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SYNTHESIS AND CATALYTIC ACTIVITY OF A NOVEL CROWN-QUAT PHASE TRANSFER CATALYST

Bronislaw P. Czech, Michael J. Pugia and Richard A. Bartsch*

Department of Chemistry, Texas Tech University, Lubbock, Texas 79409, U.S.A.

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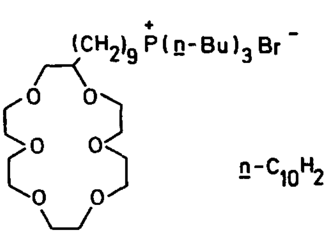
Abstract - A novel, crown-quat phase transfer catalyst has been synthesized and its catalytic activity examined in solid-liquid and liquid-liquid phase transfer systems.

INTRODUCTION

The effectiveness of quaternary onium salts and crown ethers as phase transfer catalysts has been established for more than a decade. The literature data show that crown ethers are very efficient catalysts in solid-liquid two-phase reactions[1] while ammonium and phosphonium salts are better catalysts in liquid-liquid two-phase systems.[2] Although examples of crown ethers connected via a hydrocarbon spacer chain to a quaternary ammonium group are known,[3,4] their catalytic acitivities have not been examined. Therefore the potential for synergistic interactions of crown and quat centers within a single catalyst molecule remains unknown.

In this paper, we report the syntheses of the novel crown-phosphonium quat **1** and the comparison of its catalytic activity with those of model phosphonium salt **2** and crown ether **3** in both solid-liquid and liquid-liquid phase transfer reactions.



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$n\text{-}C_{10}H_{21}\overset{+}{P}(n\text{-}Bu)_3Br^-$

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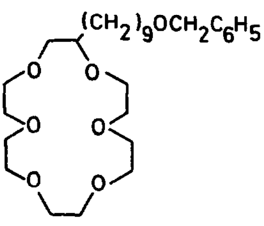

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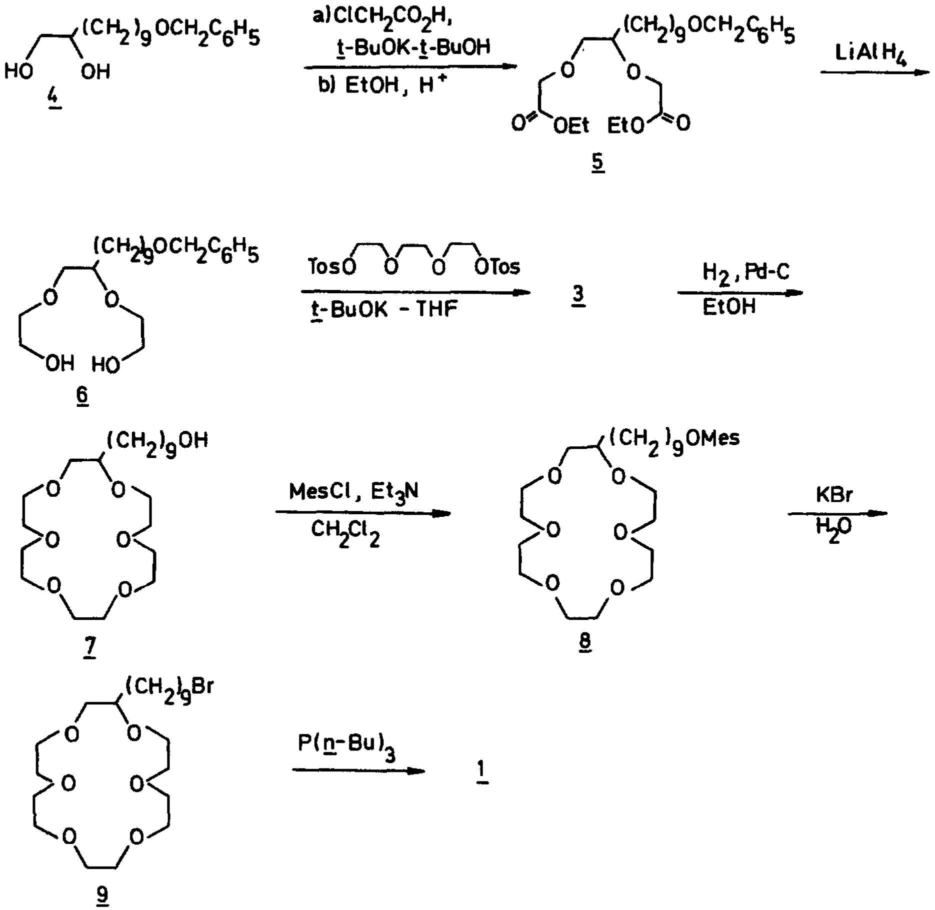
RESULTS AND DISCUSSION

Synthesis of 1-3. The synthetic routes to catalysts **1** and **3** are outlined in Scheme 1. Diol **4** was treated with t-BuOK and chloroacetic acid. The crude diacid was directly esterified to produce diester **5** in 58% yield. Reduction of **5** with $LiAlH_4$ gave diol **6** in 90% yield. Cyclization of **6** with triethylene glycol ditosylate in the presence of t-BuOK in THF afforded a 52% yield of the benzyl-protected crown ether **3**. This synthetic route to **3** provides a better yield than a reported method.[5] Hydrogenolysis of **3** afforded crown alcohol **7** in almost quantitative yield. The two subsequent steps which included mesylation of crown alcohol **7** to produce crown mesylate **8** followed by autocatalytic phase transfer conversion of **8** into the crown bromide **9** proceeded in high yields of 98 and 82%, respectively. The crown-quat bromide **1** was obtained in 60% yield by heating equimolar amounts of **9** and tributylphosphine.



Scheme 1

The model phosphonium bromide 2 was prepared in 52% yield by heating equimolar amounts of 1-bromodecane and tributylphosphine.

The structures of all new compounds were verified by IR and ^{1}H NMR spectra and by elemental analysis.

Solid-Liquid Phase Transfer Catalysis. The catalytic activities of crown-quat **1**, phosphonium salt **2**, and crown ether **3** were evaluated in the reaction of 1-chlorobutane in acetonitrile with solid KCN. A mixture of the catalyst (0.10 equiv) and KCN (2 equiv) in acetonitrile was stirred and heated at 50°C. After 0.5 h, stirring was terminated and a concentrated solution of 1-chlorobutane and heptane (internal standard) in acetonitrile was added. Samples were removed periodically and analyzed by gas chromatography. Plots for a second order reaction were satisfactorily linear and the second order rate constants are presented in Table 1. Under the same conditions but in the absence of catalyst, there was little or no conversion of 1-chlorobutane into 1-cyanobutane.

The results for quat **2** and crown ether **3** are in agreement with the observations of others that in solid-liquid two-phase systems crown ethers are often more effective catalysts than quats.[6] This has been attributed to a greater efficacy of crown ethers in disrupting the crystal lattice of the solid salt.

Crown-quat **1** is noted to be a more effective phase transfer catalyst than either quat **2** or crown ether **3**. However, a mixture of **2** and **3** which would have the same number of polyether and quat sites as in **1** exhibits essentially the same catalytic efficiency as **1**. Thus the presence of both crown ether and quat sites in a single catalyst molecule is found to produce only an additive effect with no positive synergism.

Table 1. Second Order Rate Constants for Reaction of 1-Chlorobutane with KCN in Acetonitrile at 50.0°C

Catalyst	Catalyst Concentration (mol %)	Second Order Rate Constant[a] (X 10^4, mol $L^{-1}s^{-1}$)
quat **2**	10	2.7
crown ether **3**	10	4.2
crown-quat **1**	10	7.2
quat **2** + crown ether **3**	10 + 10	6.8

[a] Second order rate constant for conversion of 1-chlorobutane into 1-cyanobutane. Observed reproduciability was ±5%.

Liquid-Liquid Phase Transfer Catalysis. The catalytic activities of **1**, **2**, and **3** were also determined in a liquid-liquid, two-phase system. The classical system of 1-bromooctane in toluene and concentrated aqueous KCN[7] was utilized at 90°C. Thus into a rapidly-stirred (1000 rpm) mixture of toluene and 7.5 M aqueous KCN was added the catalyst (0.10 equiv) and dodecane (internal standard). After 3 hours, the 1-bromooctane was added and then samples were periodically removed and analyzed by gas chromatography. Pseudo first-order plots were satisfactorily linear and the pseudo first-order rate constants are given in Table 2.

In this liquid-liquid, two-phase system, quat **2** is a much more efficient catalyst than crown ether **3**. This difference may result at least partially from a lower lipophilicity of the crown ether.[8] A mixture of **2** and **3** exhibits essentially the same activity as does **2** alone. This reveals that the crown ether **3** does not interfere with the action of quat **2**. The somewhat lower activity of crown-quat **1** compared with quat **2** probably results from the higher lipophilicity of **2** which decreases distribution of the catalyst into the aqueous phase.

Table 2. Pseudo First-Order Rate Constants for Reaction of 1-Bromooctane in Toluene with Aqueous KCN at 90.0°C

Catalyst	Catalyst Concentration (mol %)	Pseudo First Order Rate Constant[a] (X 10^6, s^{-1})
quat **2**	10	1030
crown ether **3**	10	7.2
crown-quat **1**	10	380
quat **2** + crown ether **3**	10 + 10	990

[a] Pseudo first-order rate constant for disappearance of 1-bromooctane. Observed reproduciability was ±5%.

Cloud Point Determination. To provide additional information concerning the behavior of crown-quat **1**, cloud point measurements have been conducted. Okahara has determined cloud points for 1% aqueous solutions of crown ethers with long lipophilic tails.[9] For such crown ethers, the cloud points initially increased when inorganic salt was added. Thus metal ion complexation by the crown ether enhanced its water solubility and caused a "salting-in" effect. Further salt additions diminished the cloud point (water solubility) of the lipophilic crowns ethers. However, even at high salt concentrations, the cloud points (water solubility) still exceeded that observed in the absence of salt.

Cloud point determinations for quat **2**, crown ether **3**, and crown-quat **1** were conducted in the absence and presence of added KBr. The results are presented in Figure 1. Although the addition of KBr causes only salting-out of quat **2**, salting-in of both crown quat **1** and crown ether **3** is noted with maxima at approximately 1 M aqueous KBr. In agreement with the results of Okahara,[9] the cloud point (water solubility) of crown ether **3** remains higher in even the most concentrated salt solution (5 M) than in pure water. On the other hand, the salting-in effect for crown quat **1** is less pronounced and above 4 M salt the cloud point (water solubility) for **1** becomes less than that in water. The cloud point measurements verify the rationalization that the ordering of catalytic activity in the liquid-liquid phase transfer reactions of **2** > **1** > **3** corresponds to the catalyst lipophilicity.

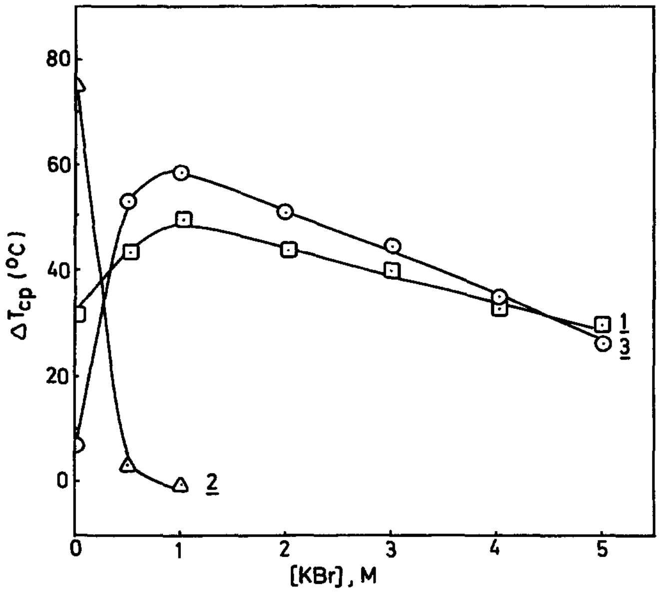


Figure 1. Cloud Points for 1% Aqueous Solutions of 1-3

CONCLUSION

For the novel phase transfer catalyst **1** which contains both crown ether and phosphonium ion functions in a common molecule, the centers act independently without positive synergism.

EXPERIMENTAL

IR spectra were obtained on neat samples (unless specified otherwise) with a Nicolet MX-S spectrometer and are reported in reciprocal centimeters. ^{1}H NMR spectra were recorded with a Varian EM 360 spectrometer in deuteriochloroform and chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane. Elemental analysis was performed by Galbraith Laboratories, Inc. of Knoxville, Tennessee.

Unless specified otherwise reagent grade reactants and solvents were obtained from chemical suppliers and used as received. THF was purified by distillation from $LiAlH_4$. *t*-BuOH was distilled from sodium metal prior to use. Acetonitrile was dried over molecular sieves (5Å). Compounds 11-(benzyloxy)-1,2-undecanediol[5] (**4**) and triethylene glycol ditosylate[10] were prepared according to published procedures.

Diethyl 3,6-Dioxa-4-[(9-benzyloxy)nonyl]-1,8-octanedicarboxylate (**5**). A solution of chloroacetic acid (23.6 g, 0.25 mol) in 80 ml of *t*-BuOH was added slowly to a stirred and refluxing mixture of diol **4** (29.4 g, 0.10 mol) and *t*-BuOK (56.1 g, 0.50 mol) in *t*-BuOH (400 ml) under nitrogen. After completion of the addition, stirring and refluxing were continued overnight. Following removal of the solvent by distillation under reduced pressure, the residue was dissolved in H_2O (100 ml), acidified with 6 N HCl, and extracted with a 1:1 (v/v) mixture of Et_2O and C_6H_6 (3 X 100 ml). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo to give the crude diacid which was dissolved in 400 ml of a 1:2 (v/v) mixture of absolute EtOH and C_6H_6 and 2.0 g of *p*-toluenesulfonic acid was added. The mixture was refluxed overnight with continuous circulation of the condensing vapors through a Soxhlet thimble which contained anhydrous Na_2SO_4. The solvent was removed in vacuo and a solution of the residue in Et_2O was washed with aqueous $NaHCO_3$ and then with H_2O. After drying ($MgSO_4$), the ethereal solution of the residue was passed through a 10 cm layer of alumina with Et_2O as eluent. Final purification by vacuum distillation produced 27.0 g (58%) of diester **5** as a colorless viscous oil, bp 232-235/7μ. IR 1755, 1736 (C=O), 1128 (C-O); ^{1}H NMR 0.9-1.8 (m,22H), 3.25-3.7 (m,5H), 3.9-4.55 (m,10H), 7.2 (s,5H). Calcd for $C_{26}H_{42}O_7$: C, 66.93; H, 9.07. Found: C, 66.93; H, 9.18%.

3,6-Dioxa-4-[(9-benzyloxy)nonyl]-1,8-octanediol (**6**). The diester **5** (22.8 g, 51.0 mmol) and 5.0 g (130 mmol) of $LiAlH_4$ were refluxed in 155 ml of THF for 2 h. The reaction mixture was cooled in a ice bath while the following additions were made slowly and consecutively: 30 ml of H_2O-THF (1:5, v/v); 5 ml of 15% aqueous NaOH, and 50 ml of H_2O-THF (1:1, v/v). The precipitated inorganic material was filtered and washed with hot THF. The combined filtrate and washings were evaporated under vacuum and the residue was vacuum distilled to give 17.6 g (90%) of a hygroscopic, colorless oil, bp. 218-220°C/7µ. IR 3420 (O-H), 1116, 1101 (C-O); ^1H NMR 1.3-1.8 (m,16H), 3.3-3.9 (m,15H), 4.48 (s,2H), 7.30 (s,5H). Calcd for $C_{22}H_{38}O_5 \cdot 0.25\ H_2O$: C, 68.27; H, 10.03. Found: C, 68.46; H, 10.14%.

2-[9-(Benzyloxy)nonyl]-18-crown-6 (**3**). A solution of diol **6** (9.56 g, 25.0 mmol) and t-BuOK (6.17 g, 55.0 mmol) in 240 ml of THF was stirred at room temperature under nitrogen for 1 h. To this solution, 12.6 g (27.5 mmol) of triethylene glycol ditosylate in 90 ml of THF was added and the mixture was stirred at room temperature for 24 h and refluxed for another 24 h. The solvent was removed in vacuo and H_2O (100 ml) was added. The mixture was neutralized with 6 N HCl and extracted with CH_2Cl_2 (3 X 20 ml). After drying ($MgSO_4$) and evaporation under vacuum, the residue was purified by chromatography on alumina with 30-60°C pet. ether - AcOEt (2:1) as eluent to yield 6.5 g (52%) of crown ether **3**.

2-(9-Hydroxynonyl)-18-crown-6 (**7**). The benzyl-protected crown ether **3** (5.84 g, 11.8 mmol) was dissolved in 100 ml of EtOH and 0.60 g of 10% Pd-C was added. Hydrogenolysis was conducted for 24 h at room temperature under 45 psi pressure of hydrogen. The catalyst was filtered and the solvent was removed in vacuo to afford 4.65 (97%) of pure **7**.

Methanesulfonate of 2-(9-Hydroxynonyl)-18-crown-6 (**8**). A solution of **7** (4.65 g, 11.4 mmol) and triethylamine (1.84 g, 18.2 mmol) in CH_2Cl_2 (50 ml) was cooled to -10°C, and a solution of methanesulfonyl chloride (1.58 g, 13.8 mmol) in 25 ml of CH_2Cl_2 was added dropwise. After stirring at 0°C for 1 h, the reaction mixture was poured over ice, extracted with cold CH_2Cl_2 (2 X 20 ml). The organic extracts were washed with cold 5% HCl, H_2O, 5% aqueous $NaHCO_3$, and H_2O again. Drying ($MgSO_4$) and evaporation of the solvent under vacuum afforded 5.40 g (98%) of a colorless oil. IR 1352, 1172 (SO_2), 1116 (C-O); ^1H NMR 0.9-2.0 (m,16H), 3.02 (s,3H), 3.15-4.4 (m,25H). Calcd for $C_{22}H_{44}O_9S$: C, 54.52; H, 9.15. Found: C, 54.41; H, 9.13%.

2-(9-Bromononyl)-18-crown-6 (**9**). Methanesulfonate **8** (5.17 g, 10.7 mmol), KBr (3.2 g, 27.0 mmol) and 3 ml of H_2O were combined and the mixture was heated at 100°C for 2 h. Water (20 ml) and CH_2Cl_2 (20 ml) were added and the organic layer was separated, washed with H_2O (10 ml), saturated aqueous $NaHCO_3$ and then H_2O again. The crude product obtained after drying ($MgSO_4$) and evaporation of the solvent under vacuum was purified by chromatography on alumina with 30-60°C pet. ether - AcOEt (2:1) as eluent to afford 4.10 g (82%) of a colorless oil. IR 1122 (C-O); ^1H NMR 1.1-2.1 (m,16H), 3.2-3.9 (m,25 H). Calcd for $C_{21}H_{41}BrO_6$: C, 53.73; H, 8.80. Found: C, 53.77; H, 8.76%.

Crown-Quat Bromide 1. Bromide **9** (0.94 g, 2.0 mmol) and tributylphosphine (0.405 g, 2.0 mmol) were combined and heated with stirring at 65°C for 3 days in a stoppered flask. The resulting thick colorless oil was washed with n-hexane to yield 0.81 g (60%) of 3 as a colorless, hygroscopic oil. ^1H NMR 0.8-2.1 (m,37H), 2.2-2.8 (m,8H), 3.4-3.9 (m,23H). Calcd for $C_{33}H_{68}BrO_6P \cdot H_2O$: C, 57.46; H, 10.23. Found: C, 57.68; H, 9.96%.

n-Decyl-tri-n-butylphosphonium Bromide (**2**). 1-Bromodecane (11.9 g, 50.0 mol) and tri-n-butyl phosphine (10.6 g, 50 mmol) were heated together in a stoppered flask at 85°C for 3 days. The crude product was washed with n-hexane to provide a pale yellow, hygroscopic oil (11.0 g, 52%). ^1H NMR 1.10 (t,12H), 1.2-1.8 (m,28H) 2.35-2.7 (m,8H). Calcd for $C_{22}H_{48}BrP \cdot H_2O$: C, 59.93; H, 11.20. Found: C, 59.84; H, 11.41%.

Solid-Liquid Phase Transfer Reaction Kinetics. A solution of the catalyst (1.06 mmol) in acetonitrile (25.0 ml) was poured over powdered, dry KCN (2.12 mmol) in a 50 ml screw-cap glass culture tube. The tube was placed in a 50.0 ± 0.1°C constant temperature bath and mechanically stirred at 600 rpm for 0.5 h. Stirring was terminated and at zero time a solution of 1-chlorobutane (10.6 mmol) and n-heptane (10.6 mmol, internal standard) in acetonitrile (5.0 ml) was added. The resulting solution was 0.0353 M in catalyst, 0.353 M in 1-chlorobutane, and 0.353 M in n-heptane. A sample which was removed within a few seconds of mixing and analyzed by gas chromatography showed no 1-cyanobutane formation. Samples were removed at 5.0 min intervals and the disappearance of 1-chlorobutane was monitored relative to the internal standard until no further reaction was apparent. A plot of $\ln b_o/a_o[(a_o-x_n)/(b_o-x_n)]$ vs. time (where x_n is the difference between the concentration of 1-chlorobutane at t_o and t_n, a_o is the initial concentration of 1-chlorobutane, and b_o, the initial concentration of cyanide, is taken to be x_n for the completed reaction)[11] gave a straight line which covered at least two half lives of the reaction. The slope was calculated with a least squares program (r = 0.98 or greater) and k_2 was evaluated from the relationship of slope = $k_2(a_o - b_o)$.

Liquid-Liquid Phase Transfer Reaction Kinetics. Into a 50 ml screw-cap glass culture tube were placed 5.0 ml of HPLC grade toluene, 5.0 ml of 7.5 M aqueous KCN, 0.30 mmol of catalyst, and 0.30 mmol of dodecane (internal standard). The tube was placed in a 90.0 ± 0.1°C constant temperature bath and the contents were stirred mechanically at 1000 rpm for 3.0 h to condition the catalyst. At zero time, 1-bromooctane (3.0 mmol) was added to the stirred mixture. Periodically samples were removed and analyzed by gas chromatography. A plot of log ($[\text{substrate}]_t/[\text{substrate}]_{init}$) vs. time was linear (r = 0.98 or greater) for three-half lives. The pseudo first-order rate constant was calculated from the line slope.

Cloud Point Determination. Into a stirred water bath were placed a precision thermometer and a test tube which contained a 1% solution of the compound. The reversible critical point at which the solution became turbid upon heating or clear upon cooling was determined 5 or more times and had a reproducibility of ± 0.6°C.

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