Molecular Recognition and Catalysis: from Macrocyclic Receptors to Molecularly Imprinted Metal Complexes†

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Summary: The results of studying a number of reactions catalyzed by several types of soluble macromolecular catalytic systems capable of selectively binding organic substrates, namely, modified cyclodextrins, calixarenes and dendrimers are presented. The use of modified cyclodextrins as components of a catalytic system in the phenol and benzene hydroxylation by hydrogen peroxide allows one both to increase the catalytic activity and to change significantly the chemical selectivity. Phosphorilated calixarene – Rh catalytic systems was found to be catalytically active in hydroformylation of linear alkenes C_7–C_{12}. The results of experiments on the oxidation of C_7–C_{16} alkenes show that, when the ligand is the dendrimer molecule, the fraction of forming methyl ketones substantially increases for the substrates C_7–C_9. For the higher alkenes, this effect is not observed.

Keywords: dendrimers; hydroformylation; macrocycles; molecular recognition; oxydation

Introduction

Homogeneous metal complex catalysts owing to their high activity under mild conditions and unique selectivity were used to perform a number of modern petrochemical processes: stereospecific polymerization of unsaturated compounds, hydroformylation, carbonylation, and oxidation of olefins.[1] The main drawback of soluble complexes is that it is too laborious or often even impossible to separate expensive transition metal compounds from reaction products. This is the reason why the last two decades were characterized by significant interest in creating catalysts that would combine the high activity of homogeneous metal complexes and the possibility of reuse, which is characteristic of heterogeneous materials. The most popular way of achieving this purpose had long been immobilization of metal complexes on various insoluble supports, both organic and inorganic. Much experimental data collected on this subject shows that the immobilization of complexes often leads to unexpected changes in their properties under the action of the support. Not only the activity and chemical selectivity of the process decrease, but also the properties of the support itself unpredictably change.[2]

An alternative to the immobilization of complexes on heterogeneous materials is two-phase catalysis.[2–5] The advantage of catalysts in this case is the possibility of catalyst reuse without loss of activity owing to easy separation of the polar phase (water, ionic liquid, etc.), which contains

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metal complex, from reaction products. However, in reactions with substrates that are slightly soluble in water, the activity of complex compounds is low.

One of the most attractive ways of solving this problem is to use compounds capable of molecular recognition as components of catalytic systems. In this context, of significant interest are macrocyclic receptors, e.g., cyclodextrins and calixarenes (whose molecules have a hydrophobic cavity and thus can form host–guest inclusion complexes with various organic molecules), and also dendrimers (which form complexes with substrates by supramolecular interactions). In this case, the conversion of reacting particles to reaction products is preceded by the formation of a supramolecule via solubilization of a nonpolar substrate by soluble polymers or via its selective binding by a receptor ligand to form inclusion complexes. As a result, the process occurs within a peculiar kind of nanoreactor, where the host molecule can stabilize the transition state of the reaction and increase the reaction rate. Such a strategy opens possibilities for creating highly active catalysts and allows one to control such important properties as regioselectivity, stereoselectivity, and substrate selectivity.[6–11]

In this work, we present the results of studying a number of reactions catalyzed by several types of soluble macromolecular catalytic systems capable of selectively binding organic substrates, namely, modified cyclodextrins, calixarenes, and dendrimers based on polypropyleneimine (Table 1, Figure 1).

1. Wacker Oxidation Using Supramolecular Catalysts

1.1. Wacker Oxidation Using Palladium Complexes with Cyclodextrins and Calixarenes

The combination of a host and a metal center into a single molecule not only retains specific features that are characteristic of catalytic systems discussed in the previous section but also gives rise to a number of new properties of the catalysts. The substrate binding by the cavity of the receptor ligand determines its orientation with respect to the metal center, which can significantly affect the product distribution and the substrate selectivity of the reaction. Noteworthily, if, in the reaction, the substrate in the host–guest complex coordinates to the metal center, then the stability of such an inclusion complex, as well as the stability of the transition state of the reaction, can be several orders of magnitude higher (''double recognition'').[6]

The effect of these phenomena related to the cooperative binding both to the metal center and to the cavity of the receptor molecule was demonstrated[5] by the example of the oxidation of unsaturated compounds to methyl ketones that is catalyzed by palladium complexes with cyclodextrins and calixarenes modified by nitrile-containing groups (Table 2). In this case, the activity and the substrate selectivity of the complexes differed from those of catalytic systems containing unmodified cyclodextrin and a palladium salt. By the example of the complex with the ligand **CD-6-CH_2CH_2CN**, it was shown that the use of

Table 1.
Using ligands

Reaction	Ligands	Metal
Wacker-oxidation	**CD,CD-2,6-E_xOH,CD-6-CH_2CH_2CN, 2,6-Me CD-3-CH_2CH_2CN, 2,6-Me CD-6-CH_2CH_2CN, calix[4]-$C_3H_7SO_3Na$, calix[4]-$(C_3H_7SO_3Na)_2$ (p-$CH_2PhCN)_2$calix[4]-$(C_3H_7SO_3Na)_2$ (o-$CH_2PhCN)_2$, calix[4]-$(C_3H_7SO_3Na)_4$; CD-TDI, CD-6-(CH_2CH_2COOH), DAB$(CN)_4$, DAB$(CN)_8$, DAB$(CN)_{16}$,**	Pd
Hydroxylation of phenol by H_2O_2	**CD, CD-6-C(O)cat, CD-6-$NHCH_2CH_2NH_2$, CD-2,6-E_xOH**	Fe, Cu
Oxidation of alkylaromatics by H_2O_2	**CD-2,6-E_xOH+dipy**	Fe
Hydroformylation	**L1,L2,L3, L4**	Rh

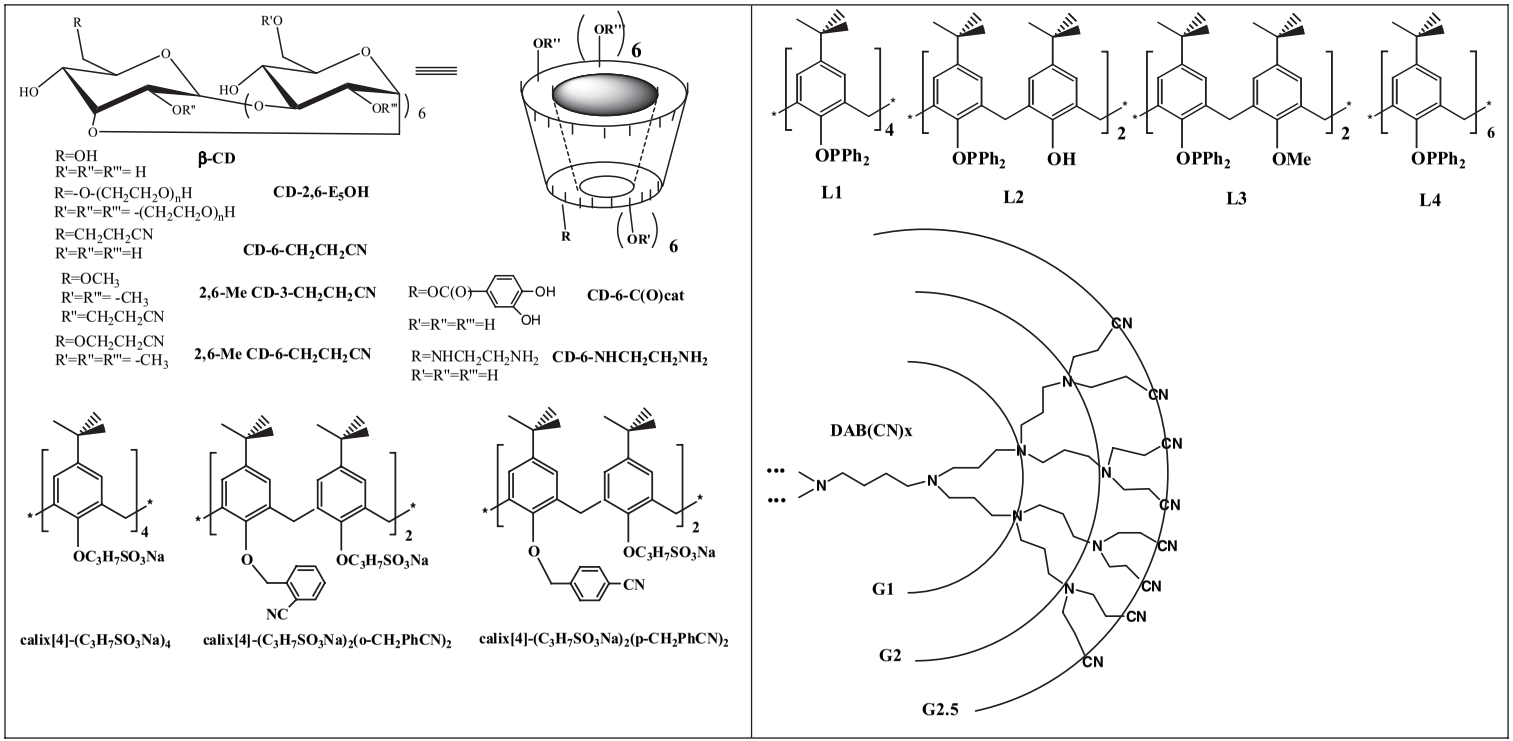


Figure 1.
Ligands

Table 2.
Oxidation of 1-octene

Catalyst	K, M^{-1}	Methylketone yield, %	Rate, mmol/(min*l)
CD-6-CH_2CH_2CN/$PdSO_4$/$CuCl_2$/HPA	210	73	9
CD/$PdSO_4$/$CuCl_2$/HPA	90	20	2.4

K – stability constant of host-guest complex

palladium macrocomplexes increases the stability constants because of the simultaneous interaction of alkene with both the cyclodextrin cavity and the metal ion. Moreover, according to our data on the apparent activation energies for catalytic systems based on **CD-6-CH_2CH_2CN**, they decrease for all the studied linear 1-alkenes in proceeding from unmodified cyclodextrin to palladium complex [7] (Tables 2, 3).

The catalyst efficiency is also affected by the position of the palladium ion with respect to the cavity of the macrocyclic receptor. For example, the activity of the metal complex in which the propionitrile group and, hence, the palladium ion are located in the wide part of the toroid on the side of secondary hydroxyls (**2,6-Me CD-3-CH_2CH_2CN**) differed significantly from the activity of the complex in which the palladium ion is bound to the modifying group in the narrow part on the side of primary hydroxyls (**2,6-Me CD-6-CH_2CH_2CN**) (Table 4).

Table 3.
Activation energy (E_A) of Wacker-oxidation of 1-alkene.

Substrate	TON_{CD-CN}/TON_{CD}	E_A, kDj/mol	
		β-CD	**CD-6-CH_2CH_2CN**
1-hexene	1.5	33	19
1-heptene	1.7	72	56
1-octene	2	74	57
1-nonene	1.5	32	16
1-decene	1.4	66	32
1- dodecene	1.4	50	21

TON_{CD-CN} - turnover numbers in the presence **CD-6-CH_2CH_2CN**; TON_{CD} – turnover numbers in the presence **β-CD**

For the first ligand, the Wacker oxidation rate increased for all C_6–C_{10} olefins, especially for 1-octene, 1-nonene, and 1-decene; and for the second ligand, such an increase was observed only for the last of the substrates. In the first case, methyl substituents favor the cooperative binding of substrates by the receptor cavity, whereas in the second, they prevent this binding.

Similarly, the activity of the catalytic system containing **calix[4]-($C_3H_7SO_3Na$)$_2$(*o*-CH_2PhCN)$_2$** was maximal in 1-hexene oxidation, whereas the product yields in 1-heptene and 1-octene oxidation catalyzed by the palladium complex with the ligand **calix[4]- ($C_3H_7SO_3Na$)$_2$(*p*-CH_2PhCN)$_2$** were higher than those for the complex with the ligand **calix[4]-($C_3H_7SO_3Na$)$_2$(*o*-CH_2PhCN)$_2$** (Table 4).

The substrate conversion in the presence of the palladium macrocomplexes with these calixarenes in the cases of **calix[4]-($C_3H_7SO_3Na$)$_2$(p-CH_2PhCN)$_2$** exceeded the product yields using a reference system that contained **calix[4]-$C_3H_7SO_3Na$**, as well as palladium and copper salts. The change

Table 4.
Oxidation of alkene-1 catalyzed by Pd macrocomplexes of modified β-cyclodextrins and calix[4]arenes

Substrate	β-CD[1]	2,6-Me CD-3-CH_2CH_2CN[1]	2,6-Me CD-6-CH_2CH_2CN[1]	calix[4] $C_3H_7SO_3Na$[2]	calix[4]-($C_3H_7SO_3Na$)$_2$ (o-CH_2PhCN)$_2$,[2]	calix[4]-($C_3H_7SO_3Na$)$_2$ (p-CH_2PhCN)$_2$[2]
1-hexene	31	37	31	41	70	46
1-heptene	20	29	16	17	35	75
1-octene	14	26	12	12	6	36
1-nonene	12	24	12	4	5	7
1-decene	7	20	15	4	5	6

[1] $P(O_2) = 5$ MPa, ($[Pd^{2+}]/[Cu^{2+}]/[CD\text{-}L]/[substrate] = 1/2/10/100$;50 °C
[2] $P(O_2) = 5$ MPa $[Pd^{2+}]/[CuCl_2]/[calixarene]/[substrate]$ - 1/10/1/50

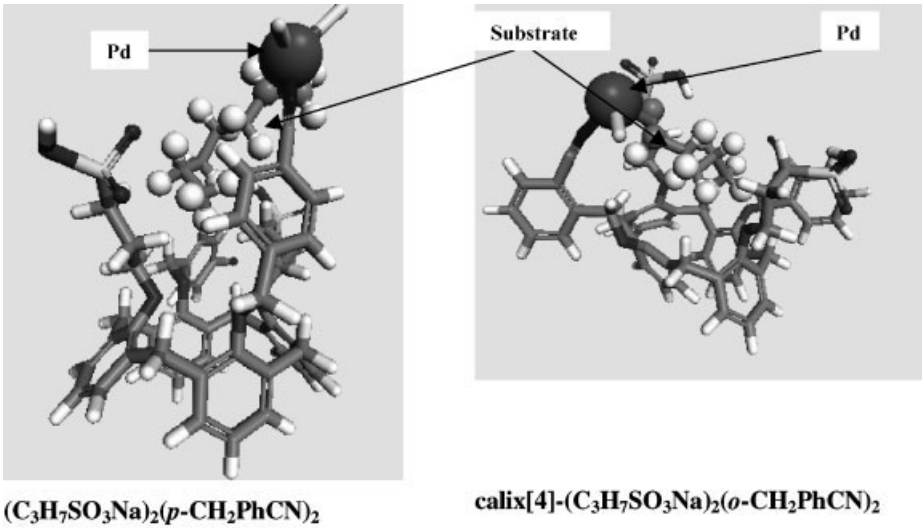


Figure 2.
The proposal structure of active complexes **$(C_3H_7SO_3Na)_2(p\text{-}CH_2PhCN)_2$** and **calix[4]-$(C_3H_7SO_3Na)_2(o\text{-}CH_2PhCN)_2$** with Pd(II) and 1-alkene

in the substrate selectivity in this case can be explained as follows. The geometry of the palladium complex with the ligand **calix[4]-$(C_3H_7SO_3Na)_2(p\text{-}CH_2PhCN)_2$** is such that the cooperative substrate binding by either the macrocycle cavity or the palladium ion for 1-hexene is unlikely (Figure 2). With an increase in the hydrocarbon chain length, the probability of this interaction increases, which leads to an increase in the reaction rates for 1-heptene and 1-octene. The larger size of the substrate rules out the cooperative binding. However, in the complex with the ligand **calix[4]-$(C_3H_7SO_3Na)_2(o\text{-}CH_2PhCN)_2$**, the coordinated palladium ion is much closer to the calixarene cavity, which favors the reaction only in the case of 1-hexene oxidation.

The relationship between the stability constants of host–guest complexes and the activity of catalytic systems was also observed in the oxidation of a number of substituted styrenes (Table 5).

For example, if the component of a catalytic system was unmodified *β*-cyclodextrin, the reaction rate was maximal in styrene oxidation and was much lower in methylstyrene and *tert*-butylstyrene oxidation. For ethoxylated cyclodextrin (**CD-2,6-E_5OH**), conversely, the *tert*-butylstyrene oxidation rate was high. The data obtained correlated with the corresponding stability constants. It proved that, for unmodified

Table 5.
Oxidation of styrenes

	TOF $\frac{\text{mol of ketone}}{\text{mol of Pd} * \text{h}}$		Stability constants, M^{-1}	
	β-CD/$PdSO_4$/$CuSO_4$/HPA	**CD-2,6-E_{30}OH**/$PdSO_4$/$CuSO_4$/HPA	**β-CD**[1)]	**CD-2,6-E_{30}OH**[2)]
Styrene	30	42	228	12
p-methylstyrene	14	36	72	14
p-tert-butylstyrene	4	58	54	34

Reaction condition: $[Pd^{2+}]$/[Ligand]/$[Cu^{2+}]$/[HPA]/[substrate] - 1/2/10/10/100, T - 50 °C, $P(O_2)$ - 0.5 MPa, reaction time - 0.5 h.
[1)] methanol/water = 1/1; HPLC, T = 25 °C
[2)] methanol/water = 1/9; UV titration, T = 25 °C

Table 6.
Oxidation of 1-alkene using ligands synthesized by molecular imprinting method*

1-alkene	Turnover frequency (TOF), $\frac{\text{mol of ketone}}{\text{mol of Pd} * \text{h}}$				
	β-CD-TDI	β-CD-TDI (C_{12})	β-CD-TDI (C_{16})	CD-6-$(CH_2CH_2COOH)_x$	CD-6-$(CH_2CH_2COOH)_x(C_{16}H_{32})$
1-heptene	2200	2350	2320	2600	4120
1-nonene	4800	3000	2800	4200	6000
1-decene	1400	2800	2600	1000	4000
1- dodecene	400	1600	2200	520	1450
1- hexadecene	66	50	110	85	120

* β-CD-TDI ligand synthesized modification by TDI without template; β-CD-TDI (C_{12}) – ligand synthesized modification by TDI using n-$C_{12}H_{24}$ as template; *β*-CD-TDI (C_{16}) ligand synthesized modification by TDI using n-$C_{16}H_{32}$ as template; CD-6-$(CH_2CH_2COOH)_x$ ligand synthesized modification by N,N′-methylenediacrylamide without template; CD-6-$(CH_2CH_2COOH)_x(C_{16}H_{32})$ ligand synthesized modification by N,N′-methylenediacrylamide using n-$C_{12}H_{24}$ as template

cyclodextrins, the introduction of a bulky substituent into the para position of the aromatic fragment decreases the constant of formation of β-cyclodextrin. The presence of oxyethyl groups substantially increases the formation constants for substituted styrenes. This increase is likely to be determined by the increase in the cavity size because of additional ethoxyl fragments in the structure of the host molecule. This assumption is confirmed by ROESY (Rotating Frame Overhauser Enhansement Specroscopy) data [8]. The spectrum exhibits a high-intensity signal characterizing the interaction between the *tert*-butyl group of styrene and C(2)-H proton of cyclodextrin.

1.2. Wacker Oxidation Using Molecular Imprinting

Previously, we used molecular imprinting approach to creating water-soluble catalysts for two-phase oxidation of unsaturated compounds to the corresponding methyl ketones on the basis of modified 2,4-toluenediisocyanate-β-cyclodextrins (TDI-β-cyclodextrins).[12] The latter acted as host molecules at the preorganization step. The activities of catalytic systems containing β-cyclodextrins synthesized according to the same procedure in the presence and absence of template molecules differed significantly. It turned out that the use of macroligands obtained in the presence of 1-dodecene and 1-hexadecene considerably increases the rate of oxidation of these substrates in comparison with systems in which macroligand was produced without adding template.

Similar results were obtained when the modifier was N,N′-methylenediacrylamide (Table 6).

After replacement of macrolig and synthesized without using template by macroligand synthesized in the presence of 1-hexadecene (**CD-6-$(CH_2CH_2COOH)_x$-$(C_{16}H_{32})$**), the reaction rate increased for all the substrates, beginning with 1-heptene, rather than only for 1-dodecene and 1-hexadecene. The activity was maximal for 1-decene.

In our opinion, the high rates of oxidation of higher alkenes using macroligands obtained under imprinting conditions can be explained by a peculiar kind of ''molecular memory''. The use of templates is likely to favor the formation of such a macroligand structure that can selectively bind template-like molecules. Comparison of the data on the composition and structure of macroligands contained in samples of modified cyclodextrins obtained in the presence and absence of templates suggests several assumptions of the optimal structure of the receptor molecule. First, for more efficient substrate binding, in the cyclodextrin molecule, hydroxyls at the C3 atom should remain unmodified. This assumption was confirmed by the data on the Wacker oxidation of 1-dodecene with

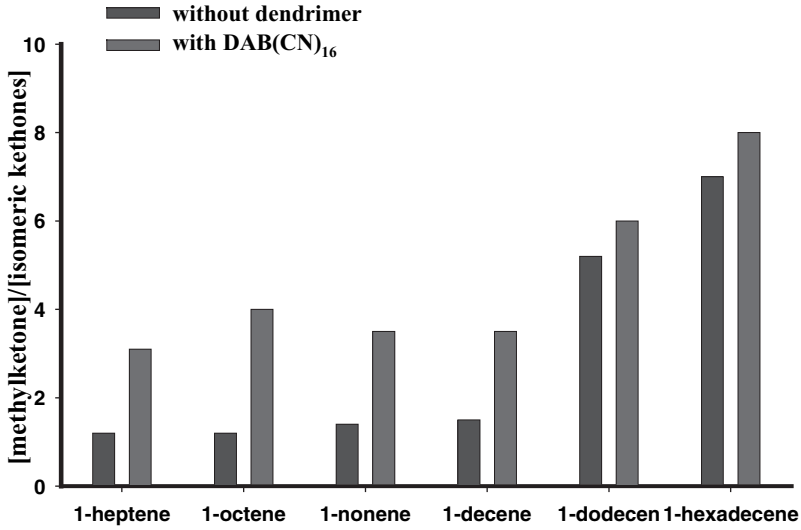


Figure 3.
Oxidation with dendrimer based catalyst

2,6-di-*O*-methyl-β-cyclodextrin modified by 2,4-toluenediisocyanate as the component of the catalytic system. With 2,6-di-*O*-methyl-β-cyclodextrin, the oxidation rate is high, whereas with the modified analog, regardless of the presence or absence of template during ligand synthesis, the Wacker oxidation product yields proved to be virtually zero. In the 2,6-di-*O*-methyl-β-cyclodextrin molecule, accessible for modification are only hydroxyl groups at the third carbon atom, which completely inhibits Wacker oxidation.

Second, of great importance to oxidation of higher alkenes is the presence of dimeric receptor molecules. When such dimers are present in a large amount according to mass spectrometry, as for *β*-cyclodextrins modified by 2,4-toluenediisocyanate in the presence of 1-dodecene and 1-hexadecene, the catalytic system on their basis is highly active with respect to higher 1-alkenes. [13]

1.3. Wacker Oxidation Using Dendrimers

As Wacker oxidation catalysts, one can also use copper and palladium complexes with other type of molecules capable of supramolecular interactions with a substrate—dendrimers based on polypropyleneimine and diaminobutane with terminal nitrile groups ($DAB(CN)_4$ –G0.5; $DAB(CN)_8$-G1.5; $DAB(CN)_{16}$-G2.5).

Various linear and aromatic 1-alkenes and also cyclohexene were taken as substrates. The reaction products were the corresponding ketones, along with the formation of which the isomerization of the double bond was also observed. It was shown that the presence of dendrimer does not affect the substrate isomerization, which has very high rate even in an inert atmosphere: in as early as 5 min, in the reaction mixture, thermodynamic equilibrium between isomeric alkenes is established (the 1-alkene content does not exceed 3%). If dendrimer is absent or the reaction is performed in a homogeneous system, the selectivity with respect to methyl ketone is low. If the reaction is carried out in a two-phase system in the presence of dendrimer, the process selectivity changes.

The results of our experiments on the oxidation of C_7–C_{16} alkenes (Figure 3, Table 7) show that, when the ligand is the dendrimer molecule, the fraction of forming methyl ketones substantially increases for the substrates C_7–C_9. For the higher alkenes, this effect is not observed.

Table 7.
Wacker-oxidation 1-alkene with denrimer-based catalysts

Ligand	1-heptene		1-octene		1-nonene		1-decene		1-dodecene		1-hexadecene	
	Yield on ketones, %	Yield of methylketone,%	Yield on ketones, %	Yield of methylketone,%	Yield on ketones, %	Yield of methylketone,%	Yield on ketones, %	Yield of methylketone,%	Yield on ketones, %	Yield of methylketone,%	Yield on ketones, %	Yield of methylketone,%
—	69	38	65	35	73	43	73	44	28	24	13	12
G 0.5	40	21	41	26	65	46	52	38	27	24	13	12
G 1.5	41	27	43	31	54	43	45	37	27	25	13	12
G 2.5	45	34	55	45	58	46	49	39	27	26	14	13

T = 90 °C, $P(O_2)$ = 0.5 MPa, [Pd]/[CN]/[Cu]/[S] = 1/2/10/180, 1 h

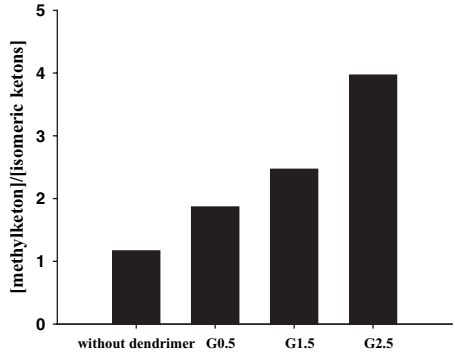


Figure 4.
Oxidation using different generation of dendrimers (substrate – 1-octene).

An increase in the ligand size also affected the process selectivity. With an increase in the generation from G0.5 to G2.5, the fraction of methyl ketones with respect to isomeric ketones increased by a factor of more than two (Figure 4).

Note that, although the use of complexes with dendrimers increases the process selectivity, the total yield of ketones decreases. With an increase in the dendrimer:palladium ratio, the selectivity rise is noticeable on reaching a ratio mol Pd to mol of nitrile groups of dendrimer average out 2. Using complexes with ratios of 4 and 8, nearly 100% selectivity can be reached, with the methyl ketone yield being the same as in a reference experiment (Figure 5).

In our opinion, this result is explained as follows. According to IR spectroscopic data, peripheral nitrile groups can bind palladium only when all the inner amino

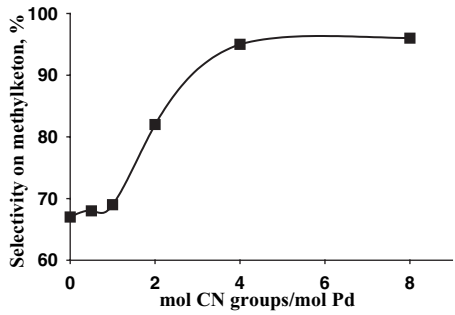


Figure 5.
Oxidation of heptene-1.

Table 8.
FTIR data on dendrimer complexes with copper and palladium

$DAB(CN)_{16}$ mol	Pd (II) mol	Cu(II) mol	ν,cm^{-1}
1	—	—	2248
1	—	32	2262
1	8	—	2249
1	8	32	2249
			2304
1	8	8	2249
			2306
1	8	2	2249
			2304–2312
1	8	160	2262
			2312

groups are occupied by (coordinated to) copper or palladium ions. For example, for palladium compounds at a metal:dendrimer ratio of 8, there is no shift of the absorption band corresponding to a unbound nitrile group (2248–2249 cm^{-1}). For complexes containing both copper and palladium, even at low copper content, along with the absorption band of an unbound nitrile group (2349), a new broad peak at 2304–2312 cm^{-1} region emerges, which characterizes a nitrile group coordinated to palladium. Probably, with an increase in the concentration of copper(II) ions, which has a high affinity for amino groups, copper ions replace palladium ions from inner amino complexes (Table 8). For the compound obtained at a dendrimer:palladium:copper ratio of 1:8:160, the IR spectra contains absorption bands at 2262 and 2312 cm^{-1}, which describe the formation of bonds between nitrile groups and copper and palladium ions, respectively.

A dendrimer-containing catalyst is likely to bind a nonpolar substrate to form a supramolecular complex in which the alkene chain interacts both with palladium ion on the dendrimer surface and with hydrophobic fragments of polymer. The stability of the complex is determined by the orientation of the substrate in the coordination to palladium ion. For internal alkenes, some of the nonpolar groups are located within the aqueous phase, which is unbeneficial from an energy standpoint. Therefore, the oxidation rate decreases.

The assumption that the reaction rates are affected by the positions of double bonds was confirmed by the data on cyclohexene and allylbenzene oxidation. In the reaction with G2.5 $DAB(CN)_{16}$, cyclohexene oxidation led to a significant (by a factor of 3.5) decrease in the cyclohexanone yield in comparison with a reference experiment without dendrimer.

Allylbenzene under the reaction conditions isomerizes to propenylbenzene, whose oxidation products can be phenyl ethyl ketone and methyl benzyl ketone. The first of them predominates in a reference experiment in the absence of dendrimer at a total ketone yield of 60%. If dendrimer-based catalysts are used, the reaction rate decreases abruptly and a small amount of only methyl benzyl ketone forms.

Table 9.
Hydroxylation of phenol by hydrogen peroxide.

Catalytic system	T, °C	Reaction time, h	Phenol conversion, %	Selectivity %	
				Hydroquinone	Catechol
$FeCl_3$/Cat/β-CD*	40	1,5	74	30	70
CD-6-C(O)cat-Fe^{3+}	50	1	65	10	90
	40	1,5	73	7	93
	20	2,5	83	4	96
CD-2,6-E_xOH -Fe^{3+}	50	0.5	45	95	5
$CuSO_4$/en/β-CD	50	0,5	57	2	2
$CuSO_4$/en	50	0,5	4	50	25
β-CD-Cu^{2+}	50	0,5	94	—	100
	40	0,5	100	—	100
	20	2	28	1	99
CD-6-$NHCH_2CH_2NH_2$-Cu^{2+}	50	0,5	70	2	98

cat-catechol, en- ethylenediamine;
$[PhOH]:[H_2O_2] = 1.1$, $[PhOH]:[Catalyst] = 100$. Solvent: water/dichloroethane 1 to 1 by volume

Table 10.
Binding constant for phenols (water/$CH_3CN = 9$, HPLC method)

Host molecule	K, M^{-1}		
	Phenol	Catechol	Hydroquinone
β-CD	132	79	170
CD-6-C(O)cat-Fe^{3+}	1995	251	631
β-CD-Cu^{2+}	1585	316	631

2. Oxidation by Hydrogen Peroxide Using Supramolecular Catalysts

The use of modified cyclodextrins as components of a catalytic system in the phenol and benzene hydroxylation by hydrogen peroxide allows one both to increase the catalytic activity and to change significantly the chemical selectivity of the process (Table 9).

Note that supramolecular catalysts ensure high phenol conversion even at room temperature and the reaction selectivity depends on the used receptor molecule and metal ion. For catalytic systems based on iron and a pyrocatechol derivative of β-cyclodextrin (**CD-6-C(O)cat-Fe^{3+}**), the selectivity with respect to pyrocatechol under optimal conditions reached 96%. Note that, in the oxidation of such a substrate as ethylphenol, only the corresponding pyrocatechol also formed and no products of alkyl chain oxidation were observed.

For copper complexes with unmodified β-cyclodextrin and β-cyclodextrin modified by ethylenediamine (**CD-6-$NHCH_2CH_2NH_2$-Cu^{2+}**), the selectivity with respect to pyrocatechol was still higher: hydroquinone hardly formed.

At the same time, for catalytic systems based on ethoxylated cyclodextrin (**CD-2,6-E_xOH-Fe^{3+}**), the selectivity with respect to hydroquinone proved to be close to 95%.

The difference in reaction selectivity is explained by the difference in substrate orientation in the cavity. In the interaction with iron complexes with β-cyclodextrin modified by pyrocatechol (**CD-6-C(O)cat-Fe^{3+}**) and with copper complexes with β-cyclodextrins (**β-CD-Cu^{2+}; CD-6-$NHCH_2CH_2NH_2$-Cu^{2+}**), phenol is coordinated to metal ion so that the para position is inaccessible for attack by an active hydroxylating particle and pyrocatechol primarily forms. In the reaction in the presence of an iron complex with ethoxylated cyclodextrin, the ortho position is shielded and hydroquinone primarily forms. The catalytic system **β-CD-Cu^{2+}** is more active under 40 °C than at 50 °C. It is possible that decreasing rate of oxidation deals with the higher rate of nonproductive hydrogen peroxide decomposition under higher temperature.

We showed that the constant of formation of phenol inclusion complexes with metal complexes is 12–15 times larger than that with unmodified cyclodextrin (Table 10), whereas the constants of formation or host–guest complexes with hydroquinone and pyrocatechol differ only by a factor of 2–3[3].

In benzene hydroxylation, high activity was reached in the presence of ethoxylated cyclodextrin and an iron(III) salt. The conversion was 75%, and the selectivity with respect to phenol was close to 100%.

The oxidation of alkyl aromatic compounds by hydrogen peroxide using catalytic systems containing cyclodextrins lead to the selective formation of ketones. This result resemble the selectivity of oxidation of alkylaromatic compounds that was observed in our early work on the oxidation of alkylaromatic compounds by H_2O_2 in homogeneous water-CH_3CN solutions and resent results by Bolm et al. [14,15] The use of macrocyclic receptors enabled one to significantly increase the catalyst activity in comparison with the activity of two-phase systems containing a phase-transfer carrier and also comparing with homogeneous system. [15] (Table 11)

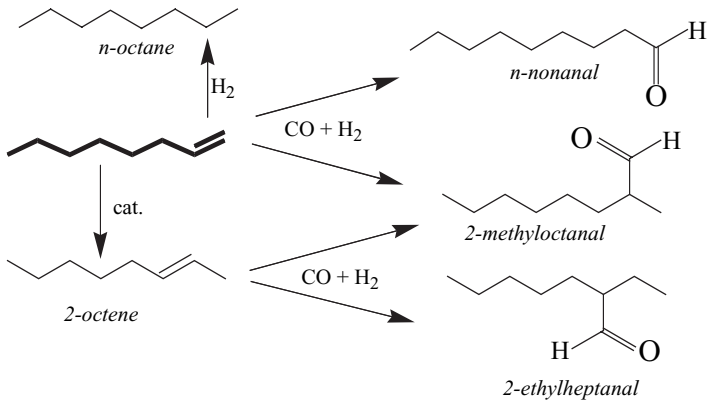
3. Hydroformylation of Unsaturated Compounds

Homogeneous hydroformylation catalysis is one of the largest volume processes in the chemical industry with a worldwide oxo-

Table 11.
Oxidation of alkylaromatic compounds by H_2O_2.

Substrate	Yield, % (product)	
	Cetyltrimethylammonium bromide/Fe^{3+}	**CD-2,6-E_xOH/Fe^{3+}/dipy**
Ethylbenzene	24 (acetophenone)	98 (acetophenone)
n-Propylbenzene	6 (propiophenone)	55 (propiophenone)
n-Amylbenzene	<1 (phenylbutylketone)	55 (phenylbutylketone)
p-Diethylbenzene	3 (p-acetylatylbenzene)	44 (p-acetylatylbenzene)
	1 (p-diacetylbenzene)	46 (p-diacetylbenzene)
Tetraline	15 (1-tetralone)	35 (1-tetralone)
		15 (2,3-dihydro-1,4-naphthoquionone)

[**CD-2,6-E_xOH**] = 40 mM; [substrate] = 0.256 M; [H_2O_2] = 0.253 M; [Fe^{3+}] = [$dipy^{+}$] = 15.4 mM; 2 h.
dipy - 2,2′ – dipyridyl



Scheme 1.
Hydroformylation reaction of 1-octene with consideration of the prior isomerization of the substrate.

aldehyde production of $7.8 \cdot 10^6$ t/a. [16] In creating new hydroformylation catalysts, greatest attention is given to synthesis of new ligands and investigation of their coordination chemistry. However, the results of oxo synthesis in the presence of expensive and hard-to-obtain metal complexes often disappointed. In spite of all efforts, no theory has been proposed to date that would relate the activity of ligands in

Table 12.
Hydroformylation of alkenes

Substrate	Calixarene	Conversion, %	Selectivity, %	
			on aldehydes	on *n*-aldehyde
1-heptene	L1	44	50	34
	L3	18	72	55
1-octene	L1	26	65	34
	L2	31	35	26
	L3	47	45	28
1-nonene	L1	36	55	38
	L3	38	39	29
1-decene	L3	20	25	20
1-undecene	L1	53	40	25
1-dodecene	L1	49	41	26
	L3	45	31	20

$Rh(acac)(CO)_2$-0.01 mmol, toluene, (substrat:Rh = 150:1, P:Rh = 3:1), 0.5 MPa, 6 h

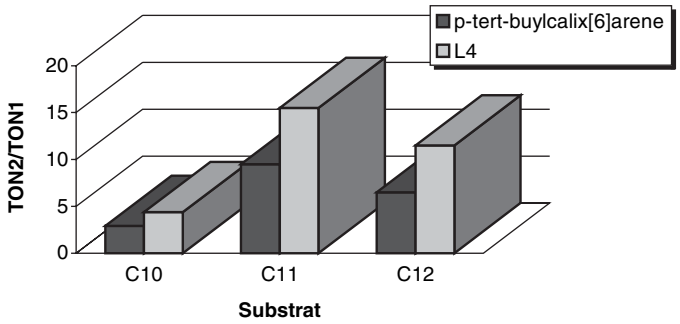
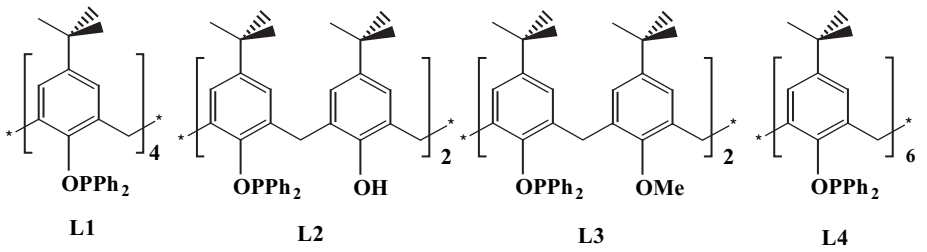


Figure 6.
Ratios of turnover numbers of C10–C12 alkenes hydroformylations. **TON-2** : Hydroformylation in the presence of calixarene; **TON-1**: No calixarene was added.

hydroformylation with their structure, although new catalytic systems have recently been developed quite intensely[17]. In our opinion, a promising way is to create bifunctional catalysts that would combine the properties of metal complex with the capability for molecular recognition within a single molecule. For this purpose, we synthesized calixarenes (**L1–L4**) functionalized by diphenylphosphine groups.



Cyclophanes were phosphorilated by the interaction of *n*-BuLi and Ph_2PCl. [18,19] Calixarene–Rh catalytic systems were found to be catalytically active in the hydroformylation of linear alkenes C_7–C_{12}.The catalytic process was carried out at 50 °C and 0.5–1.0 MPa synthesis gas pressure for 2–6 h. Catalytic complexes were obtained in the reaction mixture *in situ* from $Rh(acac)(CO)_2$ and calixarenes (**L1-L4**). The reaction was performed in a 30-ml controlled-temperature steel autoclave equipped with a magnetic stirrer. The reaction products were analyzed by gas–liquid chromatography. The corresponding aldehydes, *iso*-alkenes and alkanes were formed. (Scheme 1).

The results of alkene-1 hydroformylation obtained are presented in Table 12 and illustrated in Figure 6.

We established that, for all the alkenes studied, the activity of the catalytic system significantly increased after supplementing the reaction medium with calixarenes, both modified by complex-forming phosphine groups and unmodified by them (Figure 4). Note that the effect of macrocyclic components of catalytic systems in the case of calix[6]arenes is most pronounced in 1-undecene hydroformylation.

The data obtained can be explained as follows. A catalytic reaction occurs in two main steps: the substrate binding to form an inclusion complex and then the conversion of bound particles to products and their elimination. Of importance for both steps is the possibility of molecular recognition of a productive substrate, for which the decisive factor is the fact that this size fits the size of

the calixarene cavity. Moreover, for the reaction rates to be high, it is necessary that the substrate configuration in the substrate–calixarene inclusion complex should favor its coordination to the rhodium atom. In the case of 1-undecene and calix[6]arene the coordination to the metal center is likely to be facilitated, which eases the formation of acyl intermediate. This assumption is supported by the data on the structure of host–guest complexes of calixarenes with hydrocarbons.[20] When passing from 1-heptene to 1-octene the change in conversion and selectivity is observed for the catalytic system based on phosphorilated calix[4]arenes. Probably, it could be explained by reducing accessibility of hydrophobic cavity of macrocycle when lower rim is functionalized by bulky diphenylphosphine groups.

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