Supramolecular Catalytic Systems Based on Calixarenes and Cyclodextrins

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Summary: A number of supramolecular metal complex catalitic system based on cyclodextrins and calixarenes have been developed. Particular attention has been given to design of new metal complexes with molecular recognition abilities. Data on application catalytic systems based on receptor molecules capable to formation of inclusion "host-guest" complexes in hydroformylation and Wacker-oxidation are given. Influence of different factors on activity, stability, selectivity of metal complex supramolecular catalytic systems is discussed

Keywords: calixarene; cyclodextrin; hydroformylation; molecular recognition; two-phase catalysis; Wacker-oxidation

Introduction

Use of macromolecular complexes as catalysts for various processes attracts attention of investigators for a long time.[1,2] Yet, at the process of the metal complex fixation, preservation of or increase in activity and selectivity of the homogenous catalyst-analog does not always meet with success. By our opinion, use a components of catalytic systems molecules able to form the host-guest complexes with the substances is one of the most prospective ways of creation of high-selective macromolecular metal-complex catalysts. At their use, the reacting particle conversion into the reaction products is preceded by a "supra-molecule" creation due to selective substance binding by the molecule-receptor causing the process selectivity increase.[3-6]

Of most interest there are the macrocyclic receptors able to form the host-guest complexes between the catalyst and the substance by non-valency intermolecular interactions. Presence of various form hydrophobic cavities allows to connect the substances corresponding (by size and form) to the same of the receptor and thus we may propose their molecular recognition.[7]

In the present work, macro-molecular metal-complex systems based on the modified cyclodextrins and calixarenes were used as catalysts. The cyclodextrins are cyclic oligomers of α-D-glucose with different numbers of carbohydrate units. e.g., β-cyclodextrin contains seven such units[8] (Figure 1).

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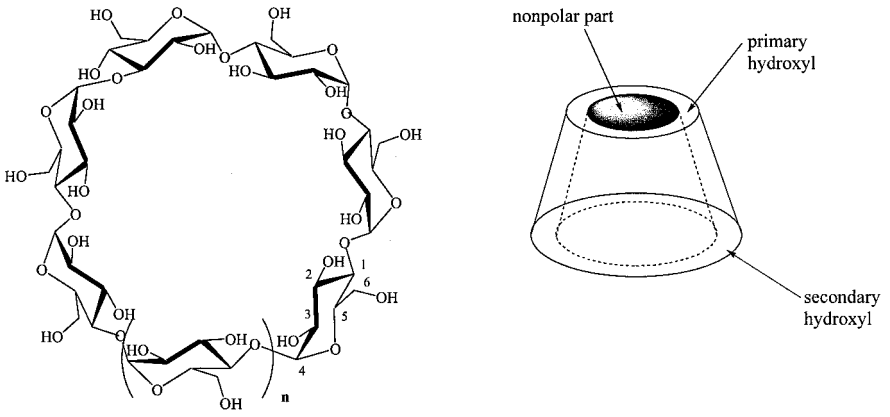


Figure 1. Cyclodextrins (n=0 - α-cyclodextrin; n=1 - β-cyclodextrin; n=2 - γ-cyclodextrin)

The H(3) and H(5) protons of cyclodextrin molecules are always oriented into the molecular cavity whereas the hydroxyl groups – outside. As a result, a hydrophobic cavity occurs in the molecule which is able to connect the molecular fragments into the host-guest complexes if the fragment size and polarity correspond with the same of the cavity.

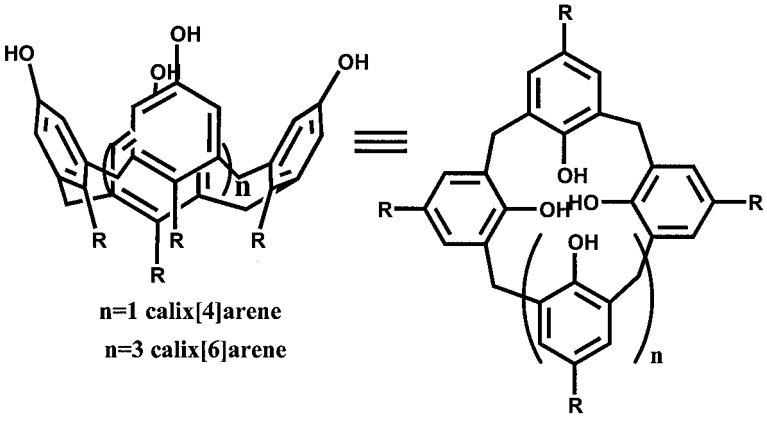


Figure 2. Calixarenes

The calixarenes are the cyclic products of the phenol oligomerization with the formaldehyde. A non-polar cavity is formed by several aromatic fragments forming a distinctive

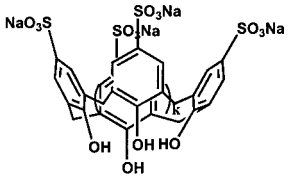
"bowl". Increase in number of such fragments from calix[4]arenes to calix[8]arenes gives rise to significant increase in size of the cycle and the cavity[9] (Figure 2).

The possession of hydrophobic cavity makes cyclodextrins or calixarenes as component of catalytic systems extremely attractive subject for study. This substances can accommodate a variety of organic compounds by forming host-guest inclusion complexes. Both cyclodextrins and calixarenes can be easily modified by various complex forming groups giving rise to further synthesizing the metal-complex catalysts with molecular recognition abilities.

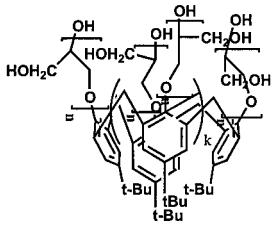
In the present paper the properties of the catalytic systems based on the modified receptor molecules were studied in the Wacker- oxidation and hydroformylation.

1. Molecule-receptors as components of catalytic systems in two-phase Wacker-oxidation and hydroformylation

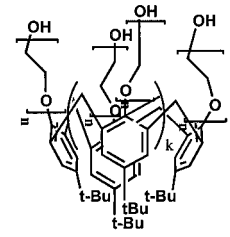
A number of water-soluble calixarenes and cyclodextrins were employed as components of the catalytic systems in two-phase Wacker-oxidation (Figure 3).



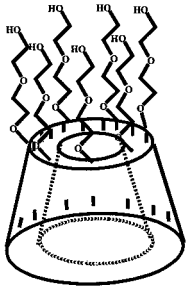
k=1 **L1**
k=3 **L2**
k=5 **L3**



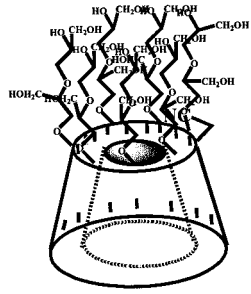
k=1 **L4**
k=3 **L5**



k=1; n=3.2 **L6**
k=3 n=3.6 **L7**



L8



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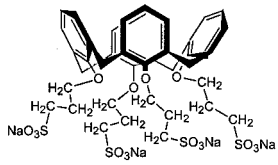


L10

Figure 3. Water-soluble calixarenes and cyclodextrins

The sulfocalixarenes (L1-L3) were obtained according to [10]. Oligoglycerol calixarenes (L4-L5) and cyclodextrin (L9) were synthesized by glycidol oligomerization in the presence of calixarenes of β-cyclodextrin. Oxyethylated β-cyclodextrin (L8) was prepared according to the literature procedure[11]. Oxyethylated calixarenes (L6-L7) were synthesized by the reaction of ethylene carbonate with potassium phenolates of calixarenes.

The oxidation was performed at pressure of 0.5 MPa in a two-phase system with use of synthesized water-soluble receptor molecule, palladium sulfate and copper chloride (II) as the catalytic system components. The methylketons were the main reaction products. Adding of water-soluble calixarenes and cyclodextrins gave rise to significant increase in the catalytic system activity without any receptor molecule (Table 1).

Table 1 Wacker-oxidation of alkene-1

Macroligand	Substrate conversion mol %				
	Hexene-1	Heptene-1	Octene-1	Nonene-1	Decene-1
No	10	8	4	3	3
L1	75	12	6	3	3
L4	60	15	16	3	4
L6	65	30	30	32	10
L2	5	7	26	6	3
L5	10	13	18	4	3
L7	75	46	25	18	11
L3	61	37	23	4	3
L8	22	22	5	7	4
L9	45	30	20	13	8

To study the effect of relation between the size of substrate molecule and the size of cavity of molecule-receptor on the catalytic system activity, the Wacker-oxidation of a unsaturated alkenes-1 with various number of carbon atoms was investigated.

Adding both oligoglycerol calixarenes and sulfo- calixarenes to catalytic system turned out to increase significantly the product yield for the case of definite alkenes: hexene-1 for the

calix[4]arenes, octene-1 for the calix[6]arenes; heptene-1 and hexene-1 for the calix[8]arenes. It should be pointed out that for oligoglycilated and particularly for oxyethylated calixarenes, such difference is less distinct. Increase or decrease in the "host" molecule size seems to cause both decrease in the binding constant for the substance in water phase and lower yields. As a result, at transition from the calix[4]arene to the calix[6]arene, the substrate selectivity changes from hexene-1 to octene-1. Note that for the calyx[8]arene, selectivity was observed similar to the same for the calix[4]arene. This fact is explained by the "twisted" conformation having two cavities that are close in size to the calix[4]arene's cavity[12]. For the case of the oxyethylated cyclodextrin, the activity turns to be minimum for the hexene-1 and the heptene-1.

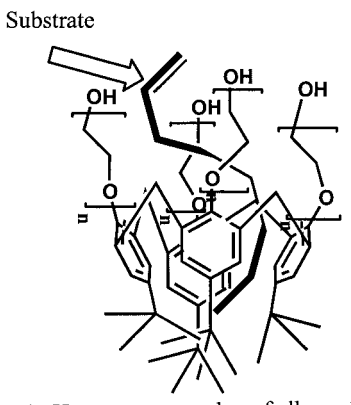


Figure 4. Host-guest complex of alkene-1 and olygoethoxylated calix[4]arene

Presence of olygoglycerol or oligoethyleneoxide fragments in the cyclodextrin or calixarene molecule causes additional solubilization of substrate (Figure 4). As a result, the influence of the calyxarene or cyclodextrin cavity size on the substrate selectivity decreases.

Considerable increase in the reaction rate was also observed when the calixarene L1 was used as the component of catalytic system for the hydroformylation of alkene-1. (Table 2)

Table 2 Hydroformylation of olefins in presence of *p*-sulfonato-calix[4]arene. Reaction conditions: toluene–water; 2 hours

Olefin	T, ^{0}C	Heptene-1			Octene-1			Nonene-1		
P, MPa		3.0	1.5	0.5	3.0	1.5	0.5	3.0	1.5	0.5
Aldehydes, %	70	68	34	2	68	15	Trace	65	23	4
Isomerisation, %		22	58	44	28	35	44	20	60	44
Aldehydes, %	50	60	41	trace	30	18	Trace	60	11	trace
Isomerisation, %		23	26	trace	12	16	7	19	24	5

The hydroformylation was performed under using the trisulfonated triphenylphosphine(TPPTS)/Rh(acac)$(CO)_2$ catalytic system at the synthesis-gas pressures of 0.5

to 3 MPa. Adding of the calyx[4]arene turned to increase significantly the rate of hydroformylation. At absence of macrocyclic receptor, the reaction proceeds at noticeable rate only at pressures above 3 MPa whereas with the calyxarene adding – already at 1.5 MPa. With pressure decrease, proportion increases of the isomerization products that dominated at the synthesis-gas pressure of 0.5 MPa.

Note that the observed properties of the catalytic systems can be treated as follows (Figure 5).

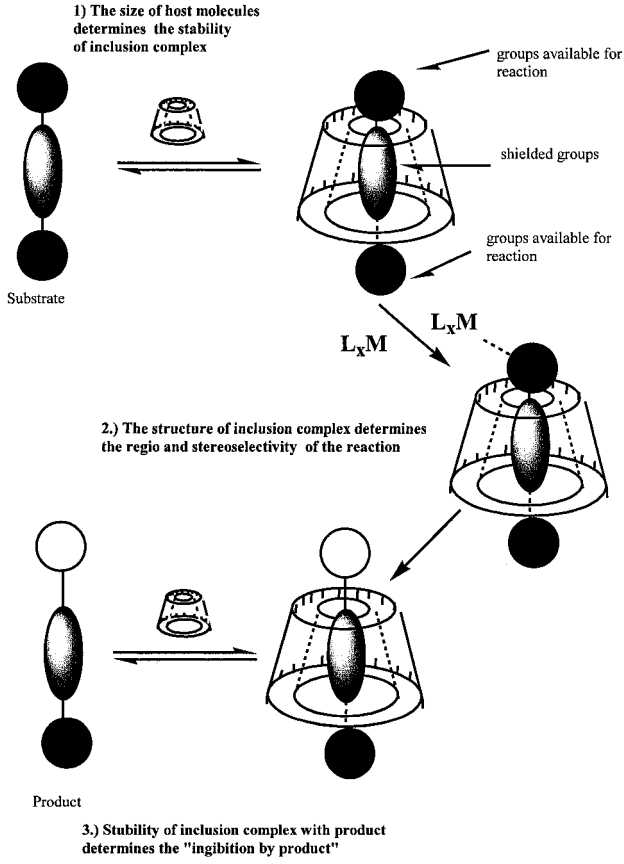


Figure 5. Supramolecular catalysis with calixarene or cyclodextrine based catalytic system

The molecule-receptor bounds the substance forming the host-guest complex that reacts in the catalytic cycle. Size and structure of the "host" molecule governs the host-guest complex stability and influences the substantial selectivity of the reaction. Being a peculiar "micro-

reactor", the "host" molecule can stabilize the transient reaction state and increase its rate. Besides, the host-guest complex creation can influence essentially the regio- and stereo-selectivity of the process due to specific substance orientation. Then, particular fragments of the substance molecule can be shielded and not involved into the reaction thus explaining absence of the products of Wacker-oxidation or hydroformylation of internal double bonds.

For the calixarenes, the selective macro-ligand modification is easily realizable; yet, for the cyclodextrins, modification by one or two modifying groups is a considerable difficulty. As a rule, the cyclodextrin modification, due to large amount of the hydroxyl groups, results in a position isomer group and their number can be large. For example, at the modification degree equal to three, more than 40 such isomers of modified β-cyclodextrins present in the mixture[13]. Each isomer forms the host-guest complexes with the substance and those complexes of different stability. As a result, the system containing the modified cyclodextrins can include large number of unequal substance-bounding compositions thus being similar to a heterogeneous catalyst (intermediate between homogeneous and heterogeneous catalyst). As for the heterogeneous catalysis, only a part of molecule-receptors, and often a small part, has high selectivity to bounding the particular substance and plays the determining role in the catalytic system activity. To produce a catalyst with high activity and selectivity, the isomer distribution should be changed to increase the proportion of compositions able to selectively bond the substance. This is possible using the molecule imprinting technique[14-15]. The imprinting process can be sketchy represented as follows (Figure 6).

Initially, complex creation takes place of "host" molecule (β-cyclodextrin) inclusion with fragments of the template molecule due to non-covalent interactions (pre-organization). Fixation of the structure resulting from the pre-organization allows to produce a macroligand including the template. Its subsequent removal results in a ligand able to the molecular recognition of the compositions similar in structure with the template molecule. Thus, one can expect that the metal complexes with such ligands will show high substrate selectivity.

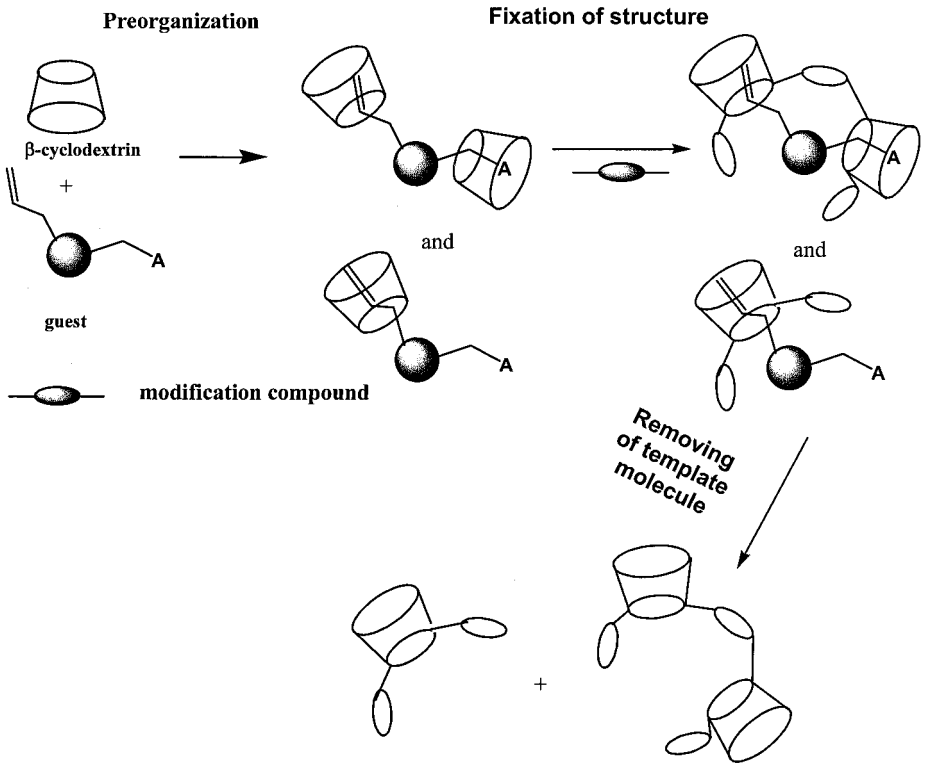
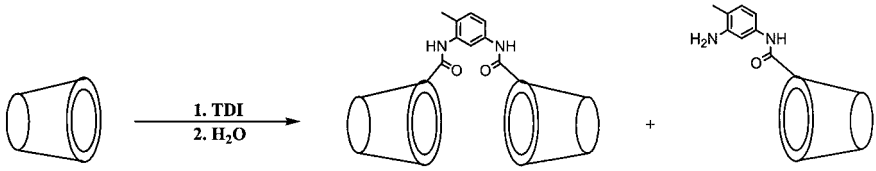


Figure 6. Modification of cyclodextrin using molecular imprinting method

In the present work, the 2-toluenediisocianate(TDI) was selected to be a modifying agent[16]. It reacts with the cyclodextrin's hydroxyl groups according to the following scheme:



Macroligands were synthesized under the template absence and when using the hexadecene-1, dodecene-1 and p-tretbutylstyrene as templates.

Figure 7 shows the data on the alkene-1 oxidation under using the cyclodextrins produced with templates as the catalytic system components with $PdSO_4$, $CuCl_2$ and heterpolyacid (HPA). The molecule-receptors obtained under the template presence show significantly higher catalytic activity.

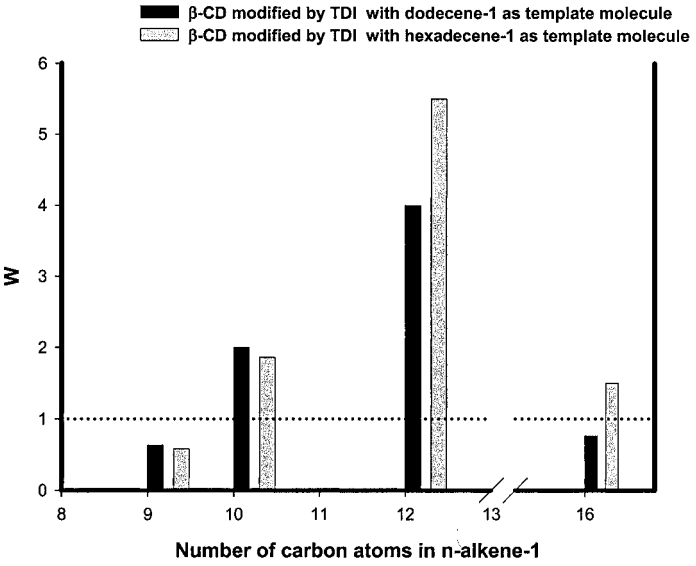


Figure 7. Wacker oxidation; Pd: CD:Cu:HPA:substrate =1:2:10:10:20; 50°C, P_{O2}=8 MPa; W= $TOF_{CD\ with\ template}$/ $TOF_{CD\ without\ template}$; TOF= mol ketone/(mol Pd^{2+} h)

The changes of activity were maximum at the dodecene-1 oxidation. When the dodecene-1 was employed as a template, the rate of oxidation increases by 4 times, and for hexadecene-1 – by 5.5 times.

For the styrene oxidation, the activity turned to be maximum for the catalytic system with use of the macroligand produced when the p-tretbutylstyrene was employ as a template molecule. The yield for the styrene oxidation increased by 1.7 times, and the p-methylbutylstyrene – by 2.4 times.

Table 3 Wacker-oxidation of alkene-1 with catalytic systems based on β-CD modified by TDI. Pd: CD:Cu:HPA:substrate =1:2:10:10:20; 50°C, P_{O2}=8 MPa

Substrate	Macroligand							
	β-CD modified by TDI		β-CD modified by TDI with hexadecene-1 as template			β-CD modified by TDI with p-tretbutylstyrene as template		
	Yield of ketone, %	TOF	Yield of ketone, %	TOF	W [a)]	Yield of ketone, %	TOF	W [a)]
styrene	24	4800	25	5000	1.0	40	8000	1.7
p-methylstyrene	10	2000	13	2600	1.3	24	4800	2.4
p-tret-buthylstyrene	14	2800	17	3400	1.2	17	3400	1.2

[a)] $W = TOF_{CD\ with\ template} / TOF_{CD\ without\ template}$; TOF= mol ketone/(mol Pd^{2+} h)

2. Palladium complexes with the modified calixarenes and cyclodextrins in the Wacker-oxidation.

The complexes of palladium with the cyclodextrins and calixarenes modified by the nitril containing groups (L11-L16) have been examined in the Wacker-oxidation of n-alkene-1 (Figure 8).

We synthesized a number of cyclodextrins with different nitrile groups – propionitrile, p- nitrile-benzil and p- nitrile-benzoil[17]. Also we prepared water soluble calix[4]arene modified by p-nitrile-benzil and o-nitrile-benzil groups[18]. The MALDI-TOF results for the solution of $PdSO_4$ and ligands indicate the formation of complex with Pd^{2+}. In FTIR spectra of complexes band corresponding of CN groups shifted to higher wavelengths that indicate coordination Pd with CN-group.

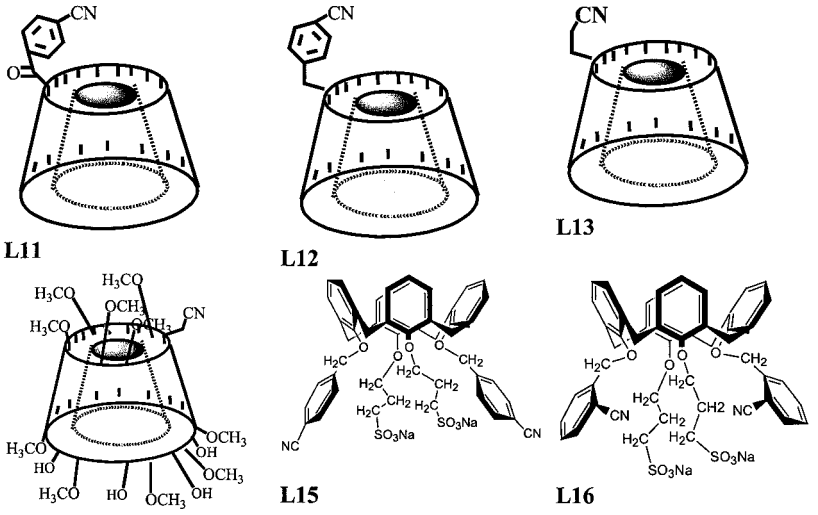


Figure 8. Cyclodextrins and calixarenes modified by nitrile containing groups

It was shown that with use of the palladium complexes with cyclodextrins L11-L13 as catalysts in the Wacker-oxidation activity of the catalytic system in the alkene-1 oxidation increases significantly (Table 4).

Table 4 Wacker-oxidation of alkene-1 catalyzed by Pd complexes with modified CD.
Pd:L:Cu: substrate=1:2:10:80; 50°C, P_{O2}=8 MPa

Substrate	Ketone yield, mol-%		
	CD	**L11**	**L12**
Hexene-1	20	55	54
Heptene-1	14	78	34
Octene-1	14	30	20
Nonene-1	7	20	14
Decene-1	1	15	6

Metal complexes obtained from modified cyclodextrins not only retain capability for producing host-guest compounds but also can change the selectivity of binding guest molecule because of the additional interaction between the substrate and the metal center bound to host molecule [6]. Stability of such inclusion complex as well as the stability of transient reaction state can increase significantly. It should be stressed that substrate selectivity strongly depends on the nature of nitrile group (Table 4).

At the methylstyrene oxidation, under use of the complexes, both ketone and aldehyde were produced (Table 5). The selectivity of the aldehyde formation increased in the following order: L14>L13=L11>CD

Table 5 Methylstyrene wacker-oxidation using Pd complexes with cyclodextrins Pd^{2+}:L:Cu^{2+}:substrate=1/2/10/80; P(O_2)=5 MPa, 2 h

Macroligand	Conversion mol-%	Selectivity on aldehyde, %
CD	6	0
L11	15	6
L13	39	5
L14	54	28

Insertion of additional methyl substituents into the ligand molecule causes change of the p-methylstyrene orientation inside the cyclodextrin cavity. In this case accessibility of the styrene methylene group increases and the aldehyde selectivity rises (Figure 9).

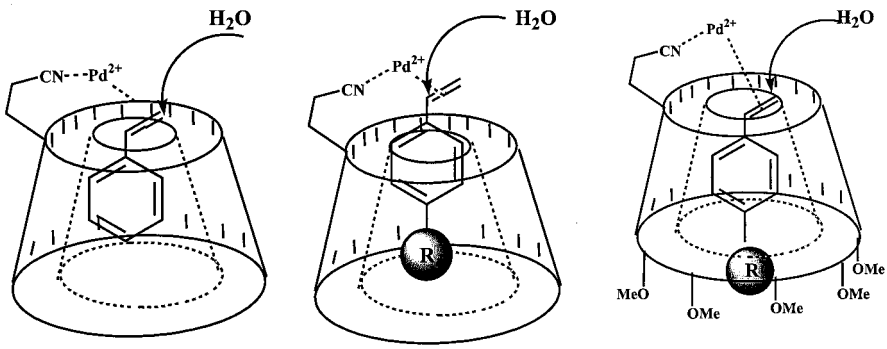


Figure 9. Possible structures of host-guest complexes with methylstyrene

Use of the palladium complexes with the L15 and L16 calixarenes as catalysts causes the activity increase as compared to the catalytic system containing the water-soluble L10 calixarene, primarily for the highest olefins. At the hexene-1oxidation, the catalytic system activity was comparable.

At the same time the catalytic activity in heptene-1 and octene-1 oxidation was several times higher then the same of the system containing the palladium complexes with the water-soluble calixarenes.

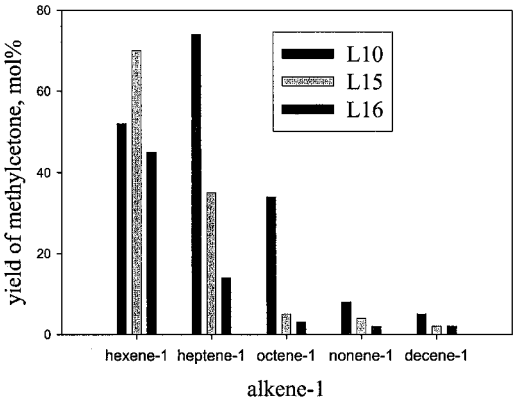


Figure 10. Activity of calixarene-based catalytic systems in oxidation of different alkenes-1; P_{O2}=0.5 MPa, [Pd^{2+}]=26 mmol/l; [Pd^{2+}]/[$CuCl_2$]/ [calixarene] /[alkene-1]=1/10/1/50

Note that for the highest alkene-1 the complex of palladium with calixarene L15 turns to be more active than the same with the L16 calixarene. In the last case at coordination the palladium apparently turns to be substantially closer to the calixarene cavity thus decreasing stability of the complexes with alkene-1 beginning from the octene-1.

3. Hydroformylation in a homogeneous calixarene based system

The hydroformylation of alkene-1 in toluene with the $Rh(acac)(CO)_2$ and triphenylphosphine (TPP) as a catalyst can serve an example of the reaction rate increase due to displacement of the equilibrium between the active species in a solution.

Catalytic process was carried out under following conditions: t = 50-70^{0}C and 0.5-3.0 MPa synthesis gas pressure, reaction time - 2 hours. The products obtained were n- and iso-

structure aldehydes respectively. Ratio of yield of aldehydes with linear and branched chain did not change notably with increase of alkene chain length (n/iso=3). The calix[4]arene and the *p-tret*-butylcalix[4]arene addition results in significant increase in the rate of hydroformylation (Figure 11).When $Rh(acac)(CO)_2$ and TPP were used the rate of the reaction was low. It was established that activity of the catalytic system increased markedly when calixarenes were added to reaction mixture. The most demonstrative is the influence of *p-tret*-butylcalix[4]arene on hydroformylation of octene-1 (conversion 78%) and calix[4]arene on hydroformylation of nonene-1 (67%).

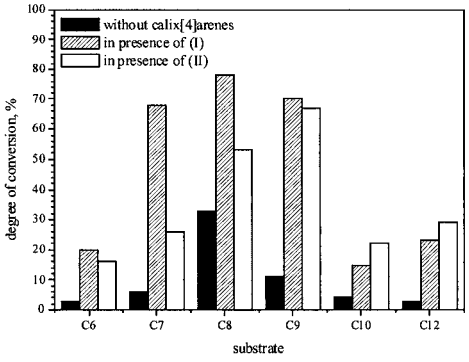


Figure 11. Hydroformylation of alkene-1 in toluene using calix[4]arenes

To our opinion, this effect is connected with the host-guest complex formation between the calixarene and the TPP thus causing the equilibrium displacement conditions sidewise more reactive rhodium particle.

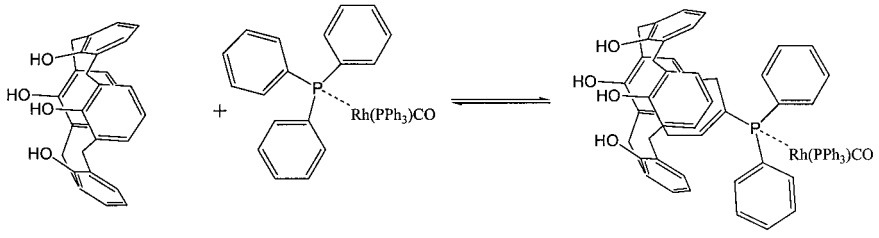


Table 6 Hydroformylation of octene-1 in toluene in the presence of calix[4]arenes

Calix[4]arene/PPh_3	Conversion, %	N/i
0	5	3
0.2	38	2.8
2.33	53	3.2
5	42	3.2

This assumption is confirmed by the data of a number of experiments. With increase of the calixarene/TPP ratio to 2.33, the octene-1 conversion increases and then decreases (Table 6)

Besides, at the twice phosphine concentration increase , the conversion decreases from 78% to 20%. Additional calixarene dope allowed to bind the extra TPP and caused the conversion increase up to 87%.

The host-guest complex formation between the calixarene and the triphenylphosphine under the reaction conditions was confirmed by the UV-spectroscopy technique. The host-guest complex constant was shown to equal to 1300 M^{-1}.

Acknowledgments

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