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CYCLODEXTRIN HOST-GUEST SYSTEMS CONTAINING AZAAROMATIC MOIETIES

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Abstract- The chemistry of cyclodextrin host-guest complexes containing azaaromatic moieties is reviewed. Systems with azaaromatic moiety appended to the host molecule and those including an azaaromatic guest are described.

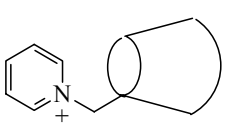
1. INTRODUCTION

Among a great number of cyclodextrin (CD) host-guest complexes, [1-4] those containing azaaromatic moieties [5,6] are of a special interest in view of their physicochemical properties and applications. As supramolecular systems of CDs and quaternary pyridinium salts are described in our previous work, [7] this theme is not included here.

The paper is a continuation of the study of azaaromatics carried out in our research group. [8,9] In the first part of the review CD host-guest systems with azaaromatic moiety appended to the host molecule will be described, and in the second part CD complexes containing an azaaromatic guest.

2. CD HOST-GUEST SYSTEMS WITH AZAAROMATIC MOIETY APPENDED TO THE HOST MOLECULE

The 1:1 inclusion complexes of modified α-, β- and γ-CDs (**1** - **3**) with naphthalene derivatives (**4** - **6**) serving as guests have been obtained. The complexation behaviour of (**1** - **3**) was examined using calorimetric titration . [10]



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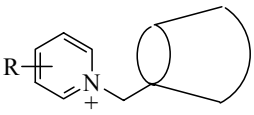
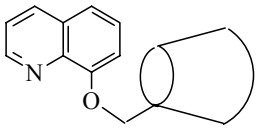


	R
2 a	3-Me
b	4-Me



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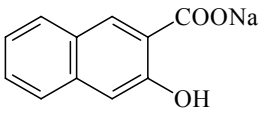

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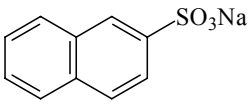

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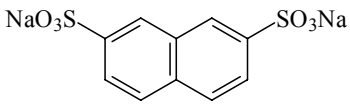
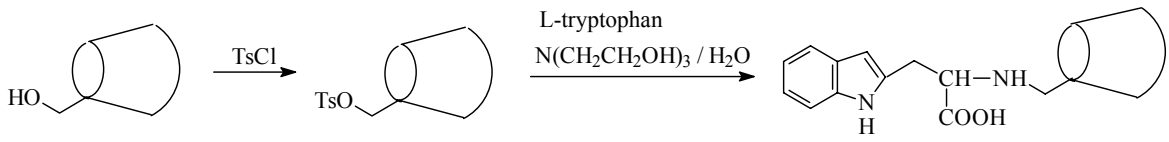


6

The molecular recognition of L-tryptophan modified β-CD (**7**) towards alcohols (**8** - **12**) has been investigated by fluorescence and circular dichroism spectrometry and by fluorescence lifetime measurement .[11-13] The indolyl group has been employed as a spectral probe for spectrofluorometric and spectropolarimetric titrations. The synthesis of **7** involves the conversion of β-CD into its tosylate and the subsequent reaction with L-tryptophan . [11-13]



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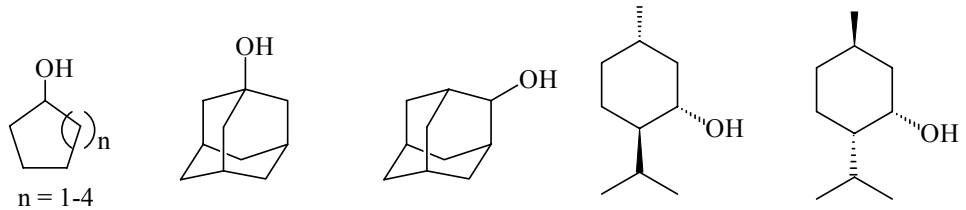
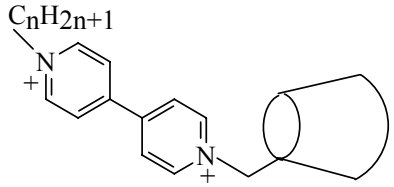


8 **9** **10** **11** **12**

It was observed that **7** may form self- and guest- inclusion complexes. The part of the tryptophan probe in the absence of the guest gives a self inclusion complex, and in the presence of the guest thehost-guest complex is formed. The indolyl moiety is originally located in an identical hydrophobic environment of the CD cavity. In the presence of the guest the indolyl moiety is driven out of the CD cavity and enters into its primary face.

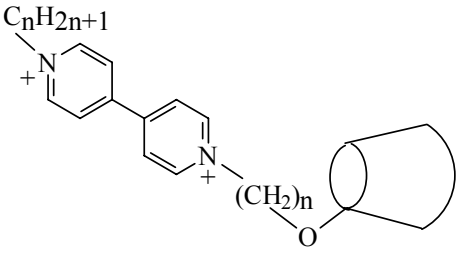
In the formation of 1:1 host-guest complexes of **7** with alcohols (**8** - **12**) it was established that it recognizes not only size and hydrophobicity of guests but also their enantiomeric and geometrical isomers.

It was found that β-CD appended **13** and **14** viologens cause the fluorescence quenching of ethers (**15** - **17**) more efficiently than methyl viologen itself. This fact is due to the inclusion complexation of fluorescent guests (**15** - **17**) into the cavity of β-CD . [14]



13

n = 1, 6, 7, 8



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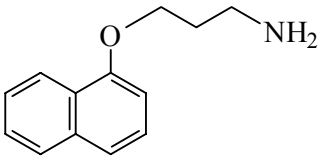
n = 4, 8



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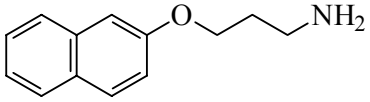

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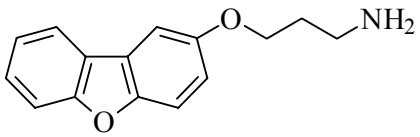
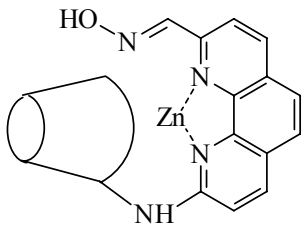


17

In order to prepare an esterase mimic two catalysts (**18**) and (**19**) consisting of β-CD bearing 1,10-phenanthroline oxime moieties coordinating Zn^{2+} ion have been investigated. In **18** the functional group is attached to the secondary face of CD and in **19** - to the primary face . [15,16]



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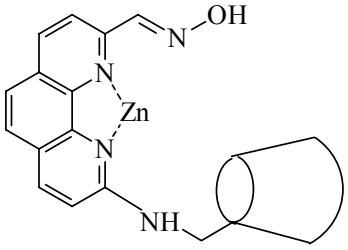

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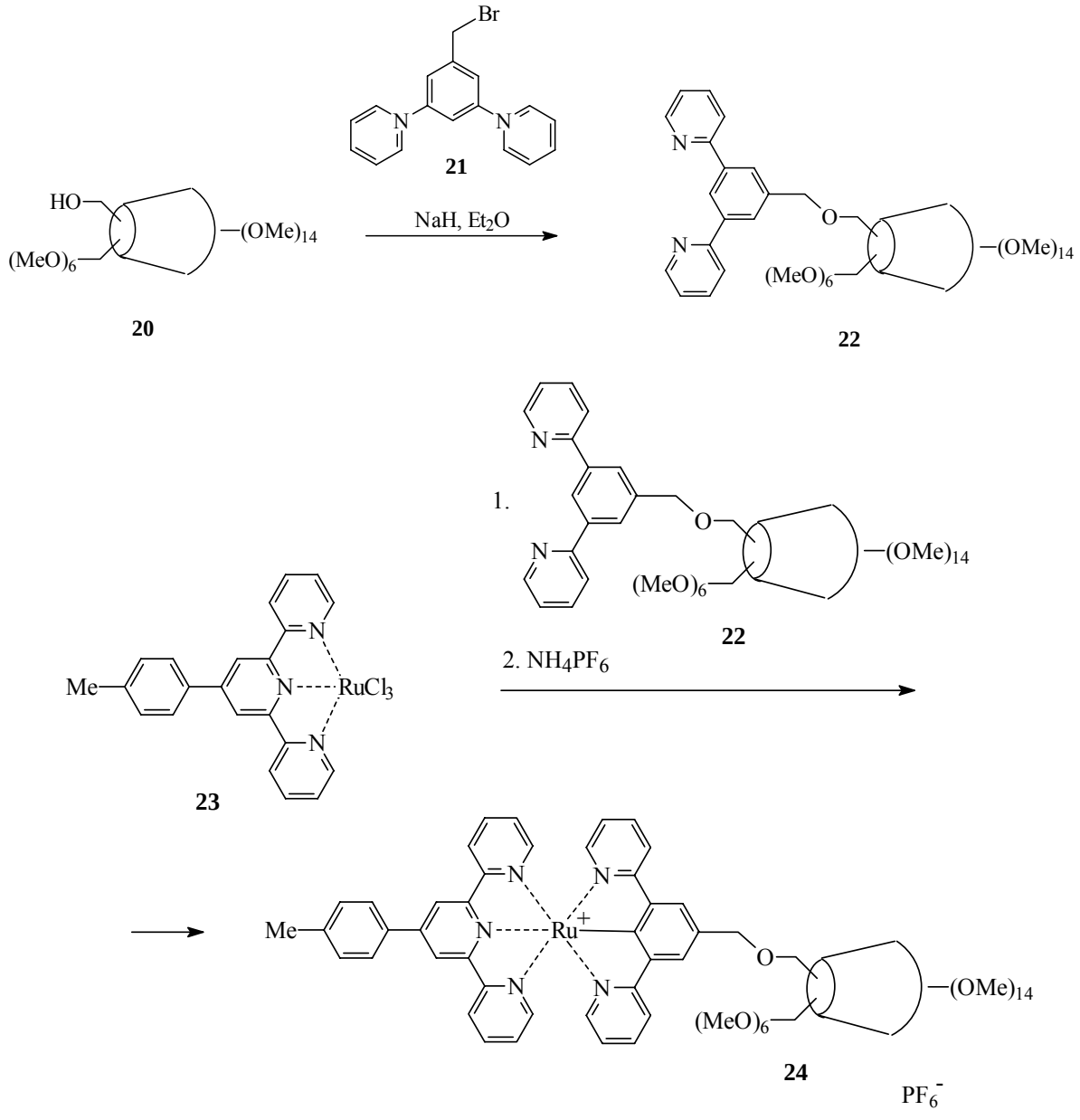
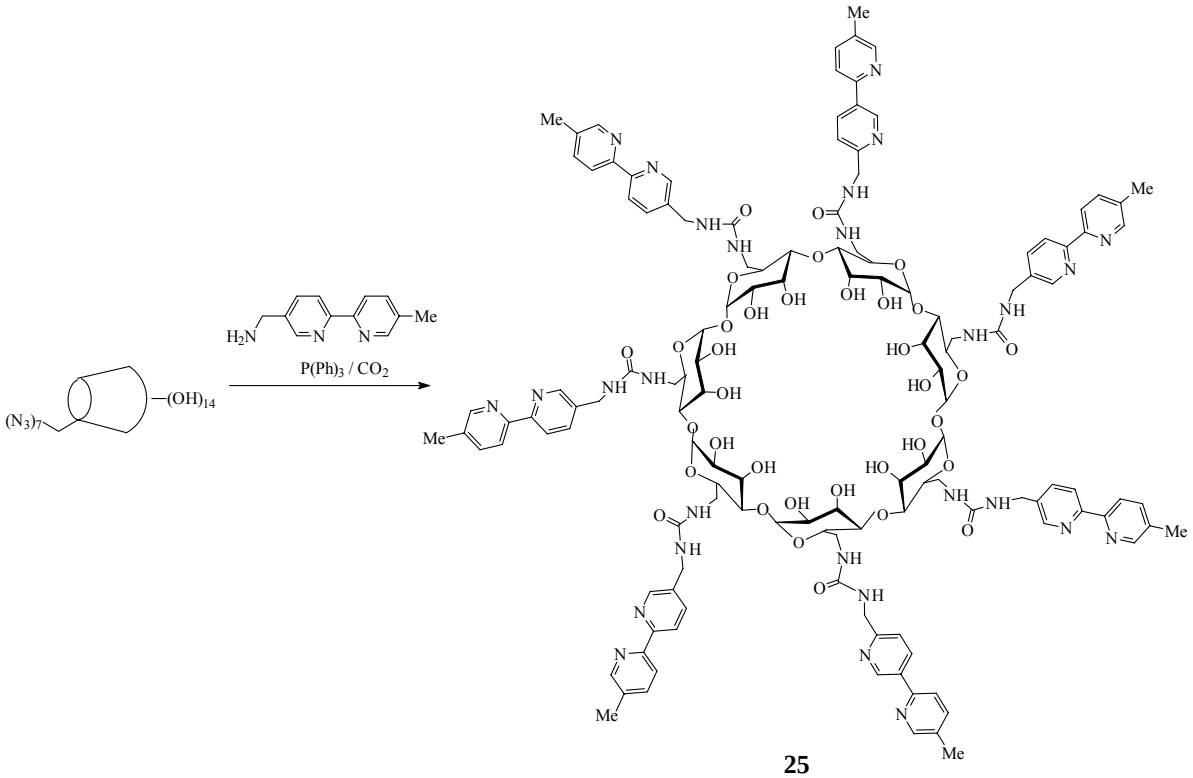
The aqueous solutions of **18** and **19** were examined as catalysts of the hydrolysis of *p*-nitrophenyl acetate, resulting in the formation of *p*-nitrophenoxide ion. It was observed that the catalytic efficiency of **18** was higher as compared with that of **19**. When Ni (II) or Cu (II) have been used instead of Zn (II), the hydrolysis was slower.

In the study of luminescent cyclometallated CDs [17] it was established that the mono-6-hydroxypermethylated β-CD (**20**) reacts with dipyridylbenzene (**21**) under Williamson ether conditions to give compound (**22**). Permethylated derivatives are convenient in such reactions due to their higher

solubility in organic solvents as compared with that of the plain CD. The subsequent reaction of [Ru(ttp)Cl_3] (ttp = tolylterpyridine) (**23**) with **22** followed by the anion exchange with NH_4PF_6 yields the cyclometallated ruthenium CD complex [Ru(**22**)(ttp)][PF_6] (**24**)**.** The complex (**24**) shows room temperature luminescence; it was obtained in order to study the interaction of the appended Ru centre with metalloguests entering the CD cavity .[18]



In the study of CDs the convenient one-pot synthesis of the full-substituted primary face β-CD (**25)** by the "phosphonimine approach" has been performed. It was observed that stirring of **25** in methanol under reflux with $EuCl_3 \cdot 6H_2O$ or $TbCl_3 \cdot 6H_2O$ leads to complexes (**26**). Complexes (**26**) have interesting fluorescence properties. [19]



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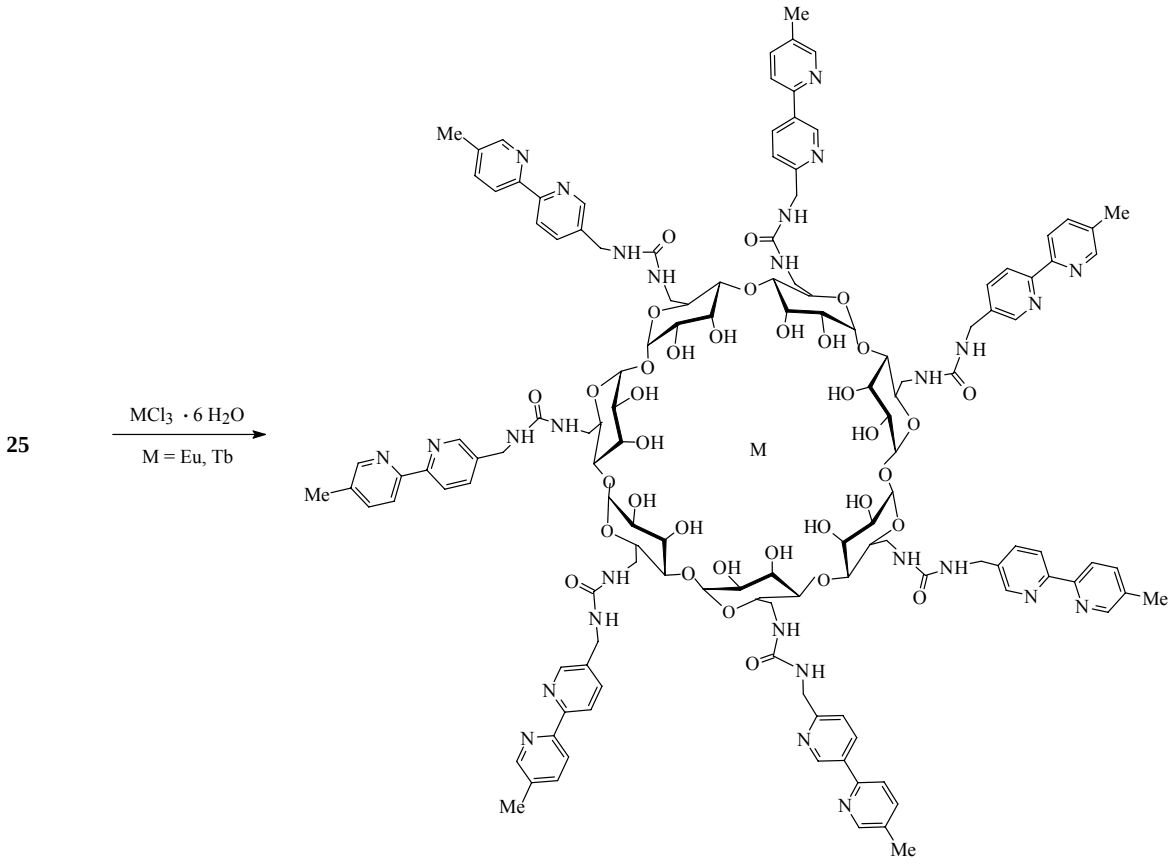

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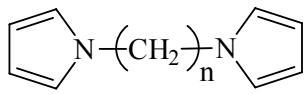
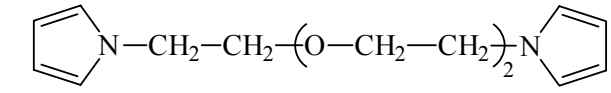
3. CD HOST-GUEST SYSTEMS CONTAINING AN AZAAROMATIC GUEST

It was found that hydroxypropyl-β-CD (**27**) forms with dipyrrolyls (**28**) and (**29**) [20] in aqueous solutions 1:2 host-guest complexes. The substituted β-CD **27** was chosen for investigations due to its higher solubility in water as compared with that of the plain β-CD.

It was established that **27** molecules encapsulate only two extremal pyrrole moieties, and the spacer remains free. [21,22]



	n
a	6
28 b	8
c	10



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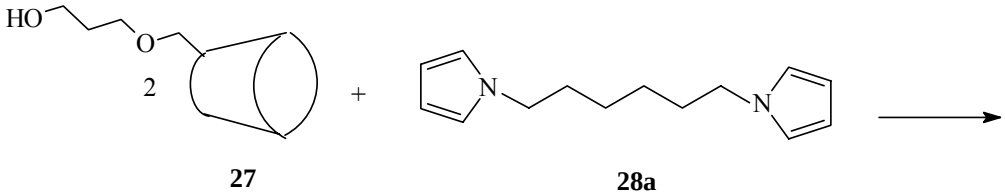
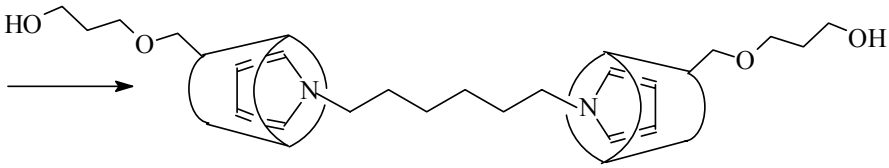


27 **28a**



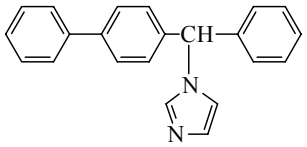
The host-guest complexes have been oxidized by electrochemical or chemical methods. Under these conditions the oxidative polymerization occurs; it was observed that the polymers are free of **27** and similar to those obtained in organic media. [22] In this way it was found that hydrophobic dipyrrolyls may polymerize in aqueous media by using their complexes with **27**. This result is promising in view of preparation of polymers in non-polluting media.

It was observed also that 3-indolyl acetate is soluble in dilute aqueous solutions of β-CD, this fact resulting from its complexation by β-CD. [23]

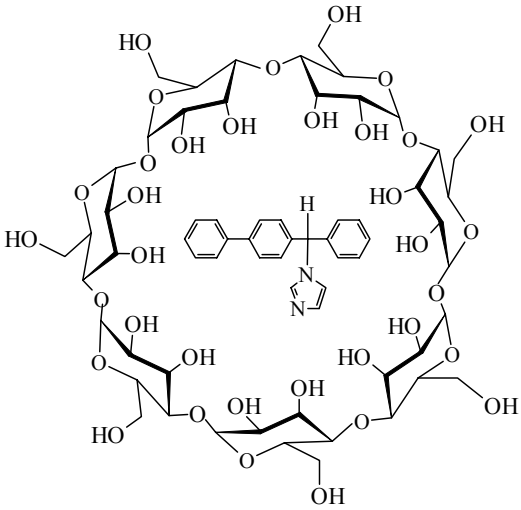
In the study of antimycotic drugs it was found that β-CD forms an inclusion complex with bifonazole (**30**). This compound and other imidazole and triazole derivatives serve as antimycotic therapeutic agents in the treatment of onychomycosis.

Bifonazole (**30**) is hydrophobic, therefore its penetration into hydrophylic human nail matrices is low. The inclusion of **30** into the apolar cavity of CD improves this process due to the hydrophilic properties of the exterior of CD molecule. The solubility in water of the complex of β-CD with **30** is higher than that

of **30** alone, this fact being of interest in the onychomycosis therapy. The solubility curves and binary phase diagrams have been drawn with the use of differential scanning calorimetry (DSC). HPLC was used in order to measure the solubility of **30** as a function of the quantity of CD in the samples. [24]

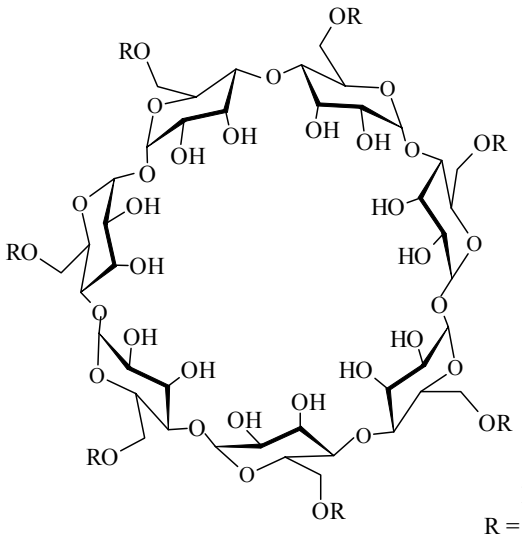


30



It was observed that β-CD containing 7 negatively charged naphthoate groups (**31**) strongly interacts with cationic surfactants, e.g. with cetylpyridinium chloride (**32**). This interaction results in the quenching of fluorescence arising from photoinduced electron transfer. The process is related to the concentration of the surfactant, therefore it can be used for sensing. The analysis of the **31** fluorescence emission allows the detecting of low concentrations of cationic surfactants in aqueous solutions, what is of interest in view of their large toxicity and a slow biodegradation.

It is proposed that the binding of **31** with **32** proceeds rather by micellization than by formation of a 1:1 inclusion complex. Here the interaction similar to that observed between cationic surfactant and anionic polyelectrolytes occurs. It should be noted that anionic surfactants do not show any fluorescence changes. [25,26]



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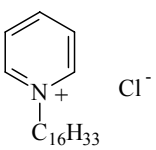

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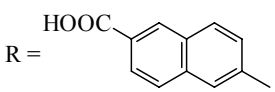
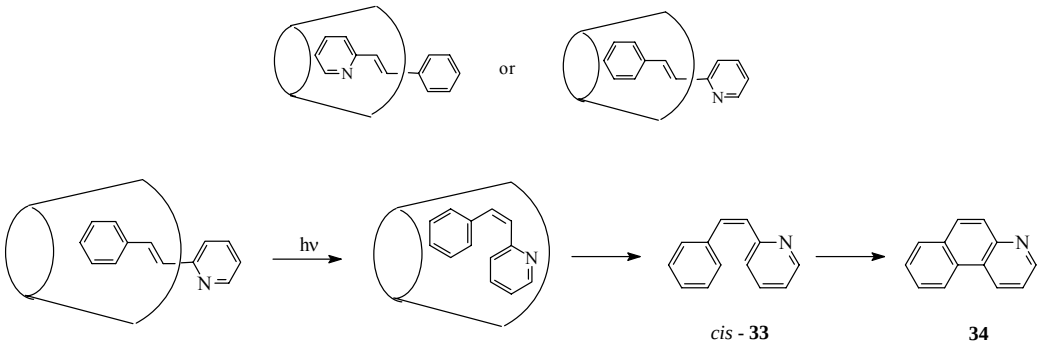
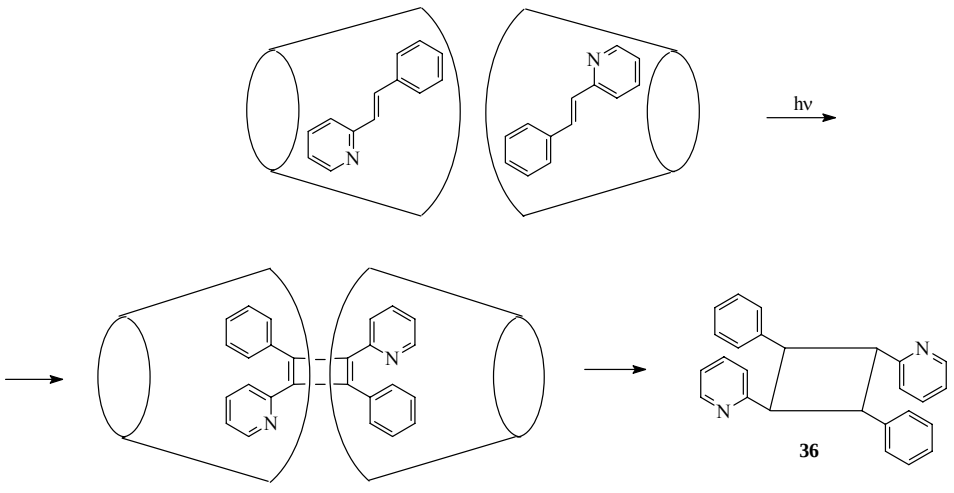


The irradiation of α-, β- and γ-CD complexes with *trans*-2-styrylpyridine (*trans*-**33)** in the solid state results in different products, depending on the kind of CD. The cavity of α -CD is small, therefore the photoisomerization of *trans*-**33** into *cis*-**33** is impossible. The cavity of β-CD is larger, allowing the isomerization of *trans*-**33** into the *cis* form; its cyclization yields azaphenanthrene (**34)**.

The largest among three CDs cavity of γ-CD allows the *trans*-*cis* isomerization of **33** and the subsequent dimerization of the *cis* form *via* **35** into **36**; here two CD molecules, each containing one molecule of *trans*-**33** take part. [27]



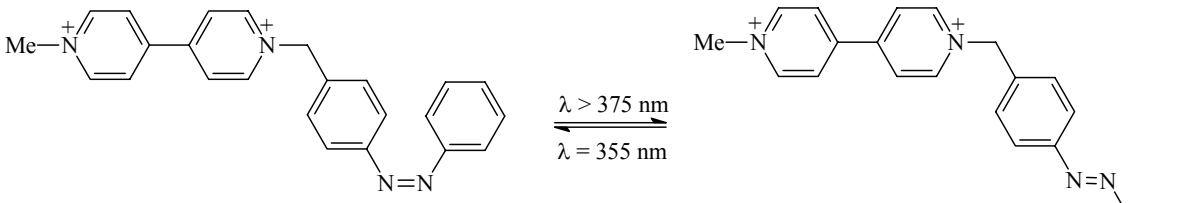
cis - **33** **34**



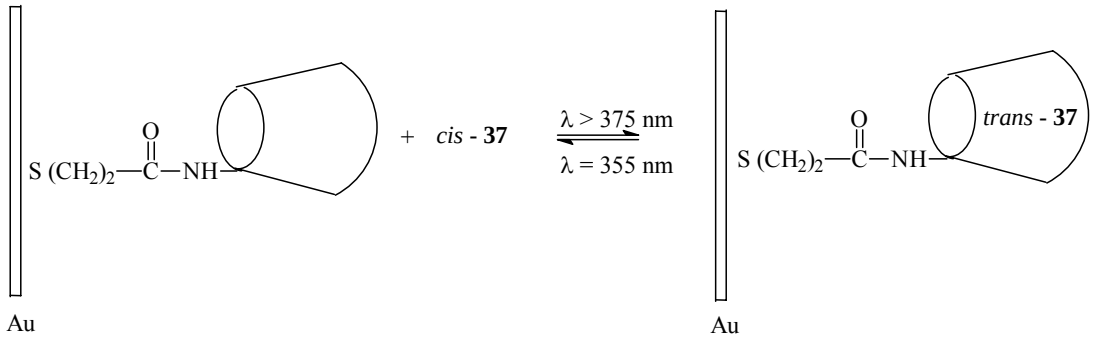
35 **36**

The construction of molecular devices is a topic of a number of works. [28-39] As an example of a molecular optoelectronic assembly may serve the following system. It was found that *cis*-bipyridinium azobenzene (**37**) shows reversible photoisomerization. Irradiation of *cis*-**37** (λ > 375 nm) yields the *trans*-**37,** and its irradiation (λ 355 nm) restores the starting *cis*-**37**.

It was observed that β-CD binds these two photoisomers in a different way: *trans*-**37** enters the cavity of CD, while for *cis*-**37** it is impossible. Amino β-CD was assembled on a Au electrode. The inclusion of **37** into the cavity of CD results in the high amperometric response of the electrode. In this way tailored molecular optoelectronic assemblies may be constructed. [40-42]



cis - **37** *trans* - **37**



4. CONCLUSION

Examples of CD host-guest systems with azaaromatic moiety appended to the host molecule are presented in the first part of the above review. Among complexes given in the second part an attention was paid to species showing photoisomerization, useful for construction of molecular devices.

CD host-guest systems containing azaaromatic moieties are interesting due to their promising properties, what has its reflection in the rapid development of this research area. [43,44]

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