Continuous Conversion of Alcohols into Alkyl Halides by Gas–Liquid Phase-Transfer Catalysis (G.L.–P.T.C.)

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A solution of a primary alcohol (propan-1-ol, butan-1-ol, and pentan-1-ol) in an aqueous halogen acid (hydrochloric or hydrobromic acid) when passed in the gaseous state over a solid porous bed (silica gel) supporting a catalyst, affords the corresponding alkyl halide. The reagent mixture is introduced continuously into a column maintained at 170 °C and the product is collected at the outlet. Since the process is catalytic, the bed is not consumed during the reaction. The reaction by-products depend on the type of catalyst used: Lewis acids (ZnCl$_2$, AlCl$_3$) lead to large quantities of alkenes and isomeric halides, while under typical g.l.–p.t.c. conditions, with a phosphonium salt as the catalyst, only the corresponding dialkyl ether, in addition to the primary alkyl halide, is obtained. The yield of the ether can be reduced progessively to zero by increasing the contact time between the reaction mixture and the catalytic bed.

The conversion of alcohols into the corresponding alkyl halides may be carried out with various types of catalysts, the most important of which are Lewis acids. However, as is shown by the Lucas test, in the case of primary alcohols this is a very slow reaction. Moreover, since the reaction mechanism involves a more or less free carbocation, considerable quantities of rearranged alkyl halides and alkenes are produced along with the primary alkyl halide.
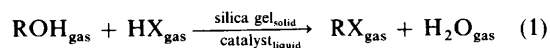
Recently it has been shown that the presence of a phase-transfer catalyst (a quaternary phosphonium salt) greatly increases the reaction rate when a water-insoluble alcohol is refluxed in aqueous hydrochloric acid under liquid–liquid phase-transfer catalysis (l.l.–p.t.c.) conditions.[1]

As regards p.t.c.,[2] depending on the phases present during the reaction, one can distinguish l.l.–p.t.c. (two liquid phases), solid–liquid phase-transfer catalysis (s.l.–p.t.c., one solid and one liquid phase), and gas–liquid phase-transfer catalysis (g.l.–p.t.c., one gas and one liquid phase). In the latter method,[3] both reagents and products are in the gaseous state.

This report describes an unusual example of anion activation involving protonation in an acidic medium, under g.l.–p.t.c. conditions: the continuous conversion of water-soluble alcohols into the corresponding alkyl halides, by means of the appropriate aqueous halogen acid.

Results and Discussion

Under g.l.–p.t.c. conditions, this reaction was run by passing the reagent mixture in the gaseous state through a column containing the solid bed on which the catalyst had been deposited [Equation (1)].

$$ROH_{gas} + HX_{gas} \xrightarrow[\text{catalyst}_{\text{liquid}}]{\text{silica gel}_{\text{solid}}} RX_{gas} + H_2O_{gas} \quad (1)$$

Since both the reagents and products have to be in the gaseous state during the reaction, the process must be carried out under suitable temperature and pressure conditions. In our case, a solution of the alcohol in an aqueous halogen acid in the liquid state was passed continuously, at a constant rate, over a solid bed contained in a column maintained at 170 °C, at which temperature the reaction mixture became gaseous at atmospheric pressure, before flowing through the solid bed. The gaseous products were condensed at the outlet and collected.

Table 1. Continuous conversion of butan-1-ol into 1-chlorobutane with aqueous 35%-HCl under g.l.–p.t.c. conditions[a]

| Catalytic bed	Collected organic phase (g)[b]	1-Chlorobutane in organic phase (%)[c]
Silica gel	0	0
Silica gel + 15% Carbowax 6000	0	0
Silica gel + 5% TsOH	0	0
Silica gel + 5% ZnCl$_2$	6.6	50[d]
Silica gel + 5% AlCl$_3$	1.7	78[e]
Silica gel + 5% Bu$_4$P$^+$Br$^-$ [f]	2.9	83[g]

[a] A mixture of butan-1-ol and aqueous 35%-HCl (1:3, mol:mol) was introduced with a peristaltic pump (liquid flow, 30 ml h^{-1}; atmospheric pressure) into the reaction column containing 50 g of catalytic bed and thermostatted at 170 °C. [b] Determined on 40.0 ml of the reagent mixture (100% conversion corresponds to 11.2 g of 1-chlorobutane). [c] By g.l.c. analysis, by comparison with authentic samples. [d] No conversion was observed when the reaction was carried out under reduced pressure (20 Torr). This fact means that a high partial pressure of the reagents on the catalytic bed must be achieved to promote the reaction. By-products: alkenes (26%); 2-chlorobutane (23%). [e] By-products: alkenes (15%); 2-chlorobutane (7%). [f] Prepared according to M. Grayson and P. T. Keough, *J. Am. Chem. Soc.*, 1960, **82**, 3919. [g] By-products: alkenes (1%); Bu$_2$O (16%).

Table 1 reports the results for the conversion of butan-1-ol into 1-chlorobutane over a bed of silica gel containing different types of catalyst.

The reaction was not promoted by the solid silica gel (pure or coated with an organic acid (toluene-*p*-sulphonic acid), or with a phase transfer catalyst of low activity [poly(ethylene glycol)]. However, it was promoted by either Lewis acids or by a phosphonium salt. Furthermore, different catalysts give different by-products in addition to 1-chlorobutane: with tetrabutylphosphonium salts, the main by-product of the reaction is dibutyl ether, while with zinc or aluminium salts both alkenes and the isomeric chlorobutane are obtained.

Comparing these results to previous reports,[4] it may be observed that in the case of the phase transfer catalyst, none of the classical by-products of a carbocation intermediate is obtained. Therefore, the reaction probably occurs by an S$_N$2-type nucleophilic substitution of –OH$_2^+$ by X$^-$ [Equation (2)].

$$RCH_2O^+H_2 + Q^+HCl_2^- \longrightarrow$$
$$RCH_2Cl + Q^+Cl^- + H_3O^+ \quad (2)$$
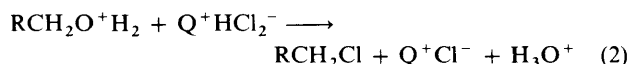
Table 2. Continuous conversion of RCH_2OH into RCH_2Cl with aqueous 35% HCl under g.l.–p.t.c. conditions[a]

| RCH$_2$OH	Collected organic phase (g)[b]	RCH$_2$Cl in the organic phase (%)[c]	Yield (%)
Propan-1-ol	9.1	94	80
Butan-1-ol	11.5	95	87[d]
Pentan-1-ol	14.5	91	99

[a] For experimental conditions, see the Experimental section. [b] Determined after 0.15 mol of the alcohol had passed over the catalytic bed. [c] By g.l.c. analysis: by-products: dipropyl ether (5%); dibutyl ether (4%); dipentyl ether (7%) respectively. [d] The n_{20}^D value determined on the crude BuCl was 1.4008, corresponding to that of an authentic sample.

In agreement with Dehmlow's results under l.l.–p.t.c. conditions,[5] the onium salt can even carry acid molecules into the organic phase through the formation of a $Q^+X^- \cdots HX$ type complex, and so protonate the alcohol.

In the case of tetrabutylphosphonium salts, increasing the time spent by the reagents in the column (by decreasing the flow rate of the reagents, or by using a larger quantity of catalytic bed) increased the conversion rate and altered the composition of the reaction mixture. In fact, the results reported in Table 2, obtained under optimized conditions (with a larger amount of catalytic bed and a lower flow rate, in comparison with those of Table 1) indicate that for butan-1-ol the reaction proceeded with higher conversion, free from alkenes and with a lower percentage yield of dialkyl ether.

If the reaction time is sufficiently long, in the presence of the phosphonium salt (which is stable at high temperatures) the primary alkyl halide is formed in high yield and without the dibutyl ether by-product.*,[6] In fact, the formation of the alkyl halide from the corresponding alcohol is not a reversible reaction under acidic conditions, while ether formation is [Equation (3)].

$$RCH_2O^+H_2 + RCH_2OH \rightleftharpoons \overset{\overset{\displaystyle H}{\displaystyle |}}{RCH_2O^+CH_2R} + H_2O \quad (3)$$
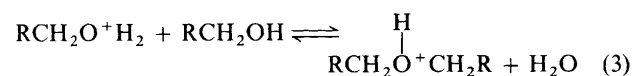
This was shown experimentally by passing, under the conditions reported in Table 1, dibutyl ether and hydrochloric acid through the catalytic column containing a tetrabutylphosphonium salt: only 1-chlorobutane was produced [Equation (4)].

$$\overset{\overset{\displaystyle H}{\displaystyle |}}{RCH_2O^+CH_2R} + Q^+HCl_2^- \longrightarrow RCH_2Cl + Q^+Cl^- + RCH_2O^+H_2 \quad (4)$$
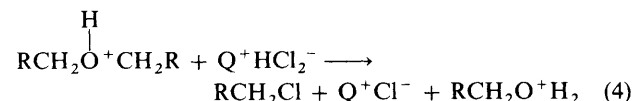
The fact that the use of a phase transfer catalyst leads to different reaction pathways than those observed with a Lewis acid may be attributed to the fact that under g.l.–p.t.c. conditions the reaction occurs in the organic phase of the molten Q^+X^- salt, on which the reagents and products are adsorbed in dynamic equilibrium from the gas phase. The presence of the aprotic liquid phase (from which comes the term g.l.–p.t.c.) that does not solvate ionic species, changes the reaction mechanism by increasing the anionic activation of the entering halide.

The process described allows the conversion of primary alcohols into the corresponding alkyl halides with no rearrangement, and the product may be isolated by simple separation of the two collected phases since there is no solvent used. The process is continuous and requires no stirring, may be run at atmospheric pressure and, since the solid catalytic bed is not consumed during the reaction, it shows no loss of activity even after 18 h of continuous use.

Experimental

Gas chromatographic analyses were carried out on a Varian Series Vista mod. 6000 apparatus, equipped with a CDS 111L integrator. A Lauda MGW ultrathermostat was used. The silica gel used was Merck art. 7734; all organic and inorganic reagents were ACS grade and were used without further purification.

Preparation of the Catalytic Bed.—In all the cases the catalytic bed was prepared by dissolving the catalyst in methanol, adding silica gel to the solution and removing the solvent under vacuum; the solid mass obtained was then oven dried at 130 °C for 5 h. The percentages given for the catalysts are weight for weight.

G.L.–P.T.C. Conversion of Alcohols into Alkyl Halides; Typical Procedure.—1-Chlorobutane. The double-jacket reaction column (50 cm in length, 1.5 cm in diameter) was filled with the catalytic bed (250 g) (catalyst Bu_4P^+, 15% by weight on silica gel); the reaction temperature and pressure were 170 °C and atmospheric respectively. A 1:3 molar mixture of butan-1-ol (11.1 g, 0.15 mol) and aqueous HCl (35%; 38.8 ml) was introduced by means of a peristaltic pump (liquid flow, 21.0 ml h^{-1}). At the end of the reaction two distinct liquid phases were collected at the column outlet: the product alkyl halide and the exhausted aqueous acid. The organic product (11.5 g) was isolated by separating the two phases and was analysed by g.l.c. analysis, and showed a 95% content of 1-chlorobutane (87% yield).

Acknowledgements

References

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* Because of the higher nucleophilicity of Br$^-$ in a protic solvent, the conversion of alcohols into alkyl halides is faster with aqueous HBr than with HCl.[6] Butan-1-ol was converted (98%) into 1-bromobutane by passing a 1:3 (mol:mol) mixture of the alcohol and 48% aqueous HBr over 50 g of silica gel coated with $Bu_4P^+Br^-$ (catalyst 15% by weight; column temperature 170 °C; reagent flow rate 140 ml h^{-1})