Supramolecular Chemistry

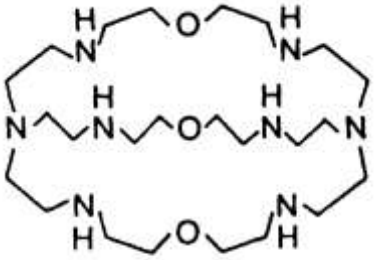
Dinuclear and Polynuclear Metal Ion Cryptates

Polytopic receptor: Macropolycyclic ligands of coreceptor type incorporating two or more binding subunits for metal ions, form dinuclear or polynuclear cryptates in which the distance and arrangement of the cations held inside the molecular cavity may be controlled through ligand design. They allow the study of cation-cation interactions (magnetic coupling, electron transfer, redox, and photochemical properties) as well as the inclusion of bridging substrates to yield cascade complexes, which are of interest for bioinorganic modelling and multicentre-multielectron catalysis. Depending on the nature and number of binding subunits and of connecting bridges used as building blocks, a variety of macropolycyclic structures may be envisaged.

Ditopic ligands that bind 2 metal ions, tritopic (3 metals or substrate) or tetratopic metal ion receptors (bind 4 substrate).

*** Bold** number represents the structure numbers.

Cascade type dinuclear copper(ll) cryptates of macrocyclic ligands (**See the structures**; e.g., **38**) or macrobicyclic ligands (e.g., **33**) containing bridging groups **(imidazolato, hydroxo, or azido**) may display antiferromagnetic or ferromagnetic coupling between the ions and bear relation to dinuclear sites of copper proteins (see, for instance, **42**). Macrobicyclic hexaimine structures, produced in a one-step multiple condensation reaction, form dinuclear and trinuclear cryptates such as the bis-Cu(l) **43,** tris-Ag(l) **44** and strongly coupled dicopper complexes.



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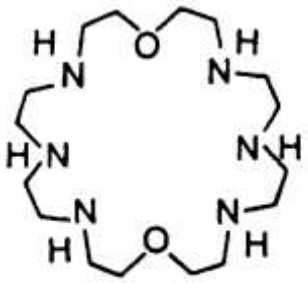

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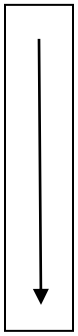

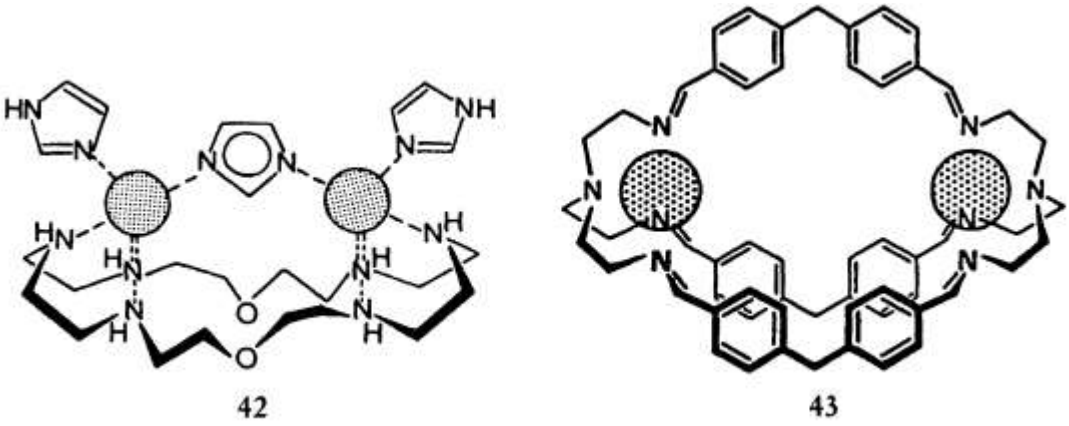

42 43

Dinuclear sites of copper proteins (**42**) Dinuclear cryptate; bis-Cu(l) (**43**)

Figure 1. Dinuclear Cryptates

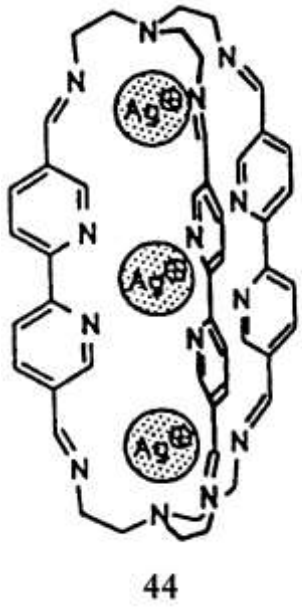

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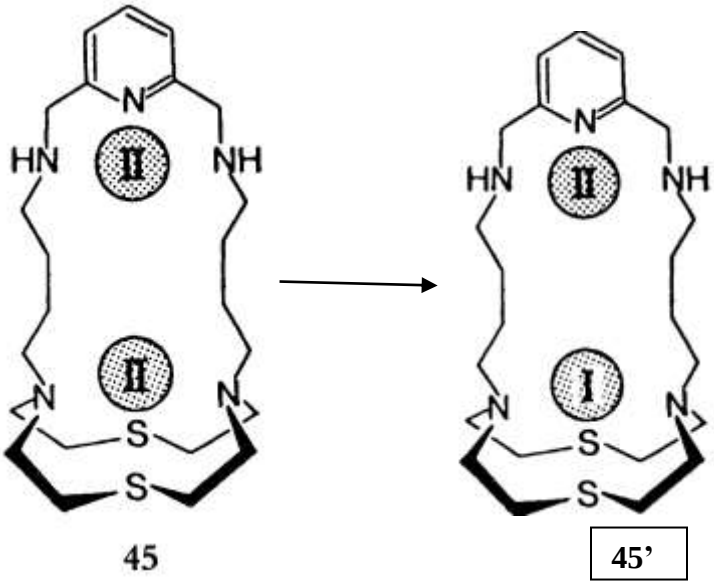
Figure 2. Trinuclear Cryptates; tris-Ag(l) (**44**)

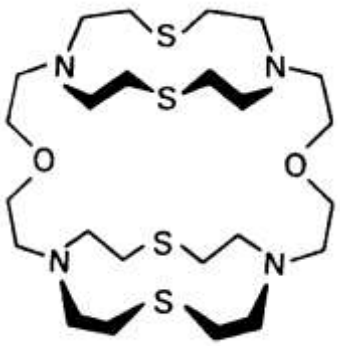


45 **45'**

Figure 3. bis-Cu(ll) cryptate (**45**) and mixed valence Cu(l)-Cu(ll) complex (**45')**

dissymmetric or asymmetric macrobicyclic: Lateral macrobicycles are dissymmetric by design; thus, monoelectronic reduction of the Cu(ll) ion bound to the N_2S_2 macrocyclic subunit in the bis-Cu(ll) cryptate (**45**), gives a mixed valence Cu(l)-Cu(ll) complex(**45**').

Macrotricycle **46** forms a dinuclear Cu(ll) cryptate that acts as a dielectronic receptor and exchanges two electrons in a single electrochemical wave. Complexes of type **47** combine a redox centre and a Lewis acid centre for the potential activation of a bound substrate.



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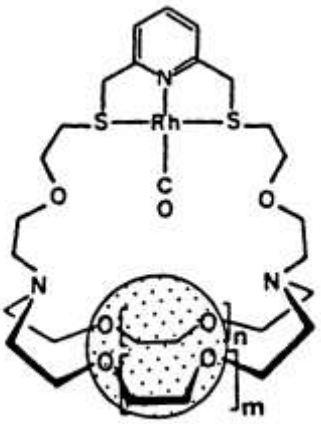

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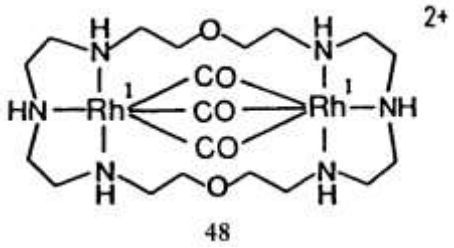
Polytopic receptors have the ability to assemble metal ions and bridging species within their molecular cavity to form *"cluster cryptates"*. The bis-chelating macrocycle **38** gives complex **48**, in which a triply bridged $[Rh(CO)_3Rh]^{2+}$ unit is built inside the ligand cavity. A trinuclear complex **49** containing a [tris-Cu(ll), bis /μ_3- hydroxo] group in the cavity is formed by a tritopic, tris-ethylene diamine macrocyclic ligand.



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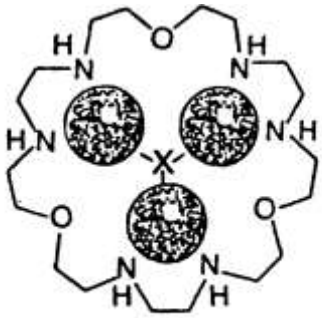

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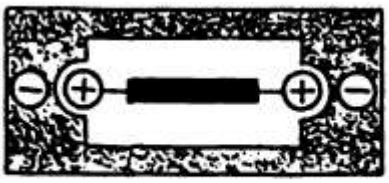
Figure 3. Triply bridged $[Rh(CO)_3Rh]^{2+}$**(48)** and [tris-Cu(ll), bis /μ_3- hydroxo] **(49)**

Linear Recognition of Molecular Length by Ditopic Coreceptors

Receptor molecules possessing two binding subunits located at the two poles of the structure will complex preferentially substrates bearing two appropriate functional groups at a distance compatible with the separation of the subunits. This distance complementarity amounts to a recognition of molecular length of the substrate by the receptor. Such *linear recognition* by ditopic coreceptors has been achieved for both dicationic and binding modes illustrated in **50** and **51**.



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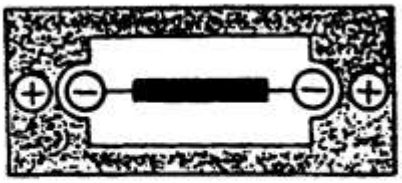

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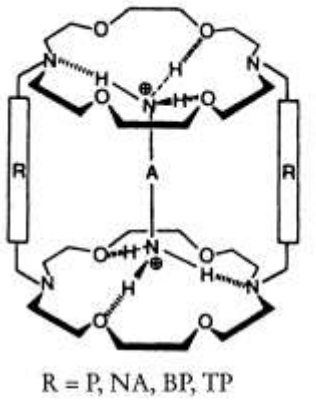
Incorporation of [18]-N_2O_4 macrocyclic subunits that bind -NH_3^+ groups into cylindrical macrotricyclic and macrotetracyclic structures yields ditopicco receptors that form molecular cryptates such as **52** with terminal diammoniumcations ^+H_3N-$(CH_2)_n$-NH_3^+. In the resulting supermolecules the substrate is located in the central molecular cavity and anchored by its two NH_3^+ groups in the macrocyclic binding sites, as shown by the crystal structure **53** of the receptor in **52**(R = NA) with its complementary substrate (A = $(CH_2)_5$). Changing the length of the bridges R in **52** modifies the binding selectivity in favor of the substrate of complementary length. Thus, complementarity in the supramolecular species expresses itself in both steric and dynamic fit. *Dianionic substrates*, such as the alkyl dicarboxylates ^-O_2C-$(CH_2)n$-CO_2^-, are bound with length discrimination by ditopic macrocycles such as **54**.



R = P, NA, BP, TP

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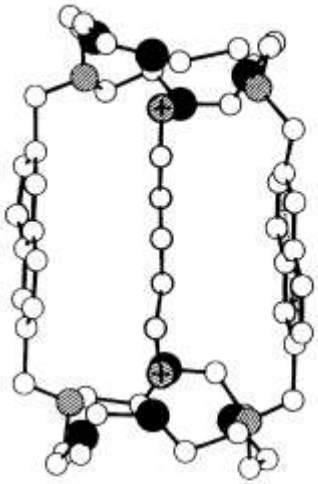

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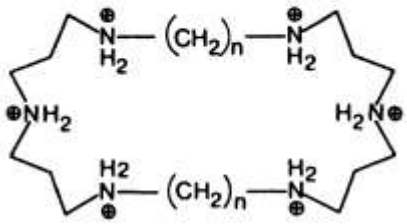

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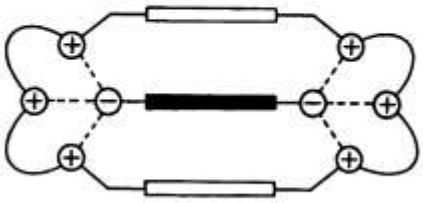

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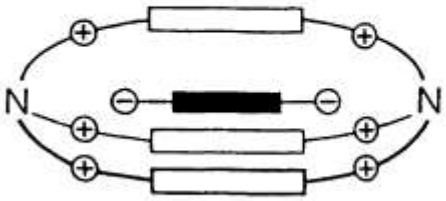
These coreceptors contain two triammonium groups as binding subunits interacting with the terminal carboxylate functions via a pattern schematically shown in **55**.

The crystal structure **57** of the strong and selective complex formed by the terephthalate dianion with a hexaprotonated macrobicyclic polyamine shows that it is a molecular cryptate **56** with the dianion tightly enclosed in the cavity and held by formation of three hydrogen bonds between each carboxylate and the ammonium groups. Both structures **53** and **57** illustrate nicely what supermolecules really are; they show two covalently built molecules bound to each other by a set of non-covalent interactions to form a well-defined novel entity of supramolecular nature.



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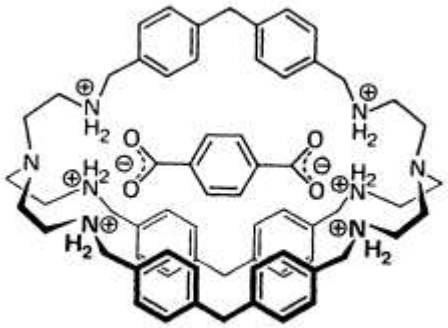

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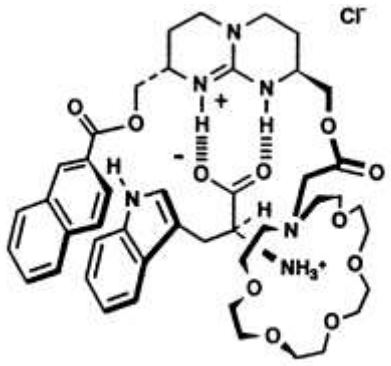
Acyclic and macrobicyclic hydrogen bonding receptors also bind dicarboxylic acids and dicarboxylates, a helicene-derived ligand effecting high diastereoselective recognition. Thus, for both the terminal diammonium and dicarboxylate substrates, selective binding by the appropriate receptors describes a linear recognition process based on length complementarity in a ditopic binding mode. Important biological species, such as poly amines, amino acid and peptide diamines, and dicarboxylates may also be bound selectively.

Heterotopic Coreceptors -Cyclophane Receptors Amphiphilic Receptors, Large Molecular Cages: Heterotopic receptors that may complex substrates by interacting simultaneously with cationic, anionic and neutral sites, making use of electrostatic and van der Waals forces as well as of donor-acceptor and solvophobic effects. Whereas homotopic coreceptors complex dicationic or dianionic substrates,

Heterotopic coreceptors may allow the binding of two different substrates, of ion pairs or of zwitterionic species. Enantioselective and diastereoselective molecular recognition is achieved by chiral coreceptors. A particularly interesting example of the latter is the binding of aromatic

amino acids with high enantioselective recognition by an acyclic tritopic receptor that contains a guanidinium, a macrocyclic and a naphthalenic unit for simultaneous interaction with, respectively, the carboxylate, the ammonium and the aromatic groups of the substrate (see structure **58**). Hydrogen bonding and stacking or ionic forces have been used for the recognition of amino acids and nucleotides, as well as of neutral heterocyclic molecules through interactions of base-pairing type.



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A short zwitterionic recognition sequence of much biological importance is the "signal" pep tide RGD (ArgGlyAsp); its binding to specific biological receptors by interaction through its guanidinium and carboxylate side chains plays a critical role in various processes involving cell adhesion.