Hofmann Decomposition of Quaternary Ammonium Salts under Phase-transfer Catalytic Conditions

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The known Hofmann degradation of quaternary ammonium salts under basic phase-transfer catalytic conditions has been studied. The base-catalysed isomerization of p-allylanisole to p-methoxy-β-methylstyrene was used as a kinetic probe to find experimentally the rate constant and activation energy of the Hofmann decomposition without isolating the quaternary ammonium basic salt $R_4N^+B^-$ (B^- = base anion). Reactions performed at various temperatures showed that the higher the temperature the greater was the initial rate but the lower the final conversion in the isomerization reaction. The quaternary ammonium hydroxide was found to catalyse the isomerization and the Hofmann degradation more effectively than the corresponding alkoxide. This indicates that the former is a stronger base in the non-polar aprotic solvents common in phase-transfer catalysis.

In phase-transfer catalytic reactions with quaternary ammonium salts as catalysts, there are two commonly acknowledged modes of catalyst deactivation. One of these involves catalyst poisoning by the anion released in the course of the reaction.[1] In such systems the affinity of the leaving anion for the quaternary ammonium cation is greater than that of the reactive anion. Saturation of the catalyst by the inactive anion then stalls the reaction.[2] The other mode of catalyst deactivation involves decomposition of the quaternary ammonium salt to give an inactive species. In general, two types of decomposition reaction are known to cause deactivation. One is the reverse Menshutkin reaction, i.e. dequaternization of the quaternary ammonium salt [equation (1)].[3] In this reaction

$$R_4N^+X^- \rightleftharpoons R_3N + RX \qquad (1)$$
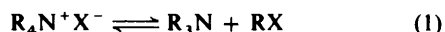
the equilibrium may be shifted to the right, usually at elevated temperatures and in non basic media. The other type of decomposition is the Hofmann degradation of the quaternary ammonium salt [equation (2)].[4] This reaction is base-catalysed

$$(R'CH_2CH_2)R_3N^+B^- \longrightarrow R_3N + R'CH=CH_2 + HB \qquad (2)$$

(B^- is a basic anion) and irreversible, and occurs even at ambient or sub-ambient temperatures.

Base-catalysed phase-transfer reactions are common, and represent a large portion of phase-transfer-catalysed reactions examined to date.[5] Although the Hofmann decomposition is known to take place in the course of many such base-catalysed reactions, little is known about the decomposition under actual phase-transfer conditions. Therefore, it seemed appropriate to perform a quantitative study under phase-transfer conditions in order to obtain a complete picture of a base-catalysed phase-transfer reaction profile. In this paper we present our results describing various factors which influence the Hofmann decomposition under phase-transfer conditions.

Results and Discussion

As stated, Hofmann decomposition of a quaternary ammonium salt (Q) occurs under basic conditions, giving a tertiary amine (A) and olefin (O), and the conjugate acid (BH) [equation (3)].

$$Q \xrightarrow{k_4} A + O + BH \qquad (3)$$

In the past, quaternary ammonium hydroxides have been synthesized and the decomposition reaction has been investigated by direct measurement of the decomposition products.[6] It has been found that the reaction is first order in quaternary ammonium salt. However, under actual phase-transfer reactions the Hofmann reaction may proceed at a different rate because of additional factors. Especially crucial may be the presence of alcohols, as in reactions such as the Williamson ether synthesis, or as an additive in carbene reactions. It has been found that when 50% NaOH, an organic solvent, and an alcohol are mixed in the presence of a quaternary ammonium salt, all the salt found in the basic form in the organic phase is alkoxide, $R_4N^+OR^-$.[7] Such a species will decompose in a Hofmann reaction, however; its isolation has not been achieved to date, and the reaction cannot be studied in the ordinary manner. Our aim, therefore, was to develop a reaction system where one could study the Hofmann decomposition indirectly without isolating the quaternary ammonium salt. To this end the isomerization of p-allylanisole (S) to p-methoxy-β-methylstyrene (P) [equation (4)] was used as a kinetic probe.

$$(4)$$
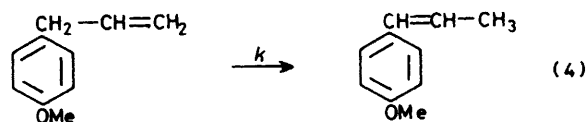
This reaction has previously been investigated and found to be first-order in the organic substrate and quaternary catalyst until catalyst decomposition becomes significant.[8] The reaction is advantageous for investigating the Hofmann decomposition, for no new anion is formed and therefore no complications due to catalyst poisoning by the leaving anion arise. The problem of catalyst poisoning can be totally eliminated if one uses as original catalyst a quaternary ammonium hydrogen sulphate such as $Bu_4N^+HSO_4^-$. Addition of a basic anion such as OH^- or the presence of OR^- formed in situ will ensure that all the catalyst is in the basic form and in the organic phase [e.g. chlorobenzene].[9]

By using the isomerization reaction as an experimental kinetic probe the Hofmann decomposition may be analysed kinetically as follows. As mentioned, the Hofmann decom-

position is first order in the quaternary salt. Thus, the concentration of the salt varies as described in equation (5) (first-

$$C_Q = C_{Q0}e^{-k_d t} \qquad (5)$$

order decay; C_Q = quaternary salt concentration). Since the isomerization reaction is first order in both quaternary salt and substrate (C_S), one obtains equation (6), which upon separation

$$-dC_S/dt = kC_{Q0}e^{-k_d t}C_S \qquad (6)$$

and integration gives equation (7). At the boundary conditions

$$\ln(C_{S0}/C_S) = kC_{Q0}(1 - e^{-k_d t})k_d \qquad (7)$$

where the time is infinite one finds[8] that the substrate concentration does not fall to zero [equation (8)]. Combining equations (7) and (8) leaves, upon rearrangement, equation (9) (x is the conversion).

$$\ln(C_{S0}/C_{S\infty}) = kC_{Q0}/k_d \qquad (8)$$

$$\ln\ln(C_S/C_{S\infty}) = \ln\ln(1 - x)/(1 - x_\infty) = $$
$$\ln(kC_{Q0}/k_d) - k_d t \qquad (9)$$

As is evident from equation (9), tracking the concentration of the isomerization reaction substrate, allylbenzene (by g.l.c. in this case), as a function of time will give the first-order rate constant of the Hofmann decomposition without isolation or measurement of the concentration of the quaternary ammonium salt or even the amine or olefin decomposition products. Naturally, performing the reaction at various temperatures will enable, in addition, the calculation of the energy of activation, E_a, by use of the Arrhenius equation.

In the first experiments the decomposition kinetics of a quaternary ammonium hydroxide were studied by the foregoing method using as original catalyst $Bu^n_4N^+HSO_4^-$. From the reaction profiles of the isomerization at various temperatures (Figure 1) one finds some interesting results. At lower temperatures the initial reaction rate is less; however, the final conversion is higher. This can be explained by increased catalyst deactivation at the higher temperatures shortening the lifespan of the catalytic reaction (without catalyst there is no reaction). Linear regression of the function described by equation (9) [$\ln\ln(1 - x)/(1 - x_\infty)$ versus t] by the method of least squares (of the results as presented in Figure 1) was performed. The results, showing the rate constants at various temperatures, are given in Table 1. The correlation coefficients show that the results fit the equation extremely well, indicating the assumptions of reaction order made were valid. Arrhenius plots of the rate constants give energies of activation of 12.5 and 17.4 kcal mol⁻¹ for the isomerization and decomposition reactions, respectively. This shows the greater effect of temperature on the degradation reaction.

As mentioned previously, many base-catalysed phase-transfer reactions are performed in the presence of alcohols. It has been shown[7] that in the presence of alcohols and aqueous NaOH, quaternary ammonium alkoxides are formed by the following series of equilibria. The first equilibrium reaction (10) takes

$$ROH + OH^- \rightleftharpoons OR^- + H_2O \qquad (10)$$

place either in the aqueous phase or at the interface, depending on the lipophilicity of the alcohol and the concentration of the aqueous phase. The second equilibrium reaction, (11), forms the
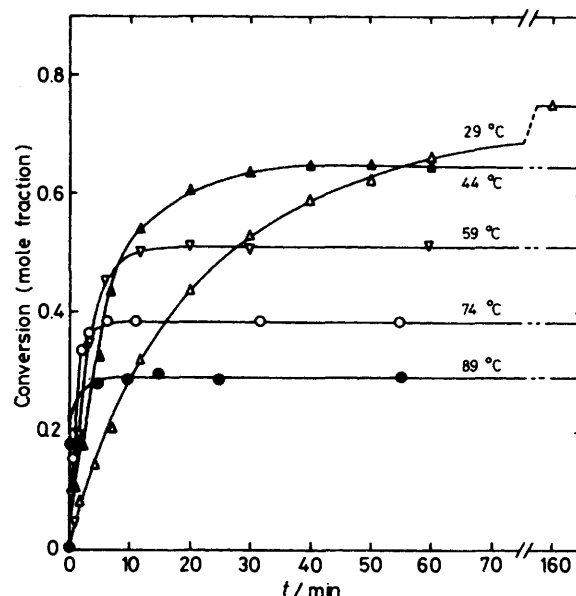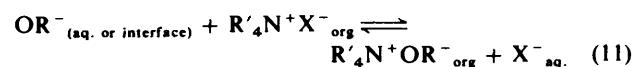
$$OR^-_{(aq.\ or\ interface)} + R'_4N^+X^-_{org} \rightleftharpoons$$
$$R'_4N^+OR^-_{org} + X^-_{aq.} \qquad (11)$$

Figure 1. Reaction profiles of isomerization reaction catalysed by quaternary ammonium hydroxide at various temperatures

Table 1. Rate constants computed by linear regression from isomerization reaction profiles catalysed by $Bu_4N^+OH^-$ at various temperatures

Temp. (°C)	k/dm³ mol⁻¹ min⁻¹	k_d/min⁻¹	x_x	r^a
29	0.472	0.0216	0.779	0.999
44	1.69	0.112	0.649	0.995
59	2.93	0.272	0.525	0.999
74	7.43	1.050	0.382	0.996
89	8.79	1.782	0.289	0.999

[a] Correlation coefficient.

quaternary ammonium alkoxide, when X^- is the bisulphate anion, and for the isomerization reaction most of the quaternary salt is the $R'_4N^+\ OR^-$ form. For such salts the Hofmann degradation has not been studied, for they have not been isolated. Reaction profiles of the isomerization reaction at various molar ratios of butan-1-ol to $Bu^n_4N^+HSO_4^-$ are drawn in Figure 2. The addition of alcohol decreases both the initial rate and the maximum conversion. Computation of the rate constants by use of equation (9), summarized in Table 2, shows conclusively that even sub-equivalent amounts of butan-1-ol reduce the rate constant of both isomerization and decomposition reactions. These results were surprising, for it is generally considered that a primary alkoxide anion is a stronger base than the hydroxide anion. The pK_a of butan-1-ol is greater than the pK_a of water for solvents such as water. Therefore, it might have been expected that both the isomerization and degradation reactions would have higher rates with the supposedly stronger alkoxide bases since both reactions are base-catalysed. This is especially true at equivalent or sub-equivalent amounts of alcohol (compared with the original amount of quaternary salt) where no solvation of the alkoxide anion by the alcohol would be expected. Such solvation would naturally have a stabilizing effect on the quaternary ammonium salt and reduce basicity, as in indeed found with super-equivalent amounts of alcohol. It seems probable that in apolar solvents such as those commonly used in phase-transfer
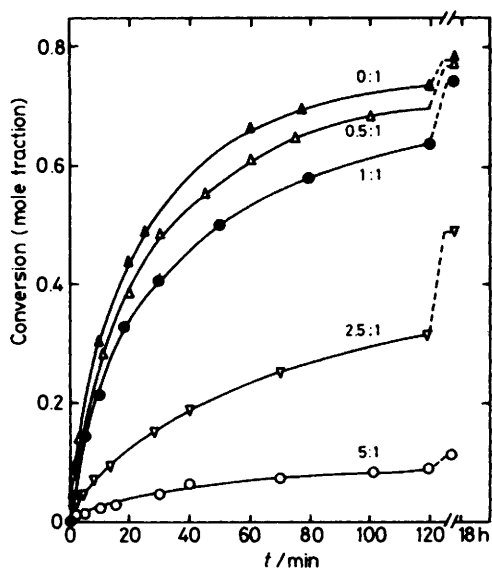
Figure 2. Reaction profiles of isomerization reaction at various molar ratios of butan-1-ol to tetrabutylammonium hydrogen sulphate, at 29 °C
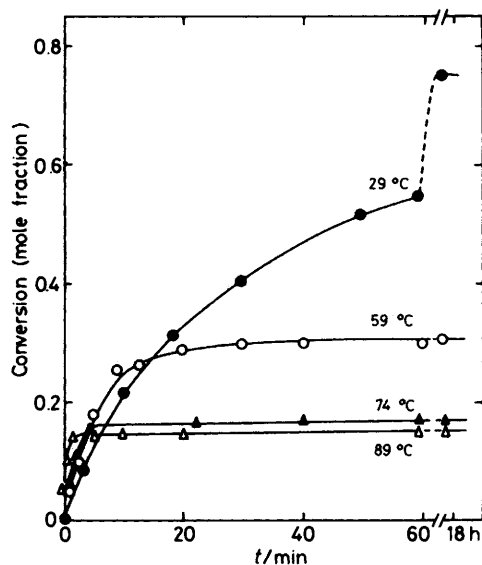

Figure 3. Reaction profiles of isomerization reaction catalysed by quaternary ammonium n-butoxide at various temperatures

Table 2. Rate constants computed by linear regression at various butanol:quaternary ammonium salt ratios[a]

Molar ratio butan-1-ol:$Bu_4N^+HSO_4^-$	k/dm^3 mol^{-1} min^{-1}	k_d/min^{-1}	x_z
0:1	0.461	0.0216	0.779
0.5:1	0.328	0.0157	0.780
1:1	0.217	0.0117	0.745
2.5:1	0.0643	0.006 93	0.487
5:1	0.0183	0.001 17	0.125

[a] Temp. 29 °C; correlation coefficients greater than 0.995.

Table 3. Rate constants computed by linear regression of reactions in the presence of alcohols[a]

Alcohol[b]	k/dm^3 mol^{-1} min^{-1}	k_d/min^{-1}	x_z
None	0.461	0.0216	0.779
MeOH	0.405	0.0194	0.816
EtOH	0.233	0.0129	0.753
Bu^nOH	0.217	0.0117	0.745
Oct^nOH	0.180	0.0093	0.683

[a] Temp. 29 °C; correlation coefficients greater than 0.992. [b] 0.8 mmol.

catalysis the order of basicity is reversed; that is, primary alkoxides are weaker bases than hydroxides when extracting from 50% NaOH. This is because in apolar aprotic solvents the hydroxide anion is small, being only slightly hydrated.[9] The smaller the basic anion the more powerful a base it is. In Table 3 the importance of the anion size is further brought out by a comparison of rate constants found for several alkoxide anions. The larger the alkoxide the less basic it is. It is important that for methoxide and hydroxide the results are very similar, indicating a similarity in size of the slightly hydrated hydroxide and methoxide anions when extracted from 50% NaOH.

In other respects the quaternary ammonium alkoxides are similar to the hydroxide. In Figure 3 one can see that, as in the case of the quaternary ammonium hydroxide, the initial isomerization rates are higher with increasing temperature but final conversions are lower. The energies of activation of the Hofmann decomposition are also similar: 13.4 kcal mol^{-1} for $Bu^n_4N^+OBu^-$ versus 17.4 for $Bu^n_4N^+OH^-$.

Conclusions

The Hofmann degradation of basic quaternary ammonium salts, $Bu^n_4N^+X^-$, where X^- is hydroxide or alkoxide, has been studied by using the isomerization of allylanisole as a reaction probe. The isomerization reaction profiles (Figures 1 and 3) ($Bu^n_4N^+OH^-$ and $Bu^n_4N^+OBu^-$ are the respective catalysts) show that lower temperatures enable higher final conversions,

albeit at lower initial rates. This phenomenon is due to the greater sensitivity to temperature of catalyst deactivation by Hofmann degradation, as is borne out by the activation energies of the decomposition and isomerization reactions. At lower temperatures the isomerization reaction is slow but the low rate of catalyst decomposition enables high final conversions. At higher temperatures the isomerization reaction is fast but the increased rate of catalyst decomposition lowers the final conversion.

The presented reaction system enabled the study of Hofmann degradation of non-isolated quaternary ammonium alkoxides commonly used in phase-transfer catalysis. The results (Table 3) show that the quaternary ammonium alkoxides are less susceptible to the degradation reaction than are the hydroxides. Increasing the size of the alkoxide anion decreases the basicity, as seen by lower rate constants, k and k_d. The presence of increasing amounts of alcohol in the organic phase decreases the rate and final conversion of both the decomposition and isomerization reaction (Figure 2 and Table 2). Since both reactions are base-catalysed one may conclude that the addition of alcohol lowers the basicity of the alkoxide anion. This is due to the formation of large anions through solvation. The larger the anion the lower the basicity in an apolar medium.

To summarize, knowledge of the reaction order, rate constant (k_d), and activation energy of the Hofmann degradation reaction under various conditions enables the general use of these parameters in the study of other phase-transfer catalytic reactions performed in basic environment.

Experimental

Reaction System.—Reactions were performed in a 50 ml round-bottom flask with a side-arm for sampling. Stirring was mechanical (Heidolph RZRI) at 500 rev. min⁻¹. The flask was placed in a 2 l thermostatically controlled oil-bath (± 0.5 °C). In a typical procedure, NaOH (50% w/w; 10 ml, 0.2 mol) chlorobenzene solvent (10 ml) and *p*-allylanisole substrate (0.01 mol) were placed in the flask. After 20 min to allow for equilibration, tetrabutylammonium hydrogen sulphate catalyst (0.0008 mol) was added. Samples were taken at regular intervals and analysed. For reactions with the addition of alcohols, the alcohol was added together with the catalyst.

Analysis.—Samples were taken and quenched with dilute HCl and analysed for *p*-allylanisole and *p*-methoxy-β-methylstyrene by g.l.c. (GOW-MAC 150 instrument equipped with thermal conductivity detector; 15% OV-17 on Chromosorb w, acid-washed; length 2 m; o.d. 1/4 in; column temp. 200 °C with He at 30 ml min⁻¹ as carrier gas).

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