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Original use of the liquid nature of the stationary phase in counter-current chromatography

II. A liquid–liquid reactor for catalytic reactions

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Abstract

Countercurrent chromatography column was used as a chemical reactor for a reaction catalyzed by a liquid catalyst. The countercurrent chromatography machine was used as a continuous reactor and as an injected-plug reactor. The reduction of benzaldehyde by sodium formate is possible at room temperature in an aqueous phase when a ruthenium–triphenylphosphine–trisulfonate complex liquid catalyst is used. Benzyl alcohol is formed. Benzaldehyde is located in a cyclohexane phase. The cyclohexane–water partition coefficients of benzaldehyde and benzyl alcohol were determined by countercurrent chromatography. The plug-flow character of the continuous countercurrent chromatography reactor is demonstrated. The chemical characteristic time is in the order of 1 h at 2 ml/min when the average benzaldehyde mass-transfer time is about 30 s in the countercurrent chromatography reactor. The chemistry kinetics is the limiting process. Using the countercurrent chromatography reactor with an injected plug of a reagent, it is shown that the profile of the band of the product obtained can be related to the kinetic characteristics of the liquid catalyst.

Keywords: Countercurrent chromatography; Stationary phases; Continuous reactor; Catalysis; Ruthenium; Benzaldehyde; Benzyl alcohol

1. Introduction

Counter-current chromatography (CCC) is a separation technique that uses a liquid stationary phase. There is absolutely no solid to support the liquid stationary phase. The CCC column contains a biphasic liquid system: phase 1 is the liquid stationary phase that should stay in the CCC column, phase 2 is the mobile phase that should percolate through the stationary phase without displacing it. Centrifugal fields and the density difference between the two liquid phases allowed us to hold the liquid stationary phase inside the CCC column [1–4]. In Part I of this series, a unique application of the liquid nature of the stationary phase in CCC was presented in the analytical chemistry field [5]. It was shown that transition metal cations could be extracted in the organic stationary phase containing a chelating agent. Using displacement chromatography, it was possible to obtain bands of pure cations in the stationary phase [5].

Catalysts are widely used in industrial chemistry. As long as the catalyst is a solid, there is a large diversity of possible reactors for liquid–liquid pro-

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cesses. Continuously stirred tank reactors or plug-flow reactors allow one to perform catalyzed reactions. A good recovery of the catalyst is desired because it is often a compound containing rare and/or noble elements such as rhodium, ruthenium, palladium or platinum. Recently liquid catalysts were introduced. For example the Rhône–Poulenc/Ruhr–Chemie Process for the hydroformylation of olefins involves a liquid catalyst and a biphasic liquid system with an aqueous phase [6]. The liquid catalyst is a water-soluble rhodium complex with the ligand triphenylphosphine–trisulfonated sodium salt (TPPTS). The process is industrially efficient because the organic phase containing the substrate and the reaction product is readily separated from the aqueous catalytic phase by simple and rapid decantation. Several industrial processes based on similar catalysts were developed [7,8]. There is a need for a better reactor than the stirred tank reactor when liquid catalysts are used.

The CCC apparatuses are possible candidates as plug-flow reactors in processes involving a biphasic liquid system. In 1990, a hydrostatic CCC machine was successfully used as an enzymatic reactor for the chiral separation of DL-amino esters [9]. The enzyme, α-chymotrypsin, was chosen as the chiral selector dissolved in the aqueous stationary phase. The L-enantiomer of an amino ester bind to the active site of the immobilized enzyme for hydrolysis while the D-enantiomer does not. As much as an 880 mg amount of DL-tryptophan methyl ester could be reacted and separated in less than 3 h into the D-tryptophan methyl ester and L-tryptophan. Another CCC machine was used as an enzymatic reactor for a simple organic synthesis [10].

This work presents the evaluation of a hydrodynamic CCC machine as a continuous catalytic reactor. The simple hydrogenation of benzaldehyde in benzyl alcohol is used to evaluate the feasibility of the technique. This reduction by sodium formate is performed in a water–cyclohexane biphasic liquid system and it needs a water-soluble catalyst which was a ruthenium–TPPTS complex. The plug-flow character of the CCC machine is demonstrated. The benzyl alcohol conversion ratio is used to establish a kinetic model and compare the capability of the CCC machine with a classical batch reactor.

2. Experimental

2.1. The counter-current chromatograph

The CCC apparatus was the model CPHV 2000 from the SFCC company (Eragny, France). The production of this machine was discontinued. Similar equipment is now produced by SEAB (Villejuif, France). The CCC machine contains three multilayer coils connected in series and spinning with a planetary motion around a central axis with a stationary gear. Each spool was filled with 133 turns of 1/8 ft PTFE tubing, (I.D. 1.6 mm), length 29 m, coiled in seven layers of 19 turns (1 ft=30.48 cm). The Ito β value is the ratio of the coil radius, r, to the spool revolution radius, R. The β ratio was 0.37 for the inner first layer with $r=2.2$ cm and $R=6$ cm. It was 0.75 for the most outer visible layer with $r=4.5$ cm and $R=6$ cm. The average β value for this CCC apparatus was 0.56. The internal volume of one coiled spool was 58 ml. The three-coil apparatus had a total internal volume, V_T, of 175 ml. The total 1/8 ft PTFE tube length was 87 m, with a total of 400 turns. The whole system is housed in an air-thermostated box. The temperature was regulated at 22°C±0.5°C. The machine usually works with the three spools serially connected ($V_T=175$ ml) for maximum efficiency and mass load capacity. It can also work with one spool only ($V_T=60$ ml) to reduce the retention volumes. The efficiency is three times lower. The two spools connected on themselves should be filled with water for rotor mass balance. For some experiments it was necessary to put the machine in a huge plastic bag that was filled by nitrogen to reduce the catalyst oxidation by oxygen diffusing through the PTFE tubing.

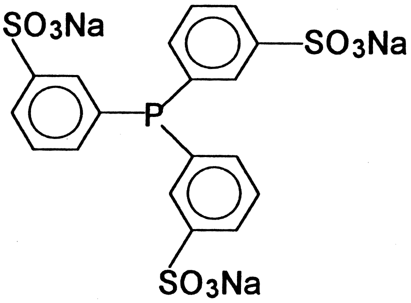
2.2. Materials

Common HPLC hardware is used with the CCC machine that can be considered as an unusual column. A Shimadzu LC6A HPLC pump (Touzart and Matignon, Vitry, France) was used for the mobile cyclohexane phase. A Shimadzu SPD6A UV–Vis detector was connected to a CR5A Shimadzu integrator.

In the batch reaction experiments, μl fractions of the cyclohexane phase were analyzed by gas chromatography using a Hewlett–Packard 5890 II GC apparatus with a 25 m BP 20 polyethylene glycol macrobore column (0.32 mm I.D.; 0.5 μm film thickness). An on-column injector, helium carrier gas and a flame ionization detector were used.

2.3. The test reaction

Benzaldehyde can be reduced in benzyl alcohol by sodium formate at room temperature [6]. A water-soluble catalyst is needed: the ruthenium–TPPTS complex of the TPPTS trisodium salt:



The reaction:

$$C_6H_5\text{-CHO} + HCOO^- + H_2O \rightarrow C_6H_5\text{-CH}_2OH + HCO_3^- \quad (1)$$

is performed in a biphasic cyclohexane–water system. The benzaldehyde molecules are essentially located in the organic phase. The benzyl alcohol partitions between the two phases.

2.4. Chemicals

The chemicals, cyclohexane, benzaldehyde (BZA), benzyl alcohol (BzlOH), sodium formate, ruthenium chloride were obtained from Sigma, Aldrich and/or Fluka, all three located at L'Isle d'Abeau Chesnes (France). TPPTS was a gift by Emile Kuntz of the CPE Lyon School of Chemical Engineering.

The ruthenium catalyst was prepared according to a described method [11]. For 100 ml of liquid catalyst, the concentrations were as follows: ruthenium 0.2 g (0.02 *M*); TPPTS 7 g (0.12 *M*); sodium formate 34 g (5 *M*). ^{31}P NMR spectra show peaks corresponding to complexes of Ru(II) such as $RuCl_2(TPPTS)_3^-\cdot 9Na^+$, $RuH_2(TPPTS)_3\cdot 9Na^+$, and $RuH_2(TPPTS)_4\cdot 12Na^+$ [11].

3. Kinetic study

Reaction 1 that takes place in the aqueous phase which contains a very large excess of sodium formate so that its concentration remains constant. In such condition, the reaction rate, *K*, in *M* s^{-1}, is defined as:

$$K = \mathrm{d}n^{\mathrm{BzlOH}}/(V_{\mathrm{aq}}\mathrm{d}t) = -\mathrm{d}n^{\mathrm{BZA}}/(V_{\mathrm{aq}}\mathrm{d}t)$$
$$= kC_{\mathrm{aq}}^{\mathrm{Ru}}C_{\mathrm{aq}}^{\mathrm{BZA}} \quad (2)$$

in which k is the intrinsic kinetic constant in M^{-1} s^{-1}, n^{BzlOH} or n^{BZA} are the number of mole of benzyl alcohol created (*M*) or benzaldehyde reduced (*M*), respectively, $C_{\mathrm{aq}}^{\mathrm{Ru}}$ and $C_{\mathrm{aq}}^{\mathrm{BZA}}$ are the molar concentration of the catalyst and benzaldehyde in the aqueous phase, respectively.

Benzyl alcohol partitions between the organic and aqueous phase:

$$n^{\mathrm{BzlOH}} = n_{\mathrm{aq}}^{\mathrm{BzlOH}} + n_{\mathrm{org}}^{\mathrm{BzlOH}} \quad (3)$$

or

$$n^{\mathrm{BzlOH}} = C_{\mathrm{aq}}^{\mathrm{BzlOH}}V_{aq} + C_{\mathrm{org}}^{\mathrm{BzlOH}}V_{\mathrm{org}} \quad (4)$$

Introducing P_{BzlOH} and P_{BZA}, the cyclohexane–water partition coefficients of the compounds and Φ, the $V_{\mathrm{org}}/V_{\mathrm{aq}}$ ratio, Eq. (4) can be written as:

$$n^{\mathrm{BzlOH}} = C_{\mathrm{aq}}^{\mathrm{BzlOH}}V_{\mathrm{aq}}(1 + \Phi P_{\mathrm{BzlOH}}) \quad (5)$$

The BzlOH and BZA concentration changes were followed by gas chromatography of the cyclohexane phase:

$$\mathrm{d}C_{\mathrm{org}}^{\mathrm{BzlOH}}/\mathrm{d}t = P_{\mathrm{BzlOH}}\mathrm{d}C_{\mathrm{aq}}^{\mathrm{BzlOH}}/\mathrm{d}t \quad (6)$$

Using Eq. (2) and Eq. (5), we can form:

$$K = \mathrm{d}C_{\mathrm{aq}}^{\mathrm{BzlOH}}/\mathrm{d}t(1 + \Phi P_{\mathrm{BzlOH}}) \quad (7)$$

and

$$\mathrm{d}C_{\mathrm{org}}^{\mathrm{BzlOH}}/\mathrm{d}t = KP_{\mathrm{BzlOH}}/(1 + \Phi P_{\mathrm{BzlOH)}} \quad (8)$$

Similarly:

$$
\begin{aligned}
-\mathrm{d}C_{\mathrm{org}}^{\mathrm{BZA}}/\mathrm{d}t &= -P_{\mathrm{BZA}}\mathrm{d}C_{\mathrm{aq}}^{\mathrm{BZA}}/\mathrm{d}t \\
&= KP_{\mathrm{BZA}}/(1+\Phi P_{\mathrm{BZA}}) \qquad (9)
\end{aligned}
$$

It should be noted that the product KP_{BZA} can be written as $k\ C_{\mathrm{aq}}^{\mathrm{Ru}}\ C_{\mathrm{org}}^{\mathrm{BZA}}$.

CCC is an excellent technique to determine the liquid–liquid partition coefficient of BZA and BzlOH. When the P values are known, the intrinsic kinetic constant, k, of the catalytic reduction of benzaldehyde by sodium formate can be estimated performing several experiments with differing initial conditions (α, $C_{\mathrm{aq}}^{\mathrm{Ru}}$ and $C_{\mathrm{org}}^{\mathrm{BZA}}$) and measuring the initial rate of reaction (d $C_{\mathrm{org}}^{\mathrm{BzlOH}}/\mathrm{d}t$ or $-$d $C_{\mathrm{org}}^{\mathrm{BZA}}/\mathrm{d}t$) in a well-mixed batch reactor.

4. Results and discussion

4.1. Partition coefficient determination

In CCC, there is no solid support. The apparatus contains only the two liquid phases. The sum of the mobile phase volume, V_{M}, and the stationary phase volume, V_{S}, is equal to the apparatus volume, V_{T}. The retention volume of a solute, V_{R}, depends only on the phase volume inside the machine and on its liquid–liquid partition coefficient, P:

$$V_{\mathrm{R}} = V_{\mathrm{M}} + PV_{\mathrm{S}} = V_{\mathrm{T}} + (P-1)V_{\mathrm{S}}. \qquad (10)$$

The retention volume of the solute gives its partition coefficient in the biphasic liquid system using [12]:

$$P = (V_{\mathrm{R}} - V_{\mathrm{M}})/V_{\mathrm{S}}. \qquad (11)$$

The cyclohexane–water biphasic liquid system was used in the CCC machine in the tail to head (ascending) mode with the cyclohexane mobile phase. The solutes benzyl alcohol, benzaldehyde and hexylbenzene were injected. The retention volumes are listed in Table 1. They allowed to calculate the solute water–cyclohexane partition coefficients. The S_{f} value, $S_{\mathrm{f}} = V_{\mathrm{S}}/V_{\mathrm{T}}$, is the phase retention parameter. The CCC machine used was able to retain more than 70% of the aqueous phase when a 3 ml/min flow-rate of cyclohexane was percolating through it. Hexylbenzene was used as a dead volume tracer, i.e. a mobile phase V_{M} volume tracer with a $P=0$ coefficient (Eq. (10)). Fig. 1 shows a typical CCC chromatogram with peak efficiencies in the hundreds of plates range. The coefficients were measured with a 1 *M* formate solution and a concentrated 5 *M* formate solution. The concentrated formate solution was better as a reaction medium. However, it was difficult to use because its viscosity is high and it is a phase difficult to handle with classical HPLC pumps due to crystallization and in-pump frit clogging problems. Since the aqueous phase is the stationary phase, a peristaltic pump was often used to fill the CCC machine at a low pressure and approximately known (~2 ml/min) flow-rate.

The water–cyclohexane partition coefficients are linked to the solute hydrophobicity. The exchange of the aldehyde –CHO function for the alcohol $-\mathrm{CH_2OH}$ function on the benzene ring produces a 40-time increase of the partition coefficient of benzyl alcohol compared to benzaldehyde. The ‘‘salting out’’ effect produced by the 5 *M* sodium formate

Table 1
Measurements of P values by CCC

Stationary phase	Compound	V_{R} (ml)	t_{R} (min)	V_{S} (ml)	S_{f} (%)	$P_{\mathrm{wat/cyclhx}}$	$\mathrm{P}_{\mathrm{cyclhx/wat}}$
Aqueous phase with 1 *M* sodium formate	Ethylbenzene	47	15.7	128	73%	0	–
	Benzaldehyde	52	17.3	128	73%	0.04	25
	Benzyl alcohol	252	84.0	128	73%	1.6	0.62
Acqueous phase with 5 *M* sodium formate	Ethylbenzene	44	14.7	131	75%	0	–
	Benzaldehyde	47	15.7	131	75%	0.02	50
	Benzyl alcohol	162	54.0	131	75%	0.9	1.2

The water–cyclohexane partition coefficient is the reverse of the cyclohexane–water partition coefficient. V_{R}: retention volume, V_{S}: aqueous (stationary) phase volume, apparatus volume: 175 ml, rotation speed: 750 rpm, flow-rate ascending cyclohexane: 3 ml/min, temperature in the machine: 27°C.

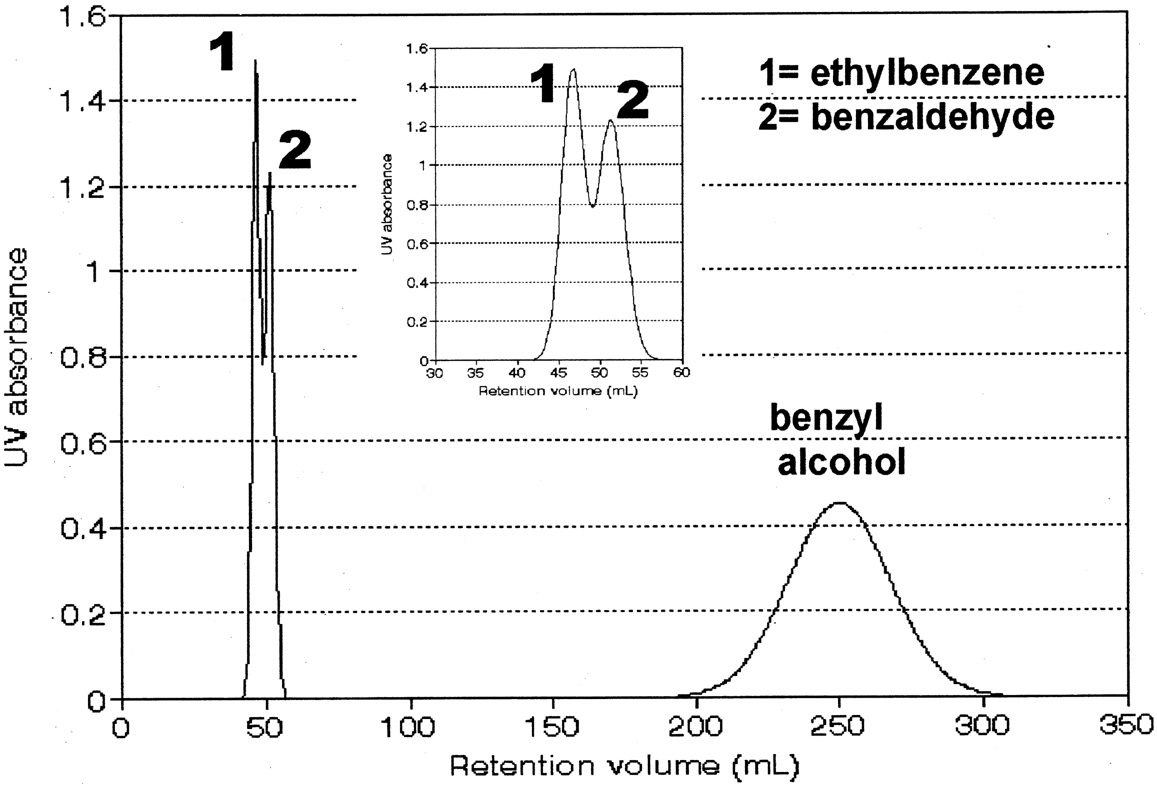


Fig. 1. Partition coefficient determination. Apparatus volume: $V_T=175$ ml, 1 *M* sodium formate aqueous stationary phase: $V_S=128$ ml, cyclohexane mobile phase 2 ml/min in the ascending tail to head mode: $V_M=47$ ml, $S_f=73\%$, rotation speed=750 rpm.

concentration is seen by the decrease of the coefficients (Table 1).

4.2. Kinetics studies in a batch reactor

The kinetics measurements were performed in a well-mixed 100 ml batch reactor. Fig. 2 shows the benzaldehyde and benzylic alcohol concentration changes obtained during a typical experiment. Microliter samples of the cyclohexane phase are taken at different times and analyzed by gas chromatography to determine the BZA and BzlOH concentrations. The organic BZA concentration decreased with time as BZA is reduced in BzlOH whose concentration increased. ~40% of the BzlOH molecules formed are extracted in the aqueous phase ($P=1.6$, Table 1) compared to 98% of the BZA mass located in the cyclohexane phase ($P=25$). The

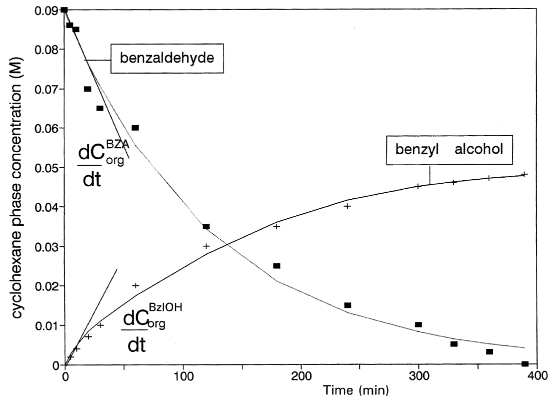


Fig. 2. BZA and BzlOH concentration evolution in a typical batch experiment. Reactor volume 100 ml, stirring speed 1100 rpm, 30°C, $C^{Ru}_{aq}=0.0095$ *M*, $C^{BZA}_{org}=0.09$ *M*, 20 ml 5 *M* formate solution, $\Phi=1$.

initial speeds of reaction, $[\mathrm{d}C_{\mathrm{org}}^{\mathrm{BzlOH}}/\mathrm{d}t]_{t=0}$ and $[\mathrm{d}C_{\mathrm{org}}^{\mathrm{BZA}}/\mathrm{d}t]_{t=}0$, are taken as the slope of the respective Fig. 2 curves at $t=0$.

Twenty one different experiments with initial BZA concentrations of 5.5, 9.0, 11.7, and $19.1\cdot10^{-2}$ M and/or initial catalyst concentration of 3.4, 4.54, 6.73, and $9.5\cdot10^{-3}$ M and/or liquid phase volume ratio of $\Phi=1$, 0.23 and 0.1 were carried out at 30°C with the 5 M sodium formate aqueous phase. According to Eq. (9), the plot of the initial speed of the benzaldehyde decrease, $[\mathrm{d}C_{\mathrm{org}}^{\mathrm{BZA}}/\mathrm{d}t]_{t=0}$ versus the term $C_{\mathrm{aq}}^{\mathrm{Ru}}\ C_{\mathrm{org}}^{\mathrm{BZA}}/(1+\Phi P_{\mathrm{BZA}})$ should produce a straight line with a slope k, the intrinsic kinetic constant of the catalytic reduction and a zero intercept. The plot of the 21 representative points gave a straight line with a 0.983 regression coefficient (intercept forced to zero) and a slope equal to 31 ± 4 M^{-1} min^{-1} or 0.51 ± 0.07 M^{-1} s^{-1}.

Taking in account the usual catalyst concentrations and the BZA partition coefficient, a characteristic time, t_{exp}, for the chemical reaction can be derived from Eq. (9):

$$-\mathrm{d}C_{\mathrm{org}}^{\mathrm{BZA}}/\mathrm{d}t = kC_{\mathrm{aq}}^{\mathrm{Ru}}C_{\mathrm{org}}^{\mathrm{BZA}}/(1+\Phi P_{\mathrm{BZA}}) = k_{\mathrm{exp}}C_{\mathrm{org}}^{\mathrm{BZA}} \qquad (12)$$

and

$$t_{\mathrm{exp}} = 1/k_{\mathrm{exp}} = (1+\Phi P_{\mathrm{BZA}})/kC_{\mathrm{aq}}^{\mathrm{Ru}} \qquad (13)$$

With the catalyst concentration in the 0.003–0.008 M range and a 80% phase retention by the CCC machine ($\Phi=0.25$), the characteristic time for benzaldehyde reduction at 30°C is in the 3300–9000 s range (1–2.5 h). Liquid–liquid reactors are characterized by the dimensionless Peclet number, Pe, defined as:

$$Pe = ul/D \qquad (14)$$

with u, the linear velocity of the mobile phase (m/s), l, the CCC reactor (or column) length and D, the solute axial diffusion coefficient (m^2/s). Using residence-time distribution analysis (RTD), the CCC machine Peclet number was measured to be 840 at 2 ml/min and 1200 at 3 ml/min [13]. These high values indicate that the CCC machine can be considered as a reactor of the plug-flow type. The Peclet number can be related to the characteristic time for solute mass transfer between the two liquid phases. For benzaldehyde, this time was estimated to 30 s at 2 ml/min and 50 s at 1 ml/min [13]. These times for solute mass transfer clearly show that, with the reduction reaction used, the limiting process in the CCC reactor is the chemical reaction.

4.3. Continuous reaction in the CCC machine

The single-spool configuration was selected to reduce the CCC reactor volume. The CCC chromatograph was filled by the aqueous 1 M or 5 M sodium formate solution containing 0.0034 M of the ruthenium–TPPTS catalyst complex. It was equilibrated with the cyclohexane–BZA solution at 3 ml/min flow-rate. The V_{M} volume was taken as the aqueous phase volume displaced by the cyclohexane phase. After the equilibration step, the cyclohexane phase leaves the CCC machine, then the flow-rate was set at the desired value (1, 0.6 or 0.3 ml/min) and μl fractions were collected at regular time intervals for GC analysis. Fig. 3 shows the benzylic alcohol formed as a function of the mobile phase volume passed in the reactor.

The flow-rate and the phase retention factor, S_{f}, are used to calculate the average BZA residence time in the CCC reactor. The values of the residence times are 47.2 min, 20.6 min, 26.5 min and 12.4 min for the Fig. 3 experiments at 0.3 ml/min, 0.6 ml/min and $S_{\mathrm{f}}=79\%$, 0.6 ml/min and $S_{\mathrm{f}}=73\%$, and 1 ml/min, respectively. Table 2 shows that the steady-state

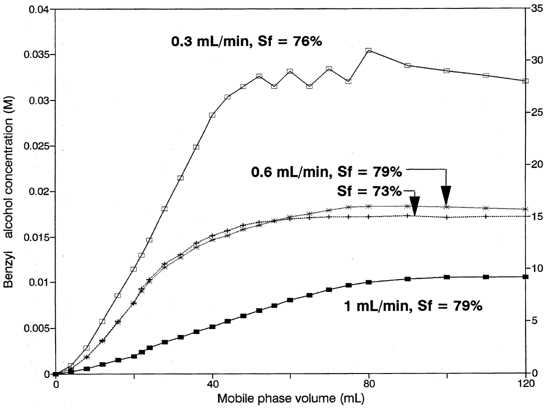


Fig. 3. Four continuous reactions in the CCC machine. $C_{\mathrm{aq}}^{\mathrm{Ru}}=0.0034$ M, $C_{\mathrm{org}}^{\mathrm{BZA}}=0.117$ M, 30°C, rotation speed=750 rpm, $V_{\mathrm{T}}=59$ ml, cyclohexane mobile phase in the ascending tail to head mode.

Table 2
Experimental conditions and yield of the reaction

Flow-rate (ml/min)	V_s (ml)	S_f	M	Cf_{CCC}	Cf_{th}
0.3	45	76%	0.31	0.29	0.254
0.6	46.5	79%	0.27	0.16	0.132
0.6	43	73%	0.37	0.15	0.139
1	46.5	79%	0.27	0.09	0.086

Experimental conditions listed in Fig. 3 legend. V_S = stationary (aqueous formate solution + catalyst); $S_f = V_S/V_T$; $\Phi = V_M/V_S$; Cf_{CCC} = experimental conversion factor (see Fig. 3); Cf_{th} = conversion factor calculated with Eq. (15).

conversion factor, Cf_{CCC}, obtained with the CCC reactor is very close to the theoretical factor, Cf_{th}, obtained by:

$$Cf_{th} = 1 - \exp[kC_{aq}^{Ru}/(1 + \Phi P_{BZA})(V_M/F)] \qquad (15)$$

The experimental conversion factors seem to be slightly (5–20%) higher than the calculated factors. This may be due to the dynamic nature of the process: the product, benzylic alcohol has a significant affinity for the aqueous stationary phase. Its extraction by the aqueous phase may favor the global yield of the reduction reaction. This point is under further investigation. The acceptable agreements between the experimental and theoretical conversion factors (Table 2) fully support the plug-flow character of the CCC machine used as a continuous liquid–liquid chemical reactor.

4.4. Plug injection for catalyst property study

The search for new efficient catalysts is an important field in chemistry. The efficiency of a new compound is checked by performing several chemical reactions in which it is used as the catalyst. These compounds are very often highly elaborated complexes of expensive and/or rare elements. When the catalyst is a liquid, a very few reactions, that are catalyst consuming, are performed. The scarce kinetic results are used to extrapolate the properties of the new catalyst.

The CCC machine could be a powerful tool to study the properties of a new catalyst for biphasic liquid reactions. The stationary phase contains the liquid catalyst and the mobile phase does not contain the reagent(s). The latter is injected as a short plug as for a classical chromatographic injection. When the reagent travels through the stationary phase, the reaction occurs and some the product is created. A continuous change of the reagent concentration is formed due to the catalyzed chemical reaction. The profile of the peak or band corresponding to remaining reagent and the profile of the peak/band corresponding to the product are both related to the properties of the liquid catalyst.

To illustrate the idea, the CCC machine, in the one-spool configuration ($V_T = 59$ ml), was loaded with the 5 M formate solution containing the liquid catalyst previously used (ruthenium–TPPTS complex). A high concentration (0.01 M) of the complex was used to be sure the chemical kinetics is fast enough. The ruthenium catalyst can be recovered after the experiment. The CCC machine was equilibrated with a pure cyclohexane mobile phase at 1.5 ml/min in the tail to head ascending mode. After equilibration ($V_M = 7$ ml, $S_f = 88\%$), a 200 μl BZA reagent plug was injected using a Rheodyne valve with a 200 μl loop. Fig. 4 shows the UV detector profile obtained. The sharp peak at 8 ml corresponds to the remaining BZA reagent that elutes close to the dead volume ($P_{BZA} = 0.02$). The peak area of a 200 μl BZA injection in the CCC machine without catalyst is about seven times higher than the Fig. 4 BZA peak area. The unreacted BZA amounts corre-

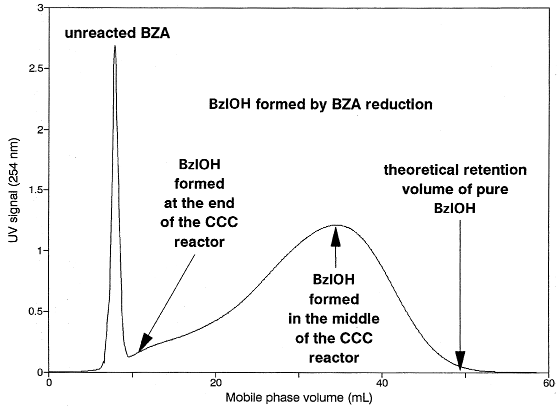


Fig. 4. BzlOH and BZA peak profiles after BZA injection in the CCC reactor loaded by the catalytic aqueous phase. $C_{aq}^{Ru} = 0.01$ M, $V_T = 59$ ml, 5 M sodium formate aqueous stationary phase: $V_S = 52$ ml, cyclohexane mobile phase 1.5 ml/min in the ascending tail to head mode, injection of 200 μl of 0.1 M BZA.

spond to less than 15% of the injected BZA (conversion higher than 85%). Fig. 4 shows the profile of the BzlOH product. The first eluted amount of BzlOH was the last formed (left part of Fig. 4) and *vice versa*. The theoretical retention volume of BzlOH is 50 ml (Eq. (10)). The main part of the BzlOH obtained was formed in the middle of the CCC reactor. It elutes with retention times in between 25 and 45 ml (Fig. 4).

The elution band profile of BzlOH should allow one to model the kinetic behavior of the Ru–TPPTS catalyst complex in the BZA reduction by sodium formate at room temperature. The idea could be pushed further: since two compounds travel in the CCC machine at a speed related to their respective partition coefficients, it is possible to imagine a sequential injection protocol. The slow traveling reagent would be injected first. The liquid catalyst travelling fast would be injected after. The reaction would take place when catalyst and reagent are superimposed. The analysis of the band profile of the product would give a lot of information on the kinetics of the catalyzed reaction. This theoretical study is under investigation and will be the topic of another work.

5. Conclusion

A CCC machine, which is a chromatographic column with a liquid stationary phase, can be used as a liquid–liquid reactor for chemical reaction involving a liquid catalyst. The CCC machine works as a plug-flow reactor. There are two significant advantages to use the CCC chemical reactor. First, the chemical process is continuous. The products may interact with the stationary phase and be retained. This could displace the chemical equilibrium toward the desired product formation. The throughput of such a reactor should be higher than that of a classical batch reactor. Second, the CCC reactor can be used to evaluate rapidly the properties and capabilities of a new liquid catalyst. This capability should allow a rapid optimization of the use of a new liquid catalyst in a given chemical reaction. The CCC chromatographs are made with Teflon tubes that are oxygen permeable. It is also difficult to raise the temperature. Specially adapted CCC machines with stainless steel tubing should be designed for chemical reactions.

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