$$\text{abundance of } m/z \text{ 106} = 0.90(\text{product from } \mathbf{4}) \quad (6)$$

$$\text{abundance of } m/z \text{ 110} = \text{product from } \mathbf{6} + 0.10(\text{product from } \mathbf{5}) \quad (7)$$

$$\text{abundance of } m/z \text{ 111} = 0.90(\text{product from } \mathbf{5}) \quad (8)$$

run 1 of expt 1, using eq 5–8 and the corrected relative abundances of 100.00, 19.50, 2.36, and 11.64, respectively, for the *m/z* 105, 106, 110, and 111 peaks, the relative amounts of products from **3–6** are calculated to be 97.83, 21.67, 12.93, and 1.07, respectively. On normalization of these results on a percentage basis, the distribution of products from **3–6** would become 73.3%, 16.2%, 9.7%, and 0.8%, respectively. In an analogous way, another set of distribution of products from **3–6** was calculated to be 83.4%, 8.6%, 6.3%, and 1.6% for the same run from the isotopomeric $(C_6H_5)_2CH^+$ ions at *m/z* 167, 168, 172, and 173.

Degradation Products. The 1,2,2-triphenylethanone was reduced with $LiAlH_4$ to give 1,2,2-triphenylethanol (**11**) which in turn was oxidized with $KMnO_4$ to give benzophenone (**12**). The procedures used have been described previously.[2]

Alcohol 11 showed ^{13}C NMR absorptions at δ (acetone-d_6) 60.8 (C-2), 76.9 (C-1), 126.8, 127.6, 127.9, 128.4, 128.8, 129.6, 130.0 (arom), 143.5, 143.9, and 145.2 (quat arom). The ^{13}C enrichments at C-1 and C-2, and hence the extents of scrambling from C-2 to C-1, were measured by using a relative intensity ratio method with a suitable absorption containing ^{13}C in its natural abundance as an internal reference standard.[11] The method utilized in calculating the extents of scrambling was the same as that described in the determination of the extents of scrambling during solvolyses of trianisyl[2-^{13}C]vinyl bromide (**2-Br-**2-^{13}C).[11b] In the work with **2-Br-**2-^{13}C,[11b] the internal reference standard was the CH_3O absorption, while in the present work, the most intense aromatic absorption at 128.8 ppm was used as the internal standard. The results obtained on the extents of scrambling of the ^{13}C label from C-2 to C-1 are given in Table III.

The CI spectra of the various samples of benzophenone (**12**) from the solvolysis experiments were obtained with 0.3 torr of NH_3 as the reagent gas. A GC/MS instrument was employed, each sample being passed through the gas chromatograph before the CI spectrum was obtained using a VG-16F mass spectrometer supplied by VG Micromass Ltd. Given in Table II are the CI spectral data in the $[M + NH_4]^+$ region for the isotopomeric benzophenones derived from the various solvolyses of 1-Br-2-^{13}C-2-Ph-d_5, the $[M + NH_4]^+$ ions for $(C_6H_5)_2CO$, $(C_6H_5)_2{}^{13}CO$, $C_6H_5(C_6D_5)CO$, and $C_6H_5(C_6D_5){}^{13}CO$ appearing at *m/z* 200, 201, 205, and 206, respectively.

As an illustration of the calculations, consider the data for run 1 of expt 1 in Table II. Since M + 1 at *m/z* 207 is 13.46% of the abundance of the *m/z* 206 peak, after the 13.46% M + 1 corrections are made, the corrected relative abundance for the peaks at *m/z* 200, 201, 205, and 206, respectively, are 10.55%, 2.29%, 22.82%, and 96.91%.

Analogous to the formulation of eq 1–4, eq 9–12 can be written

$$\mathbf{3} \rightarrow 90\%\ \mathbf{7} + 10\%\ \mathbf{7'} \rightarrow 90\%\ m/z\ 206,\ 10\%\ m/z\ 205 \quad (9)$$

$$\mathbf{4} \rightarrow 90\%\ \mathbf{8} + 10\%\ \mathbf{8'} \rightarrow 100\%\ m/z\ 205 \quad (10)$$

$$\mathbf{5} \rightarrow 90\%\ \mathbf{9} + 10\%\ \mathbf{9'} \rightarrow 100\%\ m/z\ 200 \quad (11)$$

$$\mathbf{6} \rightarrow 90\%\ \mathbf{10} + 10\%\ \mathbf{10'} \rightarrow 90\%\ m/z\ 201,\ 10\%\ m/z\ 200 \quad (12)$$

as shown. From eq 9–12, the sources of the *m/z* 200, 201, 205, and 206 peaks are given by eq 13–16.

$$\text{abundance of } m/z \text{ 200} = \text{Product from } \mathbf{5} + 0.10(\text{product from } \mathbf{6}) \quad (13)$$

$$\text{abundance of } m/z \text{ 201} = 0.90(\text{product from } \mathbf{6}) \quad (14)$$

$$\text{abundance of } m/z \text{ 205} = \text{Product from } \mathbf{4} + 0.10(\text{product from } \mathbf{3}) \quad (15)$$

$$\text{abundance of } m/z \text{ 206} = 0.90(\text{product from } \mathbf{3}) \quad (16)$$

For run 1 of expt 1 in Table II, using eq 13–16 and the corrected relative abundance of 10.55%, 2.29%, 22.82%, and 96.91%, respectively, for the *m/z* 200, 201, 205, and 206 peaks, the relative amounts of products from **3–6** are calculated to be 107.68, 12.05, 10.30, and 2.54, respectively. After normalizing these results on a percentage basis, the distribution of products from **3–6**, respectively, would become 81.2%, 9.1%, 7.8%, and 1.9%, as given in Table III.

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Registry No. 1-Br-2-^{13}C-2-Ph-d_5, 84752-76-1; **3**, 84752-77-2; **4**, 84752-78-3; **5**, 84752-79-4; **6**, 84752-80-7; **7**, 84752-81-8; **7′**, 84752-82-9; **8**, 84752-83-0; **8′**, 84752-82-9; **9**, 84752-84-1; **9′**, 84752-85-2; **10**, 84752-86-3; **10′**, 84752-85-2.

Mechanisms of Polymer-Supported Catalysis. 4. Alkylation of Phenylacetonitrile with 1-Bromobutane Catalyzed by Aqueous Sodium Hydroxide and Polystyrene-Bound Benzyltrimethylammonium Ions

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The rates of reaction of phenylacetonitrile with excess 1-bromobutane catalyzed by excess 50% aqueous sodium hydroxide and insoluble polystyrene-bound benzyltrimethylammonium ions at 80 °C depend upon several experimental variables. The rates (1) were up to 8 times faster when the phenylacetonitrile was added before the 1-bromobutane to the catalyst than when the opposite order of addition was employed, (2) increased as the stirring speed was increased up to a constant rate at ≥500 rpm with a conventional mechanical stirrer in a round-bottomed flask, (3) increased as the catalyst particle size was decreased from 250 to 50 μm in diameter at a 500-rpm stirring rate, (4) decreased markedly when polymer cross-linking was increased from 2% to 10%, and (5) were 3 times faster with the 50% ring-substituted, 2% cross-linked benzyltrimethylammonium ion catalyst than with the corresponding 17% ring-substituted catalyst. Commercial macroporous anion-exchange resins had activities comparable with the 2% cross-linked catalysts prepared in this investigation. The kinetic results are discussed in terms of mass transfer and intraparticle diffusional limitation of the rates. The 2% cross-linked polymer-bound catalysts were as selective for monobutylation of phenylacetonitrile as the best commercial anion-exchange resins or soluble phase-transfer catalysts reported earlier.

Insoluble, polymer-supported, phase-transfer catalysts can be separated easily from reaction mixtures by filtration and can be reused.[2] The activities often are lower than the activities of soluble phase-transfer catalysts, because the overall reaction rates are limited by mass transfer of reactants from bulk liquid to the catalyst surface and by intraparticle diffusion to the active site as well as by the intrinsic reactivity at the active site within the cross-linked polymer matrix.[3] The effects of mixing methods, catalyst particle size, degree of polymer cross-linking, and active site structure on the triphase reactions of alkyl halides with aqueous sodium cyanide indicate that intraparticle diffusion is a rate-limiting factor in all but a few of the slowest such reactions, and mass transfer also limits the rates unless rapid stirring is employed.[3]

We now report mass-transfer and intraparticle diffusional effects in another of the most common phase-transfer-catalyzed reactions, the alkylation of phenylacetonitrile (eq 1). Soluble phase-transfer catalysts for

$$\mathrm{PhCH_2CN + RX \xrightarrow[PTC]{50\%\ NaOH} PhCHRCN} \tag{1}$$

alkylation of active nitriles with concentrated aqueous sodium hydroxide as the base were first reported by Jarrouse[4] and have been investigated in great detail by Makosza.[5] Whereas most phase-transfer-catalyzed nucleophilic displacement reactions are thought to proceed by rate-limiting displacement in the organic phase,[6] the alkylation of active nitriles is thought to proceed by rate-limiting generation of the carbanion from the nitrile and hydroxide ion at the aqueous/organic interface.[7-9] Commercial quaternary ammonium ion anion-exchange resins[10] and soluble quaternized poly(vinylpyridines)[11] have been reported as catalysts for alkylation of phenylacetonitrile, but no study of the rate-limiting steps in these polymer-catalyzed alkylations is available. We chose insoluble, polystyrene-bound benzyltrimethylammonium and benzylquinuclidinium ions as catalysts because their ease of preparation allows study of a wide variety of particle sizes, degrees of cross-linking, and degrees of ring substitution in a reasonable time. Polystyrene-bound quaternary benzylphosphonium ions were not prepared because of their known rapid decomposition by attack of hydroxide ion.[12]

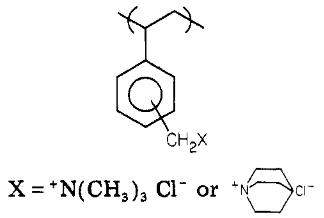
Results

Catalyst Preparation. Copolymers of styrene and 25%, 50%, and 75% (chloromethyl)styrenes (60/40 meta/para) by weight, cross-linked with 2–10% divinylbenzene by weight, were converted to quaternary ammonium salts with trimethylamine and quinuclidine. The catalysts had quaternary ammonium ions substituted on 15–18%, 27–34%, and 37–52% of the polymer aromatic rings.

Table I. Effects of Mixing Methods on Rate Constants[a]

method		10^5k, s^{-1} mequiv^{-1}	method	10^5k, s^{-1} mequiv^{-1}
stirring:	500 rpm	64.8	ultrasonic	0.0
	600 rpm	70.5	no polymer	0.0
	700 rpm	69.4	polystyrene beads[b]	0.0
vibromixer		68.0		

[a] All experiments used 0.6 g of a 60/100 mesh, 15% ring-substituted benzyltrimethylammonium ion catalyst (1.25 mequiv of Cl^-/g) at 80.0 °C with 500-rpm mechanical stirring and the inverse addition unless noted otherwise. [b] 0.6 g of 2% cross-linked, 60/100 mesh polystyrene beads used in place of a catalyst.



Kinetic Methods. Kinetic studies of the reaction of phenylacetonitrile with 1-bromobutane catalyzed by 50% aqueous sodium hydroxide and the polymer-bound quaternary ammonium ions were carried out with mechanical stirring in 100-mL, three-necked, round-bottomed flasks. The catalyst was conditioned in all but one component of the reaction mixture for 60 min at 80 °C before the kinetic run was started. In the direct addition method, the phenylacetonitrile was added at time zero. In the reverse addition method the aqueous phase and the catalyst were stirred for 50 min at 80 °C, phenylacetonitrile was added, and after another 10 min the 1-bromobutane at 80 °C was added at time zero. By both methods the molar quantities of reagents used were as follows: phenylacetonitrile, 16.6 mmol; 1 bromobutane, 233 mmol; sodium hydroxide, 860 mmol; quaternary salt, 0.125–0.9 mmol. The alkylation rates were much faster by the reverse addition method than by the direct addition method. Both methods gave pseudo-first-order kinetics. The rate constants were directly proportional to the amount of the polymer-bound catalyst. Control experiments (a) in which no polymer was used and (b) in which an unsubstituted, 2% cross-linked polystyrene was used in place of the quat salt gave no reaction.

Stirring Speed. By both addition methods the rate of reaction catalyzed by polymer-bound benzyltrimethylammonium ion depended on the speed of mechanical stirring, reaching a maximum at 500–700 rpm (see Table I and the figure in ref 13). To determine if optimum mixing was attained, we performed experiments by the faster reverse addition method with a vibromixer and with an ultrasonic mixer. The vibromixer gave the same result as conventional mechanical stirring at 500–700 rpm. The ultrasonic mixer gave no reaction at all (see Table I). The dependence of reaction rates on stirring rates indicates that the reaction rates are limited in part by mass transfer at <500 rpm and are not limited by mass transfer at ≥500 rpm. All subsequent experiments were carried out at 500 rpm to remove mass transfer as a factor limiting the reaction rates.

Swelling of Catalysts. We attribute the faster reaction rates by the reverse addition method to greater swelling

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(1) On leave 1980–1981 from Department of Physical Chemistry, University of Madras, India.

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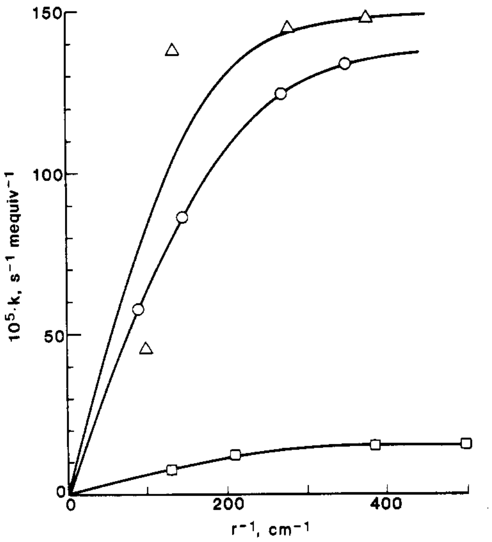

Figure 1. Effect of particle size of 2% cross-linked benzyltrimethylammonium ion catalysts on rate constant at 80.0 °C: ○, 17–18% ring-substituted catalysts by reverse addition method with 500-rpm stirring; △, 27–34% ring-substituted catalysts by reverse addition method with 500-rpm stirring; □, 17–18% ring-substituted catalysts by direct addition method with 440-rpm stirring.

Table II. Effect of the Percent Cross-Linking on Catalyst Activity[a]

% cross-linker	mequiv of Cl$^-$/g	av diameter, μm	10^5k, s^{-1} mequiv^{-1}
2	1.40	223	57.8
4	1.26	194	24.0
6	1.30	224	7.8
10	1.34	196	1.92

[a] All experiments used 0.6 g of 60/100-mesh, 16–17% ring-substituted benzyltrimethylammonium chloride catalyst at 80 °C with the reverse addition method and 500-rpm stirring.

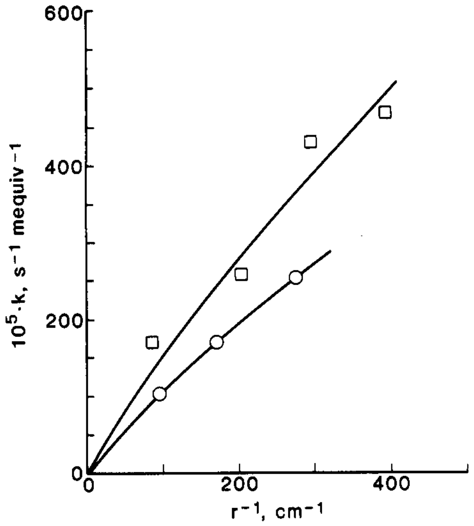

Figure 2. Effect of particle size on rate constant at 80.0 °C by the inverse addition method using the following: ○, 0.1 g of benzylquinuclidinium ion (18% ring-substituted, 2% cross-linked catalyst); □, benzyltrimethylammonium ion (50% ring-substituted, 2% cross-linked catalyst).

Table III. Comparison of 2% Cross-Linked Benzyltrimethylammonium Ion Catalysts with Commercial Macroporous Ion-Exchange Resin Catalysts[a]

catalyst	% ring subst	10^5k, s^{-1} mequiv^{-1}	mesh size[b]	av particle diameter, μm[c]
2% cross-linked	16	57.8	60/100	223
2% cross-linked	50	171	60/100	229
Amberlyst A-27[d]	40	82.2	20/40	466
Amberlyst A-27[d]	40	105	40/60	411
Amberlyst A-26[d]	90	49.5	20/40	502

[a] All experiments were performed by the reverse addition method at 80.0 °C with 500-rpm stirring. [b] Of dry particles. [c] Of particles recovered from reaction mixture. [d] Rohm and Haas Co.

of the polymeric catalyst. At 80 °C a 2% cross-linked, 17% ring-substituted benzyltrimethylammonium chloride catalyst swelled to 3.0 times its dry volume in phenylacetonitrile in 5 min. In an otherwise identical experiment using 1-bromobutane, the catalyst swelled slowly to 1.4 times its dry volume over 12 h.[13] The greater affinity of phenylacetonitrile than of 1-bromobutane for the catalysts also is shown by the organic contents of 17% and 50% ring-substituted catalysts recovered from reverse addition reaction mixtures after partial alkylation. Both catalysts contained 75 mol % of phenylacetonitrile, 20 mol % of monobutyl product, and 5 mol % of 1-bromobutane, even though the starting reaction mixture contained 93 mol % of 1-bromobutane and 7 mol % of phenylacetonitrile. Since the reverse addition method gave a rate constant 8 times that of the direct addition method at a 500–700-rpm stirring rate with a 60/100-mesh, 2% cross-linked, 17% ring-substituted catalyst, reverse addition was used in all other experiments.

Catalyst Particle Size and Cross-Linking. Rates of triphase reactions which are limited by intraparticle diffusion depend on the catalyst particle size.[3] Figures 1 and 2 show typical data for 2% cross-linked, 17–18%, 27–34%, and 50% ring-substituted benzyltrimethylammonium and 18% ring-substituted benzylquinuclidinium catalysts. Since diffusion is slower in more highly cross-linked polymer gels, presumably the rates of alkylation using more highly cross-linked catalysts also would depend upon particle size. Rate constants in Table II show that 4%, 6%, and 10% cross-linking of the 16–18 ring-substituted benzyltrimethylammonium ion catalysts markedly slowed the rate of phenylacetonitrile alkylation.

Since commercial benzyltrimethylammonium anion-exchange resins were known to catalyze phenylacetonitrile alkylation,[10] two Amberlyst resins were tested (Table III). Their activities were about the same as the activities of the 2% cross-linked catalysts, although they are macroporous, more highly cross-linked, and of larger particle size.

Catalyst Recycling. For commercial applications polymer-bound catalysts usually will need to be recycled to be economically viable. Data for catalyst recovery and reuse experiments are in Table IV. In attempts to make accurate kinetic comparisons of the recovered catalysts with the fresh catalysts, recovered catalysts were dried at 60 °C under vacuum overnight (expts A, C, and D). The recovered catalysts had a pink color that disappeared upon washing and drying. The activities were much lower in the second and third cycles. Conversion of the catalyst back to its original chloride form before drying (expt A) gave a material equal in activity to the starting catalyst on a molar equivalent basis, but the recovered catalyst had lost 18% of its ion-exchange sites. Thus the catalysts lost

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Table IV. Activities of Recovered Catalysts[a]

expt	catalyst[b]	10^5k, mequiv^{-1}, s^{-1} [c]	k_n/k_1 (wt basis)[d]
A	2% DVB, 60/100 m, 16% RS (1.25 mequiv/g)	62.6	
	recovered, dried in OH$^-$ form at 60 °C	52.2	0.70
	recovered, converted to Cl$^-$ form (1.05 mequiv/g), dried at 60 °C	60.8	0.82
B	2% DVB, 100/200 m, 18% RS (1.43 mequiv/g)	86.0	
	recovered, air-dried in OH$^-$ form at 25 °C	*e*	0.88
C	2% DVB, 100/200 m, 50% RS (2.99 mequiv/g)	133	
	recovered, dried in OH$^-$ form at 60 °C, 2.88 mequiv/g in Cl$^-$ form	25.1	0.18
	recovered again, dried in OH$^-$ form at 60 °C	*e*	0.026
D	2% DVB, 60/100 m, 17% RS, quinuclidinium Cl (1.31 mequiv/g)	65.8	
	recovered, dried in OH$^-$ form at 25 °C	*e*	0.37

[a] All experiments were performed by the reverse addition method with 500-rpm stirring at 80 °C and with 0.1–0.3 g of catalyst. [b] Benzyltrimethylammonium chloride unless noted otherwise; DVB = divinylbenzene cross-linker; m = mesh; RS = ring substitution. [c] Pseudo-first-order rate constant/mequiv of catalyst used. [d] Ratio of rate constant with recovered catalyst to rate constant with fresh catalyst on a weight basis. [e] Ion-exchange capacity of recovered catalyst was not determined.

Table V. Activities of Polymer-Bound Benzylquinuclidinium Ion Catalysts[a]

% cross-linked	stirring speed, rpm	10^5k, s^{-1} mequiv^{-1}
2	500	105
2	600	103
2	700	110
10	500	4.3

[a] Catalysts were 60/100 mesh and 17% ring substituted. Rates were measured at 80 °C by the reverse addition method.

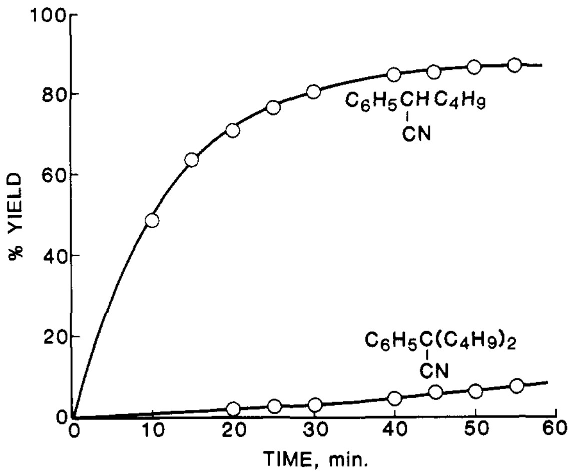

Figure 3. Percent yield of monobutyl- and dibutylphenylacetonitrile as a function of reaction time with 5.0 mol % of a 100/200-mesh, 2% cross-linked, 18% ring-substituted benzyltrimethylammonium ion catalyst with 500-rpm stirring at 80 °C by the direct addition method.

Table VI. Temperature Dependence of Rate and Swelling Ratio[a]

temp, °C	10^5k, s^{-1} mequiv^{-1}	swelling ratio[b]
60.0	22.0	2.4
70.0	71.4	2.8
80.0	133.5	3.0

[a] Catalyst was 2% cross-linked, 17% ring-substituted benzyltrimethylammonium ion, 325/400 mesh. Rates were measured by the reverse addition method with 500-rpm stirring. [b] Swollen volume in phenylacetonitrile divided by dry volume.

active sites both during the alkylation of phenylacetonitrile in the presence of 50% sodium hydroxide at 80 °C and during drying in the hydroxide form at 60 °C. Activity was not lost during drying in the chloride form at 60 °C. When the catalyst was not dried thoroughly, but only collected on a fritted filter at room temperature before recycling, 88% of the original activity on a weight basis was retained (expt B).

Benzylquinuclidinium Ion Catalysts. To test the activity of catalytic sites with a larger ionic radius than benzyltrimethylammonium ion, the corresponding quinuclidinium ion was chosen because of its resistance to base-catalyzed β-elimination reactions. The quinuclidinium catalysts were more active. (Compare data in Table V with that in Table I.) The effect of particle size of the quinuclidinium catalyst is shown in Figure 2. The 10% cross-linked quinuclidinium catalyst was much less active than the 2% cross-linked one.

Catalyst Selectivity. An important question concerning the utility of any phase-transfer catalyst for phenylacetonitrile alkylation is its selectivity for monoalkylation over dialkylation. Figure 3 reports product composition vs. time with a 2% cross-linked, 18% ring-substituted benzyltrimethylammonium ion catalyst. The yield of monobutyl product reached a maximum of 87%. Dibutyl product was limited to 3% of the reaction mixture in the presence of 80% monobutyl product and 17% of starting material. Similar results were obtained with the analogous quinuclidinium catalyst.

Temperature Effects. Rates were measured at 60, 70, and 80 °C, using both 2% cross-linked, 325/400-mesh, and 10% cross-linked, 60/100-mesh, 17% ring-substituted benzyltrimethylammonium ion catalysts. Data for the former are in Table VI. Three-data-point Arrhenius activation energies with the two catalysts were 21.5 and 19.1 kcal/mol. The swelling ratio of the 2% cross-linked catalyst was temperature dependent also (Table VI).

Discussion

Kinetics of Triphase Catalysis. Since polystyrene particles functionalized with quaternary ammonium ions were needed to achieve any measurable alkylation of phenylacetonitrile under triphase conditions at 80 °C and since the rate constants were proportional to the weight of added catalyst, the rate-limiting step of the reaction must take place at the ionic sites within or on the surface of the polymer. Under the pseudo-first-order kinetic conditions used, the rate law was

$$v = k[\mathrm{PhCH_2CN}][\mathrm{catalyst}]$$

Since the concentrations of sodium hydroxide and 1-bromobutane were not varied, we cannot tell if they were involved in the rate-limiting step(s) of the reaction. With commercial ion-exchange-resin catalysts, Dou[10] found much higher yields of alkylation of phenylacetonitrile using a 600% excess of 50% sodium hydroxide than using a 10%

excess of 10% sodium hydroxide. In conventional phase-transfer-catalyzed ethylation of phenylacetonitrile with tetra-*n*-butylammonium bromide, Chiellini[9] found a formal rate dependence of $[\mathrm{NaOH}]^{5.3}$, which was attributed to much higher activity of hydroxide ion in a 19 M solution than in an 11 M solution.

The times and temperatures required for alkylation of phenylacetonitrile with polymer-bound benzyltrimethylammonium ion catalysts are approximately the same as those with soluble quaternary onium ion catalysts.[10] In contrast to their lesser activities in nucleophilic displacement reactions, the alkyltrimethylammonium ions are effective phase-transfer catalysts for phenylacetonitrile alkylation as long as the alkyl group contains at least six carbon atoms.[9b]

Rates of triphase reactions catalyzed by polymer-supported onium ions may be limited by (1) mass transfer of one or more of the reactants to the surface of the catalyst particle, (2) diffusion of one or more of the reactants to the active sites within the gel polymer matrix, and (3) intrinsic reactivity at the active site.[3,14,15] (Steps involving transport of products out of the polymer to bulk solution could also be involved but are omitted here to simplify the discussion.)

Equations 2 and 3 show a simple mechanism for butylation of phenylacetonitrile.

$$\mathrm{PhCH_2CN + OH^-} \xrightarrow{\text{catalyst}} \mathrm{Ph^-CHCN + H_2O} \quad (2)$$

$$\mathrm{Ph^-CHCN + C_4H_9Br \rightarrow PhCH(C_4H_9)CN + Br^-} \quad (3)$$

Since the reactions of carbanions with 1-bromobutane (such as eq 3) are usually very fast, it is likely that formation of the carbanion (eq 2) is rate limiting whenever mass transfer or intraparticle diffusion does not retard the reaction rate further.

The dependence of reaction rates on stirring speeds in the figure of ref 13 shows that with a <500-rpm conventional stirring rate mass transfer is one factor limiting the rate of butylation of phenylacetonitrile.[13] The nearly identical rate constants with 500–700-rpm stirring in Table I suggest, but do not prove, that mass transfer limitations were overcome at ≥500 rpm. Vibromixing gave much finer dispersions of organic liquid in water[3] but virtually the same reaction rate as 500-rpm stirring. Ultrasonic mixing emulsified the triphase mixtures but gave no reaction at all (for which we have no good explanation).

When mass transfer is rate limiting, reaction rates are directly proportional to catalyst surface area and inversely proportional to the radius of spherical catalyst particles.[14,15] If reactants must be transported into the catalyst particle for reaction to occur, the rate depends upon some combination of the intrinsic reaction rate at an active site and the intraparticle diffusivity of the reactant. At the limit of strict intrinsic reactivity control (fast diffusion), the reaction rate does not depend upon particle size. At the limit of slow intraparticle diffusion, the rate constant approaches a limiting dependence of $(\text{particle radius})^{-1}$. The reaction rates in Figures 2 and 3 depend greatly on particle size for the larger sizes (>200 μm diameter) but less with smaller sizes (~50 μm diameter), using the faster reverse addition method. Intraparticle diffusion of one or more of the reactants or products must limit the reaction rates. The large rate differences between the direct and the reverse addition methods also indicate a large intraparticle diffusional limitation to the rates in the direct addition experiments, in which the catalysts swelled much less than in the reverse addition experiments. Diffusivities of small molecules and ions in polymer gels decrease as the fraction of mobile phase decreases. Catalyst swelling and catalyst activity also correlate well for the triphase reactions of 1-bromooctane with aqueous sodium cyanide[3] and with aqueous potassium iodide.[16] Still another indicator of the role of intraparticle diffusion is the dependence of reaction rates on the percent divinylbenzene cross-linking of the catalyst shown in Table II. The greater the degree of cross-linking of the polymer gel, the less it swells and the slower small molecules diffuse through the gel.

Figures 2 and 3 indicate that the activities of the 2% cross-linked catalysts increase as the percent of ring substitution increases from 16–18% to 27–34% to 50% (corresponding with 25%, 50%, and 75% (chloromethyl)styrenes in the original copolymers). These results are opposite many previous observations of the effect of the percent ring substitution in triphase nucleophilic displacement reactions such as the reaction between 1-bromooctane and aqueous sodium cyanide, in which catalyst activity is extremely low at ≥40% ring substitution.[17] The higher activities of the more substituted polymers suggest that transport of hydroxide ion to the active sites may be the limiting intraparticle diffusional process. The greater the number of ionic functional groups in the polymer, the more it swells in water and the faster ion transport should be. Increasing the number of ionic functional groups, however, decreases the swelling in organic liquids such as phenylacetonitrile and 1-bromobutane. Higher concentrations of ionic sites may reduce the diffusivity of organic molecules in the gel. Of course, variation of the environment within the gel may also alter the intrinsic reactivity of hydroxide ion with phenylacetonitrile.

The commercial Amberlyst catalysts in Table III are active for butylation of phenylacetonitrile, in spite of their large particle sizes. The data in Figures 2 and 3 suggest that the Amberlyst catalysts would be as active as our 50% ring substituted, 2% cross-linked catalyst if they were available as 200-μm particles. The Amberlyst catalysts are macroporous, whereas ours are only microporous. A macroporous polystyrene contains permanent pores, even when dry, due to precipitation of polymer from a nonpolymerizable solvent within each droplet during suspension polymerization.[18] Its structure contains permanent pores in addition to the micropores of the gel copolymer matrix. Under catalytic conditions both the micropores and the macropores are filled with liquid phase(s). Macroporous Amberlyst A-26 and A-27 have internal surface areas of 18.4 and 46.9 $\mathrm{m^2/g}$ and pore radius ranges of 140–220 and 210–1200 Å.[19] The large surface areas ensure that the mean distance of an active site from the surface of the macropores is much less than the mean distance of an active site from the surface of the strictly microporous polymer particles. Since the total surface areas of the macroporous catalysts are 100–1000 times greater than

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(14) For general discussions of kinetic processes in heterogeneous catalysis see: (a) Satterfield, C. N. "Mass Transfer in Heterogeneous Catalysis"; MIT Press: Cambridge, MA, 1970. (b) Thomas, J. M.; Thomas, W. J. "Introduction to the Principles of Heterogeneous Catalysis"; Academic Press: New York, 1967; Chapter 4.

(15) For discussion of the kinetics of catalysis by ion-exchange resins see: Helfferich, F. "Ion Exchange"; McGraw-Hill: New York, 1962; Chapter 11.

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those of the microporous catalysts, the active sites in the former are located much nearer the surface.

Why are the high surface area Amberlyst catalysts not even more active catalysts for butylation of phenylacetonitrile? Two other factors may limit their activities: (1) Diffusion of hydroxide ion, phenylacetonitrile, or 1-bromobutane through the macropores may be slow. (2) The macroporous catalysts are more highly cross-linked than the 2% cross-linked gel particles. To the extent that reactant diffusion through the gel phase is still necessary to reach an active site, the reaction rate may be limited by transport through a more highly cross-linked polymer. The exact levels of cross-linking of the Amberlyst catalysts are unknown. Their divinylbenzene contents are proprietary, and they are cross-linked further by intrapolymer Friedel–Crafts alkylation during chloromethylation of the cross-linked polystyrene.[20] The high activities of the Amberlyst catalysts for butylation of phenylacetonitrile contrast sharply with their total inactivity in attempted triphase reactions of 1-bromooctane with aqueous sodium cyanide.[21]

The temperature dependences of the rates of butylation of phenylacetonitrile in triphase mixtures (E_a = 21.5 and 19.1 kcal/mol) are abnormally high for reactions that are strongly limited by diffusion of reactants within a gel ion-exchange resin. Typical Arrhenius energies for ion exchange are 5–10 kcal/mol.[15] Arrhenius energies for triphase reactions of 1-bromooctane with aqueous sodium cyanide[3] and with aqueous potassium iodide[16] are 11–14 and 11–20 kcal/mol. However, the swelling data in Table VI indicate that the temperature dependence of the diffusional component in the observed kinetics should be unusually high because of increased swelling of the polymer with increased temperature (see Table VI).

Synthetic Applications. The preceding mechanistic explanation of polymer-supported phase-transfer catalysis will help in the design and selection of catalysts for future applications. Ultimately the utility of the catalysts depends on their selectivity and on recycling. Data in Table IV show reduced activity of each recovered catalyst, although the loss of activity can be minimized by not heating or drying the recovered catalyst. Active sites likely decompose by attack of hydroxide ion on the methyl carbon atoms of the benzyltrimethylammonium ions to produce methanol and polymer-bound benzyldimethylamine or on the benzyl carbon atom to produce trimethylamine and polymer-bound benzyl alcohol.[8] Nonbenzylic tetraalkylammonium ions are more stable than benzyltrimethylammonium ion.[22] Tetraalkylammonium ions separated from the polymer aromatic ring by spacer chains of three or more carbon atoms would be better candidates for recycling.

Selectivity for monoalkylation of phenylacetonitrile by phase-transfer catalysis depends upon the structure of the quaternary ammonium ion and the structure of the polymeric support. With Dowex anion-exchange-resin catalysts Dou[10] typically obtained product mixtures containing 60–70% monobutyl and 3–7% dibutyl product. The best result was 84% monobutyl and 6% dibutyl products with an approximately 70% ring-substituted, nominally 8% cross-linked resin (Dowex 1-X8). The best case of conventional biphase catalysis with benzyltriethylammonium chloride gave 84–90% monobutyl and 5% dibutyl derivatives of phenylacetonitrile.[10] Our Figure 3 shows as high a selectivity as any previously reported alkylation using aqueous alkali.[9b,23]

Experimental Section

Equipment. The temperature of the oil both used for kinetic experiments was controlled (±0.2 °C) by using a Therm-O-Watch (I^2R Corp.). Reaction mixtures were stirred by a mechanical stirrer (Con-Torque stirrer, Eberbach Co.) for speeds up to 700 rpm, a vibromixer (Model E-1, Chempec, Inc.), or a 21-KHz ultrasonic mixer (Blackstone Ultrasonics Inc., Sheffield, PA, Model SS-2A).

Gas chromatographic analyses were performed on a Hewlett-Packard Model 5840A thermal-conductivity instrument with a 6 ft × 0.125 in. column of 20% SE-30 on 80–100-mesh Gas Chrom Q at 170 °C.

Chemicals. Reagents and solvents were used without purification unless noted: phenylacetonitrile (Eastman Kodak), 1-bromobutane (Eastman Kodak), quinuclidine (Aldrich), *n*-pentadecane (Alfa). A single lot of 50% w/w sodium hydroxide (Fischer Scientific Co.) was used for all kinetic experiments. The conventional ion-exchange resins, Amberlyst A-26 and A-27, were from Rohm and Haas. Authentic samples of α-butylphenylacetonitrile and α,α-dibutylphenylacetonitrile were prepared by a known method.[10]

Polymers. Cross-linked polystyrenes containing 25%, 50%, and 75% by weight (chloromethyl)styrenes (60/40 meta/para, from Dow Chemical Co.) and the specified weight percent of divinylbenzene (from 55% active technical grade, Polysciences Inc.) were prepared as described elsewhere.[3,24]

Catalysts. Polymer-bound benzyltrimethylammonium chloride was prepared from the copolymers as described earlier.[3] Quaternization yields as mequiv of Cl^-/g of dry catalyst were determined by Volhard titration[3] to be 82–95% from 25% (chloromethyl)styrene copolymers, 67–84% from 50% (chloromethyl)styrene copolymers, and 72–74% from 75% (chloromethyl)styrene copolymers.

Polymer-Bound Benzylquinuclidinium Chloride. A 5.00-g sample of copolymer (16.4 mmol) was swelled in 150 mL of 1,2-dichloropropane in a three-necked flask fitted with a condenser, thermometer, and nitrogen inlet. Nitrogen was passed for 30 min, and 6.50 (58.5 mmol) of quinuclidine was quickly weighed and transferred to the reaction flask. The mixture was refluxed under nitrogen at 95 °C for 12 h. The catalyst was filtered, washed with dichloromethane, technical methanol, acetone, and anhydrous methanol and dried in vacuum at 60 °C. Quaternization yields were 93–94% with both the 2% and the 10% cross-linked copolymers.

All catalysts were sieved through 20, 40, 60, 100, 200, 325, or 400 U.S. standard mesh sieves in dry form and dried at 60 °C in vacuo before use.

Kinetics of Phenylacetonitrile Alkylation. (A) Direct Addition Method. In a typical run a 100 mL three-necked flask was charged with 0.1–0.6 g of the catalyst, 45.0 mL of 50% w/w NaOH (19.086 M), ~2 mL (1.52–1.53 g) of *n*-pentadecane (internal standard for GC), and 25 mL of 1-bromobutane. The mixture was placed in a thermostat at 80 ± 0.2 °C and stirred mechanically at 100 rpm with a standard 45 × 18 mm curved Teflon blade for 60 min to condition the catalyst. The stirring speed, which was measured by using a tachometer (James G. Biddle Co., Plymouth Meeting, PA) or a strobe light, was increased, an accurately weighed 2-mL portion of phenylacetonitrile was added at zero time, and 0.1-mL samples of the organic phase were analyzed periodically by GLC. GLC analysis of the starting phenylacetonitrile and 1-bromobutane showed no detectable impurities. Stirring was stopped 10–15 s each time for sampling. Every GLC analysis was done twice and average values were used in calculations. Each run consisted of 5 samples taken over periods ranging from 10 min to 150 min. Conversions of phenylacetonitrile to the monobutyl product in the last sample were 11–85% with

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2% cross-linked catalysts and 5–60% with more highly cross-linked catalysts, depending on catalyst activity, particle size, stirring rate, and reaction time.

A plot of ln $a^*/(a^* - x)$ vs. time was made, and the pseudo-first-order rate constants were evaluated from the slope of the best hand-drawn straight line. Here a^* is the concentration of phenylacetonitrile at the first data point, and x is the concentration of phenylacetonitrile at subsequent data points. Up to 30% conversion no deviations from pseudo-first-order kinetics were observed. In a few kinetic experiments, some of the catalyst splashed and stuck on the upper wall of the flask out of contact with the reaction mixture. Such runs were discarded.

(B) Reverse Addition Method. A 100-mL three-necked flask was charged with 0.1–0.6 g of the catalyst, 45 mL of 50% w/w NaOH (19.086 M), and 2 mL (1.52–1.53 g) of *n*-pentadecane (internal standard for GC), placed in a thermostat at 80 ± 0.2 °C, and stirred mechanically. After 50 min 2 mL of phenylacetonitrile was added. After 10 min the stirring speed was increased, and 25 mL of preheated 1-bromobutane at 80.0 ± 0.2 °C was quickly added at the zero time. Small samples (0.1 mL) of the organic phase were withdrawn, quenched in toluene containing anhydrous calcium chloride, and analyzed by GLC. The initial rates of disappearance of phenylacetonitrile were evaluated from plots of ln $a^*/(a^* - x)$ vs. time. Duplicate runs were carried out with seven different catalysts, and the rate constants differed by an average of 2.7%.

Particle Size Measurement. After the last sample was drawn in a kinetic run, the stirrer was stopped, and beads were removed immediately with a pipet. The beads were placed in a covered flat-bottom glass container and viewed under a microscope equipped with a calibrated movable stage. The diameters of 20 particles selected in a single area of the viewer were measured. Average diameters are used in the tables and figures. Thus the particle sizes were determined at room temperature, the particles being swollen by the reaction mixture. Every recovered catalyst consisted entirely of whole, unbroken beads.

Control Experiments. Reactions were carried out with 0.6 g of 2% cross-linked polystyrene beads containing no functional groups and with no polymer at all. Less than 0.1% butylation of phenylacetonitrile occurred in 60 min in both cases.

Experiment A, Table IV. A 2% cross-linked 60/100-mesh benzyltrimethylammonium chloride catalyst was recovered after 60 min of reaction, washed with water, methanol, tetrahydrofuran (THF), acetone, and anhydrous methanol, and dried under vacuum at 60 °C. One portion of it was used for another kinetic run. The other portion was swelled in THF, treated with 3 N HCl for 3 h, washed with water, acetone, methanol, THF, acetone, and anhydrous methanol, dried under vacuum at 60 °C, and analyzed for chloride ion. From a separate reaction mixture the recovered catalyst was converted to the chloride form by treatment with 3 N HCl in THF, washed and dried as above, and used for a new kinetic experiment.

Experiment B, Table IV. A 2% cross-linked, 100/200-mesh benzyltrimethylammonium ion catalyst was recovered after 45 min of reaction, washed with water until the washings were neutral, and dried in air on a fritted filter overnight.

Distribution of Phenylacetonitrile, 1-Bromobutane, Monobutyl Product, and *n*-Pentadecane in a Reaction Mixture. Two 2% cross-linked 60/100-mesh benzyltrimethylammonium chloride catalysts (1.27 and 2.99 mequiv of Cl^-/g) in reverse addition experiments were filtered separately as quickly as possible from reaction mixtures after 30 min and washed with water to remove the NaOH on the surface of the beads. Each catalyst was then swelled in 50 mL of THF and filtered. The beads were washed twice with 20 mL portions of THF. The THF solutions were dried over anhydrous sodium sulfate and analyzed by GLC with hexadecane as an internal standard. The various amounts (in mole percent) were as follows: phenylacetonitrile, 73.9, 75.1; 1-bromobutane, 5.5, 4.9; monobutyl product, 20.7, 20.0. The starting mixture contained 7.0 mol % of phenylacetonitrile and 93.0 mol % of 1-bromobutane.

Swelling of Catalyst. (A) Dry catalyst (1.0 mL) was placed in a graduated centrifuge tube, and 25 mL of 1-bromobutane was added. The catalyst floated.

(B) Dry catalyst (1.0 mL) was heated to 80 °C, and 3 mL of phenylacetonitrile at 80 °C was added, stirred, and allowed to stand. The catalyst sunk. The catalyst volume increased to 3.0 mL in 5 min and did not change after 12 h. Experiment B was repeated at 70 and 60 °C. The swollen volumes after 5 min were 2.8 and 2.4 mL, and they remained constant for 12 h.

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Registry No. Phenylacetonitrile, 140-29-4; 1-bromobutane, 109-65-9; sodium hydroxide, 1310-73-2.

Effect of Pressure on the 1,3-Dipolar Cycloaddition Reaction of Diphenyldiazomethane to Carbon–Carbon Multiple Bonds

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The volume profiles for the 1,3-dipolar cycloaddition reactions of diphenyldiazomethane to dimethyl acetylenedicarboxylate, diethyl maleate, diethyl fumarate, and maleic anhydride were measured in various solvents. Generally, the volumes of activation amount to ca. −20 cm^3/mol and the volumes of reaction to ca. −28 cm^3/mol. Cohesive energy densities and probably small electrostatic interactions contribute to the solvent effects in the above quantities.

1,3-Dipolar cycloaddition reactions have attracted much interest during the past 2 decades; their synthetic potential is far from being exhausted. According to mechanistic studies,[1] they belong to the concerted processes which once were called, half in jest, "no mechanism reactions",[2] because no intermediate occurs which allows interference. The electronic prototype of the 1,3-dipolar cycloaddition is the (hypothetical) combination of the allyl anion with ethylene; the π electronic description, $[_\pi 4_s + _\pi 2_s]$, is shared

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