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New reactors and methods for the investigation of homogeneous catalysis

Claude de Bellefon *, Nathalie Tanchoux, Sylvain Caravieilhes

Laboratoire de Génie des Procédés Catalytiques, CNRS URA 2211, CPE Lyon, BP 2077, F-69616 Villeurbanne Cedex, France

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Abstract

New methods and reactors for the kinetic investigation of homogeneous catalysis are described. These are oriented towards the minimisation of the amount of catalyst required for testing new catalytic reactions, kinetics determination and/or catalyst selection. The use of the centrifugal partition chromatograph (CPC) as a chromatographic catalytic reactor for steady-state and transient kinetics is reported. Examples are given which involve monophasic and biphasic reductions. The former is the enantioselective reduction of acetophenone to 2-phenylethanol by isopropanol catalysed by a Rh/chiral diamine system. The biphasic reductions are: (i) the reduction of benzaldehyde into benzylic alcohol catalysed with a Ru/TPPTS complex and (ii) the reduction of dimethylitaconate into dimethylmethylsuccinate catalysed with a Rh/TPPTS complex, both reductions taking place in cyclohexane/water mixtures with sodium formate as the hydrogen transfer reagent. Finally, for first order reactions, analytical solutions are found which demonstrate that kinetic parameters can be readily obtained by using the CPC as a chromatographic reactor in the transient (pulse) mode.

Keywords: Homogeneous catalysis; Liquid/liquid catalysis; Batch reactor; Plug flow reactor; Kinetics

1. Introduction

The separation, the recycling, the cost and the availability of the catalyst and of the ligand, the ligand/catalyst to substrate specificity and the lack of reliable kinetic data and deactivation processes constitute technological and scientific drawbacks that may seriously limit a wider application of homogeneous enantioselective catalysis.

The separation and recycling of the catalysts is a matter of active research and some reliable solutions do exist now [1]. Thus, numerous transition metal complexes based on homogeneous catalytic reactions can easily be made biphasic just by functionalisation of the ligands to make the catalyst water soluble. This is currently achieved by sulfonation of phenyl groups which are widely used as organic substituants in phosphines ligands. The Rhône-Poulenc/Ruhr Chemie Process for the hydroformylation of olefins uses a rhodium complex catalyst co-ordinated with the water soluble sodium salt of triphenylphosphinetrisulphonate (TPPTS) [2,3]. Separation of the product and recovery of the catalyst is thus achieved by simple decantation. Although the overall picture seems elegant and simple, the introduction of an other physical phase induces complexity in the process analysis.

The cost of the catalyst is determinated not only by the precious metal often used (Rh, Pt) but also by the sophisticated chiral inductor co-ordinated to the metal centre. For example, the price of commercially available diphosphine ligands lies between 100 and 500 dollars per gram whereas that of rhodium metal is only $20 per gram. With such expensive chemicals, a pre-industrial study may become very expensive. More embarrassing is the availability of the catalyst. New

* Corresponding author. Tel.: +33 4 72431754; fax: +33 4 72431673; e-mail: cdb@lobivia.cpe.fr

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catalysts and chiral ligands are often prepared at the laboratory scale in quantities required for the estimation of activities and enantioselectivity with some typical substrates. Whenever more tests are needed, then more catalyst is synthesised with possible risks of non reproducible results and lost of time and money.

In some cases, when catalysts (ligands) are readily prepared or available, the chemist is still facing a problem: which catalyst for which reaction ? Amazingly, that question comes from one of the well recognised advantages of homogeneous catalysis, i.e. its very high selectivity. In homogeneous catalysis, a very high selectivity (enantioselectivity) is generally obtained with a specific ligand for a specific substrate or class of substrate. This may be called the catalyst (ligand) to substrate specificity. The reverse of the coin is the lack of 'universal' catalysts. When a catalyst is to be chosen for an industrial production, the latter conclusion calls for numerous catalytic tests for the selection of the 'right' catalyst. Here again, investment in time and money may become prohibitive with the expensive catalysts that are used.

Quantitative investigation of kinetics with homogeneous catalysts is also a field to be developped. Most of the chemists working at the synthesis of homogeneous catalysis and ligands have been educated and trained in organic chemistry. In evaluating catalysts, they generally pay more attention to the selectivity rather than to the activity or possible deactivation. For example, in the field of enantioselective catalysis, except for few examples [4], the activity is seldom given as a result of a kinetic study but rather as 'a time to reach quantitative conversion' and catalysts deactivation is almost never investigated.

These four general remarks, which mostly apply to homogeneous enantioselective catalysis, point to the need for new methods and apparatus for the study and the selection of catalysts.

Looking to the methods that are used in the field of gas/solid heterogeneous catalysis may provide some guidelines to develop new methods and apparatus in liquid, liquid/liquid and gas/liquid/liquid homogeneous catalysis. Fixed bed plug flow like G/S continuous tubular reactors are largely used in the steady-state mode for the kinetic and deactivation studies of heterogeneous catalysts. Non steady-state or pulsed modes have also been described in the case of chromatographic reactors [5].

The picture is not the same in homogeneous catalysis where liquid catalysts are most often used. How to design a reactor that possess a liquid fixed bed? Liquid/liquid and gas/liquid columns are well known and widely used in industry [6]. However, the volume of such apparatus is still too large (> 2000 ml), even at the laboratory scale for applications with expensive catalysts. This is mainly due to the size effects. The droplets of the dispersed phase are millimetric in size which will drive strong wall effects when using small bore (< 0.04 m) columns. In a previous paper, we have reported that the centrifugal partition chromatograph (CPC) is a convenient liquid/liquid plug flow continuous reactor for the study of homogenous catalysis [7].

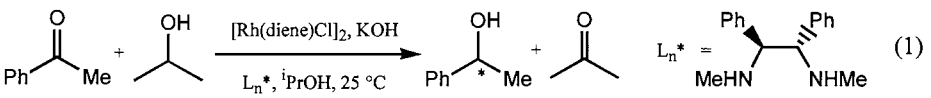
Along with this paper, technical problems linked with liquid/liquid catalysis, results obtained with the CPC and future applications of the CPC for catalysts selection will be presented and discussed.

2. Results and discussion

2.1. One (liquid) phase batch operations

When dealing with monophasic catalytic reactions, mixing during the reaction is not of tremendous importance (except for fast reactions with $t_R < 10$ s). Most of homogeneous catalytic reactions are slow enough to consider that diffusion is not the limiting process so that the chemistry is the actual process under investigation. In such cases, only mixing of the reaction mixture at the early beginning of the reaction is important. Thus, a gas phase chromatography vial may be used as a reactor which both allows kinetic investigations and the full automation of the sampling.

This technique has been used with a gas chromatograph equipped with an automatic sampler for the kinetic investigation of the enantioselective reduction of acetophenone to 2-phenylethanol by isopropanol catalysed by a Rh/chiral diamine system (Eq. 1) [8].



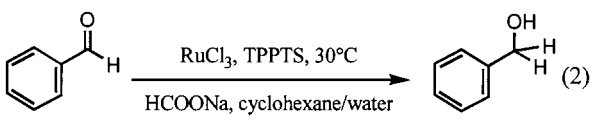
(1)

$$r_{R\text{-}PE} = \frac{k_R C^0_{Rh} C_{AP}}{K_R C_{AP} + K'_R C_{AC} + K'' C_{H2O} + K} \qquad r_{S\text{-}PE} = \frac{k_S C^0_{Rh} C_{AP}}{K_S C_{AP} + K'_S C_{AC} + K'' C_{H2O} + K}$$

Thus, out of ca. 50 tests involving more than 1000 samples, 30 have been used for the kinetic study. Complex kinetic laws have been confirmed (Eq. 1). The results have not yet been published but suffice to say that the observed complex kinetic order in acetophenone and the inhibition by water and acetone confirms the mechanism proposed for this reaction, [9] all being done with < 0.12 g of the expensive diamine ligand L^*_n.[10].

2.2. Liquid/liquid biphasic batch operations

In biphasic L/L catalytic systems, the chemicals are being transferred from the organic phase to the catalytic phase, e.g. water, where the catalytic reaction takes place [11]. Thus, the observed reaction rate depends both on the intrinsic chemical kinetics and the mass transfer kinetics. Obviously, when catalysts are compared on the bases of their activities, it should be ensured that mass transfer is not limiting, i.e. the experiments have been performed under chemical regime. Such verification of the chemical regime is of tremendous importance since results obtained under the mass transfer regime will lead to erroneous conclusions. To test the chemical regime, both the independence of the rate of reaction to the stirring speed and the proportionality of that rate to the concentration of the catalyst should be checked. The results of such tests performed in a well mixed batch reactor (Fig. 1) are shown in Fig. 2 in the case of the biphasic reduction of benzaldehyde into benzylic alcohol catalysed with a Ru/TPPTS complex in a cyclohexane/water mixture with sodium formate as the hydrogen transfer reagent (Eq. 2) [12].



(2)

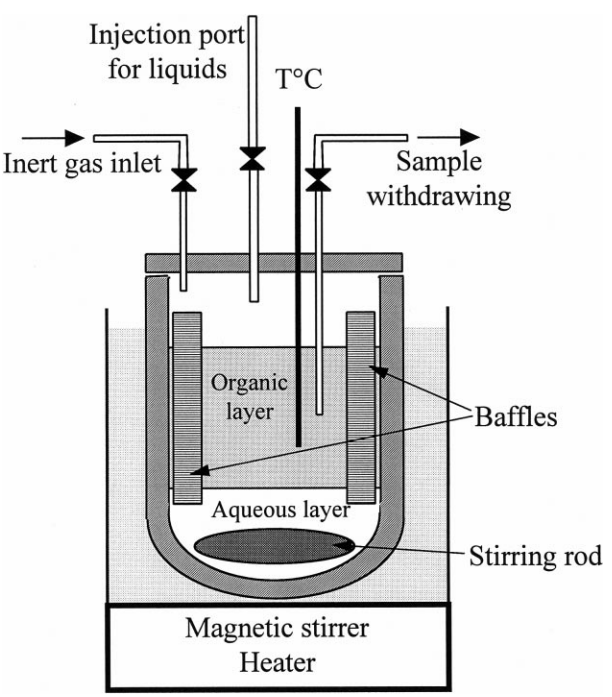


Fig. 1. Schematic representation of the well mixed batch reactor used in the study. Volume, and inner diameter: 100×10^{-6} m^3, 5×10^{-2} m. Size of the stirring bar: $4 \times 2\ 10^{-2}$ m.

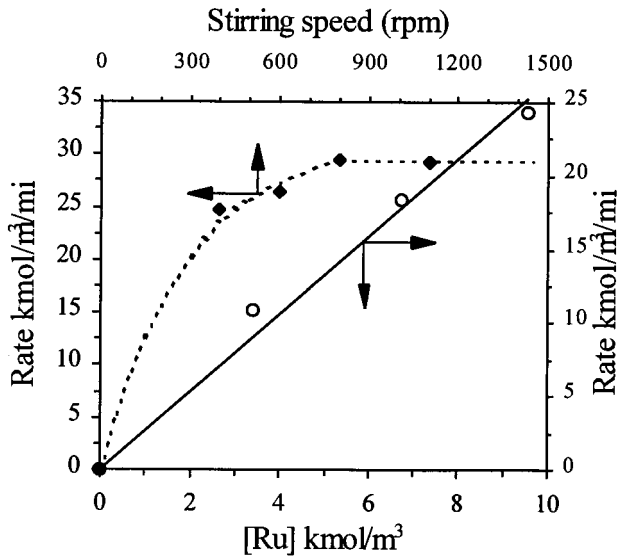
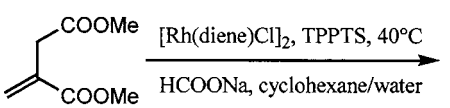


Fig. 2. Influence of the stirring speed and of the catalyst concentration on the initial rate of reduction of benzaldehyde (batch reactor, $T = 30$°C, [benzaldehyde] = 0.04 kmol^{-1} m^{-3}, P/Ru = 3, total volume = 40.10^{-6} m^3, cyclohexane/water ratio: 1/1; aqueous phase: sodium formate 5 kmol^{-1} m^{-3}).

As illustrated, the chemical regime is reached for stirring speeds above 800 rpm (Fig. 2). Consequently, the proportionality of the rate of reaction with the catalyst concentration has been checked at 1100 rpm. The results further demonstrate the chemical regime. Because mass transfer limitation depends on the mixing properties of the batch reactor used, these tests should be performed when investigating new reactions and/or new reactors.

The latter point is illustrated with another biphasic catalytic reaction, i.e. the reduction of dimethylitaconate into dimethylmethylsuccinate catalysed with a Rh/TPPTS complex in a cyclohexane/water mixture with sodium formate as the hydrogen transfer reagent (Eq. 3) [13].



(3)

Tests have been performed with two different reactors (Fig. 3). The first reactor A is the well mixed batch reactor equipped with a magnetic rod and baffles as described above (scheme 1). The second reactor is a Schlenk tube, comparable to that widely used in organometallic chemistry, of inner diameter 0.025 m and equipped with an olive shaped (0.02 m) stirring bar. Obviously, lower rates of reaction are observed with the Schlenk tube reactor.

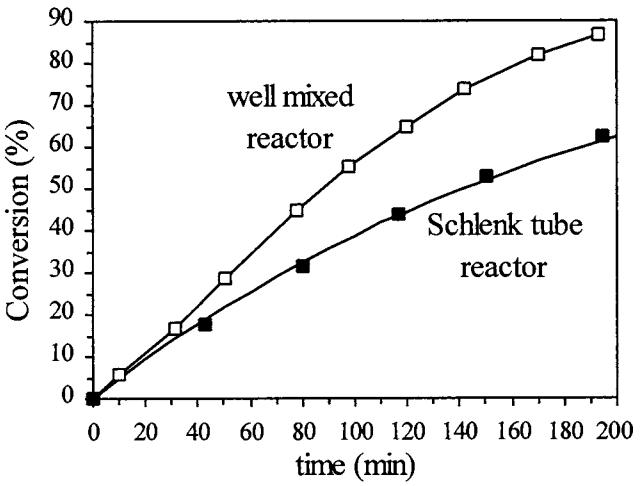


Fig. 3. Influence of the mixing on the concentration/time profiles in the reduction of dimethylitaconate (batch reactor, 40°C; [Rh] = 0.002 $kmol^{-1}\ m^{-3}$, [dimethylitaconate] = 0.1 $kmol^{-1}\ m^{-3}$, P/Rh = 6, total volume = 40.10^{-6} m^3, cyclohexane/water ratio: 1/1; aqueous phase: sodium formate 5 $kmol^{-1}\ m^{-3}$).

The purpose of this section was not to present new exiting results (these reactions are well known by chemists and mass transfer effects are well handled by chemical engineers) but rather to provide some tools which (when used!) will help to ensure good conditions for biphasic catalytic tests. Last but not least, the Schlenk tube reactor is not intrinsically a bad reactor. The results shown above just stated that it is not good enough to investigate catalytic biphasic reactions with characteristic reaction time $t_R < 2$ h (note that this limit is probably valid for most of the biphasic catalytic reactions but has been estimated under the conditions of our experiments).

2.3. Liquid/liquid biphasic steady-state operation in the CPC

In a centrifugal partition chromatograph (CPC), a stationary liquid phase is maintained in a coiled column by a centrifugal force field while a liquid mobile phase containing the mixture to be separated is pumped through. The separation of the chemicals is based upon the differences in their partition coefficients. The basic principle of the CPC used for analytical purposes has been reviewed by Ito [14] and application in homogeneous L/L catalysis has been reported recently [7]. The CPC used in this work has been described in detail and a schematic representation of the apparatus is given in Fig. 4 [15].

In the absence of the transition metal complex catalyst in the aqueous layer, the CPC is operating as a chromatograph. This is exemplified in Fig. 5 where a mixture of the substrate benzaldehyde, the product benzylic alcohol and an inert tracer ethylbenzene which does not dissolve in water, is separated.

When the aqueous layer is charged with the rhodium/TPPTS catalyst, the CPC may be operated as a continuous catalytic plug flow reactor. This is exemplified in Fig. 6 in the case of the biphasic reduction of dimethylitaconate into dimethylmethylsuccinate already mentioned in the previous section. For catalytic steady-state operations, the organic phase containing the substrate is continuously fed at the inlet of the CPC, the conversion being measured at the outlet. The results illustrate the steady state mode is reached after a transient period during which the measured conversion reflects both the kinetic and the partition of the substrate and the product between the two liquid layers. They also show that catalyst deactivation may be conveniently estimated in the CPC (note that in this example, the deactivation was due to the presence of oxygen in the reactor, the Rh/TPPTS catalyst being readily oxidised).

For a first order kinetics, the steady-state conversion χ_{out} is readily obtained from a mass balance equation assuming plug flow and no axial diffusion through the stationary catalytic aqueous phase and no mass transfer limitations (Eq. 4):

$$\chi_{out} = 1 - \mathbf{e}^{-\frac{kC_{Aq}^{Ru}}{(1+\alpha)P_{BZA}}\frac{V_r}{Q}} \quad (4)$$

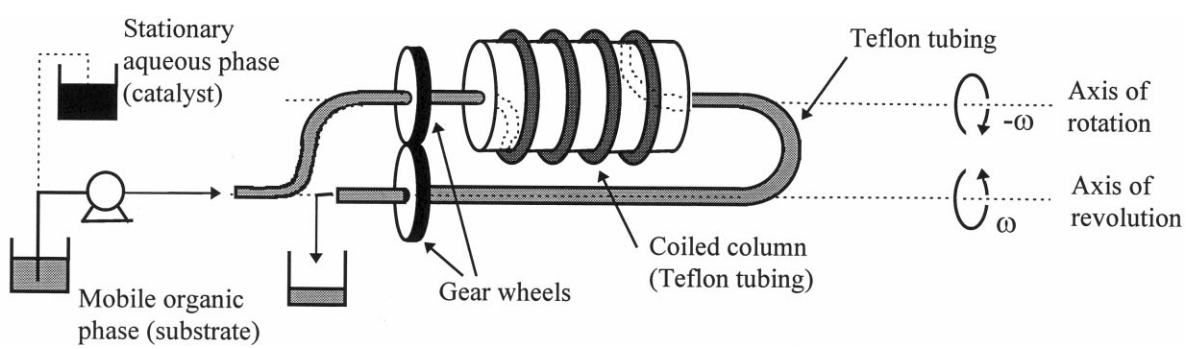


Fig. 4. Schematic representation of the CPC used in the study. Volume, length and inner diameter of the column: 55×10^{-6} m^3, 26.5 m, 1.63×10^{-3} m. Speed of revolution 750 rpm.

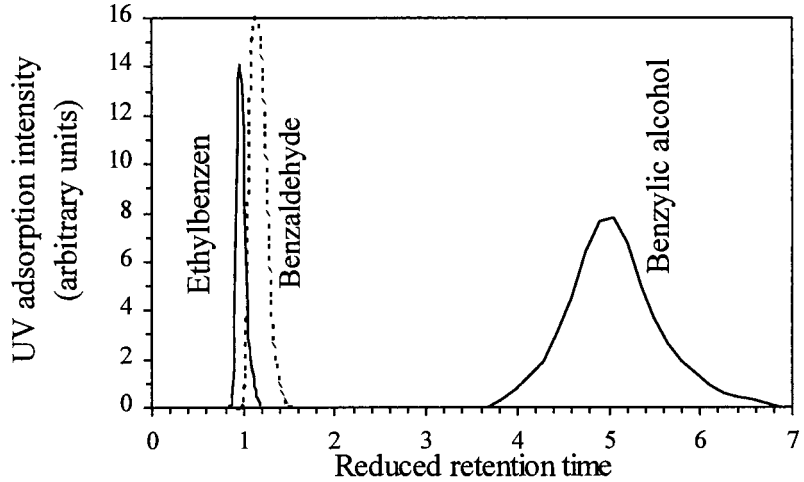


Fig. 5. The CPC as a chromatograph: illustration of the separation based on the differences in partition coefficients of the compounds (P = [organic layer]/[aqueous layer]). $P_{ethylbenzene}$ (> 1000) > > $P_{benzaldehyde}$ (50) > > $P_{benzylic\ alcohol}$ (1.2).

Where k is the intrinsic kinetic constant (m^3_{aq} $kmol^{-1}$ s^{-1}), C^{Ru}_{aq} ($kmol^{-1}$ m^{-3}) is the catalyst concentration in the aqueous layer, V_R (m^3) is the volume of the reactor (Teflon tubing), α is the volumic ratio between the organic and the aqueous phases, $P_{BZA} = [BZA]_{Org}/[BZA]_{aq}$ (m^3_{aq} m^{-3}_{Org}) is the partition coefficient of benzaldehyde and Q (m^{-3} s^{-1}) is the flow rate of the organic phase.

The good agreement found between the experimental steady-state conversion and the predicted conversion (χ_{out}) is illustrated for the biphasic reduction of benzaldehyde into benzylic alcohol catalysed with a Ru/TPPTS complex already mentioned in the previous section (Fig. 7).

These results show that the centrifugal partition chromatograph may be used as a continuous catalytic plug flow reactor for liquid/liquid reactions. Furthermore, in this example, mass transfer is fast compared to the chemical reaction since experimental data in the CPC fit perfectly with the model assuming a chemical regime. The volume of the catalytic phase in the example shown above is ca. 40 ml which is already quite low for a continuous reactor. However, future works are aiming to decrease this volume in order to minimise the quantity of catalyst required for a test. Noteworthy, the enantioselective reduction of dimethylitaconate using water soluble diphosphine ligands is under investigation.

2.4. Operating the CPC in the transient mode

So far, only the steady state operation of the CPC has been checked. One drawback of this operation mode is the time required to reach the steady-state regime. It would be time saving to operate the CPC in a transient mode. One way would be to fill the CPC with, for example, an aqueous catalytic phase like previously described and to test several substrates in a short time. That may be achieved by using the CPC as a chromatographic reactor. The liquid catalytic phase is the stationary phase and an organic solvent is the carrier mobile phase. Take the example of a reaction $A \rightarrow B$ such as the catalytic isomerisation of allylic alcohols (A) into aldehydes (B) catalysed by a TPPTS complex of Ni [16]. At a certain time, the substrate, either pure or diluted with the solvent, is injected via an injection valve very much like in gas chromatography the sample is injected through the septum. Because the partition coefficients of the enol and that of the aldehyde are quite different, the product will separate from the substrate all along the column. At the exit of the CPC, the shape of the peak of the product not only reflects the efficiency of the chromatograph, as usually found in chromatography, but also the kinetics of the reaction. In the absence of mass transfer limitation and for linear partition isotherm of the chemicals between the two liquid phases, the model described by Villermaux for gas/liquid chromatography may be applied. The following figures have been obtained by simple reverse Laplace transform of the model given by Villermaux [5] and numerical treatments (Fig. 8a–c).

The three operating parameters of importance are: (i) the efficiency of the chromatograph (in a first approximation, the efficiency can be considered equal for the substrate and the product $N = N_A = N_B$); (ii) the partition coefficients P_A and P_B of the substrate and the product are proportional to the retention time t_{RA} and t_{RB} and (iii) the isomerisation intrinsic rate constant (k).

Let's now comment on these figures. Please, note that the numbers are in arbitrary units since they do not reflect any experimental results. The intensity of the signal can be, for example, the UV detector signal. In Fig. 8a, the importance of the chromatograph efficiency

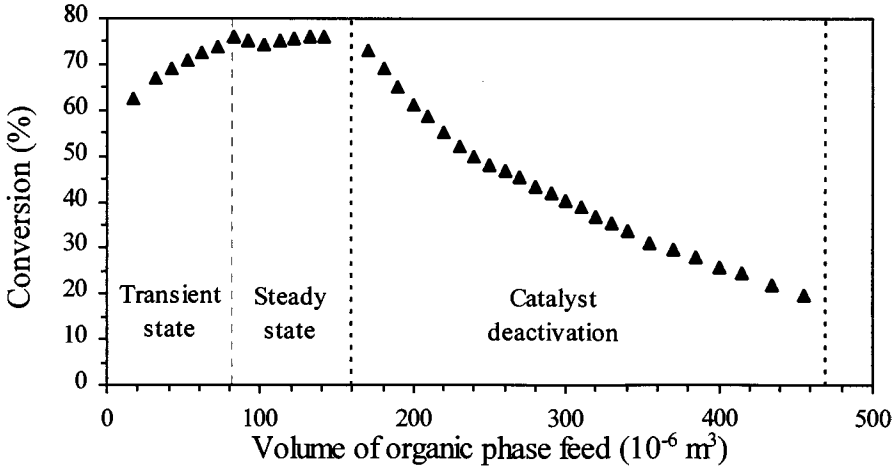


Fig. 6. Typical data obtained with the CPC. Conditions: [dimethylitaconate] = 0.1 kmol^{-1} m^{-3}, [Rh] = 0.002 kmol^{-1} m^{-3}, P/Rh = 3, total volume = 55×10^{-6} m^3, cyclohexane/water ratio: 1/10; aqueous phase: sodium formate 5 kmol^{-1} m^{-3}.

is given. N is what analysts call the plate numbers (neglecting the axial dispersion). It depends on both the mass transfer coefficient, the interfacial area between the two liquid phases, the volume of the stationary (catalytic) phase and the flow rate of the mobile phase. It is obvious that a better separation of the substrate and the product will give better data. For the CPC, the measured plate number lies between 200 and 2000 depending on the conditions and on the chemicals and solvents used.

Fig. 8b shows that the product and the substrate just need to have partition coefficients to be slightly different. This difference is quantified by the ratio $\Omega = P_B/(P_B - P_A)$. Thus, P_A and P_B should lie such as $|\Omega| < 1.3$. Note that this limit is computed for $n = 1000$. Should the efficiency of the chromatograph be better, i.e. $n = 10000$, then a higher limit of 1.5 or 2 would be acceptable. The fact that the product shows up before the substrate ($t_{RB} < t_{RA} \Leftrightarrow P_B > P_A$) or reverse ($t_{RB} > t_{RA} \Leftrightarrow P_B < P_A$) just changes the 'direction' of the profile (Fig. 9).

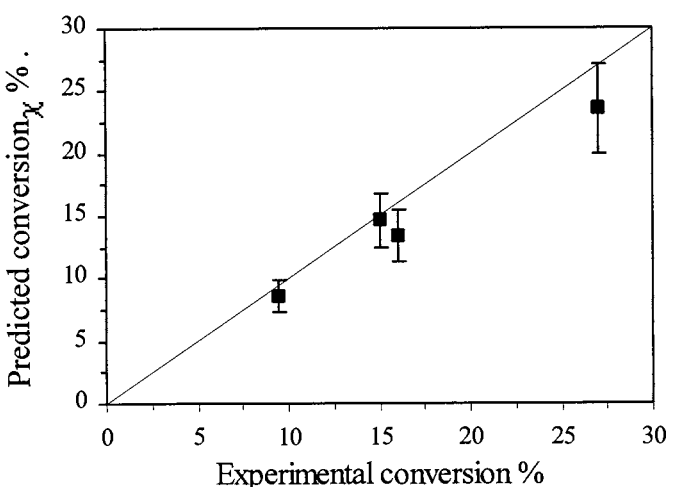


Fig. 7. Comparison between the experimental and the predicted conversion (χ_{out}). Conditions: T = 300 K; $V_R = 52.10^{-6}$m^3; = 3.4 10^{-3} kmol^{-1} m^{-3}; = 0.117 kmol m^{-3}; Q = 5.3, 9.0, 9.2 and 15.7 10^{-9} m^3 s^{-1} with α = 0.31, 0.27, 0.37 and 0.27, respectively.

Finally, the importance of the kinetic constant is outlined in Fig. 8c. Obviously, larger kinetic constants lead to higher conversion, as shown for $k = 2$, where the peak of the substrate has almost disappeared.

How can information on the catalytic reaction be extracted from such profiles? In the absence of mass transfer limitation, with negligible axial dispersion and for a first order kinetics, the theoretical model predicts an exponential variation of the profile of the product (Fig. 9).

The case where $P_A < P_B$ (exponential decrease, Fig. 9a) is given by equation 5:

$$I_B(t) = Ke^{-k(t-t_A)\frac{P_B}{(P_B-P_A)}} \quad (5)$$

The reverse situation $P_{A'} > P_{B'}$ (exponential decrease, Fig. 9b) is given by equation 6:

$$I_{B'}(t) = Ke^{-k'(t-t_{B'})\frac{P_{B'}}{(P_{B'}-P_{A'})}} \quad (6)$$

where $I_B(t)$ is variation of the intensity of the signal of the product B with time at the exit of the chromatographic reactor; t is the time after the injection of the substrate; t_A and t_B are the retention times of the substrate and the product; k is the observed kinetic constant in the mobile phase; P_A and P_B are the partition coefficients of the substrate and the product; K is a pre-exponential factor related to k, P_A, P_B.

Although the expression of K can be deduced from the model, it is rather complex and there is no need for it. A plot of $\mathrm{Ln}I_B(t)/\Omega$ with t affords a straight line which slope is k (Ω is the ratio $P_B/(P_B - P_A)$, P_A and P_B are known or measured). Integration of peaks A and B

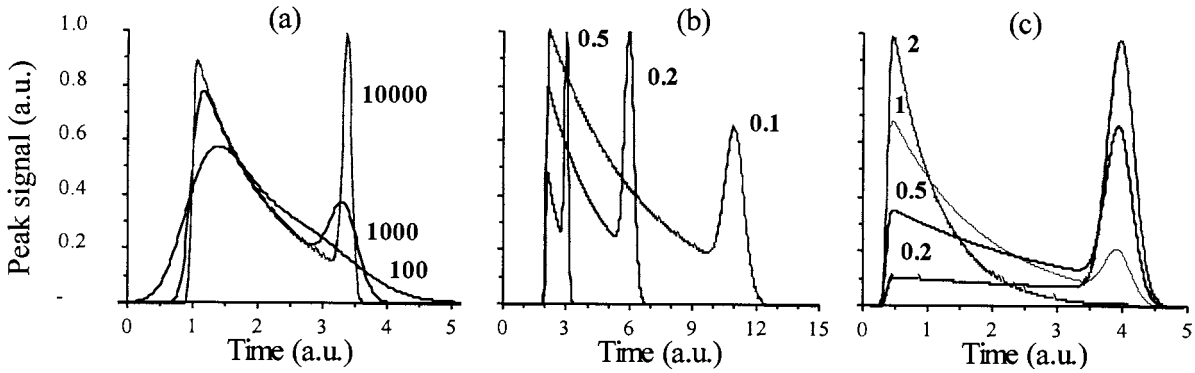


Fig. 8. Sensitivity of the simulated concentrations profile of the mixture obtained at the exit of the CPC with the operating parameters: (a) influence of the plate number of the column N ($P_A = 0.5$, $P_B = 1$, $k = 2$). (b) influence of the partition coefficient P_A ($N = 1000$, $P_B = 1$, $k = 1$). (c) influence of the rate constant k ($N = 1000$, $P_A = 0.2$, $P_B = 1$).

will give the conversion with a good approximation, depending on the integration method used and on the overlap of the peaks (quantitative analysis of A and B is then required!).

Finally, it is worth mentioning another possible use of the CPC as a catalytic reactor with the reaction occurring in the mobile phase. In this situation, the stationary phase is not chemically active and only plays a role as a separation medium. All the catalyst is in the mobile phase with no partition with the stationary phase. Such an operating mode for the CPC will be of larger interest than that described in the previous section since most of the transition metal complexes used in homogeneous catalysis are very soluble in organic media and poorly soluble in an aqueous medium. To illustrate this mode, lets take again the example of the catalytic isomerisation of allylic alcohols (A) into aldehydes (B) but this time catalysed by a triphenylphosphine complex of rhodium [17,18]. Qualitatively, the partition coefficients of the catalyst, the substrate and the product would be: $P_{Cat} > > > P_B > P_A$ or expressed as retention times, $t_{Cat} < < < t_B < t_A$. The CPC is simply filled with water as a stationary phase and a carrier organic solvent compatible with the isomerisation reaction is pumped through. At a certain time, a pulse of the substrate A, is injected at the inlet of the column. After a short time, a pulse of the catalyst, in the solvent, is injected. Because the catalyst is not held up by the stationary phase, it will join and pass the substrate and finally shows up first at the exit of the column. However, during the crossover of the catalyst and the substrate, the catalytic reaction does occurr. The product of the reaction, when partition is not strong, will appear second and, finally, the substrate will show up. In theory, very much like in the previous section, the profile of the product should contain the kinetic information. The model required for a better quantification of this approach is not yet available but it will come soon.

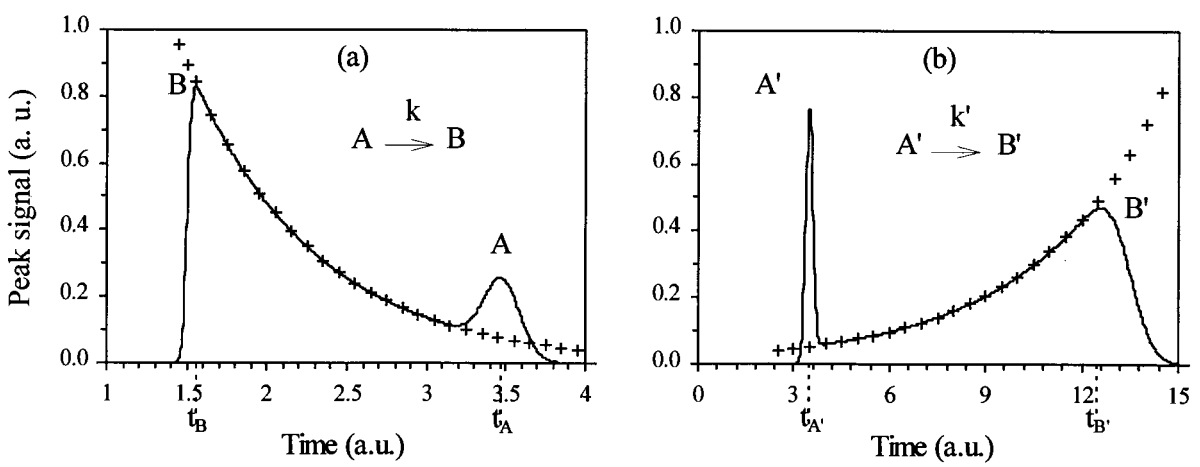


Fig. 9. Adjustment of the simulated concentrations profiles of the mixture obtained at the exit of the CPC with a first order kinetics: (a) $t_A > t_B$ or $P_A < P_B$; (b) $t_{A'} < t_{B'}$ or $P_{A'} > P_B$.

3. Conclusion

The work presented in this paper was oriented in the hope of helping chemists working with expensive or/and rare catalysts. More precisely, it represents a tentative step in solving a paradoxical situation often found in the field of enantioselective catalysis: on the one hand, catalysts (ligands) are very expensive and/or only available at the laboratory scale which speaks for as few tests as possible whereas, on the other hand, reaction mechanisms are quite complex which require numerous tests for establishing good kinetics. Within such a context, running a test with as little liquid catalyst (millilitres or microliters) represents a challenging perspective.

Acknowledgements

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