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Some Examples of Phase-Transfer Catalysis Application in Organochlorine Chemistry

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Abstract:

Kinetics of phase-transfer catalysed (PTC'd) dehydrochlorination of the α-isomer of hexachlorocyclohexane in the presence of proton donors was investigated. Carboxylic acids and picric acid act as inhibitors. Benzyl alcohol strongly promotes the reaction. The plots of observed rate constants vs phenol and pentachlorophenol concentration have a bell-shaped form that was not observed before. An example of long-chain quats application in the synthesis of the ketamine anaesthetic intermediate by dehydrochlorination in dilute alkali is shown. Another application of phase-transfer catalysis (PTC) in organochlorine chemistry is the aqueous (sodium hypochlorite) chlorination of alkyl aromatic compounds. The results of *m*-phenoxytoluene chlorination and reaction kinetics in the presence of the polymeric crown are described.

Introduction

Many industrial processes are based on the various reactions of organochlorine compounds. It is quite natural that phase-transfer catalysis has attracted a great interest of chemists working in the field. The well-known advantages of PTC answer best to the current challenge for the chemical industry, that is, the development of safer and more environmentally benign processes.[1] PTC is in many aspects nearly an ideal tool for retrofitting organochlorine chemistry processes based on dehydrochlorination or chlorination reactions.

Earlier the author had published the summary of results obtained in his laboratory.[2,3] This work is devoted to two problems, namely, alkaline dehydrochlorination in dilute alkali and the effect of proton donors in it and PTC'd chlorination. These problems have both applied and scientific importance. The use of cocatalysts in PTC had been first described by Dehmlow more than 10 years ago.[4] Nevertheless, so far there were significant discrepancies concerning the role of acidic additives in PTC reactions.

PTC'd chlorination is quite advantageous as it allows the use of large amounts of hypochlorite solutions formed as the side-products in many industrial processes. Until now this was performed using soluble catalysts; we have studied this chemistry using a solid catalyst.

1. Alkaline Dehydrochlorination in Dilute Alkali and Proton Donor Influence in PTC'd Dehydrochlorination. The topic of synergetic additives to PTC has become quite fashionable. This was caused by the recent work of Savyolova[5] who showed that in the hydrolysis of nitroaromatic esters by solid sodium hydroxide a 50:50 mixture of quaternary ammonium salt and crown ethers gives the highest reaction rates. Much earlier the analogous effect was demonstrated by Szabo[6] in the alkylation of malonic ester. However, from the viewpoint of a process chemist, the use of such a mixture in an industrial medium- or even small-scale process is hardly feasible due to large costs. The same effect can be obtained in a rather simpler and cheaper way using cocatalytic acid additives.[4,7,8] As indicated earlier, the role of proton-donating substances in PTC'd reactions is still debated. Thus, in PTC'd displacement of chloride from hexyl chloride by sodium formate the introduction of acid additives (such as phenol) resulted in the retardation of the reaction.[9] Conversely, in PTC'd dehydrobromination of dibromoethylbenzene the addition of phenol resulted in acceleration of the reaction.[10] Makosza has also shown that addition of weak H-acids strongly promotes alkaline dehydrobromination in concentrated NaOH using Bu_4NBr as the catalyst,[7] but no kinetic dependencies were obtained in either cases. It was therefore, interesting to investigate the effect of addition of proton donors on kinetics of PTC alkaline elimination.

As the model reaction we chose the dehydrochlorination of the α-isomer of hexachlorocyclohexane (HCCHX). The kinetics of this reaction in the presence of different quats was studied earlier in considerable detail,[11,12] thus making it possible to avoid some preliminaries. For the proton donor additive we have used phenol (**I**), pentachlorophenol (**II**), benzyl alcohol (**III**), picric acid (**IV**), caproic acid (**V**), and α-methyl substituted fatty acids (fraction C_7-C_9) (VIK-1) (**VI**), whilst the phase-transfer catalyst was Katamin AB ($PhCH_2(Me)_2N(C_{16}-C_{18})Cl$). The reaction in the presence and absence of additives is satisfactorily described by a first-order kinetics, that is shown in Figure 1.

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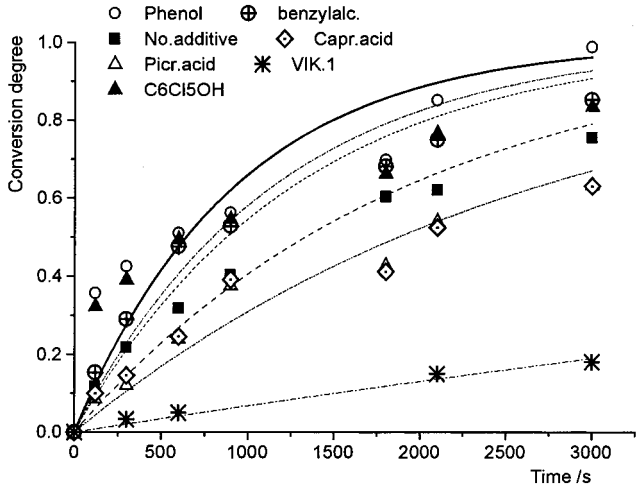


Figure 1. **Kinetic curves of HCCHX dehydrochlorination at 20 °C, $[HCCHX]_0 = 5.1 \times 10^{-2}$ M, $[cat] = 1.78 \times 10^{-4}$ M, $[I] = 7.0 \times 10^{-4}$ M, $[II] = 1.0 \times 10^{-5}$ M, $[III] = 4.0 \times 10^{-4}$ M, $[IV] = 4.7 \times 10^{-5}$ M, $[V] = 1.5 \times 10^{-5}$ M, $[VI] = 1.8 \times 10^{-4}$ M.**

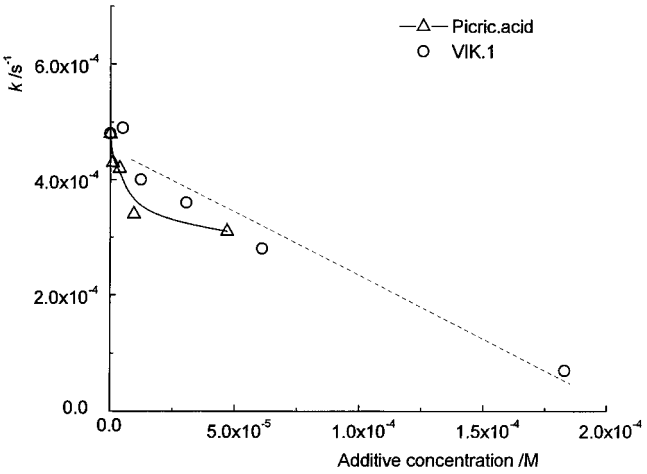


Figure 2. **Dependence of k_{obs} on VIK-1 and picric acids concentration.**

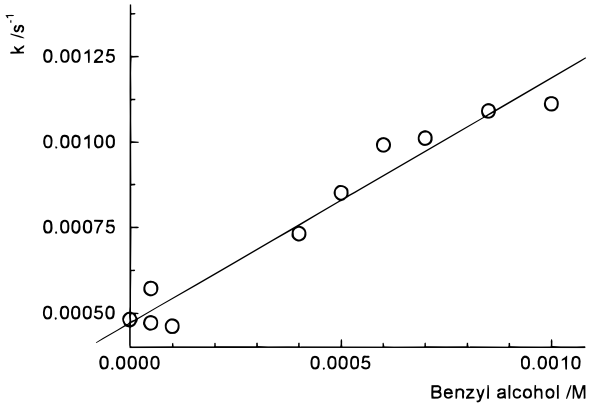


Figure 3. **Dependence of k_{obs} on benzyl alcohol concentration.**

Figures 2−5 show the dependencies of the observed first-order rate constants on cocatalyst concentration. It is seen that addition of carboxylic acid inhibits the reaction, the effect being more pronounced the more lipophilic is the acid. Picric acid also acts as the inhibitor.

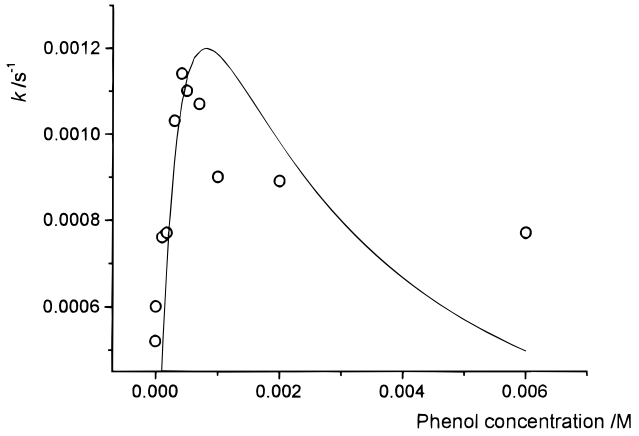


Figure 4. **Dependence of k_{obs} on phenol concentration; points: experiment, line: least-squares fit.**

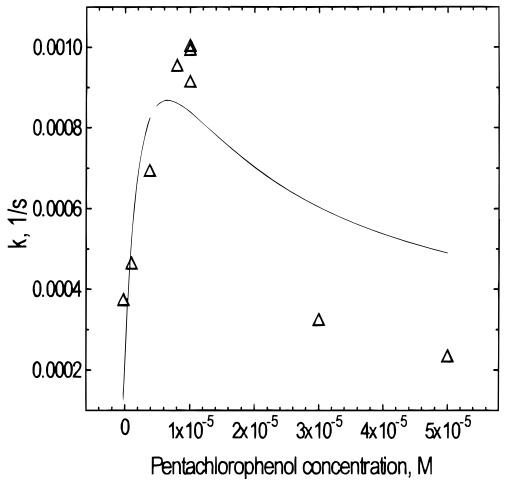


Figure 5. **Dependence of k_{obs} on pentachlorophenol concentration; points: experiment, line: least-squares fit.**

The results obtained in the presence of carboxylic and picric acids are quite fairly described by the well-known competitive inhibition scheme.[13] Makosza in his work on cocatalysts in β-elimination reactions[7] proposed a following scheme:

$$Y\text{-}H_o + NaOH_{aq} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Y^-Na^+_{if} + H_2O_{aq}$$

$$Y^-Na^+_{if} + Q^+X^-_o \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} + Y^-Q^+_o + Na^+X^-_{aq}$$

$$\left(H\text{—}C\text{—}C\text{—}X\right)_o + Y^-Q^+_o \xrightarrow{k_3} \left(C{=}C\right)_o + Y\text{-}H_o + Q^+X^-_o$$

where YH is a proton donor, Q is the quaternary ammonium cation, subscripts "o", "aq", and "if" denote respectively the organic phase, the aqueous phase, and the interface. Unfortunately, it was not supported by kinetic data.

The possible competing reaction

$$\left(H\text{—}C\text{—}C\text{—}X\right)_o + Q^+OH^-_o \xrightarrow{k_4} \left(C{=}C\right)_o + H_2O_{aq} + Q^+X^-_o$$

(13) Schmid, R.; Sapunov, V. N. *Nonformal Kinetics*, Verlag Chemie: Weinheim, 1982.

is less probable as Dehmlow[14] showed that the distribution coefficient of Q^+Cl^- is 5 orders of magnitude larger than that of Q^+OH^-. It is evident that in the absence of the promoter the reaction proceeds either at the interface or in the third phase, that is the liquid border film.

It is easy to show that the rate of product formation for the above scheme is expressed by the following differential rate equation:[15]

$$\frac{d[C=C]_{org}}{d\tau} = \frac{k_1k_2k_3[Q^+X^-]_{org}[NaOH]_{aq}[Y-H]_{org}[HCCX]_{org}}{k_{-1}k_{-2}[X^-]_{aq} + k_{-1}k_{-3}[HCCX]_{org} + k_2k_3[HCCX]_{org}[Q^+X^-]_{org}}$$

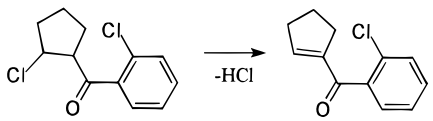
This equation validly describes the action of promoters (Y−H), such as fatty alcohols, amines, and benzyl alcohol. Benzyl alcohol acts as the promoter, confirming the results on PTC-elimination in the presence of alcohols obtained by Dehmlow and co-workers.[4] It should be noted that the distribution of quaternary ammonium hydroxides between aqueous and organic phases in the presence of alcohols was already studied by Agarwall and Diamond in 1963.[16] They showed that in benzene solution quaternary hydroxide exists as an ion pair linked with three alcohol molecules. In a more polar organic phase, such as nitrobenzene, quaternary hydroxide exists as a free ion also linked with three alcohol molecules. In the author's opinion it is most probable that the alcohol molecules are bonded with the hydroxyl ion rather then with the quaternary cation. So Makosza's scheme is not very accurate.

The most peculiar results are obtained in the presence of phenol and pentachlorophenol (Figures 4 and 5). The obtained dependence is best described by the equation of the type

$$k_{obs} = kC_{add}/(1 + K_1C_{add})(1 + K_2C_{add})$$

where C_{add} is the concentration of the cocatalyst and k, K_1, and K_2 are some reaction constants. This equation implies the mechanism where the cocatalyst forms complexes with *both* the reacting species. This kind of equation is common for micellar and acid catalysis. In the framework of existing views on PTC elimination mechanism that would mean that in this case not only does the catalyst form a complex with the additive but the substrate does so also. However, this is hardly plausible in this case, as it is difficult to conceive of a HCCHX complex with the quaternary salt or a proton donor. The species Y^- is effectively the major source of base in the organic phase (by virtue of the greater organophilicity of complex QY than that of QOH when the Y−H concentration is greater than that of QX, so that Q^+ is almost wholly associated with Y^- in place of HO^-), then the reactivity of Y^- as base in E_2 elimination is going to be inversely proportional to the stability of Y^- (e.g., as measured by its basicity). Thus, with very stable (low pK_a) anions (from the very acidic Y−H), these anions Y^- are too weak to act effectively as base (associated with Q^+ in the organic phase) but nevertheless largely tie up Q^+ with ineffective Y^- thereby preventing Q^+ from associating with more reactive hydroxide HO^- due to the greater organophilicity of Y^- than HO^-. Hence, increasing the concentration of strongly acidic Y−H inhibits the reaction by reducing Q^+ availability. Far less acidic Y−H acts as by being more easily solubilised into the organic phase than hydroxide, whilst Y^- is still a strong enough base to catalyse the E_2 elimination. As regards the phenol and pentachlorophenol results, a possible rationalisation for the kinetics observed is that at low additive concentration (less than that fully occupying the quat Q^+), increasing additive concentration increases the reactive QY base concentration. However, as additive concentration increases above that of quat concentration, then further additive can associate with QY by hydrogen bonding to give QY−HY in which the basic phenoxide is stabilised by hydrogen bonding to another phenol, thereby reducing its reactivity. Hence increasing additive HY concentration beyond that fully occupying quat Q^+ gradually decreases the reactivity of the basic species QY. It is quite plausible, as Brandstrom proved the formation of Y^-Q^+, $Y^-Q^+(Y-H)$, $Y^-Q^+(Y-H)_2$, and higher complexes on addition of the quat and base to the solution of phenol or carboxylic acid in methylene chloride.[18] This scheme is also described by the above equation. The obtained results can well explain the discrepancies concerning the action of phenol additives obtained by different authors [compare refs 9 and 10]. It is interesting to note also that even strong inhibitors, such as **VI** do not fully stop the reaction. That confirms our previous findings on dual catalytic character of long-chained quats and some of their advantages over short-chained ones.[2,3] It is that the long-chained quats are both micellar and phase transfer catalysts, and only the phase-transfer function is inhibited.

We have used the advantage of the long-chained quats, that is their ability to catalyse elimination at low alkali concentrations, in the solution of the following practical task. One of the steps in the synthesis of the short-time anaesthetic ketamine includes dehydrochlorination. This reaction is usually carried out in the presence of an amine base.



VII **VIII**

This is a bottleneck step as the yield is about 70%. It seemed interesting to try PTC in this reaction but the use of concentrated alkalis was ruled out as it would result in numerous side-processes involving the keto group. The usual catalysts (TEBA or Bu_4NBr) do not work in diluted alkali. Therefore, we had to apply our usual long-chained catalyst

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Table 1. **Dehydrochlorination of VII in the presence of NaOH, catalyst—Katamin AB, $t = 20$ °C[a]**

$[NaOH]_0$, M	C_{cat}, % mol.	reaction time, h	chromatographic yield, % theor.
0.44	0.6	2	93
1.06	0.6	2	86
3.57	0.047	3	15.1
6.92	0.1	5	10.2
10.86	0.1	4	22.1

[a] In all of the experiments the conversion was 100%.

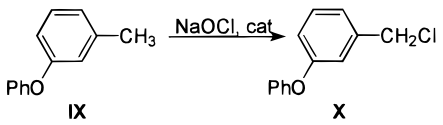
Table 2. **Dehydrochlorination of VII in the presence of KOH, $t = 20$ °C**

$[KOH]_0$, M	catalyst	C_{cat}, % mol	reaction time, h	chromatographic yield, % theor.
0.28	dibenzo-18-crown-6	1.04	3	84
0.3	dibenzo-18-crown-6	1.2	3	85
0.63	dibenzo-18-crown-6	1.04	3	84
1.14	dibenzo-18-crown-6	1.6	4	85
1.85	dibenzo-18-crown-6	1.6	3.5	82
2.1	dibenzo-18-crown-6	1.25	4	86
3.2	dibenzo-18-crown-6	1.65	2	0
0.3	Katamin AB	0.12	3	84
0.7	Katamin AB	0.12	3	84
0.22	$[(C_7-C_9)_3NMe]_2SO_4$	0.08	1	97
0.27	$[(C_7-C_9)_3NMe]_2SO_4$	0.06	1	94
0.66	$[(C_7-C_9)_3NMe]_2SO_4$	0.1	2.5	94
0.74	$[(C_7-C_9)_3NMe]_2SO_4$	0.2	1	94

[a] In all of the experiments the conversion was 100%.

$PhCH_2(Me)_2N^+(C_{16}-C_{18})Cl^-$.[17] The results are listed in Tables 1 and 2. It is seen that the increase in alkali concentration results in a sharp decrease in the product yield. At quite moderate concentration of 3.0 M the yield falls practically to zero. At the lower base concentrations the yield is much higher than in the presence of an amine base. Thus, PTC dehydrochlorination is one solution to the problem.

PTC Chlorination. The use of PTC for the chlorination of alkylaromatic compounds has some significant advantages. First, it is very selective as only side chain is chlorinated.[19] Second, it allows one to use large quantities of sodium hypochlorite solutions that are obtained as side-products in many industrial processes. Nevertheless, the use of the soluble catalyst is not very advantageous for the large-scale processes as it necessitates the purification of the final product from the catalyst or the products of its decomposition. The use of polymeric phase-transfer catalysts is widely known,[15] but till now they were not applied in chlorination reactions. We decided to test triphase catalysis in the chlorination of *m*-phenoxytoluene.



IX **X**

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Table 3. **Chlorination of *m*-phenoxytoluene by aqueous NaOCl, $t = 20$ °C, $[PhOC_6H_4Me]_0 = 0.5$ M, solvent $CHCl_3$, $[(C_7-C_9)_3NMe]_2SO_4]_0 = 1.6$ % w/w, $[C_7H_9COOH]_0 = 3.2$ % w/w, $NaOCl/PhOC_6H_4Me = 3:1$**

$[NaOCl]_0$, M	pH	reaction time, min	conversion of **IX**, %	yield of **X**, % theor.	ring-chlorinated products, %
0.98	8	170	95.0	74.8	20.2
0.98	3	30	54.0	14.5	39.5
1.65	7	90	67.6	51.4	16.2
1.65	7	20	12.1	8.9	3.2
1.65	6	40	16.1	12.4	3.7
1.65	7	70	26.4	21.8	4.6
1.65[a]	7	20	25.0	23.4	1.4
1.65[a]	7	35	41.2	38.8	2.4
1.65[a]	7	50	66.6	63.5	3.1
1.65[a]	7	130	92.8	88.8	4.0

[a] The catalyst was **XI** preliminary swelled in $CHCl_3$.

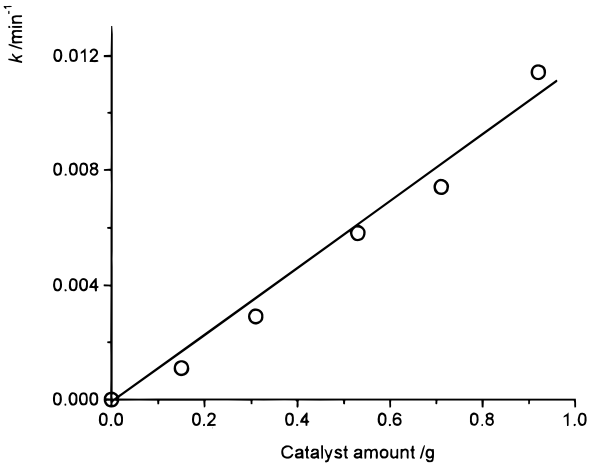
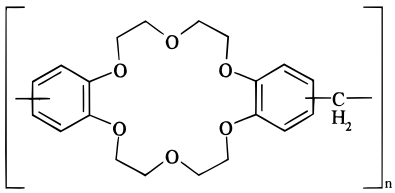


Figure 6. **Dependence of the observed rate constant on the catalyst amount.**

The resulting compound, *m*-phenoxybenzyl chloride is used in the synthesis of pyrethroid insecticides. For the catalysts we used the mixture of $[(C_7-C_9)_3NMe]_2SO_4$ with heptanoic acid that proved perfect in the bromination of cyclopentadiene[3] and polymeric dibenzo-18-crown-6 (**XI**) of the following structure:



The results are listed in Table 3. It is seen that the polymeric crown is much more selective then soluble quats. At the low pH values mostly ring-chlorinated products are formed.

These results made it worthwhile to investigate the kinetics of this reaction. The reaction was investigated at room temperature. Some of the obtained results are shown in Figures 6−8.

It should be noted that all experiments were carried out at stirring rates above 2000 rpm, that is, when it did not

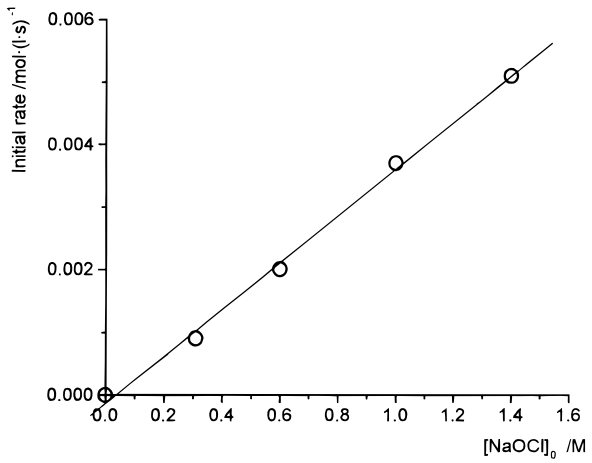


Figure 7. **Dependence of the initial rate on the hypochlorite concentration.**

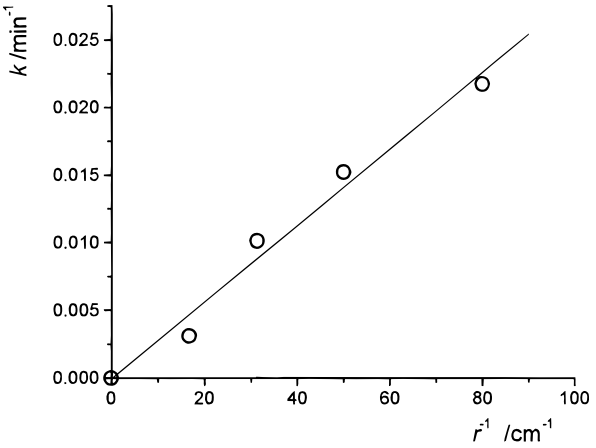


Figure 8. **Dependence of the observed rate constant on the catalyst particle size.**

influence the reaction rate. The reaction was first-order on catalyst amount and NaOCl concentration. The reaction rate was strongly dependent on the size of catalyst granules (see Figure 8). The obtained dependence is typical for reactions proceeding in the internal diffusion region. The catalyst was rather strongly cross-linked, thus resulting in internal diffusion limiting the overall reaction rate. Also it worked only in swelled state after soaking for several hours in $CHCl_3$.

The obtained results show that use of triphase catalysis for the chlorination of alkylaromatics is rather promising. The problem lies in obtaining the catalyst in the form suitable for industrial use.

Experimental Section

Materials. Solvents and reagents were commercial grade. The α-isomer of hexachlorocyclohexane was isolated from the mixture of isomers by the known methods.[20] The product used had mp 157−158° (159−160°[20]).

Product Identification and Analysis. Reaction products of *m*-phenoxytoluene chlorination were determined by GLC, using a TSVET gas chromatograph, model 152 with FI detector. Analyses were performed on a 3 m SE-30 column. Reaction products of **VII** dehydrochlorination were determined by GLC, using a Chrom-5 gas chromatograph with FI detector. Analyses were performed on a 1 m OV-17 column. Product identification was performed using GLC-MS spectroscopy. GLC-MS spectra were recorded on a Varian-MAT spectrometer, model CH7A with chromatograph model 2740 and a data treatment module SS-100.

Kinetic Experiments. Kinetics of the α-hexachlorocyclohexane dehydrochlorination was studied using NaOH concentration 2.5 M, by the methods described in ref 11. Kinetics of *m*-phenoxytoluene chlorination was investigated in a three-necked jacketed 150 mL glass reactor with baffles, equipped with high-speed stirrer and thermometer. The reaction was studied at about 1800−2000 rpm where stirring speed did not influence the reaction rate. The reaction was monitored by taking samples of the organic phase and analysing them by GLC. The polymeric catalyst **XI** was soaked in $CHCl_3$ for at least 5 h before its use until it increased its volume 3-fold.

Acknowledgment

This paper is dedicated to Professor Eckehard Volker Dehmlow on his 65th birthday.

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