

CATALYTIC ACTIVITY OF PEG-QUAT PHASE-TRANSFER CATALYSTS IN DEHYDROHALOGENATION REACTIONS

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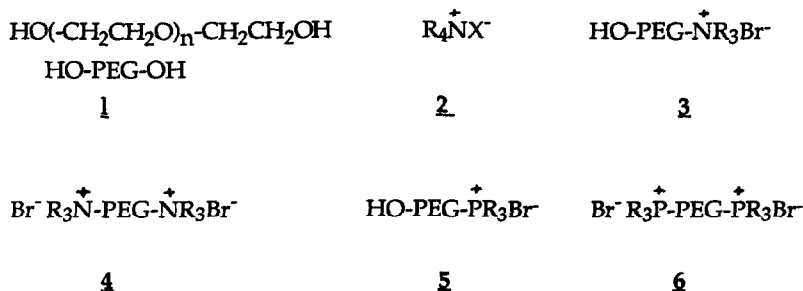
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Abstract. New polyethylene glycol ammonium and phosphonium salts (PEG-quat) phase-transfer catalysts were synthesized and their catalytic activity was studied in a dehydrohalogenation liquid-liquid phase-transfer system. The catalytic activity of the PEG-quat catalyst depended on the nature of the quaternary salt, the most effective compounds being those in which only one hydroxyl group is replaced by the quaternary function.

Recently, much interest has been shown in the use of polyethylene glycols and their derivatives as inexpensive phase-transfer catalysts in a variety of organic reactions.¹⁻⁴ The suitability of these compounds lies in their low cost; availability on an industrial scale; lack of toxicity, antigenicity and immunogenicity; high degree of stability in work reaction systems; and the fact that they attach easily to insoluble solid substrates.

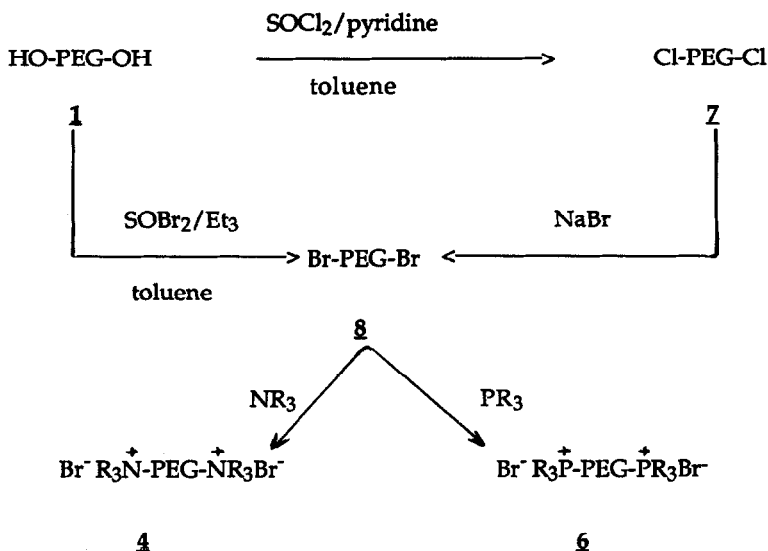
Kimura and Regen⁵ discovered that simple polyethylene glycols $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_n\text{H}$ **1** are highly active and selective in catalyzing dehydrohalogenation in organic/aqueous hydroxide two-phase systems. They suggested that polymeric alkoxides or hydroxides are involved as the active bases. Some examples of polyethylene glycols connected to a quaternary ammonium group have previously been described.⁶⁻⁸ Johansson⁸ used polyethylene glycols with charged end groups in a dextran-polyethylene glycol-water system for the partition of albumin. However, the catalytic activities of such polyethylene glycol derivatives have not yet been examined (although they have been used in separation systems).

In this work we prepared several polyethylene glycol ammonium and phosphonium salts (PEG-quat) **3-6** and studied their activity as phase-transfer catalysts in dehydrohalogenation reactions in a liquid-liquid system in comparison with polyethylene glycol **1** and quaternary salts **2** alone.



RESULTS AND DISCUSSION

A general synthetic route for the preparation of the PEG-quat catalysts is presented in Schemes 1 and 2.

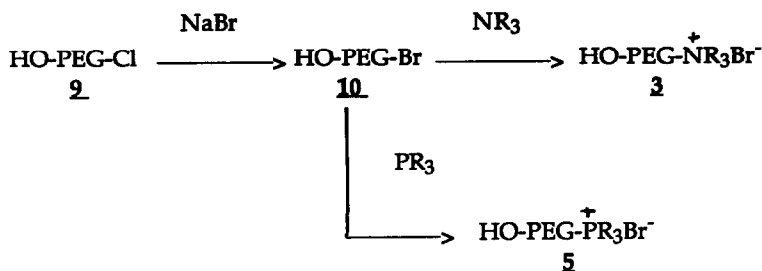


Scheme 1

The dichloroderivative **2** was prepared by chlorinating of polyethylene glycol with thionyl chloride in toluene solution in the presence of pyridine.⁹ The bromo derivative **3** was prepared in a similar way with thionyl bromide and triethylamine. The dibromo derivative **3** could also be obtained by heating the dichloro derivative with sodium bromide in a two-phase reaction for 20 h.

In the second step the polyethylene glycol dibromide **3** was converted to the ammonium derivative **4** by refluxing the dibromo derivative with an excess of trialkyl amine in ethanol for 24 h. The phosphine derivative **6** was prepared by heating the dibromide with tributyl phosphine in an oil bath at 7-0°C for about three days.

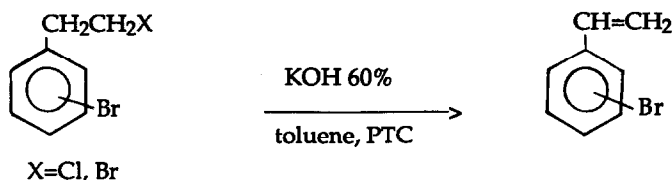
To prepare a bifunctional polyethylene glycol derivative a partially derivatized polyethylene glycol **1** was used as the starting material. This compound was obtained by limiting the amount of thionyl chloride in the chlorination of polyethylene glycol. The bifunctional derivative was then prepared according to Scheme 2.



Scheme 2

The PEG-quat compounds were identified by $^1\text{H-NMR}$ and elemental analysis.

The catalytic activities of PEG-quat, polyethylene glycol and the quaternary salts were studied in the dehydrohalogenation reaction of bromo(2-haloethyl)benzene to bromostyrene in a two-phase liquid-liquid system (Scheme 3).



Scheme 3

Similar reactions have been described by other workers. Halpern et al.¹⁰ described a procedure for the synthesis of 4-bromostyrene from 4-bromo(1-chloroethyl)benzene by dehydrohalogenation with sodium hydroxide and Aliquat 336 as the catalyst. Daren et al.¹¹ and Jackish¹² prepared halogenated styrene by treating the halogenated (β -bromoethyl)benzene with a strong aqueous alkali solution in the presence of a quaternary phase-transfer catalyst and, optionally, an inorganic nitrite salt accelerator and a tertiary alkoxide. They reported that these anions (nitrite or tert-butoxide) had a co-catalytic effect on the elimination of brominated (β -bromoethyl)benzenes to yield bromostyrenes.

We performed our reaction at 50, 65 or 85°C in a thermostated water bath. Samples were removed periodically and analyzed by gas chromatography. Fig. 1 presents the reaction profile of the elimination of hydrogen bromide from bromo(2-bromoethyl)benzene. From the figure we can see that the dehydrohalogenation reaction at 85°C is very fast. With the PEG-quat catalyst **3** (R = Bu) the reaction mixture contained only 10% of the starting material after 2 min, while with the quaternary salt or with polyethylene glycol alone about 75 and 95%, respectively, of the starting material remained after the same time. When the same reaction was performed at 50°C, the best results were obtained with a partially derivatized PEG-quat catalysts (Fig. 2).

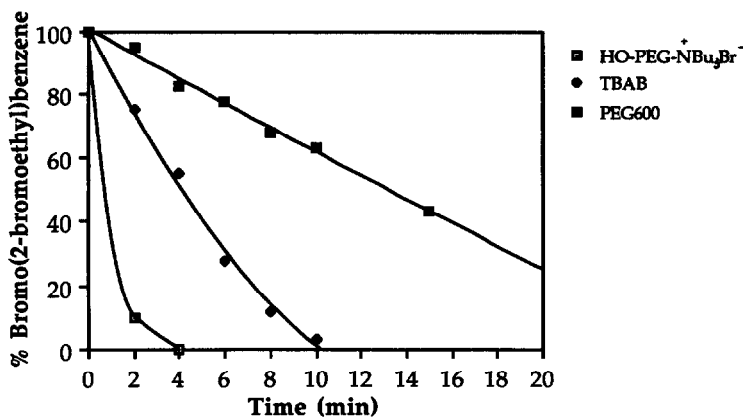


Fig. 1. Dehydrobromination of bromo(2-bromoethyl)benzene in the presence of phase-transfer catalysts at 85°C.

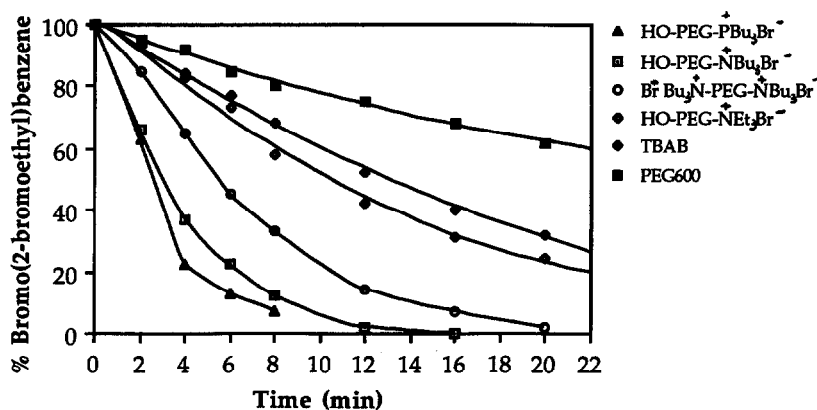


Fig. 2. Dehydrobromination of bromo(2-bromoethyl)benzene in the presence of phase-transfer catalysts at 50°C.

The activity of the PEG-phosphonium catalyst was slightly better than that of the corresponding PEG-ammonium compound. Catalyst **3**, with R = ethyl, exhibited lower catalytic activity than the catalyst with the butyl group and even lower activity than the compound with both hydroxyl groups replaced by the quaternary salt.

The dehydrobromination of dibromo(2-bromoethyl)benzene (Fig. 3) was faster than that of the corresponding monobromine compound (Fig. 2). For the dibromo compound the reaction was complete after 4 min with catalyst **3** (R = Bu), but for the dehydrohalogenation of the monobromine compound under the same reaction conditions 20% of the starting material remained unreacted. The catalytic activity of the different catalysts was the same as before.

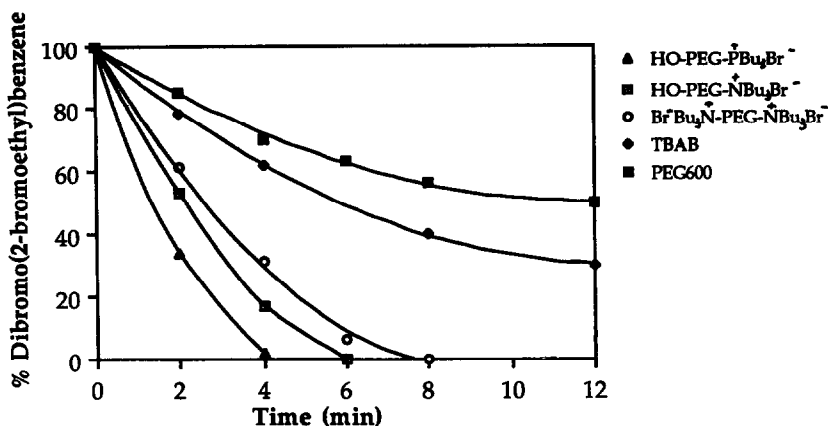


Fig. 3. Dehydrobromination of dibromo(2-bromoethyl)benzene in the presence of phase-transfer catalysts at 50°C.

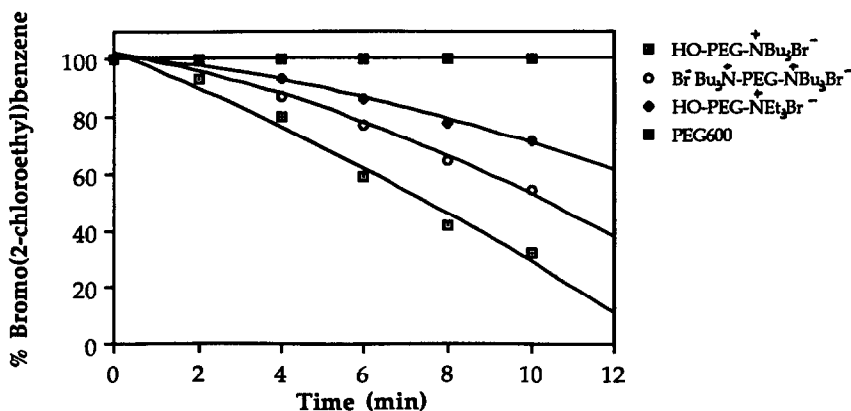


Fig. 4. Dehydrochlorination of bromo(2-chloroethyl)benzene in the presence of phase-transfer catalysts at 65°C.

From Fig. 4 we can see that with catalyst **3** (R = Bu) the dehydrochlorination of bromo(2-chloroethyl)benzene is much slower than the dehydrobromination of the corresponding bromo(2-bromoethyl)benzene. After 10 min at 65°C more than 30% of the bromo(2-chloroethyl)benzene remained, while after 5 min at 50°C only about 15% of the bromo(2-bromoethyl)benzene remained (Fig. 2).

EXPERIMENTAL

Polyethylene glycols (Fluka) were dried by azeotropic distillation with toluene before use. Thionyl chloride, thionyl bromide, tributyl amine, (2-bromoethyl)benzene, and (2-chloroethyl)benzene were obtained from Aldrich, and triethylamine was obtained from BDH.

$^1\text{H-NMR}$ spectra were recorded with a Bruker WP200SY spectrometer, in CDCl_3 solution and chemical shifts are reported in ppm downfield from tetramethyl silane. IR spectra were obtained with a Perkin Elmer 357 spectrometer and GC analysis with a Varian 3300 flame ionization instrument.

Elemental analysis was performed by the Analytical Laboratory of our Institutes.

Polyethylene glycol dichloride, 7

The dichloro polyethylene glycol derivative was prepared in accordance with the procedure of Zalipsky et al.⁹ To a solution of polyethylene glycol 600 (30 g, 0.1 mol OH) and pyridine (7.9 g, 0.1 mol) in 500 ml of toluene, thionyl chloride (16 g, 0.14 mol) was added slowly with stirring over a period of half an hour. The mixture was then refluxed for about 4-5 h. After cooling and filtering off the pyridine hydrochloride, the solvent was removed *in vacuo*. The residue was dissolved in dichloromethane and treated with activated alumina. The process was repeated twice. The dichloromethane solution was filtered and evaporated to dryness. The yield was 25 g (78%) of polyethylene glycol dichloride. $^1\text{H-NMR}$ 3.65(m, $\text{CH}_2\text{-O}$); 3.75(t, CH_2Cl); Calcd for $\text{C}_{26.4}\text{H}_{52.8}\text{O}_{12.2}\text{Cl}_2$: Cl, 11.2; Found: Cl 12.0

Polyethylene glycol dibromide, 8

a. Polyethylene glycol bromide was prepared by a modification of the procedure of Bückmann and Morr.⁶ To a solution of polyethylene glycol 600 (15 g, 0.05 mol OH) and triethylamine (8.2 g, 0.08 mol) in 100 ml of toluene, thionyl bromide (13.4 g, 0.064 mol) was added dropwise with stirring over a period of 1 h. The reaction mixture was refluxed for 1 h, and the hot solution was separated from the triethyl hydrobromide by filtration through a layer of celite. After cooling the solution was treated with active carbon, refluxed for 20 min, and filtered again. The toluene was removed by evaporation *in vacuo*. The crude product was washed with ethanol. A yield of polyethylene glycol dibromide of 15 g (85%) was obtained. $^1\text{H-NMR}$ 3.4 (t, $\text{-CH}_2\text{Br}$), 3.65 (m, CH_2O); Calcd for $\text{C}_{26.4}\text{H}_{52.8}\text{O}_{12.2}\text{Br}_2$: Br, 22.1; Found: Br, 23.0.

b. A mixture of polyethylene glycol dichloride **7** (10 g, 0.015 mol) and sodium bromide (10.3 g, 0.1 mol) was heated in an oil bath at 120°C overnight. After cooling, dichloromethane was added, the solution was filtered, and the solvent was removed *in vacuo* to obtain **8** (9.2 g, 81%). Calcd for $\text{C}_{26.4}\text{H}_{52.8}\text{O}_{12.2}\text{Br}_2$: Br, 22.1%; Found Br, 22.8.

Polyethylene glycol monohalide, 9, 10

Polyethylene glycol monochloride **9** and monobromide **10** were prepared in the same way as the dichloride or dibromide, respectively, by using half of the amount of the thionyl chloride or thionyl bromide. **9** $^1\text{H-NMR}$ 2.90 (s, OH), 3.65 (m, CH_2O), 3.75 (t, CH_2Cl); Calcd for $\text{C}_{26.4}\text{H}_{53.8}\text{O}_{13.2}\text{Cl}$: Cl, 5.7; Found: Cl, 5.9. **10** $^1\text{H-NMR}$ 2.85 (s, OH), 3.48 (t, CH_2Br), 3.7 (m, CH_2O); Calcd for $\text{C}_{26.4}\text{H}_{53.8}\text{O}_{13.2}\text{Br}$: Br, 12.1; Found: Br, 11.6.

Polyethylene glycol di(tributyl ammonium bromide), 4

A solution of polyethylene glycol dibromide **8** (14.4 g, 0.02 mol) and tributylamine (12 g, 0.06 mol) in 50 ml ethanol was refluxed overnight. Active carbon (0.5 g) was added, and refluxing was continued for one additional hour. The active carbon was filtered off, and the solvent was evaporated *in vacuo*. Ether was added to the residue and the product was separated (17.5 g, 81%). ¹H-NMR 0.9 (t, CH₃), 1.43 (m, CH₂-O), 3.0-3.3 (m, CH₂-N), 3.7 (m, CH₂-O); Calcd for C_{50.4}H_{106.8}O_{12.2}N₂Br₂: N, 2.5; Br, 14.6; Found: N, 2.2, Br, 13.8.

Polyethylene glycol di(tributyl phosphonium bromide), 6

A mixture of polyethylene glycol dibromide **8** (2.17 g, 0.003 mol) and tributyl phosphine (0.6 g, 0.003 mol) was heated with stirring at 70°C in an oil bath for 70 h. The residue was washed with petroleum ether 60-80° and the product **6** (2.8 g, 84%) was dried *in vacuo*. ¹H-NMR 0.95 (t, CH₃), 1.5(m, CH₂-C) 2.35-3.0 (m,CH₂-P), 3.75 (m, CH₂O); Calcd for C_{50.4} H_{106.8} O_{12.2} P₂Br₂ : P, 5.5, Br, 14.2; Found P, 5.0; Br, 12.7.

Polyethylene glycol monotributyl phosphonium bromide, 5

¹H-NMR 1.0 (t, CH₃), 1.5 (m, CH₂), 2.35-3.0 (m, CH₂-P, OH); 3.0 S,_{OH}); Calcd for C_{38.4}, H_{80.8}, PO_{13.2} Br: P, 3.6, Br 9.3; Found : P, 3.4, Br, 8.7.

Polyethylene glycol monotributyl ammonium bromide, 3 (R=Bu)

¹H-NMR 0.95 (t, CH₃), 1.5 (m, CH₂-C), 3.0-3.35 (m, CH₂-N, OH), 3.7 (m, CH₂O); Calcd for C_{38.4} H_{80.8} NO_{13.2}Br : N, 1.7 ,Br, 9.6; Found: N, 1.4, Br, 7.9.

Polyethylene glycol monoethylammonium bromide, 3 (R=Et)

¹H-NMR 1.3 (m, CH₃) 3.0-3.8 (m, CH₂-N, OH, CH₂-O); Calcd for C_{32.4} H_{68.8} NO_{13.2} Br: N, 1.8, Br, 10.5; Found N, 1.7 Br, 9.6

Liquid-liquid phase-transfer dehydrohalogenation reaction

Into a 25-ml round-bottomed flask were added 0.005 mol of bromo(2-haloethyl) benzene, 5 ml of toluene, 0.006 mol of the PEQ-quat catalyst and 5 ml of a 60% solution of KOH. The flask was immersed in an oil bath maintained at a constant temperature. The reaction mixture was stirred magnetically for 3 h. Samples were removed periodically and analyzed by gas chromatography. Plots of the concentration of the starting material vs. time are given in Fig. 1-4.

Monobromophenethyl bromide

A solution 5 g of (2-bromoethyl)benzene (0.08 mol) and 1 g of iron in 30 ml of carbon tetrachloride was introduced into a triple-necked round-bottomed flask equipped with a mechanical stirrer, condenser and separatory funnel. A solution of bromine (15.5 g, 0.096 mol) in 10 ml carbon tetrachloride was added dropwise from the separatory funnel over a period of 1 h. After all the bromine had been added, the reaction mixture was heated at 45°C for 2 h.

After cooling the mixture was washed with a saturated solution of sodium bisulfite. After separation the organic phase was washed with a 1:1 HCl solution and then with water and finally dried over $MgSO_4$. The solvent was removed *in vacuo*. The yield of the product was 17 g, (80%); Calcd for $C_8H_8Br_2$: Br, 60.6%; Found: Br, 59.1%.

CONCLUSIONS

In the dehydrohalogenation of the bromophenethyl system, PEG-quat catalysts that contained ether and the ammonium or phosphonium function in the same molecule showed superior catalytic activity to that of either polyethylene glycol or the quaternary salt acting alone. Furthermore, partially derivatized polyethylene glycols that still contain one hydroxyl group, the other having been replaced by the quaternary function, were more effective phase-transfer catalysts than those in which both hydroxyl groups have been replaced by the quaternary salt. It was also shown that the catalytic activity of the PEG-quat catalyst in the dehydrohalogenation reaction studied depended on the nature of the quaternary salt.

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