more readily adsorbed by the covering, but they exchange less completely. These results are also in accord with the data reported in Table IV and in Figure 2.

Conclusion

Onium salts immobilized on silica gel present a quite different situation from any previously known exchange resin. Importantly, structures can be varied relatively easily which result in markedly altered exchange properties. Conversely, in cross-linked polystyrene resins, the selectivity properties may be partially altered only if the onium salt functionalization is varied. Combined with facility for regeneration, these factors make the use of silica gel supports valuable in anion exchange and ionic and liquid chromatography as well as in phase-transfer catalysis.

Experimental Section

General Methods. Argentometric titrations were performed with a Metrohm-Erisau Multi-Dosimat E 415 with a combined silver electrode in the presence of nitric acid. The hal$^-$ titers were not corrected for the weight change of the supports due to the anion exchange and/or adsorption. Ultraviolet measurements were obtained with a Beckman UV-DGB spectrophotometer. All organic and inorganic reagents were ACS grade or have been previously described. **1** and **3** contained 0.40 and 0.69 mequiv of Br$^-$/g, respectively.

3-Chloropropyl-Functionalized Silica Gel 2. The procedure previously described for **1**[5] was followed: 40.0 g of activted silica gel and 12.0 g of 3-chloropropyltrimethoxysilane in 200 mL of anhydrous toluene yielded 48.5 g of functionalized silica gel. Determination of organic chlorine yielded 1.0 mequiv Cl$^-$/g.

Syntheses of 4–8. The precursor halogen-functionalized silica gels (10.0 g) were degassed under vacuum in tributylamine or pyridine and were then heated to 80 °C for 7 days or to 100 °C for 4 days, respectively. After cooling, the immobilized onium salts were filtered and washed several times with diethyl ether, methanol, and diethyl ether to yield 10.25, 10.75, 10.23, 10.32, and 10.25 g of **4**, **5**, **6**, **7**, and **8**, respectively. Titration of ionic halide yielded for **4**, 0.16; **5**, 0.75; **6**, 0.23; **7**, 0.34; **8**, 0.60 mequiv of Q$^+$/g.

The lower onium salt content found in the case of tributylammonium-functionalized silica gels, in comparison with the analogous pyridinium and tributylphosphonium ones, is attributable to the lower nucleophilic reactivity of tributylamine: no attempt was made to improve the functionalization.

Competitive Cl$^-$–X$^-$ Exchange. A mixture containing 2.5 mL of 0.8 M KCl aqueous solution (20 mmol), 2.5 mL of 0.8 M KX or NaX aqueous solution, 5.0 mL of deionized H_2O (no change was observed using bidistilled and nitrogen-deaerated water), and 0.1 mequiv of **4–8** corresponding to 0.59, 0.13, 0.41, 0.23, and 0.13 g respectively, was slowly stirred for 15 h at room temperature; 0.34 g of Spherosil QMA (0.29 mequiv of Q$^+$/g) was also used. The solution was then filtered and washed repeatedly with water until anions had completely disappeared from the mother liquor and then with methanol and diethyl ether. After air evaporation of the solvent, the Cl$^-$ present on the supports was measured argentometrically (0.01 N $AgNO_3$). The affinity of the systems for the various anions as compared to Cl$^-$ (Table III) was calculated with the followng formula

$$(\text{mL Ag}^+_{\text{theor}} - \text{mL Ag}^+_{\text{used}})/\text{mL Ag}^+_{\text{used}}$$

where mL Ag$^+_{\text{theor}}$ is the number of milliliters of 0.01 N $AgNO_3$ required to titrate an equal quantity of support before the exchange.

Competitive Cl$^-$–HCO_3^- in 5(Cl$^-$). Various amounts of 1.0 N NaCl aqueous solution and 1.0 N $NaHCO_3$ aqueous solution (7.8 mL in total, corresponding to 8.0 mequiv of (Cl$^-$ + HCO_3^-), 2.2 mL of H_2O, and 0.20 mequiv of **5**(Cl$^-$) (0.27 g) were slowly stirred for 15 h at room temperature. The support was then filtered and washed with water until the Cl$^-$ had disappeared; this was followed by washing with methanol and diethyl ether. After solvent evaporation, the Cl$^-$ content was determined argentometrically with 0.01 N $AgNO_3$.

***n* and *K* Determination.** A 0.25-g sample of **7**(Br$^-$) (0.58 g) was placed in 50 mL of aqueous solution containing various quantities of salt or conjugate acid (ranging from 0.10 to 5.0 mmol). The suspensions were then slowly stirred for 15 h at room temperature; 10.0-mL aliquots of each solution were then taken and potentiometrically titrated with 0.01 N $AgNO_3$ to determine the Cl$^-$ in aqueous solution. The quantity of Cl$^-$ on the support and the residual X$^-$ in solution were calculated by difference. The plots of $1/r$ vs. $1/[X^-]$ had correlation coefficients between 0.989 and 0.999.

Adsorption and Anion Exchange on 4(Br$^-$) and 7(Br$^-$). A 0.10-mequiv sample of KBr, 0.10 mequiv of **4** and **7** (0.625 and 0.290 g, respectively), and 0.20 mequiv of the acid in question (0.20 mequiv of NaOH was added in the case of the sodium salt) in 10.0 mL of H_2O, was degassed and slowly stirred for 15 h at room temperature. After suitable dilution, aliquots of the aqueous solution were analyzed by UV spectroscopy and compared with standard solutions of the compounds in question. Systems **4** and **7** were then filtered and washed thoroughly with water, methanol, and diethyl ether before air-drying. Nonexchanged bromide was titrated potentiometrically (0.01 N $AgNO_3$), and the percentage of exchanged bromine on the support was calculated. The percentage of compound present on the support was calculated from UV data. The difference between the two measurements is reported as the adsorbed percentage and is arbitrarily referred to the quantity of immobilized onium salt.

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Phase-Transfer Catalysts Immobilized and Adsorbed on Alumina and Silica Gel

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Abstract: Onium salts immobilized on alumina have been shown to be effective phase-transfer catalysts in comparison to analogous soluble catalysts adsorbed on silica or alumina. Appreciable selectivity has been observed in the nucleophilic substitution reaction with aqueous potassium iodide toward halide of different sizes (1-bromobutane, 1-bromooctane, and 1-bromohexadecane). Alumina and silica gel immobilized onium salts can also act very effectively as reagents when used in stoichiometric quantities.

Three methodologies have been developed in phase-transfer catalysis. In liquid–liquid phase-transfer catalysis (LL-PTC)[1] the reaction is run in a two-phase system: the reactant is in the organic phase while the nucleophile is located in the aqueous phase. In solid–liquid phase-transfer catalysis (SL-PTC)[2] the reaction is run in a heterogeneous solid–solvent system: a solid salt is used as the source of the reactive anion while the reagent is dissolved in the solvent. In the third and most recent method, gas–liquid phase-transfer catalysis (GL-PTC),[3] the reaction is run without solvent and the organic reagent is located in the gas phase. In

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[1] (a) Weber, W. P.; Gokel, G. W. "Phase Transfer Catalysis in Organic Synthesis"; Springer-Verlag: West Berlin, 1977. (b) Starks, C. M.; Liotta, C. "Phase Transfer Catalysis"; Academic Press: New York, 1978. (c) Dehmlow, E. V.; Dehmlow, S. S. "Phase Transfer Catalysis"; Verlag Chemie: Weinhein, 1980. (d) Montanari, F.; Landini, D.; Rolla, F. *Top. Curr. Chem.* **1982**, *101*, 147–200.

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Table I[a]

$(\text{SiO}_2)(\text{CH}_2)_3\text{N}^+\text{Bu}_3\text{Br}^-$ 1a (0.16)	$(\text{SiO}_2)(\text{CH}_2)_3\text{P}^+\text{Bu}_3\text{Br}^-$ 1b (0.34)
$(\text{SiO}_2)(\text{CH}_2)_3\text{NHCO}(\text{CH}_2)_{10}\text{N}^+\text{Bu}_3\text{Br}^-$ 2a (0.43)	$(\text{SiO}_2)(\text{CH}_2)_3\text{NHCO}(\text{CH}_2)_{10}\text{P}^+\text{Bu}_3\text{Br}^-$ 2b (0.52)
$(\text{Al}_2\text{O}_3)(\text{CH}_2)_3\text{N}^+\text{Bu}_3\text{Br}^-$ 3a (0.11)	$(\text{Al}_2\text{O}_3)(\text{CH}_2)_3\text{P}^+\text{Bu}_3\text{Br}^-$ 3b (0.31)
$(\text{Al}_2\text{O}_3)(\text{CH}_2)_3\text{NHCO}(\text{CH}_2)_{10}\text{N}^+\text{Bu}_3\text{Br}^-$ 4a (0.14)	$(\text{Al}_2\text{O}_3)(\text{CH}_2)_3\text{NHCO}(\text{CH}_2)_{10}\text{P}^+\text{Bu}_3\text{Br}^-$ 4b (0.25) or 4′b (0.11)
$\text{C}_{16}\text{H}_{33}\text{N}^+\text{Bu}_3\text{Br}^-$ 5a	$\text{C}_{16}\text{H}_{33}\text{P}^+\text{Bu}_3\text{Br}^-$ 5b

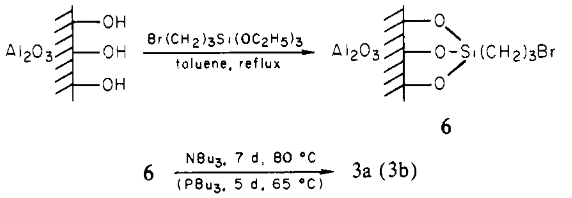
[a] The circles indicate the inorganic matrix, and the siloxane functions binding the alkyl chains are omitted; the onium salt concentration is reported in brackets as mequiv of Q^+/g.

all three methods the phase-transfer catalyst (onium salts, crown ethers, or cryptands) may be used free or immobilized on insoluble matrices. Such inherent advantages as clean reactions and catalyst recoverability have prompted increased attention on the use of immobilized phase-transfer catalysts.[4] Additionally, there may be significant effects on reactivity, reaction development, and possible reaction condition as a function of the nature of the insoluble matrix. Generally, the immobilized catalyst is expected to maintain the same activity orders as found for soluble catalysts.[5] A complex situation arises, however, on using polar matrices. On the one hand, the activity of the catalyst decreases because the microenvironment of the reaction becomes more protic and polar; on the other hand, reaction rates become high, even in the absence of stirring, since the active form of the catalyst is readily regenerated by exchange with the aqueous solution.[6]

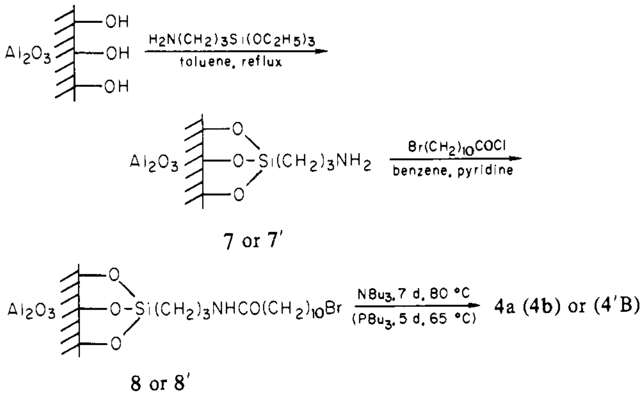
Cross-linked polystyrene and silica gel have been used as insoluble supports. Higher rates have been observed in the former since apolar polystyrene swells in polar solvents.[5,7] Swelling dilates the mesh of the resin which, in turn, allows a greater accessibility of the reagents to the catalytic sites.[8] However, the lack of uniformity precludes selectivity toward organic substrates of different dimension. Catalytic activity of silica gel in apolar solvents is twofold. First, reaction rates are higher in apolar media, and second, the substrate is more strongly adsorbed on the insoluble support. Moreover, since the three-dimensional structure does not vary with the solvent and is well defined,[9] there are greater possibilities of studying and applying the selectivity phenomena.

This paper reports the synthesis of ammonium and phosphonium salts immobilized on alumina and compares their activity with that of similar known catalysts anchored on silica gel[6] in some nucleophilic substitution reactions. Catalytic effects are also compared to those elicited by free catalysts adsorbed on insoluble matrices. Preliminary studies of the selectivity resulting from the pore diameter of the support are also reported along with the use of stoichiometric amounts of insoluble matrices supporting reactant anions.[10]

Scheme I



Scheme II



Results

The phase-transfer catalysts used in this work are shown in Table I. All of the catalysts were synthesized from silica gel (Merck No. 7734, surface area 500 m^2/g, pore diameter 60 Å), and alumina (Merck No. 1067, surface area 180–200 m^2/g, pore diameter 60 Å, in the case of catalysts **3a–4b**, and No. 1061, surface area 70 m^2/g, pore diameter 150 Å, in the case of catalyst **4′b**) by reaction of the suitable trialkoxysilane with the hydroxyl groups on the surface of the inorganic solids.

The syntheses of **1a**,[11] **1b**,[6b] **2a**,[11] and **2b**[6a] were previously reported. **3a** and **3b** were prepared by refluxing 3-bromopropyltriethoxysilane with alumina 60 in toluene and subsequent quaternization (Scheme I).

The synthesis of **4a** and **4b** involved a preliminary functionalization of the alumina with 3-aminopropyltriethoxysilane, subsequent reaction with 11-bromoundecanoyl chloride, and finally quaternization (Scheme II).

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(2) (a) Liotta, C. L.; Harris, H. P. *J. Am. Chem. Soc.* **1974**, *96*, 2250–2252. (b) Landini, D.; Rolla, F. *Synthesis*, **1976**, 389–390. (c) Fedorynski, M.; Wojciechowski, K.; Matacz, Z.; Makosza, M. *J. Org. Chem.* **1978**, *43*, 4682–4684.

(3) (a) Tundo, P. *J. Org. Chem.* **1979**, *44*, 2048–2049. (b) Tundo, P.; Venturello, P. *Synthesis* **1979**, 952–954.

(4) (a) Regen, S. L. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 421–429. (b) McKenzie, W. M.; Sherrington, D. C. *J. Chem. Soc., Chem. Commun.* **1978**, 541–543. (c) See ref 3a.

(5) (a) Molinari, H.; Montanari, F.; Tundo, P. *J. Chem. Soc., Chem. Commun.* **1977**, 639–641. (b) Molinari, H.; Montanari, F.; Quici, S.; Tundo, P. *J. Am. Chem. Soc.* **1979**, *101*, 3920–3927.

(6) (a) Tundo, P. *J. Chem. Soc., Chem. Commun.* **1977**, 641–643. (b) Tundo, P.; Venturello, P. *J. Am. Chem. Soc.* **1979**, *101*, 6606–6613. (c) Tundo, P.; Venturello, P. *Ibid.* **1981**, *103*, 856–861.

(7) Tundo, P. *Synthesis* **1978**, 315–316.

(8) Halász, I.; Vogtel, P. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 24–28.

(9) Ilor, R. K. "The Chemistry of Silica"; Wiley: New York, 1979; Chapters 5 and 6.

(10) (a) Sherrington, D. C. In "Polymer-Supported Reaction in Organic Synthesis", Hodge, P.; Sherrington, D. C., Ed.; Wiley: New York, 1980. (b) Cainelli, G.; Contento, M.; Manescalchi, F.; Musatto, M. C. *Synthesis* **1981**, 302–303, and references therein.

(11) Tundo, P.; Venturello, P.; Angeletti, E. *J. Am. Chem. Soc.*, preceding paper in this issue.

Table II. Observed Pseudo-First-Order Rate Constants for the Reaction of 1-Bromobutane with Aqueous KI ($k^{I}{}_{obsd}$) and KCN ($k^{CN}{}_{obsd}$) under Phase-Transfer Condition[a]

cat.	$10^4 k^{I}{}_{obsd}$ (s^{-1})	$10^4 \times k^{CN}{}_{obsd}$ (s^{-1})	cat.	$10^4 k^{I}{}_{obsd}$ (s^{-1})
1a	1.18 (0.19)[b]		5a	9.21 (1.52)[b]
1b	1.88 (0.22)[b]		5b	7.14 (1.14)[b]
2a	1.36 (0.21)[b]		SiO_2 + 5a	1.38[c]
2b	1.74 (0.26)[b]		SiO_2 + 5b	1.15[c]
3a	1.36	1.78	Al_2O_3 + 5a	1.92[d]
3b	3.10	5.19	Al_2O_3 + 5b	1.54[d]
4a	2.51	2.97	SiO_2	0.0[e]
4b	3.68	6.23	Al_2O_3	0.0[f]

[a] 1-Bromobutane, 10.0 mmol; KI (KCN), 30.0 mmol; H_2O, 3.25 mL; catalyst, 0.005 mequiv; $T = 80$ °C; stirring speed 1000 ± 50 rpm. [b] Reactions carried out in chlorobenzene as a solvent: 1-bromobutane, 10.0 mmol; KI, 20.0 mmol; H_2O, 2.5 mL; C_6H_5Cl, 5.0 mL; catalyst, 0.005 mequiv; $T = 80$ °C; stirring speed 1000 ± 50 rpm. [c] Conditions as in *b* plus 1.0 g of silica gel. [d] Conditions as in *b* plus 2.5 g of alumina. [e] Silica gel 1.0 g. [f] Alumina 2.5 g.

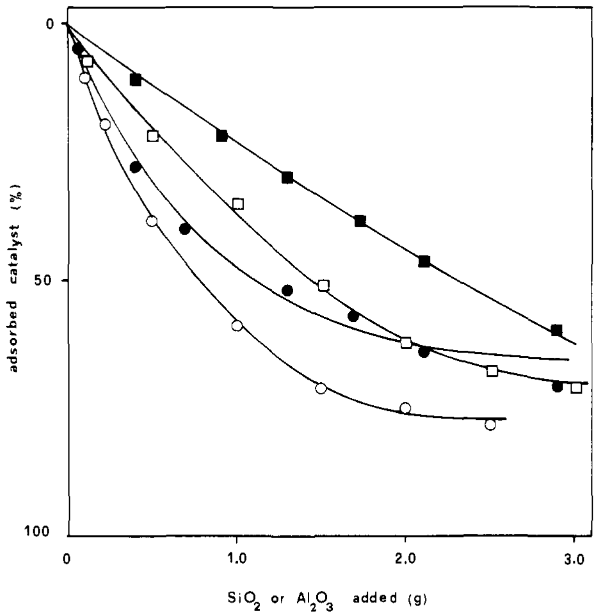

Figure 1. Adsorption of **5a** (open symbols) and **5b** (full symbols) on silica gel 60 (circles) and alumina 60 (squares). The experimental conditions were the same as in Table II for chlorobenzene and without 1-bromobutane: KI, 20.0 mmol; H_2O, 2.50 mL; C_6H_5Cl, 5.0 mL; catalyst 0.005 mequiv; $T = 80$ °C. Adsorptions were measured by ^{1}H NMR integration of the signals of the chain protons of the onium salts.

Catalytic activity of **1–4** (0.005 molar equiv) in nucleophilic substitution reactions were assessed under LL-PTC conditions in two simple reactions (eq 1 and 2).

$$\text{RBr} + \text{KI} \xrightarrow[80\ °\text{C}]{\text{cat.}} \text{RI} + \text{KBr} \tag{1}$$

$$\text{RBr} + \text{KCN} \xrightarrow[80\ °\text{C}]{\text{cat.}} \text{RCN} + \text{KBr} \tag{2}$$

Both reactions obeyed under all the conditions used pseudo-first-order kinetics, with correlation coefficients ≥0.990 for plots of ln RBr vs. time. Table II reports rate constants for reactions 1 and 2 (R = Bu) in the presence of immobilized (**1–4**) and homogeneous catalysts (**5**).

It is well known that silica gel and alumina are able to adsorb quaternary trimethylalkylammonium salts.[9] This phenomenon was investigated in chlorobenzene as solvent, in the same reaction mixture used for kinetic measurements but without the organic reagent. Figure 1 shows the % adsorption of **5a** and **5b** as a function of the number of grams of silica and alumina added. The kinetics of reaction 1 were measured under conditions of 40–60 % adsorption of **5a** and **5b** (1.0 g of silica gel and 2.5 g of alumina). The results are reported in Table I.

The utility of phase-transfer catalysts immobilized on alumina in preparative reactions was shown in the preparation of 1-nonanonitrile (eq 2) (after 24 h at 80 °C with 1.0×10^{-3} molar equiv of **4b**, without solvent and with weak stirring, the yield was 89.5%; see Experimental Section). In the 1-bromooctane–1-iodooctane reaction, the mechanism for alumina-immobilized catalysts was shown to be the same as that for the corresponding silica gel-immobilized catalysts; that is, the reaction rate is controlled by the regeneration of the onium salt in its active form, with I^- as counterion. Under the condition reported in Table II, with stirring, catalyst **3b** (0.025 molar equiv) after 0.5 h (37 % conversion) showed a content of 0.25 and 0.06 mequiv/g of I^- and Br^-, respectively. In the absence of stirring the reaction proceeded more slowly; after 3.3 h (38 % conversion), **3b** had an I^- content of 0.14 mequiv/g with the remaining 0.16 mequiv/g made up of Br^- ion from the reaction. Since the substitution reaction proceeded well when the catalyst was functionalized with the reagent nucleophile, the decreased activity in the absence of stirring was due to the difficulty of access for the aqueous phase into the catalytic centers. The greater polarity of alumina and silica gel than that of functionalized polystyrene resins renders the access of reagents easier in the former systems than that in the latter.[5b] This interpretation is supported by the observed reactivity even in the absence of stirring.

The use of stoichiometric rather than catalytic amounts of **1–4**, can be seen as an extension of Brändström's extractive alkylation,[12] where the onium salt is made insoluble. In addition to the intermediate advantages of catalyst recoverability (and easy regeneration) and predictably greater activity than commercial polystyrene resins were the benzyltrimethylammonium salt is immobilized, it may also be expected in this case that the inorganic matrix directs certain reactions. These possibilities were verified in two simple nucleophilic substitution reactions using **3b**(Br^-) and **2a**(SCN^-) as the nucleophile source. The reactions between **3b**(Br^-) and octylmethanesulfonate (see Experimental Section)

$$\mathbf{3b}(\text{Br}^-) + n\text{-C}_8\text{H}_{17}\text{OSO}_2\text{CH}_3 \xrightarrow[\substack{\text{cyclohexane} \\ \text{(acetonitrile)}}]{80\ °\text{C}} \mathbf{3b}(\text{CH}_3\text{SO}_3^-) + n\text{-C}_8\text{H}_{17}\text{Br} \tag{3}$$

was observed to be very dependent on the solvent used; 82% conversion was observed in cyclohexane after 10 min, while 74% conversion was reached in acetonitrile after 60 min. This order for solvent polarity dependence is similar to that reported for soluble catalysts,[13] and in this case it may be attributed to adsorption phenomena analogous to those reported above for functionalized silica gel.[6b]

Reaction between **2a**(SCN^-)[14] and 1-bromooctane (see Experimental Section)

$$\mathbf{2a}(\text{SCN}^-) + n\text{-C}_8\text{H}_{17}\text{Br} \xrightarrow[\text{cyclohexane}]{80\ °\text{C}} \mathbf{2a}(\text{Br}^-) + n\text{-C}_8\text{H}_{17}\text{SCN} \tag{4}$$

was run on a preparative scale and had a rate greater than that reported for thiocyanate-functionalized Amberlyst A-26.[15] Striking dependence on solvent polarity[6b] was noted in this case as well (95% conversion was reached after 2.0 h in cyclohexane and after 5.0 h in benzene).

The effect of the average pore diameter on the kinetics of reaction 1 was studied by reacting alkyl bromides of various chain lengths, using 0.005 molar equiv of **2b**, **4b**, and **4′b**. In order to

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[12] Brändström, A. "Preparative Ion Pair Extraction", Apotekarsocieteten/Hassle: Lakemedel, 1974.

[13] Landini, D.; Maia, A.; Montanari, F. *Nouv. J. Chim.* **1979**, *3*, 575–577.

[14] **2a**(SCN^-) was prepared from **2a**(Br^-) (40.0 g) by successive treatment with aqueous 5% $NaHCO_3$ (500 mL) and 3 N NaSCN (50 mL); it had a titre of 0.42 mequiv of SCN^-/g (argentometric).

[15] Cainelli, G.; Manescalchi, F.; Pannunzio, P. *Synthesis* **1979**, 141–144.

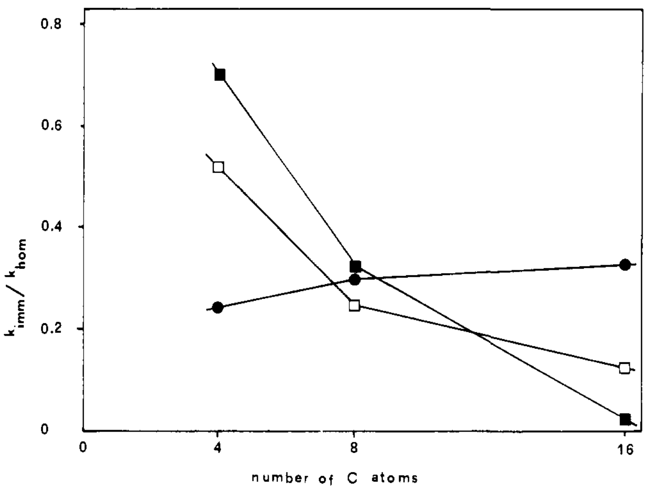

Figure 2. Selectivity induced by the micropores of the immobilized PT catalysts **2b** (full circles), **4b** (open squares), and **4′b** (full squares) on the pseudo-first-order rate constants (k_{imm}) of Br–I exchange in n-$C_nH_{2n+1}Br$ with aqueous KI as a function of the number of carbon atoms in the alkyl chain (n). These rate constants are referred to those obtained in the same reaction and under the same conditions with the homogeneous catalyst n-$C_{16}H_{33}P^+Bu_3Br^-$ (k_{hom}). For the reaction conditions see Table II, footnote *a*.

prevent interference by nonreagent molecules with access to pores of the functionalized matrix, the kinetics for n-C_4H_9Br, n-$C_8H_{17}Br$, and n-$C_{16}H_{33}Br$ were carried out in the absence of solvent. Figure 2 shows the ratio of the pseudo-first-order rate constants of these catalysts to that of **5b**, as a function of the sizes of the alkyl bromides. In this case reference to the activities of the structurally analogous homogeneous catalyst **5b** is essential, since it allows the neglect of the numerous interfering variables (i.e., variations in volume and polarity of the organic phase, intrinsic reactivity of the alkyl halide, etc.). Although little selectivity for small molecules was seen in the case of functionalized silica gel, the pore diameter had a considerable effect in the case of functionalized aluminas.

Discussion

The present results have shown that organofunctionalization of alumina with onium salts broadens the range of polymer-immobilized phase-transfer catalysts with specific properties. Since the active sites of alumina are both Brönsted and Lewis acids, it can catalyze a large and varied number of organic reactions.[16] Alumina differs from silica gel in its adsorption and ion interaction properties since it promotes nucleophilic replacements to a greater extent than silica gel. In the absence of water, alumina offers an aprotic polar environment favoring nucleophilic substitution.[17-19]

The degree of functionalization of alumina is less than that of silica gel, consistent with the fact that the surface concentration of hydroxyl groups is lower in alumina than in silica gel (0.1–2.5 OH/nm^2 and 4–10 OH/nm^2 respectively).

A functionalization level of 0.31 mequiv/g in **3b** means that on the average, 8.7 Al_2O_3 groups bear a single alkyl chain. Since the surface area of the alumina is between 180 and 200 m^2/g, there is approximately 1 organofunctionalization/nm^2 of surface. This value is very close to the concentration of surface hydroxyl groups and so the type of bond effectively present in **3**–**4** is uncertain. It may be a 3 or 2 point bridge, simply Al–O–Si(OR)$_2$R, or a multilayer of siloxane functions on the surface of the support.[20]

Activity of Inorganic Matrices Immobilized and Adsorbed Catalysts in Nucleophilic Substitution Reactions. The observed slightly lower catalytic activity of **5a** and **5b** (Table II) on silica gel than on alumina can be attributed to the different nature of the two supports. Alumina catalyzes nucleophilic substitution to a greater extent than the more protic silica gel. Catalytic activity on surface-adsorbed phase-transfer catalysts can be rationalized as a first approach by the orientation of the onium salts on these supports. While hexadecyltrimethylammonium bromide on silica gel is arranged with the polar ends toward the support,[21] in **5** the presence of three bulky butyl groups undoubtedly changes this orientation. Therefore, reaction may occur on the surface of the support, close to it, or at some distance from it in the organic phase, promoted by the nonremovable fraction of free catalysts in dynamic equilibrium with the adsorbed one. In any case, the matrix has no significant effect, as seen comparing rate constants of silica gel and alumina-adsorbed onium salts (data for **5a** and **5b** in Table II).

The use of adsorbed rather than free catalyst in LL-PTC has no effect on operating condition, since the relative catalytic activities of ammonium and phosphonium salts do not change; moreover, since the catalyst cannot be easily removed from the organic phase, conditions do not allow for a clean reaction mixture or for the recovery of the catalyst.

Data in Table II show that in reaction 1 carried out under LL-PTC conditions, ammonium salts are more active than the corresponding phosphonium ones by a factor of approximately 1.3. The same effect was reported by Montanari et al. in a different reaction.[22] However, when the onium salts are immobilized on inorganic matrices, under LL-PTC conditions the phosphonium salts are on the average 1.3 times (Table II, compare **1b**–**4b** with **1a**–**4a**) more active than the corresponding ammonium salts. The reasons for our observed inversion of the catalytic order of activities are not entirely clear, but it may be related to the polarity of the reaction medium. The many water molecules present solvate the higher charge density molecule more strongly, i.e., the ammonium salt. This could then lead to greater solvation (and so lower activity) of the reactant anion. In any case, the observed catalytic order seems to be the general behavior when the catalysts are immobilized on inorganic matrices, since it is seen with differently functionalized silica gel and alumina and in both the absence and presence of solvents (Table II).

Selectivity Arising from Micropore Diameter. For these porous inorganic solids a relation in the catalytic selectivity can be rationalized as a first approximation by considering that the distribution and shape of the micropores are quantities that can be easily measured.[23] Even more important, they do not vary appreciably as a function of the solvent used for the reaction.[24,25] Conversely, it is well known that the diameter of the pores of alumina and silica gel plays an important role in the chromatographic separation of organic compounds.[25]

The size of polystyrene mesh bearing the onium salt and the diffusability of the reagents on the support were used to justify some differences of alkyl halides of various sizes.[26] However, the corresponding homogeneous catalysts under the same reaction conditions were not studied as a comparison.

The ratios of the pseudo-first-order rate constants for immobilized and homogeneous phosphonium salts (k_{imm}/k_{hom}) for the

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(16) Posner, G. H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 487–496.

(17) (a) Regen, S. L.; Quici, S.; Liaw, S. J. *J. Org. Chem.* **1979**, *44*, 2029–2030. (b) Bram, G.; Fillebeen-Khan, T.; Geraghyt, N. *Synth. Commun.* **1980**, *10*, 279–289. (c) Angeletti, E.; Tundo, P.; Venturello, P. *J. Chem. Soc., Chem. Commun.* **1980**, 1127–1128.

(18) Egorov, M. M.; Igantjeva, L. A.; Kiselev, V. F.; Krasilnikov, K. G.; Topchieva, K. V. *Zh. Fiz. Khim.* **1962**, *36*, 1882–1889.

(19) Iler, R. K. *J. Colloid Interface Sci.* **1976**, *55*, 25–34.

(20) In 0.1 N HCl aqueous solution and in pH 9 borate buffer, **3a** showed no detectable loss of functionalization after 15 h at room temperature (argentometric titration).

(21) Bijsterbosh, B. H. *J. Colloid Interface Sci.* **1974**, *47*, 186–198.

(22) Landini, D.; Maia, A.; Montanari, F. *J. Am. Chem. Soc.* **1978**, *100*, 2796–2801.

(23) See ref 9, pp 493–505.

(24) See ref 9, pp 488–492.

(25) (a) Kiselev, A. V.; Nikitin, Ya. S.; Petrova, R. S.; Shcherbakova, K. D.; Yashin, Ya. I. *Anal. Chem.* **1964**, *36*, 1526–1533. (b) Kiselev, A. V. *J. Chromatog.* **1970**, *49*, 84–129. (c) Unger, K. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 267–278.

(26) (a) Tomoi, M.; Ford, W. T. *J. Am. Chem. Soc.* **1981**, *103*, 3828–3832. (b) Selectivity toward alkyl bromides of different sizes has been reported in the formation of phenol ethers with catalysts supported on polystyrene (Regen, S. L.; Nigam, A. *J. Am. Chem. Soc.* **1978**, *100*, 7773–7775). In this case, however, the matrix was functionalized with ethylene glycols rather than onium salts, and the selective effect was correctly attributed to the cosolvent effect of the organic function bound to the polystyrene.

reactions of some primary alkyl bromides are plotted as a function of the alkyl chain length in Figure 2. With the homogeneous catalyst $n\text{-}C_{16}H_{33}P^+Bu_4Br^-$ (**5b**) the kinetic rate constants (k_{hom}) decrease as the alkyl chain increases as expected for an S_N2 reaction (in fact this catalyst showed $k_{\text{hom}} = 7.14 \times 10^{-4}$, 2.74 $\times 10^{-4}$, and 0.98×10^{-4} (s^{-1}) for 1-bromobutane, 1-bromooctane and 1-bromohexadecane, respectively, in reaction 1 carried out according to conditions of Table II footnote *a*). In particular, for the most selective catalyst in this type of reaction (**4′b**) the ratio of the rate constant for 1-bromobutane to that for 1-bromohexadecane has been found to be 276, while for **5b** it was 7.3. Thus, the immobilized system **4′b** is 38 times more selective as a catalyst than its homogeneous counterpart (**5b**). For catalyst **4b** the same ratio of the rate constant for 1-bromobutane to that for 1-bromohexadecane was found to be 30, showing that **4b** is 4.1 times more selective than **5b**.

The relation between selectivity and micropore diameter is more complex than it appears. The larger pore diameter of the alumina used for **4′b** (150 Å) than for **4b** (60 Å) could suggest that **4′b** might be less selective than **4b**. However, **4′b** shows decreasing activity going from 1-bromobutane to 1-bromooctane to 1-bromohexadecane and is more selective than **4b**. Alteration of the geometries of the micropores consequent on the functionalization must be considered. The alkyl chains may anchor themselves in different sites of the micropore, thus leading to different geometries in the active sites. These geometries may also derive from self-aggregation of the alkyl chains as in liquid crystals. However, the geometries may vary as a function of the support, covering, and degree of organic functionalization.

Experimental Section

General Methods. Argentometric titrations were conducted on a Metrohm-Herisau Multi-Dosimat E 415, using a combined silver electrode, in the presence of nitric acid. Nuclear magnetic resonance spectra were recorded on a Hitachi Perkin-Elmer R-24B 60 MHz ^1H NMR spectrometer. Gas chromatographic analyses were conducted on a Varian Series 1440 gas chromatograph equipped with a Varian CDS 111L integrator. All organic and inorganic reagents were ACS grade and were used without purification.

Hexadecyltributylammonium bromide,[27] mp 70–72 °C, hexadecyltributylphosphonium bromide,[28] mp 54 °C, and *n*-octylmethanesulfonate,[29] bp 112–114 °C (2 mmHg), were obtained according to the literature. The synthesis of the catalysts **1a**, **2a**,[11] and **1b**, **2b**[6a] was previously described, and the anion content was 0.16, 0.43, and 0.34, 0.52 mequiv of Br^-/g, respectively.

3-Bromopropyl-Functionalized Alumina 6. Al_2O_3 (40.0 g) dried in an oven at 120 °C for 12 h (the last water traces were removed by azeotropic distillation with toluene) was suspended in 180 mL of anhydrous toluene and placed to react with 11.9 g (42 mmol) of 3-bromopropyltriethoxysilane added dropwise over 15 min. The reaction mixture was stirred and refluxed for 1.5 h; 42.0 g of **6** was obtained and the argentometric analysis (carried out transforming organic bromine into bromide anion by reaction with an excess of pyridine at 100 °C for 4 h) yielded a titer of 0.35 mequiv of Br^-/g.

3-Aminopropyl-Functionalized Alumina 7 (and 7′). According to the procedure described for **6**, a suspension of 40 g of Al_2O_3 60 (or 150) and 3-aminopropyltriethoxysilane (14.5 g, 65 mmol) in 180 mL of anhydrous toluene was refluxed under stirring for 1.5 h; 41.0 g (or 40.7) of **7** (or **7′**), respectively, was obtained. The organic functionalization was established salifying the immobilized amino groups with 0.05 N bromidric acid and titrating the bromide anion present on the matrix. Titers were 0.29 and 0.19 mequiv of $NH_3^+Br^-$/g for **7** and **7′**, respectively.

11-Bromoundecaneamidopropyl-Functionalized Alumina 8 (and 8′). 40.7 g of compound **7** (or **7′**) was dehydrated by azeotropic distillation with benzene and successively treated, under stirring, in anhydrous benzene (150 mL) in the presence of pyridine (20 mL) with 11-bromoundecanoyl chloride (7.0 g, 25 mmol), dissolved in anhydrous benzene, by cooling in a water bath. The reaction mixture was stirred for 2 h at room temperature and **8** (or **8′**) was filtered, carefully washed with ethanol, water, methanol, and diethyl ether. The organic function contents were 0.27 and 0.15 mequiv of Br^-/g for **8** and **8′**, respectively.[30]

Synthesis of 3a, 3b, 4a, 4b, and 4′b. The precursor halides **6**, **8**, and **8′** (15 g) were suspended in 15 mL of tributylamine (case a) or tributylphosphine (case b) and degassed under vacuum and left without stirring for 7 days at 80 °C (case a) or 5 days at 65 °C (case b). After cooling, they were recovered with diethyl ether, filtered, and carefully washed several times with methanol and diethyl ether. Argentometric titration of ionic halide yielded titers of 0.11, 0.31, 0.14, 0.25, and 0.11 for **3a**, **3b**, **4a**, **4b**, and **4′b**, respectively.

Kinetic Measurements. All kinetic experiments were run in a 10-mL flask fitted with a Teflon top and a Teflon-coated stirring bar, connected with a circulating *n*-butyl phthalate thermostat regulated at 80 ± 0.5 °C.

In a typical experiment, the flask was charged with water (3.25 mL), potassium iodide, or potassium cyanide (5.0 or 1.95 g, respectively, 30 mmol) and 0.005 molar equiv of catalyst corresponding to 0.31; 0.15, 0.12, 0.10, 0.45, 0.16, 0.36, 0.20, and 0.45 of **1a**, **1b**, **2a**, **2b**, **3a**, **3b**, **4a**, **4b**, and **4′b**, respectively. The mixture was equilibrated for 0.5 h and the organic substrate (10 mmol) was added; stirring speed set at 1000 ± 50 rpm.[6c] The reaction was followed by withdrawing small samples of the upper organic layer at suitable time intervals and analyzing the disappearance of the reagent and the appearance of the product by NMR in the case of bromo–iodo exchange in 1-bromobutane, as previously reported,[6c] and by GLC in the other case (SE-30 5% on Varaport, after calibration with standard mixtures).

Nonanonitrile. A mixture consisting of 19.3 g of 1-bromooctane (0.1 mol), 14.7 g of sodium cyanide (0.3 mol), 33 mL of water, and 0.5 g of **4b** (0.001 molar equiv) were mechanically stirred at ca. 100 rpm, and allowed to react at 80 °C for 24 h. After cooling, the catalyst was filtered and washed with diethyl ether; the dried organic phase was distilled under vacuum to give 12.4 g of nonanonitrile (89.5% yield); bp 119–120 °C (30 mm), $n^{20}{}_D$ 1.4262 (lit.[31] 98.4–98.6, 10 mm, $n^{20}{}_D$ 1.4255).

Reactions of 2a(SCN^-) and 3b(Br^-) as Solid Reagents. 1-Bromooctane. A mixture consisting of 0.89 g of **3b** (0.28 mmol; 2.8 molar equiv) and 0.021 g (0.1 mmol) of *n*-octylmethanesulfonate was heated at 80 °C in the presence of 0.80 mL of cyclohexane or acetonitrile. The disappearance of the reagent and the appearance of 1-bromooctane were followed by GLC analysis.

***n*-Octylthiocyanate.** A mixture consisting of 36.0 g of **2a**(SCN^-) (15.5 mmol; 2.8 molar equiv), 1.04 g (5.4 mmol) of 1-bromooctane, and 35 mL of cyclohexane was heated at 80 °C for 2.0 h. GLC analysis showed a conversion of 95%. The reaction mixture was filtered and washed with diethyl ether; the distillation of the organic phase gave 0.70 g of *n*-octylthiocyanate (76% yield); bp 135 °C (12 mm), $n^{22}{}_D$ 1.4660 (lit.[32] 141–142, 19 mm, $n^{20}{}_D$ 1.4649). The same reaction carried out in benzene showed a 95% conversion after 5.0 h. When the recovered **2b** was regenerated in its SCN^- form and allowed to react in cyclohexane and 1-bromooctane it showed unchanged reactivity.

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Registry No. 5a, 6439-67-4; **5b**, 14937-45-2; 1-bromobutane, 109-65-9; 1-bromooctane, 111-83-1; 1-bromohexadecane, 112-82-3; 3-bromopropyltriethoxysilane, 52090-18-3; 3-aminopropyltriethoxysilane, 919-30-2; 11-bromoundecanoyl chloride, 15949-84-5; tributylamine, 102-82-9; tributylphosphine, 998-40-3; nonanonitrile, 2243-27-8; *n*-octylthiocyanate, 19942-78-0; alumina, 1344-28-1.

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(27) Shelton, R. S.; Van Camper, M. G.; Tilford, C. H.; Lang, H. C.; Nisonger, L.; Bandelin, F. J.; Ruberkoenig, M. L. *J. Am. Chem. Soc.* **1946**, *68*, 753–755.

(28) Starks, C. M. *J. Am. Chem. Soc.* **1971**, *93*, 195–199.

(29) Williams, H. R.; Mosher, H. S. *J. Am. Chem. Soc.* **1954**, *76*, 2984–2987.

(30) Because the automatic titrator was not available, the different halides on silica gel could not be distinguished one from another. Therefore, the **2b** titers reported previously, measured by the Volhard method, are inexact. In fact, **2b** was later shown to contain 45% Cl^-, with the remaining 55% (0.52 mequiv/g) Br^-. The chloride ions arise from amide synthesis from acyl chloride. The hydrochloric acid generated reacts with some amine groups and prevents them from reacting to completion. These groups do not exchange with the pyridine in the reaction mixture if even small quantities of water are present on the support, probably due to obstruction of the pores of the matrix. In any case, the immobilized NH_3^+ Cl^- is inactive in the catalysis: in the conditions of Table I, 1-bromooctane showed a conversion into 1-iodooctane of 4.5% after 22 h, with this ammonium salt as a catalyst. The previously reported results for **2b** need to be corrected only as refers to activity (×1.8). We are very sorry about this error over which we had no control.

(31) Merckx, R.; Verhulst, J.; Bruylants, P. *Bull. Soc. Chim. Belg.* **1933**, *42*, 177–198.

(32) Allen, P. Jr. *J. Am. Chem. Soc.* **1935**, *57*, 198–199.