

GAS-LIQUID PHASE-TRANSFER CATALYSIS (GL-PTC)

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INTRODUCTION

Liquid catalysts supported on solids and promoting reactions in gas phase are a quite old technique in chemical industry, as many important processes are included in this category. Because of its versatility and simplicity, and due to the fact that the catalyst preserves the original structure it had in homogeneous solution, increasing attention is directed towards reactions performed under such conditions, namely under Supported Liquid-Phase Catalysis (SL-PC) [1].

The SL-PC catalysis is widely used in industry; for example in vanadia-melt oxidations (i.e., $\text{SO}_2 \rightarrow \text{SO}_3$), in supported phosphoric acid alkylations (i.e., ethylbenzene and cumene production), in ethylene oxychlorination (Deacon process) and also in hydroformylation reactions (isobutyraldehyde from propene) [2]. It is expected that SL-PC conditions will be applied in other reactions and other configurations, such as those in which membranes can be used as supports for selective transport processes.

The most important restriction in SL-PC reactions is that only relatively small molecules can be reacted since they have to be transferred in gas phase and no highly boiling compounds have to be formed neither as products nor as by-products.

Continuous flow (c.f.) operations with anions as the reagents are ideally possible in the gas phase. Regrettably, the gas phase results are of little practical importance since they can only be achieved under high vacuum conditions as exist in mass spectrophotometers. Similarly, the observed reaction rates of flowing gaseous organic substances over a solid salt would be very low because of the relatively small surface of the solid; moreover, the generally high fusion point of alkaline metal salts heavily limits

the possibility of work in the presence of fused salts [3]. Nevertheless, reactions involving anions in the gas phase are reported to occur at a high rate [4], close to diffusion-controlled limits, and may follow unusual reaction pathways which originate from the absence of solvation of the anions [5-6]. As a striking example it is known that acidity and basicity scales differ very much in gas phase and in solution [7-8] and bimolecular nucleophilic substitutions occur in the range of 10^7 - 10^{15} times faster in the gas phase than in solution [9-10].

Gas-liquid phase-transfer catalysis (GL-PTC) overcomes the problems of allowing reactions between activated anions and gaseous organic substrates in a c.f. operation. It has its basis in the well-known principles of PTC; the catalyst provides anion exchange with the aqueous phase and anion activation in the organic phase is ensured by a low-polarity solvent and by the weak cation-anion interactions. GL-PTC allows new systems to be studied [11 a-c]; it uses an actual PT catalyst immobilized on a solid bed and carries out the reaction with the reagents and the products in the gas phase; promoters of such syntheses are appropriate PT catalysts, as liquid under the reaction conditions, able not only to solubilize the salt but also to confer high anion activation and to promote anion exchange with the solid bed.

In order to provide a larger surface area to gas phase, the solid supporting the catalyst has to be porous. Many solid supports (like alumina and silica gel) contain hydroxyl groups on their surface; their interaction with the liquid film of the catalyst may produce a protic environment which will solvate the anion, conditions not suitable for their activation and therefore their use should be avoided. α -Macroporous alumina spheres (surface area in the range of 0.01 - 1 m^2/g), or small glass spheres have been

preferred [12].

Simple reactors have been employed in GL-PTC. They are constituted by a cylindrical column containing the solid support; at its entrance a compartment is present where the liquid reagents become gaseous. The apparatus is kept at the desired temperature by a continuous circulation of thermostatted oil, heated by an external device. Continuous flow was ensured by sending the liquid mixture of reagents into the column by a metering pump. Gaseous products were collected at the outlet of the column by a condenser (Fig. 1).

For high boiling compounds it is necessary to operate under suitable vacuum conditions. Otherwise substrates having a boiling point higher than the temperature used during the synthesis may be kept in the gaseous phase by compounds acting as carriers; such compounds can be either inert gases or low-boiling organic solvents. Sometimes the carrier can be an excess of the reagent itself, as in the case of the reaction using dimethyl carbonate.

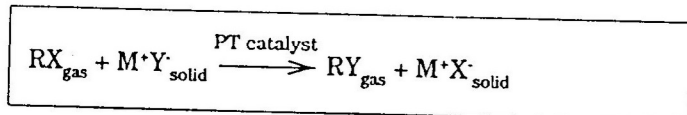
In GL-PTC systems, as usually for PTC, the more lipophilic anions are selectively transferred into the organic phase. Furthermore, phosphonium salts are more efficient than crown ethers and PEGs in carrying out the transfer process between the solid salt and the liquid organic phase [13] (See reactions 2 and 3).

In general, catalyst efficiency in GL-PTC follows the order: phosphonium salt > crown ethers > PEGs; such a trend is in agreement with SL-PTC, where the catalyst must involve anionic exchange with a solid salt to be regenerated.

METHODS IN GL-PTC

There are two main ways in which GL-PTC reactions may be classified:

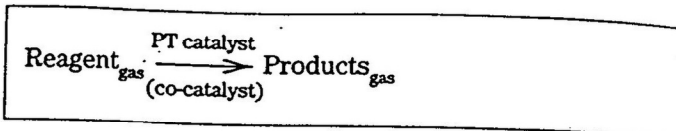
- *Reactions with reactive beds.* A gaseous reagent is reacted with a solid salt; gaseous products leave the reactor; the reagent solid salt is transformed into a new, solid product (Scheme 1):



Scheme 1

- *Reactions with catalytic beds.* Gaseous reagents are transformed into gaseous products by flow over a catalytic solid bed (Scheme 2):

tic solid bed (Scheme 2):



Scheme 2

A catalytic bed does not alter with time and, in principle, reactions can be performed indefinitely under effective c.-f. conditions. It should be noted, however, that the use of catalytic beds can not be accomplished under classical PTC conditions if the catalyst is not chemically immobilized.

GL-PTC provides four behaviour types of catalysis in which anion activation is involved. The first two cases work with reactive beds (Scheme 1); in the last two cases a catalytic bed promotes the reaction (Scheme 2).

REACTIONS WITH ALKALINE METAL SALTS

They occur *via* the transfer of reactive anions from a solid phase; deficiency in solvation in the organic phase allows the anions to be very active in S_N2 type reactions. In the absence of any stirring (plug flow reactor) small amounts of molten PT catalyst (usually 0.5 - 5% molar equivalents) are able to promote the reaction of the wholly solid salt: during the reaction, the catalyst moves from the original surface to the inner core of the crystals. Powerful PT catalysts such as quaternary phosphonium salts are required.

BASE MEDIATED REACTIONS

A base, present on the solid bed in stoichiometric quantities, acts as a mediator in producing the actual nucleophile; this latter, in turn, undergoes the nucleophilic displacement. The base is usually an alkaline carbonate; acidic compounds can be phenols, mercaptans, malonic acid esters and comparable CH-acidic compounds. This method is suitable for generating anions of pK_a up to 13 (starting from K_2CO_3 as a base). The catalyst for these types of reactions is PEGs because soft anions are mostly involved.

CONTINUOUS-FLOW PROCESSES IN NEUTRAL AND ACIDIC MEDIA

Activated halide anions react with alkyl halides [14] or protonated alcohols [15] yielding an alkyl halide.

Phosphonium salts, coated on macroporous solid supports, are the catalysts. In the first case, the reaction is an equilibrium-type reaction (thermodynamic equilibrium is reached); in the second case, the reaction is entirely shifted towards the products.

CONTINUOUS-FLOW PROCESSES IN THE PRESENCE OF BASES AS CO-CATALYSTS

PEGs are effective catalysts in this type of reactions. For example, the transesterification reaction is readily accomplished under gaseous c.-f. conditions in the presence of K_2CO_3 as a co-catalyst. Of particular relevance are the reactions of dialkyl carbonates; they behave as alkylating agents under GL-PTC conditions, by shif-

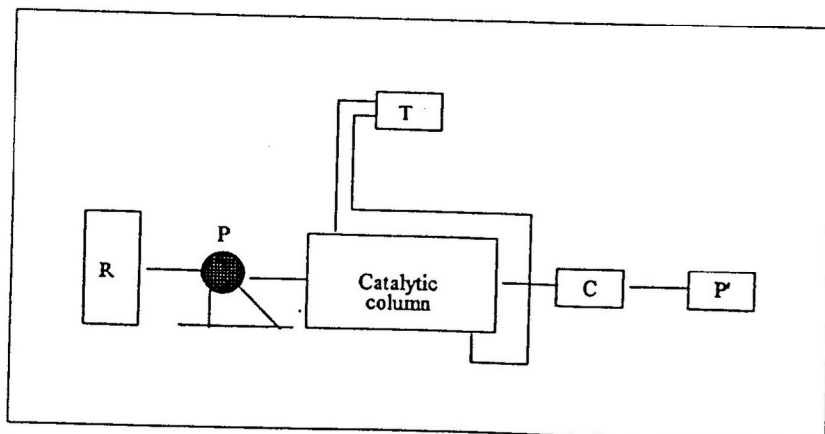


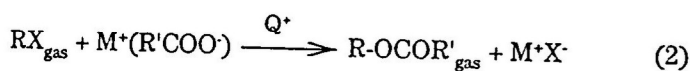
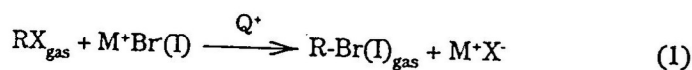
Fig. 1 - GL-PTC apparatus. R: reagent's reservoir; P: metering pump; T: thermostat; C: condenser; P': product store

ting the attack of the base-produced anions to the saturated carbon of the organic carbonate. The fact that the leaving group (methoxycarbonate anion, CH_3OCOO^-) is not stable and spontaneously decomposes into methanol and CO_2 makes the reaction catalytic (i.e. methoxide regenerated). Some reactions already carried out by GL-PTC are reported below.

REACTIONS CARRIED OUT IN GL-PTC: REACTIVE BEDS

ALKYL HALIDES AND ESTERS

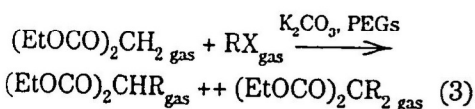
By passing alkyl halides through beds composed of alkali-metal halides, (M^+Br^- , M^+I^-) or carboxylates ($\text{M}^+\text{R}'\text{COO}^-$) and a phosphonium salt, as a PT catalyst, reactions (1) and (2) take place.



The quantity of alkyl halide fed to the reactor was near to the stoichiometric amount of the salt present on the bed. Catalyst (Q^+) concentration ranged from 0.01 to 0.05 molar equivalents to the salt. No solvent was used, so that essentially pure alkyl halides or esters were obtained [16]. The reaction does not proceed at all in the absence of a catalyst or if that catalyst melts at a higher temperature than those used in the reaction; moreover PEGs are not active with such a hard anion, nor are polyoxyethylene units containing a long alkyl chain as in Brij 35 [$n\text{-C}_{12}\text{H}_{25}(\text{OCH}_2\text{CH}_2)_{23}\text{OH}$]. With a column 50 cm in length and 2.5 cm in diameter it was possible to obtain, in about 35 min., 0.2 moles of alkyl iodides.

ALKYL ARYL ETHERS, THIOETHERS AND MALONIC ESTERS

It would be difficult to carry out reactions with anions having too high pKa values, because extensive handling may not be tolerated during the preparation of the reactive bed. This difficulty is overcome by the observation that alkyl halides react only very slowly with inorganic carbonates to produce organic carbonates: this opens the way to the use of carbonates in reactions in which, by loss of carbon dioxide, they behave as a source of bases. Accordingly, when phenol, thiols [17] or weak CH-acidic compounds such as malonate esters [18] and an alkylating agent is allowed to go through a bed composed of K_2CO_3 and PEGs or crown ethers as catalysts, the corresponding alkylated products leave the reactor; eq. 3 shows the reaction of malonate esters. In this case reactions were performed under moderate vacuum (about 20 torr).



In all cases potassium carbonate was able to produce anions having a higher pKa, up to ca. 12. In the absence of water K_2CO_3 increases its basicity by several orders of magnitude and, in addition,

PTC increases its basicity by improving anionic activation; this is so in the case of diethylmalonate anion ($\text{CH}_3\text{CH}_2\text{COOCH}^-\text{COOCH}_2\text{CH}_3$, eq. 3) which is usually obtained in solution by reaction with sodium ethoxide.

REACTIONS CARRIED OUT IN GL-PTC: CATALYTIC BEDS

Such reactions are performed by continuously feeding the catalytic bed with the reagent mixtures (Scheme 2); in relation to the reaction involved, the catalyst may vary, but in all cases it is supported on a macroporous solid. In some cases a co-catalyst has to be present, as those reactions occurring in basic or acidic media.

A distinction should be noted, depending on if the reaction involves an equilibrium reaction or if it is entirely shifted toward the products. Examples of the first kind are halogen exchange in alkyl halides and transesterification. The second type of reactions concerns isomerizations reactions, reaction of primary alcohols with hydrochloric acid to give primary alkyl chlorides and, generally speaking, the reactions of dialkyl carbonates.

TRANSHALOGENATION OF ALKYL HALIDES

When a mixture of two different alkyl halides RX and $\text{R}'\text{Y}$ are sent in a gaseous state over a solid bed containing phosphonium salts as catalysts, a very fast halogen exchange occurs (eq. 4) and all the possible halides are collected at the outlet of the reactor [19-20].



The reaction between CH_2Cl_2 and $\text{C}_2\text{H}_5\text{Br}$ (1 : 2 molar ratio) represented in Fig. 2 achieves thermodynamic equilibrium when a statistic distribution of the halides is present in all the compounds. The equilibrium is achieved more or less rapidly, as a function of the catalyst and of the supporting solid. The nature of the supporting solid is a determining factor in promoting the reaction, even when a phosphonium salt is present: this points out that the nature of the liquid phase is directly affected by the nature of the support.

It was found that reaction of Cl^- with RCH_2Br is faster than the reaction of Br^- with RCH_2Cl [12], as shown that, under steady conditions, the counteranion of Q^+ on the liquid catalytic phase was Br^- instead of Cl^- . This fact well agrees with the behaviour of PTC reactions in which, due to the absence of water, anion activation coming from lack of solvation is higher for smaller anions like Cl^- than for bigger ones [21].

TRANSESTERIFICATION

As previously reported, potassium carbonate bearing PEGs as anion activator is able to catalyze reactions that

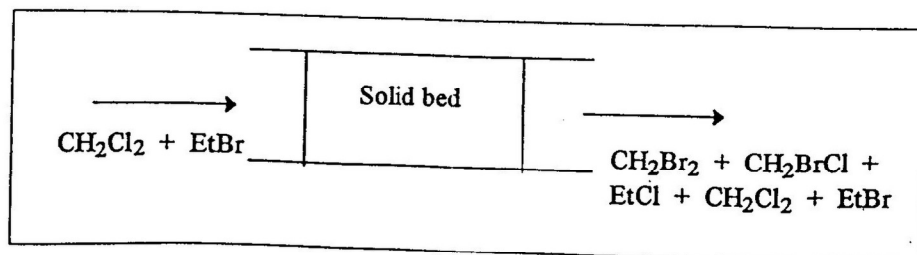


Fig. 2 - Transhalogenation in alkylhalides by GL-PTC

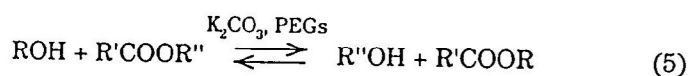
Alcohol	Catalytic bed. Effect on % conversion	
	K ₂ CO ₃ + 5 wt% PEG 6000 (400 g)	K ₂ CO ₃ + 5 wt% 18-Crown-6 (30 g)
Methanol	54	31
<i>n</i> -Propanol	33	
<i>n</i> -Butanol	42	17
<i>iso</i> -Butanol	46	
<i>sec</i> -Butanol	2	
<i>tert</i> -Butanol	Traces	

* Temperature = 170 °C; rate (liquid), 60 ml/min; ester / alcohol molar ratio, 1.2. From Ref. 22

Tab. 1 - Transesterification of ethyl acetate with several alcohols under GL-PTC conditions*

usually require strong basic media. K₂CO₃/PEGs catalysts do not produce RO⁻ able to provide S_N2 displacement. More generally, it does not allow nucleophilic substitution by hard anions (carbonate, alkoxide etc.), whereas the reactions of soft nucleophiles like ArO⁻, RS⁻ and malonate esters anions are strongly promoted.

Under such conditions hard anions behave better as bases and they attack carbonyl carbon rather than saturated alkyl carbon, according to a B_{Ac}2 mechanism. In this way, alcohols react with esters through their intermediates RO⁻ [22] and reaction (5) takes place.



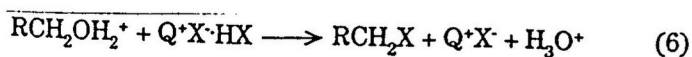
Like transhalogenation, reaction (5) is an equilibrium-type reaction; thus, by feeding the bed with an alcohol and an ester, the new alcohol and the new ester (together with the unconverted reagents) are collected at the outlet: the extent of conversion can reach the thermodynamic equilibrium of the reaction in a short time.

Some results in transesterification are reported in Tab. 1; data show that primary alcohols react better than secondary ones and that tertiary alcohols are almost inactive: this behaviour accounts for the fact that transesterification reaction in GL-PTC is controlled by an alkoxide intermediate. In fact the basicity trend in alkoxides follows the order tertiary > secondary > primary and so the first ones are present at equilibrium in lower concentration than the last ones.

It is interesting to note that the acidity scale of alcohols in the gas phase is reversed [23-24] evidencing that GL-PTC reactions occur in a liquid phase.

PRIMARY ALKYL HALIDES FROM PRIMARY ALCOHOLS

PTC is known to operate also under acidic conditions, since ion pairs Q⁺X⁻ are able to bring in organic phase small molecules like halogens, hydrogen peroxide or acids [25]. In the latter case the acid can protonate neutral molecules, enabling their reaction with the activated X⁻. Alcohols react according to eq. (6), where the rate-determining step is shown.



In GL-PTC primary alcohols and aqueous hydrochloric or hydrobromic acid are continuously injected in the gaseous state over porous silica gel supporting quaternary phosphonium salts as catalysts: at the reactor outlet the corresponding primary alkyl halides are obtained [18].

Also classic Lewis acids such as Zn or Al salts catalyze the reaction under the same conditions when supported on silica. However, they lead to large quantities of alkenes and isomeric halides as by-products: carbocation intermediates are present in the case of Lewis acids, while, on the contrary, the PT catalyzed reactions go through the mechanism of S_N2-type nucleophilic substitution.

In addition to the feasibility of the reaction in a continuous way, the practical advantage of GL-PTC conditions on LL-PTC ones lies in this case on the possibility of reacting water soluble alcohols: they do not give useful yields in LL-PTC since only one phase (aqueous-like) would be present [26].

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