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GLYCOLURILS

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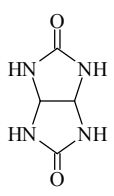
Abstract- In the first part of the review the glycoluril dimers are described, followed by molecular clips and bowl-shaped receptors; then glycoluril capsules and at last some applications of glycolurils are presented.

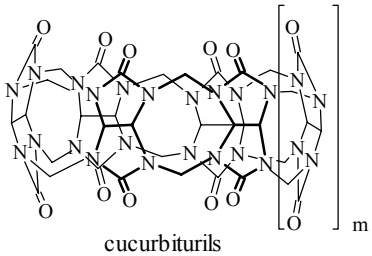
INTRODUCTION

Glycolurils are a topic of numerous reports; [1,2] these compounds are of use in supramolecular chemistry as building blocks for molecular clips [3] and molecular capsules; [4] they form self-complementary facial amphiphiles [5,6] and xerogels. [7] Among glycoluril derivatives, [8-10] their dimers [11,12] deserve a special attention.

Glycolurils are synthons of cucurbiturils, now a field of an intense research. [13-17] Cucurbiturils are components of supramolecular structures, *e.g.* interlocked molecules, [18-21] molecular switches [22,23] and systems of a fascinating shape such as necklaces, [24] gyroscopes [25] or Russian dolls. [26]

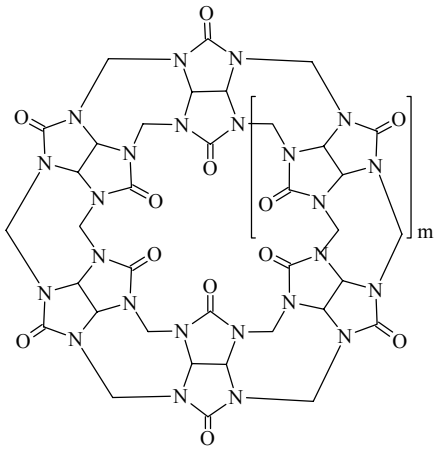


glycoluril



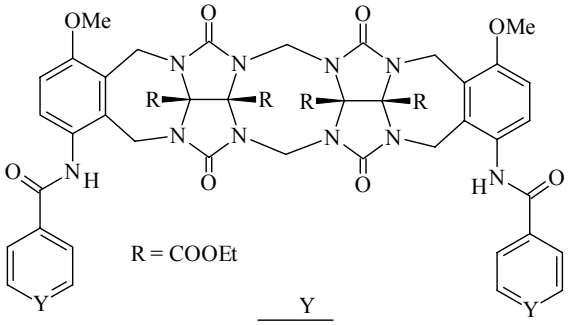
cucurbiturils

CB[n]	m
CB[5]	0
CB[6]	1
CB[7]	2
CB[8]	3

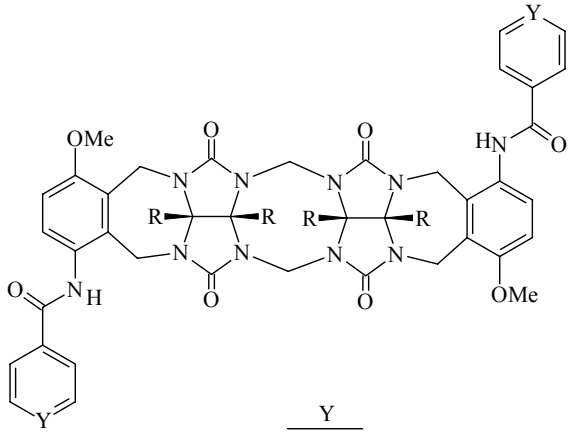


1. GLYCOLURIL DIMERS

Compounds (**1a**, **1b**, (±)-**2a**) and ((±)-**2b**) form in $CDCl_3$ tightly self-associated dimers, driven by the simultaneous formation of π - π interactions and only two C=O...HN hydrogen bonds. [27]



1 **a** CH
b N

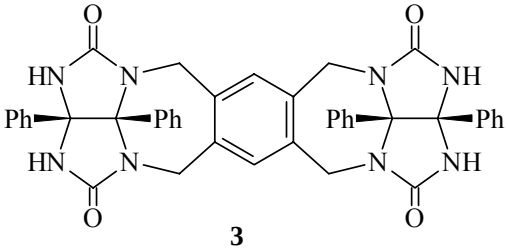


(±)-**2** **a** CH
b N

Compounds (**1a**) and (**1b**) are C_s-symmetric achiral meso forms, while (±)-**2a** and (±)-**2b** are chiral C_2-symmetric species. When **1a** and **1b** were dissolved in $CDCl_3$, homodimers (**1a·1a**) and (**1b·1b**) and heterodimer (**1a·1b**) were formed. It should be noted that in the case of heterodimers of (±)-**2a** and (±)-**2b**, a complete enantioselective discrimination of (+)**2a** between (+)**2b** and (-)**2b** was observed; the heterodimer ((+)**2a**·(-)**2b**) forms exclusively.

The properties of dimers, *i.e.* their tight binding, high levels of chiral discrimination and self-sorting [28] are promising for their applications, such as enantioselective recognition and noncovalent polymer chemistry. [27]

It was shown by ^{1}H NMR spectral measurements that mixtures of **3**-**5** undergo thermodynamic self-sorting in $CDCl_3$ solution. [29] ^{1}H NMR spectra for $\mathbf{3}_2$, $\mathbf{4}_2$ and $\mathbf{5}_2$ have been recorded. In self-sorting systems, the closely related sets of molecules (up to four molecules) aggregate exclusively with themselves, and not with other molecules present in the mixture. The fidelity of self-sorting depends on the temperature, concentration and equilibrium constants. Self-sorting involves the formation of hydrogen bonds, [30] metal-ligand interactions [31] and solvophobic effects, [32] and plays an important role in self-organization.



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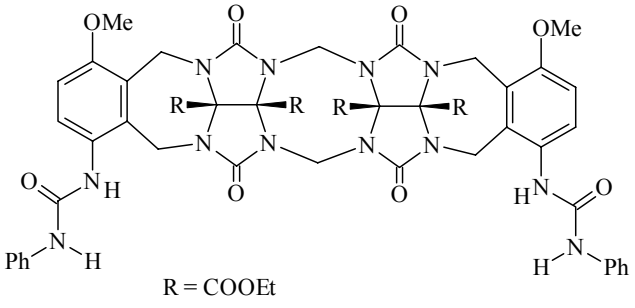

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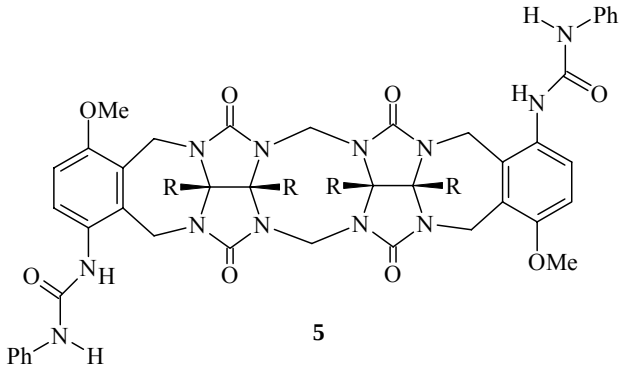
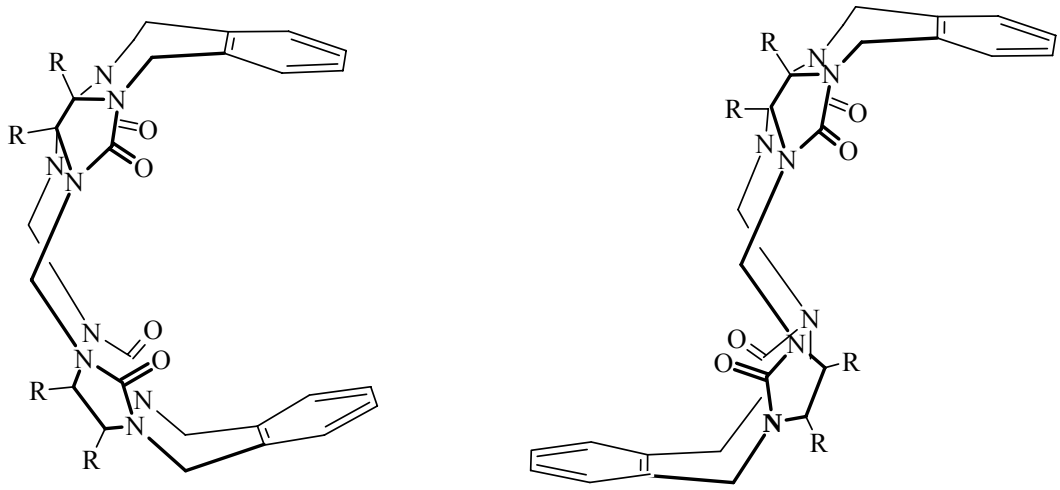


5

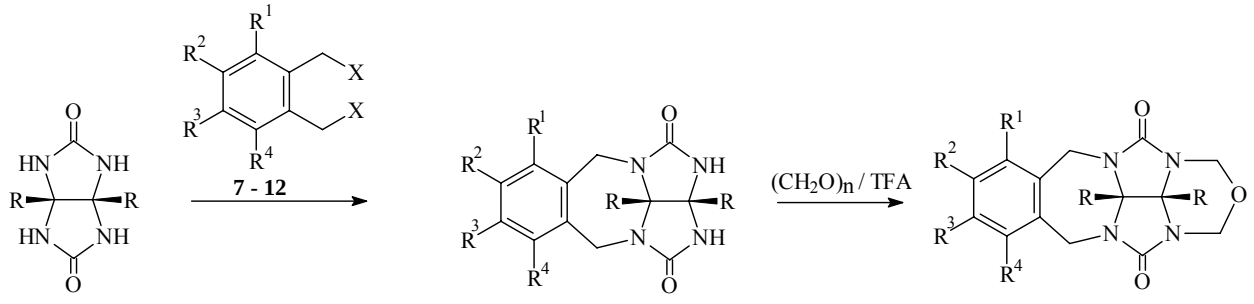
Methylene-bridged C- and S-shaped glycoluril dimers have been obtained; [5,6,27,33] selected examples of their syntheses will be described here. [34]



glycoluril dimers

C - shaped S - shaped

Glycolurils (**6a-c**) react with bis(halomethyl)aromatics (**7-12**) yielding glycoluril derivatives (**13-18**) which by treatment with formaldehyde under anhydrous conditions (TFA) afford cyclic ethers (**19-23**).

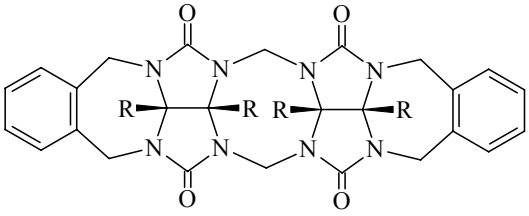


13 - 18 **19 - 23**

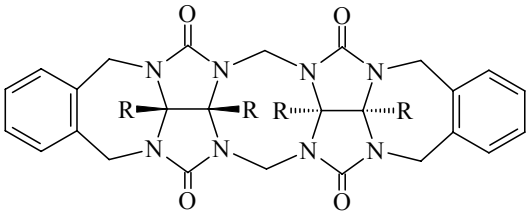
R	
a	COOEt
6 b	2-pyridyl
c	R,R=$(CH_2)_4$

	R^1	R^2	R^3	R^4	X		
7	H	H	H	H	Cl	**13**	**19**
8	H	OMe	OMe	H	Br	**14**	**20**
9	OMe	H	H	OMe	Br	**15**	**21**
10	H	Me	Me	H	Cl	**16**	**22**
11	OMe	H	H	Br	Br	**17**	**23**
12	OMe	H	H	NO_2	Br	**18**	-

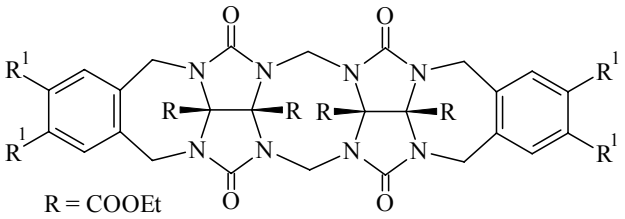
Compounds (**24*C*-30*C***) and (**24*S*-30*S***) are examples of C- and S-shaped glycoluril dimers, respectively.



	R
(from **13a**) **24*C***	COOEt
(from **13b**) **25*C***	2-pyridyl
(from **13c**) **26*C***	R,R =$(CH_2)_4$

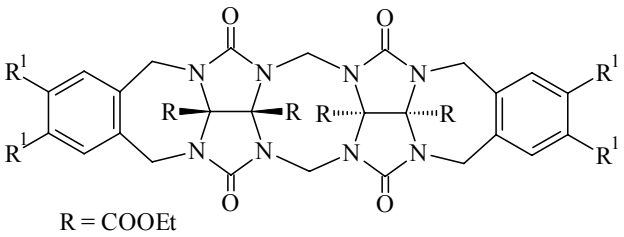


	R
24*S*	COOEt
25*S*	2-pyridyl
26*S*	R,R=$(CH_2)_4$



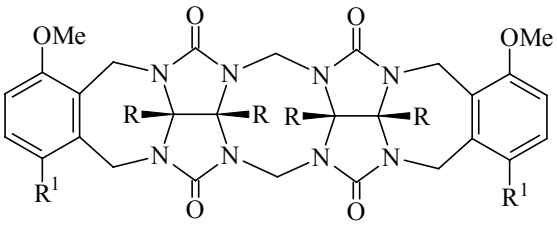
R = COOEt

	R^1
27*C*	OMe
28*C*	Me



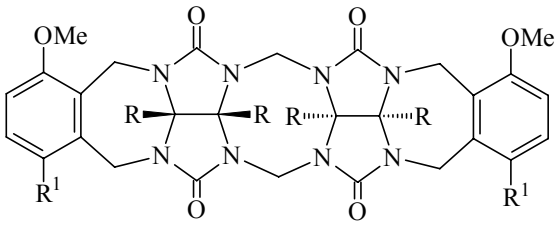
R = COOEt

	R^1
27*S*	OMe
28*S*	Me



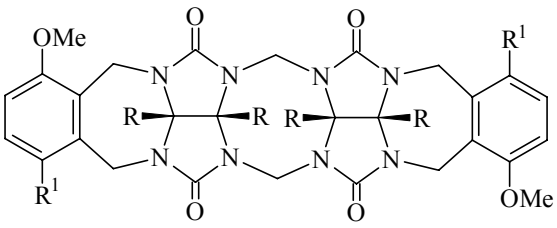
R = COOEt

		R^1
29*C*	*cis*	Br
30*C*	*cis*	NO_2



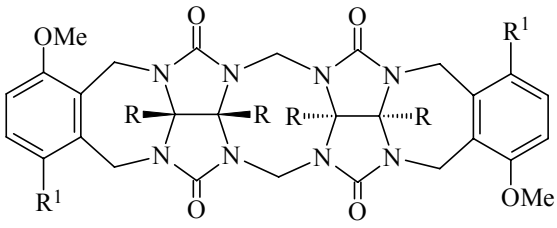
R = COOEt

		R^1
29*S*	*cis*	Br
30*S*	*cis*	NO_2



R = COOEt

		R^1
29*C*	*trans*	Br
30*C*	*trans*	NO_2

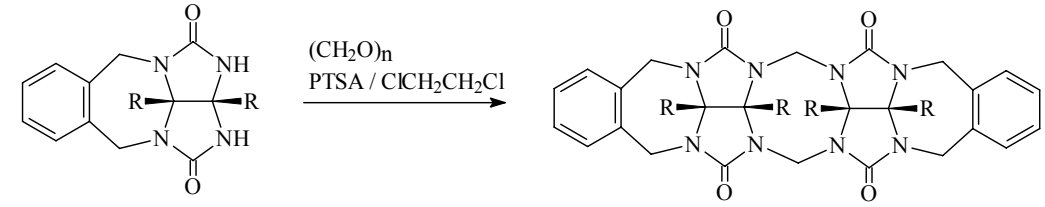


R = COOEt

		R^1
29*S*	*trans*	Br
30*S*	*trans*	NO_2

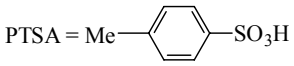
Three synthetic methods lead to methylene-bridged glycoluril dimers: A) the reaction of two equivalents of **13** with paraformaldehyde, B) the condensation of **13** with cyclic ether (**19**), and C) the reaction of two equivalents of **19** with the formal extrusion of formaldehyde.

Method A



	R	
a	COOEt	(gives only **24*C***)
13 **b**	2-pyridyl	(does not react)
c	R, R = $(CH_2)_4$	(gives only **26*C***)

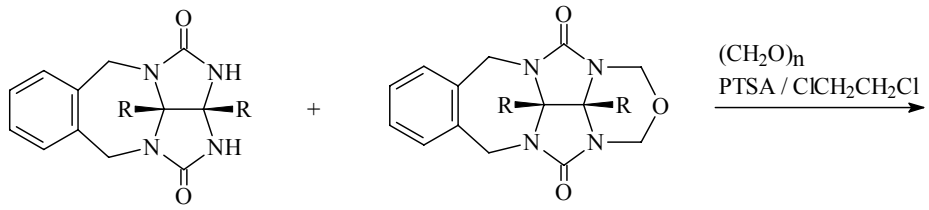
C - shaped dimer



The kind of solubilizing groups on the convex face of the glycoluril molecule significantly influences the dimerization. For example **13a** and **13c** afford exclusively C-shaped diastereomers (**24*C***) and (**26*C***) while **13b** does not give **25*C*** nor **25*S***.

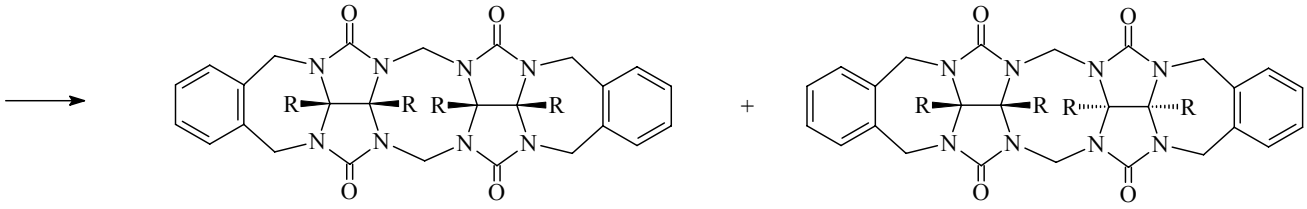
Compounds ((±)-**17**) and ((±)-**18**) are chiral. The dimerization of (±)-**17** gives exclusively C-shaped diastereomers (**29*C*** *cis*) and ((±)-**29*C*** *trans*). In contrast, in the dimerization reaction of (±)-**18** two C-shaped and two S-shaped diastereomers are formed in a nearly statistical distribution. They are: **30*C*** *cis*, (±)-**30*C*** *trans*, (±)-**30*S*** *cis* and **30*S*** *trans*.

Method B



	R	
a	COOEt	
13 **b**	2-pyridyl	
c	R, R = $(CH_2)_4$	

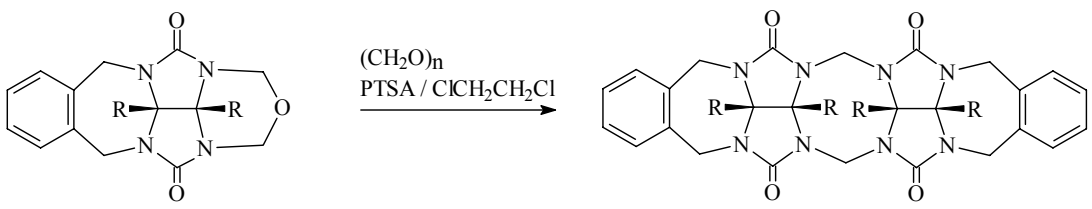
	R	
a	COOEt	(**24*C*** + **24*S*** are formed)
19 **b**	2-pyridyl	(only **25*C*** is formed)
c	R, R = $(CH_2)_4$	(only **26*C*** is formed)



C-shaped dimer

S-shaped dimer

Method C



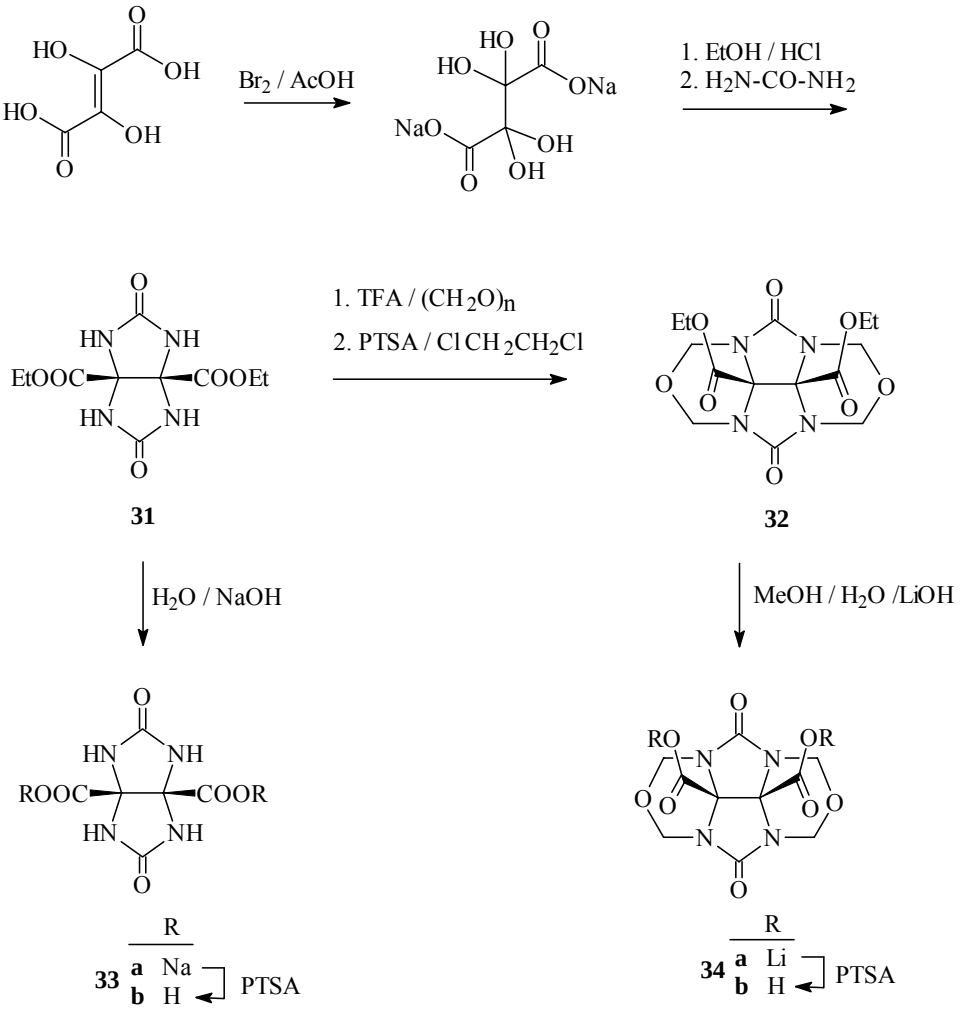
	R	
a	COOEt	(gives only **24*C***)
19 **b**	2-pyridyl	(does not react)
c	R, R = $(CH_2)_4$	(gives only **26*C***)

C-shaped dimer

In all three methods the best results have been obtained in the case of starting materials bearing ethoxycarbonyl groups, their presence allows the high yield synthesis of water soluble dimers. [5,6]

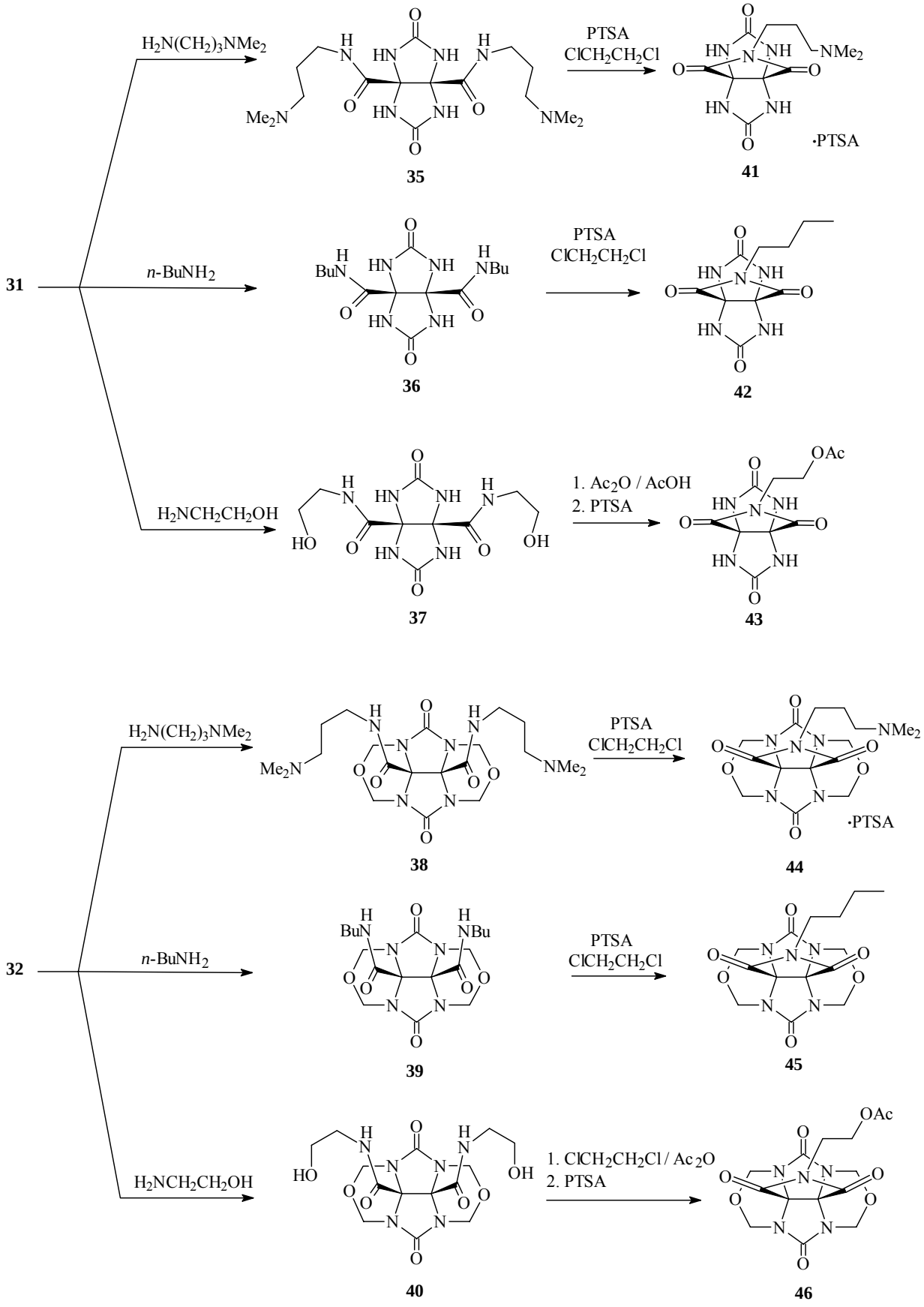
The above experiments showing the preference of C-shaped dimers suggest that the formation of the mixtures of C- and S-shaped species occurs under kinetic control and that the preference for the C-shaped species reflects the thermodynamic control. [33] From among these three procedures the method A has proven to be the most suitable.

It was found that glycoluril derivatives bearing electron withdrawing substituents (*e.g.* ester, carboxylate and amide) on their convex face are more efficient substrates for the synthesis of the methylene bridged glycoluril dimers than those containing phenyl or fused cyclohexyl groups.[34] Glycoluril derivatives bearing ester and amide substituents are soluble in organic solvents, in contrast to most other glycolurils. Compounds (**31**) and (**32**) are convenient starting materials for the synthesis of glycoluril derivatives bearing electron-withdrawing functional groups. Syntheses of **31** and **32** and their conversion into carboxylate salts (**33a**) and (**34a**) and acids (**33b**) and (**34b**) proceed as follows: [1]



Reactions of **31** and **32** with primary amines afford secondary amides (**35-40**). The conversion of **35**, **36**, **38** and **39** into tertiary amides (**41**, **42**, **44**) and (**45**) was made by treatment with *p*-toluenesulfonic acid

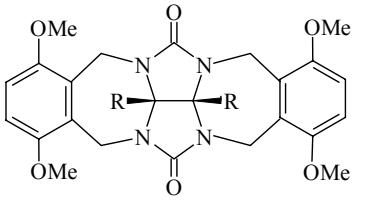
(PTSA). In order to obtain **43**, the diol (**37**) has been acetylated and induced to ring closure ; in a similar manner **40** has been converted into **46**.



2. GLYCOLURIL MOLECULAR CLIPS AND BOWL-SHAPED RECEPTORS

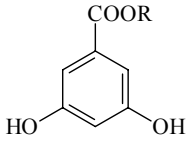
It is possible to prepare materials in which the different building blocks are oriented in the crystal by well defined and directed intermolecular interactions, such as hydrogen bonds and π-π stacking. Design of similar materials in which guest molecules are incorporated at discrete positions in the layers is also interesting; such lamellar host-guest materials are promising for a variety of applications, *e.g.* in construction of photovoltaic devices. [3] Host-guest materials may be constructed by the lamellar self-assembly of host molecules which can recognize small guests by hydrogen bonding and π-π stacking interactions.

Molecular clips (**47a,b**) functionalized on their convex side with long alkyl chains have a rigid, U-shaped cavity. They can form dimers in organic solutions and in the solid state, in which the cavity of one molecule is filled by the side-wall of the second one, resembling a rod-like mesogen (shown below). The dimers self-assemble into malleable lamellar thin films. [3]

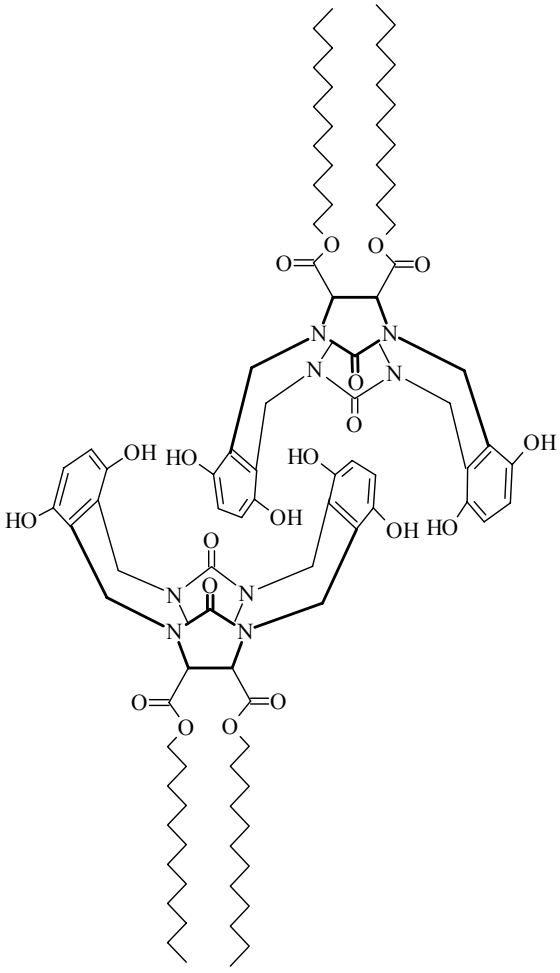


	R
a	$O(CH_2)_{11}CH_3$
b	$O(CH_2)_{17}CH_3$

47



	R
48	Me
49	H



Differential scanning calorimetry (DSC) and variable temperature X-Ray powder diffraction (XRPD) measurements have revealed that **47a,b** are crystalline; however in the case of **47b** a layered structure has

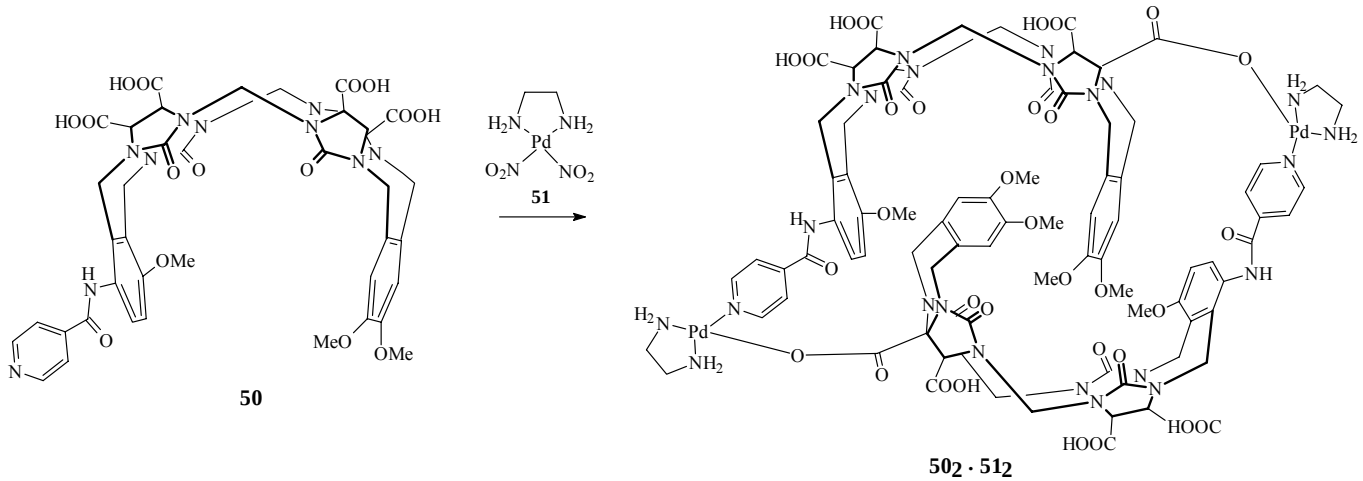
been found. The lamellar nature of **47b** is responsible for the malleability of the material at high temperatures, as observed by polarizing microscopy (PM).

In order to disrupt the dimeric structures of clips (**47a**) and (**47b**), the ester (**48**) was added affording the 1:1 host-guest complexes of **47a** and **47b** with **48**. This complexation prevents dimerization of clips and the formation of extended sheets. The result is the disappearance of the lamellar structure and the decrease of the melting point.

However, a complexation of a guest which allows the redimerization restores the lamellar organization. To investigate this, the 1:1 complex of **47b** with 3,5-dihydroxybenzoic acid (**49**) was prepared. Incorporation of **49** in the clip results in the formation of host-guest complexes which dimerize *via* hydrogen bonding interactions between carboxylic groups of the guests. Due to this dimerization, the lamellar structure of the material is restored and the film of the complex is malleable again.

Chiral molecular aggregates may be prepared by the use of enantiomerically pure molecules, [31,35] by self-association of achiral molecules [36] and by enantiomeric self-recognition of racemic mixtures of ligands. [37,38] Using the latter method, the aqueous solution of racemic compound (**50**) was treated with **51** to give single molecular aggregates (**50**$_2$·**51**$_2$) and (*ent*-**50**$_2$·**51**$_2$). [5]

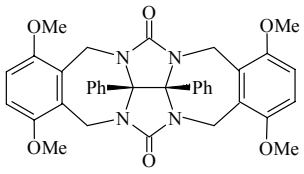
Compound (**50**) containing a hydrophobic cleft and a pyridyl ligand is an example of amphiphilic molecular clips which undergo self-association leading to dimers. [3,6,11,39] The addition of **51** to **50** results in dimerization affording coordination-driven self-assembly. [40-42] This enantiomeric self-recognition process is triggered by an additional coordination interaction between palladium centers and the carboxylate solubilizing groups. The analytical ultracentrifugation (AUC) was used for the determination of absolute stoichiometry of aggregates (**50**$_2$·**51**$_2$) and (*ent*-**50**$_2$·**51**$_2$). [6]



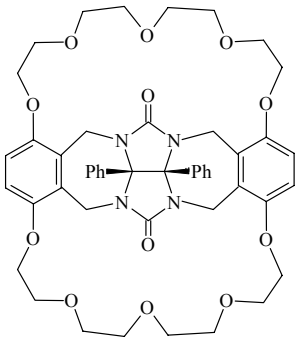
50$_2$ · **51**$_2$

Clip-shaped molecules of the type (**52**) may incorporate uncharged aromatic guest molecules; *e.g.* the binding of resorcinol by **52** occurs by π-π stacking interactions of two aromatic walls of the cavity of **52**

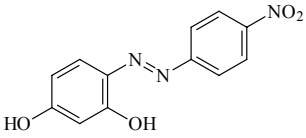
with the aromatic moiety of the guest and by hydrogen bonding of the urea carbonyl groups of **52** with phenolic hydroxyl groups. Basket-shaped derivatives of **52**, such as **53** bearing crown ether units may also complex alkali metal ions. [43]



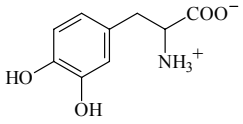
52



53

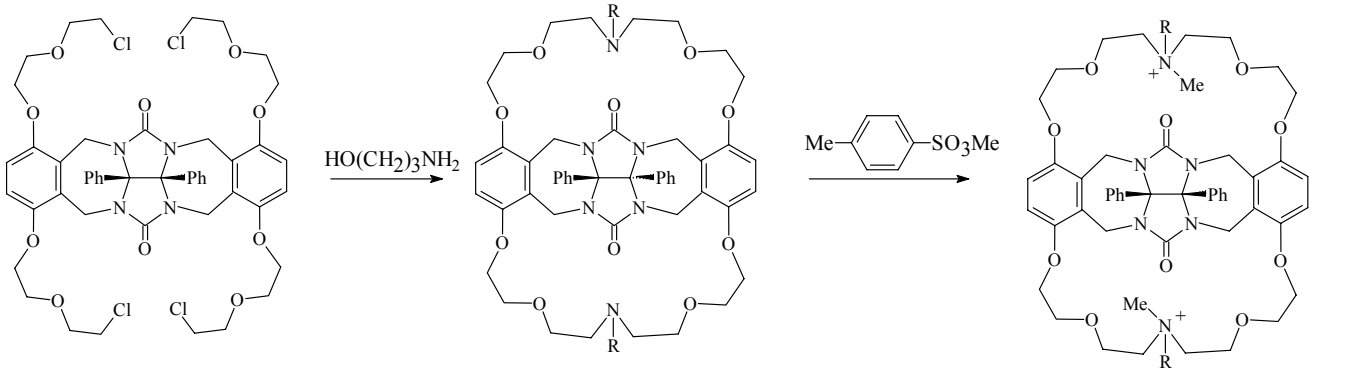


Magneson



L-dopa

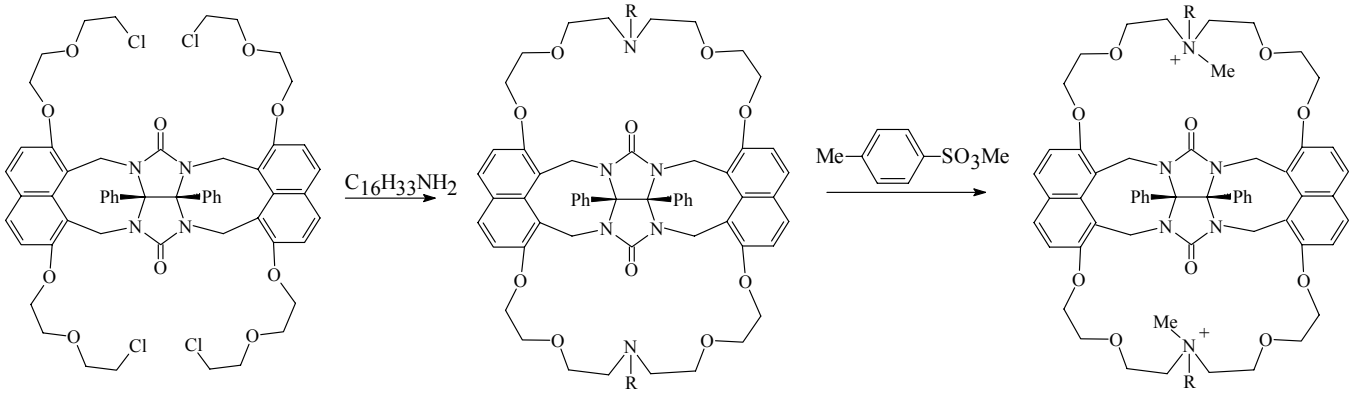
Compounds (**54-57**) containing aza-crown ether units and long aliphatic chains have been obtained as follows:



	R
a	$(CH_2)_3OH$
54 b	$(CH_2)_3OC(O)C_{11}H_{23}$
c	$C_{16}H_{33}$

55 2 TsO^-

$R = C_{16}H_{33}$



56

$R = C_{16}H_{33}$

57 2 TsO^-

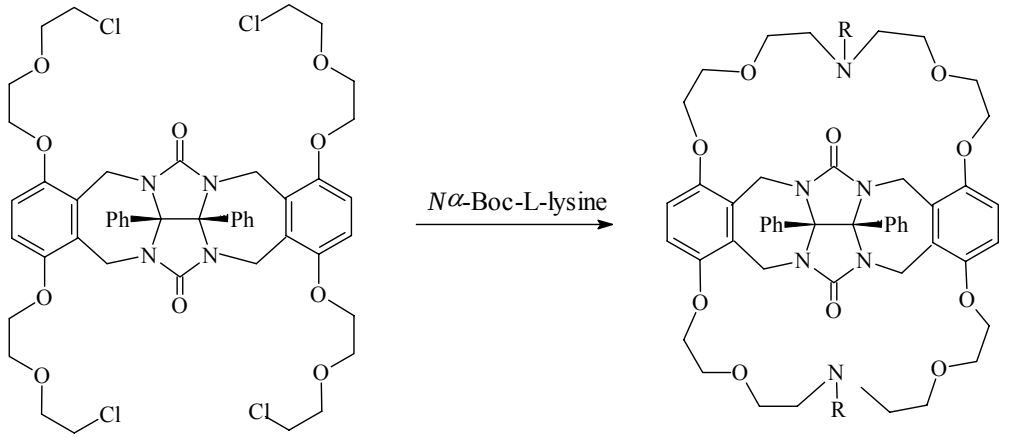
$R = C_{16}H_{33}$

Upon dispersion in water they self-assemble to form vesicles which may bind neutral guests and alkali metal ions. [43] Compounds (**52**, **54c**, **55**, **56**) and (**57**) form with resorcinol and with Magneson the 1:1 inclusion complexes.

In the study of complexation of Magneson in water by **55** and **57** it was observed that below critical aggregation concentration (CAC) of the amphiphile, the 1:1 host-guest complexes are formed with high host-guest association constants. However, above the CAC the formation of 2:1 host-guest complexes takes place, *i.e.* only the cavities on the outside of the vesicle are occupied.

Studying the aggregation of **54b** in aqueous solutions of KCl it was found that at a low pressure and high K^+ concentration the complex has a nearly flat structure with two K^+ ions bound in its two aza-crown ether rings. At high pressure the complex adopts a sandwich-like conformation with only one K^+ ion incorporated between two rings. The monolayer experiments have shown that Rb^+ and Cs^+ ions are more strongly bound by **54b** than K^+ ions. In water, molecules of **54b** have an elongated conformation which becomes a sandwich-like one upon binding alkali metal ions. Increasing the size of the alkali metal ion leads to the gradual change of the shape of aggregates from vesicles to tubules. Such tuning of supramolecular structures by addition of organic guest molecules or metal ions resembles the behavior of natural cell membranes and is promising in the chromatographic separation of organic molecules and in the drug delivery. [43]

The L-lysine appended receptor (**58**) based on diphenylglycoluril has been obtained as follows. [44]



58

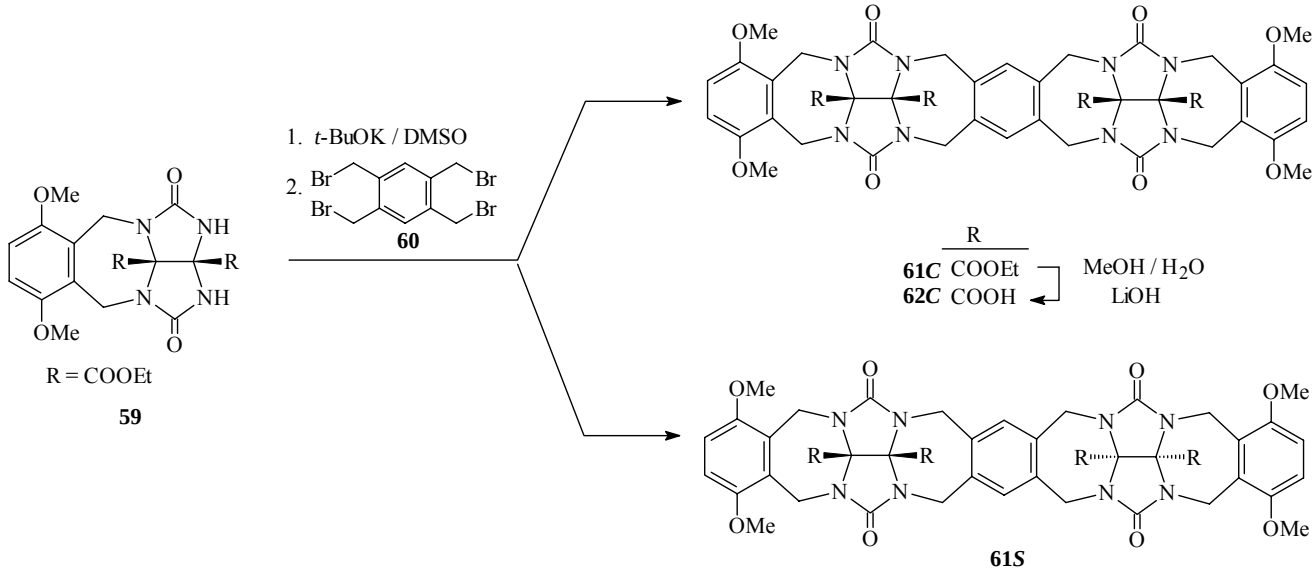
R = $(CH_2)_4$CH(NHBoc)COOH

Compound (**58**) shows a well-defined aggregation behavior in water and in organic solvents. In contrast to receptors (**54b,c-57**), [43] it contains amino acid arms which may take part in additional hydrogen bonding and electrostatic interactions.

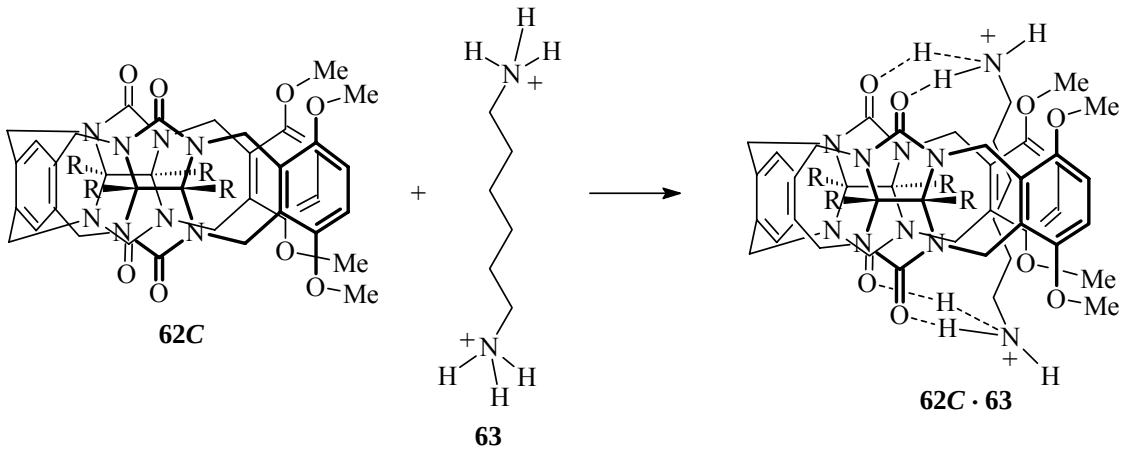
The amino acid arms also enable the recognizing of multifunctional guests, such as hydroxyaromatic amino acids and amino alcohols. For example, L-dopa is insoluble in $CHCl_3$, however in the presence of **58** it is fully solubilized. In the study of binding of adrenaline and related species by artificial receptors, [45,46] the encapsulation of L-dopa in the receptor (**58**) has been investigated. The estimated binding constant ($4.3 \pm 1.5 \times 10^3$ M^{-1}) is one of the largest ones reported for this guest in water; the high affinity of **58** to L-dopa is similar to the binding of natural receptors with guests.

The complexation of Magneson in host-molecule (**58**) was examined in $CHCl_3$ by UV-VIS titration; the association constant is higher than those observed for the binding of Magneson with other bowl-shaped receptors. [43]

One should mention also the existence of an acyclic congener of cucurbituril. [47] Synthesis begins with the deprotonation of **59** with *t*-BuOK. The subsequent reaction with **60** yields C- and S-shaped diastereomers (**61*C***) and (**61*S***). The deprotection of **61*C*** with LiOH and acidification with PTSA affords free acid (**62**) which is the acyclic congener of cucurbituril.



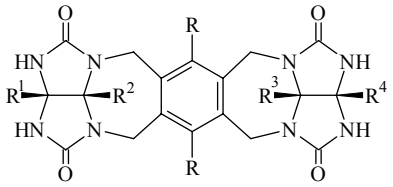
The *o*-xylylene linkages preorganize (**62*C***) into the (a,a,a,a) conformer necessary for its complexing properties. The binding of **62*C*** with amines, diols, diacids and pyridinium species have been investigated; it complexes Na^+ ion at its carbonyl- and methoxy group-lined portal in a similar manner as CB[6]. It was observed that **62*C*** binds hexanediammonium ion (**63**) only 189-fold less tightly than does CB[6], this fact being due to the greater flexibility of **62*C*** as compared to CB[6].

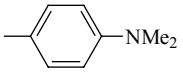
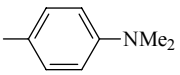
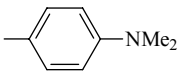
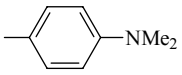
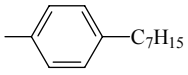


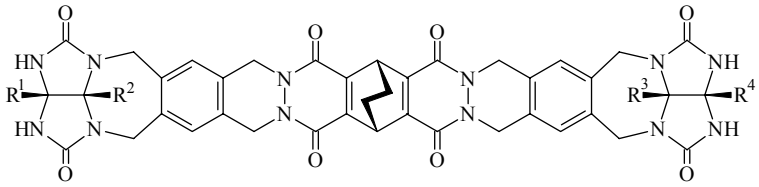
It should be pointed out that the synthesis of **62*C*** avoids the difficulties of a tailor-made approaches to cucurbiturils, and that acyclic CB congeners may complement behavior of cyclic species.

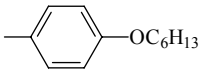
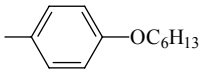
3. GLYCOLURIL CAPSULES

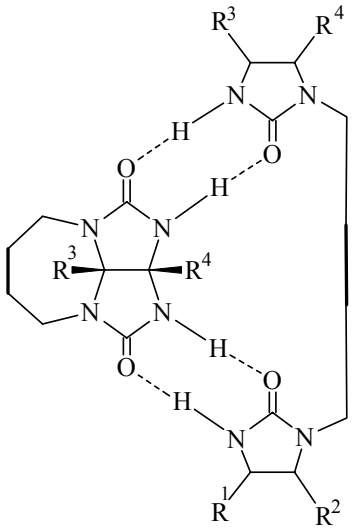
In the study of dynamic NMR spectra of supramolecular complexes, self-assembling glycoluril capsules have been investigated. [48] As examples may serve molecular capsules formed by dimerization of compounds (**64-67**). The structure of these capsules, held by hydrogen bonds resembles that of a tennis ball, as shown below. The rate of guest exchange of "tennis balls" is much higher than the dissociation rate; this indicates that the cavity can open without complete dissociation of the dimer.



	R^1	R^2	R^3	R^4	R
64	Ph	Ph	Ph	Ph	H
65					H
66	Ph		COOEt	Ph	H
67	Ph	Ph	Ph	Ph	OH



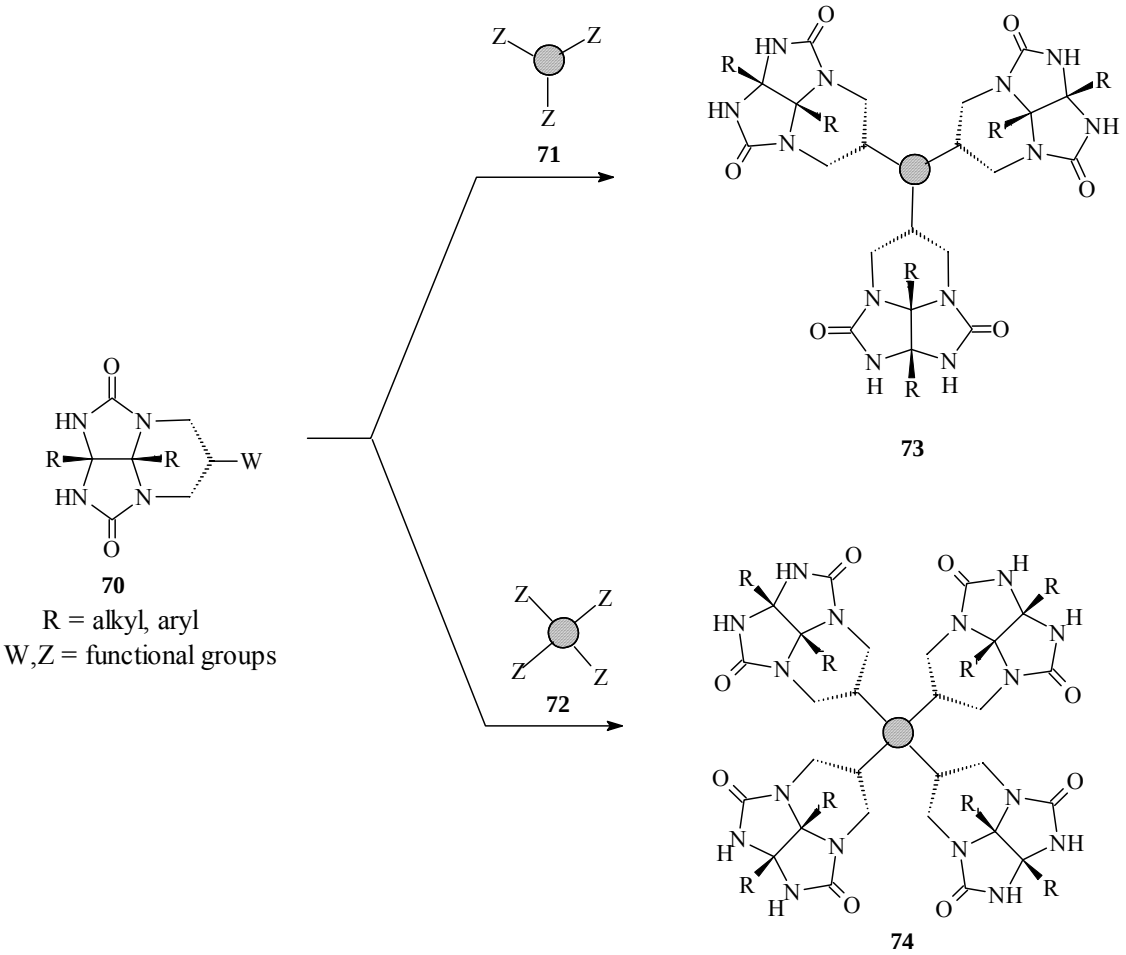
	R^1	R^2	R^3	R^4
68	Ph	Ph	Ph	Ph
69	COO-*i*-C_5H_{11}	COO-*i*-C_5H_{11}		



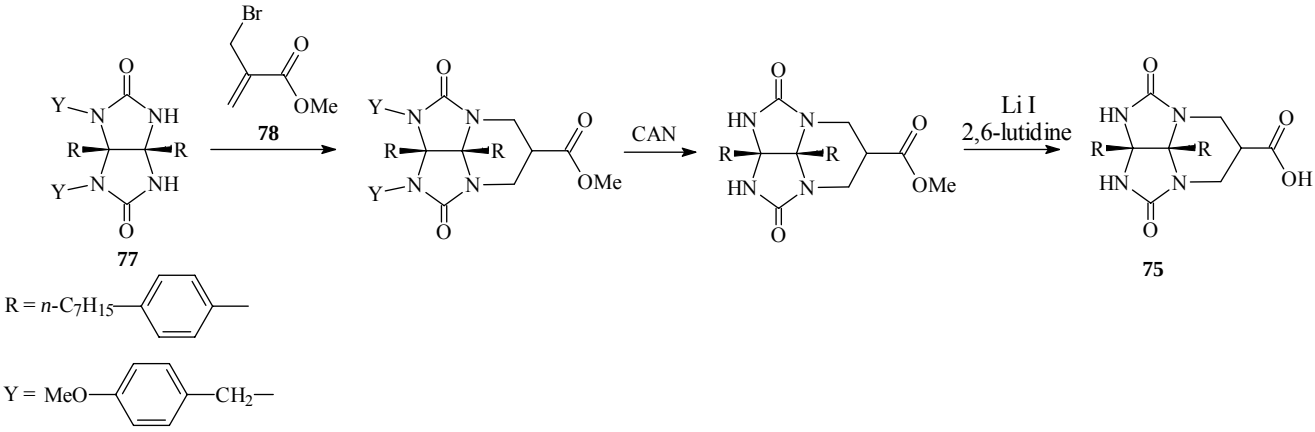
Dimer (**65**$_2$) forms in DMF-d_7 in the presence of nucleating Xe. The ^{129}Xe NMR spectral measurements allow the observation of the encapsulated Xe. In the presence of acid, the capsule is destabilized and Xe is released. The dimer may be reformed by addition of sodium carbonate, leading to reincorporation of Xe. When both glycoluril units are differently substituted, the capsule is chiral; an example is **66**$_2$. Compound (**67**) gives a heterodimer with its related quinone species.

Dimers (**68**$_2$) and (**69**$_2$) are examples of capsules with larger cavities ("soft ball" capsules). The chiral "soft ball" capsule (**69**$_2$) forms complexes with chiral guests. Due to the different rates of guest exchange and dimer dissociation, the transient excess of the less stable diastereoisomer is possible when the guest is replaced by its enantiomer. This phenomenon is an "imprinting" of the guest chirality in the host molecule, remaining after the release of the guest. [49]

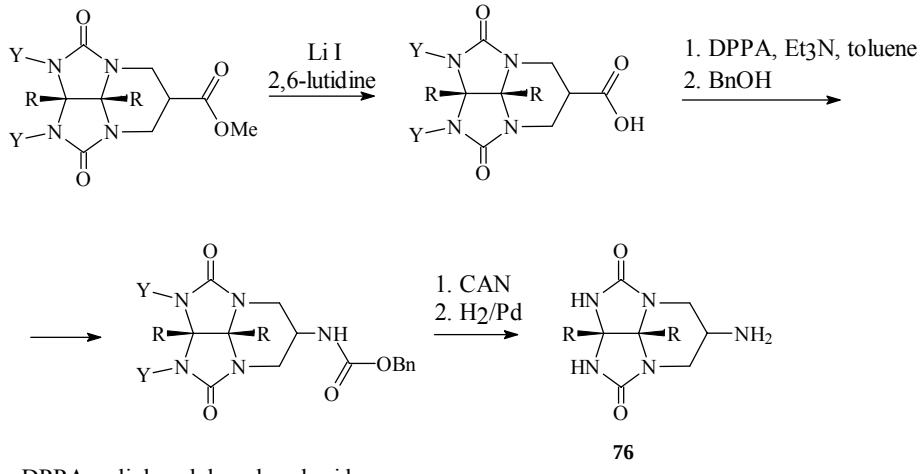
In order to obtain molecular capsules of a three- or tetrafold symmetry axis, self-assembling by hydrogen bonds, at first the functionalized glycolurils (**70**) have been condensed with tri- or tetravalent spacers (**71**) or (**72**) to give monomers (**73**) and (**74**); their subsequent dimerization afforded capsules. [50] A scheme for the synthesis of monomers (**73**) and (**74**) is shown below.



Glycolurils functionalized by carboxyl and amino groups (**75**) and (**76**), respectively, have been obtained as follows.



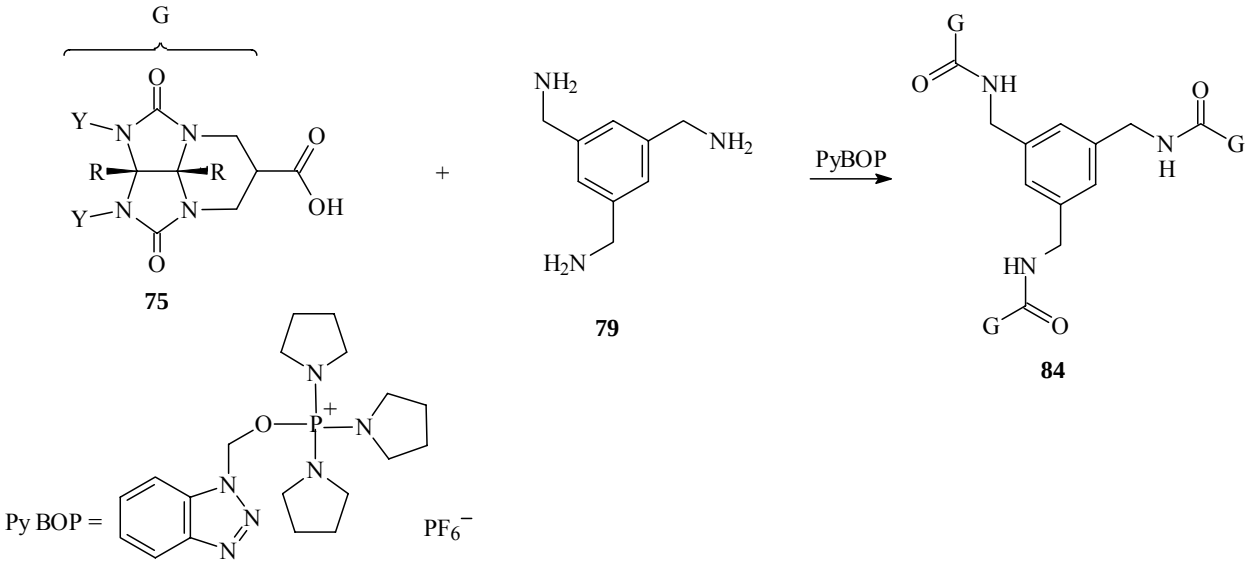
CAN = ceric ammonium nitrate

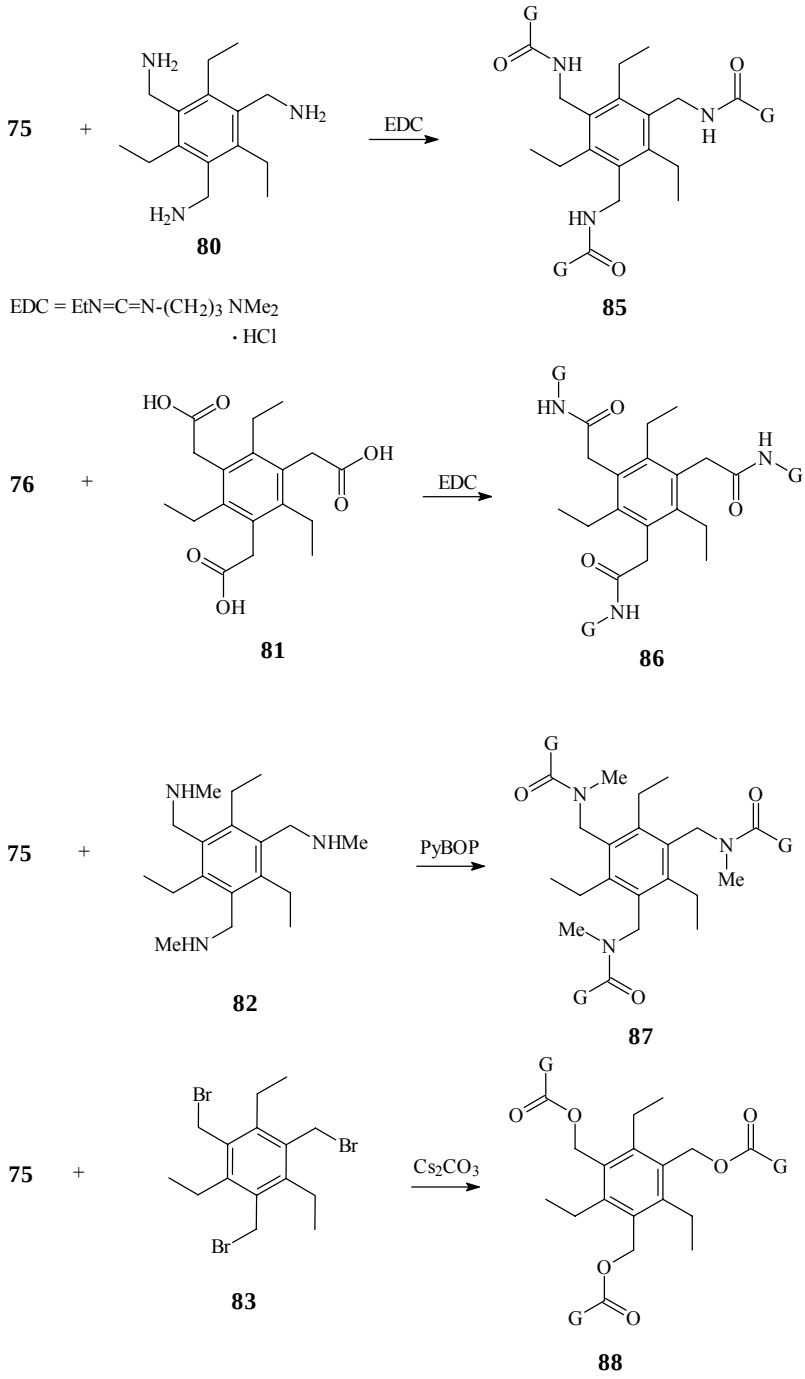


DPPA = diphenylphosphoryl azide

It should be pointed out that in the reaction of **77** with **78** the six-membered fused ring is formed, and not, as usually, the seven-membered one, which is more difficult to obtain. Molecules (**79-83**) were used as spacers. Compounds (**80-83**) are hindered spacers, more suitable than **79**.

Trivalent monomers (**84-88**) have been synthesized as follows.

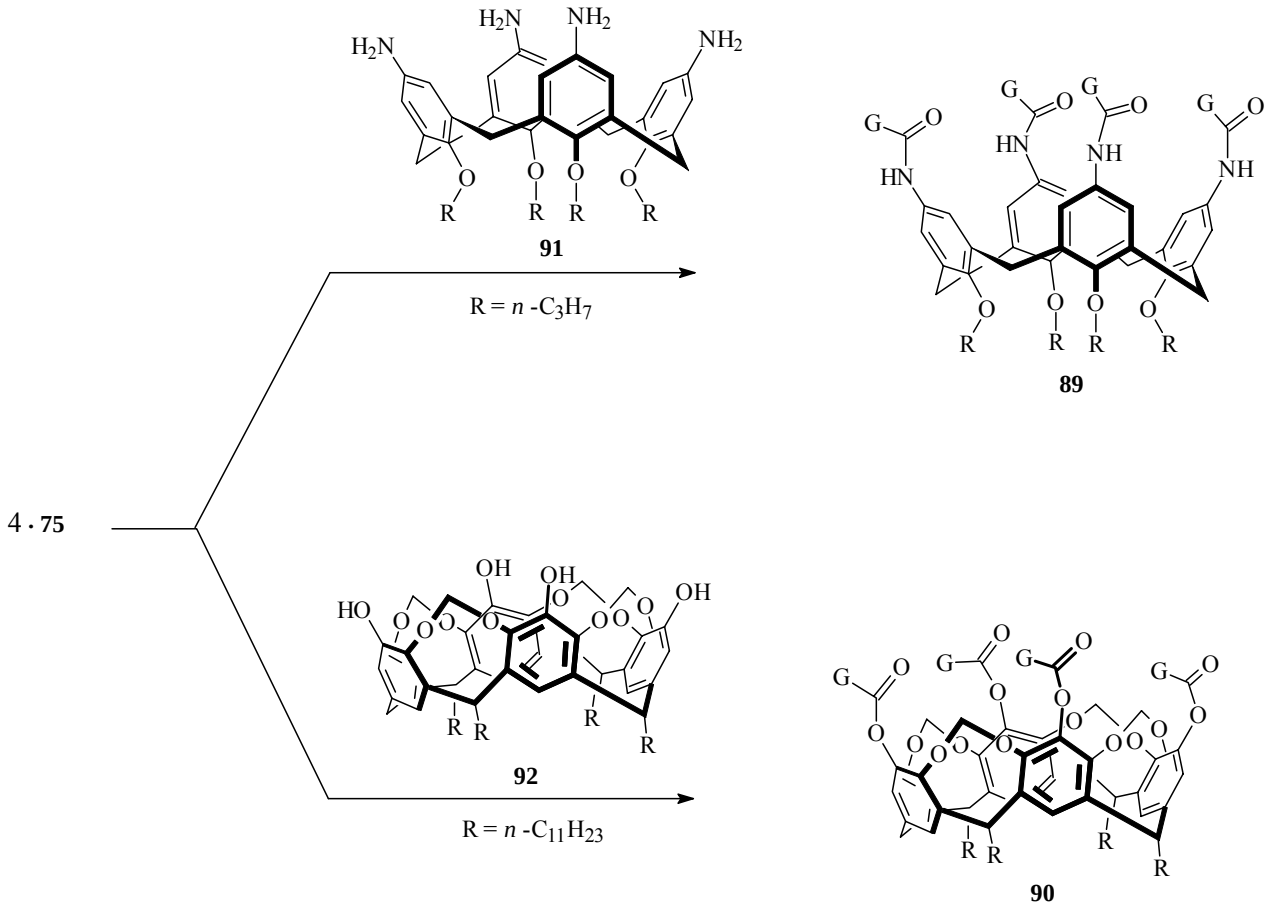




Triamide monomers (**85-87**) have been obtained by standard peptide coupling procedures. Compounds (**85**) and (**86**) were available by EDC coupling, while for the synthesis of more hindered monomer (**87**) the use of PyBOP was necessary. Triester (**88**) has been prepared by condensation of **75** with tribromide (**83**).

It was observed that **84** exists only as a disordered aggregate which does not give a discrete dimer, therefore rigid spacers (**80-83**) instead of **79** have been used for condensation, resulting in **85-88** suitable for the subsequent dimerization.

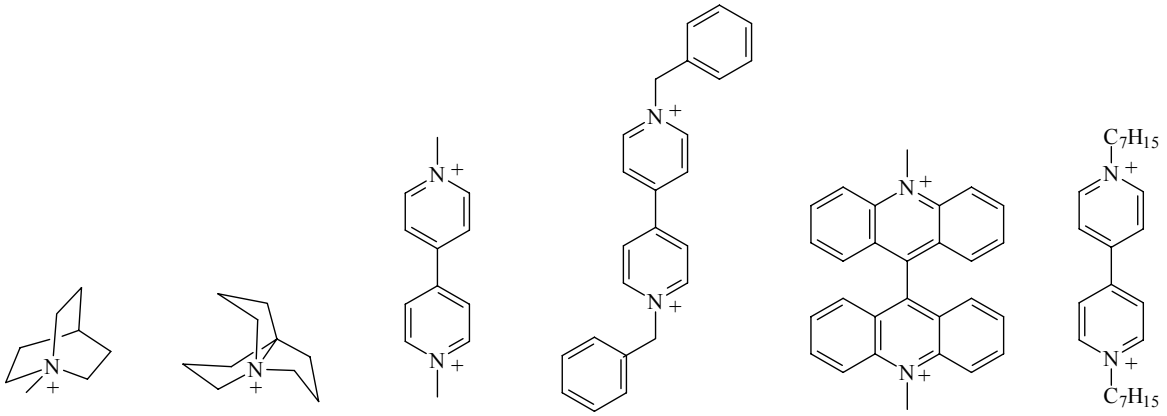
In order to obtain tetravalent monomers (**89**) and (**90**), following condensation reactions with calixarene (**91**) and cavitand (**92**) have been made.



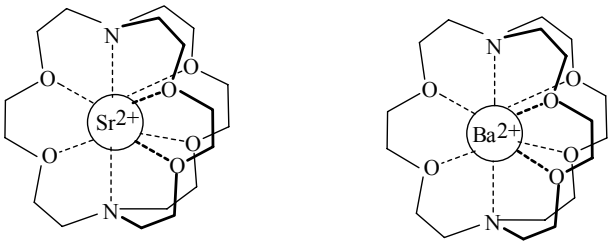
It was shown that, as in the case of **84**, the monomer (**89**) does not form discrete dimers, probably due to the fact that its cone conformation, necessary for dimerization is not a preferred one.

The monomers (**85-88**) and (**90**), more rigid than **84** and **89** have been investigated in view of their dimerization and encapsulation properties by ^{1}H NMR spectra and electrospray ionization (ESI) mass spectrometry.[50] The monomers (**85**, **86**) and (**88**) give exclusively discrete dimers. It was observed that **85**, a rigid template, complexes the less rigid monomer (**84**) to give heterodimer (**85·84**), so the rigidifying of only one monomer is sufficient to give the capsule. Monomer (**86**) forms homodimer (**86**$_2$) and heterodimer (**86·85**). Monomer (**87**) does not dimerize, and triester (**88)** gives homodimer (**88**$_2$), albeit more dynamic than are **85**$_2$ or **86**$_2$. Monomer (**90**) gives homodimer (**90**$_2$), whereas heterodimer (**90·89**) is not formed.

The capsules (homo- and heterodimers) have large cavities (0.45-0.95 nm^3) able to accomodate big species affording kinetically stable host-guest complexes. The 1:1 complexes of capsules (**85**$_2$, **86**$_2$) and (**88**$_2$) with **93**$^+$, **94**$^+$ and **98**$^{2+}$ (as BF_4^- salts) have been formed. The capsule (**88**$_2$) can adapt to the shape of guests and can accomodate large species such as **96**$^{2+}$ or **97**$^{2+}$ (as BF_4^- salts). Capsule (**90**$_2$) gives 1:1 complexes with **95**$^{2+}$, **97**$^{2+}$, **98**$^{2+}$ (as BF_4^- salts), as well as with **99**$^{2+}$ $(ClO_4^-)_2$ and **100**$^{2+}$ $(Cl^-)_2$.



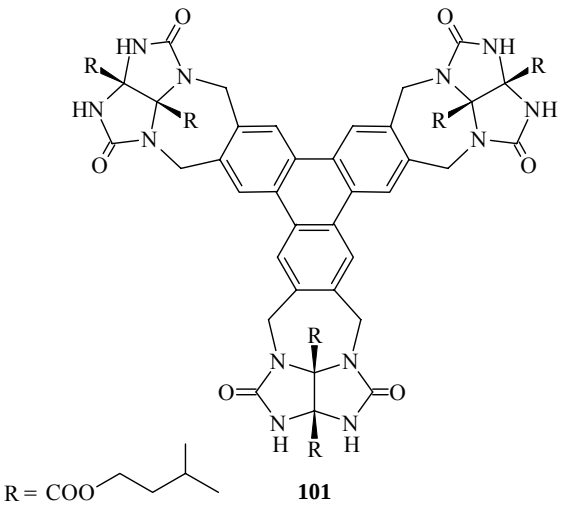
93 $^{+}$ **94** $^{+}$ **95** $^{2+}$ **96** $^{2+}$ **97** $^{2+}$ **98** $^{2+}$



99 $^{2+}$ **100** $^{2+}$

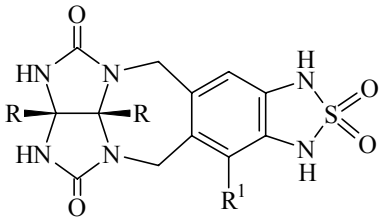
It should be pointed out that monomers (**73**) and (**74**) show some flexibility, therefore functional groups may appear on the concave surface of the capsule, this fact being rather uncommon in supramolecular structures. [51] Such endohedral functionality would change the size and the shape of the cavity, and may provide hydrogen bond donors or acceptors to the cavity. For example in the case of **85** the secondary amide protons (hydrogen bond donors) are exposed to the cavity, while in the case of **86** (its inverted analog), hydrogen bond acceptors are provided to the inside.

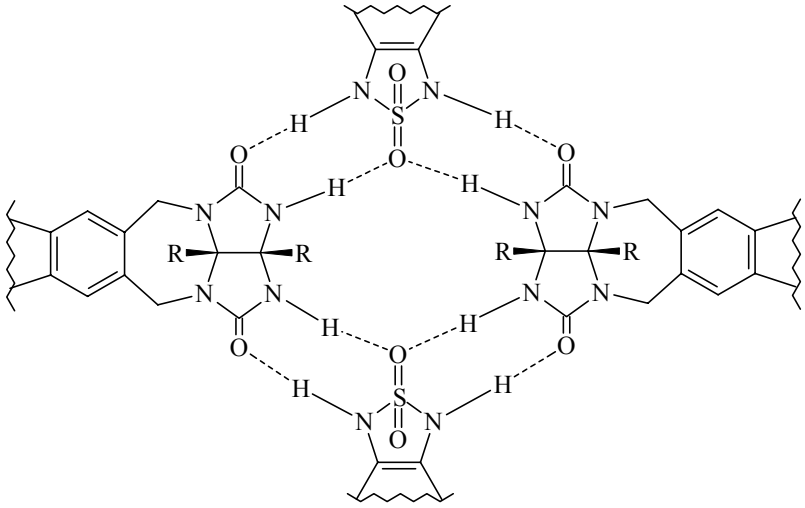
Compound (**101**) dimerizes to give **101**$_2$ which is a capsule of a D_{3d} symmetry. In ^{1}H NMR spectral study of solvent incorporation in **101**$_2$ it was observed that the included cyclohexane showed a decrease of ring inversion rate as compared with its non-encapsulated molecule. [48]



101

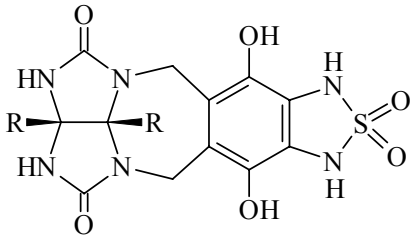
Compounds (**102a-c**) form tetrameric capsules held together by hydrogen bonding, as shown below. The inclusion of adamantane into tetrameric capsule (**102b**$_2$) of a D_{2d} symmetry was observed by ^{1}H NMR. [48] Compound (**102c**) bearing hydroxyl group is chiral; this results in the reduced (D_2) symmetry of the tetrameric capsule (**102c**$_2$). Due to its chirality this capsule may incorporate chiral guests affording diastereomeric complexes. [48]



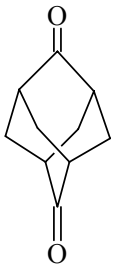


		R	R1
102	**a**	4-MeC_6H_4	H
	b	4-*n*-$C_{10}H_{21}C_6H_4$	H
	c	4-*n*-$C_{10}H_{21}C_6H_4$	OH

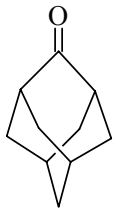
The crystallographic studies have shown that the tetramer consisting of four glycoluril derivatives (**103a**) held together by hydrogen bonds serves as a host for 2,6-adamantanedione (**104**). [52,53] In the resulting 1:1 host-guest inclusion complex the guest is filling a large amount (*ca*. 72%) of the space inside the capsule in the solid state. It was observed that the binding force in host-guest systems of **103a** with **104-106** decreases in the order **104** > **105** > **106**. Similar inclusion systems of **103b** with **104-106** guests have been formed in CD_2Cl_2 solution. [52]



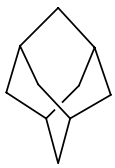
		R
103	**a**	4-MeC_6H_4
	b	4-*n*-$C_{10}H_{21}$ C_6H_4



104

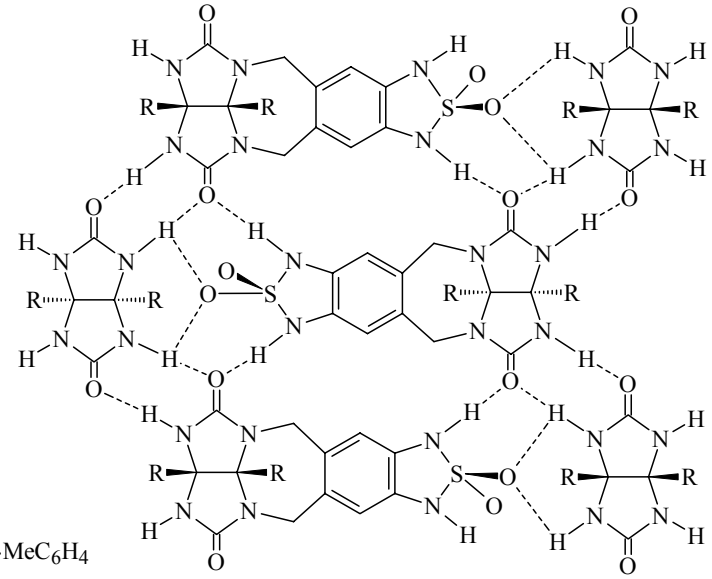


105



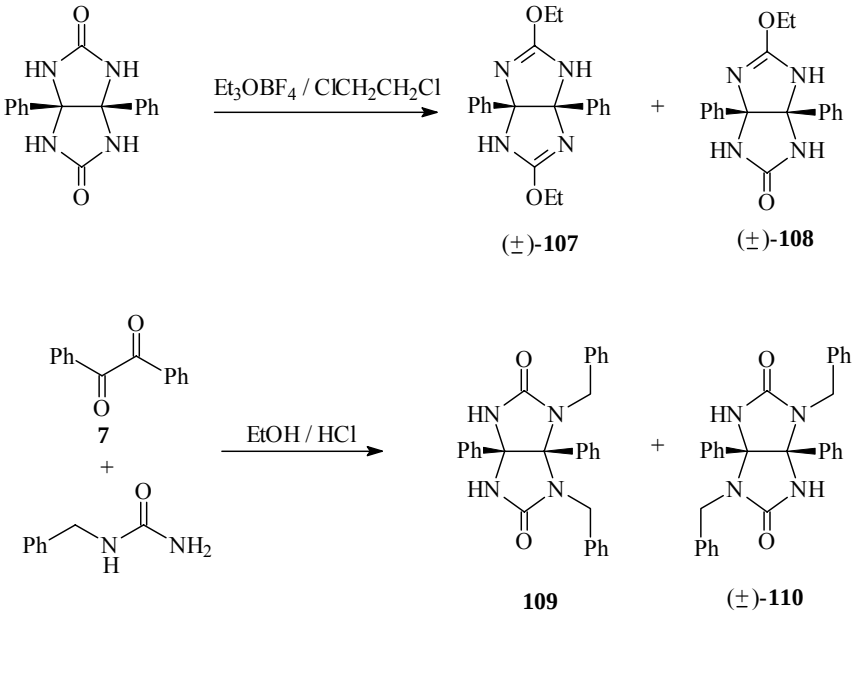
106

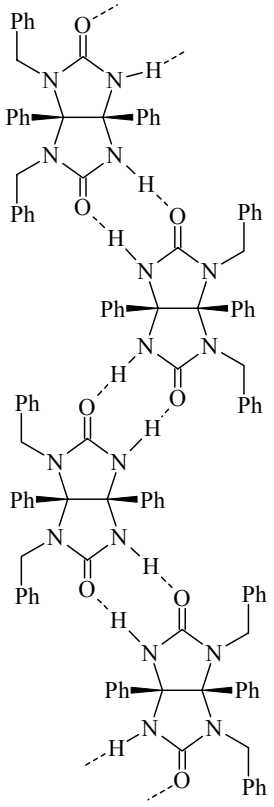
Compound (**102a**), however, does not give tetrameric capsules in the solid state, instead two-dimensional sheets held by a network of hydrogen bonds are formed. [54] They consist of adjacent, hydrogen bonded ribbons bridged by hydrogen bonds, as shown below. Such interactions between different functional groups are promising in the design of engineered solids. [55,56]



R = 4-MeC$_6$H$_4$

Some glycoluril derivatives form hydrogen bonded tapes in crystal [57,58] instead of cucurbiturils; to investigate this property glycoluril derivatives (**107-110**) have been synthesized as follows. [59]



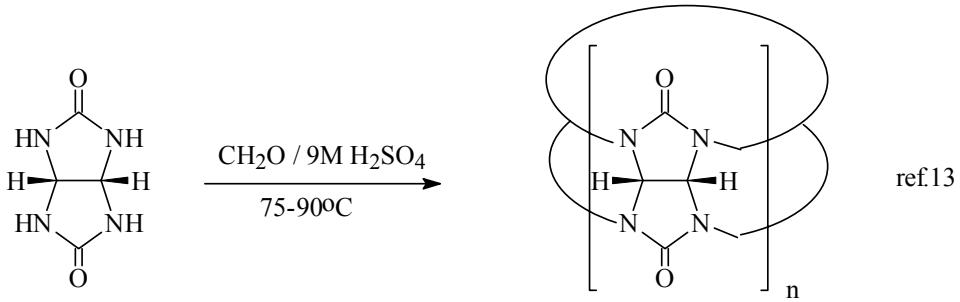


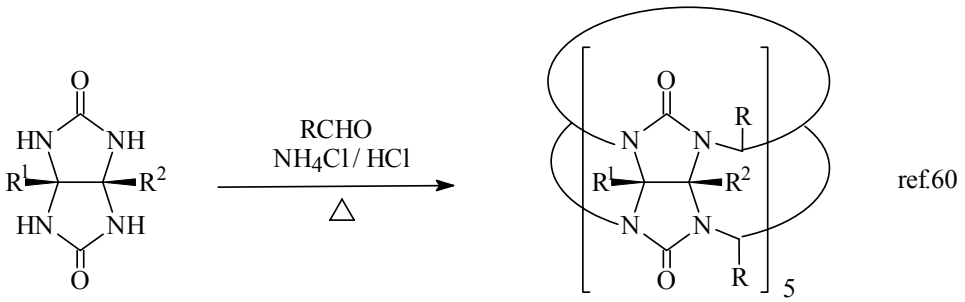
hydrogen-bonded tape of **109**

The existence of tapes is due to the presence of phenyl and benzyl substituents which enable good solubility of **107-110** in non-polar aprotic solvents. As these solvents do not compete for hydrogen bonds with the ureidyl groups, such tapes may be formed. This behavior of glycolurils may be of use in crystal engineering investigations. [57] Compounds (**107-110**) give tapes containing hydrogen bonded eight-membered rings; as an example may serve the hydrogen bonded tape of **109**.

4. APPLICATIONS OF GLYCOLURILS

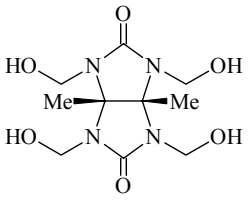
Glycolurils are precursors of cucurbiturils, an interesting class of compounds; two synthetic approaches to these species are shown below. [13,60]



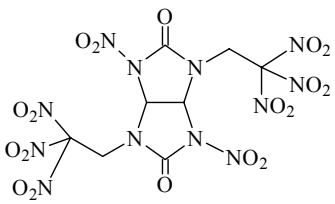


R = H, C_{1-6} (un)substituted alkyl, C_{2-6} (un)substituted alkenyl, Ph
R^1, R^2 = H, C_{1-10} (un)substituted alkyl, (un)substituted Ph

Glycolurils find various applications, for example their derivatives may serve in biological studies for ^{125}I–labelling of peptide hormones. [61,62] Compound (**111**) is used as a crosslinker for epoxy resins, [63] and **112** is promising as a high explosive. [64]



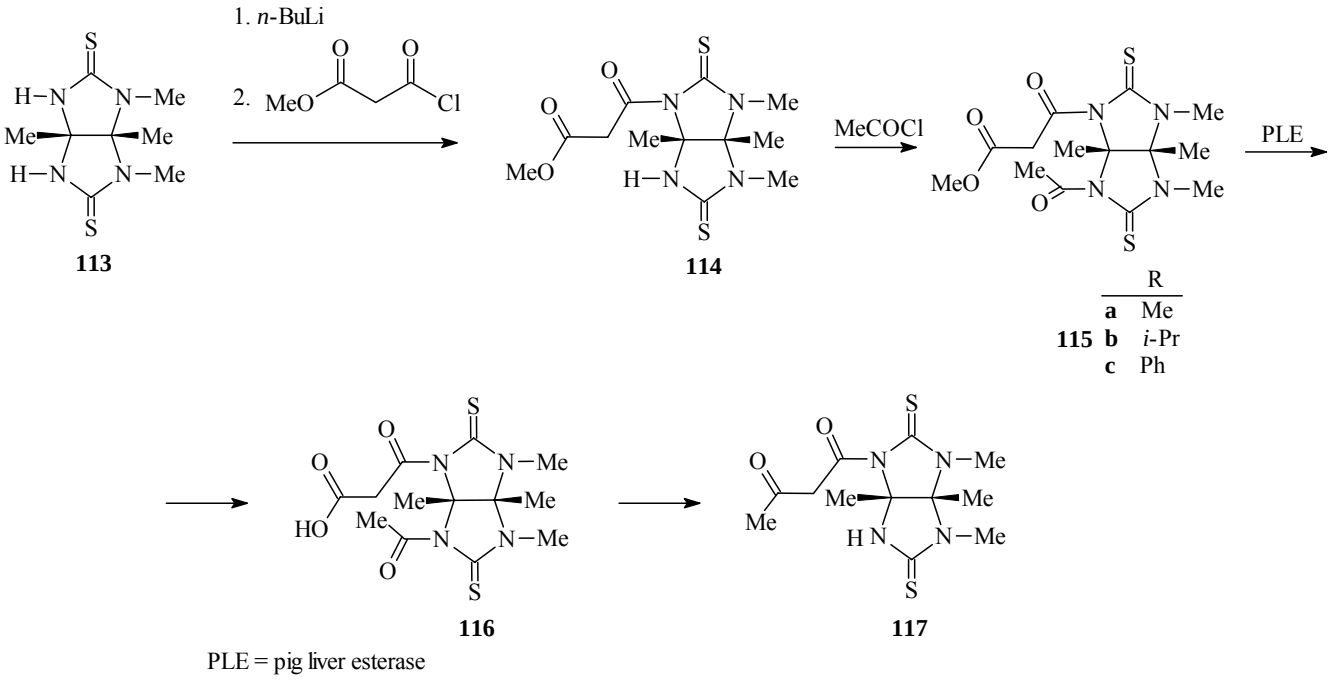
111



112

Besides glycolurils, also their sulfur analogues are known. It was observed that the biomimetic decarboxylative condensation of malonate unit with an acyl group may be promoted by a dithioglycoluril template. [65,66] In this investigation dithioglycoluril (**113**) reacted with monomethylmalonyl chloride to give **114**, converted into **115** by treatment with acetyl chloride. The cleavage of **115** by pig liver esterase (PLE) leads to compound (**116**); its attempted isolation affords acetoacetyldithioglycoluril (**117**) *via*

intramolecular Claisen-like condensation. This process may serve as a model of the carbon-carbon bond forming step in the synthesis of fatty acids and polyketides.



113 **114** **115** **116** **117**

CONCLUSION

Due to the properties of glycolurils, described above, these compounds deserve an attention. One should point out the use of glycolurils as precursors of cucurbiturils. [13,60,67] Cucurbiturils are area of an intense study, they serve as receptors in host-guest chemistry and as building blocks of supramolecular systems, promising in the design of molecular machines and devices; the investigation concerning this class of compounds is developing rapidly. [1,68-70]

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