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Inhibition and synergism in phase transfer catalysis

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ABSTRACT. Questions concerning inhibition and synergism in phase transfer catalytic reactions in various systems are examined. Effects induced by the decomposition of the catalyst during the reaction and also by the introduction of various reagents and additives are analysed. Factors giving rise to synergistic and inhibition phenomena are considered.

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I. Introduction

The phenomenon of the synergism and inhibition of catalysts is well known in homogeneous and heterogeneous catalysis. In some cases, the mechanism of the action of promoting agents and catalytic poisons has been investigated and catalytic systems ensuring a high selectivity of reactions have been created. There are numerous patents devoted to the use of the synergistic effect in industrial processes.

The same effects involving the synergism and inhibition of catalysts have been observed also in phase transfer catalytic reactions. However, in this field synergism has been studied to an extremely slight extent. Whereas inhibition, albeit induced by different causes, is encountered fairly frequently, synergism is manifested much more rarely and to date it is generally considered to be a kind of exotic phenomenon. It is therefore useful to consider initially inhibition, since this effect has been better investigated and is more common.

The inhibition of a phase transfer catalytic reaction, understood in a broad sense, can be induced by a whole series of factors which will be considered below.

For the benefit of readers who are not familiar with the details of the problem, it is useful to explain briefly the essential features of phase transfer catalysis itself before considering specific effects. It consists in the fact that contact between two reactants in immiscible phases (a liquid–liquid or a liquid–solid system) is possible by virtue of the presence of a transferring substance — the phase transfer catalyst. Such transferring agents are as a rule quaternary onium salts. These substances effect either the transfer of a reactant into one of the phases (for reactions in a liquid–liquid system with a neutral aqueous phase) or the removal of the product from the reaction zone (for reactions involving concentrated solutions of alkalis). It is hardly possible within the framework of a single review to consider in detail the principles of phase transfer catalysis.

A number of designations have been adopted in the literature on phase transfer catalysis. The quaternary onium salt is usually designated by QX or Q^+X^-, where $Q(Q^+)$ is the quaternary onium cation and $X(X^-)$ is the anion (usually inorganic) or by the term "quat" from the word "quaternary". The subscripts "wph" and "oph" or "w" and "org" refer to the reagents and the catalyst in the aqueous and organic phases respectively. The symbol $MY(M^+Y^-)$ is understood as the inorganic reagent, where M is the metal cation and Y the anion. Subsequently this notation will be used without further explanation.

II. Inhibition in a liquid–liquid system

1. Inhibition as a result of the poisoning of the catalyst by extraneous anions

This type of effect was first observed by Starks and Owens.[1] It was noted that the interphase reaction of alkyl iodides with sodium cyanide, i.e.

$$RI + NaCN \xrightarrow{quat} RCN + NaI,$$

ceases after the attainment of 15–25% conversion.[1] It is usual to explain this by differences between the mutual extractabilities of the reactant ion (Y^-) and the departing ion (X^-) or the catalyst counterion (Z^-).

Such a difference in the reaction of the type

$$RX + M^+Y^- \xrightarrow{quat} RY + M^+X^- \qquad (1)$$

can be described with the aid of the ion-selective equilibrium constant $K^{sel}_{Y/X}$ (Gordon and Kutina[2]):

$$K^{sel}_{Y/X} = (C^{X^-}_{wph} \cdot C^{QY}_{oph})/(C^{Y^-}_{wph} \cdot C^{QX}_{oph}),$$

where $C^{Y^-}_{wph}$ and $C^{X^-}_{wph}$ are the concentrations of the reactant anion and the leaving anion respectively and C^{QY}_{oph} and C^{QX}_{oph} are the concentrations of different forms of the catalyst. The above constant determines the effectiveness of the catalyst in reaction (1).

$K^{sel}_{Y/X} < 0.1$ corresponds to the "poisoning" of the catalyst. Reaction profiles corresponding to different values of $K^{sel}_{Y/X}$, which makes it possible to select approximately a catalyst effective in the given system, have been published.[2] However, the special case where the catalysts 'own' counterion Z^- differs from both the reactant ion (Y^-) and the ion of the leaving group (X^-), i.e. in the system where there are three different anions, was not considered in the above studies. Theoretical examination of this version[3] showed that, even for $K^{sel}_{Z/X} \leqslant 10$, the "poisoning" effect can be avoided by taking a

tenfold excess of the inorganic reagent (M^+Y^-) relative to the substrate (RX). If $K^{sel}_{Z/X} \leqslant 1$, there is no poisoning even for a stoichiometric ratio of the reactant and the substrate. Hence it was concluded that the catalyst should be introduced into the reaction in the form Q^+X^-, i.e. when its counterion is identical with the leaving group. For $K^{sel}_{Z/Y} < 1$, the initial rate is higher if the catalyst is added in the form Q^+Z^- and not Q^+Y^-. The opposite effect is manifested for $K^{sel}_{Z/Y} > 1$.

The study of the "poisoning" of the catalyst by extraneous anions in processes occurring in the presence of alkalis, which is associated with the presence of an admixture of chlorates in technical alkali,[4] is very important. The quantity $\lg K^{sel}_{ClO_3/OH}$ is approximately 2. This means that chlorate is a powerful catalytic poison in reactions involving the hydroxide ion. Other lipophilic anions are inhibitors in reactions of this kind. For example, in the alkylation of acetone by alkyl halides in an alkali–organic phase system (catalyst—quaternary ammonium salt), the addition of sodium tetraphenylborate to the system stopped the process as a result of the removal of the catalyst from the reaction zone.[5]

The study of the inhibiting effect of extraneous anions by chemical kinetic methods[6] in relation to alkaline dehydrochlorination of 3,4-dichlorobut-1-ene made it possible to determine the corresponding inhibition constants. For this purpose, a series of inorganic salts were added to the reaction system. The familiar reversible inhibition model was used for the description of the results.[7] The dependence of the rate of reaction on the substrate concentration was expressed in a linear form in terms of double reciprocal variables (the Lineweaver–Burke plot), the effective rate constant was then determined. The following series based on the decrease in the inhibiting capacity of the anions was obtained: ClO_3^- (1) > NO_3^- (0.6) ≃ Cl^- (0.64) ⩾ SO_4^{2-} (0.24), where the inhibition constants are given in brackets. This sequence agrees quite well with the available data[8] for the relative lipophilicities of these anions.

Table 1. The influence of the catalyst counterion on the rate constant k_{obs} in the isomerisation of allylbenzene.[9]

Catalyst	$10^3 k_{obs}$, s^{-1}	Induction period, min	e_{QZ} *
MBu_4HSO_4	114	<0.1	$5.75 \cdot 10^{-2}$
NBu_4Cl	24	1.3	0.35
NBu_4Br	2.4	10	17

Note. Reaction conditions: 40% NaOH, catalyst—5 mol%, temperature 75 °C.
* The Brandstrom extraction constants e_{QZ} were taken from Ref. 11 for the water–methylene chloride system.

The influence of the catalyst's "own" counterion on the rates of different reactions occurring in the presence of alkalis has been examined.[9,10] In the study of the isomerisation of allylbenzene under the influence of an aqueous NaOH solution to a mixture of (*Z*)- and (*E*)-β-methylstyrenes,[9] the dependence of the rate constant and the induction period of this reaction on the catalyst counterion was found (Table 1). In this case, there is no departing group, i.e. the system contains only the Y^- (in the given instance OH^-) and Z^- anions. The dependence of $\lg k_{obs}$ on $\lg e_{QZ}$ (where e_{QZ} is the Brandstrom extraction constant[11]) is linear with a correlation coefficient of 0.995. However, since these data were obtained for only three catalyst, it is difficult to make any broad generalisations.

A similar influence of the catalyst counterion on the rates of dehydrochlorination of *m*-bis(α, β-dichloromethyl)benzene and *m*-bis-(α-chlorovinyl)benzene in the presence of tetrabutylammonium salts has been noted.[10] The usual extraction system was used to describe the reaction kinetics. The catalysts were the following tetrabutylammonium salts: the bromide, chloride, sulphate, and hydroxide. The activities of the sulphate and the hydroxide were virtually identical while on passing to the chloride and even more so to the bromide the rate of reaction fell appreciably, particularly in the initial period. Thus the lipophilic properties of the leaving anion and the catalyst counterion play a significant role in reactions involving not only neutral salts but also alkalis. However, the data obtained recently show that not everything proceeds quite so simply and smoothly. If in the estimation of the influence of the anions one is guided solely by the lipophilicity, one may conclude that quaternary ammonium iodides are in general ineffective in any phase transfer catalytic reactions. This has indeed been confirmed in a number of studies[1,11] and has led to the creation of the fairly well established view that these salts have no potential as catalysts.

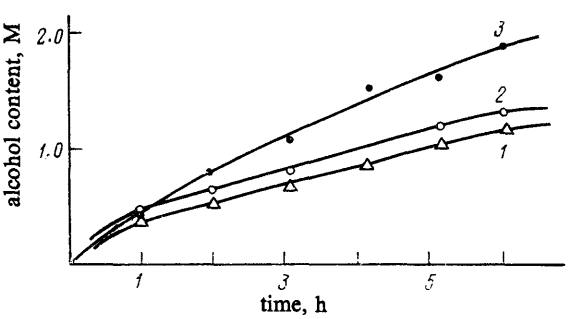


Figure 1. Hydrolysis of 2,3-dichloropropene using different phase transfer catalysts;[13] *1*, catamine; *2*, NBu_4Nr; *3*, NBu_4I. The amount of catalyst used was 10 mol% relative to the initial compound.

However the thesis that the activity of quaternary ammonium iodide is low in any phase transfer catalytic reactions is disproved both by data[12] on the alkylation of 2-methylacetoacetic ester (MAAE) and by the results of a study of the hydrolysis of 2,3-dichloroprop-1-ene to β-chloroallyl alcohol.[13] In the latter case, quaternary ammonium iodides proved to be appreciably more active as catalysis of the hydrolysis than the chlorides (Fig. 1). It was suggested[13] that the reaction proceeds via the mechanism

$$CH_2{=}CHCl{-}CH_2Cl + Q^+I^- \rightarrow [CH_2{=}CHCl{-}CH_2I],$$

$$CH_2{=}CHCl{-}CH_2I + NaOH \rightarrow CH_2{=}CHCl{-}CH_2OH,$$

which includes the intermediate formation of 2-chloro-3-iodoprop-1-ene, which should be hydrolysed much more readily than the initial compound (although the results of chromatographic analysis of the reaction mixture did not provide grounds for hypotheses of this kind). However, bearing in mind the fact that in the alkylation of MAAE by prenyl chloride in the presence of KF the exchange of chlorine for iodine does not occur when quaternary ammonium iodides are used as catalysts[12] and their increased catalytic activity is caused by the nucleophilic catalysis by the iodide anion, one may confidently postulate that the role of the iodide anion is similar also in the hydrolysis of 2,3-dichloropropene.

Table 2. The half-lives of quaternary ammonium salts in the chlorobenzene–50% NaOH two-phase system in the presence (A) and absence (B) of a molar excess of the salt NaY with a like counterion.

R_4M^+	Y^-	T, °C	ΔE^*_{act}, kJ mol^{-1}	$\tau_{1/2}$, h	
				A	B
$(C_6H_{13})_4N^+$	Cl^-	25		35	(4% after 6 days)
	Cl^-	60		0.4	8
	Cl^-	60		0.7 **	1.5 **
	Br^-	25	120	(8% after 6 days)	stable
	Br^-	60		13	stable
	Br^-	60		45 **	
	Br^-	80		1	272
	I^-	25		stable	
	I^-	60		stable	
	I^-	80		136	stable
$(C_8H_{17})_4N^+$	Cl^-	60		0.25	
	Br^-	60		3.5	stable
Bu_4N^+	Cl^-	25		18	
$C_6H_5CH_2N^+Et_3$	Cl^-	25		6.7 ***	127 ***
	Br^-	25	66	240 ***	stable***
	Br^-	35		96 ***	
$C_6H_5CH_2N^+(C_6H_{13})_3$	Cl^-	25	120	13	
	Cl^-	60		0.05	
	Br^-	25	120	432	
	Br^-	60		2.3	
$(C_8H_{17})_3N^+Me$	Cl^-	25	85	32	
	Cl^-	60		0.7	
Bu_4P^+	Cl^-	25		0.03	0.3
	Br^-	25	85	3.5	220
	Br^-	60		0.6	5.5
$Bu_3P^+C_{16}H_{33}$	Cl^-	25		0.03	0.8
	Br^-	25	68	2	220
	Br^-	60		0.25	
	Br^-	60		1.5 **	
	I^-	25		(8% after 3 days)	stable

* The quantity ΔE_{act} was estimated approximately on the basis of two temperatures.

** The reaction takes place in the solid NaOH–PhCl system.

*** The reaction takes place in the CH_2Cl_2–50% NaOH two-phase system.

In all probability, the directly opposed effects induced by the presence in the system of highly lipophilic anions such as the bromide and the iodide, i.e., on the one hand, the inhibition of the reaction, observed in a number of studies,[1,5,9,11] and, on the other hand, the acceleration of the reaction under the influence of the same iodide anion, established in other investigations,[12,13] are induced by the difference between the mechanisms of the reactions investigated.

The dehydrochlorination of chlorohydrocarbons and the isomerisation of allylbenzene take place in liquid–liquid systems and have a common rate-limiting stage—the deprotonation of the substrate by QOH at the interface between the phases or in the bulk of the organic phase. Naturally, anions more lipophilic than OH^- effectively inhibit this process. The hydrolysis of 2,3-dichloropropene is a substitution reaction of the S_N2 type and I^-, which is more nucleophilic than OH^-, catalyses it. The somewhat greater effectiveness of iodides in the alkylation of MAAE on solid KF, where deprotonation takes place on a solid surface, is believed[12] to be caused by the smaller Q^+-X^- bond energy.

These results show that, in estimating the influence of the counterion, one cannot use as a basis solely its lipophilicity without taking into account the mechanism of the main reaction.

A phenomenon of a similar nature—nucleophilic catalysis by an extraneous ion—has been observed in the alkaline hydrolysis of n-BuBr and benzoyl chloride.[14] In the presence of 60% NaOH solution, aliquat 336, NBu_4HSO_4 (or NBu_4Br), both hydrolysis and the formation of an ether are very slow: the degree of conversion of benzyl chloride into dibenzyl ether after 24 h at 100 °C is 71%. The addition of 10 mol% of sodium acetate to the solution leads to the full termination of the reaction after 3 h. In contrast to the alkylation of MAAE,[12] where there was no exchange of the halogen between the alkyl halide and the extraneous anion (I^-), the intermediate formation of acetates, which undergo alkaline hydrolysis to a much greater extent, was noted in the given instance. The alcohol formed as the alkoxide is transferred by the quaternary salt to the organic phase where an ether is formed. The ratio of the products obtained on hydrolysis makes it possible to establish the sequence based on the relative extractabilities of the ions: $OR^- > AcO^- > OH^-$.

2. Inhibition as a consequence of the decomposition of the catalyst

This version of the inhibition occurs in catalysis by the ammonium salts of reactions which take place in the presence of alkalis at a high temperature. The quaternary ammonium base decomposes via the Hofmann reaction or the Menshutkin retroreaction or via both processes simultaneously. Thus, benzoyl alcohol, dibenzyl ether, hexadecane, dimethylhexadecylamine, and dimethylbenzylamine were detected among the decomposition products of the catalyst $[C_6H_5CH_2N(CH_3)_2C_{16}H_{33}]^+Cl^-$ used to generate dichlorocarbene.[15] The decomposition products of triethylbenzylammonium chloride (TEBA) under the conditions of the acetone alkylation reaction were benzyl chloride, benzyl alcohol, and dibenzyl ether,[5] i.e. the catalyst decomposed via the Menshutkin retroreaction. The decomposition of a whole series of quaternary ammonium and phosphonium salts has been investigated semiquantitatively[16] in the chlorobenzene–50% NaOH two-phase system and the stability of the salts was estimated from the half-life.

The ammonium salt decomposed in the general case in accordance with the equation

$$RN^+R_3'Y^- + NaOH \rightarrow R_3'N + R_2'NR + R''CH{=}CH_2 + \\ + R_2O + NaY + H_2O.$$

Symmetrical and asymmetric tetraalkyl derivatives decompose mainly via the Hofmann reaction while benzyl-substituted salts decompose via the Menshutkin retroreaction. Similar data have been obtained also by other workers.[5,15] Factors such as the nature of the heteroatom and the counterion, the structure of the alkyl chain, the reaction temperature, and the presence of a salt with a like counterion were investigated. The results are presented in Table 2.

Although it has been stated in the early and familiar monograph of Weber and Gokel[17] with a reference to Herriott and Picker[18] that phosphonium ions are more thermally stable than the corresponding ammonium catalysts, the results of Landini et al.[16] contradict this view which is in general widely held. It is essential to note that in the original study of Herriott and Picker[18] it is also claimed that, although phosphonium salts are more active than ammonium salts, they undergo thermal decomposition and side reactions to a much greater extent. Thus according to the data of Herriott and Picker[18] benzyltriphenylphosphonium chloride decomposes even under mild conditions 30 °C, 2 N NaOH). It is therefore incomprehensible whence arose the idea that quaternary phosphonium salts are more stable in the presence of alkalis. This has also been repeated in the monograph of Dehmlow and Dehmlow.[19] As can be seen from Table 2, all ammonium salts are appreciably more stable than the phosphonium salts. The high stability of the symmetrical tetraalkylammonium salts falls after the introduction of the benzyl substituent and increases in the sequence chlorides $\ll$ bromides $<$ iodides. Interpretation of data [16] on the influence of the concentration of alkali on the decomposition of a quaternary salt (Table 3) showed that the observed pseudo-first-order rate constant (determined as the reciprocal of the half-life $\tau_{1/2}$) is correlated fairly well with the activity and basicity of the alkali (r = 0.955, 0.968), at any rate in the case of tetrahexylammonium chloride.

Table 3. The influence of the NaOH concentration on the half-life of quaternary onium salts in the chlorobenzene–aqueous alkali two-phase system at 60 °C.[16]

NaOH concentration, wt.%	$\tau_{1/2}$, h		
	$(C_6H_{13})_4N^+Cl^-$	$(C_6H_{13})_4N^+Br^-$	$Bu_3P^+C_{16}H_{33}Br^-$
10	78		
15	29	312	20
25	12		
30	6	30	4.5
40	0.75		
50	0.4	13	0.25

The available literature data on the stability of phosphonium salts in the presence of alkali are fairly contradictory. Compared with ammonium salts, these compounds are stable on heating, decomposing at temperatures above 300 °C.[20] On the other hand, the rate constant for the reaction of tetrabenzylphosphonium iodide with NaOH at 39 °C is 2.72 litre mol^{-1} min^{-1},[21] which is greater by approximately three orders of magnitude than the decomposition constant of benzyltrihexylammonium chloride under analogous conditions (the above value was estimated from the data of Landini et al.[16]). In another place in the same monograph,[19] it is stated that benzyl-substituted phosphonium salt are less stable than their ammonium analogues in the presence of NaOH. The contradiction between these data is due to the different reaction conditions.

It is noteworthy that the inhibition due to the decomposition of the catalyst differs kinetically from that considered in the previous section. Whereas in the inhibition induced by the poisoning of the catalyst by extraneous anions a sharp fall of the reaction rate is observed after the attainment of a specific threshold degree of conversion, in the given instance the rate of reaction falls gradually. Formally this phenomenon is described as first-order irreversible inhibition of the catalyst.[7] The kinetics of the decomposition of the catalysts were investigated in relation to the dehydrochlorination of the α-isomer of hexachlorocyclohexane catalysed by katamin AB.[22] The rate of this reaction was described adequately by the equation

$$\ln\{[C_6H_6Cl_6]/[C_6H_6Cl_6]_0\} = k_1[NaOH]c_{cat}[1-\exp(-k_2\tau)]/k_2,$$

where k_1 and k_2 are the effective rate constants for the dehydrochlorination and decomposition of the catalysts respectively and τ is the reaction time. The activation energies for these two reactions are 54 and 68 kJ mol^{-1} respectively. Istomin's data for the decomposition of the tetrabutylammonium hydroxide catalyst, which occurred independently of the main reaction, have been published.[10] The decomposition was found to be a zero-order process with a rate of reaction (r_{decomp}) independent of the current concentration of the catalyst:

$$r_{decom} = k^{eff}_{decomp},$$

where k^{eff}_{decomp} is the pseudo-zero-order rate constant for the decomposition of the catalyst.

However, the rate of reaction is a function of the initial catalyst concentration:

$$k^{eff}_{decomp} = k^0_{decomp} + k^1_{decomp}c^0_{cat},$$

where k^0_{decomp} and k^1_{decomp} are the rate constants for the decomposition of the catalyst at the interface and in the bulk of the film containing the catalyst.

This type of dependence can be achieved by the fact that, in the presence of highly concentrated alkali, the main bulk of the catalyst is concentrated in the film at the interface.[8] The catalyst in this film supplies the organic phase and the observed rate of its decomposition therefore remains constant as a function of time. The rate of decomposition of the catalyst depended very greatly on the basicity function (H_-):

$$\lg k^{eff}_{decomp} = (-17\pm1)+(0.77\pm0.09)H_-(r=0.982).$$

The activation energy for the decomposition of the catalytst is approximately 110 kJ mol^{-1}, while the activation energy for the dehydrochlorination reaction is lower by a factor of two. Thus the data in Refs. 22 and 10 agree. From this it follows that, when the dehydrochlorination takes place at a high temperature, then a constant supply of the fresh catalyst to the reaction mass is necessary to maintain its concentration at the required level.

III. Inhibition in a solid–liquid system and inhibition by onium salts

The inhibition effects are also manifested in solid–liquid systems. This is associated, firstly, with the adsorption–desorption of the substrate and catalyst on the solid surface and, secondly with the enormous role of water in phase transfer catalysis. As noted in a familiar monograph,[17] this role is "like the weather, discussed a lot but little understood". Hitherto the influence of water has been studied somewhat more effectively, but the discrepancy beween the data quoted has diminished little. Different workers reach diametrically opposite conclusions, which is apparently caused both by experimental errors and by the not always correct interpretation of the results. Nevertheless, the popularity of solid–liquid systems has been increasing, since the reaction proceeds at a higher rate in the absence of water as a consequence of the increased nucleophilicity of the anions. Furthermore, in certain cases the Gibbs free energy of reaction (2) in "dry" systems is greater and hence the equilibrium degree of conversion in substitution reactions of the type

$$RX + Y^- \rightleftarrows RY + X^- \qquad (2)$$

is higher.

The role of water in the reactions with participation of alkali is also considerable, since it is known that the basicity of the hydroxide ion in the absence of water of hydration is appreciably greater.[23]

The influence of water in substitution reactions in a solid–liquid system has been investigated.[24] It was established that, for X = Cl^- or Br^- and Y = F^-, Br^-, Cl^-, $HCOO^-$, or $MeCOO^-$ (in the forms of salts with K^+ or Na^+) and R = C_6H_{13}, C_8H_{17}, $C_{10}H_{21}$, or $PhCH_2$, reactions (2) catalysed by quaternary ammonium salts do not occur when the reactants in the solvent are thoroughly dried. This agrees with the data of Starks and Owens[1] but not with those of Zwan and Hartner.[25] Zwan and Hartner[25] investigated the reactions of benzyl chloride and hexyl bromide with solid KF, KCN, AcOK, and the potassium salt of adenine in acetonitrile catalysed by aliquat 336, 18-crown-6, and tetramethylenediamine. Aliquat 336 proved to be the most active catalyst in virtually all cases apart from the reaction with KCN. All the reactants and solvents were carefully dried and the reaction was carried out in a sealed tube in the presence of 4 Å molecular sieves. Unfortunately, the authors[25] do not quote the water content, which hinders the comparison of the results. It is of interest to note that the quaternary salt was established in the above study.

The influence of water on the kinetics of the consecutive-parallel 1,4-dichlorobutane formylation reaction has been analysed:[24]

$$Cl(C_2H_4)Cl \xrightarrow[k_1]{HCOONa} Cl(C_2H_4)OCOH \xrightarrow[k_2]{HCOONa} HCOO(CH_2)_4OCOH.$$

The constants k_1 and k_2 were calculated directly from the kinetic curves. Fig. 2 shows how the presence of water influences k_1. As can be seen, in the fully dried system there is no reaction, after the addition of traces of water the rate increases sharply, while on further addition of water it falls. A similar effect had been observed earlier.[1] According to the authors,[24] the results show that the quaternary salt is incapable of abstracting a non-hydrated ion from the crystal lattice.

An interesting effect has been observed in the study of the interaction of solid potassium formate, containing 0.015 mol% of water, with chlorodecane.[26] The reaction was carried out for a reactant ratio of 1.5:1 in *o*-dichlorobenzene at 75 °C. In the absence of the catalyst, the reaction did not occur and after 3 h the water content in the formate fell by only 10%. On the other hand, after the addition of even 5.5 mol% of aliquat 336 a rapid reaction begins with a first-order rate constant of 2×10^{-3} min^{-1} and approximately 90% of the water present in the initial formate is transferred to the organic phase. This happens also in the presence of a larger water content in the formate. The data are summarised in Table 4.

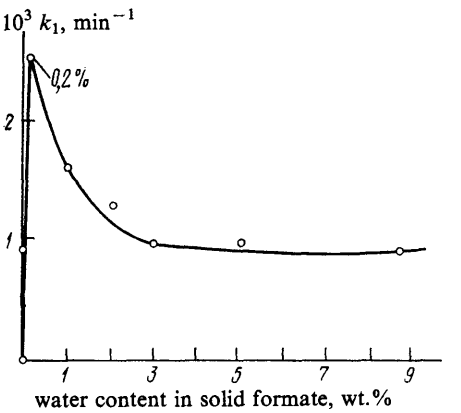


Figure 2. The influence of the water content in solid potassium formate on the observed rate constant for the formylation of dichlorobutane.[24]

Table 4. The influence of the quaternary salt on the dehydration of solid HCOOK in the alkylation of 1-chlorodecane in *o*-dichlorobenzene (T = 348 K, catalyst—aliquat 336).[26]

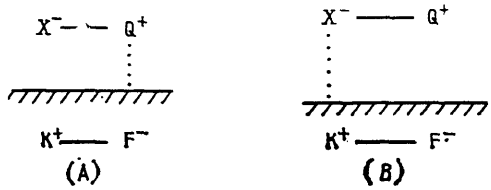
Water content in solid formate, mol%	Salt concentration*, mol%	Degree of transfer of water to organic phase, % of initial amount	k, min^{-1}
0.015	0.0	10	no reaction
0.015	5.56	88	$2 \cdot 10^{-3}$
1	5.56	51	
2	5.56	30	
0.015	19.44		$1 \cdot 10^{-3}$
0.015	39–56		$< 1 \cdot 10^{-3}$

* Relative to 1-chlorodecane.

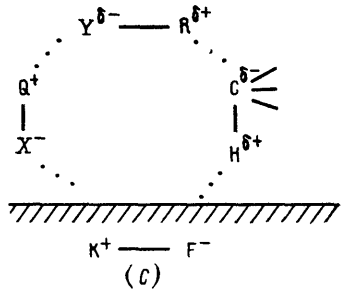
With increase in the concentration of the quaternary salt, the observed rate constant falls appreciably. This has been attributed[26] to the dehydration of the formate by the quaternary salt. The data obtained led to the conclusion that the observed effect is common to reactions in a solid–liquid system. However, it has been suggested[12] that a similar dependence, with an extremum in the dependence of the rate of reaction on the quaternary salt

concentration, is a result of effects associated with the adsorption of the catalyst on the solid surface. In the alkylation of MAAE by prenyl chloride in acetonitrile in the presence of solid KF, the dependence of the specific rate of reaction on the catalyst concentration also passed through an extremum. It was established that there is no ion exchange between QX and KF.

In earlier studies[27–29] of the reactions involving solid inorganic salts, it has been demonstrated that there are two types of adsorption of the catalyst on the surface of the solid reactant. The formation of two types of surface complexes of QX on KF was also postulated in the study described above:[12]



The MAAE adsorbed on the solid surface via the binding of the F^- ion to the CH group of MAAE is deprotonated. Complex (A) is thus of the "blind end" type since F^- is blocked. The adsorption of QX via Scheme (B) and the participation of the adsorbed complex in the alkylation process are confirmed, according to the author,[12] by data on the influence of the nature of Q^+ and X^- on the rate of alkylation (Table 5). These data agree to some extent with the nucleophilicity series quoted by Gordon.[30] Since prenyl iodide is not formed during the reaction, it was suggested that the alkylation proceeds on the surface of solid KF [Scheme (C)]:

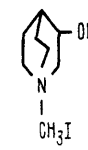


Alkylation via this scheme should lead to variable orders with respect to the component. The author[12] suggests that, if the QX concentration is higher than the MAAE concentration, the contribution of the "blind end" complex (A) increases, which explains the decrease in the rate of reaction with increase in the catalyst concentration. However, in our view, this does not agree fully with the kinetic scheme proposed by the author.

Table 5 also shows that the influence of the catalyst counterion is by no means always wholly determined by its lipophilic properties. This postulate has been confirmed by the results of Ali Abbas et al.[13]

Another interpretation of the dependence of the initial rates of reaction on the concentration of the solid reactant with an extremum has been proposed in studies[31,32] where the reaction of 1,2,4-trichlorobenzene with solid potassium phenoxide was investigated in the presence of copper and 18-crown-6. The authors explain this dependence in terms of the influence on the rate of reaction by the degree of surface coverage of the solid reactant by the catalyst (18-crown-6) and use the Langmuir equation in the description of the adsorption-desorption process involving the crown-ether–potassium phenoxide complex on the surface of the phenoxide, i.e. they used the mathematical procedures for heterogeneous catalysis in phase transfer catalysis. A synergistic effect was also noted in the above studies when two catalysts, such as metallic copper and 18-crown-6, were used.

Table 5. The influence of the nature of the phase transfer catalyst on the observed alkylation rate constant.[12]

Catalyst	$10^2 k_{obs}$, litre mol^{-1} min^{-1}	Catalyst	$10^2 k_{obs}$, litre mol^{-1} min^{-1}
Et_4NCl	0.16	Et_4NBr	0.38
Et_3NBzCl	0.14	Bu_4NBr	0.05
Bu_4NCl	0.18	Oct_4NBr	0.34
N-Benzylquininium chloride	0.06	Ph_3MePBr	0.37
Et_4NI	1.3		
Bu_4NI	0.64		0.42
Dibenzo-18-crown-6	0.065	Complex of 18-crown-6 with MeCN	0.37

Note. Reaction conditions: solvent—CH_3CN, T = 293–295 K, [PC] = [MAAE] = 0.2 M, KF/MAAE = 2, [QX] = 0.05 M.

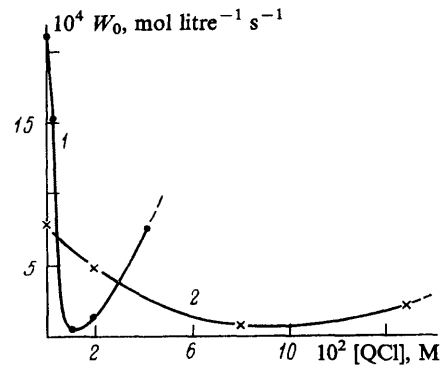
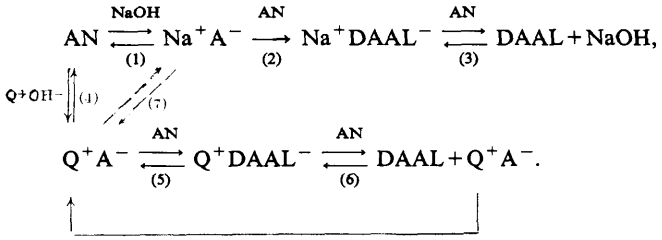


Figure 3. The influence of the new concentration of triethylbenzylammonium chloride on the initial rate of formation of diacetone alcohol at 40 °C in benzene solution in the presence of 50% aqueous NaOH at different initial molar acetone concentrations: *1*, 12; *2*, 8.[33]

Inhibition of the process by a quaternary ammonium salt has been observed not only in a solid–liquid system but also in a liquid–liquid system. Thus a study of the kinetics of the aldol condensation of acetone (AN) in the presence of 50% aqueous NaOH solution[33,34] established that, as a result of the addition of catalytic amounts of TEBA, the order of the reaction with respect to acetone changes and the initial rate of reaction falls appreciably (Fig. 3). This also entails the alteration of the composition of the

reaction products: considerable amounts of mesityl oxide (MO) and phorone (PHO) appear, while the amount of diacetone alcohol (DA) diminishes. The observed nature of the dependence of the initial rate of reaction on the Q^+Cl^- concentration persisted also on reducing the acetone concentration. The authors[33,34] explain the observed behaviour by a change in the reaction mechanism in the presence of the quaternary salt and propose the following process mechanism:



The reaction proceeds via the pathway (1)→(2)→(3) in the absence of Q^+Cl^- in the heterogeneous phase at the interface. Two molecules of acetone and water participate in it. After the introduction of the catalyst, the reaction can proceed via two pathways: (4)→(5)→(6) and (1)→(7)→(5)→(6). The heterogeneous pathway (1)→(2)→(3) is then blocked, as shown by the third order with respect to acetone of the reaction occurring in the presence of the catalyst.

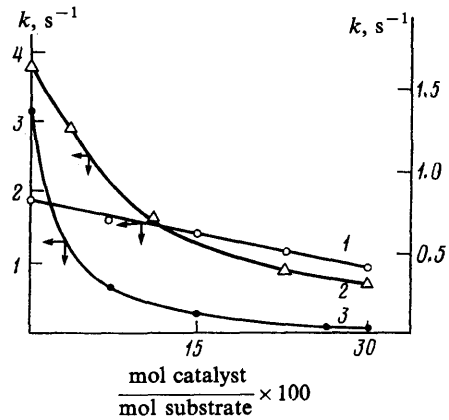


Figure 4. Dependence of the rate constant for the two-phase reaction on the catalyst concentration in the 1:1 benzene–water system at 25 °C:[35] *1*, 10^6k, t-BuCl + KNCS, $(n\text{-Bu})_4NBr$; *2*, 10^5k, hydrolysis of t-BuCl, $(n\text{-Bu})_4NBr$; *3*, 10^3k, hydrolysis of trityl chloride, $(n\text{-Bu})_4NCl$.

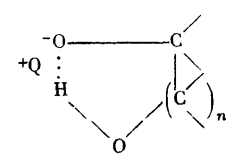
Inhibition of the reaction in a liquid–liquid system after the introduction of the phase transfer catalyst has also been observed in a study[35] of the substitution of tertiary alkyl chlorides by the thiocyanate ion (Fig. 4). Whereas in the reaction involving primary alkyl chlorides the introduction of the phase transfer catalyst accelerates the substitution, in the case of tertiary alkyl chlorides the introduction of a quaternary ammonium salt induces a marked inhibition. In the given instance, this is also a consequence of a change in the reaction mechanism, although it is not induced by the presence of the catalyst but is caused by a change in the structure of the substrate. On passing from a primary to a tertiary alkyl chloride, the S_N2 reaction mechanism changes to S_N1. This is confirmed by the fact that the hydrolysis of triphenylmethyl chloride (trityl chloride) is also inhibited sharply by tetrabutylammonium chloride.[35] Evidently, despite the fact that the quaternary salt transfers thiocyanate ions to the organic phase, the polarity of this layer is insufficient for the operation of the S_N1 mechanism. The reaction therefore takes place either in the aqueous layer or at the interface. The observed inhibition effect is induced by the removal of the thiocyanate ion from the reaction zone as a result of its extraction by the quaternary salt into the organic phase.

The inhibition of a number of other two-phase reactions by a phase transfer catalyst has been observed recently.[36] Thus the reaction of *p*-bromonitrobenzoylmethane with urotropine is inhibited by TEBA added in catalytic amounts. According to the author, this is induced by the transalkylation of TEBA with *p*-bromonitrobenzoylmethane. It was noted in the same study that, in the presence of TEBA, the acetylation of $p\text{-}O_2NC_6H_4C(O)CH_2NH_2$ by acetic anhydride in the presence of aqueous sodium carbonate proceeds with a lower yield as a consequence of the acceleration of the side reaction involving the cyclisation of the amino-derivative. However, the acetylation of 9,13-dimethyl-7-(1,1,5-trimethylcyclohex-5-enyl)nona-8,11,13-triene-10,15-diol by acetic anhydride in the presence of a phase transfer catalyst proceeds smoothly and with a satisfactory yield.[37]

All these features demonstrate that phase transfer catalysts are not a universal means of accelerating any heterophase process. In each specific case, the reaction mechanism plays the decisive role and not the presence in the system of two and more immiscible phases.

IV. Synergism and inhibition in multicomponent catalytic systems

This section is devoted to what is in our view the most interesting effect in phase transfer catalysis—the cocatalytic or, on the contrary, the inhibiting effect of compounds of substances added to the reaction system and capable of forming complexes with its components or a base of nucleophile stronger than the compounds present initially. Systems with alkalis have been most thoroughly investigated. At an early stage, in the study of the Williamson reaction under phase transfer conditions, it was observed that in the presence of alcohol an appreciably greater amount of the base passes to the organic phase than under the usual conditions.[18] The extracted alkoxide anion is a very powerful base. Thus the basicity of a 0.001 M solution of benzyltrimethylammonium t-butoxide in t-butyl alcohol is 1000 times higher than the basicity of a similar potassium t-butoxide solution.[38] It has been shown[39] that the most effective additive to quaternary ammonium salts, ensuring the maximum extraction of the base into the organic phase, is pinacol—2,3-dimethylbutane-2,3-diol. It was suggested that this is induced by the formation of a stable ion pair having the structure



It is essential to note that, in the absence of a quaternary salt, even the most effective diols increase the basicity of the organic phase extremely insignificantly, in contrast to polyglycols. This served as a basis for the application of a system comprising a quaternary ammonium salt and a diol in the synthesis of alkynes from 1,2-dihalo-derivatives,[40] because it had been shown earlier that 1,2-dibromoalkanes are readily dehydrobrominated by solid KOH in the presence of tetraoctylammonium bromide.[41] The following products are formed on elimination of 1,2-dihaloalkanes (Table 6):

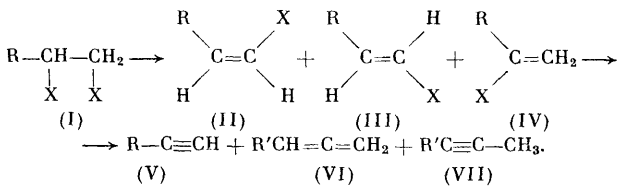


Table 6. Dehydrohalogenation of 1,2-dibromooctane by 50% KOH.[40]

Catalyst	Cocatalyst	Yield of products, %		(I)
		(V)	(II)–(IV)	
Oct_4NCl	Нет	0	70	30
	EtOH	0	88	12
	$C_5H_{11}OH$	10	90	0
	$C_7H_{15}OH$	8	92	0
	$HO(CH_2)_6OH$	48	52	0
	$HO(CH_2)_8OH$	50	50	0
	Hexane-2,5-diol	50	50	0
	2-Methylpentane-2,4-diol	44	56	0
	2,3-Dimethylbutane-2,3-diol	39	61	0
	2,5-Dimethylhexane-2,5-diol	39	61	0
	PEG 200	2	98	0
	PEG 1000	31	69	0

Note. Reaction conditions: amount of dihalo-derivative 5.36 mmol; amount of KOH 500 mmol, amount of catalyst 10^{-4} mol, amount of cocatalyst 2×10^{-4} mmol, amount of petroleum ether 5 ml, temperature 75 °C, time 2.5 h.

It has been established,[40] that apart from tertiary diols, primary diols in which the OH groups are separated by 6–8 carbon atoms are also extremely effective.

Fig. 5 shows how the yield of the elimination products varies in the presence of the cocatalyst (in the given instance pinacol) and in its absence.[40] The effect is most marked in the case of the least reactive chloro-derivative. It is extremely striking that the quaternary ammonium salt (QAS)–diol catalytic system does not ensure, in contrast to poly(ethylene glycols), the isomerisation of an alk-1-yne to an allene and an alk-2-yne. In all probability, this is induced by the completely different structure of the catalytic complexes involved in the reaction, because, as mentioned previously, we find, firstly, that, in contrast to polyglycols, diols do not increase the basicity of the organic phase in the absence of a QAS and, secondly, that the addition of a QAS to polyglycols also does not induce an increase in the basicity of the organic phase.[39] It is also noteworthy that, like other primary alcohols, ethanol is a fairly weak cocatalyst. Nevertheless, QAS–alcohol systems have been used widely by many investigators in elimination and alkylation reactions.[42] The study of the kinetics of the dehydrochlorination of 1,2-dichloroethane, catalysed by the TEBA–benzyl alcohol mixture,[43] showed that the dependence of the initial rate of reaction on the benzyl alcohol concentration passes through an extremum. The formal order of the reaction with respect to the concentration of alkali was ~2.5. In order to account for this, an extremely complex kinetic scheme was postulated. However, our calculations showed that the substitution of the activity of NaOH for its concentration leads to the first order of the reaction with respect to the above reactant, which renders the authors' entire reasoning[43] concerning the proposed mechanism extremely ill-founded. It is also essential to note that the intermediate complex, whose formation has been postulated,[43] cannot be produced for physical reasons.

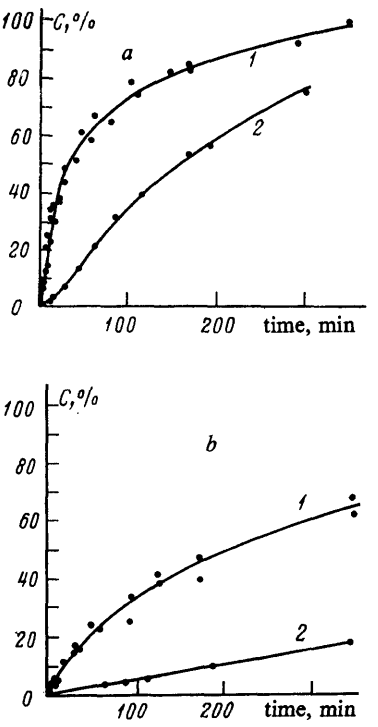


Figure 5. Elimination of 1,2-dibromooctane (*a*) and 1,2-dichlorooctane (*b*) by solid KOH in the presence of $(C_8H_{17})_4NBr$ with (curves *1*) and without (curves *2*) the addition of pinacol.[40]

The influence of a large number of different added proton-donating compounds on the katamin-catalysed dehydrochlorination of the α-isomer of hexachlorocyclohexane has been investigated.[22] Fig. 6 illustrates the dependence of the initial rate of reaction on the concentration of the additive. The dashed line represents the initial rate of reaction in the absence of the additive. Whereas the addition of a carboxylic acid inhibits the reaction, as might have been

expected, while that of benzyl alcohol accelerates it (the acceleration is directly proportional to the alcohol concentration), the addition of phenol and pentachlorophenol leads to complex relations. In our view, this is associated with the formation of complexes of the above compounds with the substrate, because according to Brandston's data,[11] phenols and other weak acids can be extracted in the presence of alkali by quaternary salts not only in the form of anions but also in the unionised form as a complex with the QAS. In particular, it has been shown that, after the addition of a base and a QAS to a phenol or carboxylic acid solution in methylene chloride or a similar solvent, the RO^-Q^+, $RO^-Q^+(ROH)$, $RO^-Q^+(ROH)_2$, etc. species are formed in the organic phase. Species of this kind can interact, in their turn, with the substrate. The formation of substrate–QAS–additive ternary complexes has been demonstrated by spectroscopic methods. The degree of association of the complex $CHCl_3/NEt_3$/TEBA calculated from IR spectroscopic data is 0.13.[44]

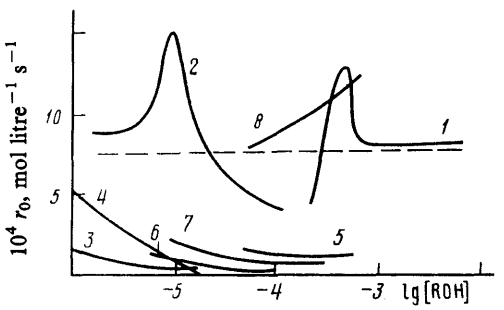


Figure 6. The influence of added proton-donating compounds on the rate of alkaline dehydrochlorination of the α-isomer of hexachlorocyclohexane in catalysis by katamin AB;[22] Additives: *1*, phenol; *2*, C_6Cl_5OH; *3*, $C_5H_{11}COOH$; *4*, picric acid; *5*, L-histidine; *6*, VIK-1 (mixture of α-methyl-substituted carboxylic acids, C_7-C_9 fraction); *7*, *o*-$HOC_6H_4SO_3H$; *8*, $C_6H_5CH_2OH$.

The available data[45] suggest that the following processes take place in the system:

$$ROH + NaOH \rightleftarrows NaOR + H_2O,$$
$$NaOR_w + QCl_w \rightleftarrows QOR_w + NaCl_w,$$
$$QOR \rightleftarrows QOR_{org},$$
$$QOR_w + nROH_w \rightleftarrows (QOR.nROH)_w,$$
$$(QOR.nROH)_w \rightleftarrows (QOR.nROH)_{org},$$
$$NaOH_w + QCl_w \rightleftarrows QOH_w + NaCl_w,$$
$$QOH_w + nROH_w \rightleftarrows (QOH.nROH)_w,$$
$$(QOH.nROH)_w \rightleftarrows (QOH.nROH)_{org}.$$

The role of the base can be assumed in the given instance by both $(QOH.nROH)_{org}$ and NaOH (through the interface). The QOR and $(QOR.nROH)_{org}$ species are most probably not reactive in the given process, which explains the extremum in the dependence of the initial rate of dehydrochlorination on the phenol concentration. The acceleration of the alkali elimination reaction after the addition of phenol to the QAS was observed also in the synthesis of phenylacetylene.[46] Unfortunately, detailed data are not available. The results of Sirovskii et al.[22] show that the effect of the additive depends on its acidity. Compounds with $pK_a < 5$ cause inhibition, those with $5 < pK_a < 10$ give rise to both synergism and inhibition, and those with $pK_a \geqslant 10$ give rise to synergism alone. On the other hand, according to another study,[47] the addition to the system of compounds more acid than water, particularly phenol, inhibits the substitution of hexyl chloride by sodium formate. The authors[47] believe that the presence in the system of compounds promoting extraction as a result of the formation of hydrogen bonds via the scheme

$$QX_{org} + HZ_w \rightleftarrows QX\ldots(HZ)_{n(org)}\ [\text{or } Q^+(HXZ)^-\ldots(HZ)_{n-1(org)}],$$

inhibits the process in all cases. In the light of the data presented below, this conclusion appears to be not entirely justified.

The synergistic effect of a mixture of two types of phase transfer catalysts has been observed in the alkylation of malonic ester by alkyl halides.[48] When a mixture of aliquat with crown-ethers was used, the initial rate of alkylation and sometimes the yield of the product were higher than would be expected from the simple summation of the catalytic effects. However, the mechanism of the cocatalytic action is not entirely clear in this instance.

It is of interest to note that the addition of an acid to the QAS increases the yield of the product in the bromination of cyclopentadiene by sodium hypobromite:[49]

$$C_5H_6 + NaOBr \xrightarrow{QX+RCOOH} C_5Br_6.$$

The corresponding data are presented in Table 7. The addition of the carboxylate anion probably promotes the extraction of the OBr^- into the organic phase.

Table 7. The influence of the catalyst on the yield of hexabromocyclopentadiene.

Concentration of $[(C_{7-9}H_{15-19})_3NMe]_2SO_4$, mM	Concentration of VIK-1*, mM	Yield of hexabromocyclopentadiene, %
0	0	56.3
7.75	0	28.0
0.775	3.05	65.4
1.55	6.1	78.1
3.10	12.2	50.0
7.75	30.5	48.4

Note. Reaction conditions: temperature from 0 to 5 °C, $V_{org}/V_w = 0.11$
*VIK-1 is a mixture of α-methyl-substituted aliphatic carboxylic acids (C_5-C_7 fraction).

In studies[44,50,51] devoted to the synthesis of cyclopropyl ethers by the addition of dichlorocarbene to olefins, the synergism, observed for the first time by the authors, occurring when mixtures of TEBA with a series of complex-forming agents are used, was investigated. Fig. 7 presents an example of the synergistic effect of TEBA and

triethylamine in the formation of 7,7-dichloronorcarane from cyclohexene and $CHCl_3$ on treatment with solid KOH. For a quantitative description of the effects of additives, the synergistic coefficient was used: $K_s = \eta_3/(\eta_1 + \eta_2)$, where η_1 and η_2 are the yields of the products when the phase transfer catalyst and the additive respectively are used separately and η_3 is the yield for the mixture comprising equimolar amounts of the catalyst and the additive. Depending on the mixture composition, an acceleration (synergism of the catalysts) or inhibition (antagonism of the catalysts) were observed (Table 8).

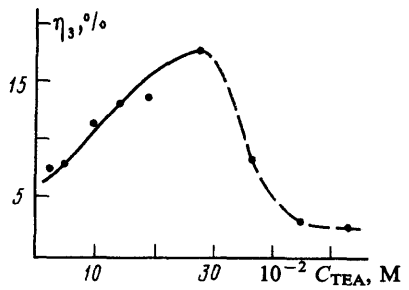


Figure 7. Dependence of the yield of 7,7-dichloronorcarane on the content of the triethylamine (TEA) in the reaction mixture (20 °C, 5 min, molar ratios cyclohexene: chloroform: solid NaOH: TEBA = 1:5:9.04:0.02; when TEBA at a concentration of 0.5 mM is used without added triethylamine, η_1 = 4.8%, while in the presence of triethylamine at a concentration of 0.5 mM without added TEBA, η_2 = 2.3%).[44]

The use of certain additives (for example, NEt_3, activated charcoal) in non-catalytic amounts leads to a complex variation of K_S (an initial increase followed by a sharp decrease). A similar picture has been observed also after the introduction into the catalytic mixture of a third component (for example, ethanol) capable of forming a complex both with the phase transfer catalyst or the additive and with $CHCl_3$. K_S depends also on the ratio of the components and the reaction temperature and is determined by the nature and content of alkali in the reaction mixture. A decrease in the amount of alkali introduced into the reaction lowers the observed synergistic effect as far as antagonism ($K_S < 1$).

In all probability the reaction is accelerated in the $CHCl_3$ deprotonation stage. Homoassociated species, in which the proton of one molecule is located between the two C–Cl bonds of a neighbouring molecule as a result of the formation of hydrogen bonds, are known to be formed in liquid $CHCl_3$.[52] Under the reaction conditions, the presence of such associated species can give rise to steric hindrance to the attack by the hydroxide ion on the C–H bond in $CHCl_3$, which leads to the formation of the anion CCl_3^-. Tertiary amines and quaternary ammonium salts exist in $CHCl_3$ as complexes with chloroform of types (VIII) and (IX):[52,53]

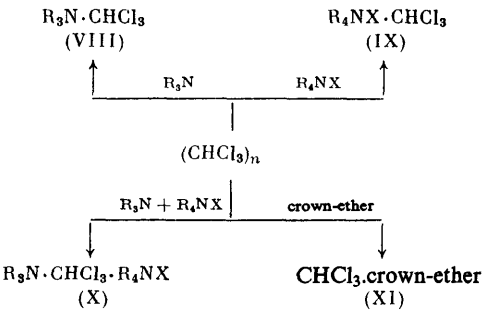


Table 8. The yields of 7,7-dichloronorcarane in the presence of various catalysts and their mixtures.[51]

Components of catalytic mixture a	Yields, %			K_S
	η_1	η_2	η_3	
TEBA/NEt_3	16.3	7.2	51.1	2.17
TEBA/PhOH	16.3	2.0	47.7	2.6
TEBA/EtOH	16.3	2.8	54.8	2.86
TEBA/Bu_3PO	16.3	2.2	55.8	3.02
NEt_3/ARA-5p* anion exchanger	7.2	1.1	3.0	0.36
NEt_3/PEG-4000	7.2	6.5	13.6	0.99
NEt_3/Sintanol DS-10**	7.2	5.5	30.7	2.42
NEt_3/15-crown-5	7.2	10.1	36.0	2.08
NEt_3/DB-18-crown-6	7.2	15.1	44.1	1.98
TEBA/activated charcoal	16.3	0.8	40.3	2.35
DB-18-crown-6/activated charcoal	15.1	0.8	17.9	1.12
TEBA/DB-18-crown-6	16.3	15.1	58.6	1.87
TEBA/15-crown-5	16.3	10.1	56.8	2.15

Note. Reaction conditions: T = 283 K, 2 mol% of catalyst, SKT charcoal.

*The ARA-5p anion-exchange resin contains the $[C_6H_5CH_2N^+.(CH_3)_3]Cl^-$ exchange groups.

**Sintanol is the monoalkyl ether of poly(ethylene glycol) $C_{10}H_{21}O.(C_2H_4O)_{10}H$.

In complexes of this kind, the C–H bond in $CHCl_3$ should be more polar than in the homoassociated species. After the simultaneous introduction into $CHCl_3$ of a phase transfer catalysis and an additive, one may expect the formation, together with complexes (VIII) and (IX), of mixed complexes (X) in which the polarisation of $CHCl_3$ is more pronounced than in two-component complexes, as shown by IR and ^1H NMR spectroscopic data.

Thus the $CHCl_3$ molecule removed from the homoassociated species as a result of binding into complexes (VIII)–(IX) is activated as a consequence of the polarising action of the catalyst, which facilitates the heterolysis of the C–H bond and the formation of CCl_3^-. In binary mixtures of catalysts, deprotonation should take place more readily, since the phase transfer catalyst and the additive exert a concerted polarising action on different centres in the $CHCl_3$

molecule [complex (X)]. Since all the catalysts and additives listed in Table 8 are capable of forming complexes of different nature with $CHCl_3$ [including complex (XI)], it becomes understandable why the independent use of compounds which are not traditional phase transfer catalysts but exhibit donor–acceptor properties leads to the formation of dichloronorcarane (η_3 = 0.8–2.8%) and why their use in a mixture with the phase transfer catalyst gives rise in most cases to a synergistic effect ($K_S > 1$). The postulate that the acceleration of the addition of dichlorocarbene takes place in the deprotonation stage is supported by the analogous influence of additives also in reactions of other CH acids when the reaction takes place under the conditions of phase transfer catalysis and involves the stage indicated: in the intramolecular cyclisation of γ-chloropropyl mesityl sulphone in the presence of dimethyl sulphoxide (DMSO) and in deuterium exchange involving DMSO.[44] Overall, the nature of the activity of the above phase transfer catalysts and catalytic mixtures in these reactions is the same as in the dichlorocarbene addition reactions.

Cases of the inhibition of the reaction (Table 8) can be best explained by steric hindrance to attack on the C–H bond of the chloroform by the hydroxide ion OH^- in the pre-reaction three-component complex. This explanation is confirmed by the finding that, when a series of $Alk_4NX/NAlk'_3$ pairs (Alk = C_1–C_4; Alk′ = C_1–C_{20}) are used, the synergistic coefficient changes from $K_S > 1$ to $K_S < 1$ with increase in the length of the Alk or Alk′ carbon chain. However, one cannot rule out additional causes of the non-additive changes in the reaction rate such as the formation of complexes between the catalyst and the additive,[54] the modification of the catalyst by the additive,[41] or the participation of the catalyst and the additive in different stages of the process.

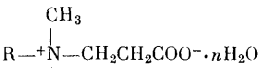
In some cases inhibition is induced by the solvent (benzene or toluene).[55] In reactions involving the alkylation of acetone by prenyl chloride, inhibition was observed after the replacement of part of the acetone by toluene despite the zero order of the reaction with respect to acetone.[55] The authors explained this effect by the "inhibiting" influence of toluene. The Lineweaver–Burk plots of the observed dependence of the rate constant on the catalyst concentration at different benzene concentrations consists of a set of straight lines intersecting in one point, which indicates inhibition of a mixed type. According to the authors,[55] in the given instance the solvent forms solvate complexes with QX and QA. Here A^- is acetone enolate, whose concentration is defined by the equation $[A^-] = K_e[AN]a_{OH^-}a_{H_2O}$, where K_e is the equilibrium constant for the deprotonation of the acid HA by OH^-, a_{OH^-} the activity of the hydroxide ion, a_{H_2O} the activity of water, and [AN] the concentration of acetone in aqueous alkali. The authors estimate the constant K_e as the ratio $K_{HA}/K_{H_2O} = 10^{-20}/10^{-16}$. According to their data,[55] 30% of acetone dissolved in 50% NaOH is enolised. Calculation of kinetic data showed that QX is bound by toluene approximately 6 times more effectively than QA. This is induced by the more pronounced lipophilicity of QA and by the fact that Cl^- is more effective solvated by toluene than A^-.[55]

Consideration of the above instances of synergism and inhibition permits the conclusion that complex formation processes in fact determine the mode of the action of the additive—synergistic or inhibiting. As a rule, synergistic action is manifested on formation of ternary complexes incorporating the phase transfer catalyst, the substrate, and the additive. The binding of the additive in a complex with only one of the components leads to inhibition.

V. Catalysis by betaines

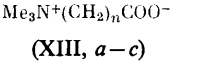
At first sight the topic of this section does not fit within the general framework of the review. However, we believe that the transition from the use of two-component catalytic systems to the construction of bifunctional catalysts is an entirely logical stage and that the use of betaines as such catalysts is one of the first steps in this direction.

It has been stated in a monograph[56] that, in the presence of the betaine $(C_{12}H_{25})_3N^+CH_2COO^-$, the interaction of alkyl halides with aqueous alkali is 10–50 times faster than in the presence of the usual onium salts. The application of betaines of the type $R_3N^+(CH_2)_nCOO^-$ and $C_{12}H_{25}N^+R_2(CH_2)_nSO_3^-$ as promoting agents for the alkaline dehydrochlorination reactions of chlorobutanes and chlorobutenes was described as early as 1973.[57] A wide scale study of betaines as phase transfer catalysts has been undertaken recently.[58,59] Gol'dberg et al.[68] synthesised a series of betaines having the following structure:

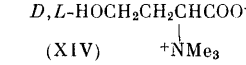


(XII, *a*–*j*)

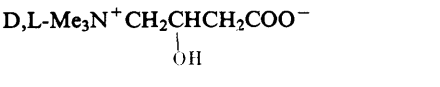
(*a*–R = CH_3, *n* = 2; *b*–R = C_2H_5, *n* = 1; *c*–R = n-C_3H_7, *n* = 0; *d*–R = iso-C_3H_7, *n* = 2; *e*–R = n-C_6H_{13}, *n* = 1; *f*–R = n-$C_{10}H_{21}$, *n* = 1; *g*–R = n-$C_{12}H_{25}$, *n* = 1; *h*–R = n-$C_{16}H_{33}$, *n* = 0; *i*–R = $CH_2C_6H_5$, *n* = 1; *j*–R = $CH_2CH_2C_6H_5$, *n* = 2)



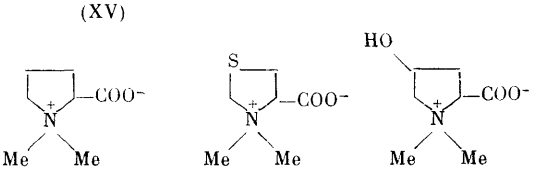
(XIII, *a*–*c*)



(XIV)



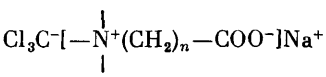
(XV)



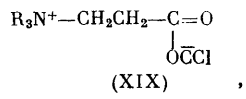
L-(XVI) L-(XVII) L-(XVIII)

The betaines (XIII)–(XVIII) were tested as catalysts of two-phase reactions involving dichlorocarbene: the conversion of styrene into dichlorocyclopropane, dehydration of benzamine, and *N*-formylation of pyrrolidine. The betaine based on *b*-alanine (XIII*b*), homoserine (XIV), proline (XVI), and carnitine (XV), in the presence of which the yields of products attained were close to those obtained with the aid of the usual phase transfer catalyst, proved to be the most effective.[58] The betaines (XII*a*–*j*) have also been used in the conversion of styrene into dichlorocyclopropane and in the dehydration of benzamine and their activity proved to be close to that of TEBA. The use of these betaines in the Williamson reaction was found to be less effective; the yield of benzyl propyl ether in the reaction of propanol with benzyl chloride was lower by a factor of approximately 3 than in the case where NBu_4HSO_4 was used.[59]

It has been suggested[58,59] that the mechanism of the catalysis by betaines differs from that proposed for the usual onium salts, because betaines are incapable of solubilising the CCl_3^- anion in the form of an ion pair. On formation of a bis-ion pair of the type



the catalytic activity should have increased with increase in the length of the chain connecting the carboxy-group to the onium centre. However, the opposite behaviour is observed: the catalytic activity falls in the sequence (XIII*a*)–(XIII*b*)–(XIII*c*). The authors[58,59] believe it to be more likely that the electrophilic dichlorocarbene interacts with the carboxylate anion to form the betaine (XIX)



(XIX) ,

which is capable of migrating into the bulk of the organic phase and acting similarly to the ylide formed when trialkylamines are used as catalysts. This mechanism is confirmed by the absence of a relation between the lipophilicity of the onium component of the catalyst and its catalytic activity (Table 9).[59]

Table 9. The reaction of styrene with dichlorocarbene in the presence of the betains (XII).[59]

Catalyst (XII)	Reaction time, h	Yield of product, % of theoretical	Catalyst (XII)	Reaction time, h	Yield of product, % of theoretical
Without catalyst	4.5	4	*f*	0.5	98
TEBA*	0.5	71	*g*	0.5	81
a	2.5	59	*h*	0.5	80
b	0.5	64	*h**	0.5	79
c	0.5	75	*i*	2.5	70
d	0.5	58	*j*	2.5	31
e	0.5	100			

Note. Reaction conditions: 1.7 mmol of styrene, 2.5 ml of $CHCl_3$, 1.5 ml of 50% aqueous NaOH, 1 mol% of catalyst, temperature 25 °C.
* 0.5 mol% of catalyst.

The high catalytic activity of betaines, comparable to the activity of the usual onium salts, leads to the possibility of "constructing" new catalytic salts, leads to the possibility of "constructing" new catalytic systems containing in one molecule both a catalyst and a promoting agent fragment. The carboxylate group need not necessarily be used as the promoting agent. There are data showing that the introduction of the OH^- or NH_2 group into the quaternary salt molecule in the β-position relative to the onium centre also increases the catalytic activity.[60] It is also known that the activity of chiral catalysts increases after the introduction of the OH group in the β-position relative to the nitrogen atom. All these features provide extensive opportunities for investigators who have a lively imagination and are skilled in the art of organic synthesis.

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