

## Synergism and antagonism in phase transfer catalysis\*

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Synergism and antagonism phenomena in phase transfer catalytic reactions have been considered. The factors responsible for the synergism in the catalysis by an onium salt — crown ether mixture have been determined. Special attention have been paid to quantitative estimation of synergism and antagonism. The influence of addition of water on the rates of the reactions in solid—liquid systems have been discussed.

**Key words:** phase-transfer catalysis, synergism, antagonism, hydrolysis, aminolysis, quaternary ammonium salts, crown ethers.

The terms synergism (Greek *synergeia*, cooperation), synergist (Greek *synergos*, acting jointly) have been used in the literature to describe an effect of a mixture of two compounds that exceeds the sum of the effects of the individual components. Applied to catalytic processes, this term means a nonadditive increase in system reactivity when a mixture of two or several catalysts is used. A decrease in reactivity will be denoted as antagonism (Greek *antagonisma* — active opposition) and the mixture components as antagonists (Greek *antagonists* — acting against each other). Contrary to the above definitions, the frequent use of the term "synergism" implying "co-catalysis" and "antagonism" meaning "inhibition" is rather common in the chemical literature.

The review<sup>1</sup> published in 1991 showed that the investigation of synergism in phase transfer catalysis (PTC) is still in its infancy. Up to now, there is no justified classification of the phenomena that should be assigned to synergistic effects in PTC.

Synergistic and antagonistic phenomena have long been known in homogeneous and heterogeneous catalysis.<sup>2</sup> These terms imply a nonadditive increase (decrease) in the catalytic reaction rate with a mixture of two or several homogeneous or heterogeneous catalysts. A rise in catalyst activity resulting from the introduction into the reaction system of substances that are not catalysts themselves is usually referred to as activation or promotion. Consequently, synergism (antagonism) in PTC is the nonadditive increase (decrease) in the reaction rate with a mixture of two or several phase transfer catalysts. To reveal this effect it is necessary to study the dependence of the reaction rate on the concentration of the individual catalysts and then on their concentrations

in the mixture while keeping their total concentration constant. This approach allows the effects of synergism and antagonism to be revealed unambiguously as well as to be described quantitatively.<sup>3–5</sup>

In the field of PTC the mentioned approach is used but partly in a few works,<sup>6–9</sup> and in some of them<sup>7,8</sup> in a very simplified variant, when instead of the reaction rate the yield of the reaction product was determined.

The term synergism is often used in PTC in a reference to the increase in the reaction rate on introduction of a phase transfer catalyst along with some organic compounds of acid-base nature (alcohols, phenols, carboxylic acids, amines, *etc.*), which themselves usually could not transfer the ions from one phase into another (see the review<sup>1</sup> and the references therein). These cases appear to deal with the phenomenon of co-catalysis rather than with that of synergism. One could mention the only work,<sup>8</sup> where the synergism was reliably established in use of the mixture of phase transfer and homogeneous catalysts. It was shown, that in the presence of the mixture of tetrabutylammonium chloride ( $\text{Bu}_4\text{NCl}$ ) and organic bases, for example, triethylamine, the yield of dichloronorcarane produced from cyclohexene and chloroform in the system with solid alkali or potassium carbonate increases as compared with the yield expected from the additivity grounds. For the quantitative characteristics of this effect the coefficient  $k_S$  was introduced.<sup>8</sup> It is equal to the ratio of the yield of the reaction product in the presence of the mixture of catalysts ( $h_3$ ) to the sum of the yields of the products in the presence of the individual catalysts ( $h_1 + h_2$ ):

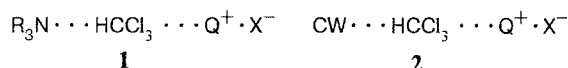
$$k_S = h_3 / (h_1 + h_2). \quad (1)$$

When  $k_S > 1$ , the synergism occurs, when  $k_S < 1$  the antagonism occurs. The positive effect resulted from the

\* In memory of the 75th anniversary of Member of the Academy of Sciences of Ukrainian SSR L. M. Litvinenko.

use of the mixture of the quaternary ammonium salt (QX) and the organic base was attributed by the authors to the formation of the triple complexes of type **1**, that results in the decrease in chloroform self-association (homogeneous catalysis) and in more effective chloro-carbene generation at the interface (PTC).

It is interesting to note that the mixture of two typical phase transfer catalysts tetrabutylammonium chloride and 18-crown-6 (CW) also exhibits synergism in the considered reaction. The function of the crown ether in this pair is considered by the authors to be similar to that of an organic base (complex **2**).

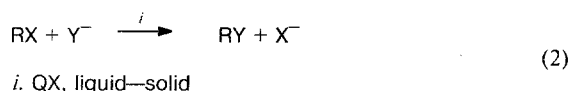


In principle, this mechanism is possible, because crown ethers are able to serve as electron donors in hydrogen bond formation. However, it does not exclude some other mechanisms of joint action, in particular, the formation of the multi-centered complexes, where both components behave as typical phase-transfer catalysts.

Water has a special place among protic additives, which strongly affects the rate of phase-transfer processes in solid—liquid (s/l) systems. Besides participating in general acid-base catalysis and solvation, water can also influence the reaction rate due to the formation of a "third" phase, the so-called omega phase. Dramatic increase in the reaction rate resulting from even minute addition of water into the s/l system<sup>10–14</sup> illustrates its outstanding role.

Solid—liquid systems, in which one of the reagents or the catalyst may be used as a solid, attract the most attention of chemists. Compared to the processes in liquid—liquid (l/l) system, these technologies are more ecological. To catalyze the reactions in s/l systems the two types of phase transfer catalysts are generally used: quaternary onium salts and crown ethers. Although the mechanisms of such processes are generally investigated,<sup>15,16</sup> the problem of the influence of water and other additives of acid-base nature still remain complex and ambiguous.

It is suggested<sup>17,18</sup> that the activity of a phase-transfer catalyst in the s/l system depends on its ability to "extract" the ion from its crystal lattice. Apart from other reasons, the lattice strength depends on the degree of hydration of ions, *i.e.*, on the amount of water in the system. The works<sup>10–14</sup> argued that substitution reactions of the following type

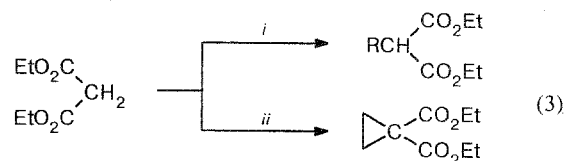


practically do not occur in nonaqueous solutions. According to the authors' opinion, the reason is that the quaternary salt is not able to abstract the non-hydrated ion out of the crystal lattice. Nevertheless it was shown<sup>19</sup>

that the reaction of benzyl and hexyl bromides with solid salts (KF, KCN, CH<sub>3</sub>COOK) occurs in dry acetonitrile using the carefully dried reagents.

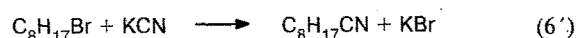
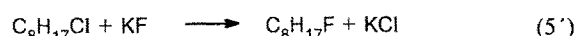
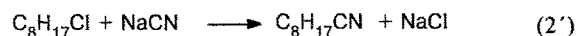
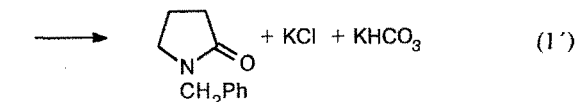
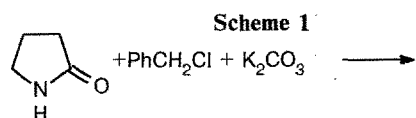
In this regard the apparent conflict of the results obtained by the authors<sup>20,21</sup> seems to be very characteristic. It was found<sup>20</sup> that the reaction of hexachlorocyclophosphazotriene [PNCI<sub>2</sub>]<sub>3</sub> phenolysis by triethylammonium aryl oxides passes tenfold faster in benzene saturated with water than in a nonaqueous solvent. At the same time the authors<sup>21</sup> report the deactivating influence of water on the PTC phenolysis of cyclic chlorophosphazone compounds [PNCI<sub>2</sub>]<sub>*n*</sub> (*n* = 3, 4) in the chlorobenzene—water system. Such a disagreement arises from the fact that the investigations of the influence of water are often carried out at different concentration ranges. In fact, some publications<sup>1,11,12,14,22,23</sup> describe an extremum dependence of the reaction rate or yield on the total amount of water in the solid—liquid system, the influence of water being the most pronounced in the low-concentration range. The authors<sup>11,12,14</sup> consider this phenomenon to be associated with the formation of a peculiar kind of water layer (the omega phase) on the solid surface. A phase-transfer catalyst is concentrated in this phase, which is responsible for the transportation of the anion into the organic phase, where the anion reacts with substrate. However the activating (deactivating) influence of water can be also caused by some other reasons: dissociation of ionic reagents, variations in the ratio of the reactivities of ions and ion pairs, specific solvation of the leaving group. The position of the extremum on the plot of rate vs. water amount seems to be an individual characteristic of the particular PTC process. It is determined mostly by the interrelation of the effects responsible on the one hand, for the transfer of reacting species (PTC), and on the other hand for their reactivity (homogeneous catalysis, promotion). Scheme 1 represents some examples of PTC reactions in a solid—liquid system where the extremum rate dependence on the total amount of water was observed. The scheme indicates, that the position of the extremum varies in a rather wide range (from 3 to 30%). From the discussion below it will follow that the problem of the influence of water in liquid—solid systems is closely related to synergism and antagonism in PTC.

One of the first examples of the quantitative approach to the investigation of the effect caused by the application of a mixture of phase-transfer catalysts was<sup>7</sup> the alkylation of malonic ester by alkyl halides in the toluene—potassium carbonate system.



*i.* QX, CW, RX

*ii.* C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>—K<sub>2</sub>CO<sub>3</sub>—XCH<sub>2</sub>CH<sub>2</sub>X



Reaction	Catalyst	Water content (%)	References
1'	QX	12	12
2'	$\text{C}_{16}\text{H}_{33}\text{P}^+\text{Bu}_3\text{Br}^-$	30	22
3'	18-Crown-6—toluene	3.6—5.4	11
4'	18-Crown-6—toluene	7	11
5'	Aliquat-336	25	24
6'	A-27	20.5	13

With the use of the mixture of quaternary ammonium salt (Aliquat) and benzo-15-crown-5 (B-15-C-5) the increase in the reaction rate by ~20 % relative to the additively expected value (Table 1) was observed. The same work discusses the yield of the alkylation products in the presence of some individual phase transfer catalysts and their mixtures (Table 2). The catalytic pairs like Aliquat—crown ether and Aliquat—polyethylene glycol were determined to be preferable. Table 2 reports the synergism coefficients  $k_s$  calculated in the present work from the equation (2) suggested previously.<sup>8</sup> Their analysis indicates that only few of the cases (runs 8, 13, 21, 23) could be attributed to synergism with a great degree of doubt. The reason is that under the conditions of experiments (Table 3) the yield increase effected by the use of the mixture of catalysts could be mainly caused by the total increase in the concentration of catalyst. A comparison of the products yield in different experiments at equal concentrations of the individual catalysts or their mixtures would be more correct.

**Table 1.** Values of initial rates ( $k$ ) of the reaction of diethyl malonate with 1-bromobutane in a toluene— $\text{K}_2\text{CO}_3$  system in the presence of phase transfer catalysts (80°C, catalyst concentration 4 mmol L<sup>-1</sup>)<sup>7</sup>

Catalyst	$k/\text{mmol (L s)}^{-1}$
Aliquat	80
B-15-C-5	20
Aliquat+ B-15-C-5	120

**Table 2.** Yields of reaction products and coefficients of synergism for the alkylation of diethyl malonate in the presence of phase transfer catalysts and their mixtures in a toluene— $\text{K}_2\text{CO}_3$  system at 80°C<sup>7</sup>

Run	Alkylating agent	Catalyst <sup>a</sup>	Yield (%)	$k_s$
1	1-Bromobutane	A	58	
2		CW	73	
3		A + CW	90	0.442
4	Benzyl bromide	A	76	
5		CW	93	
6		A + CW	94	0.556
7		PEG-300	4	
8		CW + PEG-300	93	1.16
9	Benzyl chloride	A	54	
10		CW	40	
11		A + CW	73	0.776
12		PEG-300	3	
13		A + PEG-300	75	1.32
14	1,2-Dibromoethane	A	44	
15		CW	54	
16		A + CW	73	0.745
17		PEG-300	5	
18		A + PEG-300	46	0.939
19	1,2-Dichloroethane	A	32	
20		CW	5	
21		A + CW	72	1.95
22		PEG-300	4	
23		A + PEG-300	38	1.06

<sup>a</sup> Aliquat (A) 0.025 g, dicyclohexano-18-crown-6 (CW) 0.0113 g, polyethylene glycol 300 (PEG-300) 0.025 g.

**Table 3.** Second order rate constants ( $k_2$ ) for the reaction of 1-chlorobutane with solid KCN in acetonitrile at 50 °C and pseudofirst order rate constants ( $k_1$ ) for the reaction of 1-bromooctane with KCN in a toluene—water system at 90 °C in the presence of phase transfer catalysts<sup>6</sup>

Catalyst	Concentration of the catalyst (mol. %)	$k_1 \cdot 10^6$ s <sup>-1</sup>	$k_2 \cdot 10^4$ s <sup>-1</sup>
3	10	1030	2.7
4	10	7.2	4.2
5	10	380	7.2
3+4	10+10	990	6.8

Moreover, one should take into account that equation (1) is applicable only at low degrees of reagents conversion, because  $h_3$  values and the sums ( $h_1 + h_2$ ) are limited by 100%. It is possible that in some experiments in Table 2 the "lowered" value of  $k_s$  results from the restricted applicability of the equation (1) in case of high yields of products in the presence of both individual catalysts and their mixtures.

The synergistic effect in PTC was most correctly studied<sup>9</sup> in the alkylation of 2-methylacetoacetic ester in the acetonitrile—potassium fluoride system in the pres-

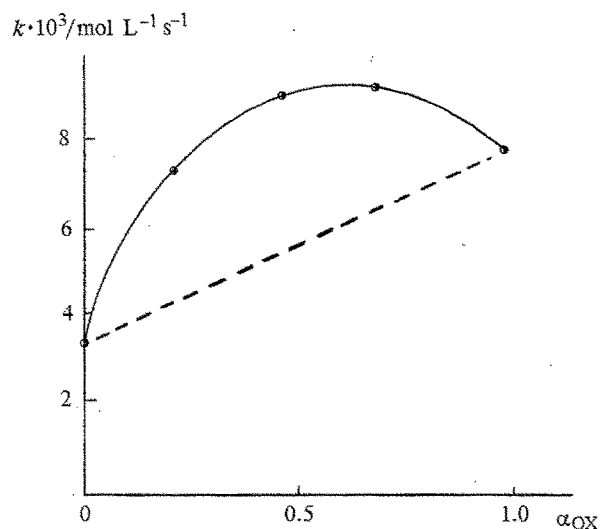
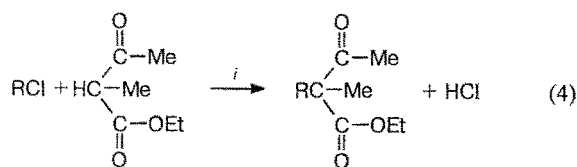


Fig. 1. Joint influence of 24-crown-8 on the rate constant of 2-methylacetoacetic ester (HA) alkylation by prenyl chloride (RY) (acetonitrile, 20°C, [RY] = 0.13 mol L<sup>-1</sup>, [QX] + [CW] = 0.1 mol L<sup>-1</sup>).<sup>9</sup>  $\alpha_{QX}$  is the mole fraction of QX in the QX + CW mixture.

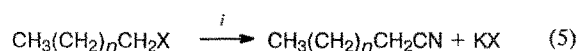
ence of a mixture of quaternary ammonium salt and crown ether.



i. QX, CW, acetonitrile—KF

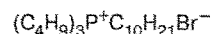
The reaction kinetics were studied at various ratios of the ingredients in the mixture and keeping the total concentration of catalysts constant. Figure 1 shows the typical example of synergism. In this work the first attempt of interpretation of the mechanism of joint action of the quaternary salt and crown ether was made. According to the authors opinion, in the presence of the quaternary salt the reaction proceeds at the interface. In the presence of crown ether it proceeds in the organic phase which extracts potassium fluoride, the latter serving as a base in the formation of a carbanion from methylacetoacetic ester. The better extraction of KF when the mixture of catalysts is used (this fact was previously known from other works) results in synergism.

A peculiar approach to investigation of the joint catalysis by onium salt and crown ether was applied<sup>6</sup> in the cyanation of alkyl halides.

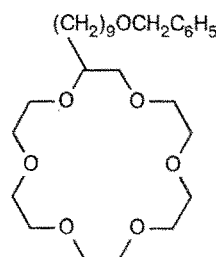


i. QX, CW, 1) acetonitrile—KCN  
2) toluene—aqueous KCN

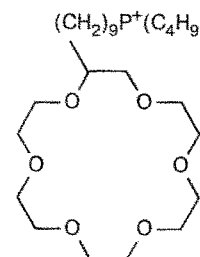
Tributyldecylphosphonium bromide **3** and crown ethers **4** and **5** were used as catalysts.



**3**



**4**



**5**

One can see from Table 3 that catalyst **5**, wherein the onium function is united with the crown ether fragment, is the most effective catalyst in the s/l system as compared with individual catalysts **3** and **4**. It is interesting that the mixture of onium salt **3** and crown ether **4** demonstrates no synergism. In the toluene—water system there is also no synergism for catalysts **3** and **4**. At the same time catalyst **5** exhibits reduced activity, which is associated by the authors with its high hydrophobicity.

Summarizing the analysis of the literature concerned with joint action of the two types of phase-transfer catalysts (quaternary onium salts and crown ethers), one should note that in the literature cited<sup>6-9</sup> the existence of the effect of synergism was established on the basis of a very few kinetic data. Some of the authors attribute the fact of the increase in product yield to the result of the action of a catalyst mixture, neglecting the rule of constancy of sum of concentrations, which is necessary to reveal the effect correctly. There are no basic criteria for quantitative determination of synergism (antagonism). The site of the reaction and its rate-limiting stage both in the presence of individual catalysts and their mixtures were not established.

We offer the following approach for revealing and establishing the synergism (antagonism) in PTC using as the example the catalysis by onium salt QX and crown ether CW.

Firstly, it is necessary to establish the site of the reaction and the rate-limiting stage of the PTC process.

Secondly, one must determine rate constants characterizing catalysis by the onium salt ( $k_{QX}$ ), by the crown ether ( $k_{CW}$ ), and by their mixture ( $k$ ) conforming to the following conditions: [QX] =  $C_1$ , [CW] =  $C_2$ , [QX + CW] =  $C_1 + C_2 = \text{const}$ .

In the case of additive action of the catalysts QX and CW the following equation is obeyed

$$k = k_{ad} = k_{QX} + k_{CW} \quad (6)$$

If synergism (antagonism) occurs, the increase (decrease) in the rate constant takes place

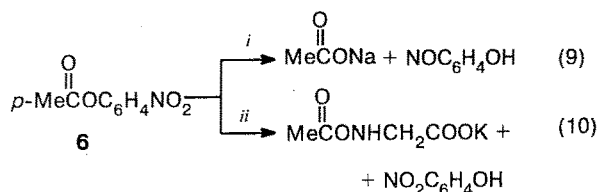
$$\Delta k = k - k_{ad} \quad (7)$$

As a quantitative measure of the effects listed above we offer the value  $S$ , equal to the ratio of the increase in the rate constant to the sum of catalytic rate constants.

$$S = \Delta k / k_{ad} \quad (8)$$

The absolute value of  $S$  indicates the part of the expected additive value constitutes this change (increase or decrease) in the rate constant.

We have studied the kinetics of the reaction of *para*-nitrophenyl acetate (**6**) with solid sodium and potassium hydroxides and with potassium glycinate (anhydrous and monohydrate) in the presence of onium salts QX (**7a-c**) and crown ethers CW (**8a-c**), as well as their mixtures in a s/l system (stirring speed 400 rpm) at 25°C.



i. QX, CW, toluene—NaOH (KOH)

ii. QX, CW, organic solvent—NH<sub>2</sub>CH<sub>2</sub>COOK

QX: Et<sub>4</sub>NBr (**7a**); C<sub>16</sub>H<sub>33</sub>Me<sub>3</sub>NBr (**7b**); Ph<sub>4</sub>PCl (**7c**)

CW: 18-crown-6 (**8a**); dibenzo-18-crown-6 (**8b**); dicyclohexano-18-crown-6 (**8c**)

Sodium and potassium hydroxides (Lachema, NaOH 96.5%, carbonates 0.2%, H<sub>2</sub>O 3.3%; KOH 84%, carbonates 4.4%, H<sub>2</sub>O 11.6%) were used. Solid reagents were crushed in a ball mill to the particle size of 20±10 μm. The water content in a solid alkali was found to influence the reaction rate. However, the results were reproduced with an accuracy of 5–10 % or better if one and the same lot of reagents was used.

All the kinetic measurements were performed under conditions providing kinetics of the pseudofirst order on ester **6**. The reaction rate in a two-phase system ( $k/s^{-1}$ ) and in an organic phase ( $k_{org}/s^{-1}$ ) was observed by the accumulation of *n*-nitrophenoxide ion in a bulk of the solvent at 410 nm. Sampling in the two-phase system was carried out using Schott filter as a nozzle at the continuous stirring. Under the experimental conditions almost all the phenol (more than 98%) was presented in the organic phase in the form of phenoxide ion.

The values of  $k$  and  $k_{org}$  are the ones determined experimentally. Their difference was assumed to be the rate constant of the reaction at the interface ( $k_{if}$ ).

$$k_{if} = k - k_{org} \quad (11)$$

In this way it was possible to establish the site of the process. When the reaction proceeds only in the organic phase,

$$k = k_{org} \quad (12)$$

When the reaction proceeds at the interface the following equation is valid

$$k = k_{if} \quad (13)$$

If the reaction proceeds both at the interface and in the organic phase, than equation (11) is obeyed.

The data presented in Table 4 for reactions (9) and (10) in the toluene—solid phase system in the presence of catalysts **7a,c** and **8b** showed that the reaction proceeds both at the interface and in the bulk of the organic phase only in the presence of potassium hydroxide containing 11.6% of water. With 5% of the water content in KOH the reaction proceeds only at the interface. This fact, together with the extremely low reactivity of an anhydrous NH<sub>2</sub>CH<sub>2</sub>COOK as compared with its monohydrate, indicates the important role of water in these processes.

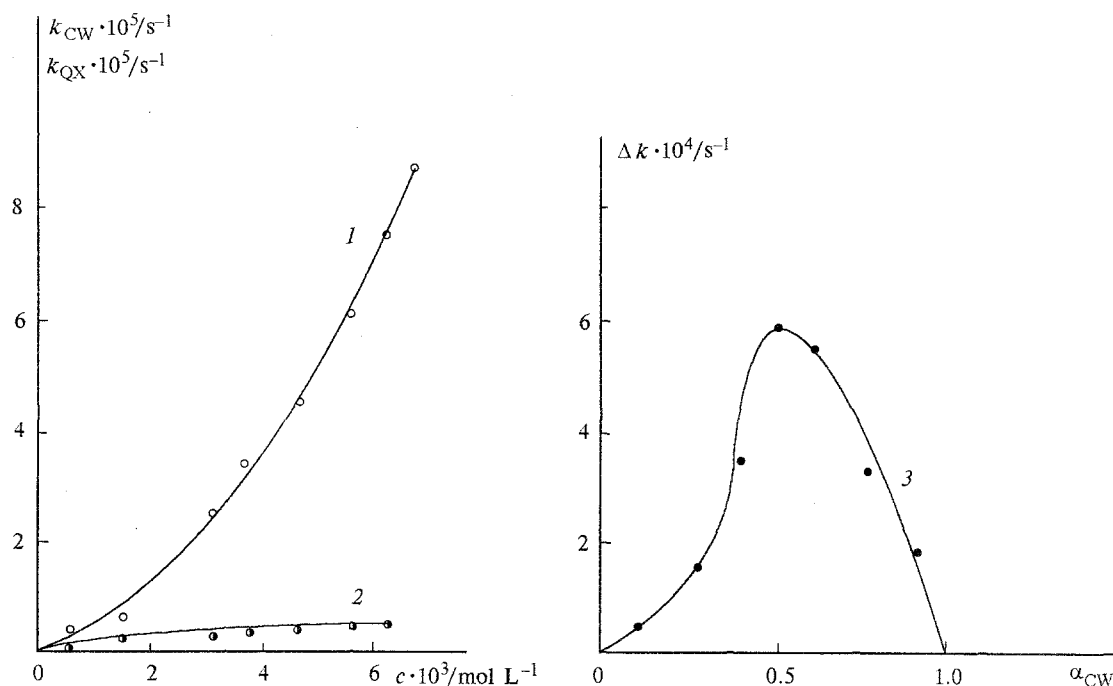
Considering the significant role of water, we believe that in the interface variant the reaction proceeds in some third phase, formed between a solid surface and toluene.<sup>11</sup> The omega phase should be considered as playing the crucial role in extractive and chemical interactions in this system. It is hard to determine the exact dimensions of this zone. They are most likely close to that of a monomolecular layer, because the content of water in NaOH and KOH ranges from 1 to 25 mol. %, so there is at most 1 water molecule to 3 alkali ones.

The influence of the mixture of phase transfer catalysts (18-crown-6 and tetraethylammonium bromide) on the rate of the processes under investigation was studied taking as the example reaction (9) which proceeds in the toluene—NaOH system only at the interface. The plots of the observed rate constants vs. the individual catalyst concentrations are given in Fig. 2 (curves 1, 2). Tetraethylammonium bromide accelerates this reaction

**Table 4.** Rate constants for hydrolysis<sup>a</sup> and aminolysis<sup>b</sup> of *para*-nitrophenyl acetate in a toluene—solid system ( $k_i$ ) and in organic phase ( $k_{org}$ ) in the presence of phase transfer catalysts at 25 °C

Nucleophile	Catalyst	$C \cdot 10^3$ <sup>c</sup> mol L <sup>-1</sup>	$k_{if} \cdot 10^3$ s <sup>-1</sup>	$k_{org} \cdot 10^3$ s <sup>-1</sup>
(solid phase)				
NaOH (3.3 % H <sub>2</sub> O)	<b>7a</b>	25	0.04±0.01	<sup>d</sup>
	<b>8b</b>	25	0.40±0.08	<sup>d</sup>
KOH (11.6 % H <sub>2</sub> O)	<b>7a</b>	25	0.22±0.04	0.24±0.02
	<b>8b</b>	25	0.79±0.10	0.30±0.07
KOH (5 % H <sub>2</sub> O)	<b>8b</b>	25	2.24±0.23	<sup>d</sup>
KOOCCH <sub>2</sub> NH <sub>2</sub> ·H <sub>2</sub> O	<b>7c</b>	2.5	<0.001	<sup>d</sup>
	<b>8b</b>	2.5	2.13±0.31	<sup>d</sup>
KOOCCH <sub>2</sub> NH <sub>2</sub>	<b>8b</b>	2.5	<0.01	<sup>d</sup>

<sup>a</sup> 0.056 g (1 mmol) KOH and 0.04 g (1 mmol) NaOH per 40 mL toluene,  $[6] = 2.5 \cdot 10^{-4}$  mol L<sup>-1</sup>. <sup>b</sup> 0.0113 g (0.086 mol) KOOCCH<sub>2</sub>NH<sub>2</sub>·H<sub>2</sub>O and 0.0113 g (0.1 mol) KOOCCH<sub>2</sub>NH<sub>2</sub> (anhydrous) per 20 mL toluene,  $[6] = 2.5 \cdot 10^{-4}$  mol L<sup>-1</sup>. <sup>c</sup>  $C$  — concentration of the catalyst in organic phase. <sup>d</sup> No reaction.



**Fig. 2.** Dependence of the observed pseudofirst order rate constants of the reaction of *p*-phenyl acetate with alkali in a toluene—NaOH system (25°C) on the concentrations of 18-crown-6 ( $k_{CW}$ , curve 1) and tetraethylammonium bromide ( $k_{QX}$ , curve 2); and dependence of the increase in the rate constant  $\Delta k$  (3) on the mole fraction of catalysts in their mixture. Reaction conditions: 0.01 g (0.25 mmol) NaOH, 40 ml toluene;  $[6] = 5 \cdot 10^{-5} \text{ mol L}^{-1}$ ;  $[7a] + [8a] = 6.25 \cdot 10^{-3} \text{ mol L}^{-1}$ ;  $\alpha_{CW}$  is the mole fraction of crown ether.

only slightly, but 18-crown-6 affects it noticeably. In accordance with this fact, the additive rate constant  $k_{ad}$  for the mixture of these catalysts at their summary concentration constant will be practically equal to that of 18-crown-6. In this system the significant increase in the rate constant is observed (Fig. 2, curve 3), thus synergism takes place. The calculation of  $S$  value using the equation (8) indicates, that the rate is 21 times higher as the expected additive one, i.e., the acceleration is of 2100%.

An even greater synergistic effect was found in the aminolysis of ester **6** (reaction (10)) in the acetonitrile—monohydrate of potassium glycinate system catalyzed by a mixture of tetraphenylphosphonium chloride and dibenzo-18-crown-6. This value is noticeably low ( $S = 19$ ) for the reaction in toluene. It was shown that in these solvents the reaction proceeds at the interface contrary to reactions in methanol, butanol, and *tert*-butanol, where reactions usually proceed in the bulk as well as at the interface. In alcohols synergism of the catalytic pair quaternary onium salt—crown ether is insignificant ( $S = 0.5\text{--}1.3$ ).

In this way, the differences in the joint action of the catalytic pair quaternary onium salt—crown ether should primarily be associated with the site of the reaction. Probably, it is at the interface where the most favourable conditions for the formation of a pre-reaction complex involving nucleophile, substrate, and both catalysts are created. This complex can also include water.<sup>25</sup>

When the reaction (9) proceeds in a toluene—aqueous NaOH system (1:1 by the volume) under the concentration conditions for the reagents and catalysts indicated in Fig. 2, we have observed antagonism in the presence of the catalytic pair — tetraethylammonium bromide—18-crown-6 ( $S = -0.8$ , i.e., the 80% decrease in the rate at the ratio of catalysts 1:1).<sup>26</sup> In the liquid—liquid system the reaction (9) proceeds also at the interface. The deceleration of the reaction by joint action of QX and CW in this case is first and foremost connected with the destruction of the omega phase, making it impossible for the reagents to organize into the pre-reaction complex.

This hypothesis is confirmed by the data concerned with the influence of methanol on the hydrolysis of *p*-nitrophenyl acetate in the presence of tetraethylammonium bromide and 18-crown-6. The addition of methanol into the system with mixture of catalysts **7a** and **8a** (Table 5) results in the following: 1) with the increase in the ionic additive concentration (see  $k_{if}/k_{org}$ ) the reaction transfers from the interface into the bulk of organic phase; 2) the synergism for the reaction in the organic phase ( $S_{org}$ ) is pronounced weaker than one for the reaction at the interface ( $S_{if}$ ); 3) as the concentration of the protic additive increases, the synergism decreases and at the addition of 0.06 mL methanol transforms into antagonism. Data of Table 5 for the mixture of catalysts **7a** and **8a** allow one to suppose that the highest effect of synergism takes place in the case of the reaction proceeding at the interface.

**Table 5.** Values of synergic effects for the reaction (9), proceeding in the presence of the mixture of catalysts QX (**7a,b**) and 18-crown-6 (**8a**) in toluene—NaOH<sup>a</sup> with methanol additives at 25 °C

Mixture of catalysts	CH <sub>3</sub> OH mL	$k_{if}/k_{org}$	Synergistic effect		
			$S_{org}$	$S$	$S_{if}$
<b>7a+8a</b>	0	$\gg 10^b$	No reaction	20.4	20.4
	0.02	6.2	0.8	3.4	4.8
	0.04	3.0	0.3	2.6	7.6
	0.06	3.0	-0.5	0.1	0.6
<b>7b+8a</b>	0	<sup>c</sup>	No reaction	<sup>c</sup>	<sup>c</sup>
	0.2	6.5	-0.6	0.1	0.1
	0.04	0.71	-0.5	-0.5	-0.4
	0.06	0.63	-0.5	-0.6	-0.7

<sup>a</sup> 0.01 g (0.25 mol) NaOH per 40 mL toluene;  $[6] = 5 \cdot 10^{-5}$  mol L<sup>-1</sup>,  $[QX] + [CW] = 6.25 \cdot 10^{-3}$  mol L<sup>-1</sup> at  $[QX] = [CW] = 3.125 \cdot 10^{-3}$  mol L<sup>-1</sup>. <sup>b</sup> The lower limit is estimated from the experimental error of 10 %. <sup>c</sup> It was not possible to measure the reaction rate due to sorption of *p*-nitrophenoxide anion on the solid surface.

Changing the salt **7a** for the pair of **7b** and crown ether **8a** results in an essentially different situation: with catalysis by the pair of **7b** and **8a** not only no synergism is demonstrated, but considerable antagonism takes place both for the reaction in the organic phase as well as at the interface. In the last case this effect is slightly lower, especially with small additives of methanol.

Thus, the data given above indicate that synergism for the mixture of phase transfer catalysts (quaternary onium salt and crown ether) is observed if the reaction proceeds at the interface in the presence of small amounts of water. On addition of methanol or greater amounts of water, the mixture of the same catalysts exhibits antagonism.

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