(10 mL) under an atmosphere of dry nitrogen. The reaction mixture was refluxed for 2 h and then poured into cold, 2 N H<sub>2</sub>SO<sub>4</sub>. The aqueous layer was separated, neutralized carefully with a solution of NaHCO<sub>3</sub>, and extracted with CH<sub>2</sub>Cl<sub>2</sub> (50 mL). After drying over MgSO<sub>4</sub>, the solvent was evaporated. The crude sultone 4b was crystallized from EtOH (85% yield): mp 143-147 °C; <sup>1</sup>H NMR  $\delta$  1.60 (s, 6 H), 1.78 (s, 6 H), 2.28 (s, 3 H), 7.0–7.8 (m, 3 H); <sup>13</sup>C NMR δ 148.4 (q), 146.9 (q), 133.5, 130.4, 127.0, 120.5, 85.58, 56.43, 29.7, 28.8, 28.5; mass spectrum, m/e (relative intensity) 254 (M<sup>+</sup>, 100), 223 (27), 72 (61), 56 (23), 43 (45). Treatment of 4b with triethylamine in boiling EtOH afforded 2b. After crystallization from EtOH, pure 2b was obtained in 95% yield: mp 182 °C; <sup>1</sup>H NMR δ 1.42 (s, 6 H), 1.66 (s, 6 H), 2.77 (s, 3 H), 3.50 (s, 1 H), 7.07-7.50 (m, 3 H); <sup>13</sup>C NMR δ 147.0 (q), 146.0 (q), 132.7, 130.6 (q), 126.0, 121.2, 73.13 (q), 61.06 (q), 31.25, 25.18; mass spectrum, m/e (relative intensity) 254 (M<sup>+</sup>, 100), 236 (25), 223 (16), 91 (28), 57 (20), 56 (42), 55 (19), 44 (64), 43 (55), 41 (25), 39 (20), 28 (62). Anal. Calcd for C<sub>13</sub>H<sub>19</sub>NO<sub>3</sub>S: C, 57.97; H, 7.11; N, 5.20; S, 11.90. Found: C, 58.02; H, 6.99; N, 5.36; S, 11.99.

Reaction Products. This sultone 3b, isolated in high yield after hydrolysis of 1b, was synthesized independently according to Sachs et al.<sup>15</sup> The sultone 4b is an intermediate in the synthesis of 2b (vide infra) and was identical with the product isolated upon hydrolysis of 2b in the presence of HCl. The product of hydrolysis of 2a, the N-protonated sultone 4b, was characterized by its <sup>1</sup>H

NMR spectrum in 1:1 (v/v) EtOD-D<sub>2</sub>O:  $\delta$  2.03 (s, 6 H), 2.57 (t, 3 H), 5.63 (s, 2 H), 7.40-8.07 (m, 4 H). Treatment of 4b with NaOH gave 6 in high yield. The sulfonic acid was isolated in quantitative yield as the corresponding sodium salt. <sup>1</sup>H NMR  $(1:1 (v/v) EtOD-D_2O) \delta 2.07 (br s, 3 H), 4.77 (br s, 1 H), 5.00 (br$ s, 1 H), 6.73-7.23 (m, 3 H), 7.57-7.80 (m, 1 H). Anal. Calcd for C<sub>9</sub>H<sub>9</sub>O<sub>3</sub>SNa: C, 49.09; H, 4.12. Found: C, 48.70; H, 4.04.

Kinetic Measurements. Pseudo-first-order rate constants  $(k_{obsd})$  for reactions having half-lives longer than 1 min were determined by using the UV (Beckman model 24 spectrophotometer) and NMR methods outlined previously.4e Faster reactions were followed by using an Aminco-Morrow stopped-flow apparatus, equipped with a data acquisition storage and retrieval (DASAR) system. The optical path length of the mixing chamber was 1.0 cm. Thermodynamic activation parameters were calculated from second-order rate constants  $(k_2 = k_{obsd} [H^+]^{-1})$  at seven different temperatures in the temperature range 25-54 °C for 1b and at six temperatures in the range 21-43 °C for 2b.

Registry No. 1a, 91190-73-7; 1b, 91190-74-8; 1c, 91190-75-9; 2a, 91190-76-0; 2b, 91190-77-1; 3b, 81403-42-1; 4b, 91190-82-8; 4b·HCl, 91190-83-9; 5a, 91190-78-2; 5b, 91190-79-3; 6, 79347-33-4; 7, 72519-75-6; 8, 91190-81-7; N,N-dimethylbenzenesulfonamide, 14417-01-7; o-(1-methyl-1-hydroxyethyl)-N-methylbenzenesulfonamide, 91190-80-6; acetaldehyde, 75-07-0.

# Mechanism of Base-Catalyzed Reactions in Phase-Transfer Systems with Poly(ethylene glycols) as Catalysts. The Isomerization of Allylanisole

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The mechanism of base-catalyzed reactions with poly(ethylene glycol) (PEG) as phase-transfer catalysts was studied by using the isomerization of allylanisole as a model reaction. The reaction kinetics showed the reaction to be chemical reaction controlled. The reaction system was a three-phase system consisting of an organic solvent phase, a PEG-potassium hydroxide complex phase, and a basic aqueous phase. The reaction mechanism included diffusion of the substrate from the solvent to the complex phase reaction and back diffusion of the product. The concentration of the aqueous phase is also important. When the aqueous phase is unsaturated there is no reaction. Concentrations above saturation increase rate because the basic complex becomes more potent under anhydrous conditions. The chain length and chain end moiety of the PEG catalysts have significant influence on the reaction rate. In general, short chain catalysts were more effective per gram but not per mole of catalyst. Etherification of the terminal hydroxyl group reduced activity. When alkoxide species were used as bases the trends were reversed, long chain catalysts being more effective and etherification increasing activity.

#### Introduction

In recent years since the first published paper by Lehmkuhl et al.<sup>1</sup> poly(ethylene glycols) (PEG) and their ethers (PEGE) have received increasing attention as phase-transfer catalysts. They have been used in a wide variety of reactions including Williamson ether synthesis,<sup>2-5</sup> reductions,<sup>6-8</sup> oxidations,<sup>2,7,9</sup> eliminations,<sup>10</sup> and substitution reactions.<sup>2,7,11-13</sup> Poly(ethylene glycol) appears to be

especially attractive for base-catalyzed reactions as it is stable to base, a condition under which the better known quaternary ammonium salts undergo Hofmann elimination and therefore deactivation. In addition, the low price and nontoxicity of the PEG catalyst may enable its use in industrial reactions. Despite the considerable number of syntheses reported using PEG as catalyst, little is known or understood about the kinetics and mechanism of a PEG-catalyzed reaction. Recently, Gokel and his coworkers<sup>14</sup> have investigated some mechanistic and kinetic aspects of aliphatic nucleophilic substitutions (cvanation of octyl chloride) but to the best of our knowledge no such studies have been made in base-catalyzed reactions.

In order to investigate the base-catalyzed, poly(ethylene glycol) phase-transfer catalytic system we have chosen as a model reaction the double bond olefin isomerization of

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of reaction has been performed with quaternary ammonium salts<sup>15,16</sup> but not with PEG. We have found that the reaction is affected by numerous parameters including the concentration of the KOH (base) aqueous phase, stirring rate, catalyst concentration, catalyst chain length, and catalyst chain end moiety among others.

## **Results and Discussion**

From a kinetic viewpoint the phase-transfer catalytic reaction can be either chemical reaction controlled or diffusion controlled. From a mechanistic point of view the former has been associated with an extraction mechanism.<sup>17</sup> The hydroxide base is extracted into the organic phase where in this case it catalyzes the isomerization reaction. The latter has been associated with an interfacial mechanism<sup>18</sup> where the hydroxide base catalyzes the reaction on the interface of the aqueous and organic phases. Reactions which are chemical reaction controlled will be of simple order in the substrate, will be of first order in catalyst, and will only be slightly influenced by the stirring rate. Activation energies will be relatively high, i.e., above 10-12 kcal/mol. On the other hand reactions that are diffusion controlled will be of complex order in the substrate, fractional order in the catalyst, greatly influenced by the stirring rate, and have low activation energies, i.e., below 10 kcal/mol.

The first stage in our kinetic studies was to determine if our model isomerization reaction was diffusion or chemical reaction controlled. Therefore, we tested what effects the above mentioned parameters would have on the reaction rate. The rate equation was defined as follows (eq 2).

$$rate = -\frac{d[allylanisole]}{dt} = k_{obsd}[allylanisole]^n \quad (2)$$

where  $k_{obsd} = k[catalyst]$  and n is the reaction order in substrate.

Furthermore, the Arrhenius equation defines the rate constant  $(k \text{ or } k_{obsd})$  as a function of temperature. A graphical representation of the reaction profile as a firstorder equation in integral form (for first-order irreversible reaction  $-\ln (1 - x_A) = k_{obsd}t$ ,  $x_A$  is the conversion, t the time) gave a straight line with  $k_{obsd} = 0.20 \pm 0.01 \text{ min}^{-1}$ . The reaction is an irreversible first-order reaction up to practically quantitative yields (96%). Reaction conditions were the same as those described in Figure 1 with a stirring rate of 500 rpm. We also found that  $k_{obsd}$  varied linearly with the catalyst concentration and therefore concluded that the reaction is also of first order in the catalyst. The effect of the stirring rate on the rate constant can be found in Figure 1. It is evident that the stirring rate has only minor influence on the reaction rate, and even at low stirring rates, 200 rpm, a plateau is reached. Even in the



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Figure 1. The observed rate constant as a function of the stirring rate. Reaction conditions: 0.05 mol 60% KOH, 0.01 mol allylanisole, 0.001 mol PEG-400, 10 mL toluene, T = 75 °C.

absence of stirring the reaction rate is significant. Lastly, the effect of the reaction temperature on the reaction rate was tested. Calculation of the activation energy by the Arrhenius equation gave a value of  $13.5 \pm 0.5 \text{ kcal/mol}$ . From the above mentioned results one can safely conclude that the isomerization reaction is chemical reaction controlled and that the mass transfer is relatively fast.

It would be very tempting at this point to conclude further as has often been done in PTC systems in the past that the reaction proceeds by an extraction mechanism. If the reaction occurs by the usual extraction mechanism, this would mean that first the poly(ethylene glycol) forms a complex with the potassium hydroxide base. This complex would then dissolve (be extracted) into the organic phase where it would catalyze the isomerization reaction. Schematically such a system would look as follows (Scheme I). However, a closer look at the reaction system revealed

Scheme I  
PEG + KOH<sub>(aq)</sub> 
$$\rightarrow$$
 PEG-KOH  
PEG-KOH  $\xrightarrow{\text{organic}}$  PEG-KOH<sub>(org)</sub>  
ArCH<sub>2</sub>CH=CH<sub>2</sub>  $\xrightarrow{\text{PEG-KOH}_{(org)}}$  ArCH=CHCH<sub>3</sub>

the following. Mixing 60% aqueous KOH with toluene and catalytic amounts of PEG-400 at 75 °C for 2 h gave in actuality a three-phase system consisting of an aqueous KOH phase, a PEG-KOH complex phase, and a toluene phase in descending order of density. Titration of the toluene phase showed only a very slight concentration,  $10^{-4}$ M, of hydroxide base. Furthermore, when the allylanisole substrate was added to the separated toluene phase there was no reaction. When adding allylanisole to the combined toluene and PEG-KOH complex phase, the reaction commenced, however, at a slightly lower rate,  $k_{obsd} = 0.15$ compared to the reaction where all phases were present,  $k_{\rm obsd} = 0.20$ . (It is probable that there were losses during separation of phases). We believe that the reaction in fact occurs in the PEG-KOH complex phase by diffusion of the allylanisole into the complex phase, reaction, and the back diffusion of the product, anethole, into the organic phase, Scheme II (see next page). In a reaction where KOH disappears during the reaction, there would be additional continuous complexation of the PEG by KOH. In support of this scheme is the fact that the yellow-brown PEG-KOH complex phase turns dark red, the typical color of the allvlanisole carbanion upon addition of the substrate. The aqueous phase is also of importance as one can see in Figure 2. If the aqueous phase is not near saturation,

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required to form a crown ether type complex with the potassium cation is about 7-8 oxyethylene units. In the second region, from 8 to 20 oxyethylene units (PEG-400 to PEG-1000) there is a drop in the reaction rate which is proportional to the drop in the molar concentration of the catalyst. Therefore, the efficiency of PEG-400 and PEG-1000 are about equal on a molar basis. In the third region, 20-130 oxyethylene units (PEG-1000 to PEG-6000), the drop in the reaction rate continues, however, more slowly. On a molar basis the PEG-6000 is the better catalyst. This phenomenon has two possible explanations. First it is possible that with increasing molecular weight there is more than one binding site per molecule. However, Gokel et al.<sup>14</sup> have shown that despite the increased number of binding sites, one molecule of PEG effects one reaction at a time. We believe that the increased molar effectiveness of PEG-6000 over low molecular weight catalysts is due to a wrap around effect. Increased molecular weights cause greater separation of the hydroxide anion from the potassium cation making it a more potent base or nucleophile. In fact others have shown increased ion separation with increasing molecular weight.<sup>20,21</sup>

From the graph in Figure 3 one can see in addition that the dihydroxy moiety is more effective than the monomethyl ether which in turn is more effective than the dimethyl and dibenzyl ethers. As the molecular weight increases these differences disappear. From this it is apparent that the end group has an effect on the complexation of the KOH base to the PEG molecule. Indeed, one can see in Table I that the free hydroxyl groups aid in complexation of hydroxide anions perhaps through hydrogen bonding as has been previously suggested.<sup>10</sup> In other words the increased complexation through the chain ends increases the reaction rate by increasing the PEG-KOH complex concentration. As the chain length increases the chain end moiety loses its importance in comparison to the large chain bulk.

In the literature one finds other examples where similar effects have been obtained.<sup>10,11,14</sup> However there are reactions where opposite effects have been observed.<sup>22-25</sup> In

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k<sub>obs</sub> , hours-80 90 60 7C Concentration of KOH in aqueous phase, weight percent

Figure 2. The observed rate constant as a function of the aqueous potassium hydroxide concentration. Reaction conditions: 0.05 mol KOH, 0.01 mol allylanisole, 0.001 mol PEG-400, 10 mL toluene, T = 75 °C, stirring rate = 500 rpm.

less than 50% KOH, there is no reaction. The reason for this is that since poly(ethylene glycol) is water soluble, it dissolves in the aqueous phase, therefore no PEG-KOH complex is formed, and there is no reaction. As the aqueous phase approaches saturation, the complex forms and the reaction rate increases dramatically. At saturation,  $\sim 60\%$  KOH, there is an inflection point. With rising aqueous-phase concentration, the reaction rate still increases but in a milder fashion. This increased rate is because the less water found in the PEG-KOH phase the more effective the deprotanation of the substrate. This is due to the fact that under increasingly anhydrous conditions the PEG-KOH becomes a more potent base because of decreasing solvation by the water molecules. It could have been argued that the water causes reprotanation of the carbanion to the substrate. However, we found that this was not the case. When the reaction was performed with 60% KOH in D<sub>2</sub>O we found no deuterium in the product (MS and NMR). This is in contrast to results found for isomerizations in homogeneous systems where a small percentage of deuteration was found.<sup>19</sup> Apparently the isomerization reaction is relatively much faster than the deuteration reaction in our system excluding intermolecular reprotonation.

Up to this point we have examined the kinetic and mechanistic aspects of the reaction itself. Nothing has been said about the nature of the PEG-KOH complex and its effect on the reaction. Specifically we examined the effect of the catalyst chain length and chain end moiety and their effect on the reaction rate. The results are found in Figure 3. The graph can be divided into three zones. It is important to emphasize that the reactions were performed by using equivalent weights of catalyst so that the catalyst molar concentration is falling along the absicca. In the first zone from zero to eight oxyethylene units (PEG-400) there is a strong increase in the reaction rate. This is because the minimal amount of oxyethylene units

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Table I. Complexation of KOH by Poly(ethylene glycol) Derivatives<sup>a</sup>

catalyst	complexation, mol %
PEG-400	43.2
PEG-350 monomethyl ether	33.0
PEG-400 dimethyl ether	14.8
PEG-400 dibenzyl ether	3.2

<sup>a</sup>For a method of determination and analysis see the Experimental Section.

Table II. Rate Constants in KOH/Methanol/PEG Isomerization Systems<sup>a</sup>

catalyst	$k_{\rm obsd},  {\rm h}^{-1}$	
PEG-400	0.035	
PEG-350 monomethyl ether	0.047	
PEG-400 dimethyl ether	0.022	
PEG-6000	0.037	

<sup>a</sup>Reaction conditions: 0.01 mol allylanisole, 0.05 mol potassium hydroxide, 0.05 mol methanol, 1.0 g catalyst, 10 mL toluene, T = 65 °C, stirring rate = 500 rpm.

these cases longer chain lengths increase catalystic activity on a weight basis, i.e., PEG-6000 is more effective than PEG-400 per gram of catalyst. Also PEG ethers were more effective than poly(ethylene glycol). The common denominator of these latter reactions was that in all cases the base or nucleophile was alkoxidic. In fact when the isomerization reactions were carried out with methanolic KOH as the hydrophilic phase instead of aqueous KOH we found a drop in the PEG-400 activity whereas PEG-6000 retained the same activity, Table II. The PEG-350 monomethyl ether had a higher reaction rate whereas the PEG-400 dimethyl ether had a slightly lower one. We believe that the methanolic KOH in this case causes partial ionization of the hydroyl group increasing solubility in the alkoxide medium and thereby reducing its effectiveness. In this case the dimethyl ether was less active than the monomethyl ether because the decreased ionization was offset by the lower complexation. When solid alkoxides such as potassium tert-butoxide<sup>25</sup> or potassium phenoxide<sup>22</sup> are used, the effects are more extreme. In these cases the short chain PEG activity drops further and the activity between nonether, monoether, and diether moieties are

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totally reversed compared with the case where the hydroxide anion is used. Unfortunately, we were unable to test our hypothesis by use of solid alkoxide bases in the isomerization reaction because the reaction rate was too high even at low temperatures.

## **Experimental Section**

**Reaction System.** Reactions were performed in a 50-mL round-bottom flask with a side arm for sampling. Stirring was by a mechanical stirrer (Heidolph RZR-1) with variable stirring speeds. The flask was placed in a 15-L thermostated water bath with a temperature precision of  $\pm 0.2$  °C. A typical procedure consisted of placing 0.05 mol of KOH with the appropriate amount of water in the flask. Toluene (10 mL) and the catalyst were added. After 20 min to allow for equilibration of the system, 0.01 mol of allylanisole was added. The materials were of commercial grade of the highest purity available.

**Complexation.** PEG (0.005 mol) was stirred with 0.005 mol of KOH for 24 h. The remaining KOH was filtered off and the PEG-KOH complex mixture was analyzed by titration.

Analysis. Samples were taken and quenched with dilute HCl and analyzed by GLC. The gas chromatograph used was a Packard 427 instrument equipped with FID detectors. The column was 15% OV-17 on Chromosorb W acid washed; length 2 m; OD  $^{1}/_{4}$  in. The column temperature was 200 °C with N<sub>2</sub> as the carrier gas. The concentration of the hydroxide anion was found by titration with HCl with phenolphthalein as the indicator.

### Conclusion

We have found that the isomerization reaction shows chemical reaction controlled kinetics. The reaction was found to occur in the PEG-KOH complex phase by diffusion of the substrate to the catalyst complex, reaction, and back diffusion. Saturation of the aqueous phase is necessary for reaction to take place. More anhydric conditions improve catalytic activity by reducing solvation of the base. PEG catalysts having more than 20 oxyethylene groups are more effective per mole of catalyst but not per gram of catalyst. We explained this through greater ion separation in the heavier catalyst. Etherification of the terminal hydroxyl groups reduce catalyst activity because of reduced complexation. When alkoxide bases are used, the trends found are reversed. Long chain catalysts become more effective and etherification increases activity.

**Registry No.** MeOC<sub>6</sub>H<sub>4</sub>-*p*-CH<sub>2</sub>CH=CH<sub>2</sub>, 140-67-0; PEG-400, 25322-68-3; PEG-350 monomethyl ether, 9004-74-4; PEG-400 dimethyl ether, 24991-55-7; PEG-400 dibenzyl ether, 26403-68-9.