perimental conditions. It follows that $\lambda_1 = \alpha + \delta a + \beta b \approx \beta b$ and $\lambda_2 = \alpha\delta a/(\alpha + \delta a + \beta b) \approx (\alpha\delta/\beta)\,(a/b)$, provided $\beta b \gg \alpha + \delta a$. Thus as the system approaches its state of equilibrium

$$[\mathrm{C}]_t - [\mathrm{C}]_e = M \exp(-\lambda_1 t) + N \exp(-\lambda_2 t)$$

the constants M and N being determined by the initial conditions. As is easily verified, $\lambda_1 \gg \lambda_2$, and therefore the first term could be neglected at later stages of the reaction and then

$$[\mathrm{C}]_t - [\mathrm{C}]_e = \text{constant} \exp(-\lambda_2 t)$$

i.e.

$$\ln \{([\mathrm{C}]_0 - [\mathrm{C}]_e)/([\mathrm{C}]_t - [\mathrm{C}]_e)\} = \text{constant} + (\alpha\delta/\beta)(a/b)t$$

This result is identical to that derived on the assumption of stationary concentration of radical anions. Hence, the slopes of the asymptotes shown in Figures 2 and 3 are given by $\alpha K_1(a/b)$ because $\delta \approx k_1$ and $\beta \approx k_{-1}$.

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Phase Transfer Catalysis. An Evaluation of Catalysts[1]

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Received August 15, 1974

Abstract: The catalytic effects of quaternary ammonium and phosphonium ions on the reaction of thiophenoxide ion with 1-bromooctane in a two-phase system have been determined. The kinetics are linearly dependent on catalyst concentration and independent of stirring rate. A wide variety of catalysts was examined with the larger and more symmetrical ions being more effective. An increase in the ionic strength of the aqueous phase or change to a more polar organic solvent also increased the rate. Correlations between rate constants and partition coefficients indicate that the major function of the catalyst is simply the solubilization of the nucleophile in the organic phase.

A variety of organic reactions have recently been reported to be catalyzed by tetraalkylammonium salts. The generation of dichlorocarbene,[3] the alkylation of carbonyl and related compounds,[4] nucleophilic substitutions,[5] and the benzoin condensation[6] are among the reactions which are facilitated by this approach.[7] Two common features of these seem essential: the system has two phases consisting of a water layer and an organic layer and involves an anion as a base or nucleophile. Several explanations have been proposed for the effectiveness of quaternary ammonium ions,[3a,5,6,8] but the phase transfer mechanism proposed by Starks accounts for the major features of the reactions.[5] An important factor which has heretofore received scant attention is the structure of the quaternary ammonium salt. We wish to report a comprehensive quantitative comparison of the efficacies of quaternary ammonium ions in catalyzing an SN2 reaction.[9] The kinetic parameters obtained also offer additional independent evidence for the phase transfer mechanism.

Results

The system chosen for study was the reaction of thiophenoxide ion ($C_6H_5S^-$) with 1-bromooctane (RBr). Despite the complexities of a two-phase system of water and an organic solvent, the reaction followed good second-order kinetics at any given concentration of quaternary ammonium ions. Plots of ln $[\mathrm{RBr}]/[C_6H_5S^-]$ vs. t were linear with correlation coefficients of 0.996 or better. Rates followed by disappearance of bromooctane and by appearance of product sulfide were in good agreement and were reproducible to ≤3%.

The stirring rate was found to have no effect on the reaction for stirring speeds of 200–2200 rpm. At lower speeds a slight induction period was noted and at very low speeds (<50 rpm), the reaction no longer followed second-order kinetics. Stirring speeds of 1000–1500 rpm were used in determination of other kinetic effects.

The rate of reaction was found to be linearly dependent on catalyst concentration. Figure 1 shows the effect of a 20-fold change in concentration of cetyltriethylammonium bromide. In subsequent work the catalyst concentration was usually fixed at 0.00137 mol, but for very slow or very rapid reactions, higher or lower concentrations were used and all the results were extrapolated to 0.00137 mol of catalyst.

The major portion of this study focused on the effects of catalyst structure on the rate. The rate constants collected in Table I show the influence of systematic variations in the structure of the quaternary ion. These data were obtained for a benzene–water system containing 2 *N* sodium hydroxide. Changes in the organic solvent or salt concentration in the aqueous phase had pronounced effects on the rates as indicated in Tables II and III.

In order to evaluate the origin of the relative catalytic efficiencies, information about the distribution of quaternary salts was also collected. The distribution of quaternary ammonium hydroxides between benzene and water was evaluated by titration of the organic layer; a comparison with the rate constants is given in Table IV. The influence of quater-

Table I. Second-Order Rate Constants for the Reaction of Thiophenoxide with 1-Bromooctane in Benzene–Water

Entry	Catalyst[a]	$k_{\mathrm{obsd}} \times 10^3, M^{-1}\ \mathrm{sec}^{-1}$[b]	Mol of catalyst	$k \times 10^3, M^{-1}\ \mathrm{sec}^{-1}$[c]
1	$(CH_3)_4NBr$	<0.0016	0.00137	<0.0016
2	$(C_3H_7)_4NBr$	0.011	0.002748	0.0056
3	$(C_4H_9)_4NBr$	0.52	0.0001362	5.2
4	$(C_4H_9)_4NI$	0.72	0.0001326	7.4
5	$(C_8H_{17})_3NCH_3Cl$	4.0	0.0001757	31
6	$(C_6H_5CH_2)N(C_2H_5)_3Br$	<0.0016	0.00137	<0.0016
7	$C_5H_5NC_4H_9Br$	<0.0016	0.00137	<0.0016
8	$C_5H_5NC_7H_{15}Br$	0.025	0.001380	0.023
9	$C_5H_5NC_{12}H_{25}Br$	0.094	0.001386	0.092
10	$C_6H_{13}N(C_2H_5)_3Br$	0.044	0.004071	0.015
11	$C_8H_{17}N(C_2H_5)_3Br$	0.16	0.001359	0.16
12	$C_{10}H_{21}N(C_2H_5)_3Br$	0.25	0.001435	0.24
13	$C_{12}H_{25}N(C_2H_5)_3Br$	0.29	0.001384	0.28
14	$C_{16}H_{33}N(C_2H_5)_3Br$	0.48	0.001375	0.48
15	$C_{16}H_{33}N(CH_3)_3Br$	0.16	0.001414	0.15
16	$(C_6H_5)_4PBr$	0.25	0.0001423	2.5
17	$(C_6H_5)_4PCl$	0.27	0.0001361	2.7
18	$(C_6H_5)_3PCH_3Br$	0.17	0.0001355	1.7
19	$(C_4H_9)_4PCl$	3.5	0.0001319	37
20	$(C_8H_{17})_3PC_2H_5Br$	0.35	0.00001341	37
21	$C_{16}H_{33}P(C_2H_5)_3Br$	1.8	0.001374	1.8
22	$(C_6H_5)_4AsCl$	0.14	0.0001428	1.4
23	Crown ether[d]	0.62	0.0000207	41

[a] All hydrocarbon groups are straight chain alkyl groups, pyridine rings (entries 7–9), or phenyl rings. [b] Observed rate constant at catalyst concentration indicated. [c] Rate constant obtained by extrapolating k_{obsd} to 0.00137 mol of catalyst. [d] Dicyclohexyl-18-crown-6.

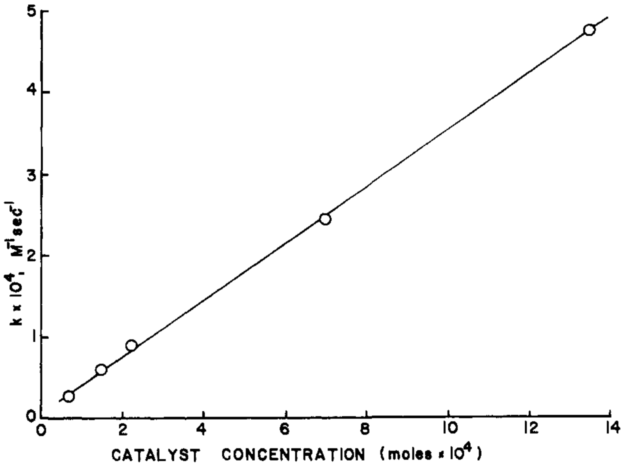

Figure 1. Dependence of rate constant on catalyst concentration using cetyltriethylammonium bromide.

Table II. Solvent Effects on Reaction Rate[a]

Entry	Catalyst	Solvent	$k \times 10^3, M^{-1}\ \mathrm{sec}^{-1}$
1	$(C_4H_9)_4NI$	Heptane	0.02
2	$(C_4H_9)_4NI$	$C_6H_4Cl_2$	88
3	$(C_3H_7)_4NBr$	$C_6H_4Cl_2$	0.45
4	$C_6H_5CH_2N(C_2H_5)_3Br$	$C_6H_4Cl_2$	0.04
5	$C_8H_{17}N(C_2H_5)_3Br$	$C_6H_4Cl_2$	28
6	$C_{10}H_{21}N(C_2H_5)_3Br$	$C_6H_4Cl_2$	75
7	$(C_6H_5)_4PBr$	Heptane	0.0093
8	$(C_6H_5)_4PBr$	$C_6H_4Cl_2$	47
9	$(C_4H_9)_4PCl$	$C_6H_4Cl_2$	180

[a] For the reaction of thiophenoxide with 1-bromooctane; rate constants are adjusted to 0.00137 mol of catalyst as in Table I.

Table III. Salt Effects in Benzene–Water with Cetyltriethylammonium Bromide[a]

Entry	NaBr	$k \times 10^3, M^{-1}\ \mathrm{sec}^{-1}$
1	0	0.48
2	0.2 M	1.7
3	0.5 M	3.7

[a] For the reaction of thiophenoxide with 1-bromooctane; rate constants are adjusted to 0.00137 mol of catalyst as in Table I.

Table IV. Comparison of Catalytic Rates and Ability to Extract Hydroxide Ion

Catalyst	No. of C atoms	$K = [OH^-]$-benzene/$[OH^-]H_2O$	Rate
$(CH_3)_4$	4	0.027	<0.001
$C_6H_5CH_2N(C_2H_5)_3Cl$	13	0.041	<0.001
$(C_3H_7)_4NBr$	12	0.11	0.034
$C_{16}H_{33}N(CH_3)_3Br$	19	0.15	0.92
$C_5H_5NC_{12}H_{25}Br$	17	0.18	0.56
$C_{10}H_{21}N(C_2H_5)_3Br$	16	0.26	1.5
$C_{12}H_{25}N(C_2H_5)_3Br$	18	0.54	1.7
$(C_4H_9)_4NBr$	16	0.68	31

nary ions on thiophenoxide distributions is given in Table V, representing not only a distribution between solvents, but also a selectivity of thiophenoxide vs. hydroxide ions.

Discussion

Examination of the relative rates with various catalysts in Table I reveals several interesting trends. (1) The larger ions (e.g., entries 3, 5, 19, 20) are the most effective. (2) As the length of the longest chain increases (entries 7-9 and 10-14), the catalytic efficiency also increases. (3) The more symmetrical ions (3, 5, 19, 20) are better than those with only one long chain (12-15);[11] similarly the cetyltriethylammonium ion is three times more effective than cetyltrimethyl. (4) Phosphonium ions (19, 20, 21) are somewhat more effective than ammonium ions bearing the same substituents (3, 5, 14); the single arsonium ion is less effective than the phosphorus analog (22 vs. 17). (5) Alkyl groups are more proficient than aryl groups (16-18 vs. 19 and 20). (6) Benzyltriethylammonium ion, the catalyst used extensively by Makosza,[3a,8] is totally ineffective in benzene and only a weak catalyst in *o*-dichlorobenzene. (7) Comparisons with Table II show that the rates are slower in heptane than in benzene, but faster in *o*-dichlorobenzene. The rate increase in going from benzene to *o*-dichlorobenzene is most pronounced for the weaker catalysts such as tetrapropylammonium bromide (80 times faster) and decyltriethylammonium bromide (300 times faster), while the highly efficient catalysts are increased by factors of 5 (tetrabutylphosphonium chloride) to 16 (tetraphenylphosphonium bromide). (8) No appreciable counterion effect was noted; the slightly

Table V. Extraction of Thiophenoxide Ion into Benzene from 2 *N* NaOH

Catalyst	% in benzene	Relative %[a]	Relative rate[b]
$(C_6H_5)_4PCl$	9	0.40	0.48
$(C_4H_9)_4NBr$	22	1.0	1.0
$(C_4H_9)_4PCl$	91	4.1	7.1
$(C_8H_{17})_3PC_2H_5Cl$	93	4.2	7.1

[a] (% extracted into benzene)/(% $(C_4H_9)_4NBr$ extracted into benzene). [b] Relative to $(C_4H_9)_4NBr$.

faster rate of tetrabutylammonium iodide than the bromide is largely due to an SN2 displacement by iodide ion followed by a more rapid reaction with thiophenoxide.

These data provide a clear choice of catalysts and solvents for synthetic purposes. Maximum rates were obtained with the large phosphonium ions, but phosphonium ions are much more prone to decomposition or side reactions with nucleophiles.[12] Trioctylmethylammonium chloride is nearly as effective and far more stable; its low cost will probably establish it as the reagent of choice. The reaction is accelerated in more polar solvents; *o*-dichlorobenzene is particularly effective in this case while methylene chloride or 1,2-dichloroethane is more convenient if stable to reaction conditions.[13] As further discussion will explain, the rates converge in more polar solvents and the choice of catalysts is less critical. For comparison, the maximum rate constant obtained by the phase transfer method (Table II, entry 9) is ten times faster than the homogeneous reaction in ethanol and about 300 times slower than in anhydrous dimethylformamide;[14] the actual rates can be accelerated if desired by increasing the catalyst concentration.

The kinetic data provide additional support for the general mechanism of phase transfer catalysis developed by Starks.[5] In our system the scheme may be depicted by eq 1, where Q is the quaternary cation. In this picture the primary role of the quaternary ammonium ion is to transport an anion into the organic phase.

$$\begin{array}{lccccccc}
\text{aqueous phase} & \mathrm{NaSC_6H_5} & + & \mathrm{QBr} & \rightleftarrows & \mathrm{QSC_6H_5} & + & \mathrm{NaX} \\
\text{interface} & \text{- - - - - -} & \text{- -} & \uparrow\downarrow & \text{- - - - -} & \downarrow\uparrow & \text{- -} & \text{- - -} \\
\text{organic phase} & \mathrm{C_6H_5SR} & + & \mathrm{QBr} & \longleftarrow & \mathrm{QSC_6H_5} & + & \mathrm{RBr}
\end{array} \qquad (1)$$

Evidence that a similar reaction occurs in the organic phase has been previously reported.[10] In the present case, the independence of reaction rate and stirring speed indicates that interface phenomena are insignificant.[15] The kinetics and dependence on quaternary ion concentration are also completely consistent with this scheme since the quaternary ion, the thiophenoxide, and the bromooctane are all involved in the rate-determining step. In particular, the linear dependence of rate on the concentration of the quaternary ammonium ion is in sharp contrast to the discontinuous behavior associated with catalysis by micelles.[16] These experiments together with the similar results reported by Starks[5b] offer compelling evidence for the scheme in eq 1[17,18] and provide a context for interpreting the catalytic effectiveness of the various quaternary ions.

In assessing the relative efficacies of the various quaternary ions in terms of eq 1, two factors can be considered. The quaternary ion must transport thiophenoxide ion into the organic phase and return to the aqueous phase to pick up another molecule of the nucleophile. Second, the reactivity in the organic phase may be dependent on the nature of aggregation between the quaternary ion and thiophenoxide ion.[19]

Assuming that transport between phases is rapid, the catalytic ability of the ions should correlate with distribution coefficients. Quaternary ammonium salts have been used to extract cobalt(II) complexes into organic solvents; symmetrical ions were found to be more effective than less symmetrical ions of comparable molecular weight.[20] The same order has been observed in the partition coefficients of quaternary ammonium permanganate salts in benzene-water.[21] A more extensive comparison is given in Table IV where the rates of the displacement reaction for several catalysts are compared with their ability to extract hydroxide ion. The correlation coefficient of 0.82 indicates a substantial parallel between catalytic effectiveness and extractive power, especially since the comparison involves the soft base thiophenoxide ion in the former case and the hard base hydroxide ion in the latter.

These efficient extractions of hydroxide and permanganate ions into benzene together with the quantitative extractions of many quaternary ammonium salts into methylene chloride as reported by Brandstrom[22] suggested that thiophenoxide might be predominantly in the organic phase. The partitioning contribution to catalysis would necessarily level off as the fraction of thiophenoxide ion in the organic phase approaches 100%. Since there is no indication of a ceiling in the rate data of Table I, either the reactivity of the thiophenoxide ion is being further enhanced by the nature of its pairing and aggregation with the quaternary ion or the thiophenoxide extraction is very incomplete.

This question is resolved by the data in Table V. Here four of the best catalysts from Table I are compared in their ability to extract thiophenoxide into benzene from 2 *N* sodium hydroxide. Again the relative rates are directly proportional to the fraction extracted into the organic phase. These data suggest that the saturation point in benzene is approached by the fastest catalysts, but the slower catalysts are not very efficient in solubilizing thiophenoxide in the organic phase. While the nature of aggregation undoubtedly plays some role, it seems clear that the partitioning coefficient is the dominant factor in determining the reactivity of a given catalyst.

Additional supportive evidence for this explanation is found in the observation that a crown ether, dicyclohexyl-18-crown-6, serves as an efficient phase transfer catalyst in the two-phase benzene–water system. Significantly, the rate constant is almost identical to that of the fastest quaternary ion catalysts. Indeed if one assumes that the crown ether forms a 1:1 complex with sodium thiophenoxide which is distributed 100% into the organic phase, the rate fits perfectly with those in Table. V. This does not require that the anions are "naked";[19b] rather the degree of association and hydration of the anions must be either very similar or of minor significance. An attempt to use tetrabutylammonium thiophenoxide in homogeneous benzene solution was complicated by irreproducibility, but was about one order of magnitude faster than the fastest heterogeneous systems.[23] The lesser reactivity of thiophenoxide under the phase transfer conditions compared to anhydrous benzene suggests that water molecules of solvation may accompany the anion into the organic phase during phase transfer. This is consistent with our earlier experiments on competitive elimination vs. substitution in a secondary alkyl bromide in which phase transfer conditions showed a preference for elimination characteristic of a nonpolar solvent, but was less selective than a homogeneous reaction in dry benzene.[10] Starks has directly measured the concentration of water in the organic phase under phase transfer conditions and shown the anions are indeed accompanied by water of hydration.[5b]

The effects of added salt and changes of solvent can also be accommodated by an interpretation based on partitioning factors. An increase in ionic strength in the aqueous phase salts out the large organic ions, increases their partitioning into the organic phases, and accelerates the rate. A change of solvent from benzene to heptane causes a substantial rate decrease by a lowering of the distribution coefficient. In going from benzene to *o*-dichlorobenzene, a mediocre catalyst such as decyltriethylammonium ion is increased by a factor of 300 while the proficient catalyst tetrabutylphosphonium ion is only accelerated fivefold. In the former case, most of the increase may be attributed to increased partitioning into the organic phase; in the latter case, the partitioning was already nearly quantitative and the rate acceleration is probably a consequence of activation of the nucleophile thiophenoxide in a looser or less solvated ion pair. There is a general converging of rates as polarity of the organic solvent is increased; for example, the difference between tetrabutylphosphonium and decyltriethylammonium ions is a factor of ca. 150 in benzene and a factor of 6 in *o*-dichlorobenzene.

Although aqueous micelles with quaternary ammonium ions can be excellent catalysts[16] and have been invoked in one example of a phase transfer reaction,[3] their involvement can be convincingly excluded in the present case. The linear dependence on catalyst concentration is in sharp contrast with the kinetic behavior of catalysis by micelles, which typically show a pronounced rate acceleration near the critical micelle concentration followed by a flat or decreasing rate at higher concentrations. Second, the relative rates indicate that the quaternary ions most prone to formation of micelles, e.g., cetyltrimethylammonium bromide, are not nearly as effective as the more symmetrical ions like tetrabutylammonium chloride.

Inverted or reversed micelles in the organic phase cannot be excluded by these data. While several examples of rate catalysis by reversed micelles show rate maxima or Michaelis-Menton behavior,[25] at least one example shows a linearly increasing rate above the critical micelle concentration.[26] Interestingly, the increased catalysis above the cmc is attributed to catalysis by monomer in equilibrium with the micelle.[26] It is possible that the linear concentration dependence observed in our work represents only a portion above the cmc of the catalysts, since the cmc's of some inverted micelles are very low and many others are undetermined. But the effectiveness of symmetrical quaternary ions like tetrabutylammonium in the present work is again in distinct contrast to the rodlike molecules used by the Fendlers in their impressive studies on catalysis by inverted micelles.[25] Finally, it should be noted that the inverted micelles can have very small aggregation numbers; nmr studies indicate that three to seven molecules is the typical micelle size for simple alkylammonium carboxylates in a variety of solvents.[27] While the phase transfer scheme is sufficient to account for our results, the ions are undoubtedly aggregated in nonpolar solvents like benzene. The question of when this aggregation could be called an inverted micelle requires identification of some discontinuity in properties as a function of concentration. The absence of such a discontinuity in our data means that it is unnecessary to invoke inverted micelles as part of the scheme, but cannot exclude them.

While the exact ordering of catalyst reactivities is specific for this system, it seems likely that similar reactivities will prevail in other instances of phase transfer catalysis. The fragmentary data on other systems[19] as well as the distribution coefficients for several anions in this and previous[21] work support this projection.[28] These results provide both a consistent picture with the phase transfer scheme and a useful guide to choice of catalyst and reaction conditions for synthetic applications.

Experimental Section

Many of the quaternary salts were commercially available.[31] Others were prepared in routine fashion by refluxing an appropriate amine and an excess of alkyl halide in ethanol. All were recrystallized from ethanol and dried in a vacuum desiccator. Tetrabutylammonium thiophenoxide was prepared by the silver oxide method of Ford.[24]

The kinetics were carried out in a 250-ml three-neck flask fitted with mechanical stirrer, a gas inlet–outlet, and rubber septum. The reactions were conducted under nitrogen to avoid oxidation of thiophenoxide. A Teflon stirring paddle was driven by a Talboy stirring motor; the stirring speed was determined using a strobe light. The reaction vessel was immersed in a constant temperature bath at 30.0 ± 0.05°.

In a typical procedure, the reaction flask was charged with 2.0115 g of 1-bromooctane, 3.0171 g of thiophenol, 1.0047 g of tetradecane as internal standard, 40.0 ml of benzene, and an appropriate amount of a quaternary salt. Fifty milliliters of 2 *N* sodium hydroxide was added, the flask was flushed with nitrogen, and the stirring and timing were commenced. Heterogeneous samples of 0.25 ml were withdrawn at regular intervals and quenched in 3 *N* HCl. After the layers separated, the organic layer was analyzed by gas chromatography using a 6 ft × ⅛ in. UCW-98 silicone rubber column programmed from 80 to 240° at 10°/min. A Hewlett-Packard Model 5750 gas chromatograph was used with a thermal conductivity detector and a Columbia Scientific Industries Digital Integrator. Appropriate calibration curves for 1-bromooctane, *n*-octyl phenyl sulfide, and tetradecane were developed. The change in concentration of 1-bromooctane was used in the rate calculations, but rate constants based on appearance of the product sulfide agreed to within 3%. The kinetics were followed to 90% completion; the yield was quantitative.

Using the equation $(1/([B_o] - [A_o])) \ln [BA_o]/[AB_o] = kt$ where $[A] = [\text{1-bromooctane}]$ and $[B] = [\text{thiophenol}]$, the rate constants were calculated using a least-squares computer program. All rates involved at least six samplings and gave correlation coefficients of 0.996 or better.

The distribution coefficients for quaternary ion hydroxides were determined by thoroughly shaking 50 ml each of benzene and 2 *N* sodium hydroxide with about 0.002 mol of quaternary salt. Aliquots were removed from the organic layer and titrated with standard HCl. Distribution coefficients for quaternary ion thiophenoxides were obtained by shaking 40 ml of benzene, 50 ml of 2 *N* sodium hydroxide, and 3 ml (an excess) of thiophenol with about 0.002 mol of quaternary salt. Aliquots were taken of the organic layer and treated with 0.5 g (excess) of 1-bromooctane and 0.500 g of tetradecane as internal standard. These were stirred under nitrogen until reaction was complete (30 min) and analyzed by gas chromatography as described above.

References and Notes

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(11) The lower reactivity of tetrapropylammonium (entry 2) compared to hexyltriethylammonium ion (entry 10) suggests that a certain minimum size is necessary before this trend is manifested.

(12) For example, even under the mild conditions used here, benzyltriphenylphosphonium chloride was rapidly consumed.

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(28) There are some indications that the quaternary ammonium ion effect in the generation of dichlorocarbene does not fit the pattern. First, vigorous stirring has been reported to be helpful[29] and interface effects have been suggested.[18] Second, benzyltriethylammonium chloride is an effective catalyst. And most significantly, tributylamine and other large tertiary amines have been found to work just as well as ammonium salts.[30] All these are in contrast to the results presented herein. We found no catalysis in our system by tributylamine, nor can permanganate be solubilized in benzene by tertiary amines.[21]

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Determination of Reaction Rate Parameters by Flow Microcalorimetry

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Abstract: Using the alkaline hydrolysis of ethyl acetate as a model reaction, the applicability of a flow microcalorimeter to measure bimolecular (or higher molecularity) reaction rates with half-times in the range of at least 5 sec to several hours is demonstrated. In addition, an experimental scheme is developed which allows the calorimetric determination of the enthalpy change of slow reactions. The precision and accuracy of both ΔH values and apparent rate constants is estimated to be better than ±2%.

The determination of reaction rate parameters is a cornerstone of chemistry and provides invaluable information about reaction mechanisms. In this communication it will be demonstrated that a flow microcalorimeter, whose usefulness for obtaining thermodynamic data is well established,[2-5] can be used to determine rates of reactions in solution that have half-lives between a few seconds and several hours. Since the production or absorption of heat is a ubiquitous property of chemical reactions, this instrument can be used to obtain both thermodynamic and kinetic information about a wide variety of chemical reactions.

Most thermal techniques previously used to determine reaction rates monitor the change in temperature[6-10] of the system as a function of time in an apparatus similar to the classical "adiabatic" calorimeter. A few methods which directly measure the rate of heat production have also been reported.[11-16] Methods of the former type require estimation of the time derivative of experimental data in order to obtain a value for the reaction velocity. Such an analytical process can significantly increase the error of the estimated reaction rate. Methods of the latter type have the advantage that the measured signal is time invariant and directly proportional to the average velocity of the reaction. The flow microcalorimetric technique to be described provides data of the second type and is similar, in principle, to the thermal method of Roughton and coworkers[17] and the stirred flow reactor described by Hammett and colleagues.[18]

The flow microcalorimeter used in this work is manufactured by LKB Instruments, Inc., based on an original design by Monk and Wadsö.[19] It can operate in two modes, one in which the rate of heat generation in a solution flowing through the calorimeter is measured (the flow-through mode) and one in which the rate of heat generation in a liquid system mixed within the calorimetric cell is measured (the mixing mode). Wadsö and coworkers[15,20] and Beezer and Tyrrell[14] have used the flow-through mode to monitor the velocity of slow reactions ($\tau_{1/2} > 10^3$ sec) initiated externally to the calorimeter. Beezer and Tyrrell[21] have also developed the theoretical relationships applicable to the special case of zero-order and pseudo-first-order reactions in both modes. However, the general characteristics of the calorimeter are such that, in principle, the reaction rate parameters can be determined for reactions of order ≥ 2 when this instrument is used in the mixing mode. Using the alkaline hydrolysis of ethyl acetate as a model reaction it will be demonstrated that the reaction rate, the reaction order, and the enthalpy change for liquid phase reactions having a half-life of 5 sec to 50 hr can be precisely determined with this technique.

Theoretical Section

Fast Reactions. The LKB flow microcalorimeter was originally designed to measure heats of essentially instantaneous reactions. Such reactions generate heat at the point of mixing which is dissipated throughout the calorimetric cell. Under constant flow conditions, a steady state temper-