Catalytic Interconversion of Alkyl Halides by Gas-liquid Phase-transfer Catalysis

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High halogen exchange conversions are achieved when a gaseous mixture of alkyl halides (chlorides, bromides, iodides) is passed over a solid bed consisting of porous inorganic supports bearing a phase-transfer catalyst under gas-liquid phase-transfer catalysis (g.l.-p.t.c.) conditions. The process is catalytic since the bed undergoes no changes once it reaches operating conditions. For example, a methylene dichloride and bromoethane mixture is converted into all the halogen-exchange products, and their statistical distribution at equilibrium depends on the original ratio of the halogens in the organic reagents. Catalytic activity is high: 200 ml of such a mixture can be converted in 1 h by passage through 200 g of alumina coated with 10% tetrabutylphosphonium bromide. The catalytic process is promoted by the halide anions present as Q^+X^- in the liquid phase constituted by the molten catalyst and as Na^+X^- in the solid inorganic support; the halide anions partition themselves between the liquid and solid phases as a function of their respective affinities. This catalysis depends on the diffusion, partition, and adsorption of the alkyl halides between the gaseous, liquid, and solid phases, as well as on their intrinsic nucleophilic reactivity. Mechanistic aspects and industrial applicability are discussed.

Gas-liquid phase-transfer catalysis (g.l.-p.t.c.)[1] is closely related to liquid-liquid (l.l.) and solid-liquid phase transfer catalysis (s.l.-p.t.c.)[2] as a technique for those reagents which may be made gaseous under reasonable temperature and pressure conditions, for running organic syntheses under continuous-flow conditions, and in the absence of solvent to minimize pollution. We have described the synthesis of alkyl halides,[1c] esters,[1d] phenol ethers, and sulphides[1e] using this procedure. In these cases, the reagent bed consisted of the nucleophile salt and the phase-transfer catalysts, and was progressively converted into the salt of the halide produced from the exchanged electrophile.

The preparation of a true catalytic bed, that is of one which may function for an indefinite period to promote reaction between reagents introduced simultaneously on the column, requires consideration of general reactions of the type (1).

$$A + B \xrightarrow{\text{cat}} \text{product(s)} \qquad (1)$$

In these reactions, one or more reagents (for example, acid and alcohol to give ester, transesterification reactions, reactions in the presence of acids or bases, *etc.*) † react as desired only in the presence of a catalyst supported on a solid or of this latter alone, acting as a catalyst.

The continuous catalysis of halogen exchange in alkyl compounds with g.l.-p.t.c. [equation (2)] has been communicated previously.[3] The present paper describes studies of the applicability and mechanism of this reaction.

$$R^1X + R^2Y \xrightleftharpoons{\text{cat}} R^1Y + R^2X \qquad (2)$$

Unlike p.t.c., in the present case a continuous phase-transfer of the reacting anions does not take place; however, we use the term g.l.-p.t.c., owing to the strict analogies existing between the herein-reported interconversions and p.t.c.: the same phase-transfer catalysts promote the process by activating the reacting anions.

Results

In accord with g.l.-p.t.c. procedures, reactions were carried out by introducing the alkyl halide mixtures, with a peristaltic pump, into a column containing different catalytic beds at the desired temperature. For the reaction to occur, the reagents, introduced into the column in the liquid state, must become gaseous. Therefore, if the b.p. of the reagents is above or near to the reaction temperature, the reaction must be run at reduced pressure. Reaction products were collected by cooling at the column outlet, and analysed quantitatively using ^1H n.m.r. and g.l.c. comparison with authentic samples.

Low molecular weight alkyl halides were used to allow operation at atmospheric pressure. However, high boiling halides give equivalent results at reduced pressure (see Experimental section; benzyl chloride–1-bromo-octane interconversion).

Two columns of different size were used: one (A) had a volume of 210 ml and a length of 50 cm, the other (B) had a volume of 115 ml and a length of 40 cm.

The inorganic supports were Merck reagents: basic alumina 60; basic alumina 90; basic alumina 150; neutral alumina 90; acidic alumina 90; silica gel 60; code number, pore diameter (Å) respectively: 1 067, 60; 1 076, 90; 1 061, 150; 1 077, 90; 1 078, 90; 7 734, 60.

R^1Cl–R^2Br *Interconversion.*—1 : 2 Molar mixtures of methylene dichloride and bromoethane, 1-bromopropane, or 1-bromobutane were forced to pass over various catalytic beds at 150 °C to afford the reaction in Scheme 1.

Table 1 reports the results for the reaction in Scheme 1 showing the percentage halogen exchange as a function of the different catalytic beds, with or without the phase-transfer catalyst tetrabutylphosphonium bromide. Once the exchange process has reached equilibrium and so the ratio of ionic halogens on the bed is constant (see below), the outgoing ratio of organic chloride to organic bromide is equal to the incoming ratio. Since this ratio was set as 1, the methylene singlet in the ^1H n.m.r. may be integrated to calculate the percentage exchange from formula (3).

$$\%\ \text{halogen exchanged} = \frac{\text{area}_{CH_2Br_2} + (\text{area}_{CH_2ClBr})/2}{\text{area}_{CH_2Cl_2} + \text{area}_{CH_2Br_2} + \text{area}_{CH_2ClBr}} \times 100 \qquad (3)$$

Figure 1 shows conversion as a function of temperature for the reaction between methylene dichloride and bromoethane

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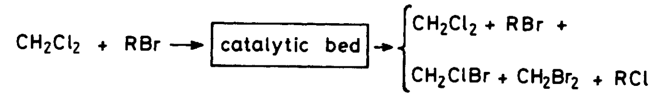
† These reactions under g.l.-p.t.c. conditions are under study in our laboratory.

Table 1. Catalytic halide interconversions of CH_2Cl_2 and C_2H_5Br, n-C_3H_7Br, or n-C_4H_9Br (Scheme 1) in the presence of different catalytic beds[a]

Catalytic bed	% Halogen exchanged[b] C_2H_5Br	n-C_3H_7Br	n-C_4H_9Br
Silica gel 60	1[c]		
Basic alumina 90	18[c]	9	9
Neutral alumina 90	30[c]	12	6
Acidic alumina 90	47[c]	10	
Basic alumina 60	12		10
Basic alumina 150	6		4
Silica gel + $Bu_4P^+Br^-$[d]	48[c] (15)[e]		
Basic alumina 90 + $Bu_4P^+Br^-$[d]	49[c] (49)[e]	49	50
Neutral alumina 90 + $Bu_4P^+Br^-$[d]	46[c] (46)[e]	46	28
Acidic alumina 90 + $Bu_4P^+Br^-$[d]	50[c] (50)[e]	49	49
Basic alumina 60 + $Bu_4P^+Br^-$[d]	50		49
Neutral alumina 90 + Carbowax 6000[d]	2		
Basic alumina 90 + NaCl[f]	8		

[a] *T* 150 °C; reagent flow rate, 0.7 ml min^{-1}; column A containing 200 g of alumina or 100 g of silica gel. [b] Calculated on the basis of equation (3). [c] Data from ref. 4, at 170 °C. [d] Catalyst 10% by weight with respect to the inorganic support. [e] Data from ref. 4, reagent flow rate 3.3 ml min^{-1}. [f] Column B containing 110 g of catalytic bed; NaCl, 10% by weight with respect to the alumina.



Scheme 1

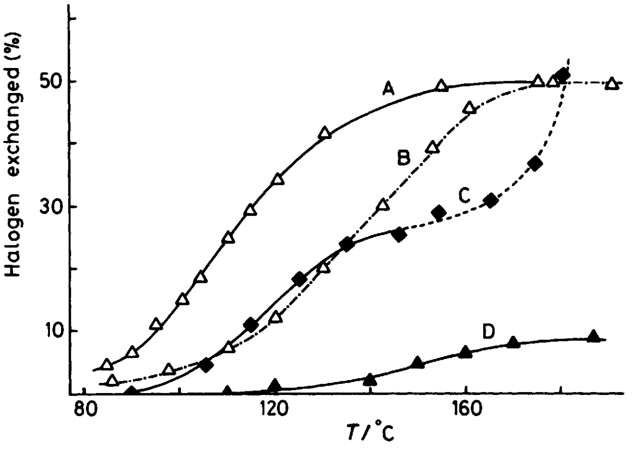


Figure 1. Percentage halogen exchanged in the reaction between CH_2Cl_2 and C_2H_5Br (1 : 2 mole : mole) as a function of the temperature over different catalytic beds (column B): A, basic alumina 90 + 10% (w/w) $Bu_4P^+Br^-$; flow rate, 0.7 ml min^{-1}; B, basic alumina 90 + 10% (w/w) $Bu_4P^+Br^-$; flow rate, 3.3 ml min^{-1}; C, acidic alumina 90; flow rate, 0.7 ml min^{-1}; at 145 °C generation of hydrogen halides is observed, HCl : HBr (6 : 1, mole : mole, dashed curve); D, basic alumina 90; flow rate, 3.3 ml min^{-1}

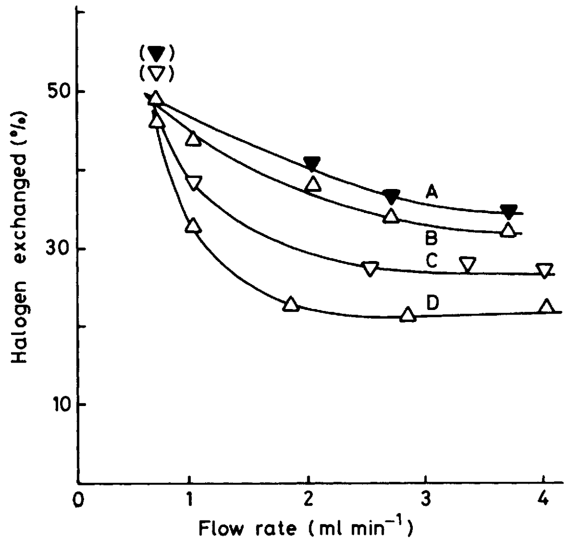


Figure 2. Percentage halogen exchanged in the reaction between CH_2Cl_2 and RBr as a function of the reagents' flow rate, over different aluminas coated with 10% (w/w) of $Bu_4P^+Br^-$: A, basic alumina 150; R = n-C_4H_9; B, basic alumina 90; R = C_2H_5; C, basic alumina 60; R = n-C_4H_9; D, neutral alumina 90; R = n-C_3H_7

in column B, filled with solid bed, with or without phase-transfer catalyst.

Figure 2 shows conversion at 150 °C as a function of the reagent flow over the column A, for various reagents and catalytic beds.

After the reaction, the catalytic beds were analysed for the presence of halides and their ratio (in this case Cl^- and Br^-). Note that in the absence of phase-transfer catalyst, the data reported in Table 2 represent the effective halogen ratio during the process. However, in the presence of phosphonium salt catalyst, this ratio and the partitioning of the halogen ions between the organic and inorganic phases are of necessity constant during the reaction, while they change during cooling and separation of the catalyst following fast partition phenomena. Therefore, analysis of Q^+X^- (not reported) always shows only $X^- = Br^-$ in the case of R^1Cl-R^2Br interconversions and $X^- = I^-$ for R^1Cl-R^2I and R^1Br-R^2I interconversions.

According to the manufacturer's specifications, the alumina had a very low Cl^- concentration. This analysis was confirmed: basic and neutral alumina contained $Cl^- < 0.004\%$, while acidic alumina contained *ca.* 0.2% Cl^-.

The high halide content on the support during the reaction

Table 2. Halide content of different catalytic beds after Cl–Br exchange reactions

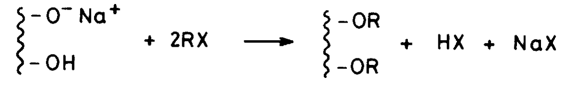
Catalytic bed	Halide content [a]	
	Cl^-	Br^-
Basic alumina 90 [b]	0.13	0.23
Neutral alumina 90 [b]	0.23	0.27
Acidic alumina 90 [c]	0.20	0.41
Basic alumina 60 [b]	0.22	0.33
Neutral alumina 90 + $Bu_4P^+Br^-$ [b,d]	0.04	0.05
Basic alumina 60 + $Bu_4P^+Br^-$ [b,d]	0.24	0.35
Basic alumina 150 + $Bu_4P^+Br^-$ [b,d]	0.18	0.11

[a] The values are expressed as mmol Hal⁻ per g of support. [b] Bed employed in the catalytic interconversion CH_2Cl_2–n-C_4H_9Br. [c] Bed employed in the catalytic interconversion CH_2Cl_2–n-C_3H_7Br. [d] Catalyst 10% by weight with respect to the inorganic support.

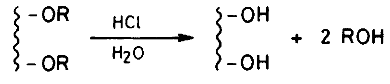
Table 3. Catalytic halide interconversion of n-C_3H_7X–CH_3I into n-C_3H_7I–CH_3X in the presence of different catalytic beds [a]

Catalytic bed	% Halogen exchanged [b]	
	n-C_3H_7Cl	n-C_3H_7Br
Basic alumina 90	35	33
Neutral alumina 90	41	33
Acidic alumina 90	*c*	*c*
Basic alumina 90 + $Bu_4P^+Br^-$ [d]	44	39
Neutral alumina 90 + $Bu_4P^+Br^-$ [d]	44	37
Acidic alumina 90 + $Bu_4P^+Br^-$ [d]	42	31

[a] T = 150 °C; reagent flow rate, 0.7 ml min⁻¹; column A. [b] Calculated on the basis of equation (4). [c] Generation of HX takes place. [d] Catalyst 10% by weight with respect to the inorganic support.



Scheme 2



Scheme 3

is a consequence of Scheme 2, in which surface hydroxy-groups react with the alkyl halide. The occurrence of the reaction in Scheme 2 was demonstrated as follows. 1-Bromo-octane (50 ml) was introduced at reduced pressure (20 Torr) at a flow rate of 0.7 ml min⁻¹ to column A thermostatted at 150 °C containing basic alumina 150 (200 g). After cooling and removal from the column, the bed was washed with diethyl ether to eliminate any traces of adsorbed organic bromide and then titrated potentiometrically to confirm the presence of NaBr. The bed was hydrolysed with 1N-HCl (150 ml) for 15 h. After filtration and washing with diethyl ether, the aqueous phase was extracted with diethyl ether, and the combined extract was dried and evaporated to dryness. G.l.c. and ^1H n.m.r. analysis showed only the presence of octan-1-ol as hydrolysis product, in accord with Scheme 3.

R^1Cl–R^2I *and* R^1Br–R^2I *Interconversions.*—These exchanges were run with methyl iodide as iodide source and 1-chloropropane or 1-bromopropane as counterpart. Table 3 reports the conversions observed for a molar ratio CH_3I : PrX = 1, using basic, neutral, or acidic alumina 90 as support, with or without the phosphonium salt. The conversions were measured using ^1H n.m.r. by integration of the triplet signals (partially overlapping in Br–I exchanges) from $-CH_2-X$ and $-CH_2-I$, after calibration with standard mixtures. Equation (4) was used to calculate the conversion. All the reported

$$\% \text{ halogen exchanged} = \frac{\text{area}_{\text{PrI}}}{\text{area}_{\text{PrI}} + \text{area}_{\text{PrX}}} \times 100 \qquad (4)$$

conversions were measured when the reaction was at equilibrium, that is when the product composition no longer varied due to exchange with the original anion of the phosphonium salt. In the case of Cl–I exchange, conversions were constant and no additional methyl bromide (from exchange between methyl iodide and the anion from the catalyst tetrabutylphosphonium bromide) was observed after reagent mixture (50 ml) had been passed over solid bed (200 g).

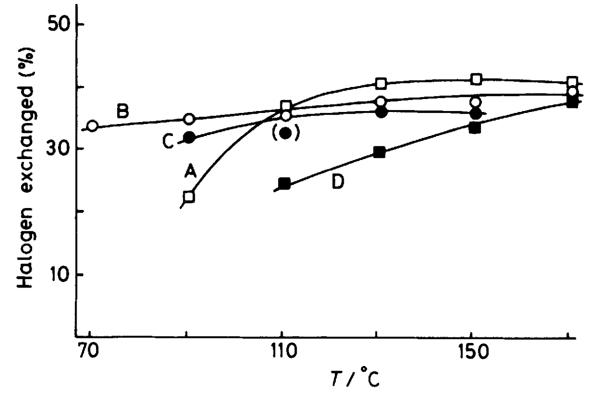


Figure 3. Percentage halogen exchanged in the reaction between CH_3I and n-C_3H_7X, as a function of the temperature over different catalytic beds (column B), at a reagent flow rate of 0.7 ml min⁻¹: A, basic alumina 90 + 10% (w/w) $Bu_4P^+Br^-$; X = Cl; B, basic alumina 90 + 10% (w/w) $Bu_4P^+Br^-$; X = Br; C, basic alumina 90; X = Cl; D, basic alumina 90; X = Br

Figure 3 shows conversions at a constant flow rate (0.7 ml min⁻¹), as a function of temperature, for basic alumina 90 support with and without phosphonium salt, on column B.

Figure 4 shows conversions at 150 °C as a function of reagent flow rate for three different catalyst beds, on column A. After the Cl–I and Br–I exchange reactions, the halogen content of the inorganic beds was measured potentiometrically as in the case of Cl–Br exchange. The results are reported in Table 4 (see observations for Table 2).

Table 5 shows the thermodynamic equilibrium of the reaction between two alkyl halides. The data reported in Table 5 were obtained either in the liquid system or in g.l.-p.t.c. conditions starting from both sides of equation (2).

The synthetic validity of the method was tested for the synthesis of chloroiodomethane and di-iodomethane from 1 : 1 and 1 : 4 molar ratios, respectively, of methylene dichloride and methyl iodide (see Experimental section). The physical properties of the chloroiodomethane and di-iodomethane isolated were compared with the literature values. Thus the process reported in Figure 5 is realistic. It involves industrial production of chloroiodomethane with a continuous catalytic process, with a pair of catalytic and distillation columns.

Table 4. Halide content of different catalytic beds after Cl–I and Br–I exchange reactions

	Halide content [a]			
Catalytic bed	Br^-	I^-	Cl^-	I^-
Neutral alumina 90	0.21	0.03 [b]	0.44	0.01 [c]
Basic alumina 90 + $Bu_4P^+Br^-$ [c,d]			0.35	0.04
Neutral alumina 90 + $Bu_4P^+Br^-$ [d,e]			0.39	0.01
Acidic alumina 90 + $Bu_4P^+Br^-$ [c,d]			0.23	0.04

[a] The values are expressed as mmol Hal^- per g of support. [b] Bed employed in the catalytic interconversion n-C_3H_7Br–CH_3I. [c] Bed employed in the catalytic interconversion n-C_3H_7Cl–CH_3I. [d] Catalyst 10% by weight with respect to the inorganic support. [e] Bed employed in the catalytic interconversion CH_2Cl_2–CH_3I.

Table 5. C_2H_5X–n-C_4H_9Y Halide interconversion under g.l.–p.t.c. and homogeneous conditions [a]

	Composition of the reaction mixture at equilibrium [b]	
Reaction	G.l.–p.t.c. conditions [c]	Homogeneous conditions [d]
C_2H_5Br + n-$C_4H_9I \longrightarrow$	48.0	48.2
C_2H_5I + n-$C_4H_9Br \longrightarrow$	47.9	48.2

[a] For the reaction procedure see Experimental section. [b] Calculated as 100 × [BuBr + EtI] : [BuBr + EtI + BuI + EtBr]. [c] At 150 °C. [d] At 25 °C; without solvent; $C_{16}H_{33}P^+Bu_3Br^-$ as catalyst.

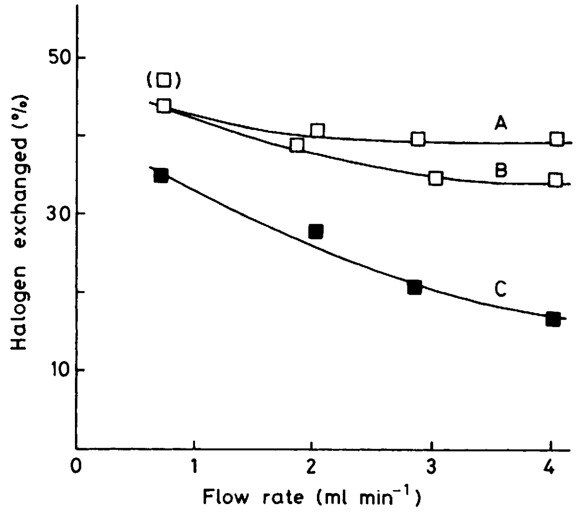


Figure 4. Percentage halogen exchanged in the reaction between CH_3I and n-C_3H_7Cl over different catalytic beds (column A), as a function of the reagent flow rate at 150 °C: A, neutral alumina 90 + 10% (w/w) $Bu_4P^+Br^-$; B, basic alumina 90 + 10% (w/w) $Bu_4P^+Br^-$; C, basic alumina 90

Discussion

As shown by the reported results, high reaction rates can be achieved when the Finkelstein reaction is run on porous solids, because of the large surface area of the inorganic supports and the anionic activation arising from the presence of the phase-transfer catalyst as well as the nature of the support.

Mechanistic aspects of the Finkelstein reaction have been studied thoroughly, involving the presence of possible equilibria, the effect of the entering and leaving groups, the polarity of the reaction medium, *etc.*[4] Therefore, this reaction was used in the study of phase-transfer catalysis in order to evaluate the effectiveness of the various catalysts. Bulky organic cations, the solvent, and the presence (l.l.-p.t.c.) or absence (s.l.-p.t.c.) of water dramatically affect anion reactivity to make them more or less ' naked '.[5]

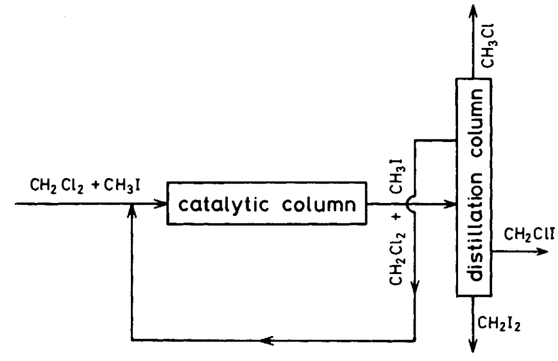


Figure 5. Possible industrial plant for the continuous and simultaneous production of CH_2ClI and CH_2I_2 with a pair of g.l.-p.t.c. and distillation columns. If one only of these exchange products is desired, the other methylene compound can be recycled with the unchanged CH_2Cl_2 and CH_3I through the catalytic column; in this case the molar ratio of the fresh CH_2Cl_2 + CH_3I mixture will be a function of the achieved conversion

Anion activation also occurs when the nucleophile source is a salt dispersed as a solid solution in a porous inorganic solid like silica gel or alumina;[6] alumina is more effective at promoting nucleophilic substitution reactions than silica gel, especially if alumina is functionalized with alkyl chains which have functional groups and play the role of the aprotic polar solvents used in classical synthesis.[7]

Alkyl halide interconversion reactions [equation (2)] have not been reported under phase-transfer conditions, where the major focus has been on reactions with an aqueous solution providing a nucleophile [equation (5)].

$$RX_{\text{liquid,org.}} + M^+Y^-_{\text{aqueous}} \xrightarrow{\text{cat}} RY_{\text{liquid,org.}} + M^+X^-_{\text{aqueous}} \quad (5)$$

Under these conditions, the reaction reaches thermodynamic equilibrium following pseudo-first-order kinetics. The said equilibrium depends mainly on the thermodynamic stability of X^- and Y^- in the aqueous phase. By definition, the catalyst does not affect the position of the equilibrium which is shifted to the right for Y = I (X = Cl, Br) and Y = Br (X = Cl) due to the different aqueous solvation of the anions involved.[8] The situation is of course quite different in the presence of two mutually exchanging alkyl halides as in equation (2). In this case, the equilibrium depends on the thermodynamic stabilities of the four compounds since they are all in the liquid or gas phase; in fact, the position of the thermodynamic equilibrium does not differ much under g.l.-p.t.c. conditions from the liquid phase (Table 5). Moreover, in g.l.-p.t.c., *i.e.* in an open system, the kinetic equilibrium may also depend on diffusion, partition, and adsorption factors, when the contact time between the reagents and the catalyst phase is not long enough to let the thermodynamic equilibrium be reached.

The effect of diffusion factors on the conversion was shown very clearly when Carbowax 6000 (Table 1), a good catalyst for soft anions like phenoxides and mercaptides under g.l.-p.t.c. conditions,[1e] was present on the surface of the neutral alumina 90. The methylene dichloride–bromoethane reaction rate fell dramatically, evidently because the Carbowax film prevents rapid exchange of the reagents with the catalytic support. Analogously, reduced reaction rates with methylene dichloride were also observed passing progressively from bromoethane to 1-bromopropane and 1-bromobutane (Table 1 and Figure 2). In addition to the intrinsically lower reactivity of long chain alkyl halides in nucleophilic substitution, in this case adsorption and partition phenomena also reduce reaction rates by increasing the time RX remains on the support and so decreasing the exchange rate.

Reactions in the Presence of a Phase-transfer Catalyst.—At a given mass of the catalytic bed, interconversion of the alkyl halides is a function of the type of reaction, the nature of the bed, and the temperature. Moreover, the mass of the catalytic bed and the reagent flow rate inversely affect the reaction rate: higher conversions are achieved if, through a given catalytic mass, the reagent flow is reduced (Figures 2 and 4), while the conversions increase as a function of the catalytic mass at a constant reagent flow (compare data in Table 1, obtained with column A, with data in Figure 1 obtained with column B).

In any case, the reported conversions attain a plateau whose value may be lower than that expected on the basis of the thermodynamic equilibrium; an increase of the reaction temperature does not considerably affect the achieved kinetic equilibrium (Figures 1 and 3).

For the reaction in Scheme 1, carried out under the same experimental conditions, Figure 1 shows inflections at different temperatures, as a function of the presence or absence of phase-transfer catalyst (compare B with D). This indicates different reaction rates for the two processes, with that occurring in the presence of alumina alone the lower.

Equations (6)—(11) apply in the presence of a phase-transfer catalyst. Equations (6)—(8) refer to the first halide,

$$R^1X_{gas} + Q^+Y^-{}_{liquid} \rightleftharpoons (R^1X + Q^+Y^-)_{liquid} \tag{6}$$

$$(R^1X + Q^+Y^-)_{liquid} \underset{k2}{\overset{k1}{\rightleftharpoons}} (R^1Y + Q^+X^-)_{liquid} \tag{7}$$

$$(R^1Y + Q^+X^-)_{liquid} \rightleftharpoons R^1Y_{gas} + Q^+X^-{}_{liquid} \tag{8}$$

$$R^2Y_{gas} + Q^+X^-{}_{liquid} \rightleftharpoons (R^2Y + Q^+X^-)_{liquid} \tag{9}$$

$$(R^2Y + Q^+X^-)_{liquid} \underset{k4}{\overset{k3}{\rightleftharpoons}} (R^2X + Q^+Y^-)_{liquid} \tag{10}$$

$$(R^2X + Q^+Y^-)_{liquid} \rightleftharpoons R^2X_{gas} + Q^+Y^-{}_{liquid} \tag{11}$$

$$R^1X_{gas} + R^2Y_{gas} \rightleftharpoons R^1Y_{gas} + R^2X_{gas} \tag{12}$$

equations (9)—(11) to the second halide, and equation (12) to the entire process. Equations (6), (8), (9), and (11) are controlled by diffusion, adsorption, and partition of the organic substrates on the melted catalyst. Equations (7) and (10) however are controlled by the nucleophilicity of the anions and the electrophilicity of the organic substrates in the reaction medium, with K_{R^1} and K_{R^2} as equilibrium constants, referred to the first and the second halide respectively [equations (13) and (14) where a is the activity of the reagents

$$K_{R^1} = \frac{a_{R^1Y}a_{Q^+X^-}}{a_{R^1X}a_{Q^+Y^-}} = \frac{k_1}{k_2} \tag{13}$$

$$K_{R^2} = \frac{a_{R^2X}a_{Q^+Y^-}}{a_{R^2Y}a_{Q^+Y^-}} = \frac{k^3}{k_4} \tag{14}$$

in the liquid phase and k is the reaction rate constant].

The greater the affinity of the reagent for the liquid phase (a function of b.p., functional groups, and partial pressure in the gas phase), the longer it will remain in this phase (in dynamic equilibrium) preventing the access of the other gaseous halides. This leads to lower conversions of the latter which, by not charging the catalyst with the anion for the exchange, also slows down reaction of the alkyl halide in the liquid phase for a longer period.

Optimal catalytic bed performance (less catalytic mass for a certain flow) is achieved when equation (15) is satisfied (written for the four halides, with k_i and t_i as rate constants and mean times of the ith reagent on the phase where the reaction occurs). However, when (as generally occurs) equation

$$k_1t_1 = k_2t_2 = k_3t_3 = k_4t_4 \tag{15}$$

(15) does not apply, the flow : mass ratio must be determined as a function of the reagent with the lowest k_it_i value. The fact that a theoretical conversion is not achieved in some cases (Figures 1 and 2), but rather a lower value is established instead, may be related to partition factors of the four alkyl halides and therefore to the k_it_i value. If k_i increases with temperature, the time the ith reagent remains on the support decreases. This demonstrates the similarities of this type of catalysis, both with and without the p.t. catalyst, with gas chromatography: in the latter case, partition between the gas and liquid phase (g.l.c.) or adsorption on the solid one (g.c.) afford compound separation, while in g.l.-p.t.c. they affect the reaction rate.

Reactions in the Absence of a Phase-transfer Catalyst.—The various types of alumina were more active than silica gel in promoting catalytic exchange reactions: this behaviour is undoubtedly due to the differing anion solvation offered by the support. Since this solvation is greater in the case of silica gel, nucleophilic activity is reduced. The data reported in Table 1 are significant in this sense: even in the presence of tetrabutylphosphonium bromide which generally increases the activity of the catalytic bed *ca.* 10-fold, silica gel was less active than alumina. Thus the nature of the phase-transfer catalyst liquid phase is affected by the nature of the underlying inorganic support.

The catalytic activities of the various types of alumina (basic, neutral, and acidic) are due to the presence of Na^+ cations, present on the support as aluminates, which can promote the exchange process in the absence of quaternary phosphonium salt.

The equations in the absence of a liquid phase are those reported above in the case of the phase-transfer catalyst, where Na^+X^- replaces Q^+X^- and partition of the reagents between the gas and liquid phase is replaced by the latter's adsorption processes on the porous support.

The catalytic bed had nearly the same content of halides ($Na^+X^- + Na^+Y^-$; see Table 2 lines 1—4) for the reactions carried out in the absence of the 'onium salt in comparison with that of the reactions run in the presence of the catalyst ($Q^+X^- + Q^+Y^-$; 10% by weight of tetrabutylphosphonium bromide implies 0.30 mmol Br^- per g). Consequently the lower reaction rates in the absence of a phase-transfer catalyst in Figures 1 and 2 indicate that the halide ions' nucleophilic activity is lower in the Na^+Y^- than in the Q^+Y^- form. The fact that added NaCl adsorbed on the alumina had no greater effect on the catalytic activity of the support (Table 1) shows that the reactive anions are only those in the form of low molecular weight non-crystalline aggregates on the surface of the porous support, with weak anion–cation interactions.

The nature of the inorganic matrix is important in determining its activity in these catalytic exchange reactions. The observed differences in activity of acid 90, neutral 90, and basic 90 alumina as well their inversion in the presence and absence of a catalyst are undoubtedly due to the different nature of the respective surfaces (Table 1). The manner in which the surface sites, which as reported in the literature[9] are different in the various types of alumina, affect this catalytic process is currently under study.

Anion Build-up on the Inorganic Supports.—Both in the absence and presence of a phase-transfer catalyst, the alumina becomes charged with anions (Tables 2 and 4). Thus, by analogy with other reactions conducted under g.l.-p.t.c. conditions, in the presence of a nucleophilic salt, Q^+X^- can effect an anion exchange between the liquid phase and the solid phase underneath.

Under operating conditions, the $(R^1Y + R^2X):(R^1X + R^2Y)$ ratio in the gas phase, predetermined by the initial molar ratio of the reagents, is constant in the various sections of the bed and so at the column outlet as well. However, this ratio does not assume the same value in the liquid phase, since the latter value depends on the partitioning of the four products between the two phases.

Under operating conditions, an equilibrium [equation (16)] between the anions is established between the liquid and solid

$$Q^+X^-{}_{\text{liquid}} + Na^+Y^-{}_{\text{solid}} \rightleftharpoons Q^+Y^-{}_{\text{liquid}} + Na^+X^-{}_{\text{solid}} \quad (16)$$

phases. However, its position is not necessarily equal to that of the ratio of the alkyl halides in the gas or liquid phase. Under these conditions the various $Q^+X^- : Na^+X^-$, $Q^+Y^- : Na^+Y^-$, $Q^+X^- : Q^+Y^-$, $Na^+X^- : Na^+Y^-$ ratios (not equal to one another) remain constant during the synthesis, at least for a given section of the bed, and depend on the relative affinities of the anions for the solid and liquid phases. The liquid phase (the phase-transfer catalyst) is a polar aprotic organic phase in which, as in l.l.-p.t.c., affinity for lipophilic anions is very high, leading to high selectivity toward halide anions ($I^- > Br^- > Cl^-$).[10]

On the other hand, the inorganic support shows very low selectivity toward the halide anions, as shown in previous studies of anion exchange of 'onion salts immobilized on silica gel.[11] This may explain the high and competitive levels of Cl^- with respect to Br^- and I^- reported in Tables 2 and 4.

Even in low concentrations, the reactivity of Cl^- during the catalytic process, carried out in the presence of the phosphonium salt should be greater than that of Br^- and I^-, since this reactivity order is found for these anions in the absence of aqueous solvation.

When the I^- anion is involved, a high reaction rate is always observed owing to the weak-medium I^- polar interactions; this fact leads (Figures 3 and 4) to high conversions in the Cl–I and Br–I exchange, even at low reaction temperature and at high reagent flow.

Conclusions.—In addition to offering a catalytic process operational for an indefinite period, the catalytic interconversion of alkyl halides under g.l.-p.t.c. conditions offers the advantage of running in the absence of aqueous and organic solvents. In this way, especially for low molecular weight halides, mixed exchange halides, requiring only fractional distillation to separate them, can be prepared at atmospheric or reduced pressure.

Experimental

All reagents were ACS grade and were used with no further purification. Argentimetric titrations (0.1N-$AgNO_3$) were carried out in water solution on a Metrohm-Herisau Multi Dosimat E-451 potentiometer, with a combined silver electrode in the presence of nitric acid. ^1H N.m.r. spectra were recorded on a Hitachi-Perkin-Elmer R-24B 60 MHz spectrometer, using tetramethylsilane as the internal standard. The gas chromatograph was a Varian series 1440, equipped with a CDS 111L integrator. A Masterflex model no. 7013 peristaltic pump and a Lauda MGW ultrathermostat were used.

Preparation of the Catalytic Beds.—Tetrabutylphosphonium bromide (10% by weight with respect to the solid support) was dissolved in methanol, the inorganic support (alumina or silica gel) was added, and the suspension evaporated to remove the solvent; the resulting solid was dried at 130 °C for 15 h. The same procedure was followed in the case of alumina coated with polyethylene glycol (Carbowax 6000). When the reaction was carried out on alumina supporting NaCl, the salt (10% by weight) was dissolved in a methanol : water (5 : 2) mixture, the alumina was added, and the suspension was then treated as described above. In the case in which the inorganic solid only was employed as catalytic bed, the support was oven-dried at 130 °C for 15 h before the reactions.

The columns were filled with a weighed mass of prepared catalytic bed, and the reagent mixture was introduced at the desired flow into the column thermostatted at a given temperature.

R^1Cl–R^2Br *Interconversions.*—1 : 2 Molar mixtures were prepared from CH_2Cl_2 (160 ml) and C_2H_5Br (373 ml), n-C_3H_7Br (454 ml), or n-C_4H_9Br (537 ml). The chemical shifts of the methylene singlets were $\delta(CCl_4)$ 5.28 (CH_2Cl_2), 5.16 (CH_2ClBr), and 4.92 (CH_2Br_2).

R^1Cl–R^2I *and* R^1Br–R^2I *Interconversions.*—1 : 1 Molar mixtures were prepared from CH_3I (311 ml) and n-C_3H_7Cl (440 ml) or n-C_3H_7Br (454 ml). The chemical shifts of the methylene triplets were δ (CCl_4) 3.44, 3.34, and 3.15 for CH_2Cl, CH_2Br, and CH_2I, respectively.

$PhCH_2Cl$–n-$C_8H_{17}Br$ *Interconversion.*—Using column B, a 1 : 1 molar mixture of $PhCH_2Cl$ (23.0 ml) and n-$C_8H_{17}Br$ (34.8 ml) was forced to pass within 1.45 h through a catalytic bed (11.0 g) consisting of basic alumina 90 and $Bu_4P^+Br^-$ (10% by weight) at 150 °C and 20 Torr. The collected reaction mixture, analysed by ^1H n.m.r., showed a 53% halide interconversion, based on the integration of the singlets of $PhCH_2X$, δ (CCl_4) 4.49 (X = Cl) and 4.38 (X = Br).

Synthesis of CH_2ClI.—Using column A, 70.0 ml of a mixture of CH_2Cl_2 (35.5 ml, 0.55 mol) and CH_3I (34.5 ml, 0.55 mol) were allowed to flow (over 1.75 h) over 200 g of a catalytic bed prepared with neutral alumina 90 and $Bu_4P^+\ I^-$ (10% by weight) at 195 °C and at atmospheric pressure. The collected reaction mixture showed, by ^1H n.m.r. analysis of the CH_2 singlets, 34% CH_2ClI and 9% CH_2I_2. The mixture was then fractionally distilled, affording CH_2ClI (29.3 g, 95% purity, 31% yield, based on CH_2Cl_2), b.p. 108—110 °C at 760 Torr.

Synthesis of CH_2I_2.—Using column B, 50.0 ml of a mixture of CH_2Cl_2 (10.2 ml, 0.16 mol) and CH_3I (39.2 ml, 0.64 mol) were forced over 110 g of a catalytic bed consisting of basic alumina 90 and $Bu_4P^+I^-$ (10% by weight) within 1.25 h, at 190 °C and at atmospheric pressure. The reaction mixture showed 50% CH_2ClI and 36% CH_2I_2, by ^1H n.m.r. analysis of the CH_2 singlets, and after distillation afforded CH_2I_2 (11.3 g, 97% purity, 26% yield based on CH_2Cl_2), b.p. 77—79 °C at 25 Torr.

EtX–BuY *Interconversion*.—A 1 : 1 molar mixture of C_2H_5Br and n-C_4H_9I (37.3 and 56.9, ml respectively) or C_2H_5I and n-C_4H_9Br (40.0 and 53.7 ml, respectively) were introduced into column B, filled with basic alumina 90 coated with $Bu_4P^+Br^-$ (10% by weight), at 150 °C and at atmospheric pressure with a flow of 0.7 ml min^{-1}. Once the exchange process had reached equilibrium, both the reaction mixtures were analysed by g.l.c. (5% SE-30 on Varaport) after calibration with 1 : 1 : 1 : 1 molar standard mixtures of the four alkyl halides.

The same reactions were carried out under homogeneous conditions at 25 °C, with n-$C_{16}H_{33}P^+Bu_3Br^-$ (0.10 mmol) and without solvent, starting in the first case from 10.0 mmol of C_2H_5Br and 10.0 mmol of n-C_4H_9I, and in the second one from 10.0 mmol of C_2H_5I and 10.0 mmol of n-C_4H_9Br. Both the reaction mixtures were analysed after 7 days, and as shown in Table 5, they had reached equilibrium.

Potentiometric Titration.—The ionic halides content of the catalytic beds, for the reactions carried out in the absence of the 'onium salt, was determined by washing the solid support with diethyl ether to eliminate the last traces of alkyl halides and by titrating in aqueous solution a weighed part (1—2 g) of the dried bed.

In the case in which the aluminas were coated with the 'onium salt, a portion of the catalytic bed was stirred for 5 min with methylene dichloride, filtered, and washed with fresh solvent. After the solvent was removed, both the solid and the inorganic residuc were separately titrated.

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