

Continuous flow homogeneous catalysis using supercritical fluids

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The continuous flow hydroformylation of 1-octene catalysed by Rh/[RMIM][Ph₂PC₆H₄SO₃] (R = 1-propyl, 1-pentyl or 1-octyl) dissolved only in the steady state reaction mixture and using scCO₂ as a transport vector for both substrates and products gives rates up to 160–240 catalyst turnovers h⁻¹ with low rhodium leaching over a 12 h period at a total pressure of 125–140 bar.

The separation of the products of a reaction from the catalyst and any solvent can be such a serious problem for reactions involving homogeneous catalysts that their commercialisation is sometimes inhibited. This is especially the case if the products are of low volatility and/or the catalyst is of low thermal stability.¹ A range of new approaches to this separation problem is being explored,^{2,3} but amongst them those which involve continuous flow processing are especially attractive, not only because the catalyst/product separation is built in as an intrinsic part of the process, but also because all of the catalyst always remains in the reactor in its active state and high throughputs can be achieved from relatively small reactors. We recently reported that the rhodium catalysed hydroformylation of long chain alkenes, a reaction of considerable potential significance for the production of plasticiser, soap and detergent range alcohols, can be carried out as a continuous process using a supercritical fluid — ionic liquid biphasic system.^{4,5} Reaction rates similar to those obtained using rhodium catalysts for commercial propene hydroformylation were obtained with very low rhodium leaching (0.012 ppm in the recovered product), when using a catalyst formed *in situ* from [PrMIM][Ph₂PC₆H₄SO₃] (PrMIM = 1-propyl-3-methylimidazolium) and [Rh(acac)(CO)₂] (acacH = 2,4-pentanedione) in [OctMIM][bistrifluoromethylsulfonyl amide] (oct = 1-octyl) and using supercritical CO₂ (scCO₂) as the transport vector.⁴ Although the linear to branched ratio of the products (l : b) was low (3–4 : 1), this could be improved to 40 : 1 albeit at a slightly lower rate using a ligand based on the xantphos skeleton.⁶ A similar process has subsequently been used for a variety of other reactions involving metal based or enzyme catalysts.⁷ The main problem with the SCF-IL biphasic system for alkene hydroformylation is that the overall pressure of the system is high at 200 bar. This high pressure is required, at least in part, because the aldehyde has to be extracted from the ionic liquid in which it is soluble.^{8,9} There is also a residual question over the long term stability and toxicity of the ionic liquid solvent; those with long alkyl chains having recently been shown to cause skin

irritation.¹⁰ These solvents may also prove to be prohibitively expensive for use in the manufacture of bulk or commodity chemicals. In this paper, we report a method for overcoming both of these problems by removing the ionic liquid altogether.

Imidazolium based ionic liquids with a long alkyl chain are capable of dissolving both the alkene substrate and the aldehyde product. This suggests that they are not very polar and we reasoned that it might be possible to dissolve the ligand and rhodium precursor in the steady state mixture of substrate and products that would be generated if no ionic liquid were present. If this were the case, it should be possible to use the steady state reaction mixture as the solvent and to transport substrates into the reactor and products from the reactor dissolved in scCO₂. Our initial studies using the reactor described previously⁴ showed that [PrMIM][Ph₂PC₆H₄SO₃] exhibits some solubility in nonanal at the reaction temperature so that the reaction can be carried out using nonanal as the initial solvent. GC analysis of liquid fractions collected downstream over a 12 h period showed that the reaction proceeded. Initially nonanal was recovered from the scCO₂ in the decompression system, but the composition of the recovered product altered with time to reach a steady state, as indicated by the linear : branched (l : b) ratio of the aldehydes. This initial reaction was carried out at 200 bar total pressure and it proved very difficult to adjust the gas and liquid flow rates so as to maintain a constant liquid volume in the reactor, such that at the end of the reaction, the reactor was almost dry and the catalyst, together with excess ligand was largely present in a solid form. In the absence of a second solvent the rate of removal of reaction products must be balanced by the rate at which products are formed within the system so as to maintain a constant volume of reaction solution. Working at 140 bar (Entry 1, Table 1), the control was easier but the overall rate was still low. In addition, substantial rhodium leaching occurred in the early part of the reaction. This suggests that the ligand may not be sufficiently soluble in the mixture for catalyst formation to take place efficiently and rhodium complexes without bound phosphines are removed because of their solubility in scCO₂.

In order to increase the solubility of the ligand and catalyst and maintain the substrate product level within the reactor, the reaction was carried out at 140 bar using the more lipophilic ligand, [OctMIM][Ph₂PC₆H₄SO₃]. Under these conditions, it was easier to adjust the CO₂, and CO/H₂ flow rates to obtain a good mass balance and a reaction rate of 239 catalyst turnovers h⁻¹ was obtained throughout the 12 h reaction (Fig. 1 and Table 1, Entry 5). Fig. 1

Table 1 Hydroformylation of 1-octene at 100 °C catalysed by rhodium complexes of different phosphines, using scCO₂ to transport the substrate and gases into and the products out of the reactor^a

Entry	Ligand R ^b	[Rh]/ mol dm ⁻³	[P]/ mol dm ⁻³	CO ₂ flow/ nL min ⁻¹	CO flow ^c / mmol min ⁻¹	Octene flow/ mmol min ⁻¹	P ^d /bar	TOF ^e / h ⁻¹	Conversion ^f (%)	[Rh] leaching ^g / ppm
1	Pr	0.012	0.19	0.47	1.2 ^h	0.042	140	22	25	35 ⁱ
2	Pent	0.011	0.16	0.55	2.89	0.32	125	80	76	0.1–0.5
3	Pent	0.0057	0.043	0.55	2.78	0.32	125	162	77	0.1–0.5
4	Oct	0.015	0.22	0.65	1.59	1.27	140	208	50	5–10
5	Oct	0.015	0.22	0.65	2.34	1.27	140	239	57	5–10

^a Starting solvent is 1-nonanal (16 cm³), nL = normal litre; ^b In [RMIM][Ph₂PC₆H₄SO₃]; ^c CO : H₂ = 1 : 1; ^d Total pressure; ^e mol product (mol catalyst h)⁻¹; ^f % aldehyde in recovered product; ^g [Rh] in recovered product; ^h CO : H₂ = 1 : 2; ⁱ High leaching early in the reaction.

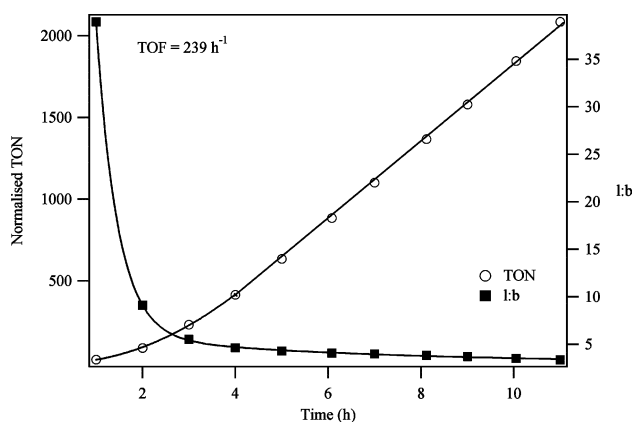


Fig. 1 Continuous flow hydroformylation of 1-octene in nonanal (initial solvent) with scCO_2 as the flowing phase. $[\text{OctMIM}][\text{Ph}_2\text{PC}_6\text{H}_4\text{SO}_3]$ (1.45 g, 2.69 mmol) and $[\text{Rh}(\text{acac})(\text{CO})_2]$ (45.9 mg, 0.18 mmol) in 1-nonanal (16 mL). Flow rates: CO_2 (0.65 nL min^{-1}), synthesis gas (1 : 1, 3.72 mmol min^{-1}), 1-octene (0.2 mL min^{-1} , 1.27 mmol min^{-1}); 100 °C, 140 bar.

also shows the change in l : b ratio of the recovered aldehydes during the reaction. Initially the only aldehyde present was nonanal (it was the starting solvent), but the l : b ratio changed smoothly towards the steady state value of 3.2 : 1 characteristic of the products expected from the reaction using this type of ligand.⁴

Reducing the flow rate of synthesis gas, but retaining the overall pressure by increasing the CO_2 partial pressure, reduces the reaction rate (compare Entries 5 and 4 of Table 1), as observed when using an ionic liquid,⁴ because the octene partitions less into the liquid phase, where the catalyst is located. Changing the alkyl chain length on the imidazolium cation has a more dramatic effect. $[\text{PrMIM}][\text{Ph}_2\text{PC}_6\text{H}_4\text{SO}_3]$ is not sufficiently soluble in the organic phase to give good catalysis. This has two effects, firstly the reaction rate is low, but secondly the rhodium leaching is high early in the reaction because rhodium complexes are formed which do not contain phosphine, and these are soluble in scCO_2 . $[\text{OctMIM}][\text{Ph}_2\text{PC}_6\text{H}_4\text{SO}_3]$ is very soluble in the organic phase and therefore gives good reaction rates but has some solubility in scCO_2 , hence the leaching. $[\text{PentMIM}][\text{Ph}_2\text{PC}_6\text{H}_4\text{SO}_3]$ has intermediate properties; it dissolves in the organic phase, but not at such high levels as $[\text{OctMIM}][\text{Ph}_2\text{PC}_6\text{H}_4\text{SO}_3]$, and shows reasonable catalytic activity but the leaching into the collected product is much reduced.

Whereas $[\text{OctMIM}][\text{Ph}_2\text{PC}_6\text{H}_4\text{SO}_3]$ is highly soluble in nonanal the $[\text{PentMIM}]$ analogue only shows appreciable solubility at elevated temperatures. Initial attempts to hydroformylate octene continuously using $[\text{PentMIM}][\text{Ph}_2\text{PC}_6\text{H}_4\text{SO}_3]$ under conditions identical to those used for $[\text{OctMIM}][\text{Ph}_2\text{PC}_6\text{H}_4\text{SO}_3]$, were unsuccessful. GC analysis of liquid fractions recovered downstream revealed a gradual drop in the % aldehyde despite some initial conversion of substrate as indicated by the presence of branched product. In this case a steady state reaction mixture was never achieved. This rapid drop in substrate conversion occurred because although the phosphine is soluble in nonanal it is insoluble in octene/aldehyde mixtures. As the concentration of alkene within the reaction solution increased, precipitation of the catalyst

occurred leading to lower rates, a higher concentration of unreacted substrate, further precipitation of catalyst and so on. In fact, to support the catalyst concentrations initially used requires a reaction solution with a composition that is at least 70 mol % aldehyde. This is illustrated further by entries 2 and 3 of Table 1; despite a large difference in the initial concentration of catalyst the same conversion is observed suggesting that not all of the catalyst is actually in solution at the higher loadings (although we note that the increased phosphine concentration will also reduce the rate). Precipitation of the catalyst was overcome by using a lower catalyst concentration and a lower flow rate of octene so as to increase its residence time within the catalyst solution thereby increasing the % conversion to products.

In conclusion, we have demonstrated that it is possible to carry out the hydroformylation of medium chain alkenes in a continuous flow system using scCO_2 as the transport vector for substrates and products, but with no other components apart from the substrates, catalyst and products. Since the scCO_2 can in principle be recycled, this represents a process which is potentially emissionless. This new approach has advantages over our previously reported systems involving ionic liquids because it can be carried out at much lower pressures and the one component of the system over which there was some environmental doubt has been removed. We anticipate that this kind of process could be applicable to a wide range of catalytic reactions. Removal of the ionic liquid offers further advantages in terms of reduced capital costs. The pressure we currently use (125 bar) is much closer to the pressure used in the commercial production of medium — long chain aldehydes, which is carried out using cobalt/phosphine catalysts at 80–100 bar, however, the temperature we use (100 °C) is much lower than that used in the commercial cobalt process (180 °C). A preliminary patent application covering this work has been filed.¹¹

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