



Experimental strategies for increasing the catalyst turnover number in a continuous Heck coupling reaction



Ludmila Peeva, Joao da Silva Burgal, Shankul Vartak, Andrew G. Livingston*

Department of Chemical Engineering and Chemical Technology, Imperial College London, Exhibition Road, London SW7 2AZ, UK

ARTICLE INFO

Article history:

Received 15 March 2013

Revised 16 May 2013

Accepted 23 June 2013

Available online 31 July 2013

Keywords:

Continuous Heck coupling reaction

Pd retention *in situ*

Organic solvent nanofiltration (OSN)

PEEK membrane

Low contamination of the product stream

High catalyst TON

ABSTRACT

This work presents a continuous Heck coupling reaction combined with organic solvent nanofiltration (OSN) separation of the catalyst *in situ*, using polymeric membranes at high temperature (80 °C) and high concentration of base ($>0.9 \text{ mol L}^{-1}$). Two reactor configurations are investigated: a continuous single stirred tank reactor/membrane separator (m-CSTR) and a plug flow reactor (PFR) followed by m-CSTR (PFR–m-CSTR). The combined PFR–m-CSTR configuration was found to be the most promising, achieving conversions above 98% and high catalyst turnover numbers (TONs) of $\sim 20,000$. In addition, low contamination of the product stream ($\sim 27 \text{ mg Pd per kg of product}$) makes this process configuration attractive for the pharmaceutical industry.

© 2013 Elsevier Inc. All rights reserved.

1. Introduction

Many organic syntheses require expensive homogeneous transition metal catalysts (TMCs) to effect the reactions. Separation of these catalysts from the reaction products and solvents is difficult, requiring the use of energy intensive and waste-generating downstream processing [1,2]. In addition, distillation, the most commonly used separation method, requires high temperatures (unless the product is very volatile), and most homogeneous catalysts are thermally labile (even at reduced pressure usually decomposition can occur). Other conventional processes such as chromatography or extraction also lead to catalyst loss [3].

Recovery of a (noble) metal catalyst is useful not only for obvious economic reasons but also because contamination of a product by heavy metal impurities is undesirable and must be limited to sub-ppm levels [2]. A lot of research has been done to heterogenise TMCs with different techniques such as encapsulation, interphase chemistry, phase-tagging for biphasic catalysis or ionic liquids and various techniques for the immobilisation of molecular catalysts on solid or colloidal supports [4]. For example, Gröschel et al. [5] employed a catalytically active membrane based on poly(acrylic acid) networks containing palladium nanoparticles for the partial hydrogenation of propyne. In order to test the long-term stability, a membrane was kept under constant reaction conditions for about 6 days (reactants flow rate of 20 mL min^{-1} and

temperature of 298 K), and a conversion and selectivity of about 50% and 88% were obtained, respectively (TON data not presented). Another work from Milano-Brusco et al. [6] used a different approach based on the potential of surfactant-based reaction media in different homogeneous catalytic reactions. The reaction under study was the enantioselective catalytic hydrogenation of dimethyl itaconate (DMI) using two different reaction media. In the first one, the Rh catalyst is complexed with the chiral ligand (2*S*,4*S*)-1-*tert*-butoxycarbonyl-4-diphenylphosphino-2-(diphenylphosphinomethyl)-pyrrolidine (BPPM) ($T = 30 \text{ °C}$ and $P = 1.1 \text{ bar}$). After complete hydrogenation was achieved, micellar-enhanced ultrafiltration (MEUF) with a polyethersulfone membrane (Nadir P010) was used to recycle the catalyst achieving up to 95% retention; in this configuration, three repetitive batches of DMI were performed, and an enantiomeric excess (ee) of up to 69% was obtained (TON data not presented). In the second reaction medium, Triton X-100 was used for the hydrogenation of DMI with a Rh catalyst complexed with the water-soluble tris(3-sulfophenyl)phosphine trisodium salt (TPPTS) at 50 °C and 1.1 bar. With this system, phase separation by temperature-induced separation allowed for up to four repetitive batches of DMI hydrogenations, resulting in a TON of 1530. Nevertheless, anchoring the catalyst on, for instance, inorganic supports or organic polymers often result in a loss of activity and selectivity [1]. Zhan et al. [7] reported a novel type of Heck reaction catalyst, composed of hydrophilic interpenetrating polymer networks (PINs) and palladium (Pd) nanoparticles that could be recycled 20 times in DMF; however, the yields were not stable from cycle-to-cycle, with variations from 60% to 90%.

* Corresponding author. Fax: +44 020 75945639.

E-mail address: a.livingston@imperial.ac.uk (A.G. Livingston).

Nomenclature

A_s	cross-sectional area (cm ² or m ²)	μ	viscosity (Pa s)
C	concentration at $T_{ref.}$ and $P_{ref.}$ (mol L ⁻¹)	ρ	density (kg m ⁻³)
D	diameter (cm)		
K	pre-exponential factor/kinetic rate constant (min ⁻¹)	<i>Subscripts</i>	
L	length (cm)	<i>cat.</i>	catalyst
\dot{m}	molar flow rate (mol min ⁻¹)	<i>CSTR</i>	continuous stirred tank reactor
n	reaction order, dimensionless	<i>gen</i>	generated in the CSTR
p	pressure (bar)	<i>i</i>	component <i>i</i> of the solution
Q	volumetric flow rate (mL min ⁻¹)	<i>IB</i>	iodobenzene
R	rejection, dimensionless (note that in a continuous filtration mode rejection and retention are equivalent terms)	<i>in</i>	system inlet stream
r	reaction rate (mol L ⁻¹ min ⁻¹)	<i>out</i>	CSTR outlet stream
Re	Reynolds number	P	product
<i>Salt</i>	triethylamine hydroiodide	<i>perm</i>	permeate
T	temperature (°C)	<i>PFR</i>	plug flow reactor
t_r	residence time (min)	<i>ref.</i>	reference
V	reactor volume (mL)	<i>ret</i>	retentate
v	velocity of the fluid (cm min ⁻¹ or m s ⁻¹)	S	substrate
X	conversion, dimensionless		

The recent development of organic solvent nanofiltration (OSN) provides an alternative to the classical heterogenisation of homogeneous complexes. An OSN membrane is used to separate the homogeneous catalyst from the reaction mixture and thus recycle the homogeneous complex. OSN has already been performed at laboratory scale to recycle homogeneous catalysts, and its importance and relevance have been emphasised by works such as Nair et al. [4], who performed a semi-continuous nanofiltration-coupled catalysis for a well-known Heck coupling reaction. They permeated the post-reaction mixture through a polyimide OSN membrane achieving an overall 90% catalyst retention after four catalyst recycles (five reaction–filtration sequences) and a total catalyst turnover number (TON, moles of product synthesised per mol catalyst added) of 1200; Datta et al. [8] developed catalysts for the Heck, Sonogashira and Suzuki type coupling reactions, which were retained by poly(dimethylsiloxane) (PDMS) membranes (retention higher than 99.5%), but the catalysts lost activity after a series of catalyst recycles; Aerts et al. [1], who used silicon-based OSN membranes to recycle the Co-Jacobsen catalyst four times in diethylether (Et₂O), achieving 98.5% retention and a minor decrease in the conversion from one cycle to another; Janssen et al. [9] reported the synthesis of multiple phosphine ligands attached to a dendritic support via ‘click’ chemistry (molecular weight enlargement – MWE – catalysts) and their application in the Pd-catalysed Suzuki coupling as well as their recovery and reuse by means of nanofiltration. In this work, the reaction performed was the Suzuki–Miyaura coupling between 4-bromotoluene and phenyl boronic acid at 60 °C for 16 h with three different ligands. A ceramic membrane (Nanofiltration Inopor[®] nano 450 Da) with retention higher than 99% for the three MWE catalysts was employed, and four catalyst recycles were performed achieving initial yields of 99% but decreasing from cycle-to-cycle (TON data not presented).

All previous examples of OSN stated above were performed in discontinuous or semi-continuous mode, but current interest in the continuous flow production of fine chemicals has motivated a re-evaluation of how synthetic transformations are performed at the laboratory, intermediary and manufacturing scales. Although continuous operations might require more time initially to set up equipment and find the optimum conditions – concentrations, temperatures and flow rates – other parameters such as mixing

and temperature can be more easily controlled when compared to batch processes [10,11]. Few works have been published in the literature about continuous flow production with catalyst retention using OSN. One of the very first works in continuous catalysis was performed by Brinkmann et al. [12]. These authors focused on the usage of diaminopropyl-type dendrimers bearing palladium phosphine complexes as catalysts for the allylic substitution in a continuously operating chemical membrane reactor. Retention rates by ultra- or nanofiltration membranes – Nadir UF-PA-5 and SELRO MPF-50, respectively – higher than 99.9% resulted in a total TON for the Pd catalyst of circa 95. However, in the reactions of $T = 25$ °C and a flow rate of 20 mL h⁻¹, the conversion starting at 100% decreased to around 80% after 40 h (80 residence times), and the experiment was stopped. Dijkstra et al. [13] developed a shape-persistent nanosize dodecakis (NCN-Pd^{II}-aqua) complex [14] that was applied as a homogeneous catalyst under continuous reaction conditions in a nanofiltration membrane reactor. The reaction performed was the double Michael reaction between methyl vinyl ketone and ethyl-cyanoacetate, and the membrane used was Koch MPF-50 flat-membrane (catalyst rejection of 99.5%). Under the reaction conditions of $T = 23$ °C and $P = 20$ bar, a TON of 3000 and a conversion of 85% were obtained (26 h, 65 exchanged reactor volumes). Smet et al. [15] have performed a continuous enantioselective hydrogenation of dimethyl itaconate with Ru-BINAP catalyst and of methyl 2-acetamidocrylate with Rh-EtDUPHOS catalyst in a hybrid process composed of a CSTR followed by a NF unit (NF-coupled catalysis). For the first reaction, they achieved a conversion of 100% throughout the entire run, and for the second reaction, the conversion was 100% initially but then decreased to 90% in the later stages. The catalyst retention was above 97% for both reactions. The TON for the hydrogenation with Ru-BINAP and Rh-EtDUPHOS was, respectively, 1950 and 1930. Fang et al. [16], reported a continuous homogeneous hydroformylation with bulky rhodium catalyst complexes retained by nanofiltration membranes (STARMEM[®]), but in practice, those experiments were performed in a semi-continuous mode. Sequential batches of 16–22 h were performed at 50–60 °C and at different pressures (maximum 3.0 MPa syngas) achieving high catalyst retention (>99%) but relatively low yields; for instance, for 1-octene hydroformylation catalysed by PBB10d at 3.0 MPa, the conversion was around 50% (TON data not presented).

Download English Version:

<https://daneshyari.com/en/article/6527657>

Download Persian Version:

<https://daneshyari.com/article/6527657>

[Daneshyari.com](https://daneshyari.com)