Calixarene- and cavitand-based capsules

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Dedicated to Professor Edmunds Lukevics on his 70th birthday

Abstract

In this paper, dimeric capsules are presented. In the first sections, selected examples of covalently bound capsules are described, then species held by hydrogen bonding and coordination with metal ions are characterized. Following chapters concern capsules bound by ionic interactions and van der Waals forces. Lastly, examples of guest-templated capsules are presented. Binding of guests within capsules is described along with application possibilities of these species.

Keywords: Binding, calixarene, capsule, cavitand, guest

Table of Contents

Introduction

Capsules formed from calixarenes, as from cavitands, have been intensively studied; due to interesting properties they are a topic of numerous reports.[1-3] The present review is a continuation of our previous papers concerning calixarenes,[4-8] resorcinarenes[9] and cavitands,[10,11] along with calixarene assemblies[12] and calixpyrroles.[13]

Capsules are formed by dimerization of calixarenes or cavitands *via* their covalent linking,[14] as well as through hydrogen bonds[15] or metal coordination.[16] Capsules are of interest in the design of molecular devices[17] and may serve as microreaction vessels;[18,19] they are promising for use in separation technologies[20] and as mimics of enzyme-substrate interactions.[21]

In the first part of the review, capsules covalently linked are presented; they are followed by species held together by hydrogen bonding and coordination with metal ions, then capsules bound by ionic interactions and van der Waals forces are described. In the last part examples of guest-templated capsules are shown. The references are cited mainly from reports appearing since 2005.

1. Covalently Bound Capsules

Covalently bound capsules are a theme of a number of works, some examples will be shown below. In the study of isotope effects, the binding of the capsules (hemicarcerands) **1** with a series of guests **2**-**8** has been investigated.[14] The guests had D_{4h} symmetry (**2**-**4**) and C_{2v} symmetry (**5**-**8**). The hemicarcerand enables the precise determination of small size differences between two incarcerated guests, even those resulting from their deuteration, by examination of chromatographic properties of both hemicarceplexes formed with these guests.

Investigating the communication of the guest of hemicarceplexes **1b**·guests with an external chromatographic stationary phase, a large increase in the HPLC retention factor k' with guest size was observed. The value of k' was the lowest for the fastest (**1b**·benzene) and highest for the slowest (**1b**·7-methoxyphthalide) eluting hemicarceplex.

It was found that ln k', which is proportional to the change in free energy ΔG, upon transferring a hemicarceplex from the mobile to stationary phase, correlates almost linearly with the guest length for hemicarceplexes having nearly D_{4h} symmetry (hemicarceplexes with guests **2**-**4**).

The reaction of capsule **9a** with **10** and butane-1,4-dimesylate in the presence of Cs_2CO_3 in HMPA and the brief irradiation of formed **9b·10** in CH_2Cl_2 affords **9b·11**; in this way it was shown that singlet phenylnitrene undergoes a thermal ring-expansion to give cyclic ketenimine **11**, its polymerization being prevented by the surrounding host.[22] This procedure allowed the NMR spectroscopic characterization of **11**.

Capsules **12b-f** served as reaction vessels for thermal decomposition of diazirines **13-15.**[23] Diazirines undergo fragmentation to carbenes and nitrogen or weakly bound carbene-nitrogen complexes, which form diazo compounds or carbene reaction products.

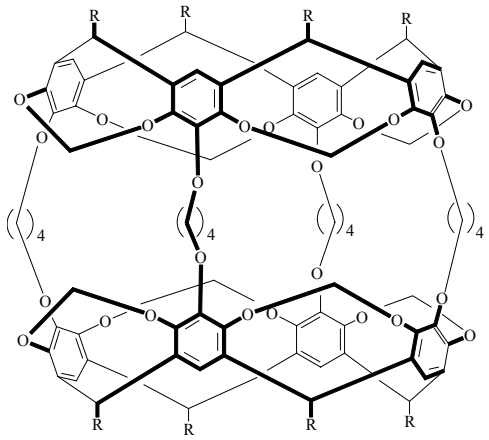
The thermal decomposition of **13** encapsulated in **12e** was accelerated due to the stabilization of transition state by dispersion forces. However, the decomposition of **14** was not affected by encapsulation in **12e** and the decomposition rate of **15** encapsulated in **12d** decreased.

In order to explain the influence of capsule on the decomposition rate of **13-15**, the shape of the host was slightly altered through variation of one linker; in this way, the center-to-center distance between two cavitands of the capsule could be changed.

Hemicarceplex **12e**·**13** was obtained by stirring **12e** with **13** in $CDCl_2CDCl_2$. Hemicarceplexes **12b**·**14**, **12c**·**14** and **12f**·**14** were obtained by reacting the diol host **12a** with linkers **16** or **17**, respectively, and Cs_2CO_3 in HMPA with excess of **14**.

The dissociation of obtained hemicarceplexes is slow enough at elevated temperature to study the thermal decomposition of the guest. Comparing diazirine decomposition processes in the bulk phase with that in the inner phase, it was observed that the hemicarcerand stabilizes the inner-phase transition states enthalpically and destabilizes the transition states entropically.

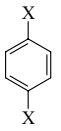
The complexation properties of hemicarcerands **18** and **19** were investigated. On the basis of AM1 calculations for host, guest and host-guest complexes a criterion for predicting guest encapsulation was determined.[24] The barriers to the exit of DMF and furan from hemicarceplexes **18b**·DMF and **18b**·furan have been computed, and the synthesis of the hemicarceplex **18b**·furan has been made.



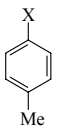
	R
1 **a**	*n*-C_5H_{11}
b	CH_2CH_2Ph

Examples of D_{4h} - symmetric guests

	X
a	none
b	F
c	Cl
2 **d**	Br
e	Me
f	CN
g	OH

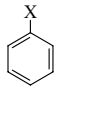


	X
a	F
3 **b**	Cl
c	Br
d	I

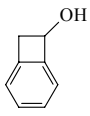


	X
a	F
4 **b**	Cl
c	Br
d	I

Examples of C_{2v} - symmetric guests



	X
a	NO_2
5 **b**	C(O)Cl
c	C(O)OMe



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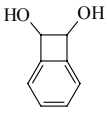

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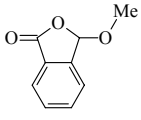

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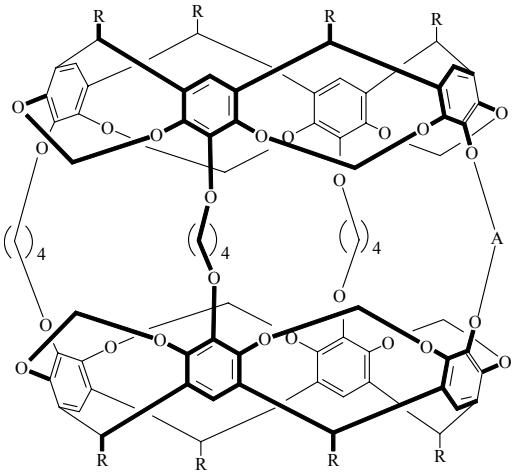
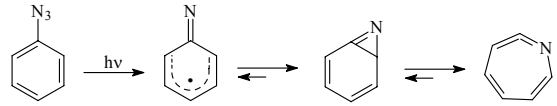
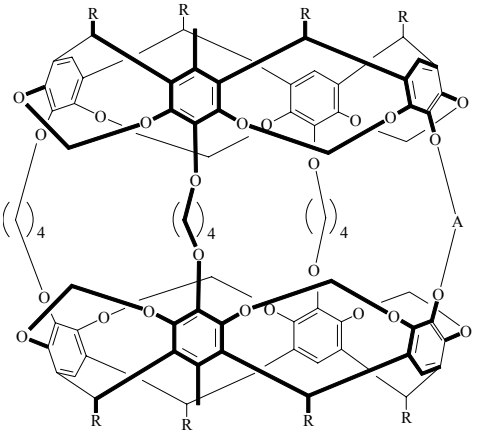


R = *n*-C_5H_{11}

		A
9	**a**	2H
	b	$(CH_2)_4$

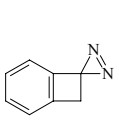


10 **11**



R = CH_2CH_2Ph

		A
12	**a**	2H
	b	$(CH_2)_2$
	c	$(CH_2)_3$
	d	$(CH_2)_4$
	e	$(CH_2)_5$
	f	



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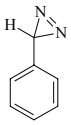

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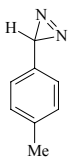
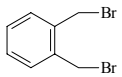


15

TsO−$(CH_2)_n$−OTs

		n
16	**a**	2
	b	3



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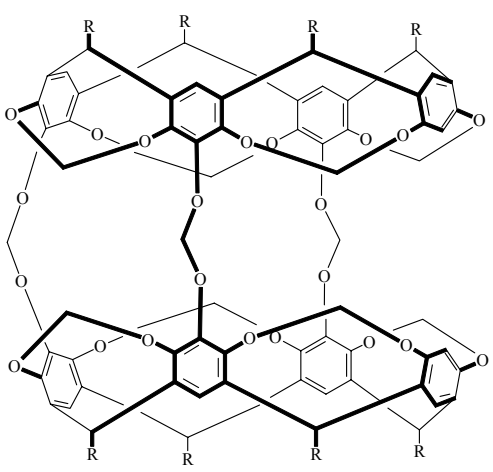
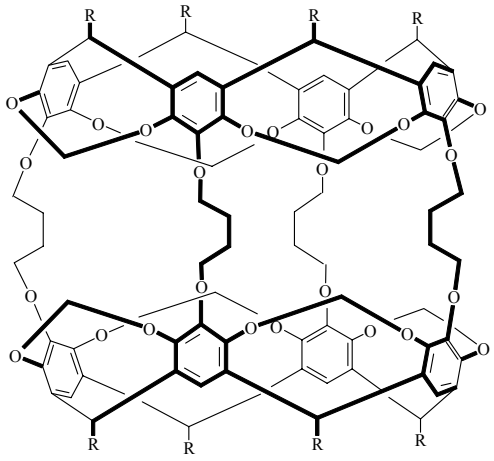


	R
18 a	Me
b	CH_2CH_2Ph



	R
19 a	Me
b	CH_2CH_2Ph

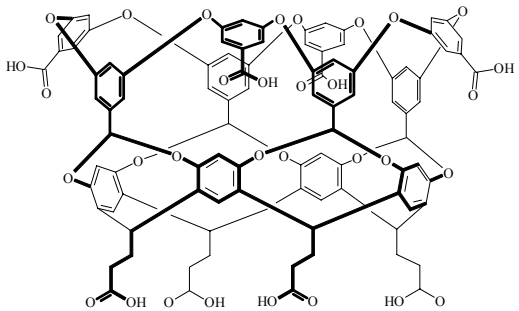
Scheme 1

It was found that the capsule $\mathbf{20}_2$ formed by the assembly of two molecules of cavitand **20** may enclose guest molecules in aqueous solution; as such naphthalene, anthracene, and tetracene have been chosen.[25]

Two molecules of either naphthalene or anthracene may be held within the capsule, this fact resulting in the enhancement of their excimer emission. However, two anthracene molecules encapsulated in $\mathbf{20}_2$ cannot achieve the geometry required for dimerization; therefore, the photodimerization of anthracene is impossible.

Since the tetracene molecule is larger, its one molecule only can be encapsulated in $\mathbf{20}_2$, and only the monomer emission is observed. The above results show that the inclusion of the guest within the cavity of the capsule $\mathbf{20}_2$ can suppress photochemical pathways that are normally favored in solution.

Mono-, bis-, and tris-hemicarceplexes **21**-**23** containing pyrazine as a guest have been obtained.[26] It was observed that they show twistomerisomerism. In bis- and tris-hemicarceplex **22** and **23** two diastereomers exist; A and B are chiral and achiral conformers of **22**, respectively.



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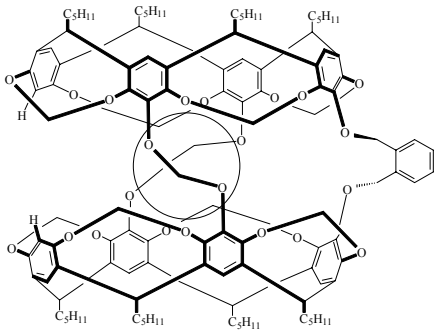

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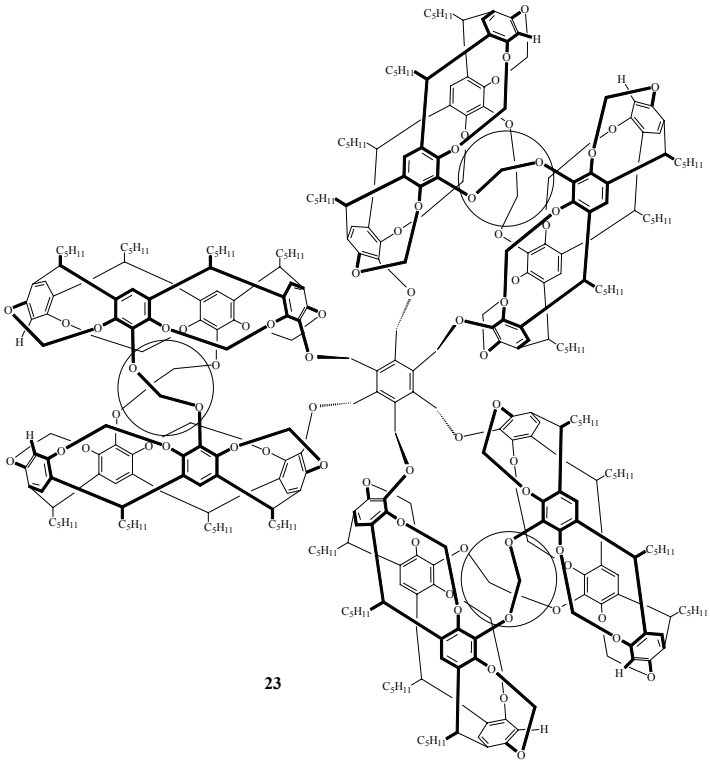

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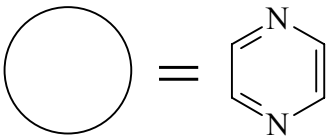
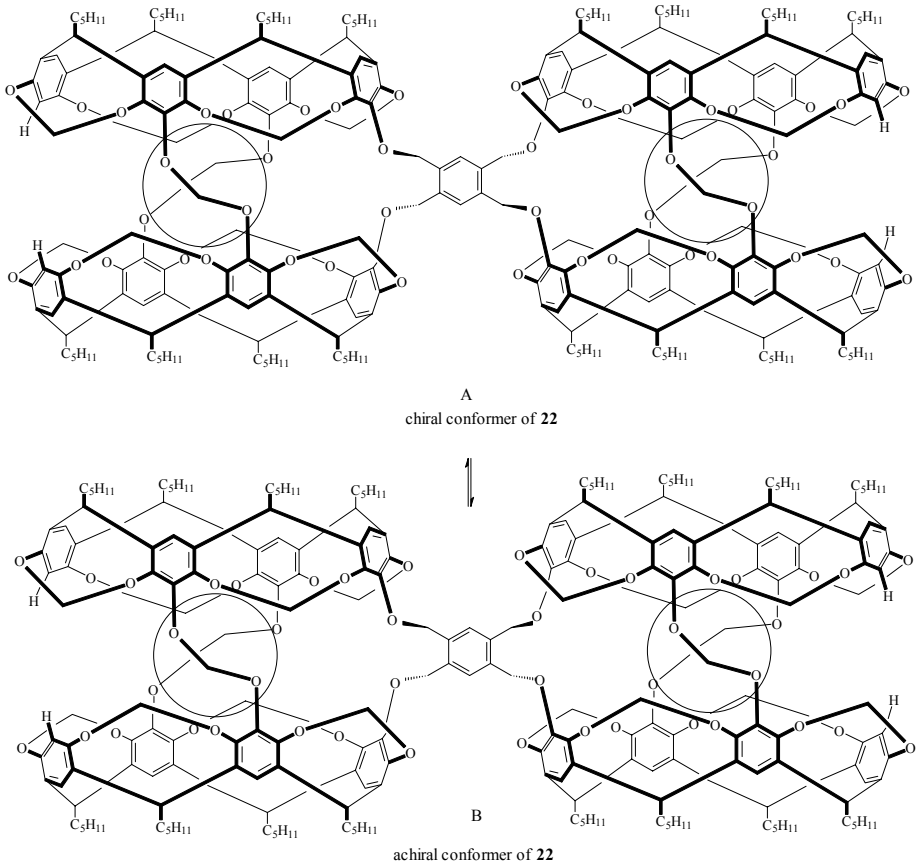




Scheme 2

2. Hydrogen-bonded Capsules

The complexation of resorcinarenes **24** with small quaternary alkyl ammonium salts, *e.g.* $\mathbf{25}^{+}Br^{-}$ affords hydrogen-bonded dimeric capsules upon crystallization from relatively hydrophilic solvents, *e.g.* alcohols. The complexation of **24** with doubly protonated and *N*,*N*'-quaternized DABCO derivatives $\mathbf{26}^{2+}$-$\mathbf{28}^{2+}$ has been studied.[27]

The crystallization of **24b** with $\mathbf{25}^{+}Br^{-}$ *i.e.* ($Me^{+}_4NBr^{-}$) from aqueous MeOH affords a dimeric capsule, $\mathbf{24b}_2$ enclosing $\mathbf{25}^{+}$, which is stabilized by four intramolecular hydrogen bonds between phenolic hydroxyl groups. The confined cation $\mathbf{25}^{+}$, as well as the co-crystallized methanol molecules and bromide ion are disordered. Complexes form hydrogen-bonded ribbons, mediated by the bromide ions.

It was observed that **24a** forms with $\mathbf{26}^{2+}$ and $\mathbf{27}^{2+}$ dimeric capsules embedding $\mathbf{26}^{2+}$ or $\mathbf{27}^{2+}$, respectively; $\mathbf{24c}_2$ forms dimeric capsule with $\mathbf{28}^{2+}$, in which $\mathbf{28}^{2+}$ interacts with two resorcinarene moieties *via* its phenyl groups. In dimeric capsules $\mathbf{24a}_2$ and $\mathbf{24c}_2$ the guests $\mathbf{26}^{2+}$-$\mathbf{28}^{2+}$ are severely disordered, as in the case of capsule $\mathbf{24b}_2$ with $\mathbf{25}^{+}$.

In the study of capsules, it was established that resorcinarene **29** treated in ethanol with terpyridine **30** and *o*-carborane affords the complex [(*ortho*-carborane)$_2$⊂ (**29**)$_2$(**30**)$_4$]·(*ortho*-carborane).[28] In this complex, the capsule held together by four terpyridine units through sixteen OH...N hydrogen bonds completely includes two *ortho*-carborane molecules.

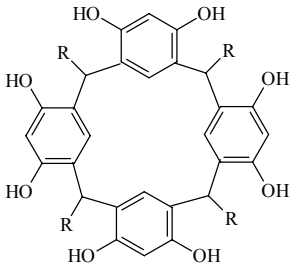
Tetra-acrylamido calix[4]arenes **31**, having cone all-trans conformation undergo dimerization in nonpolar solvents to give capsules, which may include small organic molecules.[29] It was found that **31b**$_2$ is a hydrogen bonded dimer; dimerization occurs *via* eight hydrogen bonds (NH...O=C) between C=O and N-H groups of opposing acrylamides. The electron-poor *p*-CN-aryl group interacts face-to-face with electron-rich aromatic moiety of the calixarene enhancing the stabilization.

The addition of benzene to a $CDCl_3$ solution of **31b**$_2$ leads to inclusion of benzene molecule. The pesticides thiuram **32** and triazine **33** may also be encapsulated into **31b**$_2$. It should be pointed out that the encapsulation is irreversible.

When inclusion complex **31b**$_2$·**33** is treated with **32**, no guest exchange occurs; no guest exchange occurs also when **31b**$_2$·**32** is treated with **33**. It was observed that the equimolar mixture of **31a** and **31b** in $CDCl_3$ affords heterodimeric capsule **31a**·**31b**; mixtures of **31a** with **31c** and of **31b** with **31c** also give heterodimeric capsules **31a**·**31c** and **31b**·**31c**.

Calixarenes **34** substituted by urea groups at their wide rims have been synthesized. When the chloroform solution of **34a** was treated with tetraethylammonium bromide or hexafluorophosphate, the formation of dimeric capsules **34a**$_2$ including Et_4N^+ ions occurred. Similar behavior was observed for **34b-d**, this fact indicating that the size of the amide groups does not influence dimerization. Halide anions may be hydrogen-bonded to capsules.

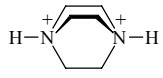
It was found that calixarenes **34a** and **34c** form with $Et_4N^+Br^-$ a single heterodimer Et_4N^+**·34a·34c·**Br^-, coexisting with the two homodimers [30].



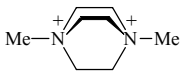
	R
a	Et
b	CH_2CH_2Ph
c	*n*-$C_{11}H_{23}$

24

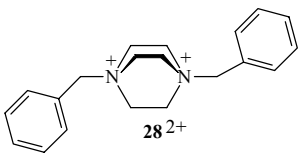
25



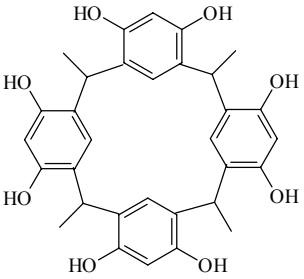
26$^+$



27$^+$



28^{2+}



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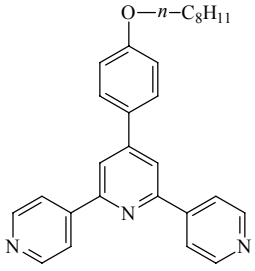

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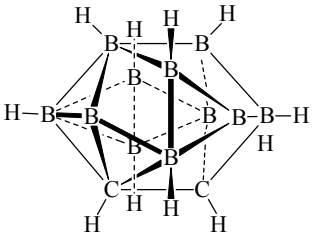
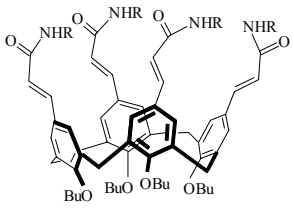
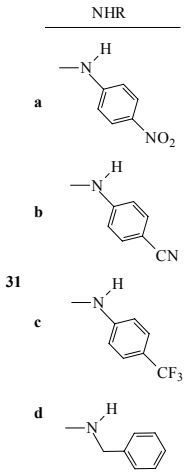


ortho-carborane





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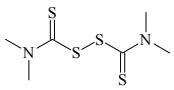

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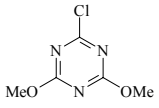

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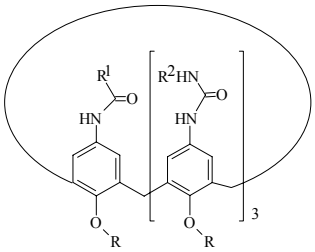


R = *n*-C_5H_{11}

		R^1	R^2
34	**a**	Me	4-C_6H_4Me
	b	Me	*n*-C_6H_{13}
	c	Et	4-C_6H_4Me
	d	*n*-Bu	4-C_6H_4Me

Scheme 3

3. Capsules bound by metal coordination

Among capsules bound by metal coordination, the homo- and heterocapsules are known, the latter being less studied as the former ones. Below some examples of both types of species will be presented.

Cavitand **35** reacts with $AgBF_4$ to give a stable D_4-symmetric capsule **36**. The silver ion coordinates two bipyridyl groups in a tetrahedral fashion. Capsule **36** may incorporate rigid guests **37b-39**; complexes with **39b** and **39c** are stable since **39b** and **39c** have the best complementary molecular length among the guests used. The K_a values decrease in the order **39c** > **39b** > **38** > **39a** > **37b**.[31,32]

When a mixture of acetic acid and **37a** is added to solution of **36**, the hetero dimer of acetic acid and **37a** in the capsule is formed; the same behavior was observed for propionic acid and **37a**.

When acetic acid, propionic acid, and **37a** were added to **36**, the exclusive formation of the hetero dimer of acetic acid and **37a** occurred. The calculation of structures has shown that both

hetero dimers – acetic acid·**37a** and propionic acid·**37a** very well fit inside **36**, and the methyl groups of acetic and propionic acids point down to the ends of the cavity, enabling CH/π interactions. However, the more acidic methyl group of acetic acid creates better CH/π interactions than methyl group of propionic acid, therefore the heterodimer acetic acid·**37a** is favored over propionic acid·**37a**.

It was observed that the reaction of cavitand **40**, cobalt (II) ions and a guest leads to the formation of a capsule including the guest, *i.e.* **41**⊃guest. A series of organic compounds were used as guest molecules; the guest encapsulation preference decreases in the order: anisole > *p*-xylene > toluene > styrene > benzene > *m*-xylene > *o*-xylene.[33] The existing selectivity of the guest inclusion should be emphasized, for example *p*-xylene is preferred over toluene which is preferred over benzene, this fact resulting from the pointing of methyl groups of xylene and toluene into the poles of the capsule, enabling formation of C-H-aryl interactions.

The reaction of cavitand **42** with palladium and platinum complexes **43** results in the self-assembly affording capsules **44** incorporating $CF_3SO_3^-$ anion. The kinetic stability of **44** and their anion encapsulation was studied by PGSE (pulsed field gradient spin-echo), NOE (nuclear Overhauser effect) and EXSY (exchange spectroscopy) NMR techniques. It was found that the kinetic stability of capsules **44** is solvent dependent.[34,35]

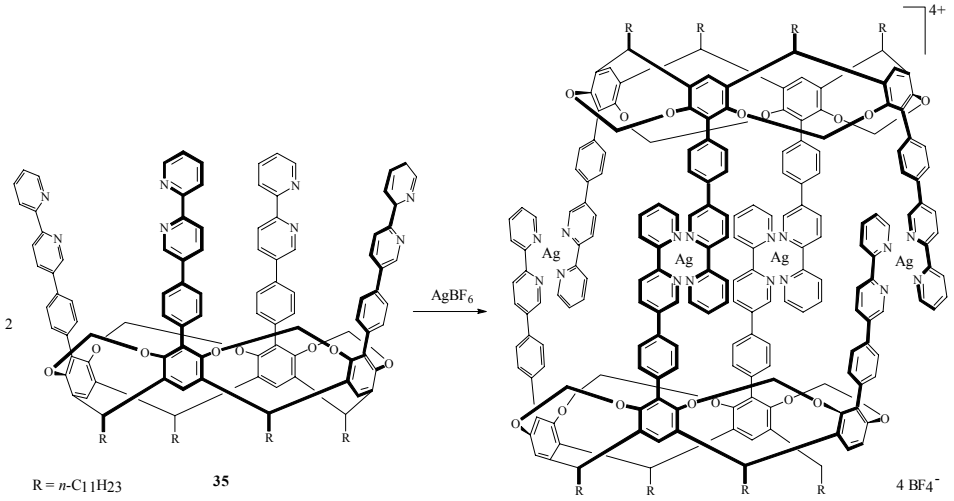
It was established that cavitand **45** reacts with **43** in $CHCl_3$/MeOH to give the capsule **46**. When in this process the $MeNO_2$ is used as a solvent, the reaction leads to the dynamic equilibrium of **46** and deep cavitand **47**.[36]

The selective self-assembling of homo- and heterocapsules *via* metal coordination of cavitands has been studied;[37,38] this process is controlled by the balance between kinetic and thermodynamic stabilities of capsules. It should be pointed out that heterocapsules are not so common as homocapsules.

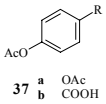
The mixture of cavitands **48** and **49** treated with **43a** or **43b** affords thermodynamically stable heterocapsules **50a** or **50b**, respectively. The Pt-NCPh bond is thermodynamically and kinetically less stable than Pt-pyridine bond; therefore, the homocapsule **51** in $CDCl_3$ at room temperature gradually underwent ligand exchange with **48** to give a mixture of **50b** and free **49**.

The treatment of a mixture of **52** and **53** in $CDCl_3$ with **43a** at room temperature leads to the formation of kinetically and thermodynamically the most stable homocapsule **54a** and the most labile homocapsule **55a**. Since the coordination ability of **52** is much higher than that of **53**, the homocapsule **54a** forms prior to homocapsule **55a**. Initially the formation of **54a** based on kinetic control is the driving force of self-assembly, and **55a** is only the byproduct. However, upon heating to 50°C the heterocapsule **56a** is formed; the product is a 1:1:1 mixture of **54a**, **55a**, and **56a**.

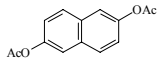
The treatment of a mixture of **52** and **53** with **43b** leads to the formation of homocapsules **54b** and **55b** along with the heterocapsule **56b**. It should be pointed out that **54b** and **55b** are stable even at 50°C.



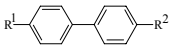
R = *n*-$C_{11}H_{23}$ **35** **36**



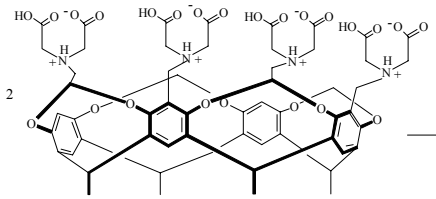
37 **a** OAc **b** COOH



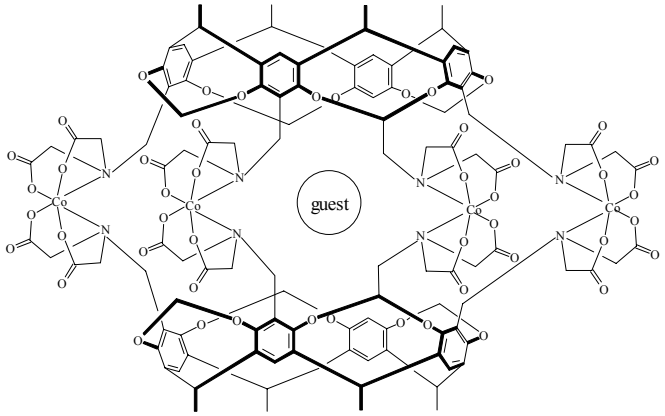
38



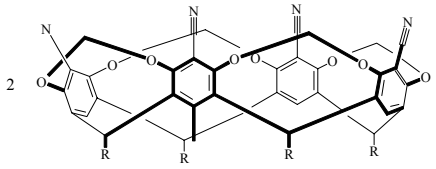
		R^1	R^2
39	**a**	H	OAc
	b	COOMe	COOMe
	c	OAc	OAc



40

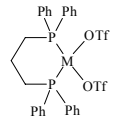


41 ⊃ guest

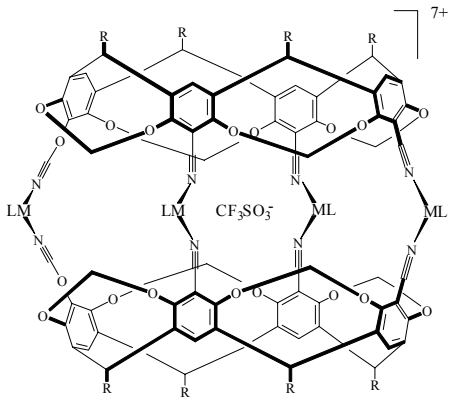


R = *n*-C_6H_{13}, *n*-$C_{11}H_{23}$

42



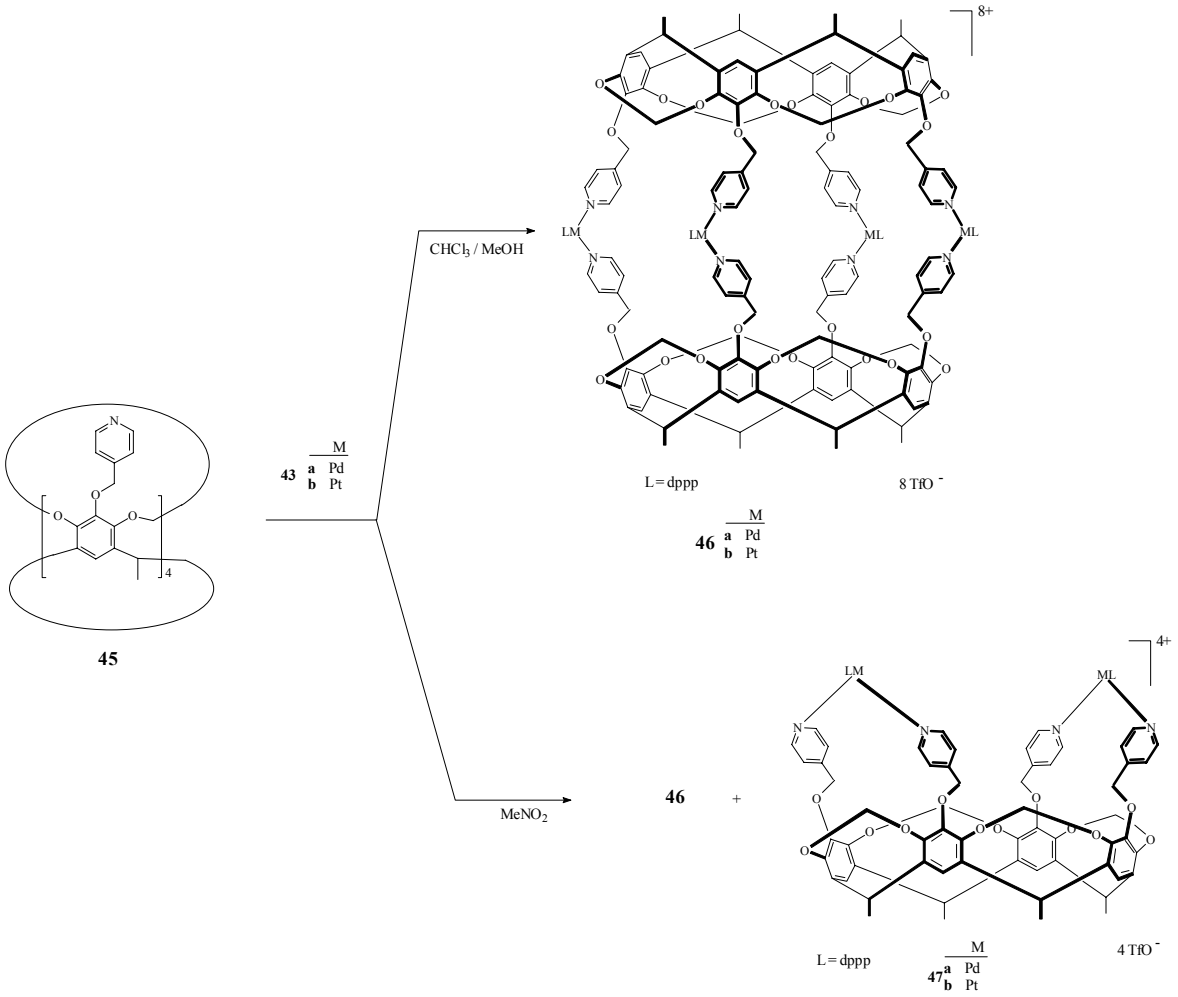
		M
43	**a**	Pd
	b	Pt



L = dppp = 1,3-bis(diphenylphosphino)propane 7 TfO -

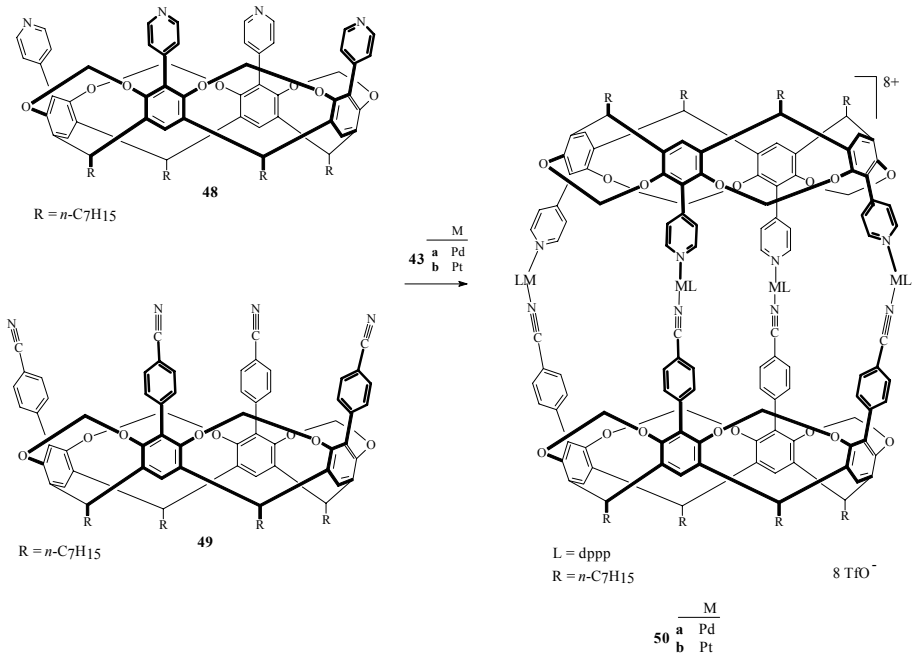
	a	M
44	a *n*-$C_{11}H_{23}$	Pd
	b *n*-C_6H_{13}	Pt
	c *n*-$C_{11}H_{23}$	Pt

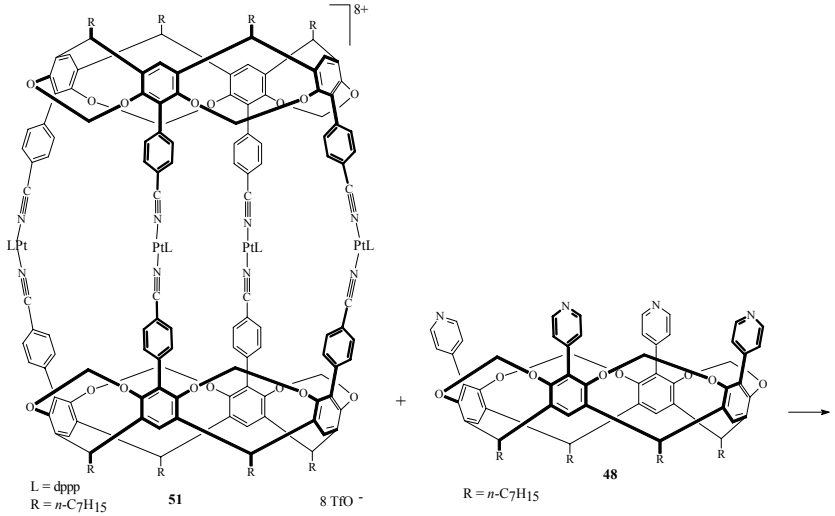
44 a-c ⊃ $CF_3SO_3^-$

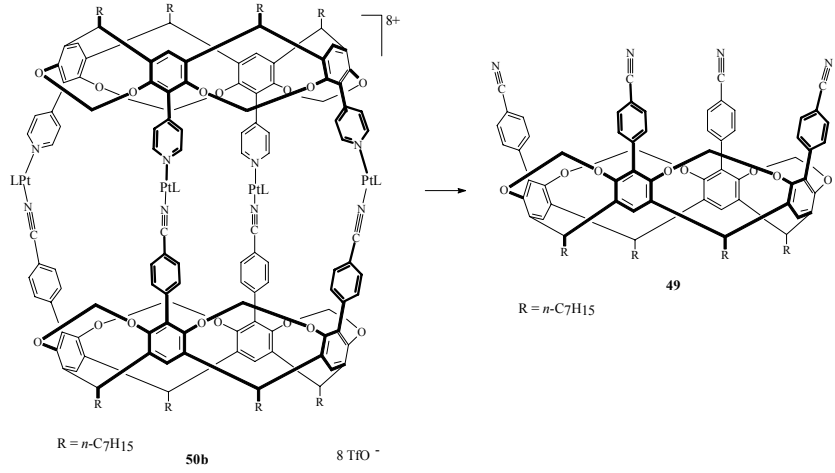


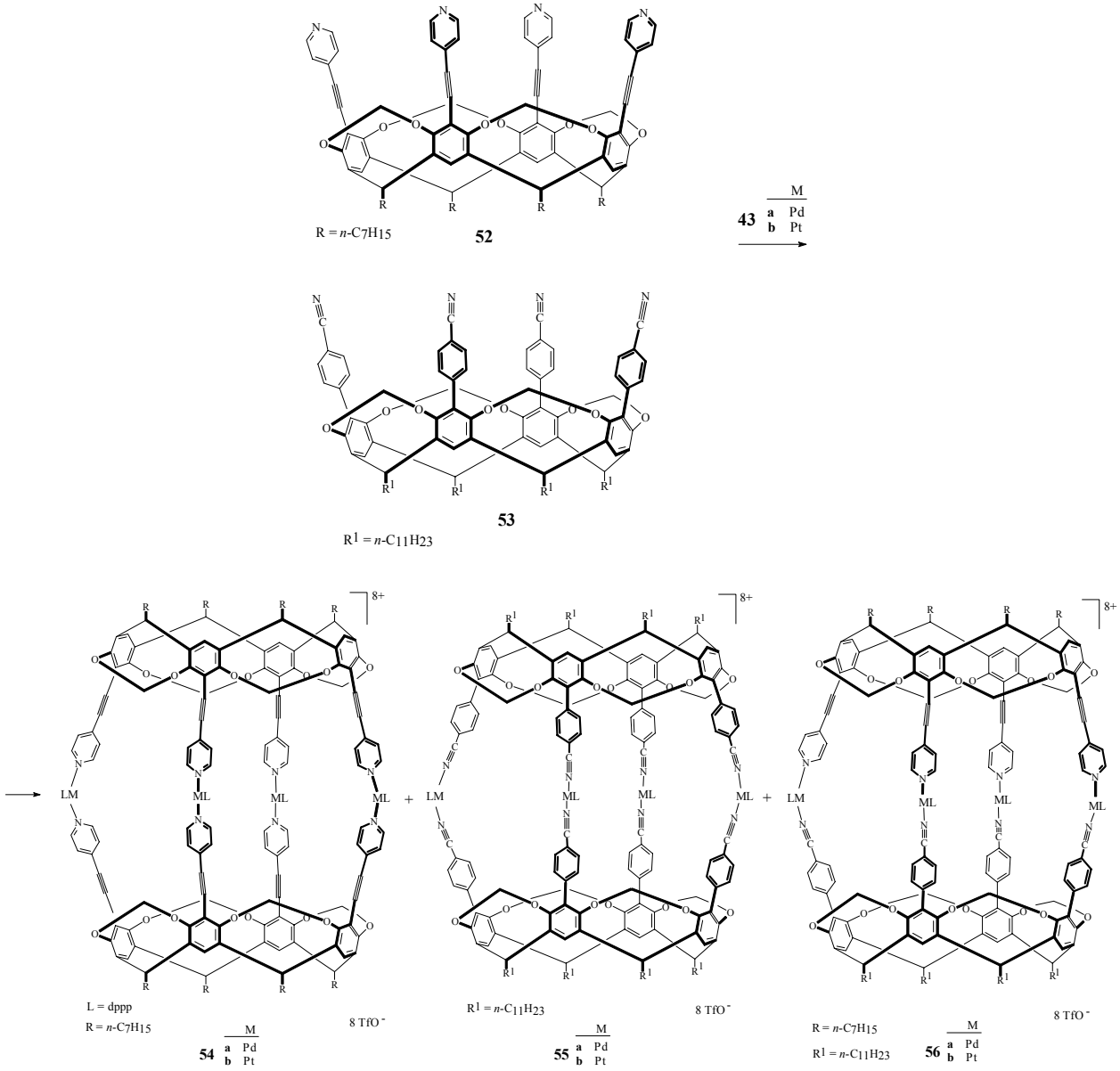
Scheme 4

By heating at 50 ^{o}C, the increase of **54b** was observed; lastly **56b** was converted completely into homocapsules **54b** and **55b**. The fact that only **54b** and **55b** exist at the final thermodynamic equilibrium shows that the average thermodynamic stability of **54b** and **55b** is much higher than the thermodynamic stability of **56b**.


48
R = n-C7H15
43
M
a Pd
b Pt
49
R = n-C7H15
L = dppp
R = n-C7H15
8 TfO -
50
M
a Pd
b Pt


L = dppp
R = n-C7H15
51
8 TfO -
48
R = n-C7H15


R = n-C7H15
50b
8 TfO -
49
R = n-C7H15



Scheme 5

4. Capsules bound by ionic interactions

The strong ionic interactions, albeit often existing in biological molecular recognition and artificial molecular building, are rather rarely used in formation of capsules; some examples of such species will be given below.

Self-assembly between oppositely charged calixarenes **57** and **58** in polar solvents like MeOH/H_2O affords capsules formed by multiple ionic interactions of amidinium moieties of **57** with sulfonate, carboxylic and phosphonate groups of **58**.[39] The association constants for

capsules **57**·**58a-c** (varying between 10^3-10^6 M^{-1}) have been determined using ITC (isothermal titration calorimetry).

The ionic interactions between amidinium groups of **57** and amino acidic residues of **59** lead to formation of water-soluble capsules **57**·**59a** and **57**·**59b**.[40] The results of ITC allow the estimation of the influence of the size of the amino acid side chains in **59a,b** and of the distance of the carboxylic groups from calixarene scaffold in the self-assembly process.

Capsule **57**·**59a** is an effective host for charged species, such as *N*-methylquinuclidinium cation **60** as well as neutral molecules, such as 6-amino-2-methylquinoline **61** in water. Molecular docking, a computational method enabling the rapid evaluation of steric and electrostatic complementarity of potential guest molecules with a host, was applied to indentify possible guest molecules for capsule **57**·**59a**.

5. Capsules bound by van der Waals interactions

Capsules, covalently linked by metal coordination or hydrogen bonding have been studied more than those formed from components that interact by van der Waals forces.[41] Such capsules are not sufficiently stable in solution since solvation forces may exceed van der Waals interactions. However, these interactions are the only source of stabilization of capsules in the solid state; since these interactions are weak, such nanocontainers have the flexibility allowing the capture and release of the guest without destroying the crystal lattice. Guest exchange in such solid matrices is important for their applications in separation science and transport of active species.

The formation of large capsules, which have the flexibility allowing the guest exchange, was studied. It was found that calixarene **62** forms hydrophobic capsule $\mathbf{62}_2$ bound by van der Waals interactions and is able to enclose a variety of guests; the capsule is robust enough to capture large guests at room temperature.[42]

Crystals obtained from a solution of **62** in $CHCl_3$ have the molecules of **62** arranged in tail-to-tail pairs; the formed hydrophobic dimeric capsules $\mathbf{62}_2$, contain four molecules of $CHCl_3$. Complex $\mathbf{62}_2$·$4CHCl_3$ is, however, thermally unstable in that it instantly releases one $CHCl_3$ molecule, even below room temperature. The heating to 80 ^oC results in the loss of two next $CHCl_3$ molecules; the fourth $CHCl_3$ molecule is removed at ca 180 ^oC.

Since $\mathbf{62}_2$·$4CHCl_3$ is not very stable, it was anticipated that the replacement of the guest $CHCl_3$ by another guest, *e.g.* dibenzyl ketone (DBK) may give a more stable structure. The size of DBK is suitable for the cavity of the capsule $\mathbf{62}_2$. For this purpose, crystals of complex $\mathbf{62}_2$·$4CHCl_3$ were placed in a saturated solution of **62** in DBK; this process leads to replacement of some $CHCl_3$ molecules by DBK without destroying the crystals. The formed complex is capsule $\mathbf{62}_2$ containing two different guests, $CHCl_3$ and DBK, *i.e.* it is $\mathbf{62}_2$·$CHCl_3$·DBK.

The TGA results show that this complex releases at 140 ^oC the residual $CHCl_3$ molecule affording complex consisting of capsule $\mathbf{62}_2$ incorporating only DBK, *i.e.* $\mathbf{62}_2$·DBK; DBK leaves the capsule upon heating to *ca*. 200 ^oC. The release of $CHCl_3$ from $\mathbf{62}_2$·$CHCl_3$·DBK proceeds

without destroying the crystal lattice; this behavior is different from that of $\mathbf{62}_2 \cdot 4CHCl_3$, in which removal of only two $CHCl_3$ molecules destroyed the crystal lattice.

The phototransformation of *cis*- and *trans*-stilbene inside capsule $\mathbf{62}_2$ bound by van der Waals interactions has been investigated.[43-45]

In bulk solution, stilbenes undergo a reversible *cis/trans* isomerization; *cis*-stilbene upon cyclization forms dihydrophenanthrene **63**, which upon oxidation afforded phenanthrene **64**; *trans*-stilbene, however, underwent dimerization to give tetraphenylcyclobutanes **65** and **66**.

It was observed that the slow evaporation of solvent from the $CHCl_3$ solution of **62** and *cis*-stilbene affords crystals in which calixarene pairs are arranged into capsules $\mathbf{62}_2$ containing two molecules of *cis*-stilbene (complex A). Complex A is thermally unstable; the TGA experiments indicate that one *cis*-stilbene molecule leaves the capsule cavity at 60-120 ^{o}C yielding complex B, *i.e.* capsule $\mathbf{62}_2$ containing one molecule of *cis*-stilbene.

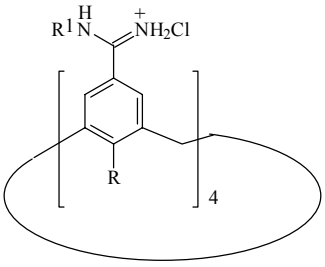
The slow cooling of a solution of calixarene **62** and *trans*-stilbene in ethanol afforded the crystalline complex C consisting of capsules $\mathbf{62}_2$ containing two *trans*-stilbene molecules and capsules $\mathbf{62}_2$ containing only one *trans*-stilbene molecule. The TGA results showed the release of one molecule of *trans*-stilbene to give the complex consisting of capsules $\mathbf{62}_2$ containing only one molecule of *trans*-stilbene.

Complexes A, B and C were irradiated by UV light (320-390 nm). The irradiation of the complex A gave rise to three photochemical reactions, which occur in the bulk solution, among them, the *cis/trans* isomerization being the fastest process. Since the situation of two *trans*-stilbene molecules in the capsule $\mathbf{62}_2$ at an appropriate distance to undergo dimerization is not probable, the yields of **65** and **66** are low.

Irradiation of complex B leads to *cis/trans* isomerization followed by cyclization of *cis*-stilbene to phenanthrene **64**; dimeric products **65** and **66** were not formed confirming that the capsule $\mathbf{62}_2$ contains only one molecule of *cis*-stilbene.

Irradiation of complex C occurs in a similar way in that only trace amounts of **65** and **66** confirmed that in complex C, capsule $\mathbf{62}_2$ contains only one molecule of *trans*-stilbene.

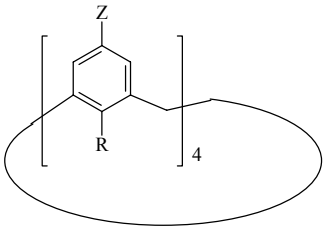
The above results show that capsule $\mathbf{62}_2$ is sufficiently robust to keep reagents close to each other and allowing their interaction. The crystals of complexes A-C remained intact after irradiation and could be investigated by single-crystal XRD. This stability is of interest in their usefulness in biological processes.



R = O OEt

R^1 = *n*-Pr

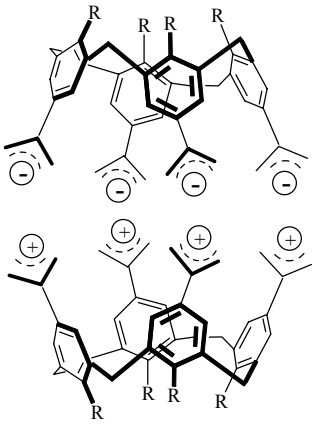
57



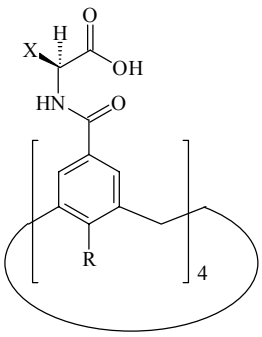
R = O OEt

	Z
a	SO_3Na
b	COOH
c	$CH_2PO_3H_2$

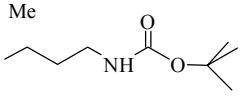
58



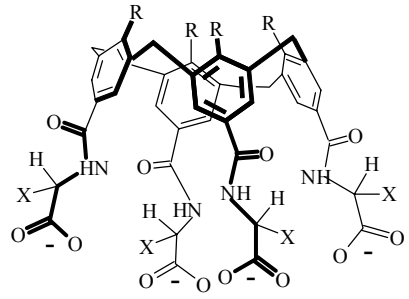
57·58a-c

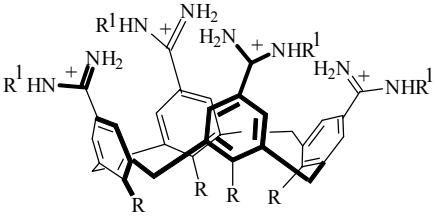


R = O OEt

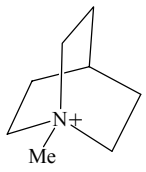
	X
a	Me
b	

59

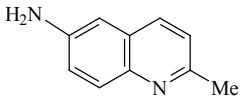




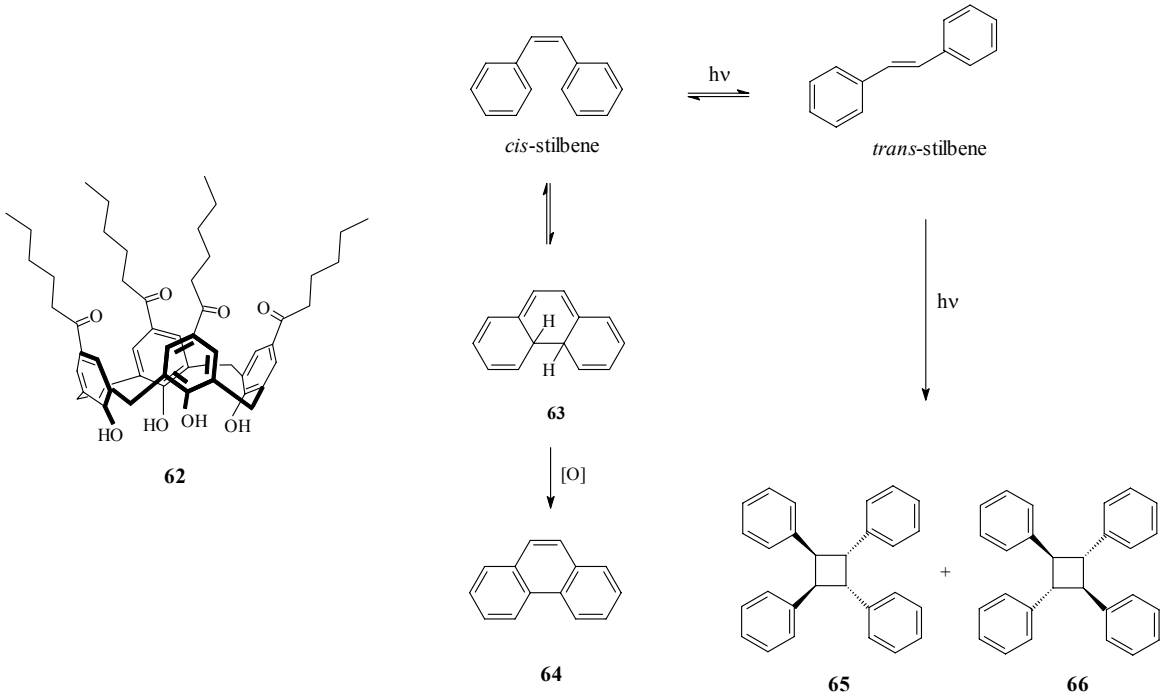
57·59a,b



60



61



Scheme 6

6. Guest-templated Capsules

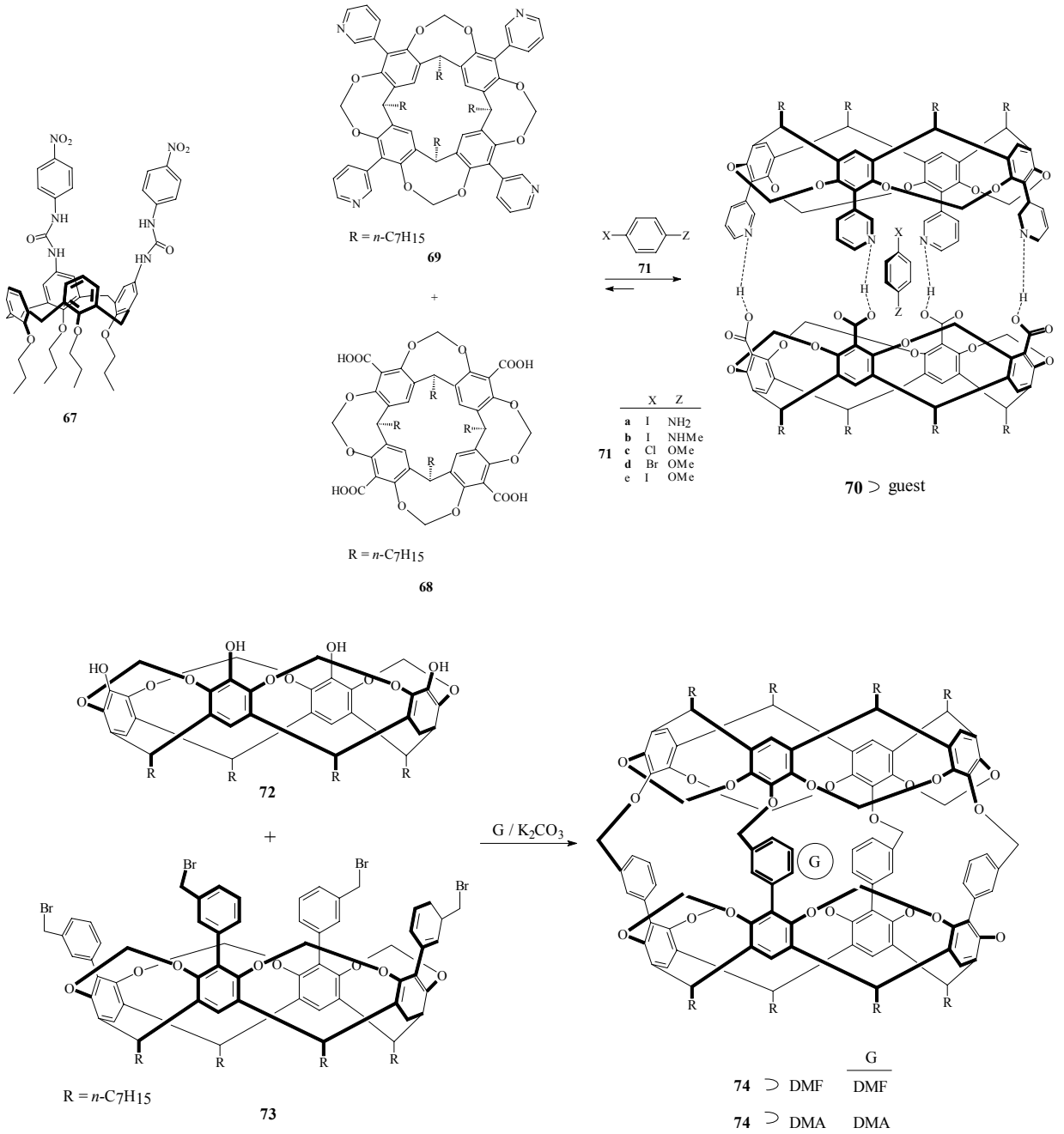
It was found that calixarene **67** with anions forms 2:1 complexes, in which anion serves as a template for dimerization of two molecules of **67**.[46] It is an interesting example of anion-induced dimerization of **67**; two molecules of **67** are interconnected by an anion, which is bound within two urea moieties of the dimer.

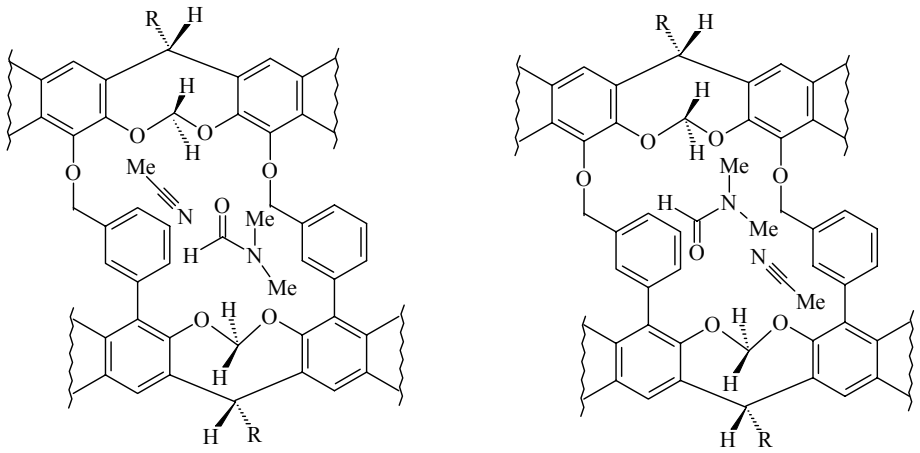
The formation of complex $\mathbf{67}_2$·anion does not depend on the geometry of anions; spherical (Cl^-, Br^-, I^-) and nonspherical (NO_3^-, AcO^-, BzO^-) anions were bound in the dimeric capsule $\mathbf{67}_2$.

Cavitands **68** and **69** in the presence of guest form the assembly heterocapsule **70**⊃guest. As guests, nonsymmetric *p*-disubstituted benzene derivatives **71** were used. The ability of the guest to induce the formation of the assembly **70**⊃guest decreases in the order **71e** > **71b** > **71d** > **71c** > **71a**. The halogen atoms of these guests are situated in the cavitand **69**.[47,48]

Cavitands **72** and **73** in solvents G [G = *N,N*-dimethylformamide (DMF) or *N,N*-dimethylacetamide (DMA)] afford carceplexes **74**⊃DMF and **74**⊃DMA.[49] It is of interest that the free capsule, *i.e.* carcerand **74** could not be obtained. When the second, non-interacting guest, *e.g.* MeCN, is added to **74**⊃DMF, the paired carceroisomers **74**⊃(DMF+ MeCN) are formed. One should mention that carceplex **74**⊂DMA does not include small guests.

The second guest may reversibly enter and escape through the portals of the carcerand. The fast movement of the first guest (DMF) is hindered by reversible inclusion of second guest (MeCN). The orientation of guests in two carceroisomers **74**⊃(DMF+ MeCN), major and minor ones shows the pairwise dipole complementarity between the C=O and –C≡N groups of two paired guests.





74 ⊃ (DMF + MeCN)

major carceroisomer minor carceroisomer

Scheme 7

Conclusions

The chemistry of capsules is developing rapidly; since the number of works concerning this class of compounds is very large [50-64], in the above review only selected examples are described. The paper does not deal with capsule-like compounds [65-67] nor with calixarene based nanotubes [68-70].

Although the review is not exhaustive, the reported works highlight to some extent the most important properties of capsules and show possibilities of their use.

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