

# Heterogeneous catalysis in Supercritical CO<sub>2</sub> applied to Friedel-Crafts acylation

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We have considered here the acylation of a benzofurane derivative by an acid chloride. In the conventional process, polluting catalysts (Lewis acids) are operated using dichlorobenzene as the solvent. In a first step, we have proposed to replace these catalysts by reusable solid catalysts. Different catalysts were tested in dichlorobenzene, and among clay, metallic oxides, heteropoly acids, ion exchange resin, mordenite zeolite, zeolite  $\beta$ ..., one of them, the zeolite Y, was found to be the most performant. In a second step, we have proposed to replace the organic solvent, here dichlorobenzene, by supercritical carbon dioxide, or by mixtures of supercritical carbon dioxide and dichlorobenzene. Indeed, in addition to the “green” aspect related to the diminution of the quantity of organic solvent, use of supercritical carbon dioxide is very advantageous for this kind of chemistry, as for instance, because of its potential to “clean” heterogeneous catalysts, that, in this case, are likely to be poisoned by heavy by-product deposit [1]. In this work, acylation reactions were carried out using a specific high pressure tubular fixed bed reactor operated in the continuous mode. The catalyst, Zeolite Y, chosen from our preliminary batch experiments in dichlorobenzene, was tested in supercritical carbon dioxide, and this catalyst proved to be active in these conditions. Results concerning yield and selectivity of the reactions, from batch and continuous experiments, are presented and compared to results in dichlorobenzene.

## INTRODUCTION

Friedel-Crafts acylation is a fundamental step in the manufacture of aromatic ketones which are used as intermediates in fine chemical (pharmaceuticals, agrochemicals and fragrances)[2]. These acylations are industrially carried out using an over-stoichiometric amount of Lewis acid catalysts, such as AlCl<sub>3</sub>. Such processes generate a high volume of unwanted polluting and corrosive by-products, and with the current drive towards “green chemistry”, it is recognised that conventional Lewis acid catalyst do need to be replaced by reusable and environmentally friendly catalysts. In this respect, a wide variety of new solid catalysts, more efficient and less polluting, can be proposed, like zeolites, ion exchange resins or heteropoly acids... [3, 4] These solid catalysts can be easily separated from liquid products, and continuous processes are easier to conceive using for instance fixed bed reactors.

Up to date the usefulness of carbon dioxide as a medium for chemical syntheses has attained greater acceptability for a variety of reasons, including the availability of pressure tunable physical properties and/or the possibility of single-phase operation when gas-liquid system are conventionally used [5-10]. Furthermore a problem frequently encountered in heterogeneous catalysis is the formation of heavy by-products [11], blocking active sites, and

thus leading to catalyst deactivation. When using supercritical media, enhanced diffusivity may accelerate the elimination of poisons from the internal and external catalyst surface, increasing catalyst lifetime. Regeneration of catalysts deactivated by coking can be accomplished by extracting the carbonaceous deposits from the catalyst surface [12]. In this work, the best catalyst found for use in a conventional solvent is briefly presented, and the work made in supercritical conditions with the continuous high pressure fixed bed is more detailed.

## MATERIALS AND METHODS

The zeolite investigated for this reaction was H-Y with  $\text{SiO}_2/\text{Al}_2\text{O}_3$  molar ratios of 15. This zeolite H-Y(15) was purchased in powder and pellet form (cylinder of 1.5mm in diameter and 2-5mm in length from Tosoh). The two zeolites were in the acidic H-form.

The water content of  $\text{CO}_2$  and  $\text{N}_2$  has to be as low as possible to avoid the degradation of the acyl chloride into the corresponding acid and HCl.  $\text{CO}_2$  (99.995%) was supplied by Air Liquide and  $\text{N}_2$  (99.995%) by Linde Gas.

In the context of this study, which is done through a collaborative industrial contract, it is not possible to disclose the exact name of the involved benzofurane derivative and the acid chloride.

### Conventional solvent batch experimental set-up

The acylation reaction was carried out in a  $250\text{ cm}^3$  batch reactor equipped with a condenser and magnetic stirrer where the acyl chloride (AC), the aromatic substrate (AS) and the solvent (dichlorobenzene, S) were mixed in the reactor. A sample of calcined zeolite\* was introduced in the reactor and the medium was heated up to the reaction temperature. The resulting suspension was stirred under reflux for 6h. The initial amounts of each compound are given for each reaction.

Samples were taken out periodically during the reaction and assayed by HPLC (Waters 600E apparatus with Symmetry C8 column).

\*Calcination procedure: the sample of catalyst is heated in a furnace with a heating rate of  $4^\circ\text{C min}^{-1}$  from room temperature to  $500^\circ\text{C}$  and then maintained at this temperature during 6 hours.

### Supercritical $\text{CO}_2$ continuous reactor

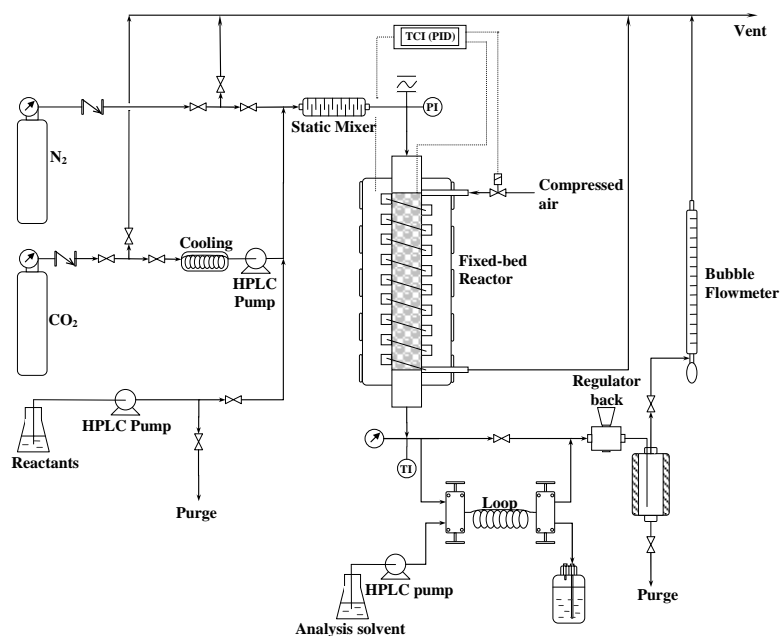
The catalytic acylation reactions in supercritical conditions were performed in a continuous fixed-bed reactor, consisting of: (i) a medium supply unit, (ii) a reaction unit; and (iii) an analytical loop (Fig. 1).

The medium supply unit comprised two HPLC pump, one for the liquid reactant mixture with a given ratio AS/AC and one for liquid  $\text{CO}_2$ . A static mixer (heated around  $60^\circ\text{C}$ ) before the reaction unit allows a good mixing of reactants and  $\text{CO}_2$ .

Our system allows in-situ calcination of the catalyst, where nitrogen is used at a flow-rate of  $250\text{ cm}^3/\text{min}$  (STP). The calcination was performed at  $500^\circ\text{C}$  during 6 h.

The reaction unit comprises a tubular reactor with an internal cartridge (14mL, 0.50 m length, 6mm inner diameter) loaded with the solid catalyst, a safety rupture disc, a pressure transducer and a K-type thermocouple located inside the catalytic bed, near the outlet. In addition a PID temperature controller and electrically heated shells allow operating at the desired temperature.

Continuous reactors for SCFs have the advantage over batch reactors that they do not require depressurisation to feed in the reactants or to recover the products. Samples can be taken out



**Figure 1:** Scheme of the continuous high pressure fixed bed (length 50 cm, inner diameter 6mm)

periodically during the reaction by using a sample loop of known volume, placed before the back-pressure regulator. The obtained sample is then decompressed in the HPLC solvent and the loop is rinsed with 10 times the volume of the loop. Each sample is assayed by HPLC (Waters 600E apparatus with Symmetry C8 column). The procedure for operation of the continuous reaction is as follow:

The cartridge is loaded with 4.3g of catalyst and calcined during the first day. The next day, the CO<sub>2</sub> is pumped and then the reactor is heated up between 150°C and 180°C, depending on the experiment. When the temperature at the outlet is stable the mixture of reactants is pumped into the system. Samples are taken each half hour. The flow of CO<sub>2</sub> was fixed to 1g/min or 2g/min, and the flow of reactants to 0.1g or 0.05g depending on experiments. The pressure was fixed at 300 bar, to compensate the bad solvating power of CO<sub>2</sub> at such high temperatures.

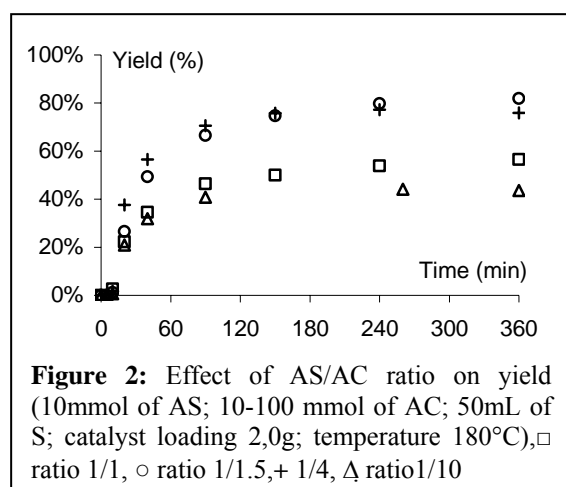
## RESULTS

### Choice of the catalyst in conventional solvent

Different kinds of catalysts were used to perform the acylation: zeolites, ion exchange resins, metallic oxides, heteropoly acids (HPA) and clay. The choice of these catalysts was made according to their reported efficiency for different aromatic acylations [5,13,14].

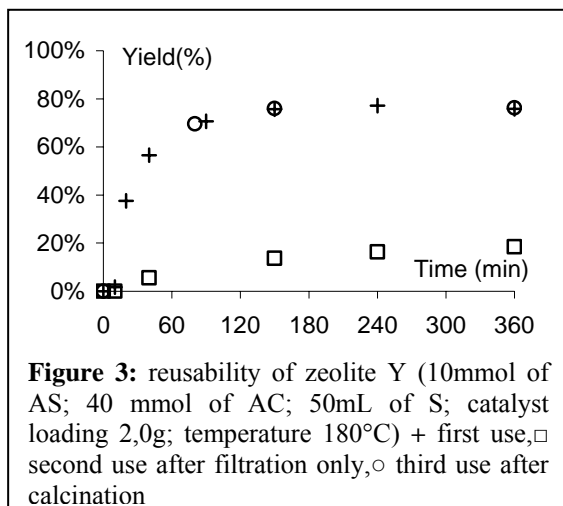
Among these heterogeneous catalysts only zeolite Y (SiO<sub>2</sub>/Al<sub>2</sub>O<sub>3</sub>=15) and indium oxide gave interesting yield. However, indium oxide was shown to be solubilized during the reaction, which is redhibitory for our studies. So, zeolite Y has been considered as the best candidate.

Other batch reaction runs have been carried out with zeolite Y to optimise the operating conditions (ratio AS/AC, catalyst loading, reusability...) before using it in the supercritical fixed bed reactor.



**Figure 2:** Effect of AS/AC ratio on yield (10mmol of AS; 10-100 mmol of AC; 50mL of S; catalyst loading 2,0g; temperature 180°C), □ ratio 1/1, ○ ratio 1/1.5, + 1/4, Δ ratio 1/10

The figures 2 and 3 summarize the best results in terms of yield and reusability of the zeolite Y. The maximal yield was shown to reach 80% (in respect to the benzofurane derivative substrate), with 2g of zeolite in 6 hours, and the reactant ratio was found to be the main parameter (fig 2).



yield drops significantly, from an initial value of 76% to 18%. The deactivation of the zeolite is very likely due to the deposition of heavy products usually termed as “coke”, and this hypothesis is currently under investigation using IR surface analysis. According to Richard *et al.* [15] this “coke” formation probably results from the acylation of compounds obtained by condensation of aromatic substrate, thus blocking the active sites. Occurrence of residues of the thermal degradation of the substrate is also a possible cause. As expected, calcination of the used zeolite allows complete recovery of its catalytic activity (see fig 3). Indeed, the need for zeolite regeneration was already observed by Guignard *et al.* and Moreau *et al.* [16, 17]. In this kind of experiments the regeneration of the catalyst becomes a prominent parameter.

#### Reaction under supercritical conditions

These previous experiments in a conventional solvent, the dichlorobenzene, have indicated which solid catalyst has the researched properties: good activity, reusable and which recovers all its activity by calcination.

For supercritical continuous experiments, zeolite Y(15) was first tested in its powder form (around 6-8µm particles). Preliminary calculations, using the Darcy law, have estimated the expected pressure drop of the fixed bed (16 bars), and this value was found acceptable for an operating pressure above 200 bar. Experiments confirmed the value of the predicted pressure drop.

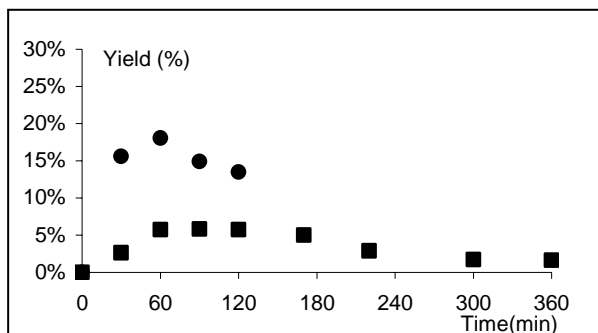
However use of zeolite powder proved to be very problematic, because all reaction runs ultimately lead to clogging of the reactor, very likely because these catalyst particles were indeed too small to be used in a fixed-bed reactor, especially when precipitation of by-products may occur, or when complete solubilisation of reactants is not insured. At T=180°C, P=200bar, although duration of experiments were not sufficient (a few hours) to be really representative, a 10% yield was observed (2g/min of CO<sub>2</sub>, 0.05g/min of reactants with a ratio AS/AC=1/2).

Fortunately, zeolite H-Y is also available in pelletized form: 1.5 mm in diameter and 2-5mm in length pellets, made with 20% inactive binder clay (“montmorillonite K-10”). These pellets are more suitable and, indeed, their use did not lead to clogging inside the reactor. The pressure drop of the bed of pellets is expected to be much smaller, the observed pressure drop being mainly due in this case to the fritted disk at the inlet and outlet of the tube, and did not exceed 5 bar.

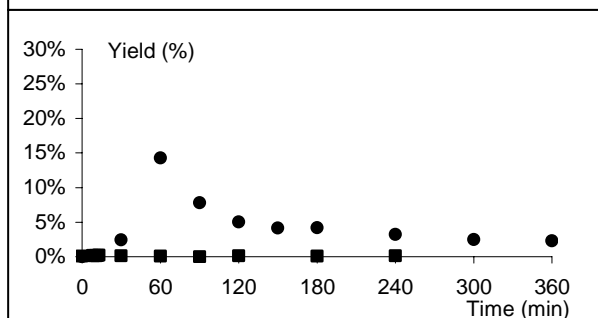
Figure 4 presents the time course of the product concentration at the output of the fixed bed. The influence of the calcination pre-treatment on the activity of the zeolite, can be seen, where 15% yield is obtained, against 5% with the non-calcined zeolite. In a conventional

The best ratio was around 1 mol of substrate AS for 1.5 mol of acylating agent AC. The results were equivalent when the ratio AS/AC increased to 1/4. With an excess of AC (ratio 1/10 fig 2), the activity of the zeolite seemed to be inhibited: active sites may have been saturated by the AC. In fact this inhibition phenomenon was also present at the end of the reaction (around 4h) when operating with a ratio of 1/4.

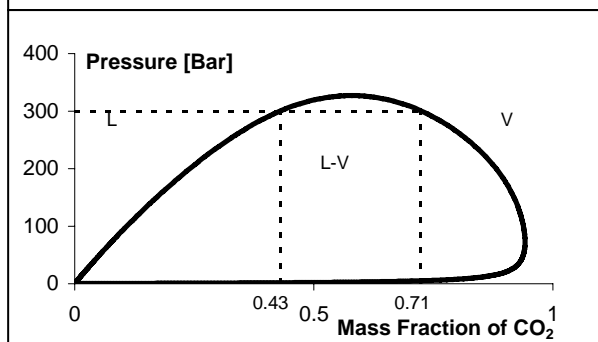
In term of reusability, figure 3 shows that the deactivation of the zeolite is relatively rapid. After a single use, if the catalyst is reused after a simple filtration on a fritted disc, the reaction



**Figure 4:** Activity of H-Y zeolite in pellet form (2g/min of CO<sub>2</sub>, 0.05g/min of reactants with a ratio AS/AC=1/2, T=150°C, P=300bars), ■ non-calcined zeolite, ● calcined zeolite.



**Figure 5:** Activity of H-Y zeolite in pellet form (0.05g/min of reactants with a ratio AS/AC=1/2, T=150°C, P=300bars), ■ 0.72 g/min of CO<sub>2</sub> and 1.2g/min of DCB (63% of DCB), ● 1.3 g/min of CO<sub>2</sub> and 0.5g/min of DCB (28% of DCB).



**Figure 6:** Isothermal fluid phase equilibrium diagram for T = 150°C - System: CO<sub>2</sub>-DCB (Peng Robinson EOS and  $k_{12}=0.1175$ [18])

solvent, the same behaviour was observed, i.e., an increase of yield when the zeolite is calcined. Figure 4 also shows that the activity of the calcined zeolite declines rapidly after 60 minutes (maximal yield was reached at this value of the time). In the case of non-calcined zeolite, the deactivation is slower and occurred significantly after 3 hours of reaction.

Some measurements using a high pressure cell (not reported here) have shown that the product of the reaction has a low solubility in pure carbon dioxide. It was supposed that with such a low solubility, the zeolite could be deactivated by deposition of the product onto the zeolite. This hypothesis was confirmed by using CO<sub>2</sub> in a batch reaction (100mL autoclave). In the same condition than in conventional solvent, a smaller yield (6%) was reached in comparison to conventional solvent (40%). Thus a soluble co-solvent, 1,2-dichlorobenzene (DCB), has been added in order to increase the product solubility and thus the yield. Figure 5 shows the influence of the quantity of DCB on the yield. Figure 6 presents the computed phase diagram of the mixture DCB-CO<sub>2</sub> (Peng Robinson equation of state with binary interaction parameter  $k_{12} = 0.1175$  [18]). This diagram shows that, at 300 bar, 150°C, two kind of mixtures are possible: an expanded liquid (CO<sub>2</sub> mass fraction < 0.43) and a dense gas phase (CO<sub>2</sub> mass fraction > 0.71). Using a high quantity of DCB (CO<sub>2</sub> mass fraction = 0.37) no reaction was detected, whereas, with a homogeneous vapour phase of CO<sub>2</sub> enriched with DCB (CO<sub>2</sub> mass fraction = 0.72), a maximum 15% yield was obtained, despite occurrence of a rapid deactivation.

Note that in these experiments the two fresh

zeolites had not been pre-treated by calcination and a comparison with the non pre-treated zeolite used in figure 4 shows that the deactivation seems to be slower with pure carbon dioxide.

Different experiments are now under progress to increase the yield, and mainly to increase the lifetime of the zeolite by varying the quantity of DCB in CO<sub>2</sub>. The study of the reusability of the zeolite by calcination is also planned.

## CONCLUSION

One of the most important challenges facing chemists is the successful development of new products, materials and chemical processes that can satisfy the social and economic requirements of the world ever-increasing population. This dual approach, aiming at changing the conventional catalysts and solvents, largely responds to green chemistry criteria.

On the one hand, a solid inexpensive catalyst (zeolite Y( $\text{SiO}_2/\text{Al}_2\text{O}_3$ 15)) was shown to be the only catalyst having the researched properties for this reaction and for its operation in a continuous fixed bed reactor (solid catalyst reusable by calcination). Moreover, it was observed in these experiments that few by-products have been generated

The experiments with supercritical  $\text{CO}_2$  in a continuous fixed bed yielded interesting and encouraging results, even if rapid deactivation of the zeolite was observed. Because of the low solubility of the expected product in pure  $\text{CO}_2$ , a co-solvent (DCB) was added. Operating conditions (temperature, pressure, residence time...) and proportions of DCB in  $\text{CO}_2$  have to be optimised to improve the yield. Batch operation of the reaction in a high pressure agitated vessel is also under progress to better understand the different phenomenon, by direct comparison with results of batch experiments in dichlorobenzene.

Anyway, this work constitutes a first step in the design of new greener route toward an important industrial pharmaceutical product using the emerging supercritical technology, applied to heterogeneously catalysed organic synthesis.

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