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Gas–liquid and gas–liquid–solid catalysis in a mesh microreactor†

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A microstructured mesh contactor that can offer residence time of more than minutes is used for gas–liquid–solid hydrogenations and gas–liquid asymmetric hydrogenations. Applications for catalyst/chiral inductor screening and for kinetic data acquisition are demonstrated.

Over the past decade, interest has grown in microstructured reactors due to their potential to conduct mass or heat transfer demanding reactions under safe conditions while maintaining and/or increasing selectivity and productivity.[1] The small volumes involved and high heat transfer capabilities allow safe handling of hazardous reactions or chemicals to be achieved. However, most reports dealing with microreactors describe reactions involving only one fluid phase, a liquid for pharmaceutical or speciality chemicals applications or a gas for heterogeneously catalysed processes.[2,3] This stems from difficulties in ensuring appropriate multiphase contact and mixing. Thus, only a few reactions involving immiscible fluids, such as fluorination of aromatics,[4,5] asymmetric hydrogenations,[6] or gas–liquid–solid hydrogenations,[7–9] have provided sufficient motivation for study in microreactors. For example, the exothermic nitroaromatic hydrogenation has been conducted in a microstructured falling film reactor,[7] the noble metal catalyst being deposited on an alumina surface by appropriate impregnation. The aim of safe and on-demand production was first noted in earlier reports, albeit using less demanding alkene hydrogenations.[8] In that work, the mass transfer capability of the microfabricated multiphase packed-bed reactors was evaluated showing mass transfer coefficients 1 to 2 orders of magnitude larger than conventional trickle-bed reactors.

While all reported microreactors were designed for fast reactions under atmospheric pressure and short reaction time (1–30 s), we felt that G–L and G–L–S microreactors offering both a large pressure range and more flexible residence times (10 s to hours) for *e.g.* batch operations would be highly desirable.

The fabrication and detailed description of the mesh microcontactor used in this work has been published.[10] The microcontactor has two 100 μm deep cavities (100 μL) separated by a micromesh (Fig. 1). The upper cavity is fed with the reacting gas hydrogen while the other, the reacting chamber, contains the reacting liquid. Roughly 20 to 25% of the mesh surface is occupied by holes of 5 μm diameter which lead to a gas–liquid interfacial area of *ca.* 2000 m^2/m^3_{liq} well above values (100–300 m^2/m^3_{liq}) obtained in traditional tank reactors. This design should allow a good mass transfer between the cavities while stabilising the interface hence ensuring gas–liquid separation.

For gas–liquid–solid reactions, the bottom glass insert in the reacting chamber is demountable allowing catalyst coating of inserts. Inserts used here had porous alumina deposits impregnated with noble metals and subjected to thermal treatment to provide well-dispersed metal (*ca.* 10 mg metal/Al_2O_3 per insert at 4% weight Pt or Pd).

In the first series of experiments, the mass transfer capability of the mesh microreactor was evaluated. A textbook test to assess mass transfer limitations *vs.* chemical regime in multiphase reactors is to measure activation energy of a known reaction. We have used the fast Pd/Al_2O_3 or slower Pt/Al_2O_3 catalysed α-methylstyrene hydrogenation as a test reaction that exhibits, considering the conditions of this study, global rate constants of roughly 56 s^{-1} and 1.4 s^{-1} for the Pd and Pt catalysts respectively.[11a] In this study methylcyclohexane is fed to the microreactor at a constant rate (0.1 $cm^3\ min^{-1}$) with pulses (100 μl) of α-methylstyrene in methylcyclohexane introduced to the flow *via* an HPLC injection loop. The product is then collected for 10 min to ensure the sampling of the entire reacting plug.

An activation energy of *ca.* 46 ± 5 kJ mol^{-1} is measured for the Pt catalyst in the mesh microcontactor (Fig. 2). A similar value of 39 kJ mol^{-1} is found for a commercial Pt/Al_2O_3 powder catalyst in

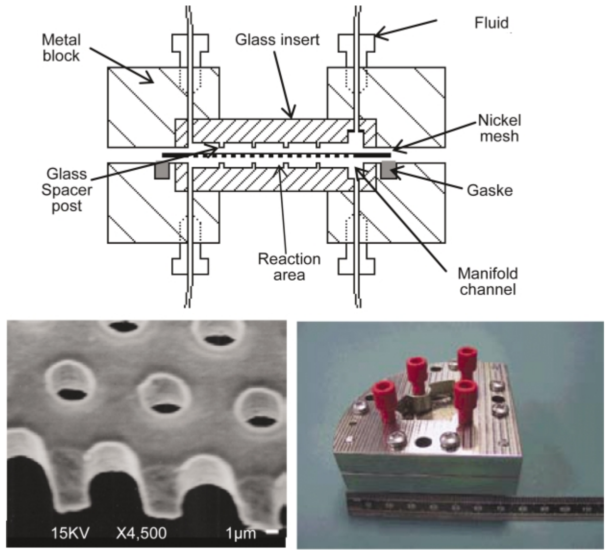

Fig. 1 Drawing of the microstructured mesh contactor and photographs of the mesh showing the micro-holes (5 μm) (SEM image) and of the mounted mesh microreactor with fluid connectors.

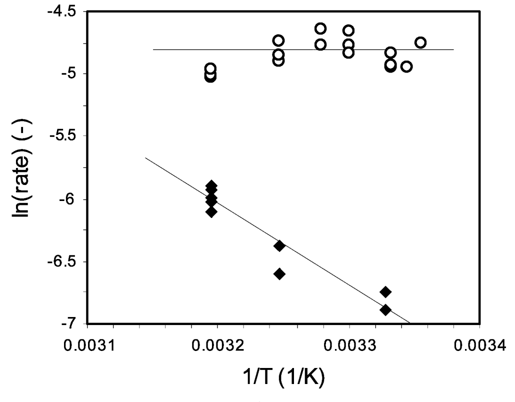

Fig. 2 Arrhenius plot for the Pd (○) and the Pt (◆) Al_2O_3 supported catalysts. Conditions: flow mode, 2–3 bar, [α-methylstyrene] 1 M in methylcyclohexane, liquid flow rate 0.1 $cm^3\ min^{-1}$.

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† Electronic supplementary information (ESI) available: experimental details and literature data. See http://www.rsc.org/suppdata/cc/b3/b312290e/

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a well behaved batch reactor demonstrating chemical regime.† The activities obtained with the mesh microcontactor are similar to those observed with the Pt or Pd inserts in the batch reactor which demonstrates similar mass transfer capabilities for both batch and micro-reactors.†

On the contrary, for the Pd inserts, the activation energy is close to zero in the mesh microreactor whereas it is about 41 kJ mol^{-1} for the same catalyst used as a powder in a well-behaved batch reactor.[11a] The activity of this catalyst is too high and mass transfer is limiting. A global mass transfer coefficient,[8] in the range $K_{l}a$ = 1–2 s^{-1} for the mesh microreactor, can be roughly estimated applying the "in series mass transfer resistances" concept,[8] and considering a fast first order reaction.[11a] These values are well in the range of those found in commercial pressure reactors equipped with baffles and turbines.[11b] It further demonstrates the efficiency of the mesh microreactor where fast mass transfer is achieved through short (~ 100 μm or less) diffusion path lengths.

The second series of experiments deals with the well-known gas–liquid asymmetric hydrogenation of *Z*-methylacetamidocinnamate (mac) with rhodium chiral diphosphine complexes. This class of reaction is of importance for the life products industry and has been the topic of the 2002 Nobel award.[12] The aim was to demonstrate the use of the mesh microreactor for ligand or catalyst screening and process evaluation. The set-up is similar to that used for gas–liquid–solid operations except that there was no solid catalyst coating on the glass insert. Also, both the molecular catalyst and the substrate mac are injected as a mixture in the organic solvent.

Up to 20 chiral diphosphines have been evaluated (Table 1). The rhodium complexes were prepared as stock solutions by mixing the $[Rh(COD)_2]BF_4$ precursor and the diphosphine using Schlenck techniques with the exception of the commercially available Rh/Binap and Rh/Dipamp catalysts (entries 2 & 15).

Mesh microreactor tests can be applied to very active catalysts such as the Rh/diop complex by operation in the continuous or flow mode enabling short residence times (1 min) (Entry 1a). When longer residence times are required, the mesh microreactor can be operated batchwise by interrupting the liquid flow using appropriate valves. For example, the conversion obtained with the Rh/Me-Duphos catalyst rises from 31% to 76% upon raising the residence time from 1 min (flow) to 30 min (batch). For the very active Rh/diop catalyst, no further conversion nor enantiomeric excess (ee) change is observed under batch operation (entry 1b). Data of this type aid evaluation of catalyst stability or deactivation.

Table 1 Screening of 20 chiral diphosphine ligands for the hydrogenation of *Z*-methylacetamidocinnamate (mac)

Entry	Chiral ligand	Operation[a]	Conv.	ee	ee lit.[b]
1a	(*R*,*R*)-Diop	Flow	> 98	61	67
1b	(*R*,*R*)-Diop	Batch	> 96	62	
2	$[Rh((R)\text{-Binap})(COD)]^+$	Flow	54	62	93
3	(*R*,*S*)-Cy-Cy-Josiphos	Flow	41	70	
4a	(*R*,*R*)-Me-Duphos	Flow	31	> 98	98
4b	(*R*,*R*)-Me-Duphos	Batch	76	95	
5	(*R*,*S*)-Josiphos	Flow	35	87	96
6	(*S*,*S*)-BPPM	Flow	32	89	93
7	(*R*,*S*)-Cy-Ph-Josiphos	Flow	9	59	
8	(*R*)-Prophos	Flow	9	81	
9	(*R*,*S*)-Ph-tBu-Josiphos	Flow	5	31	
10	(*R*,*R*)-Trost ligand	Flow	< 1	n.d.	
11	(*S*,*S*)-BDPP	Batch	79	71	
12	Carbophos	Batch	61	80	
13	(*R*,*R*)-Me-BPE	Batch	53	87	85
14	(*R*,*R*)-Et-Duphos	Batch	45	87	99
15	$[Rh((R,R)\text{-Dipamp})(COD)]^+$	Batch	34	−63	−92
16	(*R*,*R*)-Et-BPE	Batch	25	84	93
17	(*S*,*S*)-Chiraphos	Batch	12	84	
18	(*S*)-NMDPP	Batch	11	60	
19	(*R*,*R*)-Norphos	Batch	10	−51	
20	(*R*)-Quinap	Batch	< 4	−37	

[a] Flow and Batch modes see text. Reaction conditions see Fig. 3. [b] For literature data see Electronic Supplementary Information.†

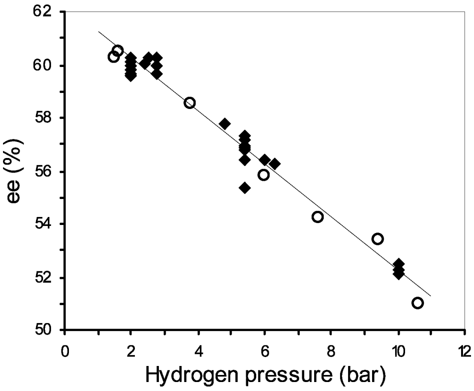

Fig. 3 Dependence of ee on pressure in a mini batch reactor (○) and in the mesh microreactor (◆). Conditions: $[Rh(COD)_2]BF_4$/(*R*,*R*)-diop; [Rh] 0.0001 M, [mac] 0.1 M, 1 min, 20 to 40 °C, MeOH.

Some complexes however are clearly not efficient catalysts for this reaction (Entries 17–20).

A straightforward comparison of activities (conversion *vs.* time) with literature data does not hold since many different reaction conditions have been used.† However, the fairly good agreement between published and measured ee's confirms the mesh microreactor's suitability for catalyst screening (Table 1).

The influence of the hydrogen pressure on the ee is a well known phenomenon in asymmetric hydrogenation that is an issue for both industrial processes and academic research.[13] This phenomenon can be efficiently investigated using the mesh microreactor as demonstrated by comparison with data obtained using a mini-batch pressure reactor (25 cm^3, Parr)[6b,11b] (Fig. 3).

In conclusion, the mesh microreactor presented here allows the accurate investigation of fast gas–liquid and gas–liquid–solid catalytic reactions and can also be used for screening applications with chiral ligand inventory down to 10 nmole.

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Notes and references

1 W. Ehrfeld, V. Hessel and H. Löwe, *Microreactors*, Wiley-VCH, Weinheim, 2000.
2 P. D. I. Fletchar, S. J. Haswell, E. Pombo-Villar, B. H. Warrington, P. Watts, S. Y. F. Wong and H. Zhang, *Tetrahedron*, 2002, **58**, 4735.
3 A. Gravilidis, P. Angeli, E. Cao, K. K. Yeong and Y. S. S. Wan, *Chem. Eng. Res. Des.*, 2002, **80**, 3.
4 K. Jahnisch, M. Baerns, V. Hessel, W. Ehrfeld, V. Haverkamp, H. Lowe, Ch. Wille and A. Guber, *J. Fluorine Chem.*, 2000, **105**, 117.
5 N. de Mas, A. Guenther, M. A. Schmidt and K. F. Jensen, *Ind. Eng. Chem. Res.*, 2003, **42**, 698.
6 (*a*) C. de Bellefon, N. Tanchoux, S. Caravieilhes, P. Grenouillet and V. Hessel, *Angew. Chem., Int. Ed.*, 2000, **39**, 3442; (*b*) C. de Bellefon, N. Pestre, T. Lamouille, P. Grenouillet and V. Hessel, *Adv. Synth. Catal.*, 2003, **345**, 190.
7 K. K. Yeong, A. Graviilidis, R. Zapf and V. Hessel, *Catal. Today*, 2003, **81**, 641.
8 M. W. Losey, M. A. Schmidt and K. F. Jensen, *Ind. Eng. Chem. Res.*, 2001, **40**, 2555.
9 R. Födisch, D. Hönicke, Y. Xu and B. Platzer, in *Microreaction Technology*, Eds. M. Matlosz, W. Ehrfeld, J. P. Baselt, Springer, Berlin, 2002, p. 408.
10 D. A. Wenn, J. E. A. Shaw and B. Mackenzie, *Lab on a Chip*, 2003, **3**, 180.
11 (*a*) V. Meille, C. de Bellefon and D. Schweich, *Ind. Chem. Eng. Res.*, 2002, **41**, 1711; (*b*) V. Meille, N. Pestre, P. Fongarland and C. de Bellefon, *Ind. Chem. Eng. Res.*, DOI: 10.1021/ie030569j.
12 Many examples can be found in *Handbook of asymmetric catalysis*, E. N. Jacobsen, A. Pfaltz and H. Yamamoto, Eds., Springer, Berlin, 2000.
13 R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, 1994, p. 33.