Continuous-Flow Reactors

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Real-Time Product Switching Using a Twin Catalyst System for the Hydrogenation of Furfural in Supercritical CO_2**

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There is an on-going debate over the relative merits of continuous and batch processing for the production of fine and speciality chemicals. Flow reactors have an inherently smaller volume than the corresponding batch reactor for a given production rate. Owing to this smaller volume, flow reactors can be operated above ambient conditions more safely than batch processes. Flow reactors have been used in organic synthesis where scale-up is possible using parallel reactors and combinatorial libraries are synthesized using divergent or convergent strategies with multireactor setups.[1–3]

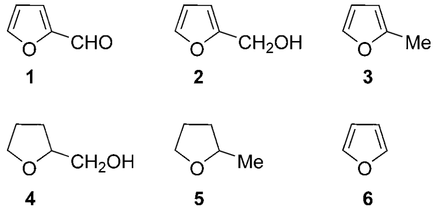
Reactions can be finely tuned much more easily in continuous flow than in batch mode because flow reactors can be operated under a wider range of conditions than batch reactors, for example, elevated temperatures and pressures, and various reactant stoichiometries by the adjustment of flow rates. However, despite many advances in continuous processing in the past decade, batch processing still predominates in the fine-chemicals and pharmaceutical industries, largely because the same batch reactor can be used for many different conversions.

Nevertheless, there is one thing that batch reactors cannot easily do, namely to switch back and forth between different products. Such "real-time" switching could potentially enable chemical industries to respond more rapidly to changing market demand for products, enhancing profitability and reducing reactor downtime.

Herein we demonstrate that such switching can be achieved remarkably simply for a set of reactions in supercritical carbon dioxide ($scCO_2$). We show that five different products can be obtained in high yields from a single feedstock, merely by switching reaction conditions—almost like getting drinks from a vending machine.[4]

Consider a flow system consisting of two reactors in tandem, such that each reactor operates only when heated. Then, if the two reactors contain different catalysts capable of promoting different reactions, *three* different products could be obtained from the same substrate, depending on whether the first, the second, or both reactors were heated. Furthermore if, as in this paper, the first catalyst could produce two different products depending on its temperature, *five* different products could be obtained by the correct combination of temperatures in the two reactors. We now demonstrate this concept in practice using furfural as the feedstock.

Furfural (**1**; Scheme 1) is obtained from the acid-catalyzed dehydration of a wide variety of renewable feedstocks, such as oats and rice husks. It is a potential platform chemical because it is easily converted into a range of useful compounds. Furfuryl alcohol (**2**) and 2-methylfuran (**3**) can be produced in various yields by hydrogenating **1** using copper-containing catalysts. Traditionally copper chromite is used at atmospheric pressure which allows the continuous production of **2** or **3** depending on the reaction temperature.[5,6]



Scheme 1. Compounds of interest in the hydrogenation of furfural: furfural (**1**), furfuryl alcohol (**2**), 2-methylfuran (**3**), tetrahydrofurfuryl alcohol (**4**), methyltetrahydrofuran (**5**), and furan (**6**).

Chromium-free catalysts such as copper on carbon or silica supports have also been reported for the hydrogenation of furfural to **2**.[7–10] Relatively few studies have been published on the selective hydrogenation of **2** to tetrahydrofurfuryl alcohol (**4**), although Chen et al. have reported high yields of **4** from **2** using supported nickel catalysts.[11] A wide range of metal-supported catalysts have been used for the hydrogenation of **3**, including ruthenium,[12] palladium or platinum,[13] and nickel catalysts.[14] Palladium has been reported as a catalyst for the decarbonylation of furfural to **6** in high yield at temperatures above 250 °C.[15,16]

Supercritical CO_2 is a highly effective medium for reactions with permanent gases such as H_2 because they are fully miscible with $scCO_2$. Mass-transfer limitations are reduced in $scCO_2$ and the viscosity is relatively low thus further enhancing hydrogenation reactions.[17,18] Furfural (**1**) is a promising candidate for hydrogenation in $scCO_2$ because it is highly soluble in $scCO_2$ and recent research has demonstrated the potential for using $scCO_2$ in the production of **1** from biomass.[19]

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Our interest in the real-time switching between multiple products was re-awakened during a detailed screening of Cu-based catalysts for the hydrogenation of **1** in $scCO_2$. One particular copper chromite catalyst (provided by Johnson Matthey) gave exceptionally high selectivity for either **2** or **3** depending on the temperature (99 % conversion of **1**; 99 % selectivity for **2** at 120 °C and 96 % selectivity for **3** at 240 °C, see Figure 1). This type of switchable selectivity is the first requirement for the "five-product" tandem reactor outlined above.

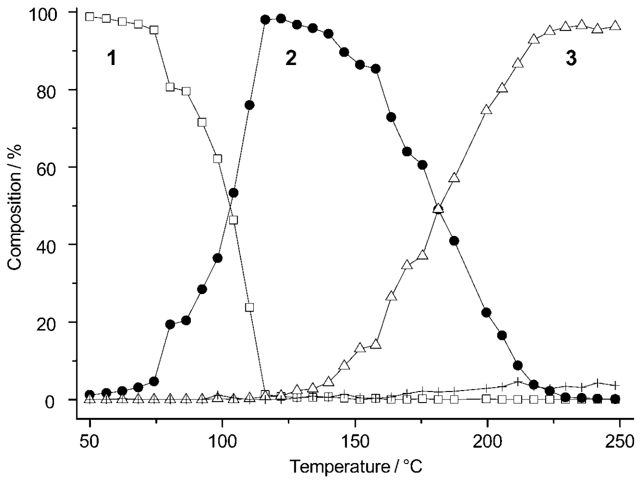

Figure 1. Traces showing the complete switch in selectivity between **2** and **3** as the temperature is increased during the hydrogenation of **1** using copper chromite in $scCO_2$. Reaction conditions: 1.0 $mL\,min^{-1}$ CO_2, 0.05 $mL\,min^{-1}$ **1**, 2 equiv H_2, total pressure 15 MPa. **1**: □, **2**: ●, **3**: △, +: other products.

Our next step was separate studies of the hydrogenation of **2** and **3** in $scCO_2$. We found that both compounds could be hydrogenated with excellent selectivity with 66 wt % Ni/silica but the catalyst was rapidly poisoned by both CO and H_2O. Such poisoning would be a serious problem if the Ni/silica catalyst were used as the second stage of the tandem flow reactor because H_2O is a co-product of **3**. We also found that copper chromite rapidly promotes the reverse water–gas shift (RWGS) reaction under these conditions [Eq. (1)].

$$H_2 + CO_2 \rightarrow H_2O + CO \tag{1}$$

H_2O can be separated relatively easily in a $scCO_2$ flow system,[20] but removal of CO is not feasible in our lab-scale reactor. Thus the Ni/silica catalyst is not suitable for our tandem reactor. Fortunately, the hydrogenation of **3** could be achieved in high yield with Pd/C over a wide temperature range (> 99 % conversion, > 99 % selectivity at 88–250 °C). The hydrogenation of **2** over Pd/C was less facile but with acceptable selectivity (82–93 %) across a wide temperature range (50–250 °C).

In the absence of H_2, the same Pd/C catalyst also promoted the decarbonylation of **1** to furan (**6**; > 99 % selectivity at 250 °C). Thus, together copper chromite and Pd/C can give the range of products, **2** to **6**, needed to demonstrate the feasibility of a "five-product" reactor.

Figure 2 shows our reactor configuration which incorporates separate H_2 feeds to the two catalyst beds (to minimize the RWGS reaction) and a water separator which permits the efficient removal of H_2O from the CO_2/organic stream without the need for depressurization.[20]

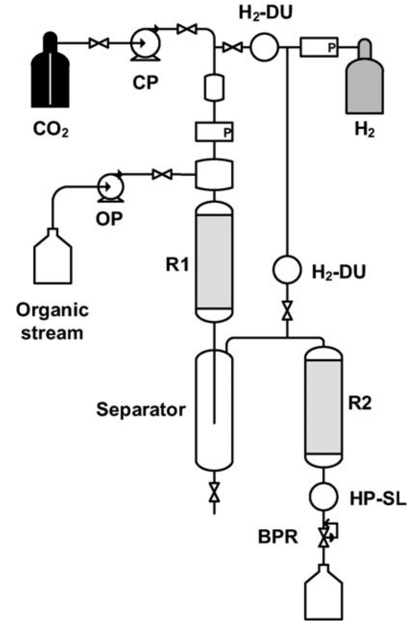

Figure 2. Schematic of our automated continuous-flow apparatus using $scCO_2$. The components are labeled as follows: CP: chilled CO_2 pump; H_2-DU: H_2 dosing units used to deliver the appropriate amount of H_2; OP: organic-stream pump; P: pressure monitor; R1, R2: independently heated reactors containing copper chromite and Pd/C catalysts, respectively; HP-SL: high-pressure sample loop connected directly to an online GC and BPR (back-pressure regulator). The separator removes liquid H_2O from the product stream emerging from R1.

Figure 3 shows the optimum results achieved over three runs when the copper chromite catalyst was used in combination with 5 wt % Pd on activated carbon. All five compounds, **2**–**6**, could be produced in high yield (> 80 % for all products) simply by changing the temperature of the reactors and amount of hydrogen dosed into the system. Online samples were taken every 20 minutes and analyzed by GC methods (see Table 1 and Figure 4 for the complete analysis). In contrast to the initial tests on the separate catalysts, the reactor containing Pd/C had to be heated to 300 °C for conversion of **3** into **5** to minimize the effects of poisoning by CO. During each run it was possible to switch between all five compounds without changing the catalyst beds or altering the system configuration. No decrease in catalyst activity was observed over the course of the experiment (14 h). In the example in Figure 4, **5** was produced initially and again after 700 minutes with no observable decrease in activity.

We have demonstrated the principle of real-time switching between multiple products by using reactions in supercritical CO_2 with a tandem flow-reactor setup to generate a choice of five products in high yield from a single biorenewable feedstock, furfural (**1**). The selective hydrogenation/

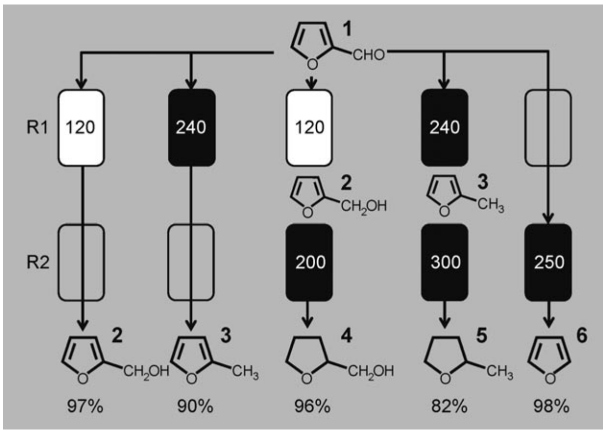

Figure 3. A switchable-product system in action. A summary of the best results achieved for the reactions of furfural (**1**) in scCO$_2$ using the apparatus shown in Figure 1. The temperatures (°C) of the two catalyst beds are indicated; R1 contained copper chromite and R2 was filled with Pd/C. By using computer control to change the H$_2$ dosing and the temperatures of the catalysts, the reactor can be switched back and forth between products with a time lay of <40 min, the re-equilibration time of the system. Note: The flow of H$_2$ was completely stopped for the conversion of **1** into **6**.

Table 1: Optimum results as an average obtained from three runs each over 1 hour.

Reactor temperature (R1, R2)		**1**[a]	**2**[a]	**3**[a]	**4**[a]	**5**[a]	**6**[a]	X[a,b]
140 °C	off	1	98	<1	0	0	0	1
120 °C	200 °C	0	0	0	96	3	0	1
240 °C	off	<1	3	90	<1	<1	0	4
240 °C	300 °C	0	0	1	6	82	<1	10
off	250 °C[c]	1	0	0	0	0	98	1

[a] Composition [%] determined by GLC analysis using known standards and an internal normalization method. [b] Other products. [c] Without H$_2$ feed.

decarbonylation of either the carbonyl or furan ring structure (or both) can be accomplished using copper chromite and supported palladium catalysts, respectively. "Real-time" switching to any of the products is possible by simply changing the reactor temperatures and/or the concentration of H$_2$.

We believe that this approach will be applicable to a wider range of feedstocks and reactions, including acid-catalyzed reactions. The approach may be particularly suited to renewable feedstocks since these are often relatively small molecules with more than one functional group.

Experimental Section

CAUTION! The experiments described in this paper involve the use of relatively high pressures and require equipment with the appropriate pressure rating.

All single-reactor experiments were carried out using a high-pressure, automated continuous-flow reactor with online GLC analysis. This reactor, described in detail previously,[21] is designed to record the effect on product yield of varying a single reaction parameter at a time (e.g. temperature, pressure, flow rate, etc). In a typical experiment, the reactors (156 mm long × 3.525 mm internal diameter) were filled with catalyst and then a 20 mm layer of sand was loaded on top of the catalyst to act as a preheated zone. After the equipment had stabilized at the required pressure and flow rate of CO$_2$, the catalyst was pre-reduced by dosing in 5% H$_2$ (BOC gases, 99.999% purity) in CO$_2$ at 200 °C. The reactor was heated to the reaction temperature and the substrate was pumped into the system. Standard reaction conditions: flow of CO$_2$ (Air Products, food grade) 1.0 mL min^{-1} (pumphead at -10 °C and 5.8 MPa), flow of the furfural (Acros 98%, distilled before use) 0.05 mL min^{-1}, 15 MPa operating pressure. The gas chromarograph was fitted with a HP-5 column (30 m, ID 0.32 mm, film thickness, 0.25 μm) held at 60 °C for 3 min, ramped at 40 °C min^{-1} to 280 °C and then held for 5.5 min. Catalyst bed R1 was loaded with approximately 1.9 g of copper chromite (provided by Johnson Matthey) and R2 was loaded with approximately 0.5 g of 5 wt% palladium on activated carbon. Wherever possible control experiments were carried out in the absence of CO$_2$.

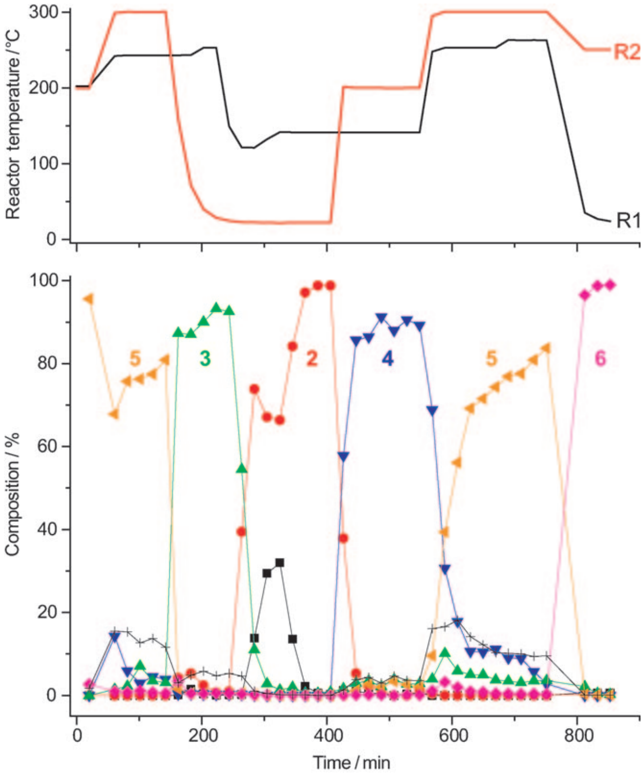

Figure 4. Real-time switching between products. Plots of reactor temperature (top) and composition of the product stream issuing from R2 determined by online GLC analysis (bottom).

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