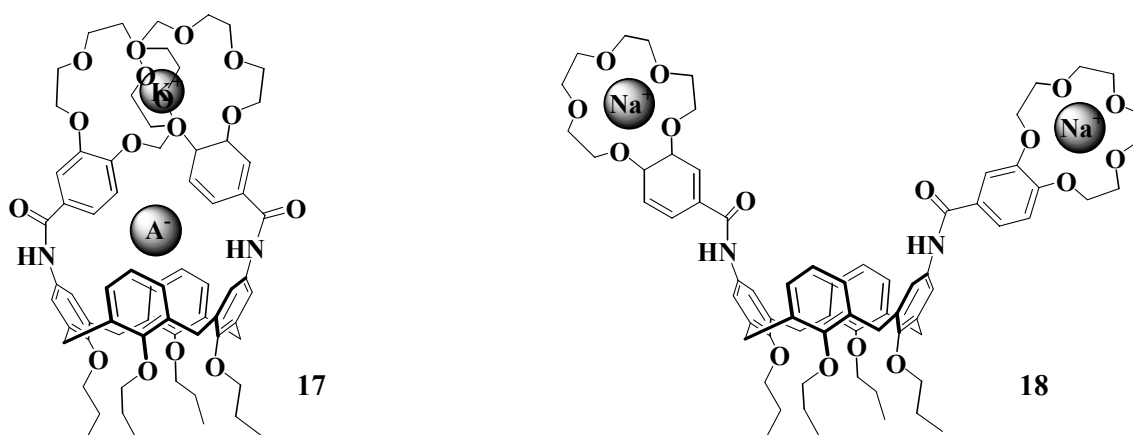
Introduction of benzocrown ethers at the lower rim of calix[4]arene results in the heterotopic receptor, in which oxygen atoms of   crown ether fragments coordinate the sodium cation, and the halide anion being bond simultaneously by the formation of H-bond with amide groups.[34]

1.2. CALIXARENE-BASED RECEPTORS

Immobilization of bridging podand to the lower rim of calix[4]arene matrix is an efficient tool to the synthesis of ditopic ligands and affords increasing a molecular cavity for the cation binding. Calix[4]arenes, modified in this way and containing urea moieties, upon addition of Na^+ demonstrate the binding ability **19** towards $H_2PO_4^-$ increased due to ion-pair enhancement.[35] Calix[4]arene **20** being in 1,3-alternate conformation is able to selective extraction of potassium halide. In this case association constant decreasing in the sequence: KCl (K_{ass} = 5420 M^{-1}) > KBr (K_{ass} = 1550 M^{-1}) > KI (K_{ass} = 880 M^{-1}).[36]
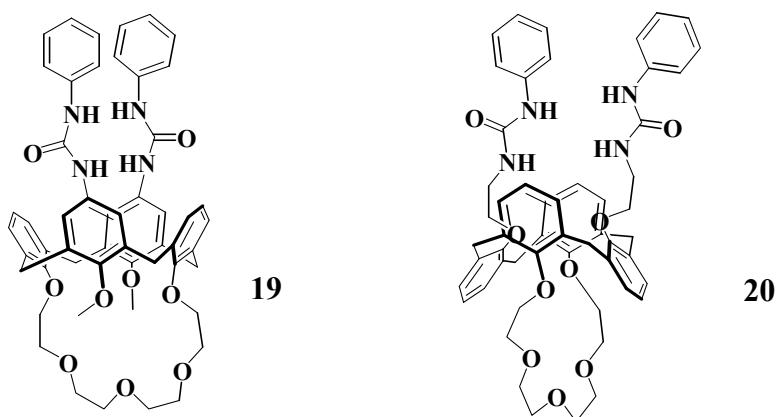

In the presence of potassium acetate the heteroditopic calix[4]arene receptor **21** in the 1,3-alternate structure and bearing two pentafluorophenyl amide groups as anion binders and crown-5 polyether for cation complexation, self-assembles in an unexpected 2:2:2 (calixarene : cation : anion) supramolecular structure, as shown in the scheme.[37]
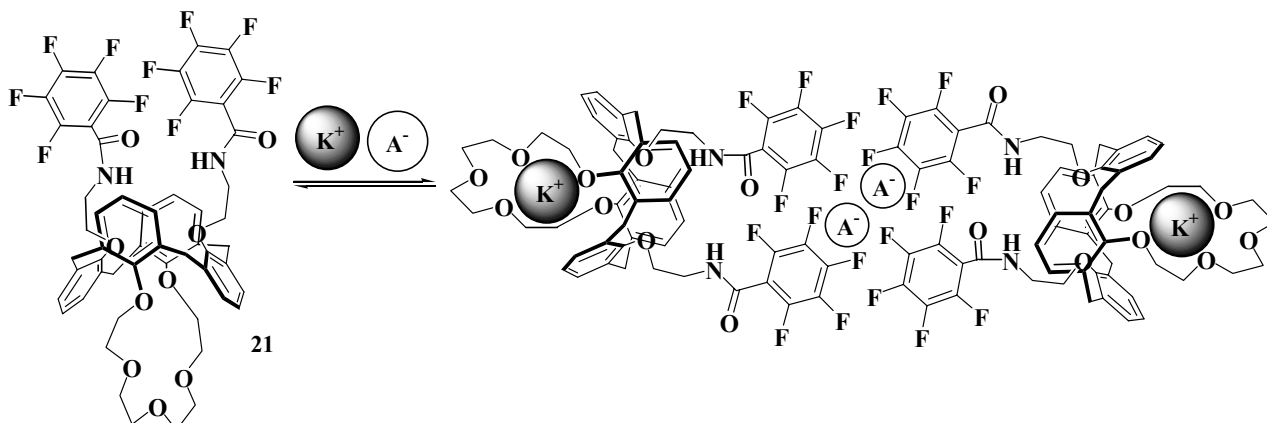
A ditopic receptor **22** comprised of a calix[4]semitube for cation recognition, and urea functionality for anion complexating displays a remarkable selectivity and fast kinetics of complexation for potassium cation over all other Group I metal cation and cooperative binding halide and acetate anions as shown in the table 1.[38]

Table 1. Stability constant (M^{-1}) data for the complexes of 22.
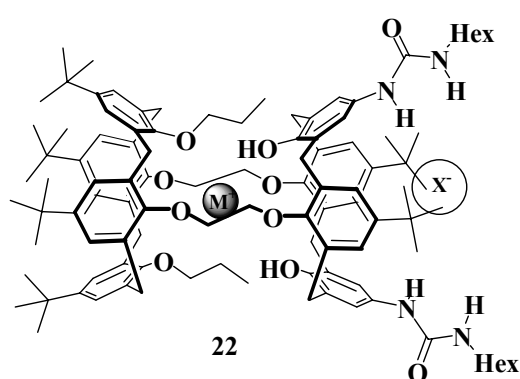
X^-	None	Na^+	K^+
Cl^-	60	-	>730
Br^-	20	620	550
I^-	15	280	310
AcO^-	110	-	710

Replacement of ureido group into thiourea fragment makes it possible to synthesize a selective receptor for CsCl.[39]

A calix[4]arene ditopic receptor **23** containing of bridging polyfunctional fragment with thiourea and amide moieties in an absence of Na^+ binds acetate anion (K_{ass} = 11000 M^{-1}) in preference to diphenylphosphate (K_{ass} = 1800 M^{-1}), but in the presence of sodium cation, the selectivity is reversed and the receptor, instead, binds diphenylphosphate (K_{ass} = 2200 M^{-1}), but not acetate, which preferentially forms a salt ion-pair in free solution.[40]
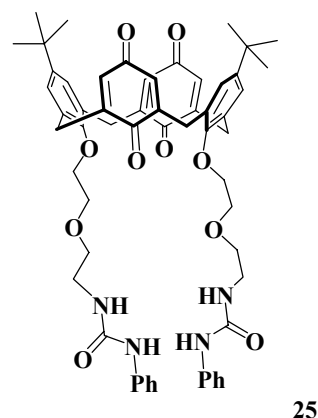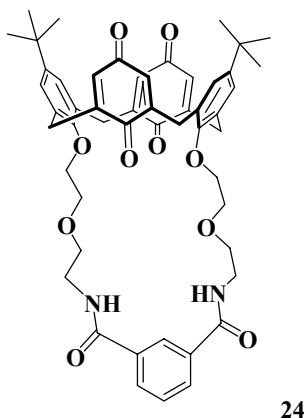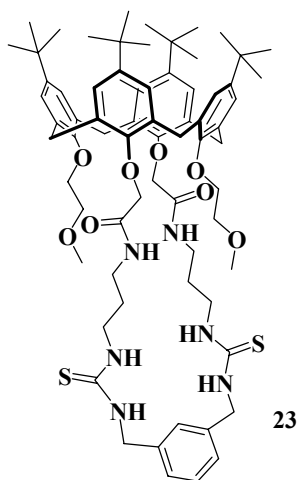
A heteroditopic calix[4]diquinone receptor **24** capable of binding an anion and a cation simultaneously in a cooperative fashion is shown only to recognize halide ions in a presence of a suitable cationic guest species.[41] Open-chain analogue of **24** – calixbiquinone **25** demonstrates selective receptor ability towards NaCl (K_{ass} = 2200 M^{-1}) over NH$_4$Cl.[42]

tert-Butylcalix[4]arene **26** containing the same substituents at the lower rim is a good receptor for alkali halides as shown in the table 2. The best results are obtained for NaCl, which can be explained a convenient conformation for complexation of these species.[43]

Table 2.   Stability constant (M^{-1}) data for the complexes of 26.
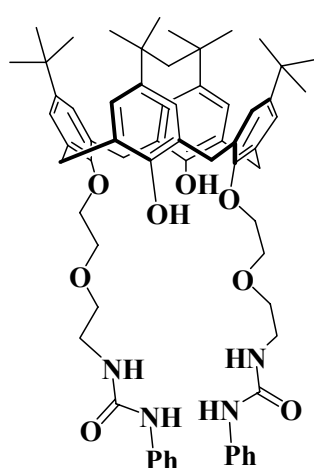
Cation	Anion	K, M^{-1}
-	Cl$^-$	624
Na$^+$	Cl$^-$	2020
Li$^+$	Cl$^-$	1600
-	Br$^-$	225
Na$^+$	Br$^-$	1620
Li$^+$	Br$^-$	704
-	I$^-$	24
Na$^+$	I$^-$	616
Li$^+$	I$^-$	461

26

Ditopic receptors **27** were synthesized by introducing of (thio)urea units at the upper rim of calixarene sodium-selective tetramide ligand in the cone conformation. They are able to complex simultaneously sodium cation at the lower rim and anion at the upper rim which greatly improves the solubility of sodium carboxylates in apolar solvents. Stability constant orders is AcO$^-$ (1200 M^{-1}) > benzoate (1100 M^{-1}) > propionate (1000 M^{-1}) > isobutyrate (800 M^{-1}).[44] Addition of one more ureido group makes it possible to increase a solubility of sodium halide in CHCl$_3$.[45]
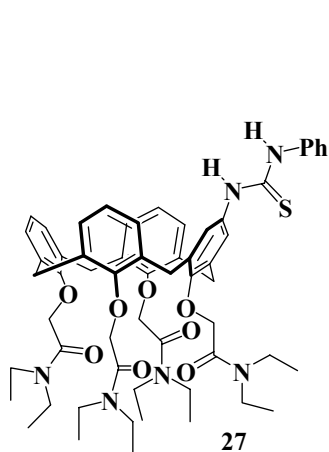
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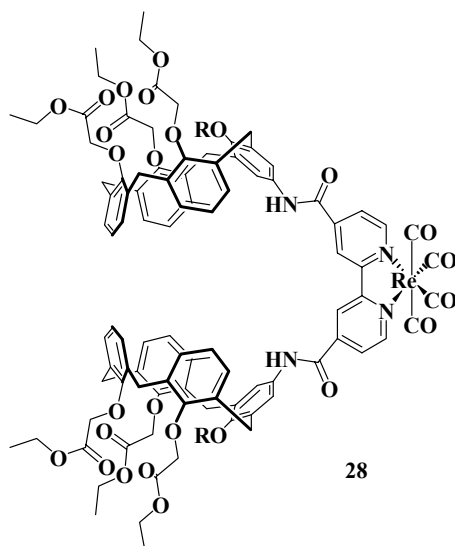
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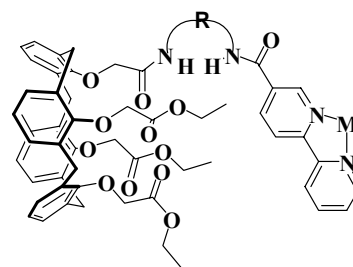
29

M = Re(CO)$_2$Cl or (biPy)$_2$Ru^{2+}(PF$_6^-$)$_2$

Sometimes recognition of ion pair occurs by interaction with dimers. Thus, calix[4]arene guanosine forms a dimer in water-saturated $CHCl_3$, extracting alkali halides from aqueous solution into organic solvent.[46]

Rhenium and ruthenium complexes **28** and **29** may be applicable for the simultaneous transfer cation and anion through lipophilic membrane.[39] These heterotopic ligands containing Re(I) and Ru(III)-bipyrodylamide fragments connected by flexible spacer to calixarene proved to be specific for ion pair containing Li^+, Na^+, Br^- and I^- ions. NMR titration showed selective binding of lithium bromide (K_{ass} = 1260 M^{-1}).[47] There are examples of applying such compounds for the simultaneous binding of NaI (K_{ass} = 320 M^{-1}) over KI (K_{ass} = 40 M^{-1}).[48,49]

1.3. RECOGNITION OF SALTS OF ALKALINE-EARTH METALS

There are few examples, devoted complexation of salts of alkaline-earth metals. 12-Crown-4 ether **30** modified with pyrido[1',2':1,2]imidazo[4,5-*b*]pyrazine exhibits complexing properties unusual for the compounds with this size of the molecular cavity. Using NMR-spectroscopy, it has been shown that these compounds effectively reacts with $Ba(SCN)_2$ giving rise to a stable complex (log K_{ass} = 3.98).[50]
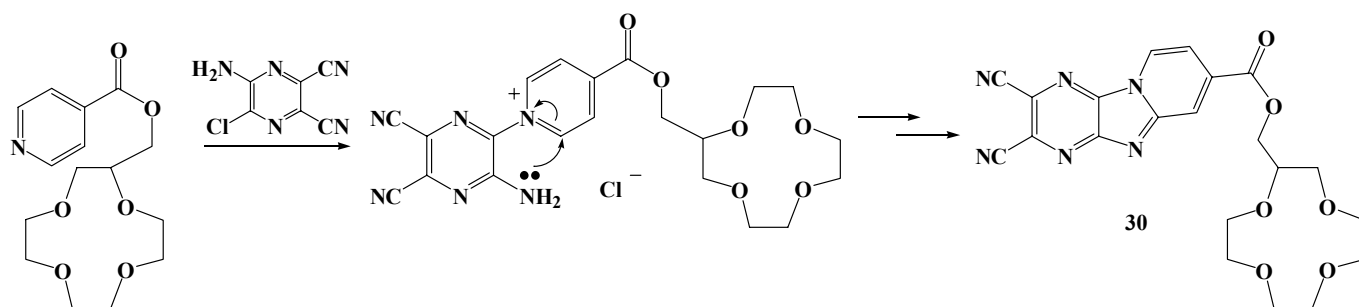
Ligand **31** is capable to complexation of Mg^{2+} and Ca^{2+} to yield stable complexes, which are demonstrated to selectivity bind HSO_4^- (or $H_2PO_4^-$) over other anions.[51]
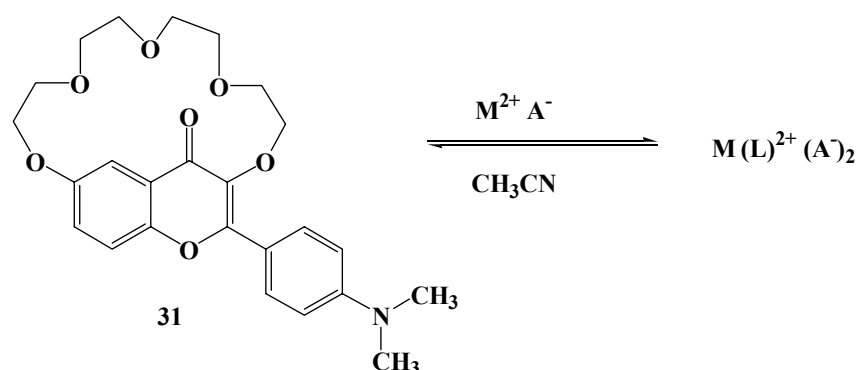
2. SYNTHESIS OF LIGANDS FOR BINDING AMMONIUM SALTS AND AMINO ACIDS

Similarity of ammonium cation to potassium cation due to proximal values of their ionic radius makes it possible to suppose that the principles and structural units, applying by the creation of potassium cation receptors will be used by design of heterotopic receptors for ammonium salts.

Indeed, in some cases crown ethers with appropriate cavity,[52,53] crown-modified calixarene with anion-binding sites,[8,21, 54, 55] and ligands, containing UO_2 fragment[56] are widely used as ammonium salts ligands. The last-mentioned receptors **32** demonstrate a different binding ability toward tetraalkylammonium chlorides in depends on substituent in aromatic ring as shown in the table 3.

Table 3. Association constant (M^{-1}) data for the complexes of 32
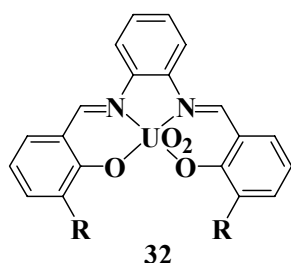
R	NBu_4Cl	NMe_4Cl
H	5600	1100
OCH_2Ph	23500	14000
OCH_2-naphthyl	24000	29000

MoO_2 also can be efficiently used as coordinating center by design of heteroditopic receptor, able to selective binding of NBu_4NO_3.[57]

Ligand **33**, characterized of two binding sites: a rapid calix[4]arene and sidearm, inserted at this rim, is able to simultaneously form strong hydrogen bonds with anion and complex ammonium cation. Stability constants decreasing in the sequence: CF_3COO^- (13000 M^{-1}) > AcO^- (5000 M^{-1}) > Cl^- (3800 M^{-1}) > TsO^- (700 M^{-1}).[58-60]
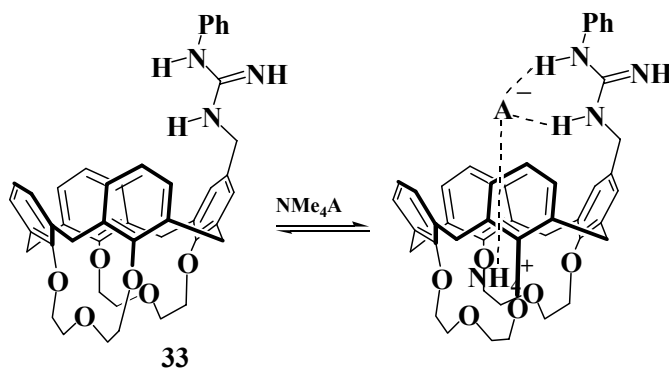
Functionalized calixarenes are widely used compounds for complexation and separation of amines, amino acids and peptides.[61] Thus, calixarene **34** in 1,3-alternate conformation binds a dicarboxylate anion in ditopic manner cooperatively with tetrabutylammonium cation. Binding constants (M^{-1}) in MeCN increases in oder: Br^- ($K = 646$) < Cl^- ($K = 1780$) < NO_3^- ($K = 3090$) < AcO^- ($K = 9550$) << Malonate ($K = 58800$).[62]

34
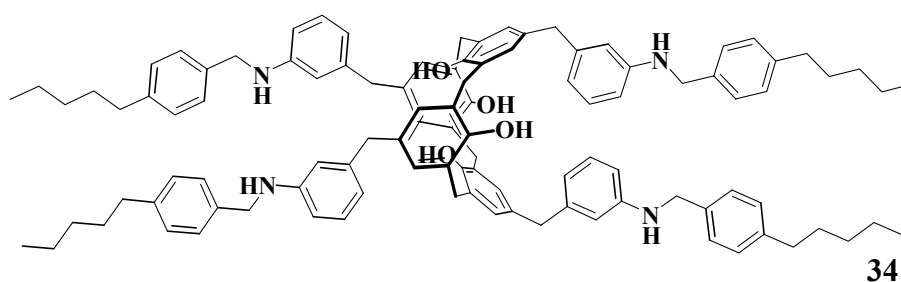
There are few examples of heteroditopic ligands based on the resorcinarene matrix. Thus, resorcinarene **35** takes part in the self-assembling process to yield dimeric capsules encapsulating small tetraalkylammonium cations. It has been indicated preference of tetramethyl ammonium cation over tetraethyl and especially tetrabutylammonium cations. All capsules form H-bonds with the solvent and ammonium cation and spherical anion (chloride or bromide) binds between the lower rim alkyl chains.[63]

Ion pair recognition can be achieved based on the sum of both electrostatic and H-bonding interaction. Resorcinarenes **36**, modified by Mannich reaction, are able to bind tetramethylammonium chloride in this manner as shown in the scheme.[64]

35   **36**
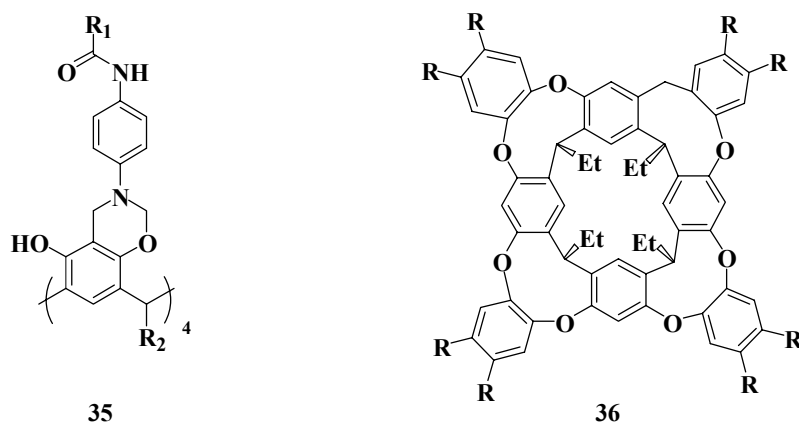
A Zn-salen-modified cavitand templates the catalytic formation of acetylcholine from choline and acetic anhydride due to the receptor ability of this compound toward ammonium cation and acetate anion.[65,66]
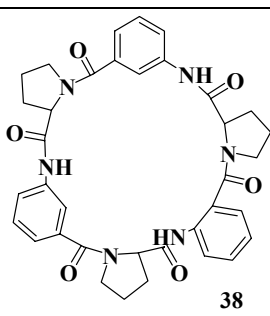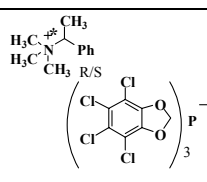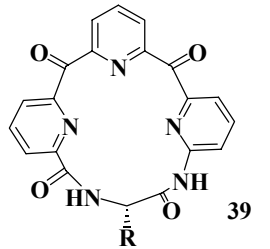
Crown-linked calixpyrroles and porphyrins can be profitably employed as heterotopic receptors due to the coupling of binding subunits of different nature in the one molecule. Thus, crowned expanded porphyrin and sapphyrin act as ligands for selective binding of NH_4F,[67] and benzo-15-crown-5-linked calixpyrrole is able to complex Bu_4NX (X = Cl, Br).[68]

A few examples of open-chain ligands for ammonium salts have been reported.[69]

A method for the development of heteroditopic receptors based on the cyclic peptides **38** has been proposed.[70] These compounds can be used for bind of ammonium iodide. In this case, the ligand is acquires a conformation similar to the cone calixarene conformation and, similarly, it binds cation through the

π-electrons of the carbonyl functions, whereas the iodide anion is bound owing to hydrogen bonding with the NH-groups of peptide. These compounds can be effectively applied not only for binding of ammonium salts but also to complex with amino acids (Table 4). A particularly interesting example is the binding of aromatic amino acids with high enantioselective recognition by an acyclic tritopic receptor **40** that contains a guanidinium a macrocyclic and naphthalinic unit for simultaneous interaction with, respectively, the carboxylate, the ammonium and the aromatic groups of the substrate.[71]
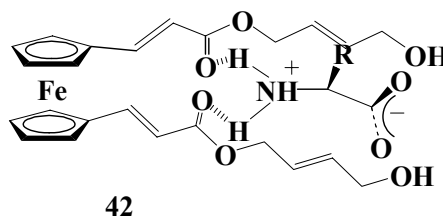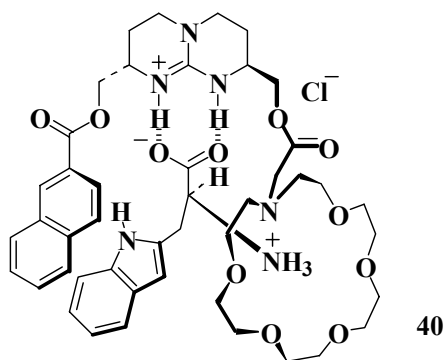
Table 4. Receptor ability of cyclic peptides.

Peptide structure	Guest	[Ref]
38	NBuI	[72]
	BTMA$^+$I$^-$	[67]
		[73]
39	NH$_4$$^+TsO^-$	[74]
	NH$_3$$^+$phenylalnine-OMe Cl$^-$ (Br$^-$)	

40

42

The coupling, within crown ether host molecule, of a fragment capable of complex formation with the NH$_3$$^+$ group and an organophosphorus moiety able to capture anion accounts for the use of compound **41** for dopamine transport.[75] The combination of a receptor fragment for hydrophobic (anionic) species with a prim ammonium group (the azacrown ether) is expected to yield a ditopic receptor for biogenic amines as shown below.[50,52]

A multiresponsible ferrocene receptor **42** having one backbone can be effectively used for the binding of amino acids.[76] Functionalization of ferrocene by amino-α-pyridyl moiety allows synthesize a selective receptor for L-phenylalanine.[77]

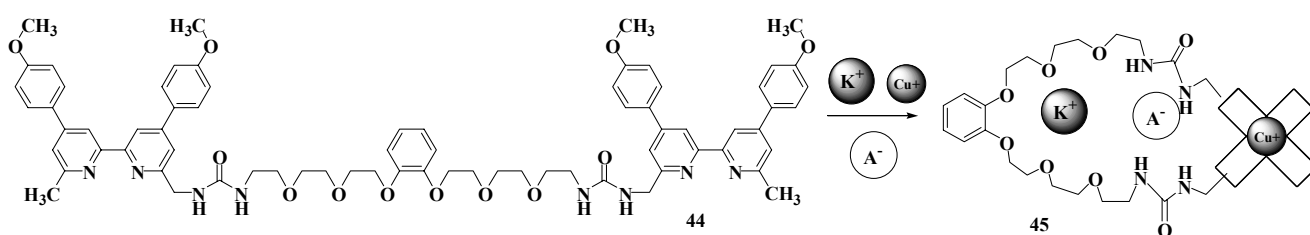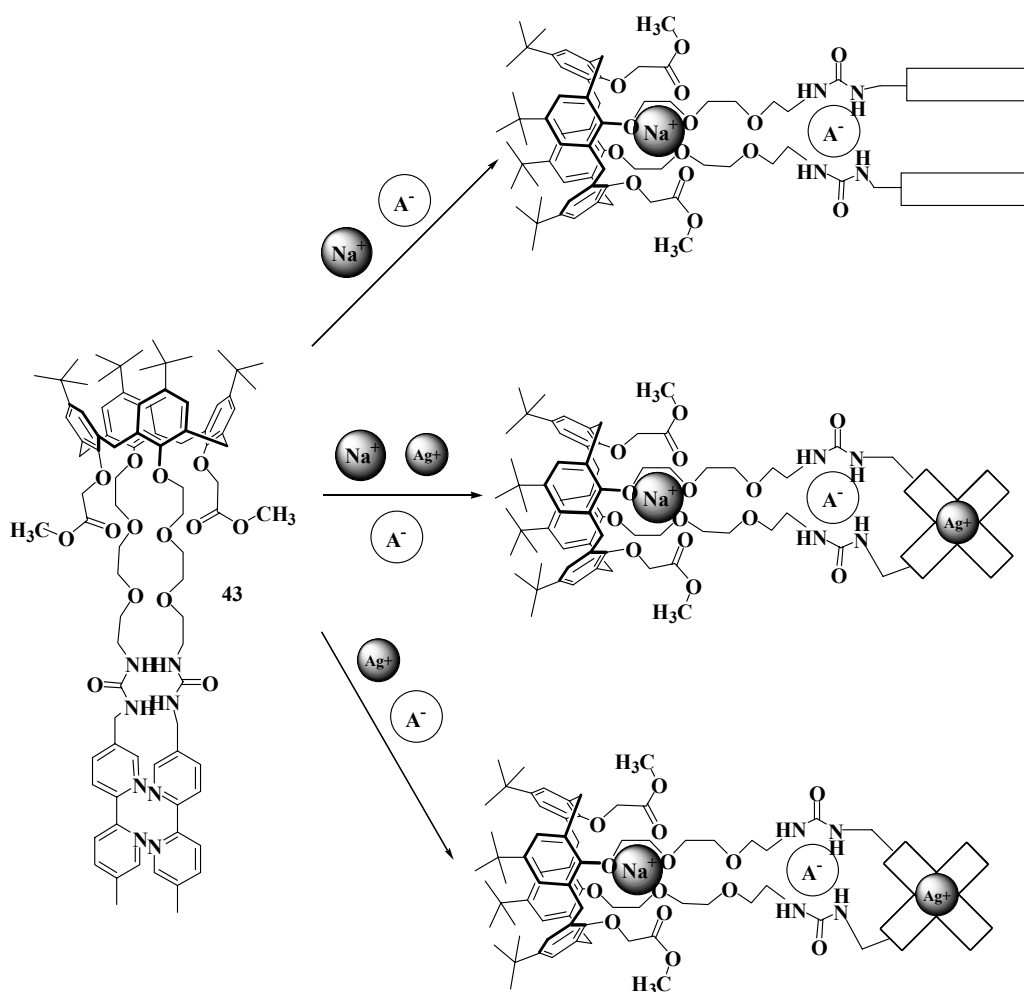It has been found that sapphyrin-lasalosid conjugates are a carrier for aromatic amino acid transport. A comparison of association constants has shown a selective binding of L-phenylalanine over L-triptophane and L-tyrosine.[78]

3.   MOLECULAR RECOGNITION OF SALTS OF TRANSITION METALS

There are some publication, devoted to the design of tritopic receptors, which are useful for complex some cations and anion. For example, tritopic receptor **43** containing of two ethers, two polyethers, two urea sites, and two bipyridyl units arranged on the calix[4]arene matrix can recognize Na^+ and Ag^+ simultaneously and quantitatively and capture an anionic guest.[79] Ability of this compound to bind anions including $CF_3SO_3^-$ and BF_4^- remarkably increases in stepwise manner using Na^+ and Ag^+ as effectors. The inhancement of the association constant eventually reaches factors of 1500 M^{-1} and 2000 M^{-1} for NO_3^- and $CF_3SO_3^-$ respectively in the presence of both Na^+ and Ag^+ compared free receptor or containing of either Na^+ or Ag^+ cation.

A tritopic receptor **44** has been prepared on the basis of pseudocrown ether modified by two urea units and two bipyridyl fragments. This compound is complexed with Cu(I) through bipyridyl groups to form closed structure **45**, whose cavity is suitable to recognition of potassium halides, receptor ability decreasing in sequence: $Cl^- \gg Br^- > I^-$.[80,81]

Due to a high binding ability of pyridyl fragments toward transition metal cation they are frequently used for design of heteroditopic receptors. Terpyridyl ligands **46** are involved in the formation of including compounds with transition metal cation and PF_6^- anion, which occurs in the outer sphere. The reaction of polypyridyl receptor **46** with $FeCl_2$, $RuCl_3$ and $Co(AcO)_2$ in the presence of NH_4PF_6 results in the stable hexafluorophosphates.[82,83]

An interesting example of the construction of supramolecular structures with simultaneous complexating of Fe^{3+} and Cl^- ions has been discovered. Ensamble **47** was obtained upon the template reaction between five tris(bipyridyl) ligands and $FeCl_3$.[84]

47

One of the most often used approach for design of ditopic receptors for salts of transition metals is a synthesis of compounds **48**. To key to the performance of these ligands is that the metal salt is bound to the zwitterionic form of the ligand generated by transfer of the phenolic protons from the cation-binding site to the pendant amine groups, thus creating a dipositive cavity wherein the anion is bound by a combination of electrostatic interactions and favorable hydrogen bonding. This zwitterionic transformation allows the formation of neutral assemblies, which can then be transported into a water-immiscible liquid in solvent extraction process, eqn. (1).

$$L + M^{n+} + A^{n-} \leftrightarrow MLA \qquad (1)$$
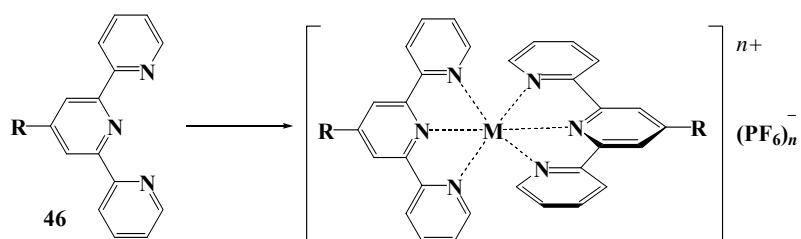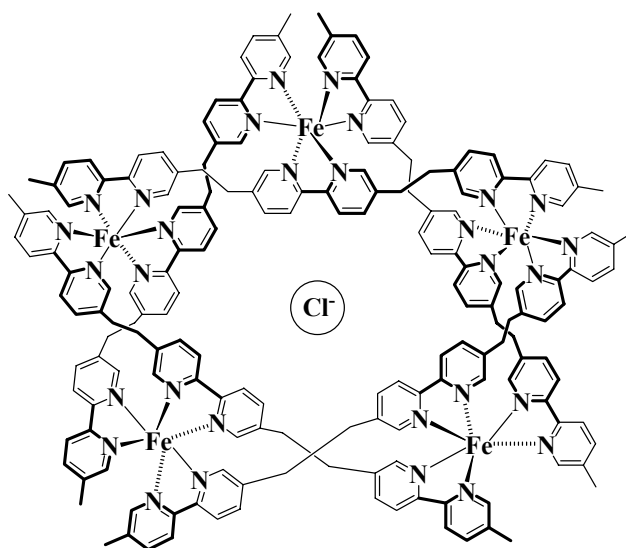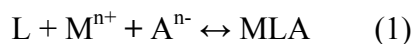
Another important feature of these zwitterionic ligands is their ditopic nature. In principle, the separation of cation and anion-binding sites should permit the sequential stripping of the cation and anion as shown in the scheme, recycling the ligand and generating a concentrated metal sulfate solution for electrowinning.
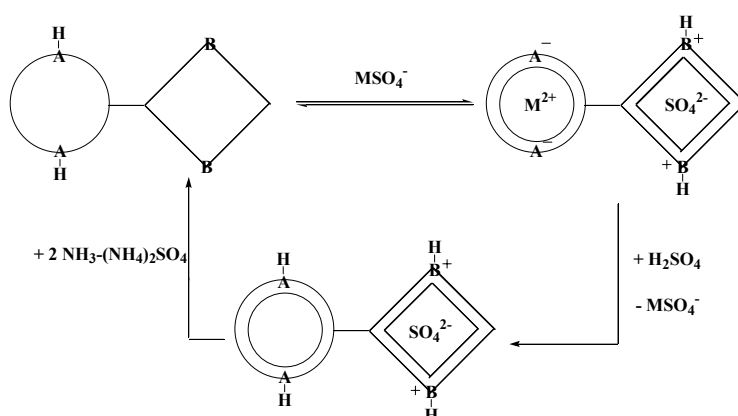
The main examples of such ditopic ligands are described below.
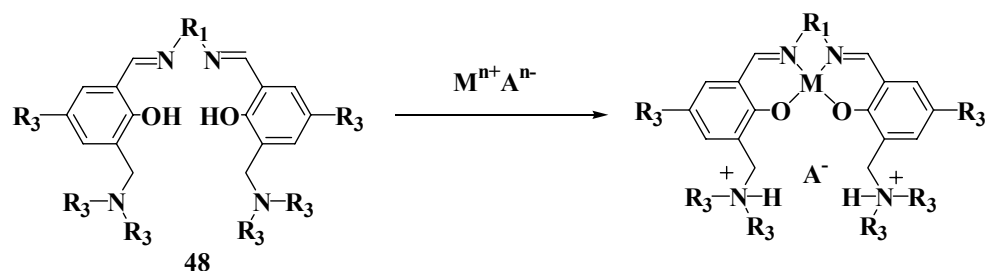
R^1	R^2	NR^3_2	Salt	[Ref]
$-CH_2-CH_2-$	t-Bu	morpholine	$NiSO_4$	[85-87]
		$n-C_6H_{13}$	$CuSO_4$	[88]
		piperidine	$NiSO_4$, $CuSO_4$, $ZnSO_4$	[86]
			$CuSO_4$	[89]
trans-Cyclohexyl	t-Bu	morpholine	$NiSO_4$, $CuSO_4$	[86, 87]
		hexyl, piperidine	$CuSO_4$	[88,90]
$o-C_6H_4$	C_9H_{19}	morpholine	$NiSO_4$, $CuSO_4$	[86,87]
	t-Bu	hexyl	$CuSO_4$	[88,90]
	Ph	piperidine	$CuSO_4$	[90]
2,2'-biphenyl	tBu	$n-C_6H_{13}$	$CuSO_4$	[88]
		piperidine	$NiSO_4$, $CuSO_4$, $ZnSO_4$	[86]
	C_9H_{19}	piperidine	$NiSO_4$, $CuSO_4$, $ZnSO_4$	[86]

Complexes of the same ligands containing additional armsubstituent were formed almost immediately upon mixing alcoholic solution of the ligand and nickel (II) sulfate and consist of 1:1:1 metal : ligand : sulfate assemblies, which exhibit characteristic absorbencies for the sulfate ion in the IR spectra, elemental analysis data and FAB mass spectrometry.[91]

The presence of amino group is not necessary for creation of ditopic receptors. Thus, compound **49** simultaneously bind Ni^{2+} or Pd^{2+} cation and F^- anion due to formation of three short and one long O-H···F bonds.[92]
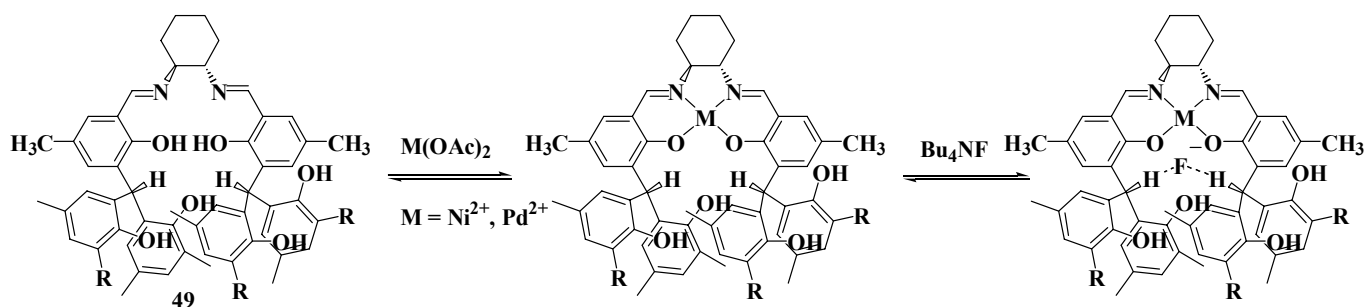
The open-chain compound **50** is able to cooperatively bind Cu^{2+} cation and HPO_4^{2-} anion. Stability constant orders is HPO_4^{2-} $(2,5 \cdot 10^4 \ M^{-1})$ = $HAsO_4^{2-}$ $(2,5 \cdot 10^4 \ M^{-1})$ > ReO_4^- $(2 \cdot 10^3 \ M^{-1})$ >> AcO^- $(900 \ M^{-1})$ > NO_3^- $(20 \ M^{-1})$.[93]
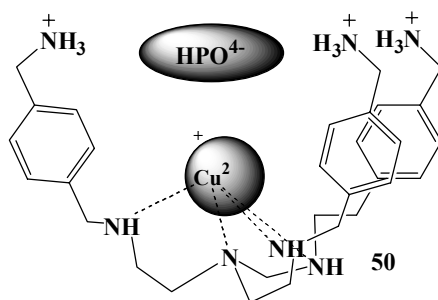
Crown ethers are also frequently used as ditopic receptors for transition metal salts. Thus, azathioethers incorporating acylurea functionalized pendant arms **51** and **52** are capable of simultaneously binding the cationic (Pd^{2+}, Cu^{2+}, Ag^+) and anionic (Cl^-, NO_3^-) species.[94]
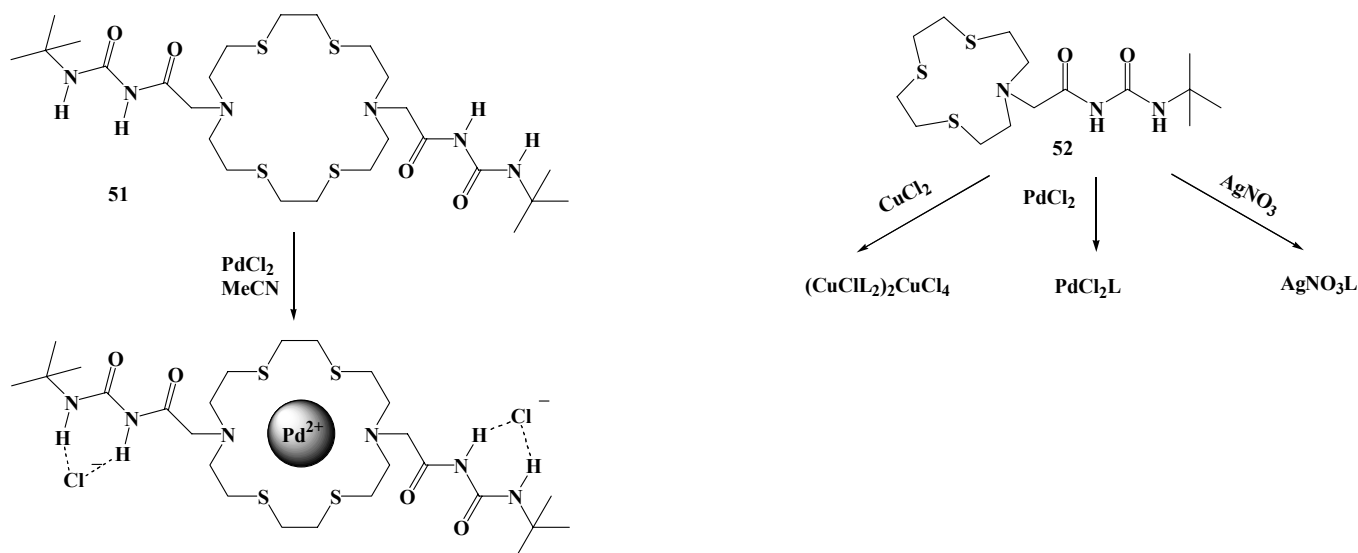
The heteroditopic receptor **53** is firmly included an Ag$^+$ into the azathio ether and establish selective H-bond interaction with anion at covalently linked urea/thiourea subunits. In the case of urea substituted crown ether, anion binding ability orders is AcO$^-$ > H$_2$PO$_4^-$ > HSO$_4^-$ > NO$_2^-$ > NO$_3^-$. Ag$^+$ coordination to the S atom of the thiourea derivative promotes the formation of unusually stable H-bonds complexes with Cl$^-$ and Br$^-$.[95]
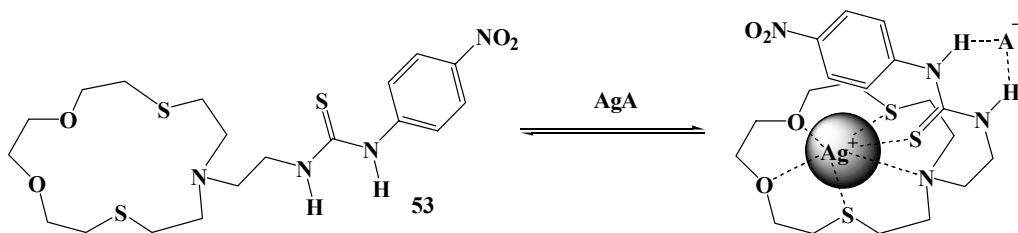
A cooperative effect between cation and anion-binding sites is of great interest given the relative simplicity of the ligand design. Thus, receptor **54** is a highly effective to bind Ag$^+$ salts, also the effect of different anions on extraction ability is probably related to the solubility of resulted metal salt complex in organic phase.[96]
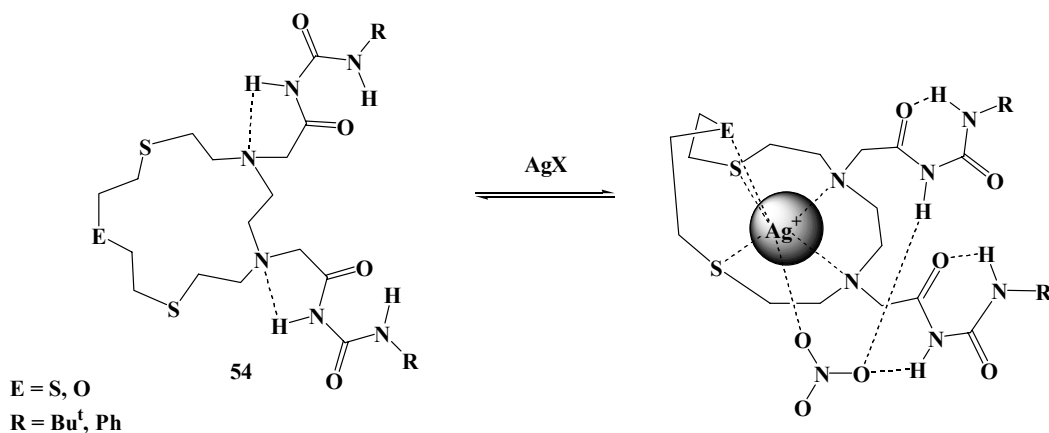
The last example demonstrates a possibility to use calix[4]pyrrole-capped metalloporphyrins as ditopic receptors. These molecules **55** being a potential host for anionic guests are able to strong binding with fluorine anion in organic solvent over other halides.[97,98]
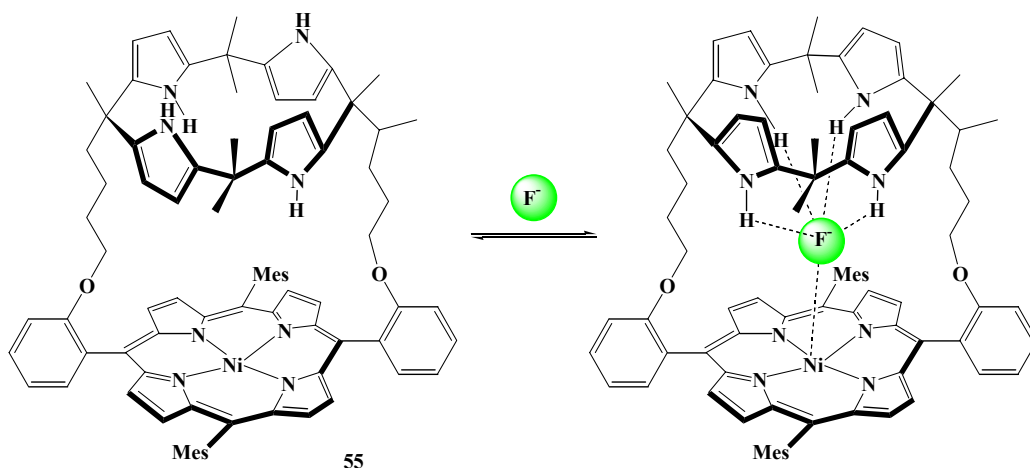
CONCLUSION

The review summarizes the data of synthesis and receptor ability of bifunctional ligands. The publications devoted to the design of heteroditopic ligands for the recognition of ion pairs and zwitterionic species are analyzed. All the described syntheses adhere to a general strategy which implies the design of the "host" molecule containing of both cation- and anion-binding sites.

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