Phase-transfer and micellar catalysis in dehydrohalogenation reaction

F. S. Sirovsky

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
47 Leninsky prosp., 117913 Moscow, Russian Federation.
Fax: +7 (095) 135 5328; E-mail: sirovsk@ioc.ac.ru

Quaternary ammonium salts with a long hydrocarbon chain are a kind of bifunctional catalysts as the reactions in their presence proceeds by two catalytic pathways, *i.e.*, phase-transfer and a micellar one. The former is inhibited by lipophilic anions such as chlorate *etc.* The structure—activity relationship for quaternary salts can be described quantitatively using Hansch π-hydrophobicity constants.

Key words: phase transfer catalysis (PTC), micellar catalysis, quaternary ammonium salts, hydrophobicity, Hansch π-hydrophobicity constants, elimination reaction kinetics.

The method of phase transfer catalysis (PTC) has been applied in organic synthesis for 30 years. The studies in the field of micellar catalysis began much earlier, and its theory is developed in more detail, although the field of its application is much more narrow. Up to the present these two types of catalysis were thought to be quite independent, although onium salts are used as catalysts in both cases. Nevertheless, it is not only synthetic organic chemists, usually quite indifferent to the meanders of high theory, who do not realize the existence of a quite close link between these two types of catalysis, but also physical chemists. Evidently all this is the result of the scarcity of kinetic information. It was noted in Prof. S. Yufit's monograph,[1] that in the field of PTC the ratio of synthetic and physicochemical works is about 7 : 1. At the same time the existence of the link between micellar and phase transfer catalysis allows one to make a number of conclusions having a theoretical as well as a practical significance. We intend to demonstrate the existence of such a link taking as an example the dehydrochlorination reactions, the kinetics of which we have studied for a number of years. These reactions are not very well investigated under PTC conditions in spite of their practical importance. These reactions are also interesting as a model ones. Organic compounds that are able to eliminate hydrogen halide are to a some extent also CH-acids. The deprotonation stage that is the first step of the elimination reaction (for E2H- and E1cb-mechanisms[2]) is a common one also for such important reactions as the addition of CH-acids and dihalocarbenes to double bonds. The kinetics of these latter reactions under PTC conditions are not investigated altogether.[3]

The problems of catalyst activity—quaternary cation structure relationship and PTC—micellar catalysis link are quite closely adjoined. At present there are practically no attempts to link the catalytic activity of the quaternary ammonium cation (quat*) with its structure. At the same time there are data on quat activity as extragents and physiologically active substances. The presence of two immiscible liquid phases is common for these two types of activity. Also there is quite a big volume of data on the structure—activity relationship for physiologically active substances, and a developed mathematical formalism exists for the structure description.[4—7] It seemed us very interesting to use data from those so different fields for obtaining the similar structure—activity model also for phase transfer catalysts.

The present work is aimed at i) elucidation of the mechanism of the catalysis of elimination reactions in two-phase systems by onium salts; ii) establishing of factors determining the type of the catalysis (micellar or PTC) prevailing in those systems; iii) analysis of the structure—activity relationship for onium cations.

1. Noncatalyzed hydrolysis and elimination in liquid-liquid systems

For catalyzed dehydrochlorination in a liquid—liquid system (organochlorine compound—aqueous NaOH) it is quite common to proceed together with an noncatalyzed one. In some cases the elimination is also accompanied with hydrolysis. We have studied the kinetics of these two processes in order to assess their contribution into the overall reaction taking as an example some aliphatic organochlorine derivatives.[8—11]

In spite of non-homogeneity of the reaction system both hydrolysis and elimination proceed not at the interface (as one can suppose on general consideration)

---

* The term "quat", meaning the quaternary ammonium cation or salt, was coined by some of the authors working in the field, and is already fairly generally used in the literature on PTC.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 11, pp. 2122—2134, November, 1995.

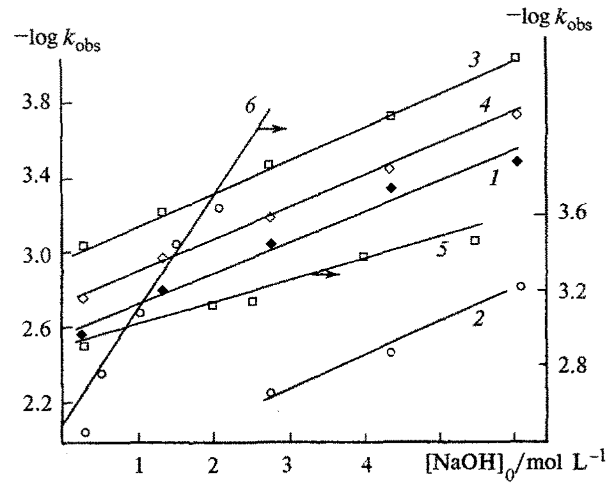


Fig. 1. Plot of the observed rate constants of the hydrolysis of the allylic chlorine atom (k/min^{-1}) *vs.* NaOH concentration at 343 K; 2,3-dichloropropene hydrolysis to alcohol (*1*) and ether (*2*), *cis-* (*3*) and *trans*-1,3-dichloropropenes (*4*), 1,1,2,3-tetrachloropropene (*5*), 1,4-dichlorobutene (*6*).

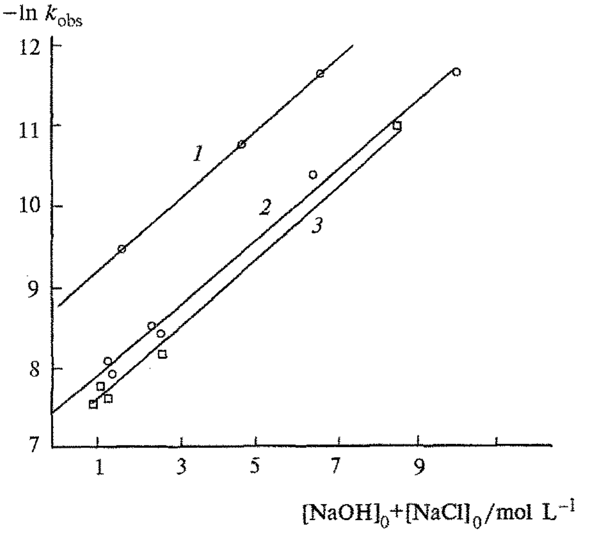


Fig. 2. Effect of the initial concentrations of alkali and sodium chloride on the observed first-order rate constant at 279 (*1*); 293 (*2*); 302 K (*3*).

but in the aqueous phase. This fact is confirmed by the first-order kinetics of these reactions in spite of their bimolecularity. Also the observed rate constants change concurrently with the substrate concentration in the aqueous phase, the latter being determined according to the Sechenov equation[12]

$$s = s_0 \cdot \exp[-\lambda C],$$

where s and s_0 are the solubilities of a non-electrolyte in an electrolyte solution and in pure water respectively, C is the concentration of the electrolyte (NaOH in our case), and λ is a salting-out constant (Figs. 1 and 2).

In order to determine the activation parameters the observed rate constants were extrapolated to the indefinite dilution of the aqueous phase. The second-order rate constants were determined by dividing these extrapolated constants on the substrate solubility in water. The authenticity of the obtained thus rate constant of the 1,1,2,2,3-pentachloropropane (PCP) dehydrochlorination was confirmed by the fact that it is satisfactorily correlated[10] with Taft's σ^*-constants together with rate constants for the dehydrochlorination of a number of chloroethanes[13] (Fig. 3). It must be underlined that unlike to our case the latter ones were obtained in a homogeneous system (the reaction was studied in water at substrate concentrations below the solubility limit).[13]

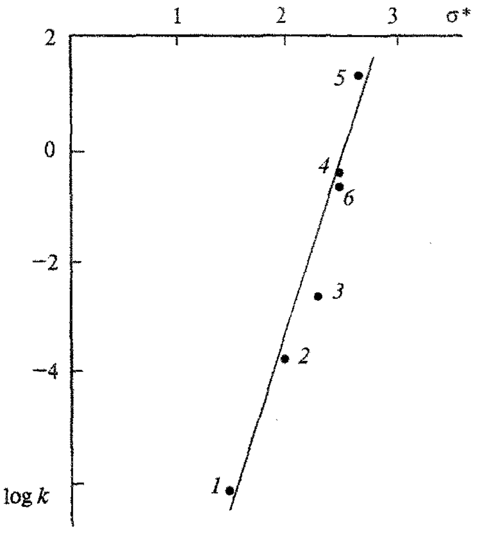


Fig. 3. Dependence of the second-order rate constants for the alkaline dehydrochlorination of chloroalkanes on Taft σ^* substituent constants: 1,2-dichloroethane (*1*); 1,1,1,2-tetrachloroethane (*2*); 1,1,2-trichloroethane (*3*); 1,1,2,2-tetrachloroethane (*4*); pentachloroethane (*5*); PCP (*6*). Data for points *1—5* were taken from the work.[13]

2. Catalyzed dehydrochlorination of chlorinated hydrocarbons in two-phase systems

The introduction of the catalytic onium salt (QX) into two-phase system results in a sharp change of the observed kinetics. The already published studies of elimination kinetics are somewhat fragmentary. Thus, kinetics of dehydrobromination of bromoethylbenzenes were studied by Sasson and Rabinovitz[14,15]. In the first work[14] the authors came to the conclusion that this reaction under PTC conditions is diffusion-controlled. This conclusion is without any doubt the result of insufficient mixing (because the experiments were evidently performed at insufficient stirring rates of 750 and 1450 rpm) and does not reflect upon the inherent properties of the reaction. The authors themselves admitted that the observed reaction rates strongly depended on stirring speed, the fact that heavily depreciates all the authors' conclusions. In their second work on the topic[15] the authors supposed that the quaternary salt itself may play the role of a base. According to this they had proposed the following mechanism:

$$\mathrm{RCH_2CH_2X + QX \rightarrow RCH{=}CH_2 + QX \cdot HX},$$

$$\mathrm{QX \cdot HX_{org} + NaOH_{aq} \rightarrow QX_{org} + NaX_{aq} + H_2O}$$

(the subscripts *org* and *aq* relate to the reagents in organic and aqueous phase respectively).

Although the elimination of hydrogen halide by quaternary salts is well known**[16]**, the reaction proceeds at fairly elevated temperatures (not less than 150 °C), and it is quite doubtful for this reaction to proceed at moderate temperatures (70 °C in the case) of PTC elimination. It is regrettable that in their review**[17]** on OH-initiated PTC-reactions Rabinovitz and his co-workers ignore Russian works on kinetics of PTC-reactions**[1]**, although they should be known to them.

We shall discuss the data on PTC-dehydrochlorination in the presence of short- and long-chained quats separately, because of the essential differences in the observed kinetics.

For dehydrochlorination of PCP in the presence of triethylbenzylammonium chloride (TEBA-Cl)**[18]** and for the same reaction of hexachlorocyclohexane α-isomer (α-HCCH) in the presence of tetrabutylammonium hydroxide,**[19]** quite similar reaction schemes were proposed and kinetic equations were determined according to the observed reaction kinetics.

In the first case the reaction scheme is as follows:

$$\mathrm{Q^+_{aq} + OH^-_{aq}} \xrightleftharpoons{K_\mathrm{I}} \mathrm{(Q^+OH^-)_{if}}, \tag{1}$$

$$\mathrm{Q^+_{aq} + Cl^-_{aq}} \xrightleftharpoons{K_\mathrm{II}} \mathrm{(Q^+Cl^-)_{if}}, \tag{2}$$

$$\mathrm{(Q^+OH^-)_{if} + CH_2Cl{-}CCl_2{-}CHCl_2} \xrightarrow{k_\mathrm{cat}} \\ \longrightarrow \mathrm{CH_2Cl{-}CCl_2{=}CCl_2 + (Q^+Cl^-)_{if}} \tag{3}$$

(the subscript if relates to the interface).

Then the rate of the catalytic reaction would be

$$r_\mathrm{cat} = k_\mathrm{cat}[\mathrm{Q^+OH^-}][\mathrm{PCP}].$$

It is known that the value of K_II is bigger than the same of K_I about 10^4 times.**[20]** The following equation was obtained by the combined solution of rate and material balance equations:

$$r_\mathrm{cat} = \frac{k_\mathrm{cat} K_\mathrm{I} \alpha^2 / (1-\alpha)^2 q([\mathrm{PCP}] + [\mathrm{PCP}]_0 \Delta n)[\mathrm{PCP}]}{1 + K_\mathrm{II}\alpha^2/(1-\alpha)^2([\mathrm{PCP}]_0 - [\mathrm{PCP}])}, \tag{4}$$

where α is the fraction of the organic phase relative to the volume of reaction mass,

$$\Delta n = ([\mathrm{NaOH}]_0 - [\mathrm{PCP}]_0)/V_\mathrm{org}[\mathrm{PCP}]_0,$$

$$q = [\mathrm{Q}]/\alpha,$$

[Q] is the catalyst concentration in the reaction volume, [PCP] is the PCP concentration in the organic phase. The value of the distribution constant K_II, determined independently by the spectrophotometric method was in a good accord with the one obtained from the kinetic measurements, thus supporting the proposed reaction scheme.

For the dehydrochlorination of α-HCCH the scheme of the reaction is

$$\mathrm{QOH_{aq}} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{QOH_{org/if}}; \quad \mathrm{K_1} = k_1/k_{-1} \tag{5}$$

$$\mathrm{QOH_{org/if} + C_6H_6Cl_6} \xrightarrow{k} \mathrm{C_6H_5Cl_5 + QCl_{org}} \tag{6}$$

$$\mathrm{QCl_{org}} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \mathrm{QCl_{aq}}; \quad \mathrm{K_2} = k_2/k_{-2} \tag{7}$$

$$\mathrm{QCl_{aq} + NaOH} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \mathrm{QOH_{aq} + NaCl}; \tag{8}$$

$$\mathrm{K_3} = k_3/k_{-3},$$

where K_1, K_2, K_3, are equilibrium constants.

(The form of the equation does not change if the catalyst is not transferred to the organic phase and is fixed at the interface.) So

$$-d\mathrm{C_6H_6Cl_6}/d\tau = K_1\mathrm{QOH_{aq}C_6H_6Cl_6}/[1+(k/k_{-1})\cdot\mathrm{C_6H_6Cl_6}], \tag{9}$$

where $\mathrm{QOH_{aq}}$ and $\mathrm{QOH_{org}}$ are the molar quantities of the quaternary ammonium base in the aqueous and organic phases; $\mathrm{C_6H_6Cl_6}$ is the molar quantity of α-HCCH. The shape of the kinetic curves shows that up to high conversion levels $(k/k_{-1})\cdot\mathrm{C_6H_6Cl_6} \gg 1$. Integration gives the equation

$$-\frac{X}{K_3} - \frac{[\mathrm{NaOH}]_0(1-\alpha)}{3K_3[\mathrm{HCCH}]_0\alpha}\ln\left(\frac{[[\mathrm{NaOH}]_0(1-\alpha) - 3[\mathrm{HCCH}]_0\alpha X]}{[\mathrm{NaOH}]_0(1-\alpha)}\right) + \\ + X = \frac{k_\mathrm{obs} q \tau}{[\mathrm{HCCH}]_0}, \tag{10}$$

where X is the conversion of α-HCCH, k_obs is the observed zero-order rate constant, mol/(L · s); $[\mathrm{NaOH}]_0$ and $[\mathrm{HCCH}]_0$ are the initial concentrations of alkali and α-HCCH in aqueous and organic phases respectively, mol/L; q is the concentration of the catalyst, referred to the organic phase volume, mol/L; α is the fraction of the organic phase relative to the reaction mass volume. Converting this equation, we obtain

$$\frac{X}{\tau} = \frac{1}{K_3}\left(\frac{X}{\tau} + \frac{a}{\tau}\ln\left(\frac{X}{a}\right)\right) + \ln\frac{k_\mathrm{obs} q}{[\mathrm{HCCH}]_0}, \tag{11}$$

where

$$a = ([\mathrm{NaOH}]_0(1-\alpha))/3[\mathrm{HCCH}]_0\alpha. \tag{12}$$

In Fig. 4 we demonstrate the linearization of the kinetic data according to the above equation. The first

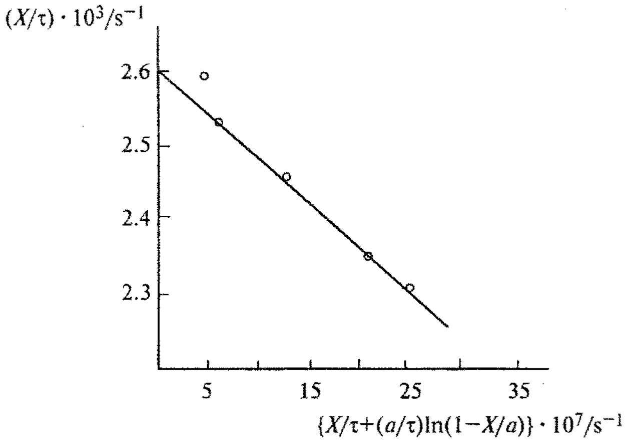


Fig. 4. Anamorphosis of the typical kinetic curve for the reaction of alkaline dehydrochlorination of α-HCCH catalyzed by Bu_4NOH (343.5 K, $[HCCH]_0 = 5.01\cdot 10^{-2}$ mol/L, $[NaOH]_0 = 6.00$ mol/L).

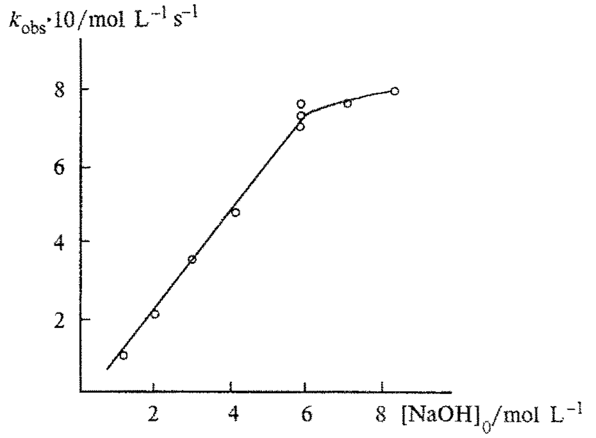


Fig. 6. Effect of the initial NaOH concentration on the observed first-order rate constant of the alkaline dehydrochlorination of α-HCCH catalyzed by Bu_4NOH (345.5 K, $[HCCH]_0 = 5.01\cdot 10^{-2}$ mol/L, $q = 7.7\cdot 10^{-5}$ mol/L).

point (60—120 s after starting the reaction), was usually an outliner and was dropped from the calculations. In all probability, during this period an equilibrium distribution of the catalyst between the phases was established.

But the dependences of the observed reaction rate constants on an initial NaOH concentration in cases of PCP and α-HCCH differ dramatically (see Figs. 5 and 6).

In case of PCP there exists an extremum dependence of $k_{cat}K_I$ (or initial rate) on initial concentration of NaOH (see Fig. 5). The increase in $k_{cat}K_I$ on the left branch of this dependence is explained by the salting-out of the catalyst out of the aqueous phase at high NaOH concentrations. On the opposite, the decrease in the NaOH concentration results in the rise of PCP concentration in the aqueous phase, caused by the salting-in effect of the quaternary ammonium salt.[12] This in turn results in the increase in the overall rate constant, thanks to the increase in the fraction of the reaction in the aqueous phase. The same dependence of the initial rate on the initial concentration of NaOH was obtained also in the dehydrochlorination of dichlorobutenes[21] and trichloroethane (Fig. 7).[22] In Fig. 8 the influence of alkali and quats on an solubility of an organic reagent in the aqueous phase is shown. It is clearly seen that the small addition of the quaternary salt winds up in the sharp rise of the concentration of this reagent in water, thus leading to the increase in the fraction of the reaction, which proceeds in the aqueous phase. In the case of α-HCCH the noncatalyzed reaction (in the aqueous phase) does not take place, so the obtained dependence of the reaction rate on an initial NaOH concentration reflects the salting-out effect of the latter (Fig. 6).

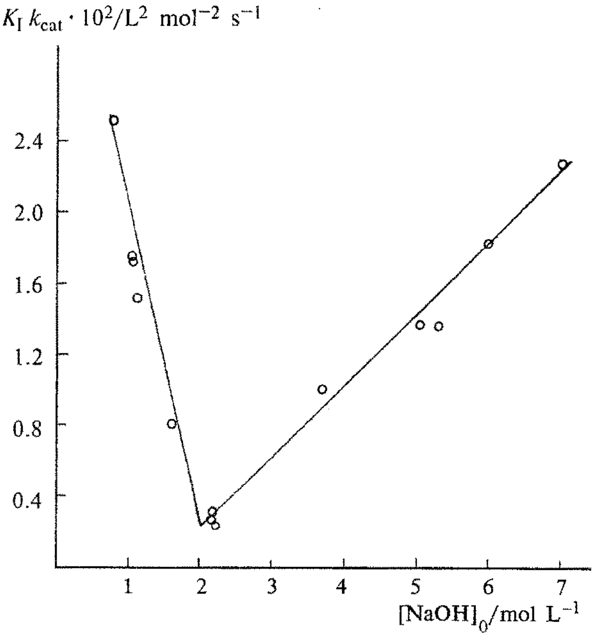


Fig. 5. Dependence of $k_{cat}\cdot K_I$ in the dehydrochlorination of PCP in the presence of TEBA-Cl on the initial NaOH concentration ($T = 293$ K).

From all the above-mentioned we can draw a conclusion that the extremum dependence of the reaction rate on the initial alkali concentration should be common for all compounds that are reactive enough to eliminate hydrogen chloride without the catalyst. The substitution of the activity of the alkali instead of its concentration did not change the appearance of the obtained dependence, thus confirming the decisive role played by the salting-out effect.

In the recent work of Makosza and Lasek[23], devoted to the alkaline PTC dehydrobromination of alkyl bromides in the presence of co-catalysts, the authors have supposed that the lipophilic alkoxide RO^-, formed as the result of the side process of hydrolysis of the substrate, or from the admixtures of alcohol already present in the latter, plays a major role in this reaction. It is a fact that

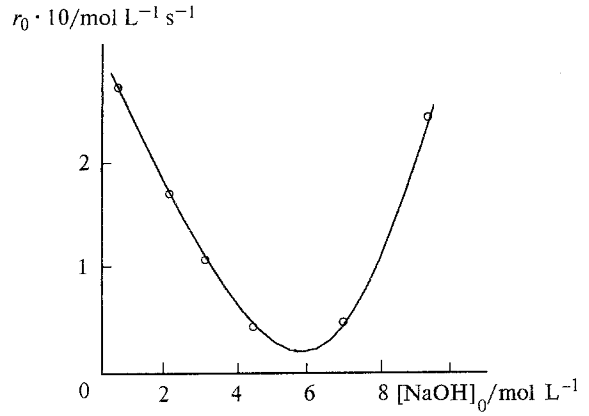


Fig. 7. Effect of the initial NaOH concentration on the initial rate of the alkaline dehydrochlorination of 1,1,2-trichloroethane (295 K, C_{cat} = 3.82 · 10^{-2} mol/L)[22].

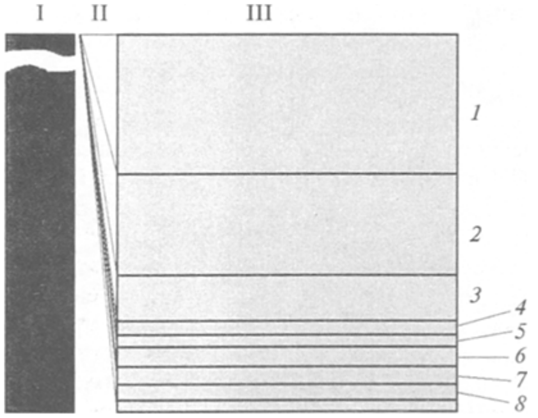


Fig. 8. Solubility of the organochlorine compound in water in the presence of alkali and quaternary ammonium salt. [Bu_4NBr^+]/mol L^{-1}: 0.25 (*1*), 0.1 (*2*), 0.05 (*3*), 0.01 (*4*); H_2O (*5*); [NaOH]/mol L^{-1}: 2 (*6*), 5 (*7*), 10 (*8*). I, organic phase; II, interface; III, aqueous phase.

the promoting effect of alcohols in the PTC elimination was observed by a number of investigators.[24,25] The authors[23] have supposed that having in view the extremely low lipophilicity of quaternary ammonium bases the above-mentioned effect is solely responsible for the proceeding of the PTC elimination. But this hypothesis is undermined by the fact that the PTC alkaline dehydrochlorination of α-HCCH proceeds quite rapidly, although there is no by-process of hydrolysis in this case. The authors themselves further have admitted that their explanation is valid only in some of the cases.[26] As an alternative hypothesis, they had proposed[26] that the intensive stirring, resulting in the sharp increase in the area of the interface where the quaternary ammonium hydroxide is absorbed, can shift the position of the extraction equilibrium in which the latter participates. So the extractability of such hydroxides under static and dynamic conditions can differ considerably. The data obtained have confirmed this hypothesis only in part. So, under static conditions Bu_4NBr does not practically change its anion for the hydroxide, but under dynamic conditions this exchange does proceed for 3—4 %. Nevertheless the authors[26] came to the conclusion that this effect is also insufficient for the explanation of the possibility of PTC elimination.

The dependences observed in the course of the PTC elimination, catalyzed by quats with surfactant properties, completely differ from the ones discussed above. This can be readily demonstrated by carrying out the alkaline elimination in the presence of inorganic salts with the anions that "poison" the phase-transfer catalyst, *i.e.*, sodium chlorate. This salt is the most common impurity in the aqueous alkali (especially in the technical grade). If the catalyst is TEBA-Cl, then the reaction stops completely even at moderate concentrations of the chlorate. But if the catalyst possesses the properties of the surfactant, such as, $PhCH_2N^+(CH_2CH_2OH)_2(C_{12}H_{25}—C_{16}H_3)Cl^-$ (katanol), than the reaction rate does not drop to zero.[21,27] In Fig. 9 are shown the kinetic curves of 3,4-dichlorobutene-1 dehydrochlorination catalyzed by katanol in the presence of ions, that poison usual phase transfer catalysts. It is seen that even at high chlorate concentrations the inhibition of the catalyst is not complete. This fact indicates the existence of the second catalytic pathway, *i.e.*, the micellar one.

It is known that surfactants, unlike the phase transfer catalysts, can catalyze reactions in strongly diluted solutions that occur, as a rule, in the absence of the bulk organic phase in so-called pseudo-homogeneous systems. The already published works[28,29] on elimination catalyzed by the long-chain quats, were performed at exactly same conditions, *i.e.*, in the absence of the bulk

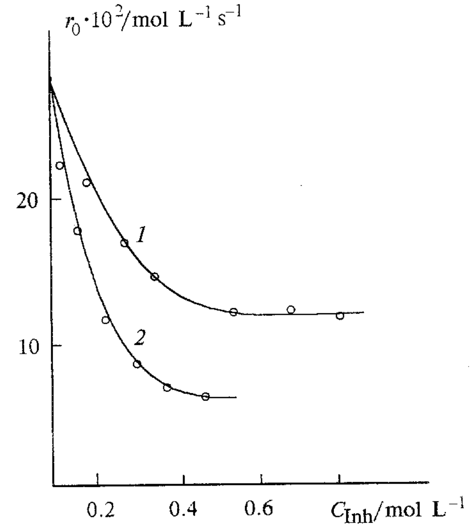
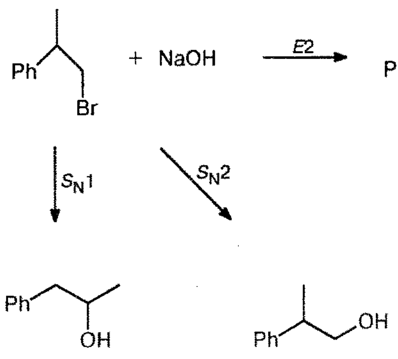


Fig. 9. Dependence of the initial rate of the dehydrochlorination of 3,4-dichlorobutene on the concentration of the inhibitor (C_{Inh})[21,27] (catalyst—katanol, 4.24 · 10^{-3} mol L^{-1}, 303 K): *1*, Cl^-; *2*, ClO_3^-.

organic phase. Thus there was investigated[28] the reaction of 1-bromo-2-phenyl propane with NaOH catalyzed by $C_{16}H_{33}N^+(CH_3)_3Br^-$ (Scheme 1):

Scheme 1



The catalytic and noncatalytic reaction rate constants on each pathway were determined. It is interesting to note that in the presence of the catalyst with the hydroxy group in a β-position[29] the reaction rate is much higher. The obtained results[28,29] are listed in Table 1.

These data show that cationic micelles are selective catalysts of *E*2-reactions. This effect was explained[28] by the stabilization of the negative charge of the *E*2-transition state by the high positive charge of the cationic micelle. The increase in *E*2-reaction rate can also be explained by lowering the microscopic dielectric constant inside the micelle. The dependence of the reaction rate on the catalyst concentration is the characteristic *S*-like curve. In the second work[29] of the same authors it was shown that the change of the methyl group for the β-hydroxyethyl one in the catalyst molecule results in the pronounced increase in the catalytic effect together with inhibition of the side processes (see run 3 in Table 1). The authors[29] supposed that this is the result of the lowering of the activity of the substrate and the increase in the hydroxide activity.

On Jencks' opinion[30], this rise of the reaction rate is the consequence of the increase in the local concentration of the hydroxide ion in the immediate vicinity of the substrate molecule that is absorbed on the surface of the micelle.

Table 1. The rate constants of the reaction of 1-bromo-2-phenyl propane with NaOH[28,29]

Run	Catalyst concentration mol L^{-1}	$k_{E2} \cdot 10^4$ s^{-1}	$k_{S_N2} \cdot 10^4$ s^{-1}	$k_{S_N1} \cdot 10^4$ s^{-1}
1	0	0.55	0.10	0.35
2	10^{-2}	2.55	0.22	0.22
3*	10^{-2}	16.20	0.60	0.25

* Catalyst is $C_{16}H_{33}N^+(CH_3)_2CH_2CH_2OHBr^-$.[29]

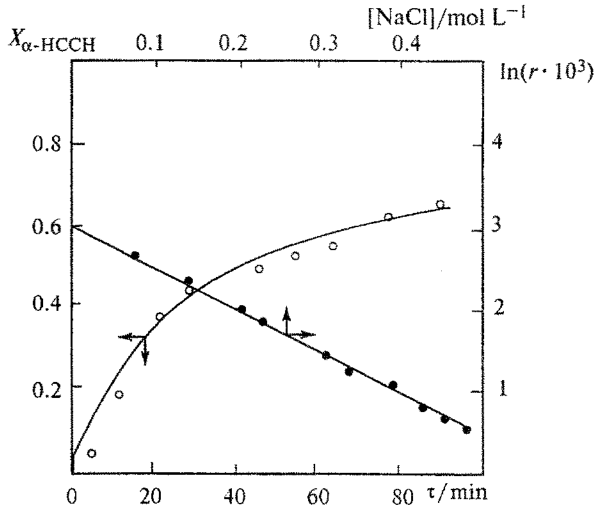


Fig. 10. Determination of the rate constant of the dehydrochlorination of α-HCCH ([HCCH] = 1.40 mol/L; C_{cat} = $6.0 \cdot 10^{-4}$ mol/L; pH 10; V_{aq}/V_{org} = 10.31). *X* is the conversion of α-HCCH; *r* is the rate of the reaction.

It was interesting to investigate whether a long-chain quat— $PhCH_2N^+Me_2(C_{12}H_{25}—C_{16}H_{33})Cl^-$ (katamin AB) would catalyze the dehydrochlorination reaction at low alkali concentrations in a true two-phase system and not in a pseudo-homogeneous one. This is important also from the practical viewpoint.

The investigation of the α-HCCH dehydrochlorination[31] revealed that unlike TEBA-Cl the katamin can catalyze the reaction even at pH 8—10, when the noncatalyzed reaction does not proceed. The reaction rate at the constant pH fell in time parallel to the increase in Cl^- concentration in the aqueous phase (Fig. 10). The likewise lowering of a solubility of non-electrolytes in water with the increase in the NaCl concentration was observed elsewhere.[12] The reaction proceeds in the micelles of the catalyst in the aqueous phase, the α-HCCH being solubilized in its trichlorobenzene (TCB) solution. The fall in the reaction rate is caused by the salting-out of the latter from the aqueous phase by sodium chloride. The micellar type of the catalysis is also indicated by the extremum dependence of the rate constant on the catalyst concentration (Fig. 11).

The rate of the micellar catalyzed second-order reaction is described by the equation[32—34]

$$r = k_m[C_6H_6Cl_6]_m[OH]_m(C_{cat} - CMC)\bar{V}, \qquad (13)$$

where k_m is the second-order reaction rate constant in the micellar pseudo-phase, $[C_6H_6Cl_6]_m$, $[OH]_m$ are the concentrations of the reagents in the same phase, $\bar{V}$ is the molar volume of the catalyst, *CMC* is the critical micellar concentration.

One can usually determine the concentrations of the reagents in the micellar pseudo-phase, starting from the

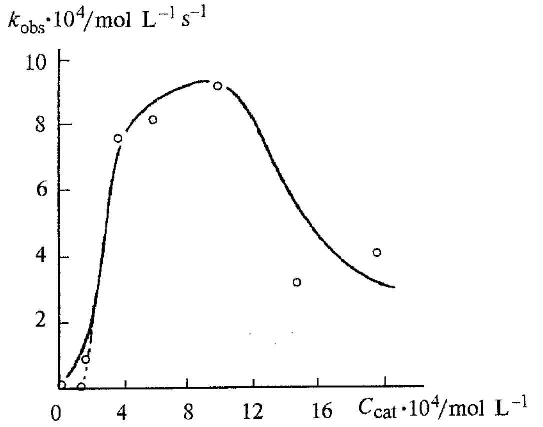


Fig. 11. Dependence of the observed rate constant of the dehydrochlorination of α-HCCH on the concentration of the catalyst.

hypothesis of their distribution between the micellar and aqueous phases. In our case the problem is additionally complicated by the presence of the bulk organic phase. Assuming that the concentration of α-HCCH in TCB on transition from the organic phase to the micellar one does not change, we obtain:

$$P_{OH^-} = [OH]_m/[OH]_{aq}, \quad (14)$$

$$P_{ТХБ} = [TCB]_m/[TCB]_{aq}, \quad (15)$$

$$P_{NaOH} = [NaOH]_m/[NaOH]_{aq}, \quad (16)$$

where P is the coefficient of the distribution of the reagents between the micellar and aqueous phases.

The reagents′ material balance is described by the following equations:

$$[NaOH] = (C_{cat} - CMC)\bar{V}]([NaOH]_{aq} + [OH^-]_{aq}) + \\ + \bar{V}(C_{cat} - CMC)(NaOH]_m + [OH^-]_m) \quad (17)$$

$$[C_6H_6Cl_6] = [1 - (C_{cat} - CMC)\bar{V}][C_6H_6Cl_6]_{aq} + \\ + \bar{V}(C_{cat} - CMC)[C_6H_6Cl_6]_m \quad (18)$$

Considering that

$$(P - 1)\bar{V} = K,$$

where K is the constant of the solubilization, we obtain:

$$r = \frac{k_m K_{TCB} K_{OH}(C_{cat} - CMC)[NaOH][HCCH]\exp[-\lambda C]}{\{1 + K_{TCB}(C_{cat} - CMC)\}\{1 + K_{OH}(C_{cat} - CMC)\}}. \quad (19)$$

If [HCCH] = const. and [NaOH] = const., than

$$r = k_{obs}\exp[-\lambda C], \ \lambda=4.3,$$

where C is the concentration of NaCl in the aqueous phase.

The beginning of the plot of k_{obs} *vs.* C_{cat} has a significant bend because the catalyst concentration is not corrected for the *CMC* value. The point of the intersection of the tangent with the C_{cat}-axis is approximately equal to the *CMC* and is about $1.9 \cdot 10^{-4}$ mol/L.

The value of K_{TCB} determined by the independent stalagmometric procedure is in quite satisfactorily agreement with the one obtained from the kinetic calculations.

The obtained results demonstrate that the kinetic model of micellar catalysis that was developed for the pseudo-homogeneous systems is valid also for the heterogeneous ones. It is quite possible that the catalytic effect of long-chain onium salts in alkaline dehydrochlorination at low concentrations of NaOH (up to 5 mass. %) is brought about by micelles. Evidently at higher NaOH concentrations there are two catalytic pathways — the micellar and the phase transfer one. It was interesting to determine their contributions into the overall rate of the model reaction, dehydrochlorination of 3,4-dichlorobutene-1.[35,36]

$$CH_2ClCHClCH{=}CH_2 + NaOH \rightarrow CH_2{=}CClCH{=}CH_2$$

The kinetic curves of the substrate consumption (Fig. 12) consist of two parts. At first there is a sharp fall in the substrate concentration during short time, than it is slow consumed according to the first-order kinetics. This confirms our hypothesis about two catalytic pathways caused by the dualistic nature of the onium salt catalyst. The phase-transfer pathway is blocked in the course of the reaction by the evolving Cl^- ion. The micellar pathway is caused by the surfactant properties of the catalysts. The rate of the reaction neglecting the noncatalyzed one is the sum of rates along both pathways.

The equation for the phase-transfer pathway was obtained earlier[18,19]

$$-d[RCl]/d\tau = k_{obs}C_{cat}[RCl]/(1 + K[RCl]), \quad (20)$$

where k_{obs} is the effective rate constant, and K is a gross-

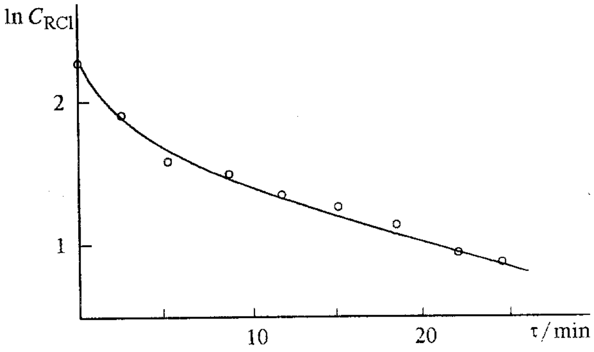


Fig. 12. Semi-logarithmic anamorphosis of the typical kinetic curve ([RCl] = 9.04 mol/L, 323 K, $[NaOH]_0$ = 4.2 mol/L, katanol, C_{cat} = $2.8 \cdot 10^{-3}$ mol/L).[36]

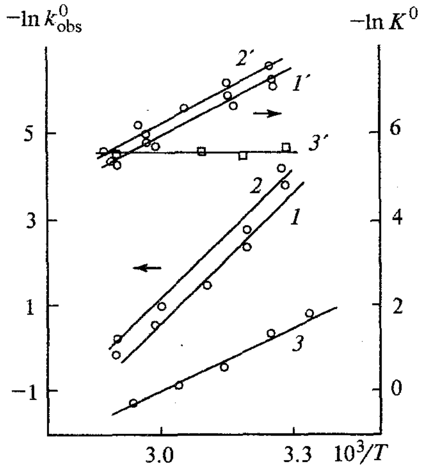


Fig. 13. Temperature dependence of the equilibrium (K) (*1′*, *2′*, *3′*) and rate constants (k_{obs}) (*1, 2, 3*) in the reactions of the 3,4-dichlorobutene-1 dehydrochlorination in the presence of TEBA-Br. [NaOH]/mol L^{-1}: 1.1 (*1, 1′*); 6.2 (*2, 2′*); 12.0 (*3, 3′*).

constant describing both the phase transfer and anion exchange.

The equation for the micellar pathway in the case of only one reagent solubilization is as follows

$$r_m = \frac{k_m K_s([Q] - CMC)[OH]_0[RCl]}{[1 + K_s([Q] - CMC]}, \qquad (21)$$

where k_m is the rate constant of the reaction along the micellar pathway, K_s is the constant of the solubilization of the reagent.

In case of lipophilic cations the obtained gross values of the activation energy are 1.5—2 times higher than the energy of phase transfer.

The observed dehydrochlorination rate constants of the TEBA-Br catalyzed reaction rise sharply (about 5—7 times) at an NaOH concentration of 12 mol/L, the effect being the result of the essential lowering of the water activity and practically complete salting-out of the catalyst from the aqueous phase. In Fig. 13 the temperature dependences of k^0_{obs} and K^0 in the case of TEBA-Br are shown. This dependence at an NaOH concentration of 12 mol/L in the case of k^0_{obs} becomes less distinct, and K^0 becomes temperature-independent (k^0_{obs} and K^0 are constants of equation (20) extrapolated to infinite dilution in order to eliminate the salting-out effect).

The catalysts having the larger anion-exchange constant K, and providing for the larger reaction rate along the micellar pathway are the most active. The rate of the reaction along the phase transfer pathway shortly after the start sharply falls due to the effect of the so-called "chloride poisoning" of the catalyst. So the substrate is consumed mainly thanks to the reaction along the micellar pathway.

Thus one can conclude that the long-chain quaternary onium salts are a kind of a missing link, which can bind PTC and micellar catalysis thanks to their "bifunctionality". In other words, they can be both micellar and phase transfer catalysts simultaneously.

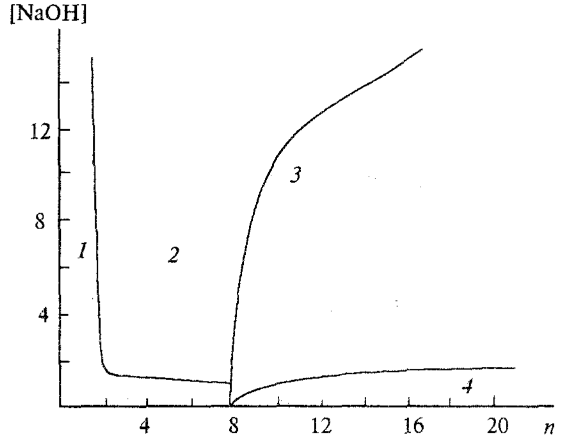


Fig. 14. Realms of catalysis: *1*, no catalysis; *2*, phase transfer catalysis; *3*, intermediate region; *4*, micellar catalysis.

The obtained results allow us to propose the following diagram showing the different fields of catalysis of dehydrochlorination reaction by various quaternary ammonium salts (Fig. 14). The realm of pure PTC is confined between the chain length of 2 to 8 carbon atoms and an NaOH concentration higher 1 mol/L. The field of the purely micellar catalysis extends from the chain length of 8 carbon atoms and is bordered by NaOH concentrations from 0.01 to 1.5 mol/L. Between these two fields the scarcely investigated wilderness extends where two types of catalysis coexist. Surely, this diagram is very rough, but nevertheless it can be helpful in the choice of the catalyst and reaction conditions. This diagram also makes it clear that the long-chain quats are more active catalysts, as they display catalytic activity in a wider range of alkali concentrations due to their dualistic catalytic properties.

3. Catalysts' structure—activity relationship under PTC conditions

The problem of the catalysts' structure—activity relationship is one of the chief ones in the theory of PTC. We will leave out the also very important question of the counter-ion influence and are going to concentrate on the influence of cation structure. Some investigators[3,37] have operated with the coefficient of the distribution of the quat between the phases of the reaction mass, using it for the estimation of the catalyst hydrophilic—lipophilic balance.[38] Fukunaga and co-workers[39] proposed a fresh but arguable approach to the problem, using for this aim the Hildebrand[40] solubility parameter δ. For the calculation of the catalyst hydrophilic-lipophilic balance $D(\delta)$ they used the equation[39]

$$D(\delta) = (\delta - \delta_{aq})^2/(\delta - \delta_{org})^2, \qquad (22)$$

where δ, δ_{aq}, and δ_{org} are respectively the solubility parameters of the catalyst (quat), water, and the organic solvent. It is a matter of fact that D(δ) is somewhat linked with the change in the standard free energy of the catalyst on its transition from one phase to another. This change is the natural and quite sensitive parameter that reflects the alteration of the catalyst structure. The partial free energy of the solute in terms of the theory of regular solutions is expressed by the following equation[40]:

$$\Delta G_2 = RT\ln X_2 + V_2\varphi_1^2(\delta_2 - \delta_1)^2, \tag{23}$$

where X_2, V_2, and δ_2 are respectively the molar fraction, the molar volume, and the solubility parameter of the solute; δ_1 and φ_1 are respectively the solubility parameter and the volume fraction of the solvent.

Nevertheless the link between the values of D(δ) and reaction rate constants is more qualitative than quantitative. The scarcity of values of δ for quats also restricts the possibilities of the wide application of Fukunaga's equation (23) for the picking of the catalyst. It is also quite doubtful that the theory of the regular solutions, that was destined for the solutions of nonelectrolytes, would correctly describe the interactions with the participation of the quats, which are usually strong electrolytes.

The parameter reflecting the change in the standard free energy of the catalyst on its phase transfer is the distribution coefficient. It is known[41] that

$$\mu^0_{org} - \mu^0_{aq} = RT\ln P', \tag{24}$$

where μ^0_{org} and μ^0_{aq} are the standard chemical potentials of the solute in the organic and the aqueous phase; P' is the "thermodynamic" distribution coefficient (the ratio of the molar fractions of the solute in organic and aqueous phases).

Nevertheless the distribution coefficient is determined by the whole quat, although it is known that isomeric quats display different catalytic activity. So this integral parameter is not always fitting for the description of the catalyst structure. Beside this, the distribution coefficients of the same quat determined in different solvents vary strongly. In some solvents due to their ion-selective properties the distribution coefficient strongly depends on the anion. In order to eliminate the vagueness caused by this effects we had used the Hansch' π-constants of hydrophobicity for the description of the quat structure. It is known[41] that these constants are defined analogously to Hammett and Taft constants:

$$\pi_X = \log P_X - \log P_H, \tag{25}$$

where P_H is the distribution coefficient for the standard compound; P_X is the same for its derivative with the X substitutient.

The standard is the 1-octanol—water system, as it is only slightly ion-selective in relation to halide and hydroxide ions.

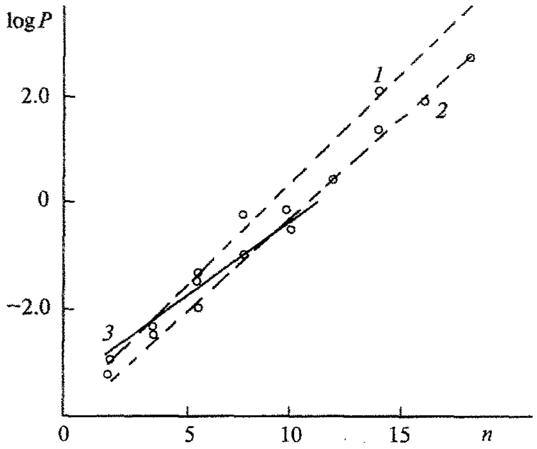
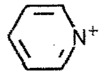
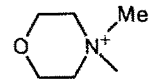


Fig. 15. Dependence of the distribution coefficients of the quaternary ammonium salts on the length of the alkyl radical in 1-octanol—water system: *1*, salts of the $C_6H_5CH_2N(Me)_2C_nH_{2n+1}$ type; *2*, salts of the PyC_nH_{2n+1} type; *3*, salts of the $Me_3NC_nH_{2n+1}$ type.

Table 2. Hydrophobicity constants of different functional groups

Ammonium "head"	$\pi_{R_3N^+}$	π_{CH_2}
Me_3N^+	−3.91	0.35
Et_3N^+	−3.00	0.35
Bu_3N^+	−0.80	0.35
$(C_8H_{17})_3N^+$	4.49	0.35
$PhCH_2N^+Me_2$	−4.09	0.45
	−4.28	0.39
	−4.66	0.35

The cation of the quat can be pictured as consisting of two fragments, *i.e.*, the hydrophilic ammonium "head" and the hydrophobic hydrocarbon "tail". This predetermines the choice of the two π-constants ($\pi_{R_3N^+}$ for the ‘head" and $\pi_{R'} = n \cdot \pi_{CH_2}$ for the "tail") for the description of the quat structure. The values of the π-constants were calculated according to the Eq. (25) from the known in the literature[41—43] distribution coefficients for quats. As the result we obtained the values of the slope (π_{CH_2}), and the intercept ($\pi_{R_3N^+}$) (Fig. 15). Table 2 lists the values of the hydrophobicity constants for the various ammonium "heads".[44]

The determined by us values of π_{CH_2} somewhat differ from the most common value of 0.5 found by other investigators.[7,41] This can be explained by the conformation effect or the "folding" of the long hydrocarbon chain.[41] In order to validate our approach we have treated the kinetic data published in a few works that compare the activity of different quats.

In the known work[37] of Herriott and Picker such a comparison was made in the following model reaction:

$$C_8H_{17}Br + PhSNa \rightarrow PhSC_8H_{17} + NaBr,$$

which was carried out in the benzene—water system. The treatment of their results by the method of the multi-parameter correlation yielded the following equation[44]:

$$\ln k_2 = 1.41\pm0.64 + (1.33\pm0.18)\pi_{R_3N^+} + (0.94\pm0.29)\pi_{R'} - (0.21\pm0.04)\pi^2_{R_3N^+}, \qquad (26)$$

where k_2 is the second-order reaction rate constant, $L\cdot(mol\ s)^{-1}$; the corrected for the degrees of freedom correlation coefficient is 0.969; the root mean square is 0.76.

Other investigators[45] have studied the reaction in the solid—liquid system:

$$AcONa_{solid} + PhCH_2Cl_{org} \xrightarrow{Q^+X^-} AcOCH_2Ph + NaCl$$

The treatment of their data yielded other correlation equation[44]:

$$\ln k_2 = (1.15\pm0.20)\pi_{R_3N^+} + (1.05\pm0.15)\pi_{R'}, \qquad (27)$$

(the corrected for the degrees of freedom correlation coefficient is 0.986, the root mean square is 0.55).

It is interesting to note that if the same reaction is carried out in the liquid—liquid[46] system and not in a solid—liquid one than the quadric member $\pi^2_{R_3N^+}$ appears again (comp. Eqs. (27) and (28)).

$$\ln k_2 = -2.85 + 0.19(\pi_{R'} + \pi_{R_3N^+}) - 0.11\pi^2_{R_3N^+} \qquad (28)$$

The same equation was obtained for the model reaction of the dehydrochlorination of PCP.[47]

$$\log k_{cat}K_I = -(1.80\pm0.47) + (0.11\pm0.06)\pi_{R_3N^+} + (0.53\pm0.16)\pi_{R'} - (0.049\pm0.016)\pi^2_{R_3N^+}, \qquad (29)$$

the root mean square is 0.47.

The presence of the quadric member also means that for the given reaction there exists the quat with the optimal $\pi_{R_3N^+}$ value.

The same very interesting parabolic dependence of the catalyst activity on the length of its hydrocarbon chain was obtained by Sasson and co-workers[48] in the study of allylbenzene isomerisation in the liquid—liquid system catalyzed by the quaternary salts of R_4NX type. The existence of this dependence confirm our conclusion that in such systems quaternary salts with the optimal value of the distribution coefficient P exist.

The generality of this approach was authenticated by the investigation of the quats catalytic activity in the reaction in the protic solvent.[49] The rate of the reaction that proceeds in an aprotic solvent rises with the increase in the catalyst hydrophobicity.[1,3] We supposed that in a protic solvent it would be just the opposite, *i.e.* the quat catalytic activity would rise with the increase in its hydrophilicity. As the model we choose the oxidation of durene to pyromellitic acid on the cobalt bromide catalyst in acetic acid in the presence of various quaternary ammonium bromides as co-catalysts. It is known from the literature that amine and ammonium salts accelerate the oxidation of alkyl aromatics.[50]

The formal scheme of the reaction is as follows:

$$\mathbf{1} \xrightarrow{k_1} \mathbf{2} \xrightarrow{k_2} \mathbf{3} \xrightarrow{k_3} \mathbf{5},$$

$$\mathbf{4} \xrightarrow{k_4} \mathbf{3},$$

where **1** is the sum of isomeric 4,6-dimethylisophthalic and 2,5-dimethylterephthalic acids, **2** is the corresponding methylcarboxyphthalide, **3** is 5-methyl trimellitic acid, **4** is 4,5-dimethylphthalic acid, **5** is pyromellitic acid.

The rate constant of the rate-limiting step of the formation of 5-methyltrimellitic acid was used as the measure of the catalytic activity. Also log P was used as the measure of the hydrophobicity (hydrophilicity) because there was no sense in dividing the cation of symmetric quats, used as catalysts, on fragments. The obtained values of log k_2/k_2^{NaBr} were plotted against the calculated values of log P (k_2^{NaBr} is the same constant of the formation of 5-methyl trimellitic acid in the presence of NaBr instead of the quat). The k_2/k_2^{NaBr} ratio is the measure of the quaternary cation catalytic activity relative to sodium ion.

The obtained dependence was satisfactorily described by the equation[49]

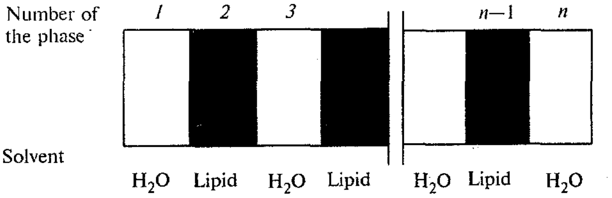
$$\log(k_2/k_2^{NaBr}) = -(4.88\pm0.85)\cdot10^{-2}\log P + (1.59\pm0.43)\cdot(\log P)^2 \qquad (30)$$

with the correlation coefficient equal to 0.95. That confirms the assumption that catalytic activity of the quats in protic solvents rises with the increase in the hydrophilicity of the former. The presence of the quadric member in the obtained relationship also demonstrates the importance of the hydrophobic interactions in this case.

The obtained data show that the relationships of the quat catalytic activity—lipophilicity in the protic and the aprotic solvents are the mirror reflections of each other (comp. signs of the quadric members in Eqs. 26, 28, 29, and 30).

It should be noted that the like parabolic relationships link the biologic activity of the quats with their structure.[4—7] There were also determined the values of $(\log P)_{max}$ for the maximum biologically active quats. The comparison of these values with the ones for $(\pi_{R_3N^+})_{max}$ in the PTC reactions demonstrate their closeness.

The necessity of the introduction of the quadric member was shown in the works.[51–52] Let us look at the scheme:



Let us denote the rate constant of the transfer of the active molecule form any aqueous phase to the neighboring lipid phase as *k*, the one of the opposite process as *l*. The distribution coefficient is equal to *k*/*l*. If the concentration of the active substance in the *i* phase is A_i, than

$$dA_{2i}/d\tau = -2lA_{2i} + k(A_{2i-1} + A_{2i+1}),$$

$$dA_{2i+1}/d\tau = -kA_{2i+1} + l(A_{2i} + A_{2i+2}),$$

$$dA_{n-1}/d\tau = \begin{cases} -(l+m)\,A_{n-1} + kA_{n-2} & \text{for odd } n \\ -(k+m)\,A_{n-1} + lA_{n-2} & \text{for even } n \end{cases}$$

$$dA_n/d\tau = mA_{n-1},$$

where *m* is the rate constant of the interaction of the active substance with the receptor.

It was shown[51,52] that the numerical solution of the above system yields the function of the type

$$\log(1/C) = k_1(\log P)^2 + k_2\log P + k_3, \qquad (31)$$

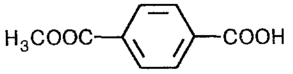
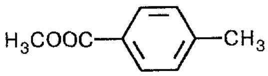
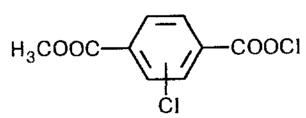
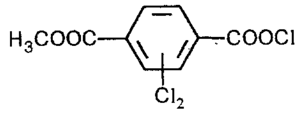
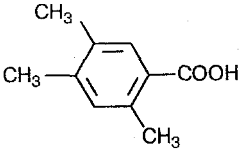
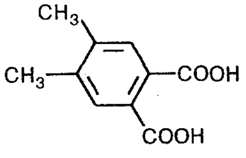
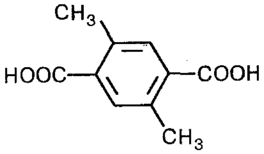
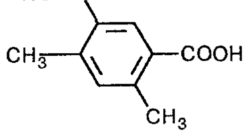
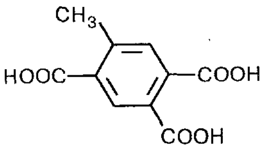
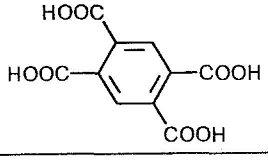
analogous to Eqs. 26 and 28—30.

What is the physical cause of the obtained parabolic relationships? In all probability they are the result of the interplay of the two opposite trends. Small highly hydrophilic cations are located mainly in the aqueous phase. On the opposite, large cations are located in the organic phase. The phase transfer is the most easy at some optimal intermediate size of the cation, thus determining the parabolic form of the structure—activity relationship.

The similitude of the mathematical model of PTC in liquid—liquid systems and the same of the quaternary salts interaction with the biological substrates reflects, in our opinion, the likeness of the mechanisms of these processes. The transfer of the quat molecule from the water (protein) phase to the lipid one accompanies its interaction with the biological substrates. Thus the PTC reactions in the liquid—liquid systems in a very approximate degree mimic the processes in biological membranes.

It should be noted that the values of log*P* are also the very useful and versatile parameter for the prediction of the chromatographic behavior[54,55]. We have successfully

Table 3. Retention coefficients, retention increments and log*P* of some aromatic acids and their derivatives[56]

Compound	log*k*′	Σs_i	log*P*	Compound	log*k*′	Σs_i	log*P*
	−0.477	−2.38	1.40		−0.071	−1.27	1.86
	0.082	−0.92	2.27		0.485	−0.16	2.11
	0.641	0.05	2.82		0.900	0.26	3.53
	1.23	−0.12	3.08		0.19	−1.84	0.99
	0.51	−1.84	2.75		0.76	−1.84	2.75
	−0.097	−2.52	0.64		−0.22	−3.72	0.18

used them for the obtaining structure—retention relationship for the reversed-phase HPLC.[56] The retention coefficients of the aromatic acids, k', were correlated with their retention increments[57] (s) and the logarithm of the distribution coefficient $\log P$. The obtained results are listed in Table 3.

The plot of $\log k'$ vs. $\log P$ is a line with a correlation coefficient about 0.880. This is a very rough model that neglects the selectivity of the chromatographic system, which could not be described in terms of the liquid—liquid distribution. Nevertheless the values of $\log P$ are listed for a large set of compounds and they can be calculated very simply. The selectivity of the chromatographic system can be described with the help of the retention increments that can be added to the above model with Leo—Hansch parameters. For the terephthalic acid and its derivatives the following equation was obtained:

$$\log k' = -(0.244\pm0.048)+(0.0309\pm0.0022)\cdot(\log P + \Sigma s_i) \quad (32)$$

$(r = 0.990)$.

And the like equation was obtained for the polycarboxylic acids and their derivatives:

$$\log k' = -(0.393\pm0.073)+(0.218\pm0.033)\cdot(\log P + \Sigma s_i). \quad (33)$$

In the reversed-phase HPLC two main factors determine the retention of aromatic acids and their esters: the interaction of the sorbate with the "brush" of the alkyl radicals of the sorbent, and the interaction of the sorbate with the mobile phase that coats the surface of the sorbent. First of them can be described by the retention increment and the second one — by the distribution coefficient $\log P$. The contributions from both these factors are homogeneous as show the Eqs. (32) and (33).

The generality of the Leo—Hansch parameters makes it possible to describe with their help not only the structure of the quaternary cation, but also to predict the retention parameters in HPLC.

In the conclusion, the author sincerely hopes that this work would serve to attract the attention to the following problems.

The first of them is the interrelation of the micellar and phase-transfer catalysis and the observed duality of properties of the long-chain quats. It seems that the described effects should not be observed solely in the dehydrochlorination reactions.

The second problem is the frequently obtained extremum (most often parabolic) dependence of the catalyst effectiveness (alias the catalytic rate constant) on the size of the quat cation. The proposed method of the preliminary estimation of the extractability of the catalytic quat using its π-constants of hydrophobicity (we mean just the extractability neglecting the inherent catalyst activity, which is called intrinsic activity) is simple enough to be used by synthetic organic chemists.

The third problem is the relation of the PTC reactions to processes in biological membranes.

References

1. S. S. Yufit, *Mekhanizm mezhfaznogo kataliza* [*Phase-Transfer Catalysis Mechanism*], Nauka, Moscow, 1984, 264 p. (in Russian).
2. D. V. Banthorpe, *Elimination Reactions*, Elsevier, London, 1973.
3. E. V. Dehmlow and S. S. Dehmlow, *Phase Transfer Catalysis, 2nd rev. ed.*, Verlag Chemie, Weinheim, 1987.
4. J. M. van Rossum and L. J. Ariens, *Arch. Int. Pharmacodyn.*, 1959, **118**, 447.
5. C. Hansch and W. Fujita, *J. Am. Chem. Soc.*, **86**, 1616.
6. C. Hansch and J. M. Clayton, *J. Pharm. Sci.*, 1973, **6**, 1.
7. E. J. Lien, E. J. Ariens, and A. J. Beld, *Eur. J. Pharmacol.*, 1976, **35**, 245.
8. T. I. Zabrodina, S. V. Levanova, F. S. Sirovsky, and S. M. Velichko, *Khim. Prom-st*, 1985, 593 (in Russian).
9. T. I. Zabrodina, S. V. Levanova, F. S. Sirovsky, and Yu. A. Treger, *Kinet. Catal.*, 1986, **27** (Engl. Transl.).
10. F. S. Sirovsky, S. M. Velichko, Yu. A. Treger, A. L. Chimishkyan, and V. D. Koptelov, *Kinet. Catal.*, 1985, **26**, 8 (Engl. Transl.).
11. L. V. Istomin, S. A. Mulyashov, F. S. Sirovsky, Yu. A. Treger, and V. F. Shvets, USSR Pat. 1816751, 1993, *Method of manufacturing of propargylic alcohol*, Byull. Izobr., 1993, **19**, 55.
12. V. F. Sergeeva, *Russ. Chem. Rev.*, **34**, 309 (Engl. Transl.).
13. R. Walraevens, P. Trouillet, and A. Devos. *Int. J. Chem. Kinet.*, 1974, **6**, 777.
14. M. Halpern, Y. Sasson, and M. Rabinovitz, *J. Org. Chem.*, 1984, **49**, 2011.
15. M. Halpern, H. Zahalka, Y. Sasson, and M. Rabinovitz, *J. Org. Chem.*, 1985, **50**, 5088.
16. E. F. Lutz, J. T. Kelly, and D. W. Hall, Brit. Pat. 1112068, 1968.
17. M. Rabinowitz, Y. Cohen, and M. Halpern, *Angew. Chem.*, 1986, **98**, 958.
18. F. S. Sirovsky, S. M. Velichko, A. V. Neimark, Yu. A. Treger, A. L. Chimishkyan, and L. I. Kheifets, *Kinet. Catal.*, 1985, **26**, 11 (Engl. Transl.).
19. F. S. Sirovsky, S. M. Velichko, M. V. Panova, Yu. A. Treger, and A. L. Chimishkyan, *Kinet. Catal.*, 1985, **26**, 731 (Engl. Transl.).
20. E. Dehmlow, M. Slopianka, and J. Heider, *Tetrahedron Lett.*, 1977, 2361.
21. S. V. Levanova, V. A. Revyakin, F. S. Sirovsky, R. M. Rodova, G. T. Martirosyan, E. M. Asatryan, and A. Ts. Malkhasyan, *Zh. Vses. Khim. O-va.*, 1986, **31**, 237.
22. F. S. Sirovsky, Yu. A. Treger, M. V. Panova, and A. V. Voronkina, *Zh. Vses. Khim. O-va.*, 1985, **30**, 580.
23. M. Makosza and W. Lasek, *Tetrahedron*, 1991, **47**, 2843.
24. E. Dehmlow, R. Thieser, Y. Sasson, and R. Neumann, *Tetrahedron*, 1986, **13**, 3569.
25. S. S. Shavanov, G. A. Tolstikov, T. V. Shutenkova, and G. A. Viktorov, *J. Gen. Chem.*, 1987, **7** (Engl. Transl.).
26. W. Lasek and M. Makosza, *J. Phys. Org. Chem.*, 1993, **6**, 412.
27. V. A. Revyakin, A. L. Zabotin, and S. V. Levanova, *Kinet. Catal.*, 1991, **32** (Engl. Transl.).
28. C. Lapinte and P. Viout, *Tetrahedron Lett.*, 1973, 1113.

29. V. Gani, C. Lapinte, and P. Viout, *Tetrahedron Lett.*, 1973, 4435.
30. W. P. Jencks, *Catalysis in Chemistry and Enzymology* McGraw Hill Book Co., New York, San Francisco, London, Sydney, 1969.
31. F. S. Sirovsky, M. B. Skibinskaya, E. R. Berlin, Yu. A. Treger, N. N. Stepanova, and S. I. Molodchikov, *Kinet. Catal.*, 1986, **27** (Engl. Transl.).
32. C. A. Bunton, *Catal. Rev. Sci. Eng.*, 1979, **20**, 56.
33. L. S. Romsted, in *Micellization, Solubilization, and Microemulsions*, **1**, **2**, Ed. K. L. Mittal, Plenum Press, New York—London, 1977.
34. I. V. Berezin, K. Martinek, and A. K. Yatsimirsky, *Russ. Chem. Rev.*, 1973, **42**, 787 (Engl. Transl.).
35. V. A. Revyakin, S. V. Levanova, and F. S. Sirovsky, *Kinet. Catal.*, 1988, **28** (Engl. Transl.).
36. V. A. Revyakin, S. V. Levanova, N. N. Semochkina, and F. S. Sirovsky, *Kinet. Catal.*, 1990, **31** (Engl. Transl.).
37. A. Herriott and W. Picker, *J. Am. Chem. Soc.*, 1975, **97**, 2345.1
38. W. G. Griffin, *J. Soc. Cosmet. Chem.*, 1943, **1**, 311.
39. K. Fukunaga, M. Shirai, S. Ide, and M. Kimura, *J. Chem. Soc. Jpn., Chem. Ind. Chem.*, 1980, 1148.
40. H. Hildebrand and R. L. Scott, *Regular Solutions*, Prentice-Hall, New York, 1962.
41. A. Leo, C. Hansch, and D. Elkins, *Chem. Rev.*, 1971, **71**, 525.
42. B. Czapkiewicz-Tutaj and J. Czapkiewicz, *Rocz. Chem.*, 1975, **49**, 1353.
43. B. Zapior and B. Czapkiewicz-Tutaj, *Zesz. Nauk. Uniw. Jagiellon., Pr. Chem.*, 1972, **17**, 87.
44. F. S. Sirovsky, S. M. Velichko, Yu. A. Treger, and A. L. Chimishkyan, *Russ. J. Phys. Chem.*, 1983, **57** (Engl. Transl.).
45. D. Yadav and M. M. Sharma, *Ind. Eng. Chem., Process Des. Dev.*, 1981, **20**, 385.
46. L. K. Wang, *J. Am. Oil Chem. Soc.*, 1975, **52**, 339.
47. F. S. Sirovsky, S. M. Velichko, Yu. A. Treger, A. L. Chimishkyan, and M. V. Panova, *Kinet. Catal.*, 1985, **26** (Engl. Transl.).
48. M. Halpern, Y. Sasson, and M. Rabinowitz, *J. Org. Chem.*, 1983, **48**, 1022.
49. S. A. Mulyashov, F. S. Sirovsky, and O. S. Grechishkina, *Kinet. Catal.*, 1989, **30** (Engl. Transl.).
50. CSSR Pat. 157932, R. Zh., Khim. 1977, 9N156P.
51. J. T. Penniston, L. Beckett, D. L. Bentley, and C. Hansch, *Mol. Pharmacol.*, 1969, **5**, 333.
52. J. C. Dearden and M. S. Townsend, *Proc. Symp. on Chemical Structure—Biological Activity Relationships, Quantitative Approaches*, Suhl, G.D.R., October 1976.
53. J. W. McFarland, *J. Med. Chem.*, 1975, **13**, 1192.
54. R. M. Carlson, R. E. Carlson, and H. L. Kopperman, *J. Chromatogr.*, 1975, **107**, 219.
55. J. M. McCall, *J. Med. Chem.*, 1975, **18**, 549.
56. S. A. Mulyashov, F. S. Sirovsky, and O. S. Grechishkina, *Russ. J. Phys. Chem.*, 1991, **65** (Engl. Transl.).
57. V. D. Shats, O. V. Sakhartova, *Vysokoeffektivnaya Zhidkostnaya Khromatografiya* [*High-Pressure Liquid Chromatography*], Zinatne, Riga, 1988, 390 (in Russian).

Received August 17, 1995;
in revised form September 22, 1995