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Poly(Ethylene Glycol) and Derivatives as Phase Transfer Catalysts

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1. INTRODUCTION

The application of poly(ethylene glycol) (PEG) and its derivatives as phase transfer catalysts for a variety of organic reactions was reviewed previously [1]. It was shown that PEGs and their derivatives could be used to replace crown ethers in many applications. PEGs provide a lower cost, nontoxic phase transfer catalyst relative to crown ethers. This is true even in cases in which the PEGs must be used at substantially higher concentrations than crown ethers.

Since the earlier review, numerous developments related to the use of PEGs and their derivatives as phase transfer catalysts have been reported [2, 3]. These include elucidation of the PEG-catalyzed reaction mechanism, the use of PEGs to catalyze organometallic reactions, the advantageous use of polymer-supported PEGs to catalyze a wide variety of gas–liquid reactions and a further broadening of the utility of PEGs to catalyze classical organic reactions. The objective of this paper is to review examples of phase transfer reactions using PEGs and their derivatives that have been reported since the first review [1]. These reactions include liquid–liquid, solid–liquid, gas–solid, gas–liquid, and triphase reactions. Selected examples of PEG derivatives, copolymers, and solid-supported PEGs are also discussed.

2. DISCUSSION

2.1. Poly(ethylene Glycol)-Catalyzed Reaction Mechanisms

To react an organic compound with the anion of an inorganic salt, it is necessary to facilitate molecular contact between the two. The salt is insoluble in organic media due to high crystal lattice stabilization, which thus inhibits the reaction. The inorganic salt may be dissolved in water since oxygen atoms of water will strongly interact with the cations, and hydrogen bonding will stabilize the anions. If these interactions overcome the crystal binding energy, the salt will dissolve. However, the organic reactant will probably be insoluble in the aqueous salt solution. This mutual insolubility in water will inhibit the desired reaction.

One approach to facilitate molecular contact is to use solvents that will dissolve both the organic reactant and the inorganic salt. Dipolar aprotic solvents will dissolve many inorganic salts. These solvents have organic groups that facilitate solubilization of organic compounds and polar groups for the cation of solution. Aprotic solvents include acetonitrile, dimethylformamide (DMF), dimethylsulfoxide (DMSO), and hexamethylphosphoramide (HMPA). Typically, these solvents are costly and difficult to purify, dry (and keep dry), and recover after reaction [4].

Starks developed the phase transfer catalysis (PTC) process to provide a solution to these problems [5]. In PTC, the inorganic salt is dissolved in water, and the organic material is dissolved in a water-insoluble organic solvent. This is a two-phase system in which the salt resides almost exclusively in the aqueous phase and the organic reactant resides almost exclusively in the organic phase. No (or very little) reaction occurs since the two reactants have virtually no contact. If the anion of the salt is introduced into the organic phase, then reaction may occur. This is achieved with a catalyst that is soluble in the organic phase and either has a positive charge or can strongly coordinate with a cation. Either approach will solubilize a cation into the organic phase, thus solubilizing the anion. As the reaction proceeds, the concentration of the anion in the organic phase will be depleted. Phase equilibrium will bring more anion into the organic phase to complete the reaction. Only catalytic quantities of the PTC are generally required. The PTC process is illustrated in Fig. 1.

An organic cation facilitates solution of the desired anion into the organic phase. Classically, an ammonium salt, which undergoes an anion exchange in the aqueous phase and then dissolves in the organic phase, is used to "transfer" the desired anion into the organic phase.

The second case, in which a crown ether transfers both the cation and anion into the organic phase, is illustrated in Fig. 2. In this example, the anion is not exchanged with a soluble salt. Instead, the inorganic salt dissolves in the organic phase through complexation of the cation.

There are a number of variations of these basic approaches. The system of two liquid phases is classified as a liquid–liquid (L-L) system. Alternatively, the salt may be present as a solid with no aqueous phase. Here, the phase transfer agent transfers the anion into the organic solution directly from the solid state (S-L). It is also possible to use a phase transfer agent bonded to an insoluble support. This facilitates removal of the PTC at the conclusion of the reaction. These "supported catalysts" can be used in a
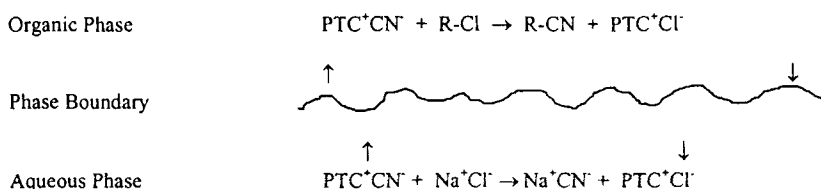
Organic Phase $\qquad$ $PTC^+CN^- + R\text{-}Cl \rightarrow R\text{-}CN + PTC^+Cl^-$

Phase Boundary

Aqueous Phase $\qquad$ $PTC^+CN^- + Na^+Cl^- \rightarrow Na^+CN^- + PTC^+Cl^-$

FIG. 1. Phase transfer catalysis process.

Organic Phase $[PTC \bullet K]^+CN^- + R\text{-}Cl \rightarrow R\text{-}CN + [PTC \bullet K]^+Cl^-$

Phase Boundary

Aqueous $[PTC \bullet K]^+CN^- + Na^+Cl^- \rightarrow Na^+CN^- + [PTC \bullet K]^+Cl^-$
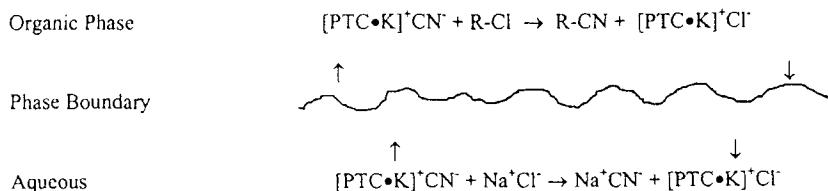
FIG. 2. Transfer of both anion and cation into the organic phase by the crown ether.

three-phase system with the organic phase, an aqueous phase, and the solid all present (L-L-S). Alternatively, the supported catalyst can be used with only an organic phase and the solid salt (L-S-S). Finally, recent studies have been conducted with gas–solid reactions. The salt of the desired anion is coated with the phase transfer agent and dried. Reaction then occurs when the organic reactant is passed over a heated bed with either a liquid coating (G-L) or by a direct reaction with a solid (G-S).

Crown ethers are classical cyclic ether phase transfer reagents by which alternating oxygen atoms (every third position in the ring) provide cation coordination. The cation fits into the cavity of the ring and is surrounded by the electronegative oxygens (see Fig. 3). Specific cations will achieve optimum coordination with a specific ring size. When the size of the cavity and the cation are matched, then maximum interaction will occur.

This review examines the ability of open-chain, noncyclic analogues of crown ethers to function as phase transfer agents. These open-chain analogues are called poly(ethylene glycols) (PEGs). A wide range of molecular weights of unsubstituted PEGs ($\sim 100\text{-} > 20{,}000$) is commercially available. The monomethyl ethers (MPEG) are also commercially available, while the dimethyl ethers are known as *glymes*. The nomenclature for the PEGs and MPEGs uses either PEG or MPEG to identify the class of compound, followed by a number that refers to the molecular weight. In principal, these are formed by reaction of water or methanol with ethylene oxide in a reaction that produces a mixture consisting of a homologous series of adducts differing only in the number of ethyloxy groups ($-CH_2-CH_2-O-$) incorporated in the structure. Except for the lower molecular weight members of the class, the PEGs and MPEGs exist as mixtures of varying molecular weights, and the name refers to an average molecular weight for the mixture. The PEGs can be synthesized with end groups other than methyl and may also have alkyl group substitution on the "backbone" of the polymer or oligmer chain (see Fig. 3). Most of the available information on
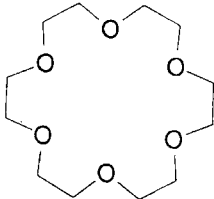
Class	Example	Name
Crown Ether		18-Crown-6
PEG	$HO\text{-}(CH_2CH_2O)_7\text{-}H$	PEG-326
	$CH_3O\text{-}(CH_2CH_2O)_4\text{-}H$	MPEG-208
	$HO\text{-}(CH_3CHCH_2O)_n\text{-}H$	Poly(propylene glycol)
	$HO\text{-}(PhCHCH_2O)_n\text{-}H$	Poly(styrene oxide)

**FIG. 3.** Crown ether as a cyclic ether transfer reagent.

PEGs and their derivatives as phase transfer catalysis deals with either unsubstituted poly(ethylene glycol) or with terminal ether derivatives.

Fundamentally, PEGs differ from the crown ethers only in topology and possibly in cation-ligand stoichiometry. However, PEGs are less expensive than the crown ethers. For example, 18-crown-6 is almost 100 times more expensive per gram [6] than PEG-300. Polyether functional derivatives designated as "cryptands" surround a cation in a three-dimensional structure, but cost more than 1000 to 5000 [7] times as much as PEGs. In many cases, PEGs are as effective as crown ethers and cryptands, which is why PEGs have been called "the poor chemist's crown" [8]. As an example, consider the results shown in Table 1 [9].

The results presented in Table 1 were generated using the reaction of aqueous potassium thiocyanate with *p*-nitrobenzyl bromide in chloroform.

TABLE 1

Rate of Reaction as a Function of Catalyst Type

| Catalyst	Relative rate
18-Crown-6	1.44
Benzo-18-crown-6	1.23
Dibenzo-18-crown-6	1.00
Dicyclohexano-18-crown-6	1.65
Crypt 2,2,2	5.10
n-Decyl crypt 2,2,2	6.15
Decaglyme	1.41
Tetrabutylammonium perchlorate	1.29
Hexadecyltetrobutylammonium bromide	1.00
Carbowax 20M	0.83

Crypt 2,2,2
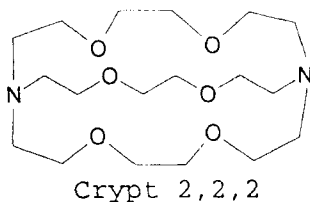
Given the relative cost of the ligands, it is apparent that the PEGs and their derivatives, glymes, are the most cost-effective catalyst for the reaction.

In phase transfer catalysts, the anion is separated from the cation sterically by the organic salt or complexing agent. This shift toward solvent-separated ion pairs with the phase transfer catalyst is discussed in detail below. This separation, combined with the relatively poor solvation of the anion by the organic solvent, results in enhanced anion reactivity. Enhanced reactivity is a critical factor in phase transfer catalysis. In comparing the rate of a standard reaction with various phase transfer reagents, the ability of the agent to transfer the anion to the organic phase is critical, but the "activation" of the anion due to poor solvation is also a significant factor.

Crown ethers typically solvate a cation two dimensionally [6], so there can be appreciable interaction between the cation and the anion. The PEGs solvate cations in a less planar fashion, but there is still potential for strong interaction between the coordinated cation and the anion. Cryptands solvate three dimensionally [6]; thus, the anion is even more reactive (see Table 1).

The ability of PEGs, crown ethers, and cryptands to function as effective phase transfer agents is not simply due to ether coordination of the cation, but is also a function of geometry. Molecular models show that the structure of crown ethers permits a cation to fit into a cavity with maximum coordination of ether oxygens. The PEGs can assume a similar structure without significant strain at any point in the chain. However, this is not true of other types of polyethers. This point is illustrated in Table 2 [10] for the rate of the Williamson reaction between sodium phenoxide and n-butyl bromide in 1,4-dioxane.

The ability of a ligand to bind a cation is defined by K_s, the equilibrium constant for the complexation reaction.

$$M^+ + L \rightleftharpoons [M \cdot L]^+$$
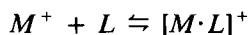
The equilibrium constant is also defined as the ratio of the rate constants for the forward and reverse reactions.

If the solubility of a salt in an organic solvent is plotted against the concentration of phase transfer agent, three general types of plots are obtained [11]. If the equilibrium constant K_s behaves in an ideal manner, the plot of salt concentration (in the presence of excess salt) will vary linearly with the phase transfer agent (see Fig. 4A). If the complex in solution has other than a 1:1 ratio, then a plot such as that in Fig. 4B will be obtained. Finally if there is a solubility limit for the complexed salt, then a plot similar to that in Fig. 4C will be obtained.

For PEG-300, the solubility of sodium 2,4-dinitrophenolate is found to be solvent dependent as shown in Fig. 5 [11]. The plots are linear over the concentration range examined, with the exception of benzene, for which a solubility limit is achieved. Figure 5 illustrates that more-polar solvents

TABLE 2

Reaction Rate as a Function of Ether Structure

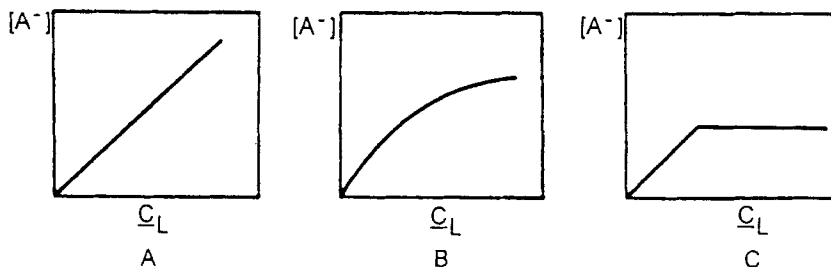| Catalyst	Structure	Relative rate
None		0.35
Poly(ethylene glycol)	$HO-(CH_2CH_2O)_n-H$	39.00
Poly(oxetane)	$-(CH_2CH_2CH_2O)_n-$	0.40
Poly(tetrahydrofuran)	$-(CH_2CH_2CH_2CH_2O)_n-$	0.80
Poly(ethylvinylether)	$-(CH_2CH_2)_n-$ $\|$ OCH_2CH_3	0.40

FIG. 4.   Types of solubility isotherms.

increase the solubility of the salt. The presence of a solubility limit for the PEG–sodium 2,4-dinitrophenolate–benzene system depends on the molecular weight of the PEG, as shown in Fig. 6 [3]. A wide variety of K_s values for PEGs and their derivatives (with a variety of cations) have been compiled from the literature by Gokel and Trafton [12].

Figures 5 and 6 demonstrate that the presence of PEGs leads to solubilization of salts in even nonpolar organic solvents. Thermodynamic factors that control the rates and free energies of reaction between the PEGs and
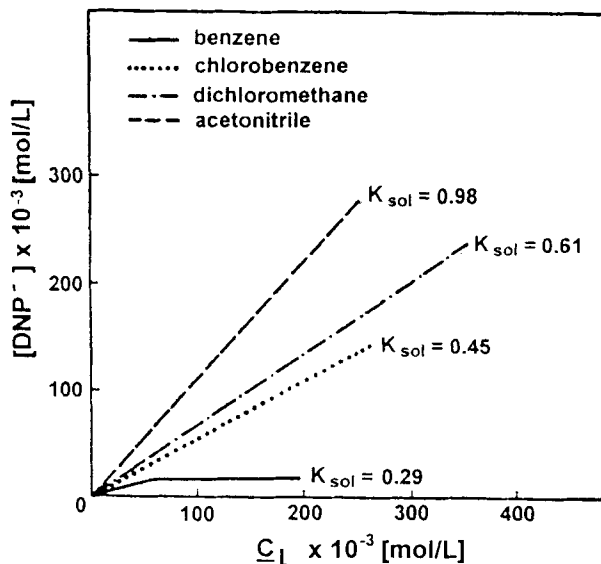

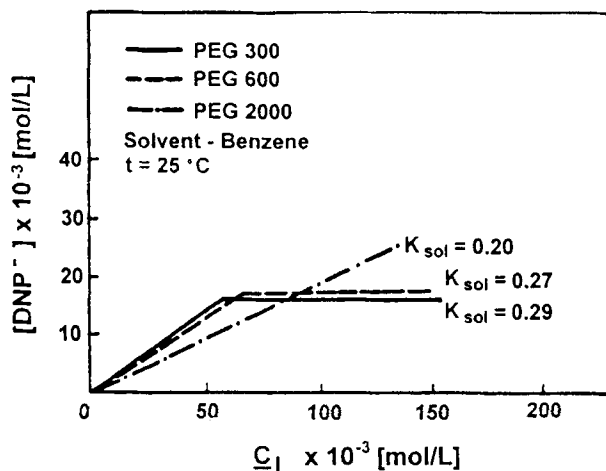**FIG. 5.**   Solubility of 2,4-dinitrophenolate for PEG-300.

FIG. 6. Dependence of solubility limit on molecular weight of PEG.

salts are very complex. Inoue and Hakushi [13] have examined the thermo-dynamics for complexation in detail. With oxygen donors, the major inter-action between the donor and the cation is charge-charge, charge-dipole, and/or charge-induced dipole interactions. These are the interactions gener-ally presented for the crown ethers. Formation of strong interactions be-tween a PEG and a cation requires an extensive reorganization of the con-formation of the PEG. Based on thermodynamic relationships proposed by Leffler [14] and elaborated by Leffler and Grundwald [15], Inoue and Hakushi plotted ΔH values against $T\Delta S$ values for a large number of differ-ent classes of ligands. For the open-chain PEG derivatives (and related structures), the plot is shown in Fig. 7 [13]. With 151 data points selected from the literature, an excellent correlation coefficient of 0.98 is obtained. The slope is found to be 1.02. As the cation-ligand bonding becomes stronger, there is a negative impact on the energy of the system due to greater restrictions in the degrees of freedom of motion in the ligand. The negative change in $T\Delta S$ will partly offset the gain in energy due to the stronger binding of the cation.

The intercept of the ΔH versus $T\Delta S$ plot also provides information re-lated to complex stability. The formation of the complex has an impact on the solvation of the uncomplexed cation and the ligand. The uncomplexed cation will be strongly solvated. Much of this solvation will be lost as the interaction with the cation occurs. The intercept in Fig. 7 is positive. Therefore, even if ΔH is zero, there is a positive entropy contribution to the
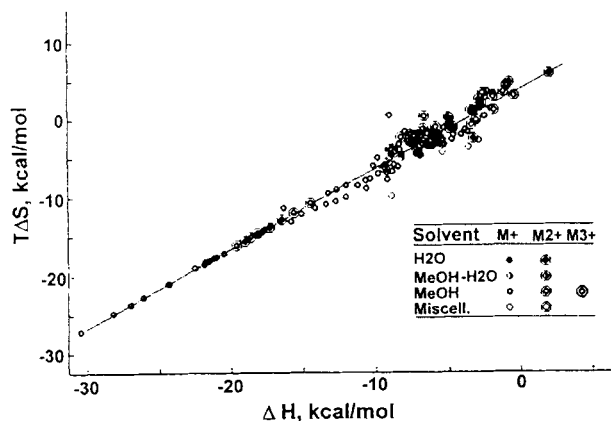
FIG. 7.   Plot of ΔH values against $T\Delta S$ values.

stability of the complex due to desolvation of the ligand and the cation. This is a major contributor to the stability of the complex.

Details of the rates and equilibrium between the various steps of complexation of a cation with a PEG (or PEG derivative) have not been elucidated. Electronegative oxygens of a PEG displace solvent molecules coordinating the cation in a sequential series of steps. The PEGs will undergo some internal reorganization between each coordination step to position the oxygen atom for the most effective coordination with the cation. In fact, coordination may be even more complex, with the approaching ligand first becoming part of the outer coordination sphere of the cation before becoming part of the inner sphere. To describe the process completely, the displacement of solvent coordinating the PEG should be included. Studies conducted in water have shown a strong and specific coordination of water through hydrogen bonding with the PEG [16]. The mechanistic aspects of the complexation process have yet to be elucidated in detail.

The binding strengths of cations to PEGs are a function of the PEGs' molecular weights. Using data collected by Gokel and coworkers [17] and Toke and coworkers [18, 19], K_s values for sodium in anhydrous methanol are plotted against the log of the number of oxyethylene groups in the PEG catalyst as shown in Fig. 8. The data cover a PEG molecular weight range of 200 to 14,000 and a log K_s range of 1.64 to 4.08. In this region, data can be reasonably fit to a straight line (with the exception of the lowest molecular weight compound, which does not have the six oxygen atoms required to coordinate the sodium cation fully). The monomethyl and dimethyl ethers also result in straight lines with similar, but not identical, slopes
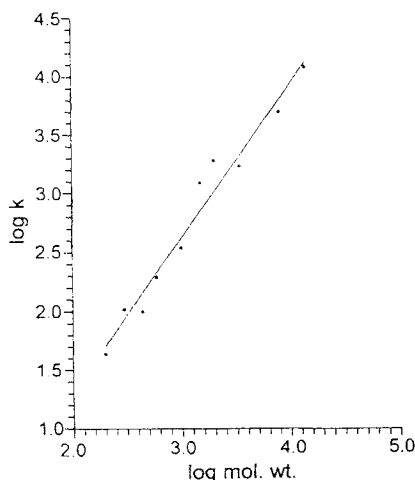
FIG. 8. Plot of K_s values of sodium in anhydrous methanol against the log of the number of oxyethylene groups in PEG catalyst.

(Figs. 9A and 9B). A plot of crown ether data shows a very different behavior (see Fig. 9C). A size-specific molecule best "fits" the cation.

The stoichiometry of cation coordination by PEGs can also be examined. The conductivities of salt solutions with equal weights of PEG-500 and PEG-14,000 were found to be the same. This indicates that binding is dependent on number of binding sites present but not on the number of molecules [17] since long chains may bind more than one cation. The phase transfer process is used to initiate the reaction between two species that would otherwise not react at an acceptable rate. Therefore, the utility of phase transfer catalysts is determined by reaction rate. To understand what determines this rate, more than the K_s value (stability or binding constant) must be examined. Gokel et al. showed (see Table 3) that the reactions catalyzed by PEG (PEG-400 and PEG-3400) between n-octylchloride and sodium cyanide are similar when the PEG is used at the same molar amount. Increasing the PEG-400 amount increases the rate significantly [17]. Comparison of both PEGs at the same weight of catalyst (approximately the same number of binding sites) shows that the lower molecular weight material is much more effective. These data suggest that each PEG molecule transfers only one ion pair at a time across the phase boundary [17]. This is consistent with the above discussion of the extensive reorganization required for coordination of an ion pair to occur. Two processes occurring at the phase boundary at the same time are unlikely. With PEG-
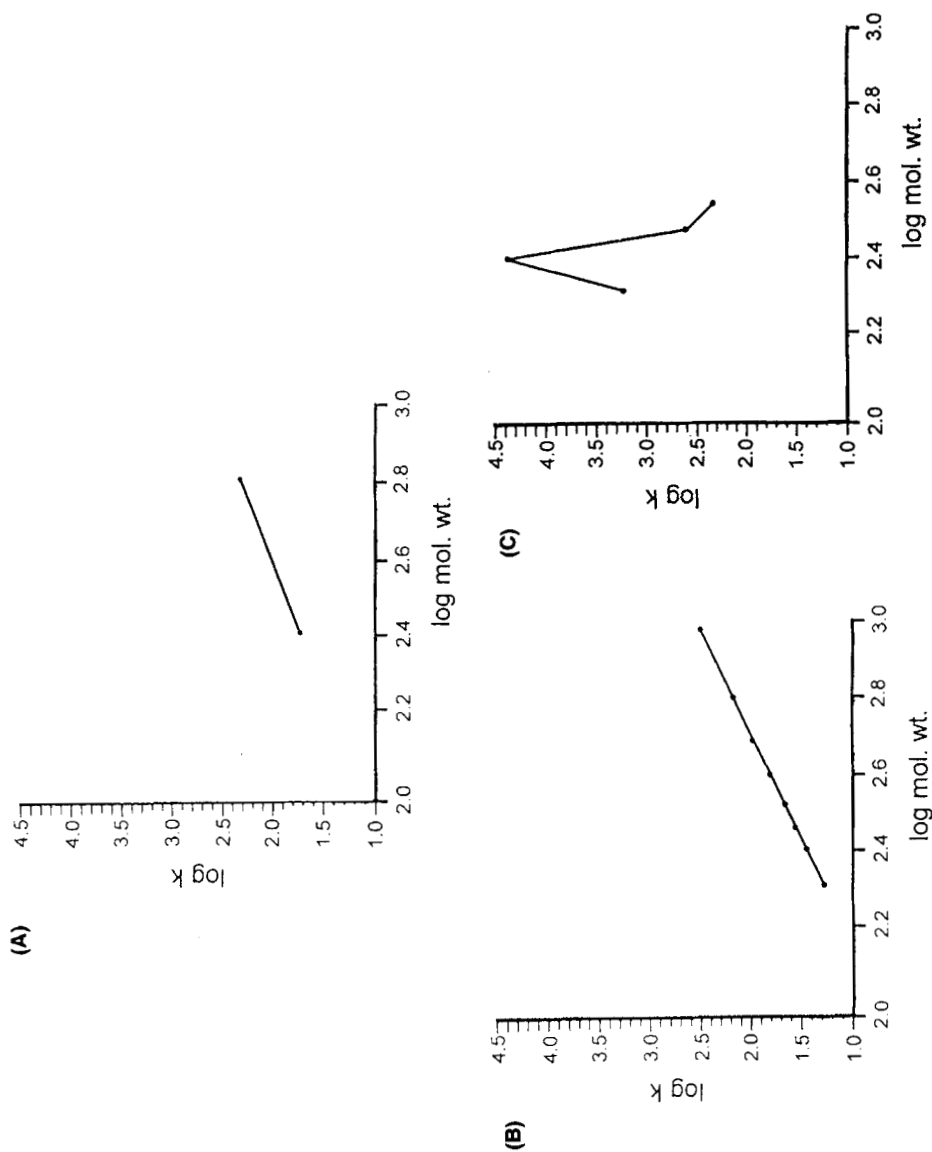
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FIG. 9. Plots of (A) monomethyl ether, (B) dimethyl ether, and (C) crown ether data.

TABLE 3

Reaction Between n-Octylchloride and Sodium Cyanide

Catalyst	Grams	Mole%	Relative rate
18-Crown-6	0.264	1.5	0.8
PEG-400	0.400	1.5	1.0
PEG-3400	3.400	1.5	1.5
MPEG-750	0.750	1.5	0.3
18-Crown-6	3.400	19.3	27.0
PEG-400	3.400	12.8	18.7
PEG-3400	3.400	1.5	1.5
MPEG-750	3.400	6.8	2.5

400 and PEG-3400, the reaction was faster (at the same molar amount of catalyst) than the reaction catalyzed with 18-crown-6.

A study of the rate of a Williamson ether synthesis as a function of the molecular weight of the PEG has been examined with a wide range of molecular weights [20]. These reactions were conducted using a constant weight of oxyethylene units. The results are given in Table 4. In this case, the reaction rate is similar to that of the PEGs when using either the poly-

TABLE 4

Relative Rate as a Function of Molecular Weight

| Phase transfer agent	Molecular weight $\times 10^{-4}$	Relative rate
PEG-1000	0.1	2.6
PEG-2000	0.2	3.7
PEG-4000	0.4	3.1
PEG-27,000	2.7	2.0
PEO-1[a]	16–20	3.2
PEO-8	170–220	6.4
PEO-15	330–380	10.8
PEO-18	380–430	10.8
PPG[b]	0.3	3.3
PSO[c]	0.2	1.4

[a]PEO is polyox.
[b]PPG is poly(propylene glycol).
[c]PSO is poly(styrene oxide).

(propylene glycol) (PPG) or the poly (styrene oxide) (PSO). Catalysts iden-
tified as PEOs are high molecular weight PEGs (MW > 50,000) and are
commercially available. Reaction rates for the lower molecular weight
PEGs are similar, and a significant rate increase occurs only with high
molecular weight polymers (PEOs). The terminal hydroxyl groups of the
PEGs have the potential to hydrogen bond to the anion, which reduces the
activation that occurs due to a weakly solvated ion. Thus, with high molec-
ular weight PEGs (which have a low concentration of end groups), the
anion is less solvated and much more reactive.

To function as an effective phase transfer agent, the ligand must form a
sufficiently stable complex and be soluble in the organic phase [21]. Anion
reactivity will be determined by the amount of association with the cation.
Thus, the anion is more reactive as a solvent-separated ion pair than as a
tighter ion pair. A study of PEG complexes of alkali metal 2,4-dinitrophen-
olates showed that a spectral shift occurred when these were reacted with
bulky onium ions [22]. This was attributed to formation of a solvent-
separated ion pair between the 2,4-dinitrophenolate and the onium cation.
Increasing spectral shifts indicate that more of the PEG salt was originally
present as a tight ion pair. The data given in Table 5 indicate the order of
dissociation of tight ion pairs to solvent-separated ion pairs in the PEG salts:

$$Li^+ < Na^+ < K^+$$
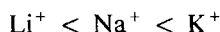
This is in agreement with kinetic measurements of anion reactivity [22]. The
data in Table 5 also demonstrate that the ion pair structure is dependent

TABLE 5

Ion Pair Structure as a Function of Solvent and Cation

Solvent	Cation	Shift (cm^{-1})
Benzene	Lithium	1300
Benzene	Sodium	1100
Benzene	Potassium	1000
Chlorobenzene	Lithium	1600
Chlorobenzene	Sodium	740
Chlorobenzene	Potassium	670
Dichloromethane	Lithium	1100
Dichloromethane	Sodium	730
Dichloromethane	Potassium	360
Acetonitrile	Lithium	0
Acetonitrile	Sodium	0
Acetonitrile	Potassium	0

on the polarity of the solvent with the more polar solvents supporting solvent-separated ion pairs.

Formation of solvent-separated ion pairs increases anion reactivity. The anion is transferred into the organic phase with only weak solvation, and ion pair aggregates are broken. These factors influence the basicity or nucleophilicity of the anion and also significantly affect the steric environment around the anion.

This was studied using the elimination reaction of 2-iodobutane by potassium t-butoxide [23]. Potassium t-butoxide is normally present in organic media as ion pair aggregates. Table 6 provides the amount of 1-butene and the E/Z ratio of the 2-butene for this reaction, which was carried out in toluene and dimethylsulfoxide (DMSO). In toluene, the potassium salt is present as an aggregate, while in the more polar DMSO the structure shifted toward solvent-separated ion pairs.

Results in Table 6 show a significant change in amount of 1-butene and in the E/Z ratio for the 2-butene when t-butoxide (or its analogue) is reacted in different solvents. The ion pair aggregates have a larger effective steric size in toluene, which favors formation of a product mix with more 1-butene and a low E/Z ratio. In DMSO, the smaller solvent-separated ion pairs favor more 2-butene and a larger E/Z ratio.

The potassium alkoxide derived from PEG is insensitive to the change of solvent from toluene to DMSO. This is because PEGs and the PEG monoethers have a terminal hydroxyl group that reacts to form an alkoxide. On formation of the alkoxide, the remainder of the PEG chain surrounds the cation to provide "self-solvation." With self-solvation, the effective steric size of the PEG alkoxide is relatively unaffected by the change in solvent from toluene to DMSO, as shown in Table 6. In both solvents, the self-solvated complex is expected to be present as a single species.

TABLE 6

Reaction of 2-Iodobutane with Base

	DMSO as solvent		Toluene as solvent	
Catalyst	Percentage 1-butene	E/Z 2-butene	Percentage 1-butene	E/Z 2-butene
t-BuO$^-$K$^+$	20	3.5	36	1.7
Et$_3$CO$^-$K$^+$	21	3.8	47	1.8
PEG$^-$K$^+$ [a]	19	3.4	20	3.7

[a]PEG$^-$K$^+$ is CH$_3$O(CH$_2$CH$_2$O)$_7^-$K$^+$.

Cation–PEG alkoxides have a different reactivity than the corresponding cation–PEG hydroxide salt. This has been demonstrated in a study of the reaction of the base-catalyzed dehydrohalogenation of (2-bromoethyl)benzene [24]. In this study, the phase transfer catalyst partitioned between a benzene and a basic aqueous phase. The percentage of the total PTC and the amount of base in the organic phase (mole of base/mole of PTC) were determined along with the reaction rate. The data in Table 7 show that the reaction rate was very slow for the reaction using ethylene glycol and diethylene glycol, which were present in the aqueous phase and therefore did not act to transfer base to the organic phase. Higher molecular weight PEGs and their mono- and diethers were soluble in the organic phase. However, only the structures with a terminal hydroxyl group were active in transferring base to the organic phase.

To determine the form of the base, a benzene solution of pentaethylene glycol was stirred with aqueous KOH and reacted with benzyl chloride. The sole product was alkylated polyether, indicating that the active species was the alkoxide. Reaction rates reported in Table 7 are not only a function of the amount of base in the organic phase, but are also dependent on the molecular weight of the PEG. The distribution of catalyst between benzene and a 60% aqueous potassium hydroxide solution is illustrated in Table 7. Higher molecular weight PEGs were not very soluble in the aqueous phase due to high salt content.

Harris and Case [25] examined the reaction of PEGs as phase transfer agents for permanganate oxidation of 1-octene. In this study, the concen-

TABLE 7

Dehydrohalogenation of (2-Bromoethyl)benzene

Phase transfer catalyst	Relative rate	Percentage catalyst in organic phase	Equivalents of base in organic phase
$HO(CH_2CH_2O)_1H$	<0.01	0	0
$HO(CH_2CH_2O)_2H$	<0.01	0	0
$HO(CH_2CH_2O)_3H$	1	14	1.0
$HO(CH_2CH_2O)_4H$	88	100	1.0
$HO(CH_2CH_2O)_5H$	208	100	1.0
$HO(CH_2CH_2O)_{13.2}H$	130	100	0.5
$BuO(CH_2CH_2O)_{13.2}Bu$	<0.01	100	0
$MeO(CH_2CH_2O)_{7.2}H$	24	100	0.2

Note: This reaction was conducted as 1.5 mL of 0.2 M (2-bromoethyl) benzene in benzene containing 0.03 mmol of *n*-decone as an internal standard with 0.5 mL of 60% aqueous KOH in the presence of 0.1 equivalent of catalyst at 35°C.

tration of salt in the aqueous phase was relatively low, and the partitioning of the PEG strongly favored the aqueous phase. In general, the PEGs partition almost exclusively in water relative to an organic phase (e.g., 99% in water v. benzene). Methylene chloride is an exception, with PEGs partitioning 75–99% in the organic layer. The PEGs can be made more efficient phase transfer agents by making them more soluble in the organic phase. This enhancement in solubility can be achieved by converting PEGs to their alkyl ethers. Table 8 shows the catalyst structure, the ratio of the number of oxyethylene groups to the number of carbons in the ether end groups, the percentage of the PEG derivative that partitions to the organic phase, and the relative rate of the phase-transfer-catalyzed reaction of aqueous potassium permanganate with the 1-octene in benzene. The fastest rate is found for the phase transfer agent that is present in appreciable amounts in both phases. Increasing the number of carbons in the polymer terminal groups increases the solubility of the PEG derivative in the organic phase. Therefore, it is possible to optimize the PEG derivative for specific solvents and salt concentrations.

The anion of a PEG-complexed salt may affect relative solubility and stability of the complex in the water and organic phases and then affect reaction rates. If the anion produced by the desired PTC reaction gives a

TABLE 8

Reaction Rates and Partitioning of PEG Ethers

Catalyst	Ratio[a]	Percentage in organic phase	Relative rate
$C_4H_9-(PEG-5000)-CH_3$	23.8	13	<1
$C_8H_{17}-(PEG-5000)-CH_3$	12.7	12	4
$C_{18}H_{37}-(PEG-5000)-CH_3$	6.0	37	8
$C_4H_9-(PEG-1500)-C_4H_9$	4.3	14	4
$C_{18}H_{36}-(PEG-6000)-C_{18}H_{36}$	3.8	Emulsion	20
$C_{18}H_{36}-(PEG-1900)-CH_3$	2.3	39	29
$C_{18}H_{36}-(PEG-750)-CH_3$	0.98	108	9
PEG-6000	0	<1	<0.1

Note: The PEG ether (0.000526 mole) in 4 mL of dry benzene was added to a suspension of KP-t—Bu (10% excess, 0.065 g, 0.0005% mole) in 2 mL of dry benzene. This mixture was stirred for 1 hour at 35°C. One-fifth of the molar equivalent of octyl bromide (0.020 g1 0.000105 mole) in 1.5 mL dry benzene was added. Samples were withdrawn periodically and disappearance of octyl bromide was followed by gas chromatography.

[a]Ratio = number of ethyloxy groups divided by the number of carbon atoms in the end groups.

salt that is more soluble in the organic phase than the initial complex, then "catalyst poisoning" can occur [26]. The phase transfer reaction between sodium hydroxide and β-bromoethylbenzene to give styrene and sodium bromide has an unexpected rate profile. As shown in Fig. 10, this reaction profile is not due to the total depletion of the base since there is an equal molar amount of base and organic halide. The PEG–sodium cation salt of bromide is more soluble than that of the hydroxide (at least in the organic phase). Thus, while there is still hydroxide in the system, it is not transferred to the organic phase and is unreactive with the organic bromide.

Catalyst poisoning may also occur in systems with more than one cation present. Brunelle reports the reaction of 4-chloronitrobenzene with aryl alkoxides occurs with PEGs and PEG monomethyl ethers as catalysts [27]. The reaction rate is faster with potassium alkoxide than with sodium alkoxides, as shown in Table 9. This is consistent with the relative stability of the solvent-separated ion pairs. In the presence of both potassium and sodium cations, the rate is proportional to the amount of sodium species. It appears that sodium is selectively bound to the PEG, and, even in the presence of 75% potassium ion, the reaction occurs via the sodium ion pair. Thus, the selective binding of the sodium dominates the reaction even though the potassium ion pair is more reactive.

Reactions using 60% aqueous potassium hydroxide and toluene to isomerize allylanisole have been found to follow a different mechanistic path [28]. Instead of a system of the expected two liquid phases, a third phase was formed. A toluene phase, a PEG–KOH complex phase, and an aqueous KOH phase were present. Reaction was found to occur in the PEG–KOH
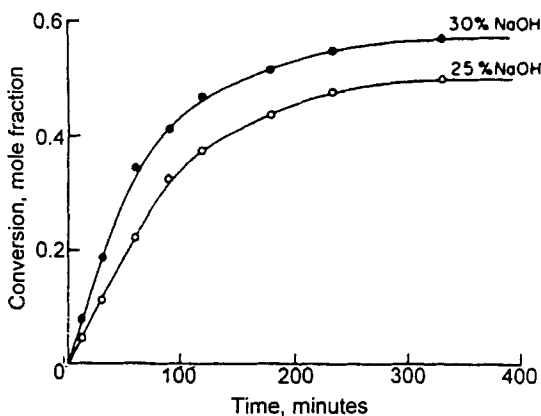
FIG. 10. Reaction profile between sodium hydroxide and β-bromoethylbenzene.

TABLE 9

Effect of Cation on Rate

Potassium percentage	Sodium percentage	Yield (1 h)
0	100	23
100	0	43
50	50	22
67	33	23
75	25	24
90	10	28

phase. The proposed reaction mechanism is shown in Fig. 11. At lower concentrations of KOH, the PEG is soluble in the water, and no new phase forms. This new phase appears only above about 50% KOH. The reaction rate is very sensitive to the presence of this phase, as shown in the rate profile of Fig. 12. In the absence of the third phase, almost no reaction occurs. As the concentration of base is increased beyond that required for the formation of the third phase, the reaction rate increases, presumably due to the higher basicity of the new phase.

The reaction rate in the new phase is a function of the molecular weight of the PEG, as shown in Fig. 13. The data were developed at a constant weight of PEG. In the region from 1 to about 8 oxyethylene units, there is a strong increase of rate with increasing molecular weight. This rate increase is presumably due to the fact that there is a minimum number of
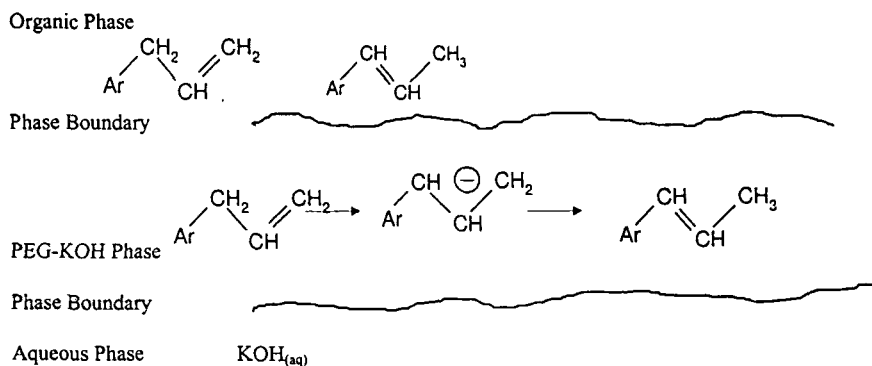
FIG. 11. Reaction mechanism of 60% aqueous potassium hydroxide and toluene isomerization of allylanisole.
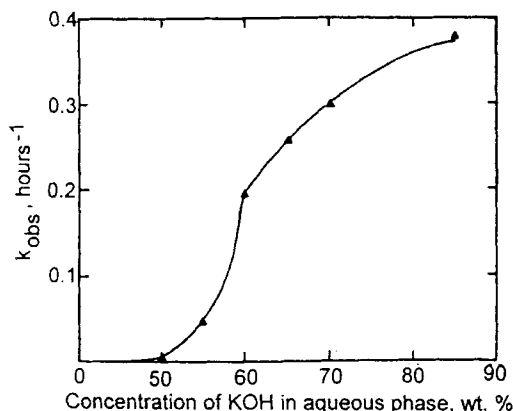
FIG. 12.   Reaction rate profile.

oxyethylene groups required to give the most effective complexation of the potassium. In the region of about 8 to about 20 ethyloxy units, there is a drop in solution rate proportional to the change in molar concentration. In this region, the PEGs have an almost equal effect on rate (on a molar basis). In the region above 20 ethyloxy units, the reaction rate continues to decrease, but at a reduced pace. High molecular weight PEGs are therefore more effective on a molar basis (but less effective on a weight basis) than their lower molecular weight analogues. This is due to the ability of the higher molecular weight PEG to surround the cation more completely, resulting in a greater ion pair separation of the hydroxide, which, in turn, results in an increase in the basicity of the PEG–KOH phase.

The use of polymer-supported PEG catalysts raises new mechanistic questions. MacKenzie and Sherrington [29] addressed a number of these
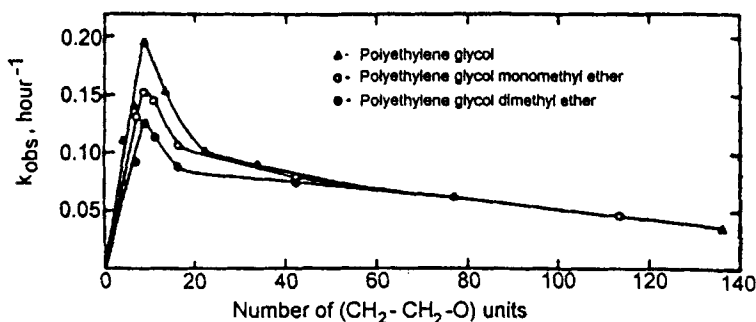
FIG. 13.   Reaction rate as a function of molecular weight of PEG.

questions in a study using a series of polystyrene-resin-supported PEG catalysts for reaction of potassium phenoxide with 1-bromobutane in toluene. This is a system utilizing a solid catalyst, solid salt, and a liquid reactant (an S-S-L system). The rate law was found to be first order in butyl bromide, 0.9 order in supported catalyst, and zero order in potassium phenoxide. This is the same rate law as that found for the unsupported catalyst with the exception that the order in catalyst is then 1.2. Activation energies for reaction with the supported catalyst are 42 kJ mole^{-1} and 47 kJ mole^{-1} for the unsupported catalyst. The similarity of rate laws and activation energies suggests that the rate-controlling step for the two reactions is similar. The rate of reaction was not dependent on the catalyst loading, catalyst particle size, or agitation rate (except at very low agitation rates).

Three possible mechanisms were suggested for the reaction of the bound catalyst. The first involves a reaction in which the potassium phenoxide both has a sufficient equilibrium concentration and dissolves at a rate sufficient to provide the base needed for the reaction. This mechanism would involve the two components of the liquid phase reacting with a solid support (an S-L-L system). However, the solubility of the potassium phenoxide was found to be significantly less than 0.5 ppm, which seems insufficient for this reaction mechanism.

The reaction was examined in a partitioned cell in which the supported catalyst was separated from the solid potassium phenoxide by a glass frit. In this reactor, the reaction rate decreased to approximately that of the uncatalyzed reaction. These two observations strongly suggest that potassium phenoxide from the bulk solvent is not responsible for the reaction.

A second potential mechanism requires the presence of a low concentration of unbound catalysts. This would solubilize the salt either to react directly with the butyl bromide or to act as a means of transporting the salt to the polymer-bound PEG. Again, slow reaction rates in the partitioned reactor suggest that this is not the mechanism. The polymer-supported systems were carefully washed to remove any unbound PEG, and it was found that the supported catalyst could be removed from the reactor, washed, and reused with no decrease in rate being observed. These observations demonstrate that this mechanism is also not responsible for the reaction.

The mechanism that seems to be consistent with the observed facts involves PEG groups on the exterior of the resin reacting directly with the solid salt to "dissolve" the salt. The salt is then transferred to the interior of the resin. The salt is pictured as being passed from PEG chain to PEG chain. In this model, the polyether is pictured as an interpenetrating network throughout the polystyrene structure, almost as if it were a separate liquid phase with an ionic mobility like that found for a liquid solution of a

PEG. Refluxing solid potassium phenoxide with the supported catalyst in the absence of butyl bromide results in the rapid apparent loss of the salt as it dissolves in the polymer matrix. This mechanism fits the observed rate law and the observed slow rate in the partitioned reactor.

Water exhibits an important influence on the rate of solid–liquid (S-L) phase transfer systems, as shown in Table 10 [29]. The reaction of potassium phenoxide with 1-bromobutane was conducted in a solvent carefully dried over lithium aluminum hydride and fractionated. Reactions listed as "normal" in Table 10 used anhydrous "as supplied" commercial solvents. Water concentrations are in microliters added to the reaction. The catalyst was the 3-mole MPEG ether used in solution or bound to the polystyrene resin.

There are a number of reports [30, 31] of the effect of low levels of water on solid–liquid phase transfer systems. Traces of water facilitate the transfer of ions from the crystalline salt. A microsolubilization of the salt is thought to occur before the salt is coordinated by the PEG. It may be necessary to have water at the surface of the crystal to solvate the cation. This would counterbalance the crystal lattice energy and allow the cation to become coordinated by the polyether.

2.2. Liquid–Liquid and Solid–Liquid Reactions

2.2.1. Dichlorocarbene Insertion Reactions

Poly(ethylene glycol) and its derivatives have been shown to be excellent catalysts for the solid–liquid chlorocarbene insertion reaction with cyclo-

TABLE 10

Reaction Rate as a Function of Water Concentration

Catalyst	Initial rate	Amount of water
Resin bound	3.7	Anhydrous
	5.0	Normal
	5.5	20
	3.3	100
	~0.1	2000
Free	3.9	Anhydrous
	4.1	Normal
	5.4	20
	2.0	100
	0.1	2000

hexene (Eq. 1) when compared to dibenzo-18-crown-6 (DB-18-C-6) and N,N,N-triethylbenzyl ammonium chloride [32]. Results are shown in Table 11, which illustrates that the optimal degree of polymerization (DP) for the underivatized PEG catalyst for this reaction is 15. Reaction yields were slightly better with PEGs than for nonionic surfactants (PEGs terminated with a fatty alcohol or alkyl phenol) with similar degrees of ethoxylation. A random copolymer of ethylene oxide (EO) and propylene oxide (PO) was evaluated that did not exhibit significant catalytic activity, showing that, in this case, the pendant methyl group present in propylene oxide polymers and copolymers inhibit cation complexation. The preferred catalyst level is between 1 and 5 mole%.

$$
\text{cyclohexene} + H_2C\begin{matrix} Cl \\ \\ Cl \end{matrix} + NaOH \xrightarrow[\text{RT, 3 Hr}]{\text{Cat. (1 mole\%)}} \text{bicyclic} \begin{matrix} Cl \\ Cl \end{matrix} \tag{1}
$$
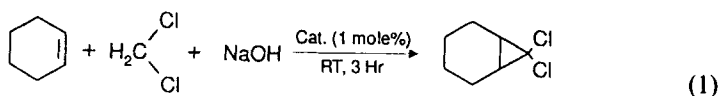
TABLE 11

Dichlorocarbene Reaction with Cyclohexene

Catalyst	n	Yield (%)
$HO-(EO)_n-H$	3	28
	5	85
	10	84
	15	92
	30	94
$C_{12}H_{25}O-(EO)_n-H$	3	36
	5	67
	10	72
	15	78
$C_8H_{17}-Ph-(EO)_n-H$	3	45
	5	65
	10	86
	20	85
$HO-(PO)_{30}(EO)_{15}-H$		<5
DB-18-C-6[a]		61
TEBA[b]		77

Note: Reactions were conducted in chloroform at room temperature for approximately 3 hours using 0.25 mole of NaOH powder, 0.05 mole of alkene substrate, and 1 mole% of catalyst.

[a]Dibenzo-18-crown-6.

[b]Triethylbenzyl ammonium chloride.

   Under liquid–liquid reaction conditions, 50% aqueous sodium hydroxide did not produce significant yields. Aqueous potassium hydroxide formed a "lump" in the reaction mixture after 60% yields were formed, with no further reaction occurring.

   Dichlorocarbene reactions conducted using PEG with a DP of 15 as the phase transfer catalyst gave an 81% yield with σ-pinene [32].

2.2.2.   Williamson Ether Synthesis

   2.2.2.1.   Alkylated Pyrocatechol Synthesis.   Pyrocatechol ethers (*O*-dialkoxybenzenes) are used in the synthesis of various natural products. Pyrocatechol is typically used as the starting intermediate in the systhesis of pyrocatechol ethers (Eq. 2). Although relatively modest yields are obtained if the classic noncatalyzed Williamson ether synthesis is used to prepare these derivatives, improvements in reaction yields are obtained if a PEG is added as a phase transfer catalyst under liquid–liquid conditions [33]. Synthesis was carried out under ethanol reflux in an inert atmosphere. Results are shown in Table 12.

$$\text{(2)}$$
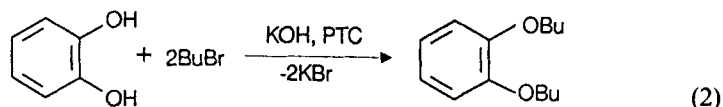
   2.2.2.2.   Phenol Alkylation Reactions.   The effect of varying DP of PEG on the reaction yield of the reaction of potassium phenoxide with

TABLE 12

Alkylation of Pyrochatechol

Alkylbromide	Mole PEG-400 per mole pyrochatechol	Reaction time (h)	Reaction yield (%)
n-Butyl	0	4	74.0
	0.0028	4	74.8
	0.003	4	77.5
	0.005	4	80.2
	0.006	4	80.2
	0.006	4	85.6
	0.013	4	87.4
i-Butyl	0	10	35.0
	0.003	10	49.0
	0.006	10	59.0
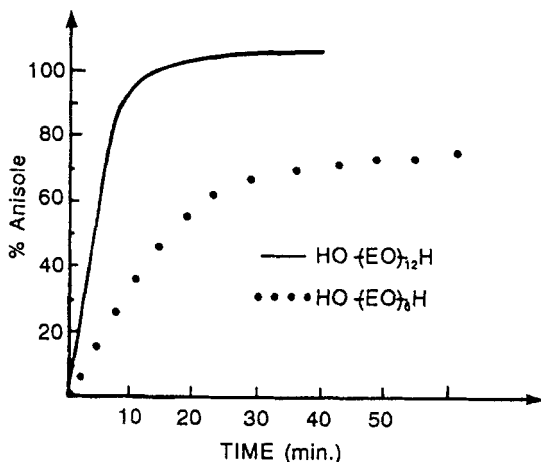
FIG. 14. Optimal catalytic activity of PEG with degree of polymerization equal to 15.

methyl iodide (Eq. 3) was studied by Slaoui et al. [34]. PEG with DP $= 12$ exhibited optimal catalytic activity, as shown in Fig. 14 [34].

$$(3)$$
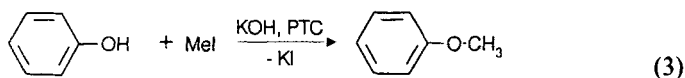
Excellent reaction yields were obtained using a PEG catalyst (DP $= 12$) for both phenol and the more sterically hindered catechol, as shown in Table 13 [34].

TABLE 13

Methylation of Phenolic Derivatives

			Yield (%)	
Phenol	Solvent	Reaction time (h)	No catalyst	$H(EO)_{12}OH$
Phenol	$H_2O/CHCl_3$	30	0	100
	H_2O/CH_2Cl_2	30	0	100
	H_2O/C_6Cl_6	30	0	0
2,4,6-Trimethyl-phenol	$H_2O/CHCl_3$	60	0	60
	H_2O/CH_2Cl_2	60	0	50

2.2.2.3. Diaryl Ether and Thioether Synthesis.   In another recent example, diaryl ethers were prepared using methoxyphenol and p-chloronitrobenzene with PEG-400 as the phase transfer catalyst using varying temperatures and solvents (Eq. 4) [35]. The results are shown in Table 14. These examples show that reaction yields comparable to 18-crown-6 can be achieved.

$$H_3C-O-\langle\bigcirc\rangle-OH + Cl-\langle\bigcirc\rangle-NO_2 \xrightarrow[\text{NaOH, 4 Hr.}]{\text{Catalyst, 5 mole \%}} H_3C-O-\langle\bigcirc\rangle-O-\langle\bigcirc\rangle-NO_2$$

(4)
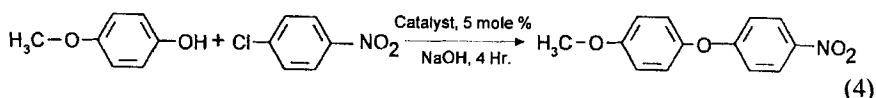
Examples of the preparation of benzylic ethers (Eq. 5) are shown in Table 15 [35].

$$Ar\text{-}OH + ClCH_2-\langle\bigcirc\rangle-Cl \xrightarrow[135^\circ C]{\text{PEG 400/NaOH/MeCN}} ArOCH_2-\langle\bigcirc\rangle-Cl + HCl$$

(5)
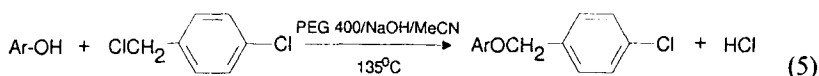
Arylthioethers were prepared using PEG-400 as the phase transfer catalyst (Eq. 6) [36]. Reaction yields were somewhat lower than those reactions catalyzed with N,N,N-tetrabutylammonium bromide (TBAB), as shown in Table 16 [36].

$$Ar\text{-}S\text{-}H + Cl\text{-}R \xrightarrow{\text{PEG 400}} Ar\text{-}S\text{-}R + H\text{-}Cl$$

(6)
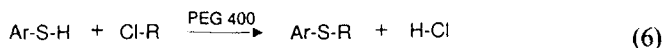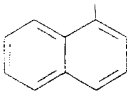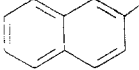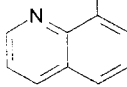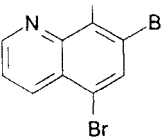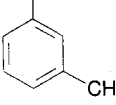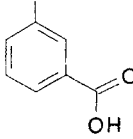
2.2.3.   Horner–Emmons Reaction

The Horner–Emmons reaction is commonly used for the synthesis of aromatic alkene derivatives (Eq. 7). PEG-400 and the corresponding dodecyl and octylphenol ethoxylates are excellent catalysts for this reaction, as shown in Table 17 [37].

TABLE 14

Condensation of p-Methoxyphenol
and p-Chloronitrobenzene

Catalyst	Solvent	Temperature (°C)	Yield (%)
PEG-400	Acetonitrile	135	81
PEG-400	Acetonitrile	100	71
18-Crown-6	Acetonitrile	135	80
PEG-400	Toluene	135	0
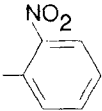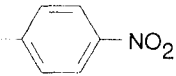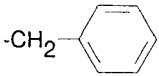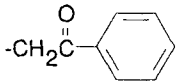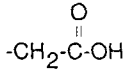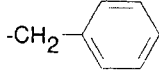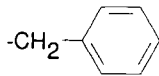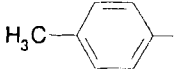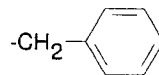
TABLE 15

Synthesis of Diaryl Ethers from Phenols
and *p*-Chlorobenzylchloride

Ar	Yield (%)
	81.0
	70.8
	71.0
	25.7
	83.8
	30.5

$$(EtO)_2\overset{O}{\overset{||}{P}}CH_2-C_6H_5 + \begin{array}{c}OCH_3\\ | \\ C_6H_4 \\ | \\ CHO\end{array} \xrightarrow[\text{RT, 2 Hr.}]{\text{PEG, 2-3 mole \%}} \begin{array}{c}OCH_3\\ | \\ C_6H_4 \\ | \\ CH=CH(Ph)\end{array} + (EtO)_2\overset{O}{\overset{||}{P}}O^- \qquad (7)$$
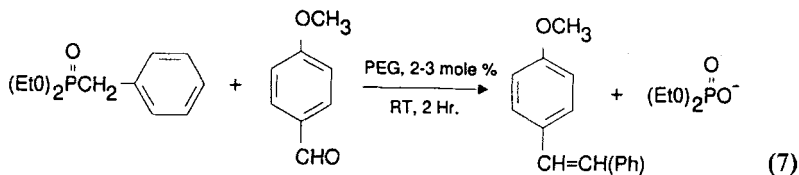
The Horner–Emmons reaction was investigated extensively using PEG-400 as the catalyst [37]. A summary of these reactions and yields is provided in Table 18.

TABLE 16

Preparation of Arylthioethers
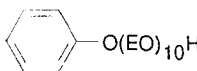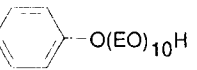
Ar	R	Catalyst[a]	Yield (%)
phenyl	o-NO_2-phenyl	TBAB	86.0
		PEG-400 (B)	74.7
phenyl	p-NO_2-phenyl	TBAB	79.5
		PEG-400 (B)	69.3
phenyl	$-CH_2-$phenyl	TBAB	79.2
		PEG-400 (B)	62.0
phenyl	$-CH_2\overset{O}{\overset{\|}{C}}-$phenyl	TBAB	72.4
		PEG-400 (A)	52.0
		PEG-400 (B)	60.4
phenyl	$-CH_2-\overset{O}{\overset{\|}{C}}-OH$	TBAB	77.4
		PEG-400 (A)	59.5
		PEG-400 (B)	72.0
phenyl	$-CH_2-$phenyl	PEG-400 (A)	85.0
		PEG-400 (B)	91.7
Cl-phenyl	$-CH_2-$phenyl	PEG-400 (A)	88.9[b]
H_3C-phenyl	$-CH_2-$phenyl	PEG-400 (A)	64.4

Note: The reactions were conducted by mixing 0.02 of sodium hydroxide, 0.02 mole of reagents with 40 mL of solvent. Catalyst at 5 mole% was added at room temperature. The reaction mixture was heated at 80°C for 2 hours unless noted otherwise above.

[a]A = Benzene solvent and B = acetonitrile.

[b]The reaction time was 2.5 hours.

TABLE 17

Phase Transfer Catalysts for the
Horner–Emmons Reaction

PEG catalyst	Reaction yield (%)
PEG-400	98
$C_{12}H_{25}O$——〈 〉——$O(EO)_{10}H$	95
C_8H_{17}——〈 〉——$O(EO)_{10}H$	98
None	26

2.2.4. Synthesis of Diacyl Sulfides

Diacyl sulfides may be prepared by the reaction of an acyl halide with sodium sulfide. A comparison of reaction yields for the synthesis of dibenzoylsulfide (Eq. 8) with different PEG catalysts is shown in Table 19 [38]. For these reactions, 0.5 mmole of phase transfer catalyst was used with 20 mmole of acyl halide and 11 mmole of $Na_2S \bullet 9H_2O$. Table 20 provides yields of various diacyl sulfides synthesized under solid–liquid reaction conditions [38].

$$2 \; \text{PhC(O)Cl} \; + \; Na_2S\text{-}9H_2O \; \xrightarrow[\text{Solvent, } 0°C]{\text{Cat., 2.5 Hrs}} \; \text{PhC(O)SC(O)Ph} \; + \; 2NaCl \tag{8}$$
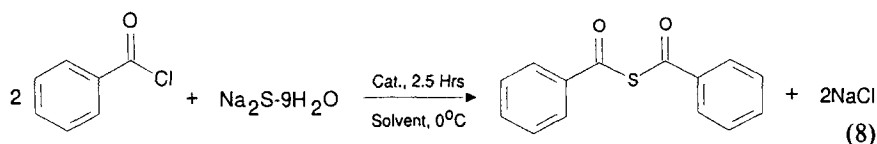
2.2.5. Synthesis of Dithiocarbamate in Aqueous Solution

Dithiocarbamates are synthesized in aqueous solution from amines and carbon disulfide (Eq. 9), a reaction catalyzed by sodium hydroxide [39]. In a side reaction, the carbon disulfide reacts with hydroxyl anion to form the unstable dithiocarbonate ion (Eq. 10), which may lead to significant contamination of the dithiocarbamate product. The use of a phase transfer catalyst will minimize the side reactions.
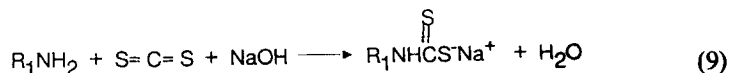
$$R_1NH_2 \; + \; S=C=S \; + \; NaOH \; \longrightarrow \; R_1NH\overset{S}{\overset{\|}{C}}S^-Na^+ \; + \; H_2O \tag{9}$$

TABLE 18

Summary of Horner–Emmons Reactions
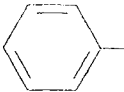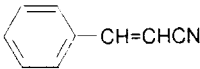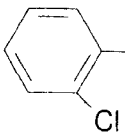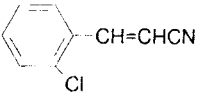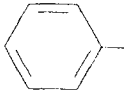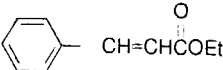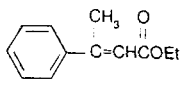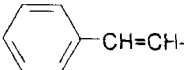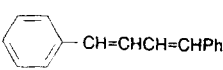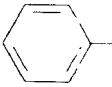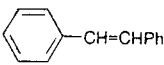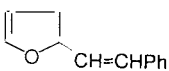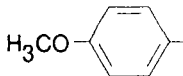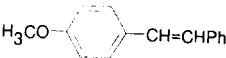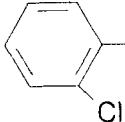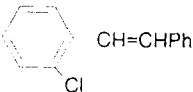
Z	R^1	R^2	Product	Cis/trans	Yield (%)
—CN		—H	CH=CHCN	9/95	90
—CN	Cl	—H	CH=CHCN Cl	10/90	83
—CO$_2$Et		—CH$_3$	CH=CHCOEt	5/95	95
—CO$_2$Et		—H	C=CHCOEt	15/85	60
—Ph	CH=CH-	—H	CH=CHCH=CHPh	0/100	94
—Ph		—H	CH=CHPh	0/100	82
—Ph		—H	CH=CHPh	0/100	92
—Ph	H$_3$CO	—H	H$_3$CO CH=CHPh	0/100	98
—Ph	Cl	—H	CH=CHPh Cl	0/100	78

TABLE 19

Phase Transfer Catalysts for Diacyl Sulfide Synthesis

Catalyst	Solvent	Yield (%)
C_8H_{17}—⟨⟩—$O(EO)_{10}H$	CH_2Cl_2	98.0
C_8H_{17}—⟨⟩—$O(EO)_{10}H$	Benzene	78.1
PEG-400	CH_2Cl_2	93.0
None	CH_2Cl_2	67.0

$$S=C=S + {}^-OH \xrightarrow[-H^+]{} {}^-S\overset{\overset{S}{\|}}{C}O^- \xrightarrow{CS_2} {}^-S\overset{\overset{S}{\|}}{C}S^- + O=C=S \qquad (10)$$

Table 21 illustrates the effect of the phase transfer catalyst; it shows that the use of PEG as a phase transfer catalyst gave yields almost as good as the tetraalkyl ammonium catalysts.

2.2.6. Synthesis of Benzyl Thiocyanate

The reaction of benzyl chloride and potassium thiocyanate (Eq. 11) was conducted in 85% yield using PEG-1500 as the phase transfer catalyst [40]. A slight improvement in reaction yield (90%) was obtained using the dimethyl ether of PEG-1500.

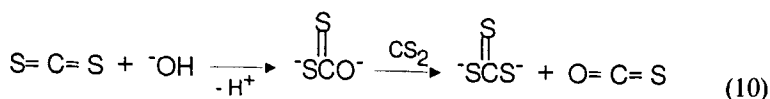$$\text{⟨⟩}{-}CH_2Cl + KSCN \xrightarrow[CHCl_3]{PEG, 2 Hr.} \text{⟨⟩}{-}CH_2SCN + KCl \qquad (11)$$
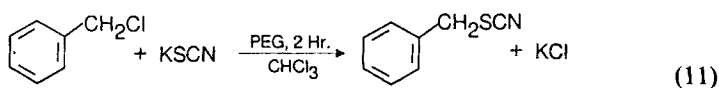
2.2.7. Preparation of Z-2-(2-Amino-4-Thioazoyl)-2-Alkoxyiminoacetic Acid Esters

Z-2-(2-Amino-4-thioazoyl)-2-alkoxyiminoacetic acid esters are prepared by nitrosation of an alkylacetoacetate, followed by alkylation of the alkyl-2-hydroxyiminoacetate, then condensation of the alkyl-4-halo-2-alkoxyiminoacetate with thiourea [41]. R_1 is a lower alkyl group, and R_2 is an unsaturated lower alkyl group or substituted carboxyl or ester group. When

TABLE 20

Diacylsulfide Synthesis Under Solid–Liquid Phase
Transfer Reaction Conditions

Diacylsulfide	Reaction yield (%)
$(CH_3\overset{O}{\overset{\|}{C}})_2S$	61.7, 92.0[a]
(⟨phenyl⟩-$\overset{O}{\overset{\|}{C}}$)$_2$S	98.0
$(O_2N$-⟨phenyl⟩-$\overset{O}{\overset{\|}{C}})_2S$	91.9
$(t\text{-Bu}\overset{O}{\overset{\|}{C}})_2S$	92.8
(O_2N-⟨phenyl⟩(O_2N)-$\overset{O}{\overset{\|}{C}}$)$_2$S	91.3
$((CH_3)_3CCH_2CH(CH_3)CH_2\overset{O}{\overset{\|}{C}})_2S$	89.2
$CH_3(CH_2)_{10}\overset{O}{\overset{\|}{C}})_2S$	95.0

Note: All reactions were conducted at 0–2°C for 2.5 hours using 0.5
mmole of the *n*-octylphenyl ether ethoxylate, with DP = 9, 10 mmole of
the acyl chloride and 11 mmole of $Na_2S \bullet 9H_2O$.
  [a]This reaction was conducted with anhydrous sodium sulfide.

all three steps are carried out with a phase transfer catalyst such as PEG,
the product could be isolated with minimal degradation of the intermediate
products. Overall reaction yields of more than 50% were reported. Unfor-
tunately, comparative yields as a function of catalyst type were not re-
ported.

### 2.2.8. N-*Alkylation of Heterocycles*

  2.2.8.1. N-*Substituted Imidazole.* The alkylation of *N*-heterocycles
such as imidazole was reviewed earlier. Since that time, Hanming and
Chengye have also reported PEG-catalyzed *N*-alkylations of imidazoles

TABLE 21

Sodium Dipentyldithiocarbamate Synthesis
Using Phase Transfer Catalysts

Phase transfer catalyst	Yield after 2 h (%)
None	38
Tetrabutyl ammonium bromide	97
N-Cetyl-N,N,N-trimethyl-ammonium bromide	100
Tetrabenzyl ammonium bromide	100
PEG-1500	94

Note: The dithiocarbamate reactions were conducted in a liquid–liquid medium by mixing 200 mL water, 0.2 mole of amine, 0.2 mole sodium hydroxide, 0.4 mole carbon disulfide, and the phase transfer catalyst (PEG-1500) at 20°C for 3 hours. The amount of phase transfer catalyst was 1% of the weight of the reactants.

(Eq. 12) [42]. A summary of the *N*-substituted imidazoles prepared is given in Table 22.

$$\text{imidazole-NH} + RX \xrightarrow{\text{PEG, MOH}} \text{imidazole-N-R} + MX \tag{12}$$
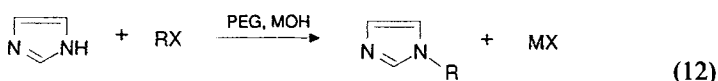
The effect of reaction temperature on the *N*-butylation of imidazole was studied and showed that essentially equivalent yields (68–70%) were obtained over the temperature range 52°C to 73°C [42]. Optimal yields were obtained with PEG-400 and PEG-600. Salt effects were found. Aqueous KOH and NaOH produced reaction yields of 75% and 70%, respectively, while only 16.6% product yield was obtained with aqueous LiOH.

2.2.8.2. N-Substituted Benzotriazole. The alkylation of 1,2,3-benzotriazole using PEG-800 as a catalyst and potassium carbonate as the base (Eq. 13) has been reported [43]. The reaction products and yields obtained are summarized in Table 23.
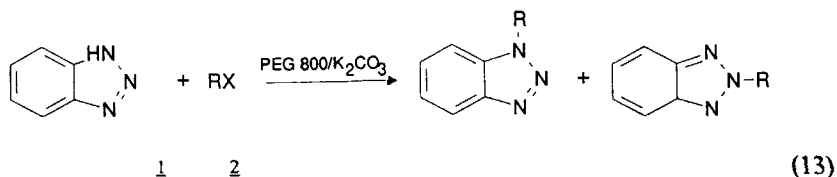
$$\text{benzotriazole-HN} + RX \xrightarrow{\text{PEG 800/K}_2\text{CO}_3} \text{product } \underline{1} + \text{product } \underline{2} \tag{13}$$

$$\underline{1} \qquad \underline{2}$$

TABLE 22

N-Alkylation of Imidazole

R-Br	PEG-400		$RO\,(EO)_{10}OH$, $R\ =\ C_8H_{17}, C_{12}H_{25}$	
	Reaction time (h)	Yield (%)	Reaction time (h)	Yield (%)
n-C_4H_9	2.70	70	4.0	78
iso-C_4H_9	7.30	19		
sec-C_4H_9	7.00	10		
n-C_5H_{11}	3.50	75	3.0	70
iso-C_5H_{11}	5.00	70	9.3	60
c-C_6H_{11}	8.00	5		
n-C_8H_{17}	4.10	73	3.5	80
iso-C_8H_{11}	5.00	66	7.8	75
$C_{12}H_{23}$	5.60	77	6.7	75
$C_{16}H_{33}$	5.75	78	5.2	70
$C_6H_5CH_2$	7.20	30	2.0	84

TABLE 23

Alkylation of 1,2,3-Benzotriazole Using PEG-800

Alkylating agent	Yield (1 + 2) (%)		1/2 by gas chromatography	
	Reaction a[a]	Reaction b[b]	Reaction a[a]	Reaction b[b]
n-C_4H_9Br	78.1	57.5	0.35	0.18
sec-C_4H_9Br	68.5	—	1.45	—
n-$C_8H_{17}Br$	82.6	—	0.55	—
n-$C_{14}H_{29}Br$	88.2	61.0	0.62	0.44
$CH_2{=}CHCH_2Cl$	84.0	—	0.19	—
$ClCH_2CO_2C_2H_5$	87.8	—	0.23	—
$C_6H_5CH_2Cl$	90.1	65.2	0.09	0.04

[a]Reaction a was conducted as a solid–liquid reaction using 0.4 grams of PEG-800 and 10 mmole of substrate.

[b]Reaction b was conducted as a liquid–liquid reaction using 50% aqueous NaOH, 0.8 grams TEBAC, and 10 mmole of substrate.

2.2.9. Chloroacetic Acid Condensation Reactions to Form Aryloxyacetic Acids

In a reaction related to the Williamson ether synthesis, aromatic alcohols react with chloroacetic acid to form aryloxyacetic acid under solid–liquid and liquid–liquid reaction conditions (Eq. 14) [44]. PEG-400 was used as the phase transfer catalyst under solid–liquid and liquid–liquid reaction conditions. The reaction products and yields are given in Table 24. As the results in Table 24 show, significantly better yields were obtained under solid–liquid conditions than under liquid–liquid conditions.

$$\text{ArOH} \; + \; \text{ClCH}_2\overset{\overset{O}{\|}}{\text{C}}\text{OH} \; \xrightarrow[\text{MeCN, 125}^\circ\text{C}]{\text{PEG-400/NaOH}} \; \text{ArOCH}_2\overset{\overset{O}{\|}}{\text{C}}\text{OH} \qquad (14)$$
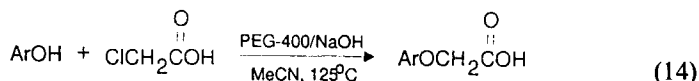
2.2.10. Oxidation Reactions

The use of PEGs as phase transfer catalysts for the autooxidation of nitroaromatic compounds (Eq. 15) was studied using mechanical and ultrasonic agitation [45]. Interesting selectivity differences were observed between the two forms of agitation, with the mechanical agitation giving exclusively dimer, while significant amounts of carboxylic acids were formed by ultrasonic agitation. Dimer was always formed whenever the carboxylic acid was formed. The reaction conditions call for 0.01 mole substrate, 0.05 moles KOH, 0.001 moles catalyst, and 10 mL toluene under an oxygen atmosphere. Results are given in Table 25.
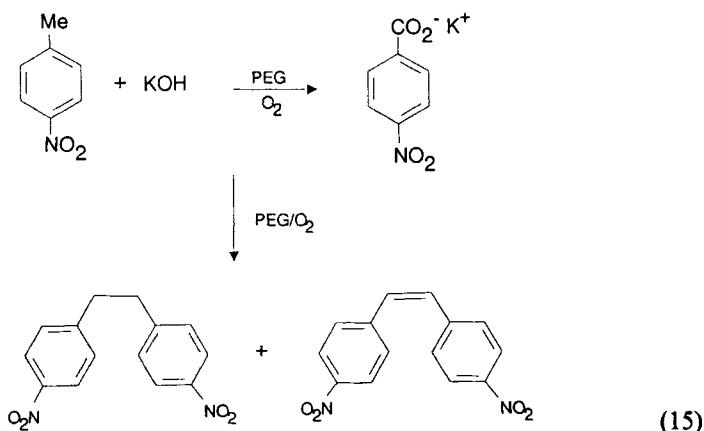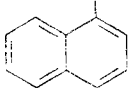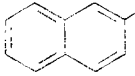

(15)
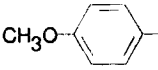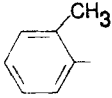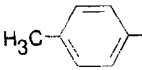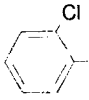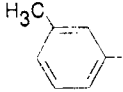
TABLE 24

Preparation of Aryloxyacetic Acids

Ar =	Reaction Yield (%)	
	Solid–Liquid[a]	Liquid–Liquid
	73.4	67.0
	66.4	40.0
	67.3	–
CH_3O–	38.1	32.7
	90.6	59.0
H_3C–	76.7	56.0
	85.2	–
H_3C–	76.0	39.0

[a]This reaction was conducted with 0.0173 mole of the substituted phena-
loc derivative, 0.0396 mole of solid NaOH, 0.022 mole of chloracetic acid,
0.35 g of PEG-400 (5 mole%), 100 mL acetonitrile at 125 °C for 3 hours.

TABLE 25

Base-Catalyzed Oxidation of Alkylated Benzene[a]

			Yield (mole%)	
Agitation	Substrate	Catalyst	Carboxylic acid	Dimer
Mechanical[b]	*p*-Nitrotoluene	PEG-6000	0	5.4
"	*p*-Nitrotoluene	PEG-400	0	26.8
"	*p*-Nitrotoluene[d]	PEG-400	0	19.3
"	*p*-Nitrotoluene[e,f]	PEG-400	0	38.7
"	*o*-Nitrotoluene	PEG-400	0	18.1
"	*o*-Ethylnitrotoluene	PEG-400	0	17.2
"	*p*-Ethylnitrotoluene	PEG-400	0	22.0
Ultrasonic[c]	*p*-Nitrotoluene	PEG-400	21.1	34.9
"	*o*-Nitrotoluene	PEG-400	1.6	2.4
"	*p*-Ethylnitrotoluene	PEG-400	22.2	5.8
"	*o*-Ethylnitrotoluene	PEG-400	0.5	1.3
"	*p*-Nitrotoluene	None	0	0
"	*p*-Nitrotoluene	PEG-6000	5.6	7.7
"	*p*-Nitrotoluene[d]	PEG-400	43.1	2.3
"	*p*-Nitrotoluene[g]	PEG-400	16.7	17.1

[a]The reaction conditions were 0.01 mole substrate, 0.05 mole KOH, 0.001 mole catalyst, and 10 mL toluene under oxygen.

[b]Mechanical agitation was provided with a R7R-01 stirrer at 1500 rpm for 3 hours at 25°C.

[c]Ultrasonic agitation was provided with a Sonicor ultrasound bath for 1 hour.

[d]Used 0.001 mole of *p*-nitro toluene.

[e]Reaction conducted under 75 psi oxygen.

[f]Agitation was provided by shaking in an autoclave.

[g]Use NaOH instead of KOH.

2.2.11. Aldol Condensations

Zupanic and Kokalj examined the use of PEG-400 diethyl ether to catalyze the formation of α,β-unsaturated nitriles by an aldol condensation (Eq. 16) [46]. The reaction medium employed 52% aqueous sodium hydroxide/toluene, and the reaction time was 60 minutes. The molar ratio of the substrates nitrile/aldehyde/NaOH/catalyst was 1/1/6/0.2. The products formed in the two-phase reaction are summarized in Table 26. Yields varied from poor to good.
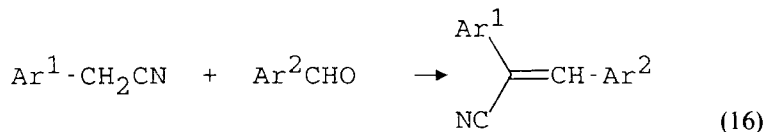
$$Ar^1\text{-}CH_2CN \quad + \quad Ar^2CHO \quad \longrightarrow \quad \underset{NC}{\overset{Ar^1}{>}}\!\!=\!\!CH\text{-}Ar^2 \qquad (16)$$
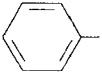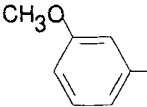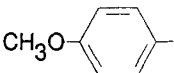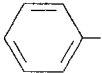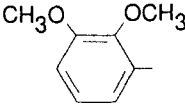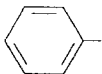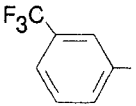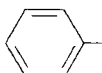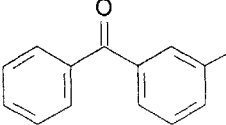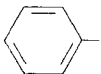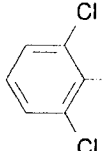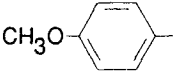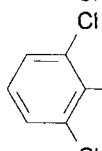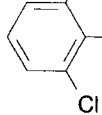
TABLE 26

Formation of α,β-Unsaturated Nitriles

Ar^1	Ar^2	Yield (%)
(see structure)	(see structure)	71
CH_3O— (see structure)	(see structure)	59
CH_3O OCH_3 (see structure)	(see structure)	64
F_3C— (see structure)	(see structure)	69
(see structure)	(see structure)	29
(see structure)	Cl ... Cl (see structure)	11
CH_3O— (see structure)	Cl ... Cl (see structure)	62
		55

Note: Reactions were conducted in toluene solution. The reaction stoichi-ometry was nitrile/NaOH/PEG-400 dimethylether = 1/1/6/0.2. The NaOH was added to the reaction medium as a 52% aqueous solution. These reactions were conducted at 20°C for 60 minutes.

2.2.12. Fluorination of Activated Halogens

Fluorides can be used to replace other halides in organic compounds, including acid chlorides, sulfonyl chlorides, and alkyl bromides and chlorides (Eq. 17). This reaction can be catalyzed by PEG catalysts [47]. The results for a series of typical reactions using a variety of PEG catalysts can be found in Table 27. The lower molecular weight PEGs are more effective catalysts than the higher molecular weight analogues. However, under the

TABLE 27

Formation of Alkyl Fluorides from Alkyl Halides

Activated chloride	Catalyst	Temperature (°C)	Time (h)	Yield (%)
Benzoylchloride	PEG-200	20	3	97
"	PEG-300	20	3	96
"	PEG-400	20	3	98
"	PEG-600	20	3	96
"	PEG-4000	20	3	48
"	None	20	3	19
Butyrylchloride	None	20	3	13
"	PEG-600	20	3	97
"	PEG-4000	20	3	61
Benzenesulfonylchloride	None	20	3	5
"	PEG-400	20	3	98
"	PEG-600	20	3	97
p-Toluenesulfonylchloride	None	20	3	11
"	PEG-300	20	3	86
"	PEG-400	20	3	80
Benzyl bromide	None	Reflux	6	0
"	PEG-300	Reflux	6	19
"	PEG-400	Reflux	6	21
Cyclohexylbromide	None	Reflux	6	0[a]
"	PEG-300	Reflux	6	76
"	PEG-400	Reflux	6	81
2,4-Dinitro-chlorobenzene	None	Reflux	24	0
"	PEG-300	Reflux	24	56
"	PEG-400	Reflux	24	41

Note: These reactions were conducted under the conditions shown by stirring 1 g of the indicated PEG, 20 mmole of calcinated KF, and 10 mmole of the acid chloride in 10 mL of dried acetonitrile.
[a]Cyclohexene was the only product observed.

reaction conditions employed, the PEG catalysts were somewhat less effective than crown ethers in previous studies.

$$RCl + KF \xrightarrow[CH_3CN]{PEG} RF + KCl \tag{17}$$

2.2.13. Organometallic Reactions

Ferrocene may be produced by the room temperature reaction of ferrous chloride with cyclopentadiene using sodium hydroxide as the base through the action of a PEG phase transfer catalyst (Eq. 18) [48]. The reaction, performed under nitrogen in DMSO, takes an hour. The normal method of preparation involves the use of metallic potassium or sodium. Although quantitative yields were not reported, they were reported to be high.

$$\tag{18}$$
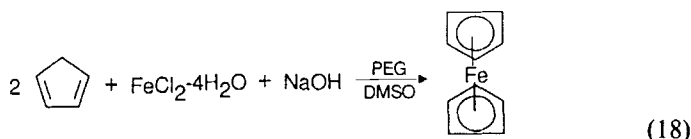
Huang and Wu reported the use of PEGs as catalysts for the palladium(II)-catalyzed carbonylation of aromatic halides (Eq. 19) [49]. It was found that increasing molecular weight of the PEG catalyst produced corresponding increases in reaction yields, as shown in Table 28. Carbonylation

TABLE 28

Carbonylation of Aryl Halides with Palladium Catalyst

Reactant	Product	Yield (%)		
		PEG-400	PEG-600	PEG-1000
PhCl	—	—	—	—
PhBr	$PhCO_2H$	41	46	86
PhI	$PhCO_2H$	71	78	91
$4\text{-}MeC_6H_4I$	$4\text{-}MeC_6H_4CO_2H$	83	91	96
$4\text{-}ClC_6H_4I$	$4\text{-}ClC_6H_4CO_2H$	—	89	98
$4\text{-}BrC_6H_4Br$	$4\text{-}BrC_6H_4CO_2H$	—	88	91
$1\text{-}C_{10}H_7Br$	$1\text{-}C_{10}H_7CO_2H$	—	56	60
$2\text{-}C_{10}H_7Br$	$2\text{-}C_{10}H_7CO_2H$	—	57	63
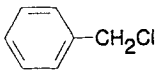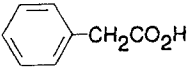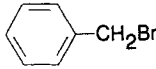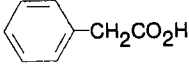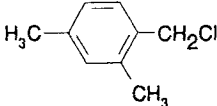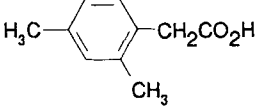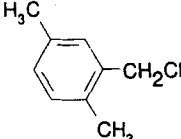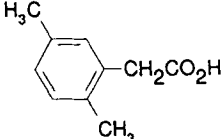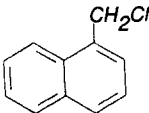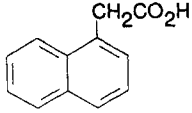
could be conducted under an unusually low pressure of one atmosphere of carbon monoxide. The reactions were performed in anisole at 80°C, followed by addition of aqueous sodium hydroxide and additional heating. Yields in some cases were quite high.

$$ArX + CO + NaOH \xrightarrow[\text{2) } H^+/H_2O]{\text{1) } Pd(PPh_3)/PEG} ArCO_2H \qquad (19)$$
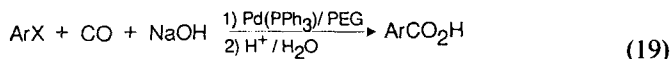
The carbonylation of benzylic halides has also been reported [50]. The substrates and reaction yields are summarized in Table 29.

Calet and Alper studied the use of PEG-400 to catalyze the carbonylation of thiiranes to β-mercapto acids using cobalt carbonyl, carbon monoxide, methyl iodide, or benzyl bromide (Eq. 20) [51]. The use of PEG-400 catalyst was reported to double the reaction yields when compared to quaternary ammonium salt catalysts such as cetyltrimethylammonium bromide. Reaction yields are summarized in Table 30.

TABLE 29

Carbonylation of Benzylic Halides

Substrate	Product	Yield (%)
—CH$_2$Cl	—CH$_2$CO$_2$H	85
—CH$_2$Br	—CH$_2$CO$_2$H	86
H$_3$C— —CH$_2$Cl CH$_3$	H$_3$C— —CH$_2$CO$_2$H CH$_3$	84
H$_3$C —CH$_2$Cl CH$_3$	H$_3$C —CH$_2$CO$_2$H CH$_3$	86
CH$_2$Cl	CH$_2$CO$_2$H	78

$$\text{(structure)} \quad + \text{ CO } + \text{ CH}_3\text{I} \quad \frac{\text{3N KOH, PEG-400}}{\text{Co}_2(\text{CO})_8, \text{ Benzene, RT, 1 Atm.}} \longrightarrow \text{(structure)} \tag{20}$$
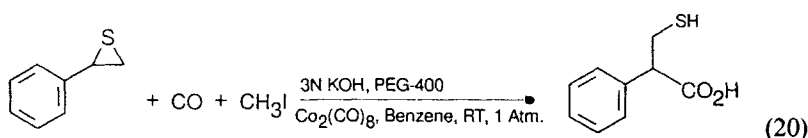
2.2.14. Acetal and Ethylene Oxide Purification

Fenton reported that acetals such as trioxane could be purified by refluxing with sodium in the presence of a PEG phase transfer catalyst [52]. Acetals purified in this way were capable of being reacted to form high molecular weight polymers.

Wu et al. stirred PEG-600 with a 5% solution of NaOH at approximately 0°C to remove aldehyde impurities from ethylene oxide [53]. The reaction time was approximately 15 hours. This reaction procedure is reported to be safer than the reaction of aqueous KOH with ethylene oxide under 72-hour refluxing conditions.

2.3.   Gas–Liquid Phase Transfer Reactions

Phase transfer catalysts are well known for reactions occurring with liquid–liquid or with liquid–solid contact. Recent studies by Tundo and coworkers [54–62] have examined reactions occurring between a gas stream and a solid. A phase transfer catalyst coated on a solid can be visualized as catalyzing reactions between the gaseous reagents and the substrate in a thin layer of liquid that coats the solid, therefore, the term gas–liquid phase transfer catalysis (GL-PTC) applies. The phase transfer agent acts to transfer a reagent from the solid state and provides the liquid medium in which the reaction occurs. With GL-PTC, the solid state consists of a salt of the active nucleophile or a strong base that generates the desired nucleophile from a gaseous reagent.

The PTC is dissolved in a solvent to which the solid is added. The solvent is removed, and the substrate is dried in an oven. The supported PTC is then placed in a column that can be held at an elevated temperature. The temperature for the experiment must be maintained so that the PTC is molten, and the temperature and pressure must be selected to keep the reagent in the vapor state as it is fed to the reactor.

Two general types of reactions have been described and the data summarized [54]. In one case, the reaction consumes an anion from the bed. An example of this type of reaction would be halide displacement (Eq. 21).

$$\text{RX (gas)} + \text{M}^+\text{Y}^- \text{ (solid)} \rightarrow \text{RY (gas)} + \text{M}^+\text{X}^- \text{ (solid)} \tag{21}$$
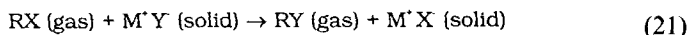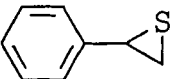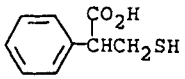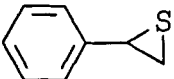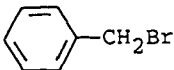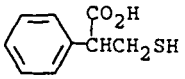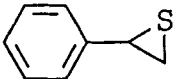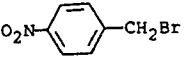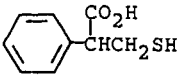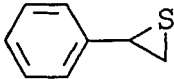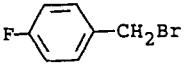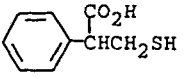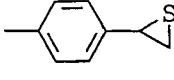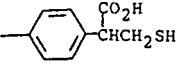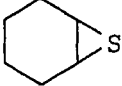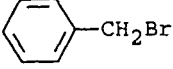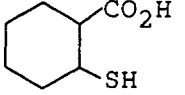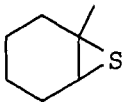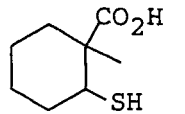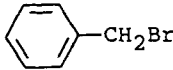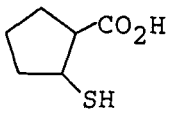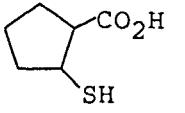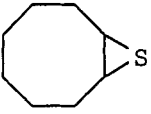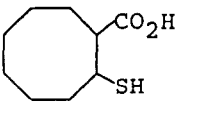
TABLE 30

β-Mercapto Acids from $Co_2(CO)_8$/PEG-Catalyzed Reaction of Substituted Thiiranes and CO

Thiirane	Halide	Reaction time (h)	Product	Yield (%)
(phenyl thiirane)	CH_3I	18	(phenyl-CH(CO$_2$H)CH$_2$SH)	78
(phenyl thiirane)	(benzyl)–CH_2Br	18	(phenyl-CH(CO$_2$H)CH$_2$SH)	55
(phenyl thiirane)	O_2N–(phenyl)–CH_2Br	18	(phenyl-CH(CO$_2$H)CH$_2$SH)	12
(phenyl thiirane)	F–(phenyl)–CH_2Br	18	(phenyl-CH(CO$_2$H)CH$_2$SH)	39
(4-methylphenyl thiirane)	CH_3I	18	(4-methylphenyl-CH(CO$_2$H)CH$_2$SH)	49
(cyclohexane-fused thiirane)	(benzyl)–CH_2Br	60	(cyclohexane CO_2H, SH)	51
(methyl cyclohexane-fused thiirane)	CH_3I	48	(cyclohexane CO_2H, methyl, SH)	24
(cyclopentane-fused thiirane)	(benzyl)–CH_2Br	60	(cyclopentane CO_2H, SH)	33
(cyclopentane-fused thiirane)	CH_3I	60	(cyclopentane CO_2H, SH)	24
(cyclooctane-fused thiirane)	CH_3I	60	(cyclooctane CO_2H, SH)	49

In the other case, the bed acts as a catalyst and is not consumed. An example would be transesterification between an acid and an ester (Eq. 22) catalyzed by sodium carbonate with a phase transfer catalyst. Since the bed is not consumed, the reaction will continue as long as the reactants are fed to the reactor.

$$R' \, X + R'' \, Y + PTC - Base \rightarrow R' \, Y + R'' \, X + PTC - Base \qquad (22)$$
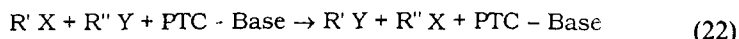
2.3.1. Preparation of Alkyl Iodides

Alkyl iodides can be prepared by passing alkyl chlorides or bromides over a bed of potassium iodide [54]. Table 31 provides results obtained at a reaction temperature of 160°C. In the absence of a PTC, essentially no reaction occurs with butylbromide, while in the presence of a PTC the reaction proceeds with a high conversion. Silica gel by itself can activate the potassium iodide, but the reaction proceeds with a much higher conversion in the presence of a phase transfer catalyst.

2.3.2. Synthesis of Carboxylate Esters

Carboxylate esters can be synthesized using GL-PTC with either the salt of an organic acid or by forming the salt *in situ* by reaction of a base in the bed with an organic acid. The reaction of ethyl bromide with sodium acetate at 150°C is shown in Table 32 [54].

The failure of the higher melting PTCs is attributable to the lack of a liquid phase. In contrast to the results in Table 31, these reactions do not proceed well with either the crown ether or PEGs.

TABLE 31

Reaction of *n*-Butyl Bromide to Form Butyl Iodide

Bed	PTC	Conversion (%)
KI (10.3 meq/BuBr)	—	2
KI (10.3 meq/BuBr)	$Bu_4P^+I^-$	96
KI (1.5 meq/BuBr)	Silica gel	50
KI (1.5 meq/BuBr)	Silica gel + $Bu_4P^+I^-$	93

$^{\sharp}$NaOH substituted for KOH.

TABLE 32

Reactions of Ethyl Bromide and Sodium Acetate

Catalyst	mp (°C)	Conversion (%)
$Bu_4P^+Br^-$	87	96
$C_{16}H_{33}P^+Bu_3Br^-$	54	86
$Bu_3P^+MeI^-$	135	59
$C_{16}H_{33}P^+Et_3Br^-$	145	86
$C_{16}H_{33}P^+Me_3Br^-$	203	0
$Et_3P^+MeI^-$	324	0
18-Crown-6	38	32
Carbowax 6000	55–62	4

2.3.3. Phenyl Ethers

Using GL-PTC, phenols and thiophenols are reacted with alkyl halides to give phenyl ethers and thio ethers. Table 33 gives data reported for reactions catalyzed by Carbowax 6000 at 150°C [55]. The high yields generated under the GL-PTC conditions are not the result of the presence alone of bases at the high temperatures employed. Common basic materials such as basic alumina, basic alumina plus sodium methoxide, magnesium oxide, or magnesium oxide plus PEG-6000 all failed to give more than trivial yields of butyl phenyl ether from phenol and butyl bromide. Even basic alumina, sodium methoxide, and PEG-6000 gave only 5% conversion.

Under GL-PTC conditions, the PEG–sodium carbonate combination produces anions up to pK_a of 12. Carbonate acts as a strong base in the absence of water. Under these conditions, PEG-6000 acts as a polar aprotic

TABLE 33

Alkylation of Phenols and Thiophenols

Phenol	Alkyl halide	Base	Product	Conversion (%)
PhOH	BuBr	K_2CO_3	PhOBu	86
PhOH	EtBr	K_2CO_3	PhOEt	81
$3,5-Me_2C_6H_3OH$	BuBr	K_2CO_3	$3,5-Me_2C_6H_3OBu$	91
$2-AcC_6H_4OH$	BuBr	K_2CO_3	$2-AcC_6H_4OBu$	96
C_6H_5SH	$CH_3(CH_2)_7Cl$	K_2CO_3	$C_6H_5S(CH_2)_7Me$	92
2-OH-Np	MeI	K_2CO_3	2-Np-OMe	72
$HSCH_2CH_2OH$	BuBr	K_2CO_3	$HOCH_2CH_2SBu$	85

solvent, allowing the generation of phenoxide and phenylthio anions. Under typical liquid–liquid phase transfer conditions using aqueous potassium carbonate and PEG as catalyst, 2% phenyl ether yields were obtained [62].

The PEGs have a stability advantage over ionic PTCs under the basic high-temperature conditions employed here. Both phosphonium salts and ammonium salts are either temperature or base unstable at 170°C.

2.3.4. Wittig Reactions

The Witting reaction (Eq. 23) has been carried out under GL-PTC conditions [56]. In this procedure, potassium carbonate is coated with PEG-6000 and dried. The desired phosphonium halide is mixed with the PEG-6000–sodium carbonate mixture. The aldehyde is then passed through a heated bed of the solid mixture, and the product is condensed as it exits the bed. Reactions have been examined using either 150°C or 170°C. The high-boiling triphenylphosphine oxide generated is left behind in the column, where it can be recovered with solvent. Table 34 gives results.

$$Ph_3P^+CH_2R_1 \text{ (solid)} + R_2CHO \text{ (gas)} \longrightarrow R_1CH=CHR_2 \text{ (gas)} + Ph_3P=O \text{ (liquid)}$$

$$(23)$$

A wide range of aldehydes may be used, including water-soluble formaldehyde and acetaldehyde. Ketones, however, will not work. The cis-trans ratios were typical for the Wittig reaction.

TABLE 34
Wittig Reaction Under GL-PTC Conditions

R_1	R_2	X^-	PEG-6000	Temperature (°C)	Yield (%)
H	Ph	I	—	170	56
H	Ph	I	+	150	98
Me	Ph	Br	—	170	20
Me	Ph	Br	+	150	77
$CH=CH_2$	Ph	Br	—	170	14
$CH=CH_2$	Ph	Br	+	150	90
H	$Me(CH_2)_8$	I	—	170	95
H	$Me(CH_2)_8$	I	+	150	100
Ph	H	Cl	+	150	100
Ph	Me	Cl	+	150	96
Ph	$MeCH_2$	Cl	—	170	97
$(CH_2)_2Me$	Ph	Br	+	150	100

As was true in the phenyl ether syntheses described above, under these conditions the potassium carbonate was basic enough to generate the ylid. In a few examples, the potassium carbonate itself was basic enough to drive the reaction. The phosphonium salts had to be handled with care or they would partially decompose before they could react with aldehyde.

2.3.5. Transesterification Reactions

Transesterification can be carried out using GL-PTC on a potassium carbonate bed coated with either a crown ether or PEG-6000 [57] (Eq. 24). All reactions were run until the ratios of reactant to product were constant. This was done to give an indication that the equilibrium mixture under the reaction conditions had been obtained. This is not necessarily the thermodynamic equilibrium, but rather the equilibrium of the entire system. Larger beds, for instance, gave higher conversions for the same reaction, and beds were not increased in size to the point of no further change. The molar ratio of ester to alcohol was 1:2 in each case studied. Both PEG-6000 and 18-crown-6 were effective PTCs. Without PTC, little conversion occurred.

$$Ph_3P^+CH_2R_1 \text{ (solid)} + R_2CHO \text{ (gas)} \longrightarrow R_1CH=CHR_2 \text{ (gas)} + Ph_3P=O \text{ (liquid)}$$

$$(24)$$
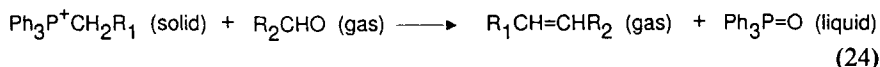
Tables 35 and 36 demonstrate some representative transesterifications. Alcohols demonstrated the following reactivity order: MeOH > primary ≫ secondary > tertiary. One of the effects demonstrated is the ease with which anions are formed from the alcohols. Anions are the expected reactive species for transesterification.

Tables 35 and 36 show that conversion is in the order of alcohol acidity: MeOH > EtOH > n-propanol > n-butanol. In addition, primary alcohols are more acidic than secondary and tertiary alcohols. Secondary and

TABLE 35

Transesterification of n-Amyl Acetate
Under GL-PTC Conditions

Alcohol	Yield (%)
Methanol	91
Ethanol	75
n-Propanol	65
n-Butanol	58

tertiary alcohols are also more stearically hindered, and conversions can be expected to be lower for this reason as well, as shown in Table 36.

Ester structure also has an effect on conversion. Higher boiling esters have a longer residence time on the beds and will have a higher degree of conversion. Examples using amyl acetate gave correspondingly higher conversions than the ethyl acetate equivalents. In addition, stearically hindered esters like *t*-butyl acetate gave very low conversions (5%), even when being reacted with an *n*-butanol, a reaction that would have relieved stearic crowding around the ester.

Although alkoxide is the suspected reactive intermediate, the yield of ethyl ether from ethanol and ethyl bromide was very low, even with crown ether. This indicates either that the concentration of alkoxide was very low or that other mechanisms like carbonyl activation contribute to conversion.

P-Toluene sulfonic acid on silica gel was ineffective as a catalyst for the transesterification reaction under the conditions employed.

2.3.6. Malonate Alkylation

GL-PTC has also been examined as a technique for carrying out the malonate alkylation. Table 37 gives the results for the reaction of diethyl-

TABLE 36

Transesterification of Ethyl Acetate

Alcohol	Catalysts	Bed size (grams)	Yield (%)
Methanol	PEG-6000	400	53
Methanol	PEG-6000	180	34
Methanol	18-Crown-6	30	31
n-Propanol	PEG-6000	400	33
n-Butanol	PEG-6000	400	42
n-Butanol	PEG-6000	180	34
n-Butanol	18-Crown-6	30	17
Isobutanol	PEG-6000	400	46
sec-Butanol	PEG-6000	400	2
t-Butanol	PEG-6000	400	Trace
1-Pentanol	None	400	36
1-Pentanol	PEG-6000	400	53
1-Pentanol	18-Crown-6	30	61

TABLE 37

Malonate Synthesis Using GL-PTC

Catalyst	Total yield (%)	Monoalkylated (%)	Dialkylated (%)
None	2.6	100	
PEG-6000	25.0	100	
18-Crown-6	58.9	83.2	16.8
$Bu_4P^+Br^-$	74.8	69.5	30.5

malonate with 1-bromobutane over a bed of potassium carbonate and phase transfer catalyst [58]. The selectivity to the monoalkylated product depends on the base strength. Monoalkylated malonates are less acidic than malonic esters. Use of PEG-6000 with potassium carbonate gave exclusively the monoalkylated product. 18-Crown-6 and tetrabutylammonium bromide gave both mono- and dialkylated product with potassium carbonate. Apparently, the PEG-6000 system was not sufficiently basic to deprotonate the monoalkylated product, which would explain the lower total conversion as well.

The alkylation of ethylacetoacetate under GL-PTC conditions using potassium carbonate is not as clean as in the case of malonates [61]. Besides carbon–carbon dialkylation, oxygen alkylation and carbon–oxygen dialkylation result. The use of PEG-6000 as the PTC is the most selective to the monoalkylated product, with tetrabutylammonium bromide and 18-crown-6 giving higher conversions but with little selectivity. Results are given in Table 38.

TABLE 38

Alkylation of Ethylacetoacetate with 1-Bromobutane

Catalyst	Conversion (%)	Product distribution			
		C-Alkylation	O-Alkylation	C,C-Dialkylation	C,O-Dialkylation
None	3.0	100.0	—	—	—
PEG-6000	52.0	72.5	25.2	2.3	—
$Bu_4P^+Br^-$	86.1	17.9	30.2	34.4	17.5
18-Crown-6	88.6	37.5	29.4	29.4	11.1

2.4. Polymer-Supported Poly(ethylene Glycol) Catalysts (Triphase Systems)

The PEGs or other phase transfer catalysts can be attached to insoluble polymer supports to facilitate subsequent catalyst recycling and separation. Systems using insoluble-polymer-supported phase transfer catalysts are designated as "triphase" systems. The discussion below provides illustrations of the use of polymer-supported PEGs to catalyze typical organic chemical reactions. When available, a comparison of unanchored PEGs is also provided. The objective of this section is to provide an overview of the synthesis and use of polymer-supported and inorganic-substrate-supported PEG catalysts.

2.4.1. Poly(ethylene Glycol)s Attached to Polystyrene

By far the most widely investigated immobilization technique applied to PEGs is to chloromethylate polystyrene followed by reaction with the sodium alkoxide salt of the desired PEG, as shown in Eq. 25. The polystyrene polymer is also modified by cross-linking with divinyl benzene. The extent and nature of this cross-linking reaction determines the hardness and porosity of the polymer matrix. Polymers of this type are insoluble in most reaction media. This type of polymer substrate is the most common type encountered in common ion exchange beads. Synthesis of these resins is not covered here. The reader should consult the cited references.

$$\text{P} - \text{C}_6\text{H}_4 - CH_2Cl + Na(OCH_2CH_2)_nOR \dashrightarrow \text{P} - \text{C}_6\text{H}_4 - CH_2(OCH_2CH_2)_nOR$$

(25)

2.4.1.1. Williamson Ether Synthesis. The most studied reaction using polystyrene-supported PEGs is the reaction of *n*-butylbromide with phenol to form butylphenyl ether. This was first studied by Regen, who found that 60% yields of butylphenyl ether could be obtained with MPEG-750 grafted onto polystyrene compared to a yield of 5% in its absence [63].

Sherrington and coworkers examined the details of the reaction of *n*-bromobutane with sodium phenoxide to form butylphenyl ether [64, 65]. The supported phase transfer catalyst used for the majority of the work was formed by reacting chloromethylated polystyrenes with the sodium salt of the 3-mole ethylene oxide adduct of methanol, $MeO(CH_2CH_2O)_3Na$. This resulted in a polymer with appended methyl-capped poly(ethylene glycol) groups with a degree of polymerization of three. The focus of the work was on the mechanistic aspects of the reaction.

The solid PTC interacted with solid sodium phenoxide to dissolve the sodium phenoxide in the resin. This could be observed in the absence of butyl bromide. In addition,

- In the absence of water and catalyst, no significant reaction occurred.
- In the presence of an aqueous phase, the desired product was formed in low yield, even with the use of a catalyst, indicating that water was absorbing the sodium phenoxide and preventing the phase transfer catalyst from activating it.
- The rate of reaction was nearly independent of supported-catalyst particle size, cross-link ratio, or support morphology (gel type, macroporous, or macroreticular).
- Yields, rates, and activation energies were equivalent to reactions catalyzed by free $MeO(CH_2CH_2O)_3H$.

In an earlier paper, Sherrington, MacKenzie, and Heffernan reported faster reactions using polymer-bound PEGs than their unsupported analogs [64]. Examples are shown in Table 39. In each system for which a comparison could be made, the higher rates were found with the polymer-supported catalyst. In comparative examples, not shown in Table 39, potassium phenoxide was found to react faster than sodium phenoxide.
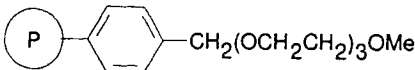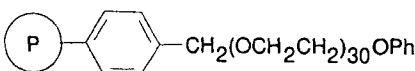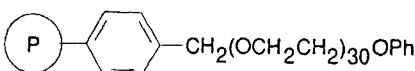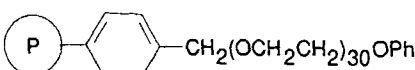
Itsuno and coworkers found that supported MPEGs were faster than PEGs of the same corresponding molecular weights [66]. Results are given in Table 40. For comparison purposes, Itsuno's group used the same number of millimoles of polyether for each experiment. They also observed that the rate using PEG alone was the same as for a mixture of PEG and polystyrene. The work of Itsuno's group was unique in that they synthesized their polymers. While most workers would chloromethylate polystyrene and then react that with the sodium salt of the polyether, Itsuno et al. reacted chloromethylated styrene with the sodium salt of the polyether and polymerized the resulting monomer with styrene.

Additional work was done on a variety of other supported poly(ethylene glycol) adducts [67]. Table 41 gives some examples using different supported ethoxylates. The results in Table 41 suggest that higher degrees of polymerization give higher rates, even though the end groups vary. Despite the different rates of reaction, all of the supported substrates gave good conversions.

By careful selection of the ethoxylate substitution, supported phase transfer catalysts may facilitate the reaction of butyl bromide with sodium phenoxide more effectively than dibenzo-18-crown-6.

In addition to the widely studied alkylation of phenol, Kimura, Kirszensztejn, and Regen used supported MPEG-750 to catalyze the reaction of cyclohexanol and butyl bromide (77% yield) and the reaction of 1-octylalcohol with butyl bromide (79% yield) or allyl bromide (75% yield) [68].
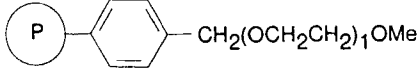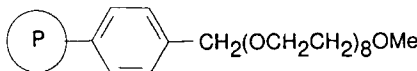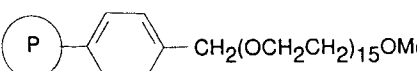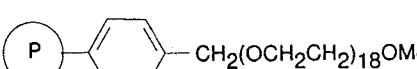
TABLE 39

Rate of 1-Bromobutane Displacement by Phenoxide

Catalyst	Initial rate × 10^5	Polyether (mmole)	Form of phenoxide
None	–	–	Aqueous NaOPh
None	0.26	–	Solid KOPh
$Me(OCH_2CH_2)_3OH$	4.80	0.830	Solid NaOPh
$Ph(OCH_2CH_2)_{30}OH$	0.66	0.039	Aqueous NaOPh
$Ph(OCH_2CH_2)_{30}OH$	16.00	0.039	Solid KOPh
(P)—⟨⟩—$CH_2(OCH_2CH_2)_3OMe$	12.00	0.640	Solid NaOPh
(P)—⟨⟩—$CH_2(OCH_2CH_2)_{30}OPh$	1.20	0.039	Aqueous NaOPh
(P)—⟨⟩—$CH_2(OCH_2CH_2)_{30}OPh$	28.00	0.039	Solid KOPh
(P)—⟨⟩—$CH_2(OCH_2CH_2)_{30}OPh$	40.00	0.039	Solid KOPh

2.4.1.2. Phenylacetonitrile Alkylation. Kimura et al. investigated the use of polymer-supported PEGs in the monoalkylation of phenylacetonitrile with 1-bromobutane [68]. Typical results are given in Table 42. These results show the usual increased effectiveness with higher degrees of ethoxylation. In addition, Kimura's group was able to separate and reuse the catalyst with no decrease in effectiveness. In addition to the alkylation of phenylacetonitrile, they were able to use supported MPEG-750 to alkylate phenylacetonitrile with cyclohexylbromide in 52% yield and to alkylate ethylphenylacetonitrile with bromobutane in 75% yield and with allyl bromide in 76% yield [68].

Ragaini et al. have also investigated polymer-bound phase transfer catalysts in the alkylation of phenylacetonitrile [69]. A wide variety of bound

TABLE 40

Rate of 1-Bromobutane Displacement by Phenoxide,
MPEGs versus PEGs

Catalyst[a]	Relative rate
PEG-1000	2.6
PEG-2000	3.7
PEG-4000	3.1
(P)—C6H4—CH2(OCH2CH2)1OMe	3.2
(P)—C6H4—CH2(OCH2CH2)8OMe	6.4
(P)—C6H4—CH2(OCH2CH2)15OMe	10.8
(P)—C6H4—CH2(OCH2CH2)18OMe	10.8
18-Crown-6	11.5

Note: Reaction conditions consisted of 0.2 mmole 1-bromobutane in toluene, 2.0 mmole KOPh, 1.16 mmole $-CH_2CH_2O-$ functionality, 20 μL water, and 50 μL n-octane. All were heated to 100°C.

[a]Polymer support represented a different polymer in each case. Molecular weights were approximately $1.7-4.8 \times 10^5$.

TABLE 41

Butyl Phenyl Ether Synthesis Using Supported Ethoxylates

(P)—C6H4—CH2(OCH2CH2)nOR
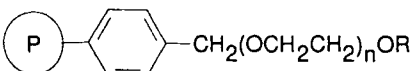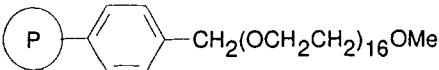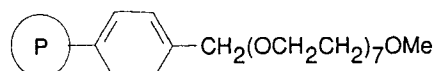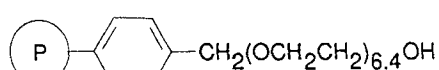
		$10^5 \times$ initial rate	Loss of bromobutane	
R	n	$(1\ mole^{-1}\ sec^{-1})$	Percentage	Time (h)
CH3	3	10.0	93	3
C9H19 to C11H23	9	11.8	98	3
Ph	30	16.0	96	3
2-Methoxyphenyl	4	7.56	96	2
2-Naphthyl	4	9.77	93	2

TABLE 42

Monoalkylation of Phenyacetonitrile with 1-Bromobutane

Catalyst	Conversion (%)	Yield (%)
None	0.3	0.3
(P)—⟨⟩—CH$_2$(OCH$_2$CH$_2$)$_{16}$OMe	96, 94[a], 97[b]	92.0
(P)—⟨⟩—CH$_2$(OCH$_2$CH$_2$)$_7$OMe	71	63.0
(P)—⟨⟩—CH$_2$(OCH$_2$CH$_2$)$_{6.4}$OH	54	52.0

[a]Second use.
[b]Third use.

catalysts was investigated, including two PEGs: PEG-200 and MPEG-200. Reactions were typically run by pumping a benzene solution containing the organic reagents and aqueous sodium hydroxide across a fixed bed of polymer-bound catalyst. A wide variety of reactor configurations and temperatures was used. The authors concluded that PEGs gave somewhat slower rates than quaternary ammonium salts like tributylbenzyl ammonium, or triethylbenzyl ammonium salts. In addition, polymer-bound quaternary ammonium salts were slower than unbound phase transfer catalysts.

2.4.1.3. Sodium Borohydride Reduction of Ketones. Kelly and Sherrington have investigated the use of polymer-bound phase transfer catalysts to catalyze the reduction of ketones with sodium borohydride [70]. In this study, the authors attached chiral end groups to the phase transfer catalysts in hopes of inducing an enantiomeric excess in the products. No such enantiomeric excess was found in any of the reactions. The PEGs in this study were capped with chiral residues. Table 43 gives some results for the reduction of octan-2-one. In this case, the bound PEG catalyst does not work as well as an unbound analogue. The quaternary phosphines, bound or free, are more effective in this system.

Table 44 gives some results for the reduction of acetophenone [70]. In these examples, the polymer-bound PEGs compared favorably, in terms of yield, to unbound triglyme or crown ether. The quaternary phosphines

TABLE 43

Sodium Borohydride Reduction of Octan-2-One
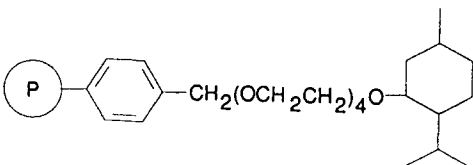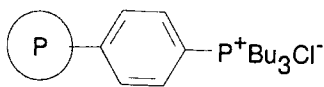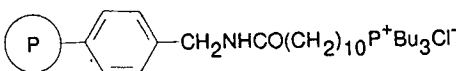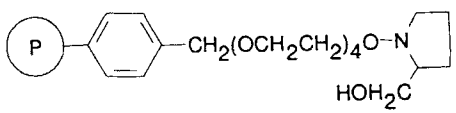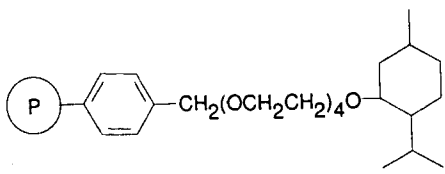
Catalyst	Water (mL)	Time (h)	Yield (%)
None	0.1	7	0
Triglyme	None	7	100
$Bu_4P^+Cl^-$	0.1	3	100
(P)—C₆H₄—$CH_2(OCH_2CH_2)_4O$—menthyl	None	7	42
(P)—C₆H₄—$P^+Bu_3Cl^-$	0.1	7.5	96
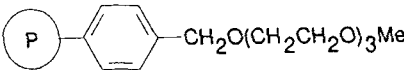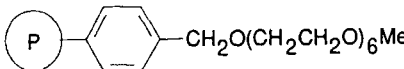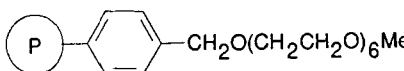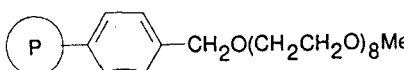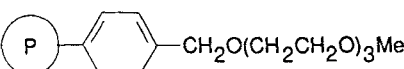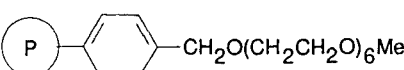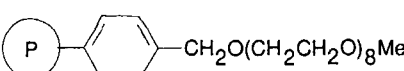
TABLE 44

Sodium Borohydride Reduction of Acetophenone to 1-Phenylethanol

Catalyst	Water (mL)	Time (h)	Yield (%)
None	0.1	24	4
$Bu_4P^+Cl^-$	0.1	2	100
Triglyme	None	6	63
Dibenzo-18-crown-6	None	1	85
(P)—C₆H₄—$CH_2NHCO(CH_2)_{10}P^+Bu_3Cl^-$	0.1	4	94
(P)—C₆H₄—$CH_2(OCH_2CH_2)_4O$–N (prolinol) HOH_2C	None	72	84
(P)—C₆H₄—$CH_2(OCH_2CH_2)_4O$—menthyl	None	24	97

were faster than the comparable PEGs, however, and tended to give higher yields.

2.4.1.4. Preparation of Alkyl Iodides. Poly(styrene)-bound MPEGs can be used to catalyze the halide exchange reaction between alkyl iodides and 1-bromooctane [71]. The powdered metal iodide was suspended in benzene. Some typical reactions are shown in Table 45. These results demonstrate the positive effect, in terms of rate and yield, of increasing the chain length of the bound PEG. Although polymer-bound PEGs allow, in principal, easy separation and reuse of the catalyst, when this was done, the

TABLE 45

Formation of 1-Octyliodide from 1-Octylbromide and Metal Iodides

Catalyst	Metal iodide	Yield (%)	$k_{obs} \times 10^5$ (sec)
None	NaI	3.6	—
18-Crown-6	NaI	90.0	130.00
(P)—⟨phenyl⟩—$CH_2O(CH_2CH_2O)_3Me$	NaI	71.0	2.30
(P)—⟨phenyl⟩—$CH_2O(CH_2CH_2O)_6Me$	NaI	78.0	25.00
(P)—⟨phenyl⟩—$CH_2O(CH_2CH_2O)_6Me$	NaI	73.0	9.00
Reused			
(P)—⟨phenyl⟩—$CH_2O(CH_2CH_2O)_8Me$	NaI	88.0	19.00
None	KI	3.6	—
18-Crown-6	KI	93.0	37.00
(P)—⟨phenyl⟩—$CH_2O(CH_2CH_2O)_3Me$	KI	14.0	0.18
(P)—⟨phenyl⟩—$CH_2O(CH_2CH_2O)_6Me$	KI	83.0	3.20
(P)—⟨phenyl⟩—$CH_2O(CH_2CH_2O)_8Me$	KI	97.0	12.00

reused catalyst, while effective, showed a drop in both yield and rate. None of the bound PEGs could equal the rate of 18-crown-6, although equivalent yields could be obtained.

2.4.1.5. Reactions of Dichlorocarbene. Yanagida, Takahashi, and Okahara used poly(styrene)-bound MPEGs to catalyze the formation and reaction of dichlorocarbene [72]. In these reactions, chloroform was used as the solvent to which the substrate was added. The polymer-bound phase transfer catalyst and sodium hydroxide were suspended in the chloroform. All of the dichlorocarbene reactions were run at room temperature.
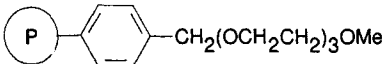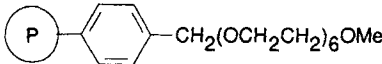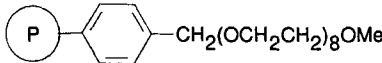
The reactions studied included dichlorocarbene insertion (Eq. 26). Details of the dichlorocarbene insertion reaction can be found in Table 46. These results demonstrate the importance of using poly(ethylene oxide) chains of at least six repeating units.

$$
\text{cyclohexene} + H_2C \underset{Cl}{\overset{Cl}{<}} + \text{NaOH} \longrightarrow \text{bicyclic} \underset{Cl}{\overset{Cl}{<}} \tag{26}
$$

Dichlorocarbene generated under triphase conditions would convert alcohols to the corresponding chloride. This reaction generated significant by-products consisting primarily of formates and ethers. Benzamide could be converted by dichlorocarbene to benzonitrile in near-quantitative yield under similar reaction conditions [72].

2.4.1.6. Nucleophilic Substitutions. Yanagida and coworkers investigated the use of polymer-bound MPEGs in simple nucleophilic substitu-

TABLE 46

Dichlorocarbene Insertion Reaction Catalyzed Under Triphase Conditions

Catalyst	Time (h)	Yield (%)
None	3.5	20–56
(P)—⟨benzene⟩—$CH_2(OCH_2CH_2)_3OMe$	3.5	46
(P)—⟨benzene⟩—$CH_2(OCH_2CH_2)_6OMe$	3.5	100
(P)—⟨benzene⟩—$CH_2(OCH_2CH_2)_8OMe$	3.5	100

tions [71, 73]. A comparison of rate was made for bromide substitution in octyl bromide by iodide, cyanide, and phenoxide. Results are shown in Table 47. These results indicate how system dependent phase transfer results can be. In the case of iodine substitution, polymer-bound MPEG is most effective, while it is least effective for substitution by potassium phenoxide.

2.4.1.7.   Ketone Alkylation.   Kimura and Regen give one example of ketone alkylation using polymer-supported PEGs [74]. In this case, MPEG-750 supported on polystyrene was used. Phenylacetophenone was alkylated in 75% yield with butyl bromide and in 76% yield with allyl bromide.
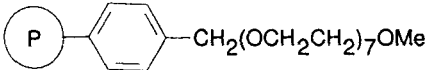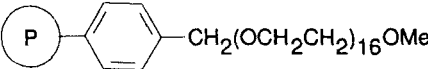
2.4.1.8.   Alkyl Halide Hydrolysis.   Regen and coworkers have studied the hydrolysis of 1-bromoadamantane and *t*-butyl chloride [63, 75]. In the presence of supported MPEG-750, the half life for 1-bromoadamantane hydrolysis was 3.4 hours compared to 84 hours in its absence.

A kinetic study using 14 different PEG- and MPEG-supported catalysts was performed to elucidate the mechanism of this triphase reaction system [75]. One possible mechanism is for the solid supported resin to act as a cosolvent for the aqueous and toluene organic phases, allowing for a high concentration of reactants, compared to the uncatalyzed case, to provide a low-energy pathway.

A second possibility is for the resin to act as a support for small water and toluene droplets, increasing the surface area between the water and toluene, thus increasing the rate of reaction based on increased surface area alone. Regen, Besse, and Mclick concluded that the cosolvent mechanism

TABLE 47

Rate of Reaction of KI, KCN, KOPH with 1-Octylbromide
Using Different Phase Transfer Catalysts

| Catalyst | k_{obs} (sec^{-1}g^{-1}) $\times$ 10^5 | | |
	KI	KCN	KOPh
PEG-2000	15	1	11
Dibenzo-18-crown-6	18	4	14
P—⟨benzene⟩—CH$_2$(OCH$_2$CH$_2$)$_7$OMe	16	1	2
P—⟨benzene⟩—CH$_2$(OCH$_2$CH$_2$)$_{16}$OMe	116	1	1

was the operative one [75]. This was based on the observation that the enthalpy of activation, the entropy of activation, and the overall free energy of activation were lower for the catalyzed case than for the noncatalyzed case. This was true in every instance. If the phase transfer catalyst was only acting to increase the surface area between the two phases, the activation parameters would be the same whether the catalyst was present or not.

In Table 48, a few examples are shown. Besides giving some examples of the thermodynamic measurements determined, the examples demonstrate the rate advantage of using higher molecular weight ethoxylates as the phase transfer catalyst.

2.4.1.9. Dehydrohalogenation. Kimura and Regen also investigated triphase catalysis for the dehydrohalogenation of organic substrates [76]. The degree of polymerization of the grafted PEG had a dramatic effect on rate. As with the PEGs alone, the rate is at a maximum if the degree of polymerization is at least five. This can be seen in Table 49. These results mirror the unbound polyethylene glycols, for which pentaethylene glycol was the preferred catalyst. This was interpreted as being the degree of ethoxylation that formed a crownlike structure, with the five-mole adduct forming the most energetically favorable structure.

A series of organic transformations using bound pentaethylene glycol is given in Table 50. As Table 50 shows, both acetylenes and olefins can be formed in high yield [76].

TABLE 48

Hydrolysis of 1-Bromoadamantane at 90°C
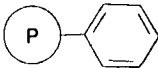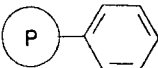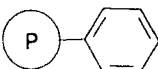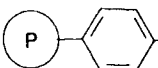
Catalyst	$k_{obs} \times 10^5$, (sec^{-1})	ΔH (kcal/mole)	ΔS (eu)	ΔG (kcal/mole)
None	—	27.9	−10.4	31.8
(P)—⟨benzene⟩—CH$_2$(OCH$_2$CH$_2$)$_1$OMe	1.99	16.6	−35.0	30.0
(P)—⟨benzene⟩—CH$_2$(OCH$_2$CH$_2$)$_2$OMe	1.65	17.8	−31.7	29.7
(P)—⟨benzene⟩—CH$_2$(OCH$_2$CH$_2$)$_3$OMe	2.08	16.8	−34.2	29.6
(P)—⟨benzene⟩—CH$_2$(OCH$_2$CH$_2$)$_{16}$OMe	9.00	16.2	−37.5	30.2

TABLE 49

Rate of Dehydrohalogenation of (2-Bromoethyl)benzene
Under Triphase Conditions
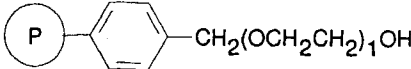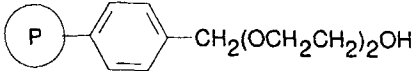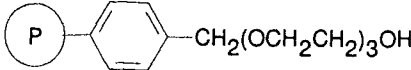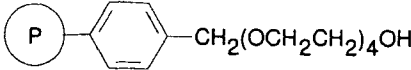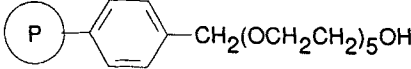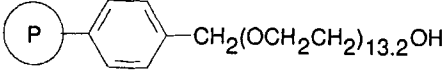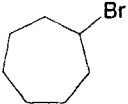
Catalyst	$k_{obs} \times 10^5 \ (\text{sec}^{-1})$
P—⟨benzene⟩—$CH_2(OCH_2CH_2)_1OH$	< 0.01
P—⟨benzene⟩—$CH_2(OCH_2CH_2)_2OH$	1.2
P—⟨benzene⟩—$CH_2(OCH_2CH_2)_3OH$	13.9
P—⟨benzene⟩—$CH_2(OCH_2CH_2)_4OH$	30.0
P—⟨benzene⟩—$CH_2(OCH_2CH_2)_5OH$	35.0
P—⟨benzene⟩—$CH_2(OCH_2CH_2)_{13.2}OH$	9.4

TABLE 50

Dehydrohalogenation Using Polymer-Bound Pentaethylene Glycol

Reactant	Product	Solvent	Yield (%)
$PhCHBrCH_2Br$	$PhC{\equiv}CH$	n-Hexane	96
$CH_3CHBr(CH_2)_5CH_3$	1- and 2-octenes	None	99 $(21/79)^a$
$CH_3(CH_2)_7CHBrCH_2Br$	$CH_3(CH_2)_7C{\equiv}CH$	None	65
$PhCH_2CHBrCH_3$	$PhCH{=}CHCH_3$	n-Hexane	98
$threo\text{-}C_4H_9CHBrCHBrC_4H_9$	$C_4H_9{\equiv}CC_4H_9$	None	95
⟨cycloheptyl-Br⟩	⟨cycloheptene⟩	None	95

^{a}Ratio of 1-octene/cis- + $trans$-2-octene.

2.4.2. Other Polystyrene–Ethylene Oxide Copolymers

The polystyrene–PEG-supported catalysts described thus far have been graft copolymers, with PEG chains grafted onto some of the aromatic rings in the polyether chain. Besides this type of insoluble system, Itsuno et al. have synthesized other types of polymer systems as well [66]. These include block copolymers, block-graft copolymers, and double-comb graft copolymers. All of these polymers were investigated as phase transfer catalysts in the synthesis of phenylbutylether from sodium phenoxide and n-bromobutane.

Because of the number of polymers studied and the difficulty of comparing their specific activities, suffice it to say that those examples that have polystyrene as part of the polymer increase the catalytic activity by as much as a factor of three compared to an equivalent amount of free PEG of the same degree of polymerization. This was explained as being due to increased solubility in the organic phase as a result of the presence of the polystyrene.

2.4.3. Poly(ethylene Glycol)–Glycidylmethacrylate–
Ethylenediaminemethacrylate Copolymers

Hradil and Svec have investigated immobilizing PEGs on copolymers of glycidylmethacrylate and ethylenediaminemethacrylates [77, 78]. The resulting gel-type polymers were active as catalysts for the formation of phenylbutylether from sodium and potassium phenoxide and n-butylbromide. Some results are given in Table 51. These examples demonstrate that the immobilized PEGs are slightly more active than the corresponding unbound PEG. The activity is much higher than when no catalyst is present. Faster rates with higher degrees of ethoxylation are also demonstrated.

TABLE 51

Reaction of Sodium Phenoxide with Butyl Bromide Catalyzed by
PEG–Glycidylmethacrylate–Ethylenediamineacrylate Copolymers

Immobilized PEG	Rate relative to free PEG	Rate relative to no catalyst
PEG-600	1.68	21
PEG-1550	0.56	78
PEG-2000	2.75	168
PEG-4000	1.64	105

2.4.4. Cross-Linked Ethoxylate Glucose

   Gruber and Greber immobilized poly(ethylene glycol)s based on glucose [79]. Glucose was ethoxylated in DMSO. The resulting multihydroxy ethoxylate was treated to convert the hydroxyl end groups to acrylic esters. These esters were then polymerized by addition of a radical initiator. The result was an insoluble gel with polyether chains. These have proved to be active in a variety of reactions typically catalyzed by phase transfer catalysts.

   Although the authors synthesized a variety of ethoxylated sucrose derivatives, the most active proved to require an average degree of ethoxylation of 15 or more. Lower degrees of ethoxylation gave lower rates. The catalysts used to study a reaction generally included PEG-10,000, dibenzo-18-crown-6, ethoxylated sucrose with an average degree of ethoxylation of each hydroxyl of 15 (which is referred to as glucose-ethoxylate), and ethoxylated sucrose with an average degree of ethoxylation of each hydroxyl of 15 and cross-linked as described above (referred to as glucose-ethoxylate gel).

   Table 52 gives the results of a series of displacement reactions carried out under solid–liquid reaction conditions. Yields are those present after 8

TABLE 52

Nucleophilic Displacement Reactions of Benzyl Bromide
Using Glucose-Ethoxylates

Reactant	Product	Catalyst	Yield (% at 8 h)
KOAc	PhCH$_2$OAc	Glucose-ethoxylate	100
		Glucose-ethoxylate gel	100
		PEG-1000	98
		Dibenzo-18-crown-6	100
		None	29
KCN	PhCH$_2$CN	Glucose-ethoxylate	100
		Glucose-ethoxylate gel	61
		PEG-1000	87
		Dibenzo-18-crown-6	100
		None	31
KI	PhCH$_2$I	Glucose-ethoxylate	58
		Glucose-ethoxylate gel	55
		PEG-1000	54
		Dibenzo-18-crown-6	59
		None	13

hours. The same weight of catalyst was present in each case (versus the more common way to make catalysts comparable: an equal number of millimoles of ethyloxy groups). As the results in Table 52 show, the supported catalyst was generally less effective than the equivalent unsupported catalyst. All of the studied reactions proceeded to a considerable extent with no catalyst at all.

Oxidation of alcohols to ketones was studied. Results are given in Table 53. Surprisingly, dibenzo-18-crown-6 was not effective in these transformations, while all of the PEGs were. The immobilized glucose-ethoxylate was as effective as the other ethoxylate catalysts tested.

The immobilized catalysts could be used repeatedly with no loss in activity. The catalysts were separated and reused five consecutive times with no loss of activity. This was shown with acetate and cyanide nucleophilic displacement and with oxidation with permanganate.

3. CONCLUSION

In this review, advances in the understanding of the PEG-catalyzed phase transfer reaction mechanism have been discussed. The overview of recently reported PEG-catalyzed reactions includes organometallic and gas–liquid examples. Finally, an overview of the increasing number of polymer-supported PEGs used to catalyze solid–solid–liquid reactions has been presented. Taken together, these reactions show that PEGs and PEG deriv-

TABLE 53

Oxidation of Alcohols with Potassium Permanganate
Using Glucose-Ethoxylates

Reactant	Product	Catalyst	Yield (% at 8 h)
Cyclohexanol	Cyclohexanone	Glucose-ethoxylate	88
		Glucose-ethoxylate gel	76
		PEG-1000	78
		Dibenzo-18-crown-6	4
		None	2
2-Octanol	2-Octanone	Glucose-ethoxylate	32
		Glucose-ethoxylate gel	46
		PEG-1000	37
		Dibenzo-18-crown-6	8
		None	3

atives continue to be an increasingly viable and often substantially improved alternative to crown ethers as phase transfer reaction catalysts.

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