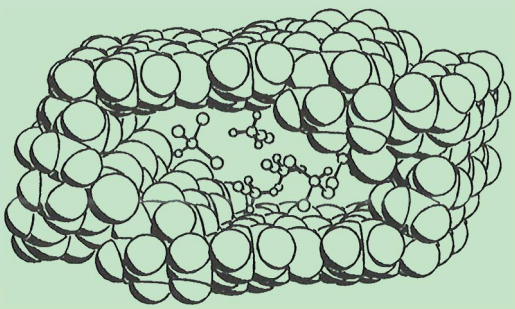
DEPARTMENT OF CHEMISTRY, UNIVERSITY OF JYVÄSKYLÄ
RESEARCH REPORT No. 55

SYNTHESIS AND STRUCTURAL STUDIES OF SOME SUPRAMOLECULAR COMPOUNDS

BY

JUHANI HUUSKONEN



Academic Dissertation
for the Degree of
Doctor of Philosophy

Jyväskylä, Finland 1995
ISBN 951–34–0649–0
ISSN 0357–346X

DEPARTMENT OF CHEMISTRY, UNIVERSITY OF JYVÄSKYLÄ
RESEARCH REPORT No. 55

SYNTHESIS AND STRUCTURAL STUDIES OF SOME SUPRAMOLECULAR COMPOUNDS

BY

JUHANI HUUSKONEN

Academic Dissertation
for the Degree of
Doctor of Philosophy

To be presented, by permission of the Faculty of Mathematics and Natural Sciences of the University of Jyväskylä, for public examination in Auditorium S-212, on November 24th, 1995, at 12 o'clock noon.

Jyväskylä, Finland
ISBN 951–34–0649–0
ISSN 0357–346X

URN:ISBN:978-951-39-9907-0
ISBN 978-951-39-9907-0 (PDF)
ISSN 0357-346X

Jyväskylän yliopisto, 2024

List of original publications

This thesis is based on the following original publications, which are referred to in the text by their Roman numerals.

I Rissanen, K., Huuskonen, J., Windscheif, P.-M., Vögtle, F., Self-assembly by co-ordination and strong hydrogen bonding. X-ray crystal structures of a dimeric trisodium complex of a new acidic complexing ligand and its dihydrate *Supramolecular Chem. 2* (1993) 247-250.
https://doi.org/10.1080/10610279308038323

II Rissanen, K., Huuskonen, J., Koskinen, A., $1^2,5^2,9^2,13^2$-Tetranitro-1,5,9,13(1,3)-tetrabenzena-3,7,11,15(1,4)-tetrapiperazinacyclohexadecaphane, a New Host Compound *J. Chem. Soc., Chem. Commun.* (1993) 771-772.
https://doi.org/10.1002/chin.199334200

III Rissanen, K., Breitenbach, J., Huuskonen, J., An Unusual Copper(I) Complex of a New Macrocyclic Ligand *J. Chem. Soc., Chem. Commun.* (1994) 1265-1266.
https://doi.org/10.1039/C39940001265

IV Huuskonen, J., Schulz, J., Kolehmainen, E., Rissanen, K., Photoresponsive Piperazine Macrocycles *Chem. Ber. 127* (1994) 2267-2272 .
https://doi.org/10.1002/cber.1491271127

V Huuskonen, J., Rissanen, K., Acetonitrile Inclusion Complexes of Piperazine-Based Macrocycles *Liebigs Ann.* (1995) 1611-1615.
https://doi.org/10.1002/jlac.1995199509224

VI Huuskonen, J., Schulz, J., Rissanen, K., Macrocyclic (1,3)- and (1,4)-Benzena-(1,4)-Piperazinacyclophanes *Liebigs Ann.* (1995) 1515-1519.
https://doi.org/10.1002/jlac.1995199508207

PREFACE

The present investigations were carried out in the Department of Chemistry, University of Jyväskylä from 1991 to 1995.

First of all, I wish to express my deepest gratitude to my supervisor, Professor Kari Rissanen, who gave me the opportunity to join his research group and start the studies in the fascinating world of supramolecular chemistry. His support, guidance and especially encouragement throughout this study were extremely valuable. I am also grateful to my supervisor Professor Jussi Valkonen for providing the possibility of carrying out this work in the Inorganic and Analytical Chemistry Section.

I also wish to thank Professor Fritz Vögtle (Institut für Organische Chemie und Biochemie der Universität Bonn) and Dr. Paul-Michael Windscheif for many useful and valuable hints especially at the beginning of this investigation. I owe my sincere thanks to my German colleagues Dr. Jörg Breitenbach (BASF AG, Germany), Dr. Jürgen Schulz (University of St. Andrews, Scotland) and Dr. Martin Bauer (University of Oulu, Finland) for their collaboration, discussion and hints in the synthetical work. I wish to thank Docent Erkki Kolehmainen for the NMR assistance and Mr. Reijo Kauppinen for running the NMR spectra. I also wish to thank Dr. Sirpa Kotila for the X-ray structure determination assistance and discussions. Moreover, I wish to extend my sincere thanks to the whole staff of the Department of Chemistry for providing a pleasant and supporting atmosphere.

I wish to express my special thanks to Professor Edwin Weber (Institut für Organische Chemie, Bergacademi, Freiberg, Germany) and Professor Rocco Ungaro (Dipartimento di Chimica Organica e Industriale, Universita Parma, Italy), the referees for this study, for their constructive criticism and suggestions. Mark Woods is thanked for the revision of the language.

Last, but most of all, I owe my warmest thanks to my wife Leena for endless support and understanding during this work.

Financial support from the Academy of Finland (project no. 1031137) is gratefully acknowledged.

Jyväskylä, November 1995

Juhani Huuskonen

I dedicate this work to Leena

ABSTRACT

Acidic complexing ligand and neutral macrocyclic compounds were synthesised as receptors for either ions or uncharged organic molecules. The compounds were purified and characterised using normal methods and the X-ray structures of 14 compounds were determined.

The acidic ligand (TEATA) formed a Na complex with two ligand molecules, both with one Na^+ ion interaction and both co-ordinated to a third, central, Na^+ ion (established in solid state by X-ray structure determination) (**VII**, **VIII**). Inside this extraordinary dimeric assembly (a pseudo-cryptate) the three sodium ions are encapsulated, as in cryptates. The macrocyclic compounds were synthesised in two ways, one-step and two-step reactions, using piperazine as a building block. These piperazine macrocycles show 4 different types of structural properties in solid state: metal-complexing (**II**), self-assembly /self-complementary (**IV**, **V**, **VI**), crystal lattice inclusion (clathrate) (**IX**) and molecular inclusion (**X**, **XI**, **XII**, **XIII**, **XIV**) compounds. In addition, azobenzene units have been incorporated into some of these piperazine macrocycles (**XIII**, **XIV**) enable variation of the shape and size of the cavity by UV-light.

A short review of the literature concerning the place of the supramolecular chemistry in the field of chemistry precedes the summary of experimental results. The reader is recommended to preview the author's original publications (papers I-VI, end of this thesis) before the summary of experimental results. The summary of experimental results contains additions to the publications, especially to that of the packing structures.

CONTENTS

ABBREVIATIONS

ADP	adenosine diphosphate
ATP	adenosine triphosphate
DMF	dimethyl formamide
EDTA	ethylenediaminetetraacetic acid
EPR	electron paramagnetic resonance
EtOH	ethyl alcohol
MeCN	acetonitrile
NTA	nitrilotriacetic acid
TEATA	triethanolamine-*O*,*O*,*O*-triacetic acid
THF	tetrahydrofuran

1. INTRODUCTION

1.1 Supramolecular chemistry

Supramolecular chemistry is a young research area in its infancy. One starting point came with the discovery of crown ethers (*Fig. 1*)[1] in 1967 by C.J. Pedersen (Nobel prize winner with J.-M. Lehn and D.J. Cram in 1987). The development of supramolecular chemistry has followed the development of the chemistry of crown ethers and cryptands and, on the other hand made inroads into the studies on the self-organisation of molecules (for example membranes and micelles). There exists no sharply defined limits for the supramolecular chemistry, but one important point is to look for the intermolecular interactions between two or more molecular components also including ionic interactions in solution.[2]

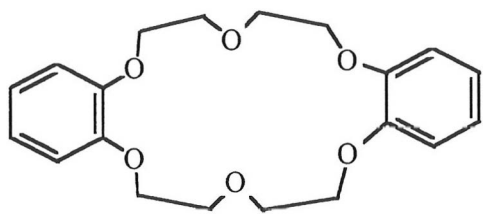


Figure 1. The first crown ether synthesised by C.J. Pedersen.[1]

Synthesis of macrocycles and studies of their receptor properties has become a very important area for research, because of its close relationship to molecular recognition in biological systems. In Nature self-organisation and intermolecular interactions are of the utmost importance. These interacting molecules are large making studies of the interaction processes very difficult and sometimes almost impossible. Small synthetic model compounds, open-chain or cyclic, have proved very important when mimicking *e.g.* enzyme functions, antiserums, receptors and ion transport through membranes (*e.g.* cell membrane). In addition some of these new compounds have turned out to possess industrial importance as *e.g.* catalysts.

Research into water soluble macrocycles with hydrophobic cavity as host compounds for non-polar guest molecules has expanded in recent decades. The hydrophobic interactions (*Fig. 2*) between interacting molecules are of great importance when modelling the substrate binding into receptors in biological systems.

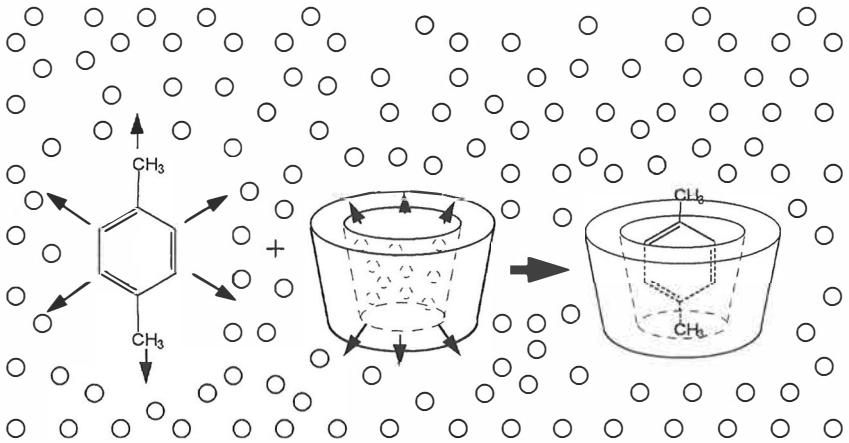
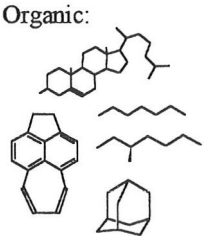
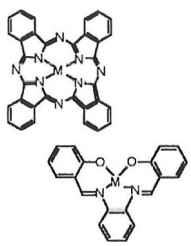
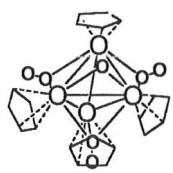


Figure 2. An example of hydrophobic interactions.[6] Cyclodextrin is the host molecule and *p*-xylene is the guest molecule, the small circles represent the water molecules.

In Nature supramolecular systems are frequent, *e.g.* enzyme and protein functions are based on supramolecular assemblies. Almost all 4. row metals have been detected from active enzymes and proteins. Co-ordination of the metal ion into a specific location, creates so-called active sites, where all the action takes place. These active sites are very large Werner-type co-ordination compounds. The co-ordination which specifies the metal atom in these sites, can be studied by using different kinds of analytical methods like EPR, UV-Vis, Mössbauer, Raman spectroscopy, magnetic susceptibility, and magnetic circular dichroism. When the structure and co-ordination of the metal atom in the active site has been found, the next step is the preparation of model compound with a similar co-ordination site. By studying its stereochemistry, reactions and biological activity, new information can be obtained for *e.g.* the functioning of enzymes.

Molecules consist of atoms, which have been bound together by strong covalent bonds. These compounds can be described unambiguously using stereochemical terms like structure, configuration and conformation. Supramolecular structures consist of coalition of suitable molecules (molecular building blocks). Molecular subunits can be prepared by selective chemical reactions and are identified by their physical properties (melting point, chirality, spectroscopic properties etc.). Their organizational parameters divide them up into inorganic, organic, metallo-organic and organometallic compounds (*Table 1*).

Table 1. Molecular building blocks and organizational parameters for the corresponding molecular material.[2,3]

CHEMISTRY	Organizational parameters
Inorganic: 	- Type of order - Strength and anisotropy of interactions between subunits - Symmetry of packing - Intermolecular vibrations
Organic: 	- Symmetry of molecules - Polarizability of a molecule's backbone - Type, number and polarity of substituents - Degree of flexibility of submolecular components - Hydrophilic and hydrophobic properties
Metalloorganic: 	- Strength of the covalent part of the bond between the metal ion and the coordination atoms of the ligand - Electrostatic forces - Oxidation state of the metal, usually high - Charge density - Weak polarizability of the metal ion
Organometallic: 	- Strong covalent bonding - Low oxidation state of the metal ion - High polarizability of the metal ion - d-d; d-f; f-f orbital interactions

Supramolecular chemistry focuses on the co-operative interactions of two (or more) different species (*Fig. 3*).[1,4] In contrast to molecular chemistry, which is predominantly based on covalently joined atoms, supramolecular chemistry is an extension to it meaning studies of the association of two or more molecules, which are bound together by weak intermolecular bonds.

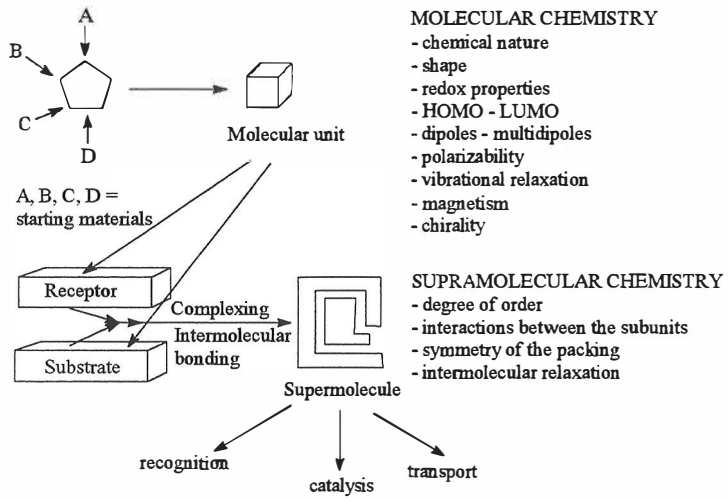


Figure 3. The relationship between supramolecular chemistry and molecular chemistry.[2]

Figure 4 describes the connection of life sciences and materials science to functional supramolecular systems. Besides molecular self-organisation, another crucial property of Nature's supramolecular systems is their capability for molecular recognition, which leads to specific interactions. Such studies have become, over the last two decades, an increasingly important part of organic chemistry.

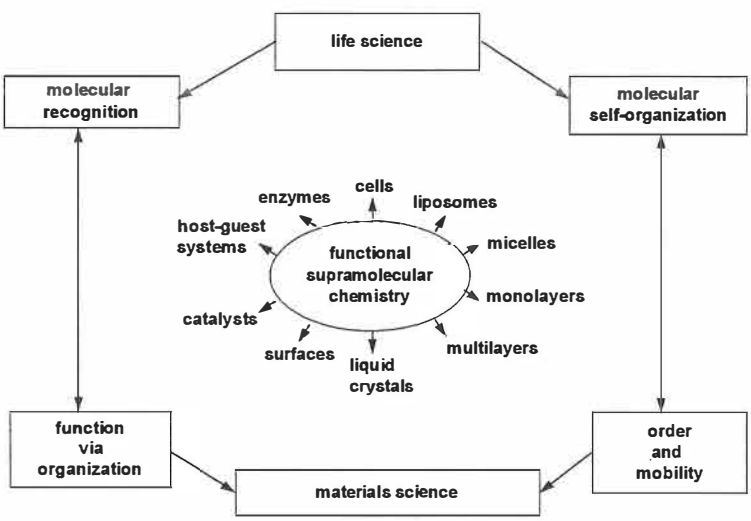


Figure 4. Functional supramolecular systems - link between life science and materials science.[5]

1.2 Host-Guest compounds e.g. the inclusion phenomenon

Inclusion complexes are supramolecular systems, where a guest molecule or ion (substrate) is included into the cavity of a host molecule (receptor) (*Fig. 3 and 5*). The guest molecule enters the interior of the cavity of the host molecule in such a fashion that the structure of the host molecule changes only slightly.[6] Using these as models it is possible to mimic and describe *e.g.* the functions of enzymes, molecular recognition and catalysis of reactions.

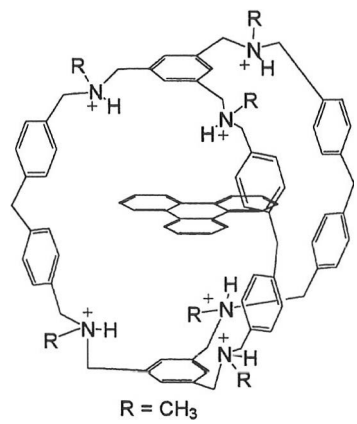


Figure 5. A host-guest complex.[7]

1.3 Receptor molecules and molecular recognition

Research with receptor molecules started in the 1960's, when the first crown ether was synthesised.[1,8] After this the synthesis of organic compounds (rings), which can make complex compounds with cations, has developed remarkably. It was also found that large rings can complex and even selectively recognise small neutral guest compounds. These kinds of systems have been developed from cyclodextrin derivatives and synthetical cyclophanes.[6,9,10] In these receptor-substrate systems host and guest complement each other sterically, viz. the shape and chemical nature of the substrate and the size of the cavity of the receptor play a very important role. In addition the binding sites of the receptor should be correctly positioned such that the interactions between receptor and substrate are as efficient as possible.[11,12] *Figure 6* shows an example of a synthetic receptor molecule which is able to recognise barbituric acid derivatives. The recognition process has been verified in the solid state, but what is more important, the interaction between guest and host also happens in the solution state (established by ^{1}H-NMR). The

X-ray structure shows the six hydrogen bonds in the inclusion complex of the receptor and diethylbarbituric acid.

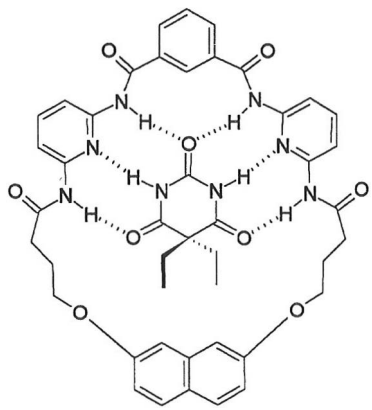


Figure 6. Receptor-substrate system, diethylbarbituric acid as guest.[13,14]

1.4 Catalysis and transport processes

Supramolecular chemistry is based on intermolecular interactions (non-covalent bonds), which are weaker but have energy and geometry as the covalent bonds. In a receptor-substrate system it can be supposed that the chemical reactivity comes from the formation and breakage of the intermolecular bonds. The reactivity depends on the structure, stereochemistry, stability and selectivity of the receptor-substrate system and also the rate of complexation and dissociation. Supramolecules should therefore possess various functions:[15]

1) Recognition of the substrate from the other substrates.
2) Molecular catalysis, catalytic effect to reactivity of substrate.
3) Transport of substrate through membranes.

Artificial, effective and selective supramolecular catalysts are models for investigation of the functions of enzymes. On the other hand they also represent new kinds of chemical reagents for research into reaction mechanisms and synthetic applications. Such catalyst have properties as:[15]

1) Selective binding of substrate.
2) Fast and selective reactions with substrate.
3) Regeneration of active centre after reaction.
4) Fast release of reaction products.

Cyclodextrins and their derivatives (modified cyclodextrins) have been found to possess catalytic properties for some reactions.[6] A classic example of such derivatives is the so-called Breslow's enzyme[16] which combines two properties of an enzyme: the hydrophobic cavity and prosthetic group (metal-ion) (*Fig. 7*). This artificial receptor has been found to raise strongly the hydrolysis rate of p-nitrophenyl acetate (reaction rate is 1000 times faster than without the receptor).

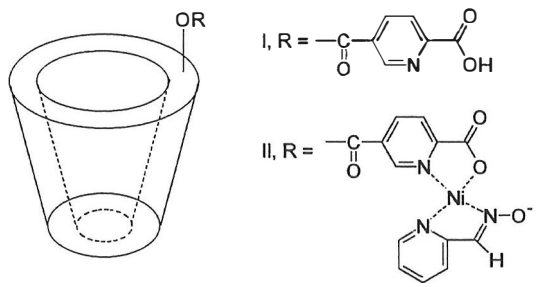
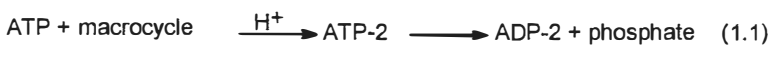


Figure 7. A classic catalytic active cyclodextrin derivative, the so-called Breslow's enzyme.[16]

Another example is macrocyclic polyamides (*Fig. 8*) which have been found to catalyse hydrolysation of adenosine triphosphate (ATP) to adenosine diphosphate (ADP) (*Formula 1.1*). The catalytic effect can be over 100 times faster compared to the reaction without catalysis.



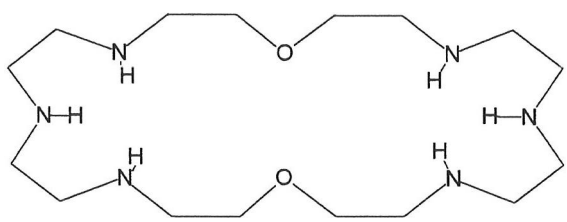


Figure 8. A catalytic active macrocyclic polyamine for hydrolysation of ATP.[17,18]

2. EXPERIMENTAL

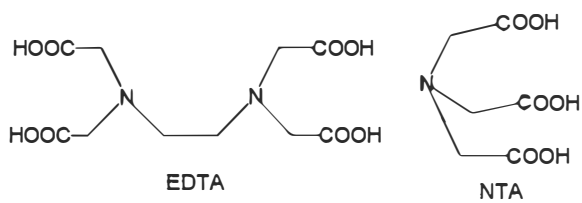
2.1 The aim of this study

The research for new ligands for complexing of metal-ions continues intensively to replace e.g. EDTA, very good and durable complexant in Nature. On the other hand macrocycles with cavity for inclusion of small molecules are important for the study of weak molecular interactions and possible catalytic properties. The aim of this work was to synthesise a new type of water soluble podand for cation complexation and neutral monocyclic receptor macrocycles and to study their structural properties in solution and in solid state.

2.2 Complexones

2.2.1 Background

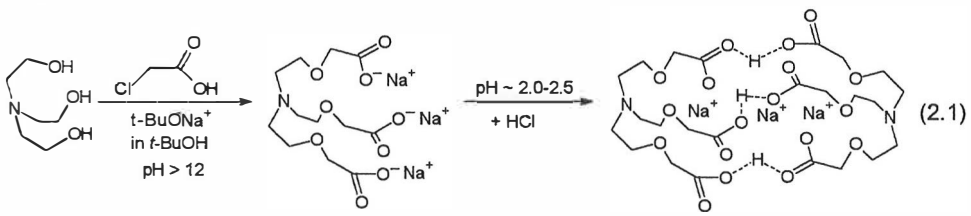
The name complexone was proposed first by G. Schwarzenbach[19] for organic ligands, which contain one or more iminodiacetic acid group(s) [$-N(CH_2CO_2H)_2$] or two amino acetic acid groups [$-NHCH_2CO_2H$)] and which form stable complexes with almost all metal cations. He also found that aminopolycarboxyl anions can bind calcium and other cations very strongly, which was not observed with classical precipitation or colorimetric methods. Well known complexones are EDTA and NTA. Being very good complexing agents, complexones have also recently been studied as sequestering agents for radioisotopes, for tumour-imaging and for other new applications.[20]



2.2.2 Synthesis of triethanolaminetriacetic acid (TEATA)

In this work TEATA was synthesised starting from chloroacetic acid and triethanol amine using sodium *t*-butoxide as base in *t*-butanol (*Formula 2.1*).[I] The reaction mixture was poured in ice/water and *t*-butanol removed in a vacuum. After adjusting the pH of the aqueous phase to 2.0-2.5, it was evaporated off. The residue was extracted by hot

methanol. After cooling, TEATA crystallised as Na-salt. The compound was purified by recrystallisation from methanol.



(2.1)

2.3 Piperazinophanes

Since biological reactions of enzymes, antiserums and receptors occur in water-based systems, the model compounds to study such interactions should also be water soluble. If macrocycles are designed to contain protonable *N*-atoms, the hydrochloric salts of these compounds can often be made water-soluble.

2.3.1 Piperazine

Piperazine or 1,4-diazacyclohexane is an alicyclic diazine with a quite rigid cyclohexane conformation and it readily undergoes nucleophilic substitution reactions (*Fig. 9*).

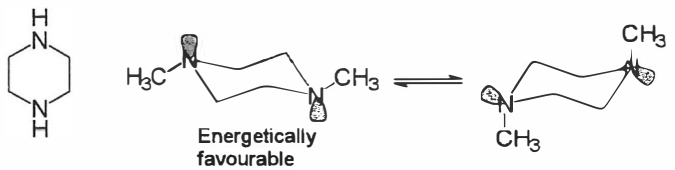


Figure 9. Piperazine (left) and the conformations of *N,N'*-substituted piperazines (right).

It is also noticeable that ring is flexible and it can change conformation from equatorial to axial. *N,N'*-alkylated piperazines favour chair conformation, where *N*-substituents have been located to equatorial positions.[21]

In addition piperazine can form both metal complexes and hydrogen bonds; both good properties in supramolecular chemistry. In medicine piperazine and its *N*-substituted derivatives have been used as sedatives, antihelmintics and local anaesthetics.[22,23]

2.3.2 Piperazine in macrocyclic compounds

Piperazine has been incorporated into small and sometimes into larger macrocycles. The first cyclic piperazine derivative was DABCO (1,4-diazabicyclo[2.2.2]octane),[24] which is an important catalyst in the condensation reaction of δ-keto-α-β-unsaturated esters and β-ketoesters.[25] As a side-product the synthesis of DABCO produces the first macrocyclic piperazine compound, a modified aza-4-crown (*Fig. 10*).

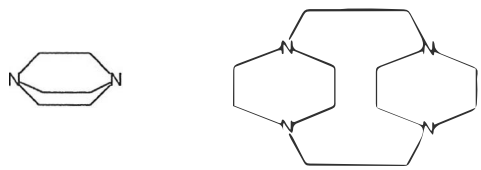


Figure 10. 1,4-diazabicyclo[2.2.2]octane (DABCO) (left) and the first piperazine macrocycle (right).

Chénevert and Plante[26] prepared crown ether macrocycles from piperazine and ditosylated polyethylene glycols, producing large macrocycles with two piperazine units (*Fig. 11*).

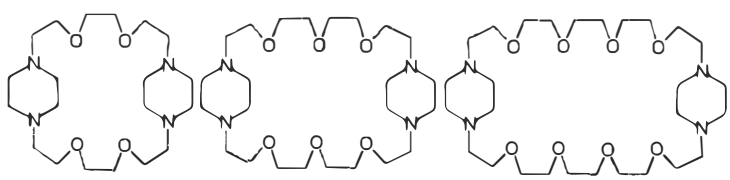


Figure 11. Piperazine-crown ether macrocycles prepared by Chénevert and Plante.[26]

Larkins and Hamilton[27] used diphenyl methane acid chloride and monoprotected piperazine in two-step syntheses and finally the cyclic tetra-amide was reduced by diborane (*Fig. 12*). This macrocycle has a suitable cavity for the inclusion of small molecules, but no inclusion was detected. The same research group also synthesised macrocycles where diphenyl methane groups were replaced by aminophenylene groups.

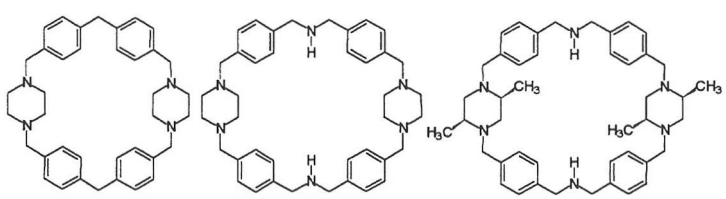


Figure 12. Piperazine macrocycles synthesised by Larkins and Hamilton.[27]

Krakowiak *et al.* used piperazine or benzyl amine and bis(2-chloroacetyl) piperazine as starting material yielding piperazine macrocycles (*Fig. 13*).[28]

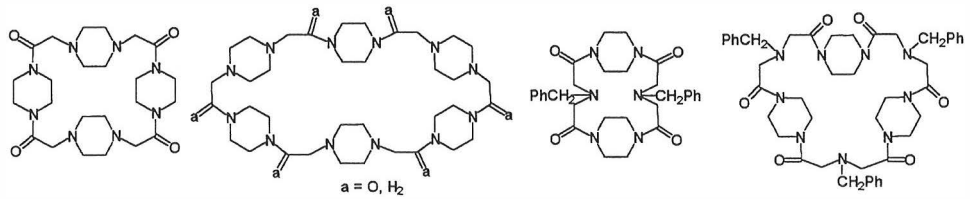


Figure 13. Piperazine macrocycles synthesised by Krakowiak *et al.*[28]

Kihara *et al.* prepared piperazine macrocycle (*Fig. 14*), which has been found to co-ordinate alkali metals, especially Li- and ammonium cations.[29]

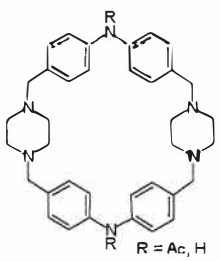


Figure 14. Macrocycle synthesised by Kihara *et al.*[29]

A giant-sized (60-membered ring) piperazine macrocycle has been prepared by Bazzicalupi *et al.* This gigandocycle forms a dinuclear complex with cadmium-ion.[30] A few piperazine macrocycles, which have co-ordination properties with metal-ions, have also been synthesised.[31-35]

2.3.3 Preparation of the piperazine macrocycles

2.3.3.1 High-dilution synthesis

High-dilution synthesis is commonly used for cyclisation reaction, where the starting compounds have at least two reactive parts in the molecular skeleton (*Fig. 9*) e.g. in the case of piperazine and bis(bromomethyl) arene compounds. The tendency towards polymerisation is the dominating reaction path unless the cyclisation reagents are present in very low concentrations, especially when the *effective molarity*[36,37] of the process is low.

The macrocycles in this work were synthesised[II-VI] using the *high-dilution technique*.[38,39] Low concentrations of the reactants can be obtained by using a large amount of solvent, but there are commercially available high-dilution apparatuses, where optimal conditions for cyclisation are obtained under appropriate reaction conditions (meaning using smaller volumes of solvent). High-dilution conditions can be created inside a glass apparatus (*Fig. 15*), where refluxing solvent is returned to the flask by side glass bends where the starting materials, dissolved in suitable solvent, are dropped slowly. Another possibility is to use syringe pumps, which add reagents at a very slow rate into the refluxing reaction mixture.

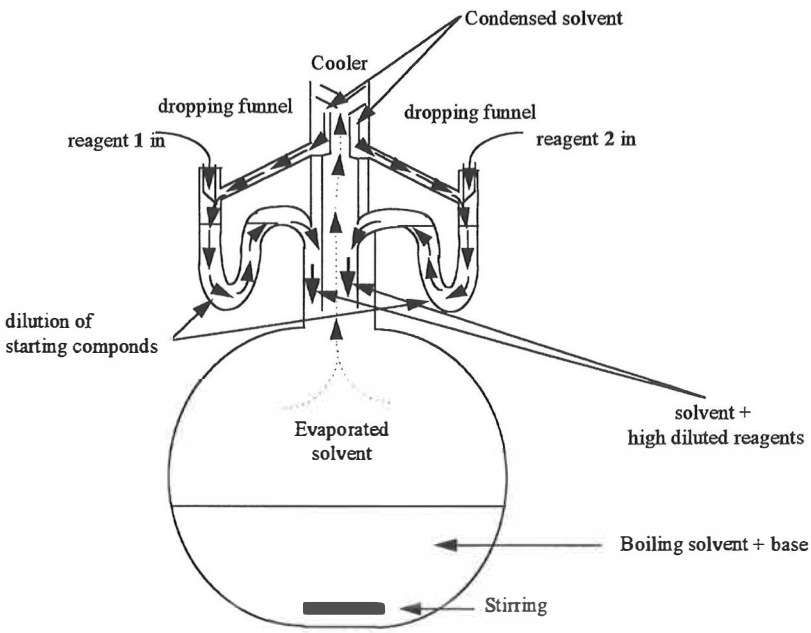


Figure 15. Principle of high-dilution apparatus.

Most of the polyazamacrocycles have been prepared by using the method developed by Richman and Atkins[40] or a modification of it. In this method the cyclisation process takes place in DMF (dimethyl formamide) or MeCN (acetonitrile) in the presence of metal carbonates. Especially caesium carbonate (Cs_2CO_3) has been found to increase cyclic products, a phenomenon defined as the *caesium effect*.[41] The term caesium effect is misleading, because the caesium atom itself is not responsible for the rate acceleration, the higher yield, or cyclo-oligomer selectivity. The effect is postulated to be caused by aggregation of caesium carbonate (often added as an auxiliary base), which sets up specific basicity/nucleophilicity of the reaction medium.[41,42] That the metal ion affects the course of organic reactions has been known for decades. In the preparation of large ring

compounds by condensation reactions such an effect has been used intentionally by the addition of suitable cations into the reaction and it has gained considerable importance. In the 1980s it was found that a neutral molecule can co-ordinate into a ligand or a host molecule, thus bringing the reactant into a suitable conformation for the formation of a specific (most often cyclic) product. This neutral guest can be a solvent molecule of the reaction mixture, viz. benzene[29] or acetonitrile,[V] improving the yield of the cyclic products. This process is generally called the *template* effect (*Fig. 16*)[43] and it was first used and defined at the beginning of the sixties.[44] Generally, all intermolecular forces that play a role in host-guest complexes affect the stabilisation of the reactive binary or tertiary complexes.

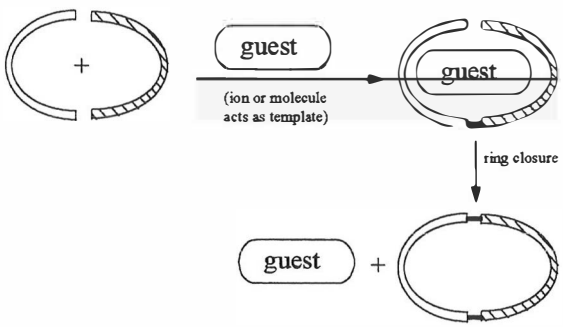
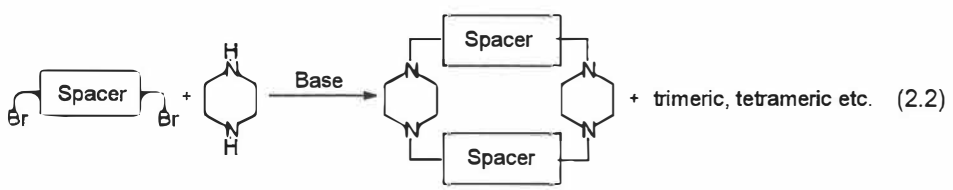


Figure 16. Principle of the template effect: The guest ion or molecule acts as a template, favouring connection of the decisive ("strategic") bond.[43]

It is also obvious that the ring closure reaction often produces different sizes of macrocycles, dimers, trimers, etc. depending on the size of starting materials (building blocks), degree of high dilution and the used base or template. This leads to difficulties in the purification of products and in some cases decreases their yields thus making the optimisation of reaction conditions very important.

2.3.3.2 Symmetrical piperazine macrocycles

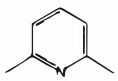
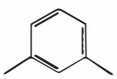
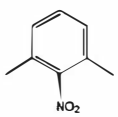
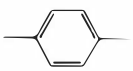
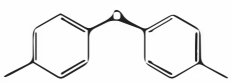
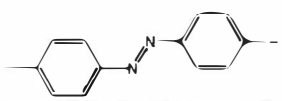
Symmetrical piperazine macrocycles were obtained using direct cyclisation reaction (*Formula 2.2*) between piperazine and desired bis(bromomethyl) arene.[II-VI]



(2.2)

The piperazinophanes obtained from dimeric up to tetrameric structures (in some cases pentameric compound was detected) (*Table 2*).

Table 2. The size of the piperazine macrocycles depending on spacer.

Spacer	dimeric	trimeric	tetra-meric	penta-meric
	+++	o	–	–
	++	++	+	o
	–	–	+++	o
	–	+++	+	–
	+++	–	–	–
	+++	–	–	–

+++, ++ = main product
+ = side product
o = detected
– = not detected

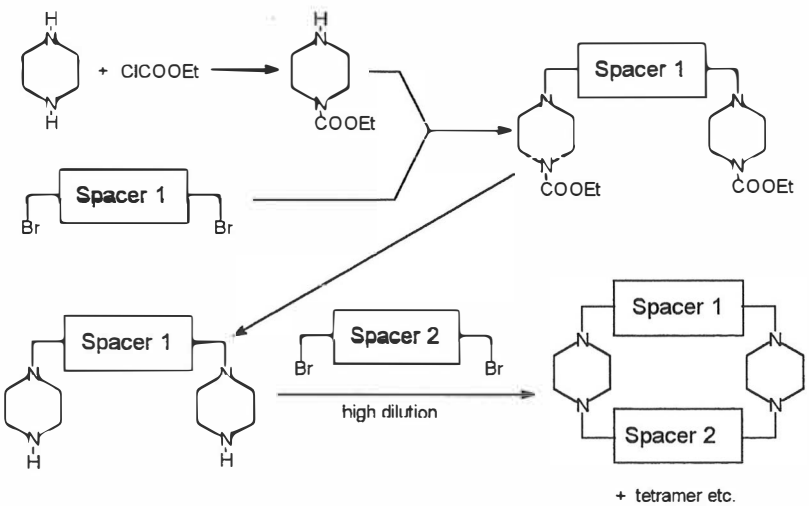
The difference between the size of cyclic products depends, especially in the case of 1,3-bis(bromomethyl) arenes, on the group between the methylene groups. The nitro group in the benzene ring is so large that it spatially hinders the dimeric cyclic structure, but in 2,6-bis(bromomethyl)pyridine no such effect appears and the main cyclic product is the dimer. In 1,3-bis(bromomethyl) xylene there is hydrogen between the methylene groups which cannot prevent production of dimer, but it increases the formation of the larger trimer and tetramer formations.

The effect of the group between the methylene groups can be observed when the cyclic products between the case of pyridine and xylene are compared. It seems that the nitrogen of the pyridine improves the formation of the dimeric product, probably via the

interactions with the caesium ion and the pyridine nitrogen (piperazine also has interactions with the caesium ion).

2.3.3.3 Unsymmetrical piperazine macrocycles

Unsymmetrical piperazine macrocycles have been prepared by using a multi-step reaction (*Formula 2.3*) where one of the piperazine *N*-atoms is protected by ethyl carboxyl group and then reacted with the desired bis(bromomethyl) arene. The protecting group is removed by treatment of hydrobromic acid and then by ammonium hydroxide causing the open-chain product to precipitate from the aqueous solution which after recrystallisation from acetonitrile gives good yields (70-90%).

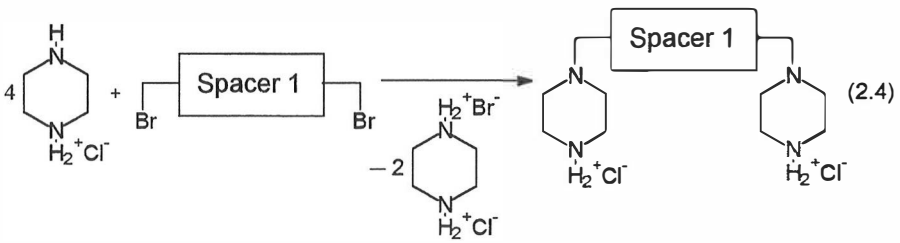


(2.3)

The open chain compound [bis(4-(1-piperazinylmethyl)) arene] is reacted with another bis(bromomethyl) arene in high dilution conditions in MeCN/THF (4:1) solvent to give unsymmetrical piperazine macrocycles. In most cases purification of the cyclic products can be performed by silica gel column chromatography (except in those cases where the compounds crystallised upon cooling from the reaction mixture) and can then be recrystallized. The best solvent for crystal growth for X-ray structure determination proved to be MeCN, $MeCN/CH_2Cl_2$ or $MeCN/CHCl_3$.

Another possibility for making these open chain building blocks is to react the bis(bromomethyl) arene with piperazine monohydrochloride salt (*Formula 2.4*) (where

one *N*-atom of piperazine is protected as ammonium salt[45]) in ethanol solution. The piperazine monohydrochloride salt is used in twofold excess compared to bis(bromomethyl) arene. The excess of monochloride salt acts as a base to neutralise formed hydrobromide. The mixed piperazine hydrochloride/hydrobromide salt is removed by filtration. The filtrate is evaporated and the residue is neutralised with ammonium hydroxide. The isolation of the desired product is done by column chromatography on silica gel. The yields were lower and the purification more complicated than in the first method (*Formula 2.3*).



2.4 Structural studies

2.4.1 General

Structural studies has been performed by single crystal X-ray diffraction and measurements were performed on an automatic Enraf-Nonius CAD-4 diffractometer. Crystals were mounted on a glass fibre and measured in an air atmosphere (crystals without solvent molecule inclusion) or they were measured in a glass capillary containing a drop of a mother liquor to prevent the crystals from breaking. The cell parameters were determined by automatic centring of 25 reflections and refined by the least-square method. Intensities were collected with graphite-monochromatized MoK_α radiation (λ = 0.71073 Å) using ω / 2θ scan (some cases ω scan) technique. An intensity check was made by monitoring two standard reflections every 60 minutes and crystal orientation was checked after every 400 or 600 reflections. Reflections were measured in the range $2° \leq \theta \leq 23 - 25°$ and were used as observed by applying the conditions $I \geq (1\text{-}3)\sigma(I)$. An absorption correction was applied to the data by the DIFABS.[46] The structures were solved by direct methods using the SHELXS-86[47] and subjected to full-matrix refinement using the CRYSTALS[48] program package. All non-H atoms were refined anisotropically. The hydrogen atoms were located from the ΔF-map (after isotropic refinement of heavier atoms) and refined isotropically in the final refinement or they were calculated to their idealised positions (C–H distance 1.00 Å or 1.05 Å for methylene H-atoms) and

subjected to final refinement with fixed isotropic temperature factors. The calculations were carried out on a MicroVAX 3100 computer and 486 (66 MHz) PC.

The structures of macrocycles are given in references I-VI. The numbering of the compounds, which is used in this thesis, is given in Appendix I. Space groups and unit cell parameters are given in Appendix II.

2.4.2. Metal-complex of piperazinophane

As mentioned on page 16, the favoured conformation of *N,N*-alkyl disubstituted piperazines is the chair conformation with the *N*-substituents in equatorial positions,[21] but piperazine has been found also in the boat conformation in some piperazine macrocyclic metal complexes.[31-35]

The reaction between 2,6-bis(chloromethyl)pyridine and piperazine produced, after purification, a yield of 25% of the macrocycle **I**.[II] The suitable crystals of **I** were obtained by slow evaporation of the MeCN/EtOH solution (MeCN/EtOH, 15:1, *v/v*, same mixture as the eluent in chromatographic purification). The Cu-complex of **II** has been synthesised dissolving ligand **I** and CuCl (1:1) in 25 ml of water giving a dark yellowish green solution. The suitable crystals of Cu-complex were crown by the diffusion method setting the water-complex mixture into an unsealed flask and then placing it into a 250 ml beaker containing 50 ml of ethanol. This whole system was sealed and left to stand at room temperature. The diffusion between water solution and ethanol took time and the crystal growth took several months. The formed crystals grew on the wall of the flask above the solvent surface and they were collected for X-ray crystal analysis. Upon further standing the diffusion system did not produce more crystals, but precipitated a syrupy, dark green residue.

The crystal structure of the uncomplexed **I** shows macrocycle, which has inversion symmetry (only half of the macrocycle have to be defined) and the cavity which is very crowded (*Fig. 17*). The piperazine rings are in the chair conformation and the N-atoms point to the same direction leaving no room inside the cavity.

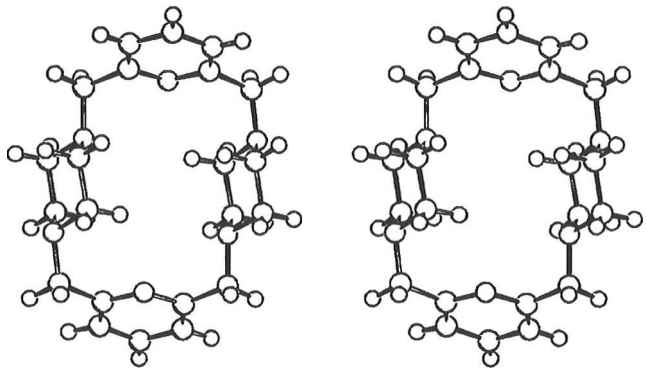
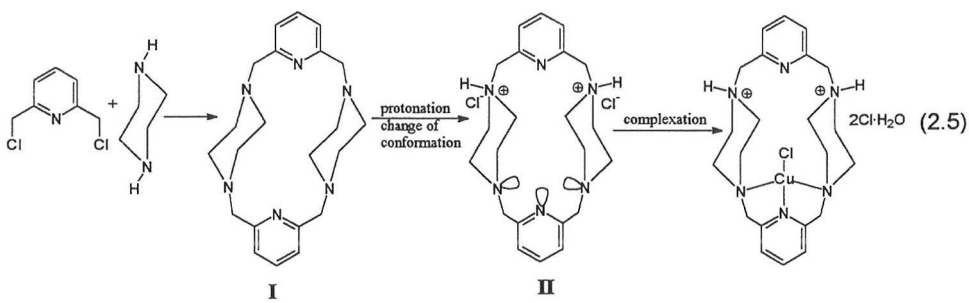


Figure 17. The stereo plot of uncomplexed ligand **I**.

The uncomplexed **I** has to change its conformation, somehow, before complexation. The conformational change occurred probably by protonation of the second piperazine N-atom of both piperazine groups following the complexation of CuCl (*Formula 2.5*).



The X-ray crystal analysis of Cu-complex of **I** (*Fig. 18*) shows interesting co-ordination geometry of Cu^{+}-ion. In the Cu-complex **II**, copper has an unusual twisted tetrahedral co-ordination sphere, where the angles of the tetrahedron have drastically changed and vary from 75.2(1)° to 164.5(1)° (*Fig. 19*). The most common types of Cu(I) complexes are those of simple halides or amine ligands that are almost invariably tetrahedral as in complexes such as $[Cu(CN)_4]^{3-}$ and $[Cu(Py)_4]^{+}$. Even those with stoichiometries such as K_2CuCl_3 still have tetrahedral co-ordination.[49]

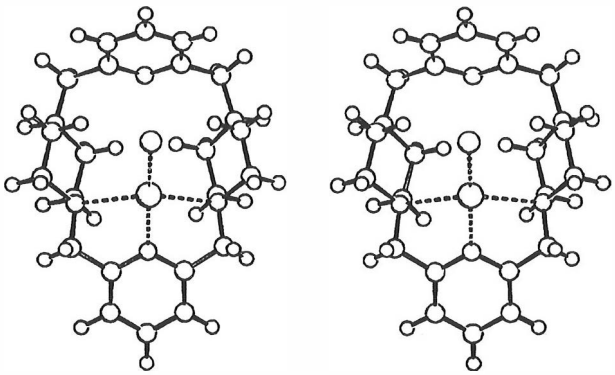


Figure 18. The stereo plot of Cu-complex of ligand **I** (compound **II**). Methanol molecules and Cl^--ions are excluded.

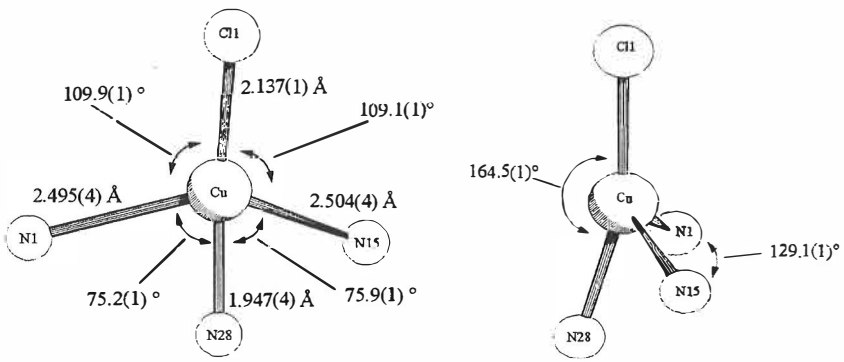


Figure 19. Co-ordination geometry of Cu^+ in complex **II**.

Similarly a chiral (*meso*-form) pyridine macrocycle **III** was prepared, (analogue to **I**) using 2,6-bis(chloromethyl) benzene and *trans*-2,5-dimethylpiperazine.[IV] It crystallises from methanol nicely as its dihydrochloride salt. The X-ray crystal analysis shows a similarly oriented macrocycle as **I** (*Fig. 20*). It seems that the methyl groups in piperazine "guide" the conformation to a similar orientation as in the case of **I**. Other conformations, such as in Cu-complex **II**, are improbable due to the methyl groups which prevent the conformational changes. A similar complexing experiment has been performed as in the case of **I**, but no complexing ability was found (only a very slight colour change).

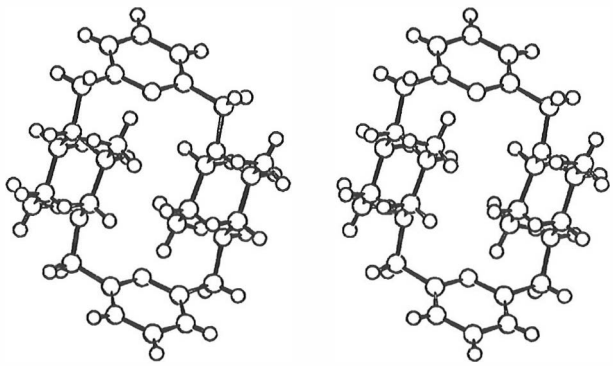


Figure 20. The stereo plot of macrocycle **III**.

2.4.3 Self-assembly / self-complementary structures

Supramolecular chemistry has focused on more or less rigidly organised, synthetically built up, molecular receptors for molecular recognition, catalysis, and transport processes. Beyond preorganisation lies the design of systems undergoing *self-organisation*, that is, systems capable of spontaneously generating a well-defined (functional) supramolecular architecture by *self-assembly* from their components under a well-defined set of conditions. Self-assembly requires binding; self-organisation additionally implies information. The information which is needed for the process to take place and the algorithm that the process follows must be stored in the components and operate via selective molecular interactions. A simple and general concept for generating molecular order is based on the recognition-directed spontaneous assembly of a supramolecular strand from complementary molecular components, which presents two identical recognition sites (*Fig. 21*).[89] Self-organisation represents a basic feature of supramolecular chemistry, since it rests on intermolecular interactions, whereas preorganisation makes use of covalent bonding.

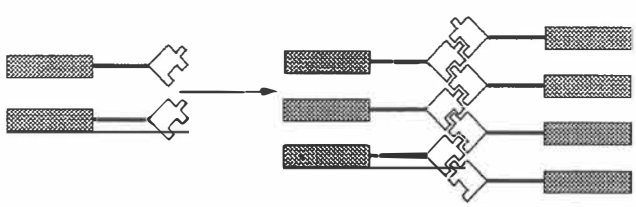


Figure 21. Schematic representation of the formation of an ordered supramolecular strand by the molecular-recognition-induced association of two (similar or different) molecular units.[89]

Self-organisation may occur in solution, in liquid crystalline phase, or in the solid state and make use of hydrogen bonding, electrostatic and donor-acceptor effects, or metal-ion co-ordination as basic interactions between components, as well as of medium (solvophobic) effects.[89,90-92,98,99]

Numerous biological supramolecular structures result from self-assembly, such as the spontaneous formation of the double helix of nucleic acids, the viral protein coat, and multiprotein complexes.[50,51] Several approaches have been pursued in the search for synthetic self-organising systems: the formation of double- and triple-helical metal complexes,[93-95,102] the generation of mesophases and liquid crystalline polymers of supramolecular nature from complementary components,[96] and the molecular-recognition-directed formation of ordered solid-state structures.[90,97]

In the assembly of supramolecules from metal ions and ligands, the latter must contain the steric program that is read by the metal ions following the algorithm represented by their co-ordination geometry.[89] The self-assembly of a given superstructure involves three stages: recognition between the components, correct orientation so as to allow growth, and termination of the process leading to a discrete, finite supramolecular species.[89,100,101]

2.4.3.1 The self-assembly structures of triethanolamine-*O*,*O*,*O*-triacetic acid sodium salt

The reaction between chloroacetic acid and triethanol amine after adjusting the pH to 2-2.5, produces triethanol-*O*,*O*,*O*-triacetic acid (TEATA) sodium salt as described earlier (section 2.2.2.).[I] Crystals suitable for X-ray analysis were grown from hot DMF by cooling (compound **VII**) and by evaporating the previous solution (compound **VIII**).

The X-ray structure of **VII** shows highly symmetrical self-organisation of two ligand molecules and three sodium cations (*Fig. 22*). The two TEATA ligands are joined together to pseudo-cryptate by three strong, crystallographically symmetrical hydrogen bonds (O—O distance 2.421(7) Å).[52] One possible route for formation of this pseudo-cryptate is presented in (*Formula 2.6*). In a very basic media one sodium cation is co-ordinated inside the ligand and other two sodium cations are positioned normally in salt structure. When the pH is changed to ~2.5 probably two forms of the ligand exist in the solution; one where there is only one sodium ion and the other one where are two. These

two forms shape with self-organisation of strong hydrogen bonds between the ligands encapsulate three sodium ions inside the pseudo-cryptate.

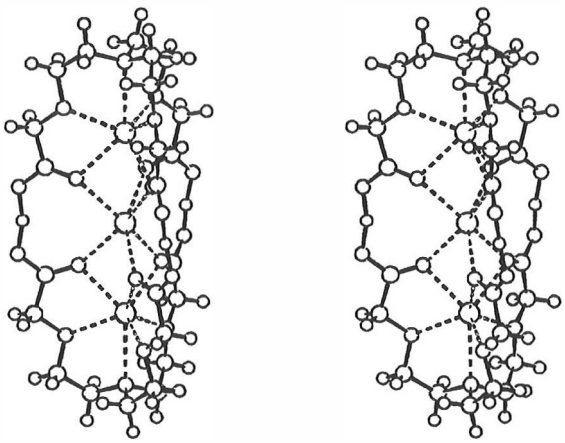
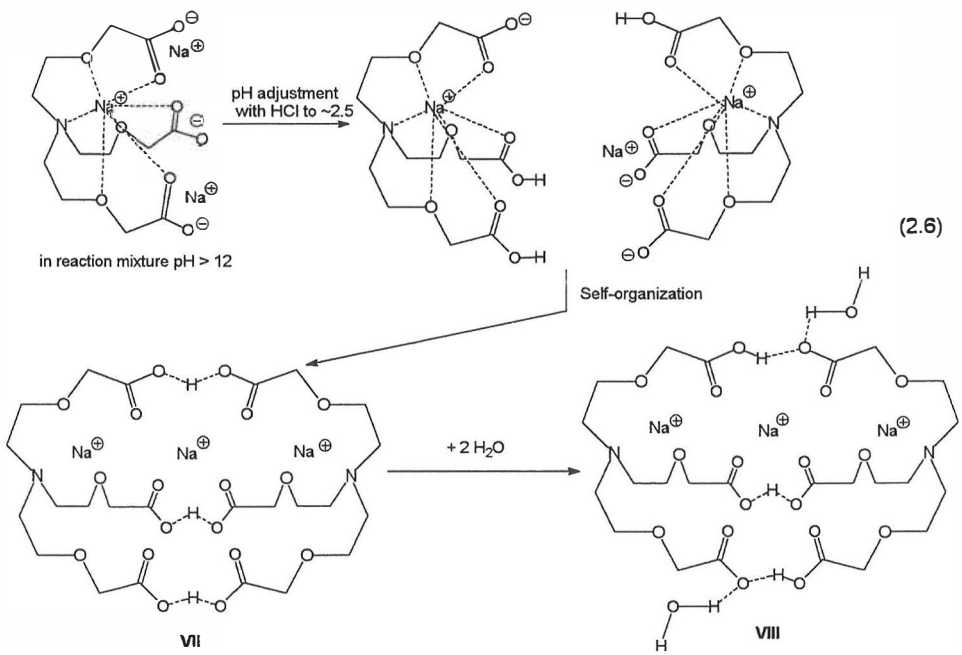


Figure 22. A Stereo plot of **VII**.



(2.6)

After one day (24 h) a new type of crystals started to crystallise from the DMF solution. These crystals proved to be pseudo-cryptate dihydrate **VIII** (*Fig. 23*), which was formed from the **VII** and a small amount of water (impurity in DMF and diffusion of water from

air). The two water molecules are bound to two oxygen of carbonyl groups breaking down the symmetry of the **VII** (symmetry of **VII** is trigonal and **VIII** monoclinic). This results a change of the two crystallographic hydrogen bonds to normal hydrogen bonds viz. the two O—-O distances changes to 2.466(4) Å and one remains in 2.419(6) Å (*Fig. 24*).

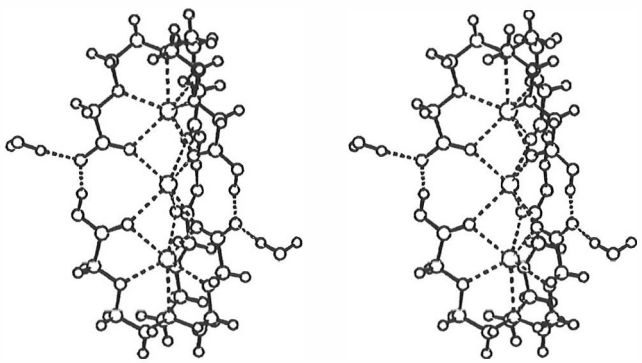


Figure 23. Stereo plot of **VIII**.

Sodium ions have 6 co-ordination, a slightly twisted trigonal prism (the central Na-ion), and 7 co-ordination, a slightly twisted mono-capped trigonal prism (the side Na-ions). The side Na-ions are co-ordinated to nitrogen and oxygen atoms (*Fig. 24*). In the **VII** the bond distances between oxygen and sodium atoms are 2.439(4) Å and between nitrogen and second sodium atom (Na2) 2.643(7) Å. The Na—O distances in **VIII** are from 2.357(3) Å to 2.517(3) Å because of lower symmetry (breaking of crystallographic hydrogen bonds) and Na—N 2.620(4) Å. The Na1—Na2 distance is 3.357(3) Å in compound **VII** and 3.325(2) Å in compound **VIII**. The packing of the **VII** showing high packing symmetry along the *c*-axis (*Fig. 25*)

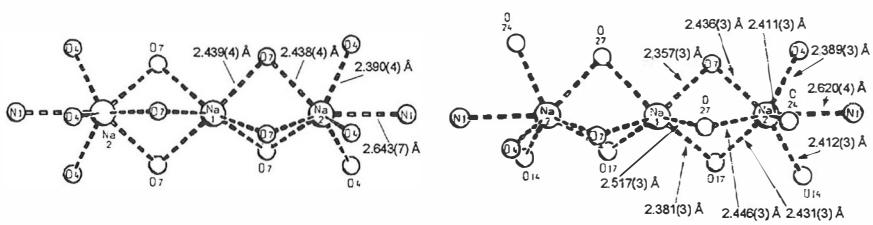


Figure 24. Co-ordination of Na-atoms in **VII** (left) and **VIII** (right).

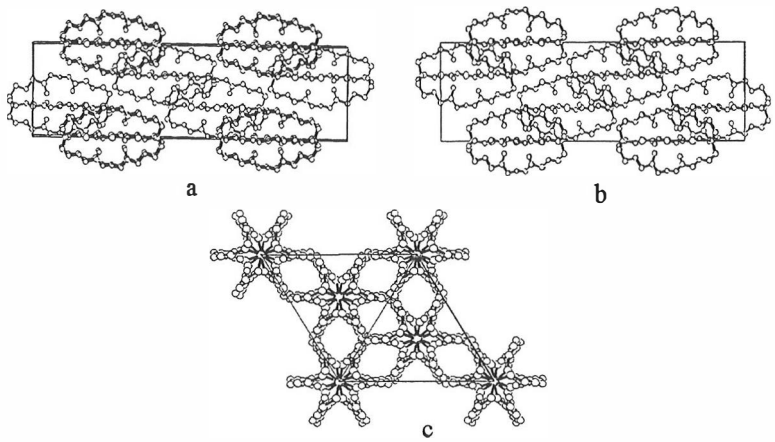


Figure 25. Packing of **VII** along *a*-, *b*- and *c*-axis, respectively.

2.4.3.2 The self complementary structures of the piperazinophanes

Complementary of shape, size and chemical surface drives molecular recognition, and *self-complementary* is the unique feature of biological molecules capable of self-assembly. A tennis ball provides a minimalist, "visible" life analogy.[103] The ball comprises two identical pieces; in shape, the ends are complementary to the middle, and the subunits feature curvatures that dictate the overall spherical shape of the dimer (*Fig. 26*).

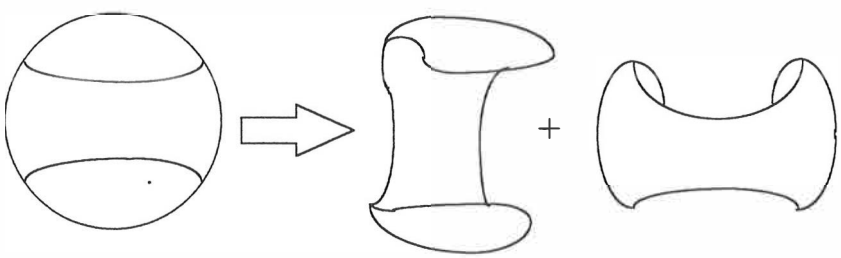


Figure 26. Tennis ball assembly from self-complementary, interlocking subunits.[103]

The cyclisation reaction between piperazine and 1,3-bis(bromomethyl) xylene produced di, tri and tetrameric products as described earlier (*Table 2*, page 21). All these three compounds showed self-complementary or self-assembly in the crystalline state. The crystal growth for each macrocycle was achieved from acetonitrile solution by slow evaporation, which yielded suitable crystals for X-ray analysis. An exception was the tetramer, the data of which was defective, due to the poor crystal quality and prevented

full X-ray determination. Later in this section a preliminary structure of the tetramer is presented.

Dimer crystallises in a monoclinic space group ($P\ 2_1/c$, no 14) and has three molecules in an asymmetric unit (*Fig. 27*).[VI] These molecules are bound together by weak intermolecular interactions between hydrogen atoms. The packing structure of the dimer shows a tape/layer structure especially when observed along its *c*-axis (*Fig. 28*). Distances between these layers alternate from ≈ 3.0 – 3.5 Å.

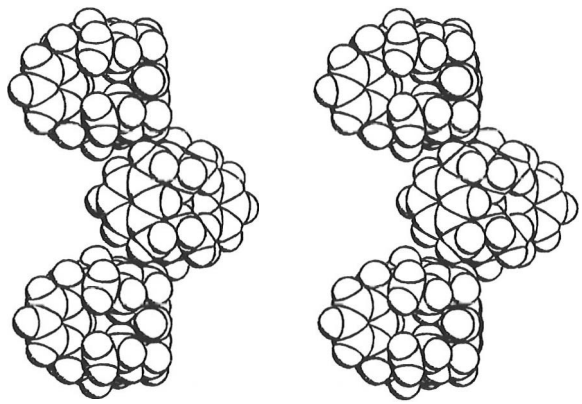


Figure 27. Stereo plot of the dimer macrocycle **IV**. Three molecules in the asymmetric unit.

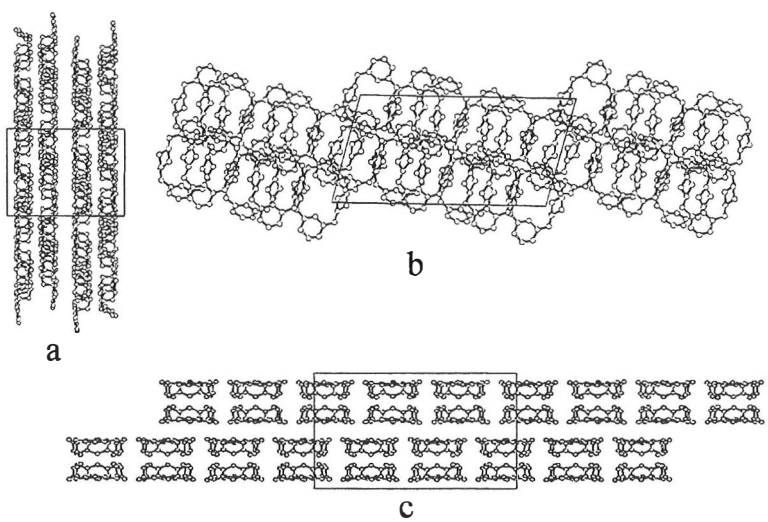


Figure 28. Packing of the dimer **IV** along *a*-, *b*-, and *c*-axis, respectively.

Trimeric compound **V** crystallises in a triclinic spacegroup (*P*-1, no 2) and the asymmetric unit contains one macrocycle (*Fig. 29*). The cavity is rather small because the hydrogens of the piperazine fill it and therefore inhibit the inclusion of even a small guest. The crystal lattice did not contain any solvent molecules either included inside the cycle or clathrated between the cycles.

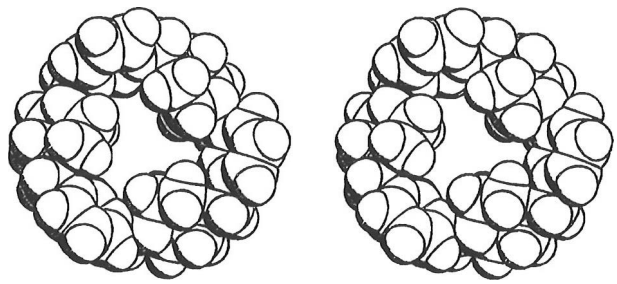


Figure 29. A Stereo plot of trimer **V** (space filling model).

The structure of **V** is interesting in another way. The two cycles possess a self-complementary structure (*Fig. 30*), which is analogous to the tennis ball structure (*Fig. 26*). A similar dimeric structure has been reported earlier e.g. with molecular basket compound.[111] There are some weak interaction contacts between these two cycles. The packing diagram shows that the dimers form piles by stacking onto each other (*Fig. 31*).

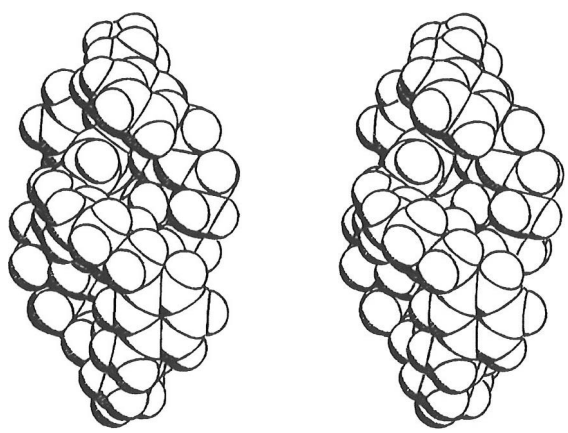


Figure 30. A Stereo plot of dimeric structure of trimer **V** (space filling model).

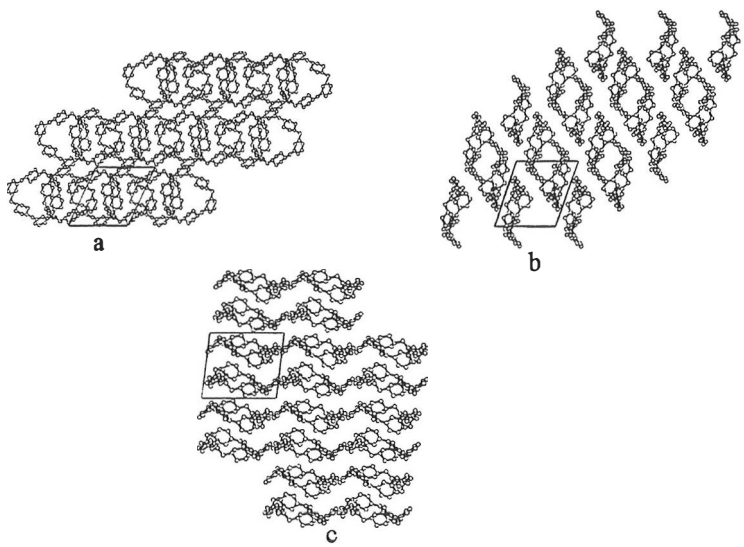


Figure 31. Packing structures of **V** along *a*-, *b*-, and *c*-axis, respectively.

Also the tetramer **VI** crystallises in a triclinic space group (*P* -1, no 2), but due to the poor quality of the crystals, the structure solution is in a preliminary stage (*R* value ≈ 0.14 during the isotropic refinement, co-ordinates of **VI** are presented in Appendix III). The preliminary structure solution shows a suitable cavity for complexation of small guest molecules e.g. acetonitrile (*Fig. 32*).

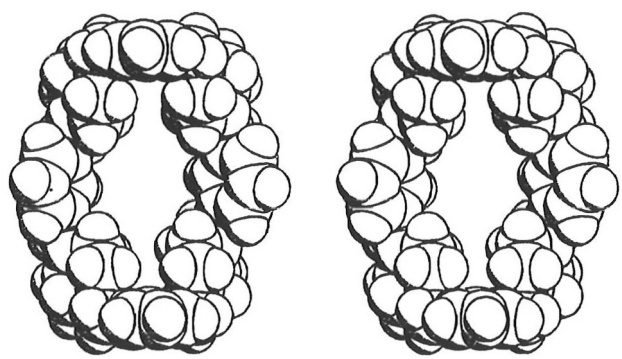


Figure 32. A stereo plot of tetramer **VI** (space filling model).

Even though acetonitrile was used as the crystallisation solvent, no solvent molecules were found inside the cavity, but the crystal structure of **VI** shows similar complementary structure as in the case of trimer **V**, where the two cycles form a tight

dimeric structure (*Fig. 33*). The packing diagram (*Fig. 34*) shows a "staple" structure which interlock into each other creating a continuous tape-like structure.

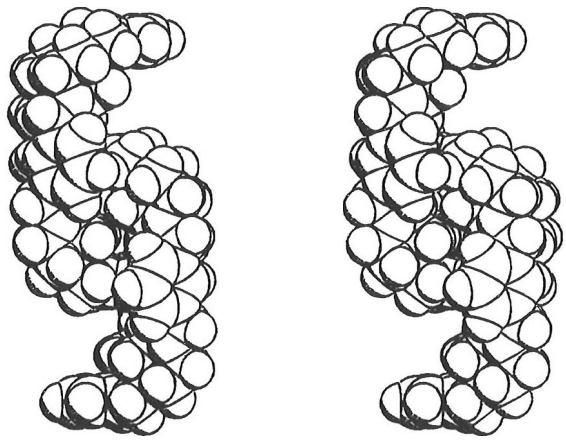


Figure 33. A Stereo plot of the dimeric structure of tetramer **VI** (space filling model).

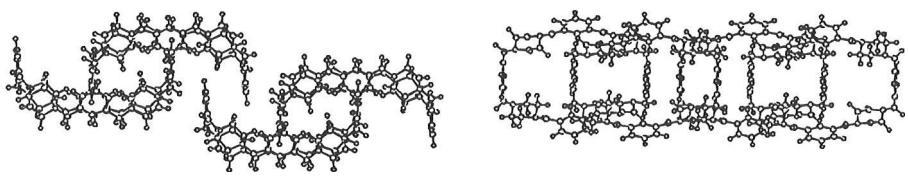


Figure 34. Packing structure of tetramer **VI** showing the interlocking "staple" structure.

2.4.4 Acetonitrile inclusion compounds

2.4.4.1 General

Inclusion compounds have been known since the beginning of the last century. The fundamental feature of this type of compound is the fact that a cavity-containing host component incorporates one or several guest components, without any covalent bonding. The inclusion can be either molecular inclusion (host-guest systems) or crystal lattice inclusion (clathrates) (*Fig. 35*). Piperazinophanes synthesised in this work have been found to form both types of inclusion compounds.[II,III-V]

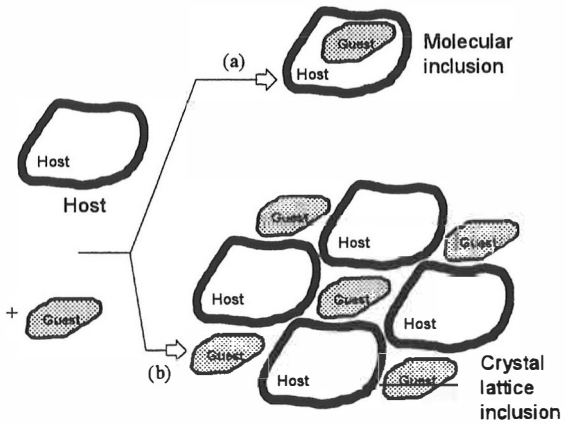


Figure 35. The molecular and lattice inclusions: (a) formation of a molecular complex, where a convex guest fits into the cavity of one host molecule; (b) inclusion of guest molecules into cavities between different host molecules in the crystal lattice (clathrate formation).[53]

2.4.4.2 Clathrate inclusion compounds

Any crystalline lattice inclusion compound is called a clathrate,[53] a term which was introduced by Powell[54] in 1948. In a clathrate, several molecules of the host compound form extramolecular cavities, where guest molecules can be incorporated or induced, on crystallisation, structures of the host lattice with guest-specific interstices (*Fig. 35*). The occurrence of clathrates, therefore, is normally limited to the solid state, but there are also reports of clathrate formation in liquid state.[55] Research activity in the field of clathrate inclusion chemistry has increased remarkably in recent years. New approaches to the systematic design of novel clathrate-forming host compounds have been reported, those leading to selective interaction between hosts and different classes of guest molecule attracting particular attention.[70] The possible applications for clathrate inclusion compounds could be: separations of mixtures (isomers, homologues), separation of racemates, solidification of gases and liquids, stabilisation of sensitive or toxic substances, polymerisation inside inclusion channels (topochemistry) and battery systems and inorganic conductors.[2,70] Clathrates where acetonitrile is included to the crystal lattice have been reported in recent decades.[56-58, 61-69]

The reaction between 4,4'-bis(bromomethyl) diphenyl ether and piperazine, yielded macrocycle **IX**, which was crystallised by slow evaporation of the acetonitrile solution

(*Fig. 36*). The X-ray diffraction analysis gave the structure,[v] where diphenyl ether groups form a small niche. The torsion angle between benzene rings in diphenyl ether is 59 degrees. In this system acetonitrile is included into the crystal lattice as a clathrate structure.

The packing diagram (*Fig. 37*) shows that clathrate formation occurs, when the macrocycles are stacking together and forming small cavities between each other. The packing does not leave any room for solvent molecules between the 'piles' (*Fig. 37*). The acetonitrile is disordered in this system having a population parameter of 0.5, and because the macrocycle is centro-symmetric (space group, monoclinic $P\ 2_1/n$) only one-half of the molecule has to be determined. This means that the acetonitrile can be located on either side of the macrocycle.

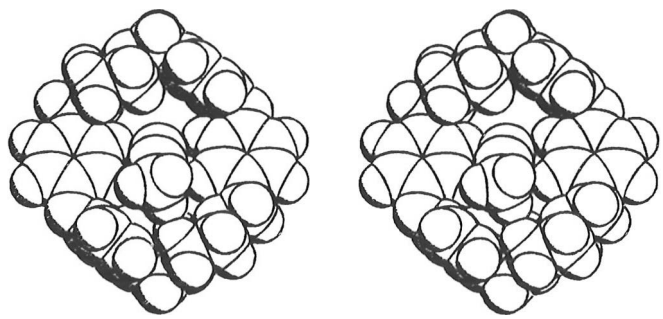


Figure 36. Stereo-plot of macrocycle **IX** (space filling model).

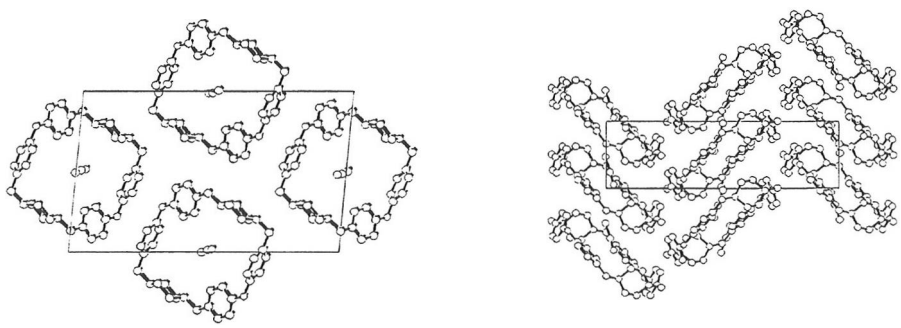
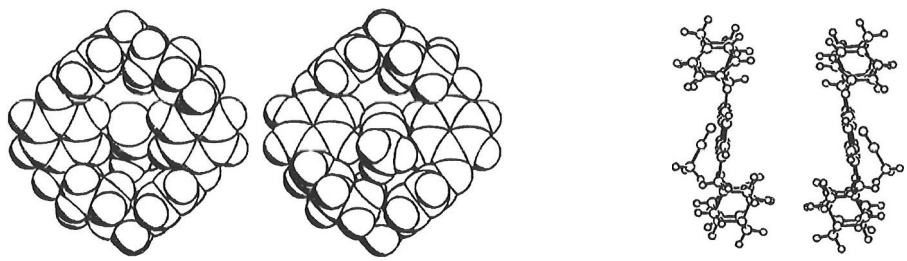


Figure 37. The packing diagram of macrocycle **IX** acetonitrile complex. Molecular piles formed by stacking along the *b*-axis .

On the other hand the reason for the disorder of the acetonitrile is that the complex of the macrocycle **IX** exists as "*R*"- or "*S*"- conformers in the solid state (*Fig. 38*). The molecular piles are "chiral", because one 'pile' consists of only "*R*"-conformers or only "*S*"-conformers. Thus, "*R*"-conformers make "*R*"-piles and "*S*"-conformers make "*S*"-piles. The crystals of **IX** are racemic consisting both "*R*"- and "*S*"-piles (*Fig. 37*). Similar systems have been found earlier for *N,N',N'',N'''*-tetramethyl-2,11,20,29-tetra-aza[3.3.3.3]*para*-cyclophane.[71] The clathrate crystals are stable only in acetonitrile solution and when taken out from the solution the crystals break down and dissipate the acetonitrile in a few hours.



"*S*" "*R*"

Figure 38. The "*R*"- and "*S*"-conformers of macrocycle **IX**, front view on left (space filled model) and side view on right (ball-stick model).

2.4.4.3. Molecular inclusion compounds

Molecular inclusion compounds, where acetonitrile (solvent, guest) was included inside the cavity of macrocycle (host), have been reported during the last two decades.[59,60,104-110] The piperazine macrocycles **X**, **XI**, **XII**, **XIII**, **XIV** show molecular inclusion with acetonitrile[III-VI] and chloroform[IV] molecules.

Structure of 1² - Nitro - 1(1,3),5,7(1,4) - tribenzena - 3,9(1,4) - dipiperazinacyclodeca-phane **X:**

The compound **X** crystallises from acetonitrile as an inclusion compound in space group *P* $2_1/n$.[V] The crystal structure shows that acetonitrile is included inside the cavity from the methylene part of CH_3CN (*Fig. 39*).

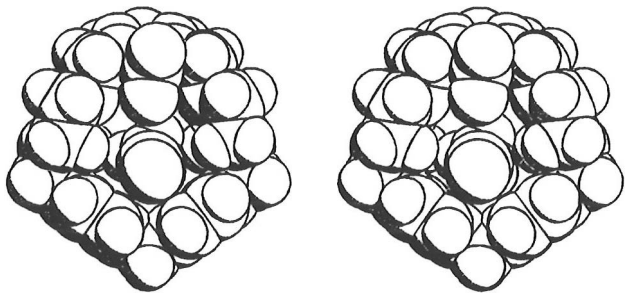


Figure 39. A Stereo plot of inclusion compound **X** (space filling model).

The packing diagram shows that the methylene part of the diphenylmethane moiety is slightly included in the cavity of the adjacent cycle leaving space on the other side of the cavity for the acetonitrile inclusion. The dimeric structure resembles the self-complementary structures of **V** and **VI**. Arrows in the packing diagram show how the structure continues in the space (*Fig. 40*). The very tight packing means that the acetonitrile is bound very strongly and one indication is the stability of the crystals at room temperature (several days). The thermal gravimetry (TG) investigation (APPENDIX IV) shows that the inclusion system breaks down in a temperature range of 80-110 °C.

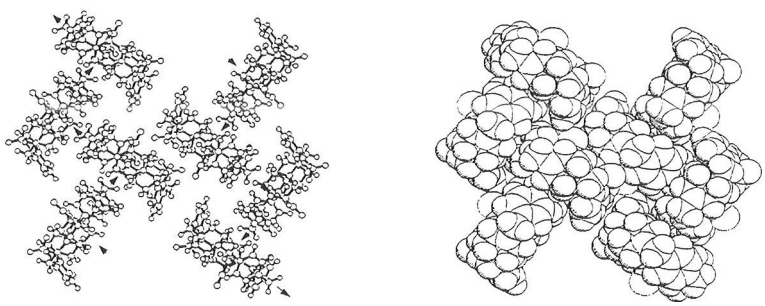


Figure 40. Packing diagram of **X** showing the close contacts between cycles (space filling model on the right).

Structure of 1^2 - Amino - 1(1,3),5,7(1,4) - tribenzena - 3,9(1,4) - dipiperazinacyclodeca-phane **XI**:

The macrocycle **XI** was synthesised by reduction of **X** with $SnCl_2 \cdot 2\ H_2O$ in THF. **XI** crystallises in space group *A* 2/*c* from acetonitrile solution. The crystal structure of **XI**

shows a similar inclusion of acetonitrile as for **X** (*Fig. 41*). The amino group locks the acetonitrile inside the cavity by hydrogen bonds to piperazine *N*-atoms. The packing diagram (*Fig. 42*, *Fig. 43* and *Fig. 44*) shows that two of these inclusion compounds form a complementary structure, in the same way as **V**, **VI** and **X**. The crystal structure also contains disordered water molecules, which are located in the channels between dimeric assemblies.

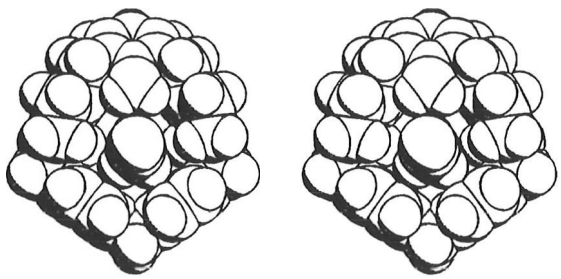


Figure 41. A Stereo plot of inclusion compound **XI** (space filling model).

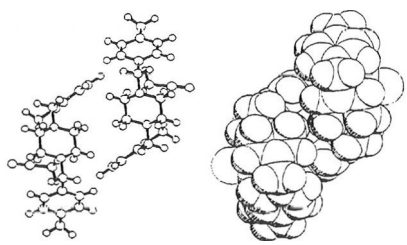


Figure 42. Dimeric structure of **XI**, a 4-component supramolecule (space filling model on the right).

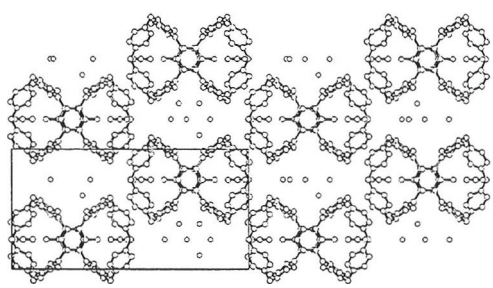


Figure 43. Packing along *a*-axis of **XI** showing small channels between dimeric self-assemblies.

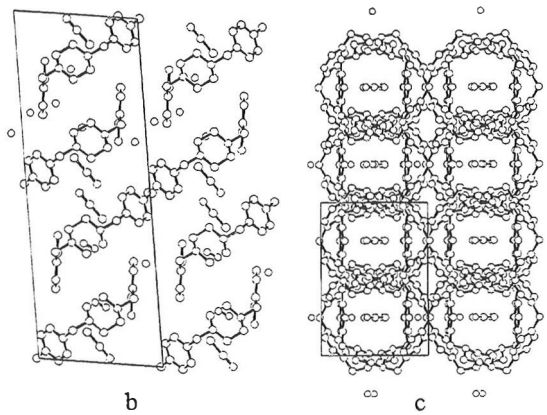


Figure 44. Packing along the *b*- and *c*-axis of **XI**, respectively.

Structure of $1^2,5^2,9^2,13^2$-Tetranitro-1,5,9,13(1,3)-tetrabenzena-3,7,11,15(1,4)-tetra-piperazinacyclohexadecaphane **XII**:

The macrocycle **XII** was recrystallized from acetonitrile-ethanol solution. The X-ray structure proved that it crystallises as an inclusion complex, where acetonitrile is included into the 'corners' of the cavity (*Fig. 45*). Because of the disorder of the acetonitrile, it has two places in the cavity, but both places can't be reserved at the same time (no room for two acetonitrile molecules at the same time). On the other hand similar self-complementary is also present as with compounds **V**, **VI**, **X**, **XI** (*Fig. 46*).

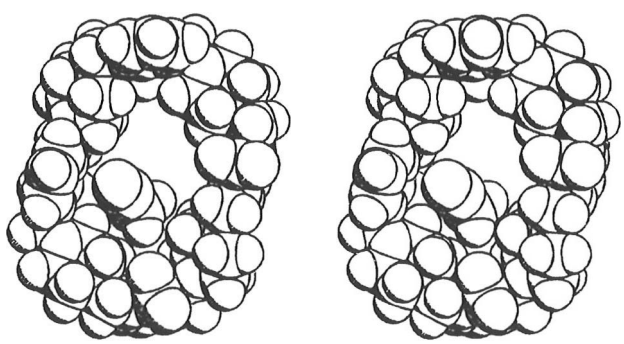


Figure 45. A Stereo plot of inclusion compound **XII** (space filling model).

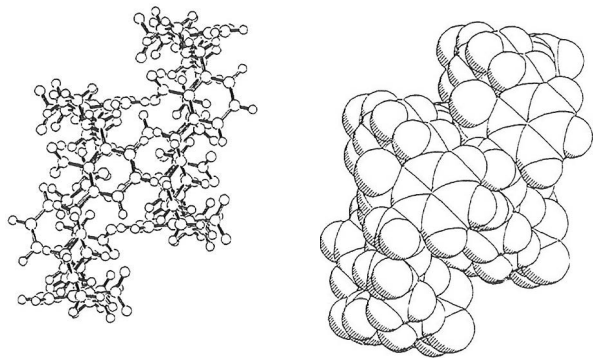


Figure 46. Dimeric complementary structure of **XII** (space filling model on the right).

The packing diagram (*Fig. 47*) of **XII** shows that cycles form piles by stacking as macrocycle **IX**. The piles can't be "chiral" in this case due to the symmetry of the molecule.

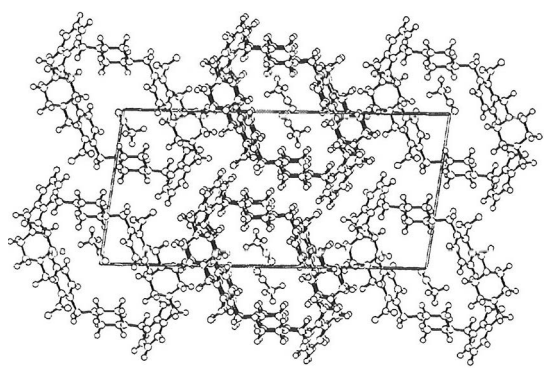


Figure 47. Packing diagram of **XII** along *b*-axis showing the stacking of the macrocycles.

2.4.4.4 Structures of photoactive piperazinophanes

Photochemistry plays an important role in nature, for example, photosynthesis in plants and the processing of optical signals in the eye. Many of these processes are still unexplained and of such complexity that simpler models are needed for their investigation. Photoactive compounds such as stilbenes and azobenzenes have been

extensively studied. Chemists are interested in these compounds because their theoretical and practical use.[2,72,73,74] One example of their application is optically switchable liquid crystals.[75,76] Similarly, the incorporation of photoactive group(s) into macrocyclic compounds[77,78] expands host-guest chemistry to switchable hosts, where position **A** is ON (inclusion of guest is possible) and position **B** is OFF (inclusion of guest is blocked) (*Fig. 48*). This switchability is carried out by the isomerisation of the double bond(s) and it causes a change in conformation, thus changing the inclusion capability.

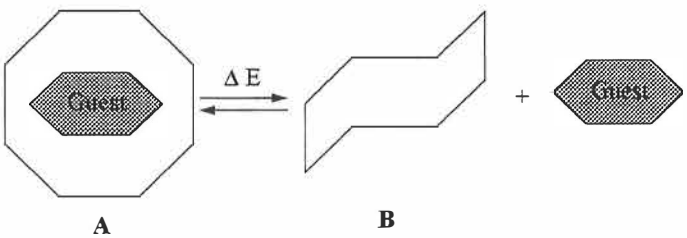


Figure 48. Principle of a switchable host molecule.

Azobenzene was first described in 1834 by Mitscherlich.[79] One hundred years later it was found that when azobenzene solution was exposed to light, the configuration of the N=N double bond change (*Fig. 49*). This photoisomerisation occurs in the UV-region and always leads to a photostationary state. For example when irradiating at λ=313 nm 80% (*Z*)-isomer is obtained and using λ=365 nm the isomerisation is 40%.[80] In addition, a dependence of the solvent has been also found.[81] The (*E*)-isomer is the thermodynamically favoured form, but the (*Z*)–isomer can also be stable in the solid state, but in the solutions it isomerises back to the (*E*)–isomer.[82] The isomerisation is increased by temperature and decreased by polarity of the solvent.

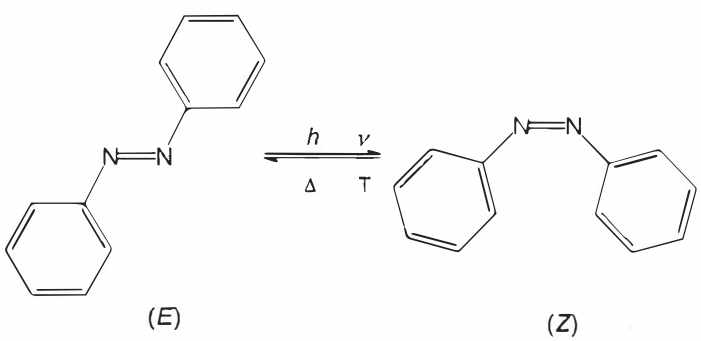


Figure 49. (*E*)- and (*Z*)-forms (*trans* and *cis*) of azobenzene.

Examples of macrocyclic azobenzene compounds are known[83-88] and they can be classified as cyclophanes due to the presence of bridged aromatic nuclei. In this thesis four photoactive piperazinophanes were synthesised using the reaction of 4,4'-bis(bromomethyl)azobenzene and piperazine or with N-monosubstituted piperazine. The structure of two of these azobenzene piperazinophanes (**XIII** and **XIV**) was solved by X-ray diffraction.[IV]

*The Structure of 1,3,7,9(1,4)-Tetrabenzena-2-diazena-5,11(1,4)-dipiperazinacyclodecaphane (**XIII**):*

The compound **XIII** crystallises from acetonitrile and X-ray structure shows a self-assembly structure, where two cycles and three acetonitriles forms the asymmetric unit (*Fig. 50*). One actonitrile is included inside one cycle, which blocks the cavity of the other cycle. Two acetonitriles are situated in between the dimers. These two cycles are enantiomers to each other (*Figs. 51* and *52*), due to the different conformation of the (*E*)-form.

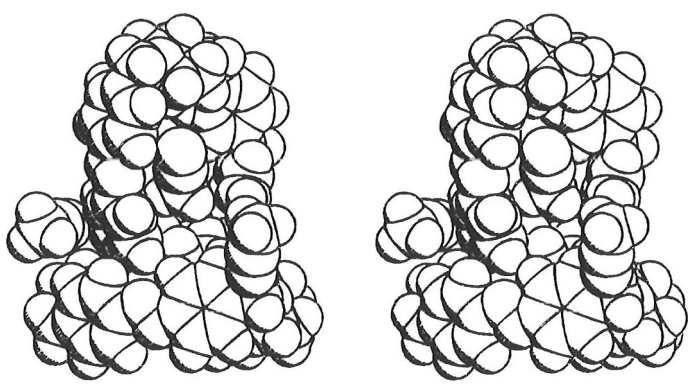


Figure 50. A Stereo plot of the self-assembly structure of **XIII** (space filling model).

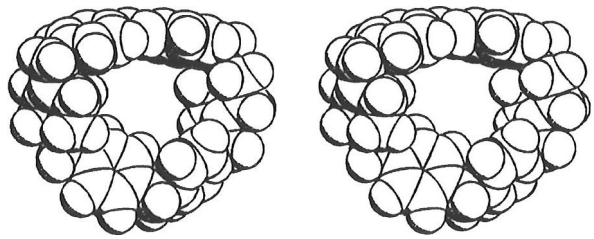


Figure 51. A stereo plot of the enantiomer **A** of **XIII** in the crystalline state (space filling model).

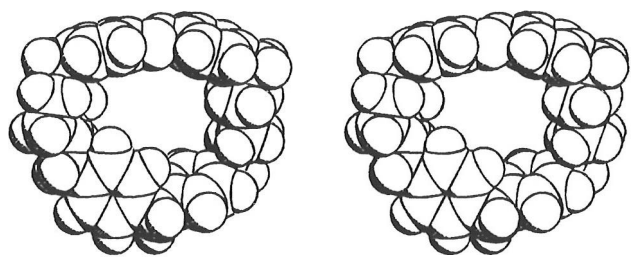


Figure 52. A Stereo plot of the enantiomer **B** of **XIII** in the crystalline state (space filling).

*$7^2,17^2$-Nitro-1,3,11,13(1,4),7,17(1,3)-hexabenzena-2,12-bis(diazena)-5,9,15,19-tetra-piperazinacycloeicosaphane (**XIV**):*

The compound **XVI** crystallises from $CHCl_3$: CH_3CN in a monoclinic $P\ 2_1/c$ space group. The X-ray structure shows a large cavity which contains both chloroform and acetonitrile molecules (*Fig. 53*). The cycles are organised into a channel structure by stacking. These tubes are packed along the *b*-axis leaving small room between the cycles. The crystal lattice also contains chloroform molecules which are located between the cycles for chloroform molecules (*Fig. 54*).

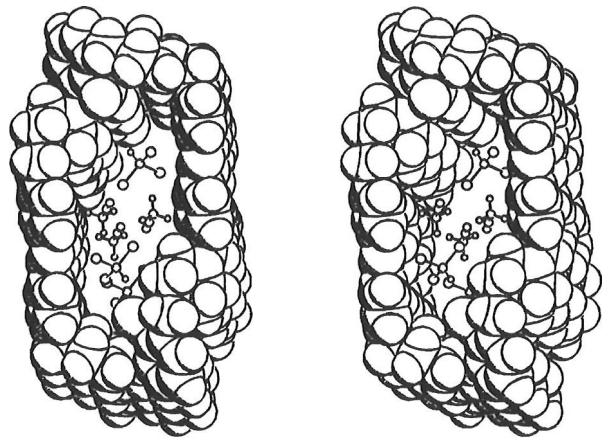


Figure 53. A Stereo plot of the tube structure of **XIV** (space filling model, radii of the solvent molecules are reduced).

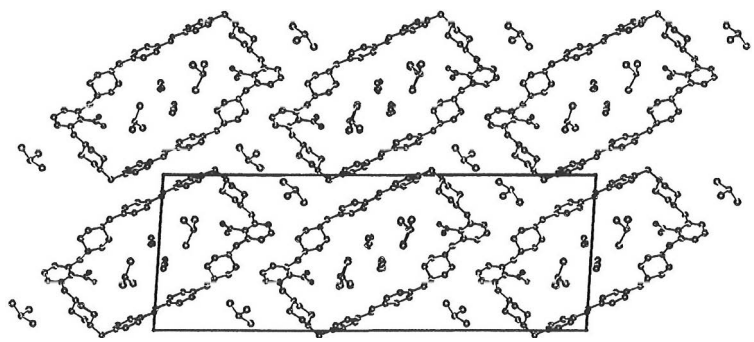


Figure 54. Packing structure of **XIV** along the *b*-axis.

3. SUMMARY AND CONCLUSIONS

In this work 18 new macrocycles and one acidic ligand were synthesised. The preparation of piperazine macrocycles were performed by two synthesis routes. The direct one-step route (*Formula 2.2*) is useful for producing symmetrical piperazine macrocycles. The weakness in this method is the number of cyclic products, which means problems in the purification of the compounds and the impossibility of affecting of the size of the formed cycles. Another method, the two-step route (*Formula 2.3*), is useful for preparation piperazine macrocycles, which contain two different kinds of spacers. The good point in this procedure is usually that it yields only one cyclic product and an easier purification process than in the first method.

The structural studies in the solid state were performed for 14 of these compounds. Remarkably, almost all determined compounds show supramolecular properties in the solid state. The acidic ligand triethanol amine-*O*,*O*,*O*-triacetic acid forms new kinds of dimeric assembly where three Na^+ ions are encapsulated inside the cage (**VII**, **VIII**), as in cryptates. This opens up a new field of structural supramolecular chemistry where spatially compatible species can interact by self-organisation via complexation. Another interesting metal-complex system was found in the copper(I) complex of pyridine-piperazine dimeric macrocycle (**II**), which shows an allosteric effect upon complexation caused by pH. In this system copper(I), has unusual twisted tetrahedral co-ordination geometry.

The self-complementary structures have also been found for piperazine macrocycles (**IV**, **V**, **VI**). In this self-complementary structure two molecules complete their own structure as in the case of a tennis ball (*Fig. 26*). The piperazine macrocycles have also shown two kind of inclusion types in the solid state; crystal lattice and molecular inclusion. The crystal lattice inclusion e.g. clathrate structure has been observed when compound (**IX**) was recrystallised from acetonitrile. The acetonitrile is included between the macrocycles, which form piles by stacking. These piles proved to be "chiral" (mirror images for each other) due to the disorder of the acetonitrile. Molecular inclusion has been found especially for small predefined cavities (**X**, **XI**, **XIII**), but also for larger rings like **XII**, **XIV**. The inclusion of **X** proved to be unusually stable in the solid state. According to the TG-measurement the crystals are stable up to 80 °C and the breakdown is complete at 120 ° (mean point for weight loss is 95 °C). In addition these inclusion compounds also show similar self-complementary structures as compounds **V**, **VI**. In

addition, azobenzene units have been incorporated into piperazine macrocycles making the variation of the shape and the size of the cavity possible.

In summary, piperazine has been found to be a good spacer for preparation of large macrocycles, suitable for the inclusion of small organic guests, and also small macrocycles for metal-complexing. The prepared macrocycles show promising supramolecular properties, especially the acetonitrile inclusion to small cavity of the **X** and copper(I) complex of **I**.

4. REFERENCES

List of the original publications by the author:

I Rissanen, K., Huuskonen, J., Windscheif, P.-M., Vögtle, F., Self-assembly by co-ordination and strong hydrogen bonding. X-ray crystal structures of a dimeric trisodium complex of a new acidic complexing ligand and its dihydrate *Supramolecular Chem. 2* (1993) 247–250.

II Rissanen, K., Huuskonen, J., Koskinen, A., 1^2,5^2,9^2,13^2-Tetranitro-1,5,9,13(1,3)-tetrabenzena-3,7,11,15(1,4)-tetrapiperazinacyclohexadecaphane, a New Host Compound *J. Chem. Soc., Chem. Commun.* (1993) 771–772.

III Rissanen, K., Breitenbach, J., Huuskonen, J., An Unusual Copper(I) Complex of a New Macrocyclic Ligand *J. Chem. Soc., Chem. Commun.* (1994) 1265–1266.

IV Huuskonen, J., Schulz, J., Kolehmainen, E., Rissanen, K., Photoresponsive Piperazine Macrocycles *Chem. Ber. 127* (1994) 2267–2272 .

V Huuskonen, J., Rissanen, K., Acetonitrile Inclusion Complexes of Piperazine-Based Macrocycles *Liebigs Ann.* (1995) 1611-1615.

VI Huuskonen, J., Schulz, J., Rissanen, K., Macrocyclic (1,3)- and (1,4)-Benzena-(1,4)-Piperazinacyclophanes *Liebigs Ann.* (1995) 1515–1519.

Literature references:

1. Pedersen, C. J. *J. Am. Chem. Soc. 89* (1967) 2495–2496, 7017–7036.
2. Vögtle, F. *Supramolecular Chemistry*, John Wiley & Sons, Chichester, New York, Brisbane, Toronto 1991.
3. Simon, J., Andre, J. J., Skoulios, A. *Nouv. J. Chem. 10* (1986) 295–311.
4. Lehn, J.-M. *Angew. Chem. 100* (1988) 91–116.
5. Ahlers, M., Müller, W., Reichert, A., Ringsdorf, H. Venzmer, J. *Angew. Chem. Int. Engl. 29* (1990) 1269–1285.

6. Szejtli, J., *Cyclodextrin technolgy*, Kluwer Academic Publishers, Dodrecht, Netherlands, 1988.
7. Seel, C., Vögtle, F. *Angew. Chem. Int. Ed. Engl. 31* (1992) 528–549.
8. Pedersen, C. J. *Angew. Chem. 100* (1988) 1053–1059.
9. Thiem, H.-J., Brandl, M., Breslow, R. *J. Am. Chem. Soc. 110* (1988) 8012–8016.
10. Diederich, F. *Angew. Chem. 100* (1988) 372–396.
11. Hamilton, A. D. *J. Chem. Educ. 67* (1990) 821–828.
12. Hamilton, A. D. *Pure & Appl. Chem. 60* (1988) 533–538.
13. Chang, S. K., Hamilton, A. D. *J. Am. Chem. Soc. 110* (1988) 1318–1319.
14. Chang, S. K., Van Engen, D., Fan, E., Hamilton, A. D. *J. Am. Chem. Soc. 113* (1991) 7640–7645.
15. Lehn, J.-M. *Pure & Appl. Chem. 51* (1979) 979–997.
16. Breslow, R., Overman, L. E., *J. Am. Chem. Soc. 92* (1970) 1075–1077.
17. Hosseini, M. W., Lehn, J.-M., Mertes, M. P. *Helv. Chim. Acta 66* (1983) 2454–2466.
18. Hosseini, M. W., Lehn, J.-M. *Helv. Chim. Acta 70* (1987) 1312–1319.
19. Schwarzenbach, G., Kampitsch, E., Steiner, R. *Helv. Chim. Acta 28* (1945) 1133–1143.
20. Kaim, W., Schwederski, B. *Bioorganische Chemie*, Teubner, Stuttgart 1991.
21. Allinger, N. L., Carpenter, J. G. D., Karkowski, F. M. *J. Am. Chem. Soc. 87* (1965) 1232–1236.
22. Stewart, H. W., Turner, R. J., Denton, J. J., Kushner, S., Brancone, L. M., McEven, W. L., Hewitt, R. I., Subbarrow, Y. *J. Org. Chem. 13* (1948) 134–143.
23. Kushner, S., Brancone, L. M., Hewitt, R. I., McEven, W. L., Subbarow, Y., Stewart, H. W., Turner, R. J., Denton, J. J. *J. Org. Chem. 13* (1948) 144–153.
24. Mann, F. G., Mukherjee, P. *J. Chem. Soc.* (1949) 2298–2302.
25. Parish, E. P. *J. Org. Chem. 39* (1974) 1592–1593.
26. Chénevert, R., Plante, R. *Synthesis* (1983) 847–848.
27. Larkins, H. L., Hamilton, A. D. *Tetrahedron Lett.* (1986) 2721–2724.
28. Krakowiak, K. E., Bradshaw, J. S, Jiang, W., Dalley, N. K., Wu, G., Izatt, R. M. *J. Org. Chem. 56* (1991) 2675–2680.
29. Kihara, N., Saigo, K., Kabata, Y., Ohno, M., Hasegawa, M. *Chem. Lett.* (1989) 1289–1292.
30. Bazzicalupi, C., Bencini, A., Fusi, V., Micheloni, M., Valtancoli, B. *J. Chem. Soc., Chem. Commun.* (1994) 1119–1120.
31. Wade, P. W., Hancock, R. D. *J. Chem. Soc. Dalton Trans.* (1990) 1323–1327.

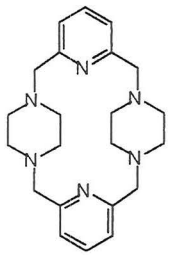
32. Hancock, R. D., Ngwenya, M. P., Evers, A., Wade, P. W., Boeyens, J. C. A., Dobson, S. M. *Inorg. Chem. 29* (1990) 264–270.
33. Wade, P. W., Hancock, R. D., Boeyens, J. C. A., Dobson, S. M. *J. Chem. Soc. Dalton Trans.* (1990) 483–488.
34. Hancock, R. D, Ngwenya, M. P., Wade, P. W., Boeyens, J. C. A., Dobson, S. M. *Inorganica Chimica Acta 164* (1989) 73–84.
35. Hancock, R. D., Dobson, S. M., Evers, A., Wade, P. W., Ngwenya, M. P., Boeyens, J. C. A., Wainwright, K. P. *J. Am. Chem. Soc. 110* (1988) 2788–2794.
36. Galli, C., Mandolini, L. *J. Chem. Soc., Chem. Commun.* (1982) 251–253.
37. Illuminati, G., Mandolini, L. *Acc. Chem. Res. 14* (1981) 95–102.
38. Vögtle, F., Wolz, U. *Chem. Exp. Didakt. 1* (1975) 15–18.
39. Vögtle, F. *Chemiker-Zeitung 96* (1972) 396–403.
40. Richman, J. E., Atkins, T. J. *J. Am. Chem. Soc. 96* (1974) 2268–2270.
41. Ostrowicki, A., Koepp, E., Vögtle, F. *Top. Curr. Chem. 161* (1992) 37–67.
42. Galli, C. *Org. Prep. Proced. Int. 24* (1992) 285–307.
43. Hoss, R., Vögtle, F. *Angew. Chem. Int. Ed. Engl. 33* (1994) 375–384.
44. Thompson, M. C., Busch, D. H. *J. Am. Chem. Soc. 84* (1962) 1762–1763.
45. Craig, J. C., Young, R. *J. Org. Synth. Coll. Vol 5* 88.
46. Walker, N., Stuart, D. *Acta Crystallogr., Sect. A. 39* (1983) 158–166.
47. Sheldrick, G. M., in *Crystallographic Computing*, (Eds. G. M. Sheldrick, C. Krüger, R. Goddard), *vol. 3*, Oxford University Press, Oxford 1985, pp. 175–189.
48. Watkin, D., Carruthers, B., Betteridge, P. W. *CRYSTALS*, Chemical Crystallography Laboratory, Oxford, England 1990.
49. Greenwood, N. N., Earnshaw, A. *Chemistry of Elements*, Pergamon Press, Oxford, New York, Toronto, Sydney, Paris, Frankfurt 1984, pp. 1386–1390.
50. Klug, A. *Angew. Chem. 95* (1983) 579–596.
51. Jaenicke, R., *Angew. Chem. 96* (1984) 385–454.
52. Howard-Lock, H. E., Lock, C. J. L., Martins, M. L., Faggiani, R., Duarte, M. *Can. J. Chem. 65* (1987) 878–883.
53. Ref. 2 pp.172–193.
54. Powell, H. M. *J. Chem. Soc.* (1948) 61–73.
55. Atwood, J. L., Davies, J. E. D., MacNicol, D. D. (Eds.) *Inclusion Compounds*, Academic Press, New York 1984.
56. Gokel, G. W., Cram, D. J., Liotta, C. L., Harris, H. P., Cook, F. L. *J. Org. Chem. 39* (1974) 2445–2446.
57. Goldberg, I. *Acta Crystallogr., Sect. B31* (1975) 754–762.
58. Mak, T. C. W., Lee, K.-S. *Acta Crystallogr., Sect. B34* (1978) 3631–3634.

59. Tanaka, I., Tajima, I., Hayakawa, Y., Okada, M., Bitoh, M., Ashida, T., Sumimoto, H. *J. Am. Chem. Soc. 102* (1980) 7873–7876.
60. Sakuragi, I., Tanaka, I., Ashida, T., Tajima, I., Okada, M., Sumimoto, H. *J. Am. Chem.Soc. 104* (1982) 6035–6039.
61. Chan, T.-L., Mak, T. C. W. *J. Chem. Soc., Perkin Trans. 2* (1983) 777–781.
62. Gilmore, C. J., MacNicol, D. D., Murphy, A., Russell, M. A. *Tetrahedron Lett. 24* (1983) 3269–3272.
63. Rogers, R. D., Kurihara, L. K., Richards, P. D. *J. Chem. Soc., Chem. Commun.* (1987) 604–606.
64. Weber, E., Franken, S., Ahrendt, J., Puff, H. *J. Org. Chem. 52* (1987) 5291–5292.
65. Rogers, R. D., Richards, P. D., Voss, E. J. *J. Incl. Phenom. 6* (1988) 65–71.
66. Garrell, R. L., Smyth, J. C., Fronczek, F. R., Gandour, R. D. *J. Incl. Phenom. 6* (1988) 73–78.
67. Rogers, R. D. *J. Incl. Phenom. 6* (1988) 629–645.
68. Grootenhuis, P. D. J., Kollman, P. A. *J. Am. Chem. Soc. 111* (1989) 4046–4051.
69. Panneerselvam, K., Chacko, K. K., Weber, E., Köhler, H. J. *J. Incl. Phenom. 9* (1990) 337–347.
70. Goldberg, I., in *Inclusion Compounds vol. 4* ed. Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Oxford University Press, Oxford, New York, Tokyo 1991, pp. 406–447.
71. Hirotsu, K., Kamitori, S., Higutschi, T., Tabushi, I., Yamamura, K., Nonoguchi, H. *J. Incl. Phenom. 2* (1984) 215–222.
72. Meier, H., *Angew. Chem. Int. Ed. Engl. 31* (1992) 1399–1420.
73. Meier, H., Zertani, R., Noller, K., Oelkrug, D. *Chem. Ber. 119* (1986) 1716–1724.
74. Bortolus, P., Monti, S. *J. Phys. Chem. 91* (1987) 5046–5050.
75. Meier, H., Kosteyn, N., Hanold, N., Rau, H., Gauglitz, G. *Chem. Ber. 125* (1992) 889–892.
76. Kosteyn, F., Zerban, G., Meier, H. *Chem. Ber. 125* (1992) 893–897.
77. Desvergne, J.-P., Fages, F., Bouas-Laurent, H., Marsau, P., *Pure & Appl. Chem. 64* (1992) 1231–1238.
78. Wild, U. P., Bernet, S., Kohler, B., Renn, A. *Pure & Appl. Chem. 64* (1992) 1335–1342.
79. Mitscherlich, E. *Ann. Pharm. 12* (1834) 311.
80. Hausser, I. *Naturwissenschaften 36* (1949) 315–317.
81. Fischer, E., Frankel, M., Wolovsky, R. *J. Chem. Phys. 23* (1955) 1367.
82. Bortolus, P., Monti, S. *J. Chem. Phys. 83* (1979) 648–652.
83. Vögtle, F., Bauer, M., Thiligen, C., Knops, P. *Chimia 45* (1991) 319–321.

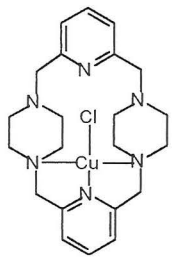
84. Losensky, H.-W., Spelthann, H., Ehlen, A., Vögtle, F., Bargon J. *Angew. Chem. 100* (1988) 1225–1227.
85. Tamaoki, N., Koseki, K., Yamaoka, T. *Angew. Chem. Int. Ed. Engl. 29* (1990) 105–106.
86. Rau, H., Lüddecke, E., *J. Am. Chem. Soc. 104* (1982) 1616–1620.
87. Gräf, D., Nitsch, H., Ufermann, D., Sawitzki, G., Patzelt, H., Rau, H. *Angew. Chem. 94* (1982) 385–386.
88. Tanner, D., Wennerström, O. *Tetrahedron Lett. 22* (1981) 2313–2316.
89. Lehn, J.-L. *Angew. Chem. Int. Ed. Engl. 29* (1990) 1304–1319.
90. Ducharme, Y., Wuest, J. D. *J. Org. Chem. 53* (1988) 5789–5791.
91. Tecilla, P., Dixon, R. P., Slobodkin, G., Alavi, D. S., Waldeck, D. H., Hamilton, A. D. *J. Am. Chem. Soc. 112* (1990) 9408–9410.
92. Tjivikua, T., Ballester, P., Rebek Jr., J. *J. Am. Chem. Soc. 112* (1990) 1249–1250.
93. Lehn, J.-L., Rigault, A. *Angew. Chem. 100* (1988) 1121–1122.
94. Constable, E. C. *Tetrahedron 48* (1992) 10013–10059.
95. Krämer, R., Lehn, J.-L., DeCian, A., Fischer, J. *Angew. Chem. Int. Ed. Engl. 32* (1993) 703–706.
96. Eidenschink, R. *Angew. Chem. Adv. Mater. 101* (1989) 1454–1458.
97. Ward, M. D. *Pure & Appl. Chem. 64* (1992) 1623–1627.
98. Seto, C. T., Whitesides, G. M. *J. Am. Chem. Soc. 113* (1991) 712–713.
99. Hunter, C. A., Sarson, L. D. *Angew. Chem. Int. Ed. Engl. 33* (1994) 2313–2316.
100. Baxter, P. N. W., Lehn, J.-L., Fischer, J., Youinou, M.-T. *Angew. Chem. Int. Ed. Engl. 33* (1994) 2284–2287.
101. Baxter, P., Lehn, J.-L., DeCian, A., Fischer, J. *Angew. Chem. Int. Ed. Engl. 32* (1993) 69–71.
102. Rüttimann, S., Piguet, C., Bernardinelli, G., Bocquet, B., Williams, A. F. *J. Am. Chem. Soc. 114* (1992) 4230–4237.
103. Wyler, R., de Mendoza, J., Rebek Jr., J. *Angew. Chem. Int. Ed. Engl. 32* (1993) 1699–1701.
104. Sakuragi, I., Tanaka, I., Ashida, T., Tajima, I., Okada, M., Sumimoto, H. *J. Am. Chem. Soc. 104* (1982) 6035–6039.
105. Allwood, B. L., Fuller, S. E., Ning, P. C. Y. K., Slawin, A. M. Z., Stoddart, J. F., Williams, D. J. *J. Chem. Soc., Chem. Commun.* (1984) 1356–1360.
106. Weber, E., Köhler, H.-J., Panneerselvam, K., Chacko, K. K. *J. Chem. Soc. Perkin Trans. 2* (1990) 1599–1605.
107. Cram, D. J., Tanner, M. E., Knobler, C. B. *J. Am. Chem. Soc. 113* (1991) 7717–7727.

108. Weber, E., Köhler, H.-J., Reuter, H. *J. Org. Chem. 56* (1991) 1236–1242.
109. Tanner, M. E., Knobler, C. B., Cram, D. J. *J. Org. Chem. 57* (1992) 40–46.
110. Cram, D. J., Tunstad, L. M., Knobler, C. B. *J. Org. Chem. 57* (1992) 528–535.
111. Breitenbach, J., Rissanen, K., Wolf, U. U., Vögtle, F. *Chem. Ber. 124* (1991) 2323–2327.

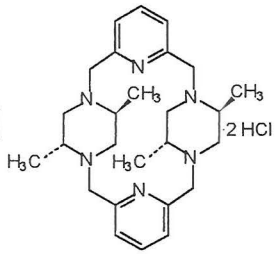
APPENDIX I The numbering of the compounds mentioned in the text.



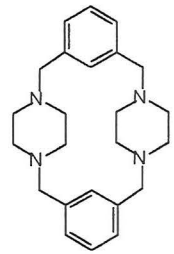
I



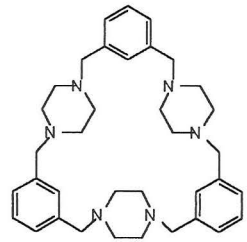
II



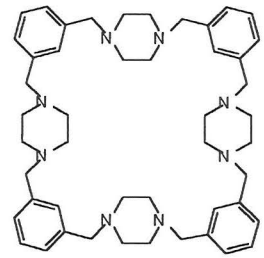
III



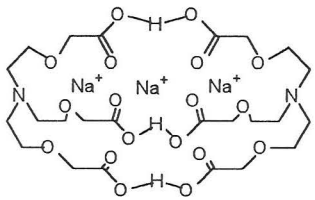
IV



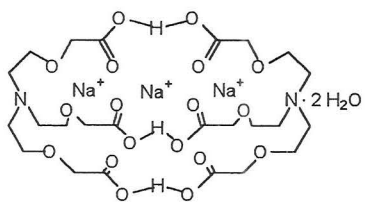
V



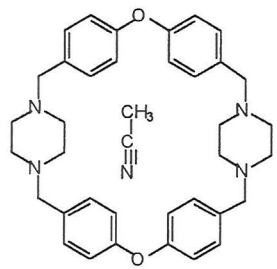
VI



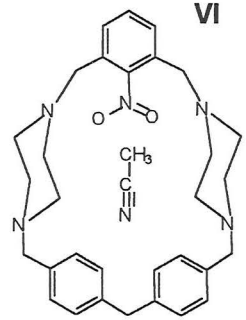
VII



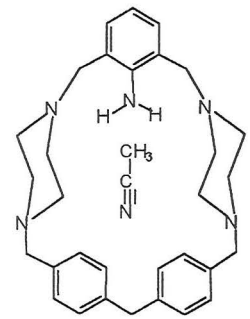
VIII



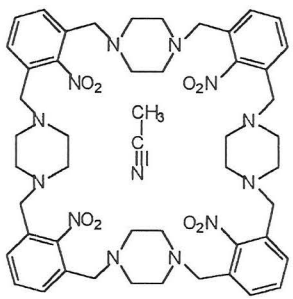
IX



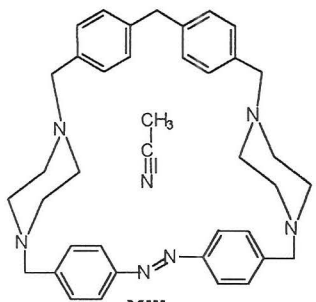
X



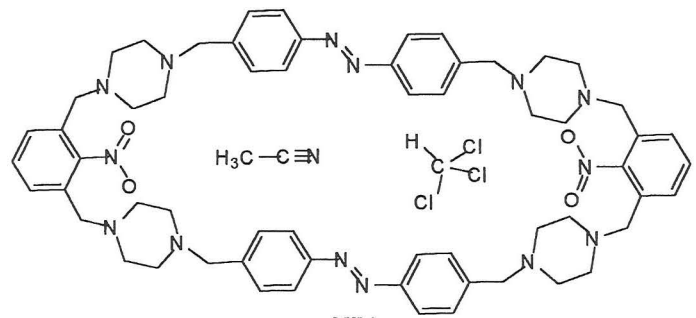
XI



XII



XIII



XIV

APPENDIX II Space groups and unit-cell parameters of the measured compounds.

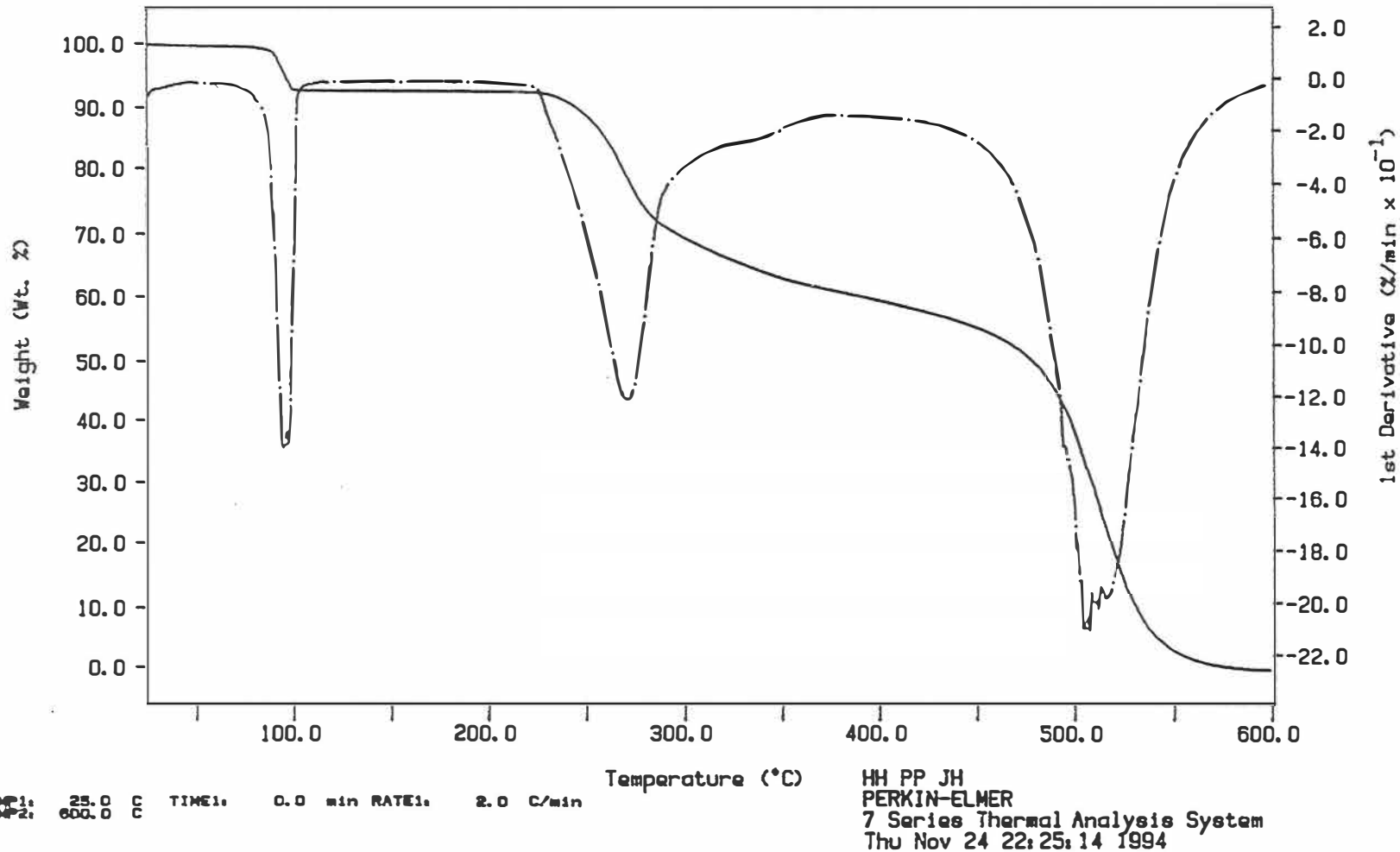
Compound	Space group (n:o)	a [Å]	b [Å]	c [Å]	α [°]	β [°]	γ [°]	V [Å^3]	ref.
I	*C* 2/*c* (15)	17.615(2)	9.696(1)	12.654(1)	90	111.69(1)	90	2008.3(4)	III
II	*P* 2_1/*n* (14)*	10.762(1)	13.714(2)	17.802(5)	90	98.16(2)	90	2600.7(8)	III
III	*P* -1 (2)	10.252(2)	10.750(2)	9.329(2)	106.14(1)	116.14(1)	104.69(1)	791.3(3)	V
IV	*P* -1 (2)	11.151(2)	13.460(2)	13.473(2)	115.645(9)	116.21(2)	88.80(1)	1721.5(5)	V
V	*P* 2_1/*c* (14)	26.255(4)	18.401(3)	13.522(3)	90	104.73(3)	90	6317(3)	V
VI	*P* -1 (2)	14.312(2)	15.032(3)	13.753(3)	103.71(1)	110.87(2)	107.30(1)	2316(1)	–
VII	*R* -3*c* (157)	12.198(1)	12.198(1)	40.926 (5)	90	90	120	5274(3)	I
VIII	*C* 2/*c* (15)	25.045(5)	11.373(2)	14.301(2)	90	122.38(1)	90	3440(1)	I
IX	*P* 2_1/*n* (14)*	13.141(2)	6.224(1)	20.360(2)	90	95.03(1)	90	1658(4)	VI
X	*P* 2_1/*n* (14)*	13.856(2)	11.201(3)	20.700(3)	90	106.15(1)	90	3086(1)	VI
XI	*A* 2/*c* (15)*	9.355(2)	13.599(2)	27.144(3)	90	98.14(1)	90	3415(1)	VI
XII	*P* 2_1/*c* (14)	13.286(1)	7.437(1)	27.985(12)	90	97.95(2)	90	2738(1)	II
XIII	*P* 2_1/*c* (14)	11.089(4)	20.074(3)	36.637(7)	90	116.21(2)	90	7317(3)	IV
XIV	*P* 2_1/*c* (14)	15.305(1)	6.136(1)	42.477(4)	90	93.65(1)	90	3982.2(6)	IV

* Non-standard space group

APPENDIX III Fractional co-ordinates of 1,5,9(1,3)-Tetrabenzena-3,7,11(1,4)-tetra-piperazina-cyclohexaphane (**VI**).

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
N(1)	0.561(2)	0.578(2)	0.797(2)	N(29)	0.858(3)	0.577(3)	0.160(3)
C(2)	0.490(3)	0.622(3)	0.824(3)	C(30)	0.844(4)	0.499(3)	0.066(4)
C(3)	0.567(3)	0.713(3)	0.928(3)	C(31)	0.941(4)	0.479(3)	0.094(4)
N(4)	0.650(3)	0.792(3)	0.928(3)	N(32)	0.965(3)	0.443(2)	0.188(3)
C(5)	0.723(3)	0.744(2)	0.900(3)	C(33)	0.979(3)	0.523(3)	0.284(3)
C(6)	0.652(3)	0.652(3)	0.786(3)	C(34)	0.883(3)	0.546(3)	0.258(3)
C(7)	0.721(4)	0.887(3)	1.016(4)	C(35)	1.055(4)	0.418(3)	0.212(4)
C(8)	0.790(3)	0.968(3)	1.002(4)	C(36)	1.083(3)	0.370(3)	0.297(3)
C(9)	0.899(3)	1.025(3)	1.086(3)	C(37)	1.186(2)	0.400(2)	0.388(3)
C(10)	0.970(2)	1.103(3)	1.074(3)	C(38)	1.194(2)	0.358(3)	0.469(3)
C(11)	0.932(3)	1.127(2)	0.979(4)	C(39)	1.103(3)	0.278(3)	0.456(3)
C(12)	0.821(3)	1.075(3)	0.898(3)	C(40)	0.997(3)	0.247(2)	0.363(3)
C(13)	0.752(2)	0.992(3)	0.907(3)	C(41)	0.986(3)	0.294(2)	0.287(3)
C(14)	0.759(4)	1.085(4)	0.792(4)	C(42)	0.893(4)	0.166(3)	0.351(3)
N(15)	0.715(3)	1.012(3)	0.686(3)	N(43)	0.807(3)	0.198(3)	0.346(3)
C(16)	0.663(4)	1.025(3)	0.578(4)	C(44)	0.711(4)	0.111(3)	0.319(3)
C(17)	0.608(3)	0.944(3)	0.474(3)	C(45)	0.623(3)	0.140(3)	0.321(3)
N(18)	0.694(3)	0.913(3)	0.459(3)	N(46)	0.651(3)	0.224(2)	0.425(3)
C(19)	0.746(4)	0.893(3)	0.560(4)	C(47)	0.745(3)	0.306(3)	0.443(3)
C(20)	0.796(3)	0.967(3)	0.667(3)	C(48)	0.840(3)	0.281(3)	0.454(3)
C(21)	0.664(4)	0.838(4)	0.359(4)	C(49)	0.563(4)	0.248(3)	0.430(3)
C(22)	0.741(2)	0.818(2)	0.326(3)	C(50)	0.588(3)	0.307(2)	0.545(2)
C(23)	0.847(2)	0.897(2)	0.371(2)	C(51)	0.655(2)	0.291(2)	0.635(2)
C(24)	0.925(2)	0.880(2)	0.341(3)	C(52)	0.675(2)	0.342(2)	0.745(2)
C(25)	0.898(2)	0.786(3)	0.262(3)	C(53)	0.623(3)	0.405(2)	0.763(2)
C(26)	0.794(3)	0.707(2)	0.219(3)	C(54)	0.556(3)	0.422(2)	0.673(2)
C(27)	0.716(2)	0.723(2)	0.253(3)	C(55)	0.540(2)	0.374(2)	0.564(2)
C(28)	0.779(4)	0.612(3)	0.142(3)	C(56)	0.506(3)	0.487(3)	0.702(3)

APPENDIX IV The Thermogravimetric (TG) measurement of inclusion compound **X**.



PAPER I

https://doi.org/10.1080/10610279308038323

PAPER II

https://doi.org/10.1002/chin.199334200

PAPER III

(Reprinted with the permission of *the Royal Society of Chemistry*)

https://doi.org/10.1039/C39940001265

PAPER IV

https://doi.org/10.1002/cber.1491271127

PAPER V

https://doi.org/10.1002/jlac.1995199509224

PAPER VI

https://doi.org/10.1002/jlac.1995199508207