

# First heterogenisation of Rh–MeDuPHOS by occlusion in PDMS (polydimethylsiloxane) membranes

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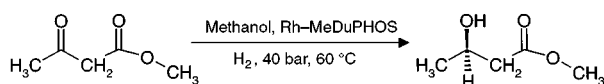
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The first heterogeneous system of Rh–MeDuPHOS, obtained by occlusion of the complex in a PDMS membrane, is reported and tested in the hydrogenation of methylacetoacetate (MAA).

Asymmetric synthesis with homogeneous chiral complexes is one of the best methods to prepare enantiopure compounds.<sup>1</sup> In 1991, Burk developed a set of new chiral biphosphine ligands referred to as DuPHOS [1,2-bis(phospholano)benzene] and BPE [1,2-bis(phospholano)ethane],<sup>2</sup> both commercially available nowadays. The Rh and Ru complexes of these ligands were found to be extremely effective in the enantioselective hydrogenation of a vast array of unsaturated substrates.<sup>3–8</sup> All reactions are characterized by high convenience, selectivity, catalytic productivity and activity, adaptability and durability. A major class of these substrates form the  $\beta$ -ketoesters. Their reduction was recently reviewed by Klabunovskii and Sheldon.<sup>9</sup> The authors stated that chiral metal complexes constitute the most elegant and efficient way to asymmetric hydrogenation with the broadest scope, but that facilitation of their recycling by immobilizing them, still remained an important future challenge.

We report here the first heterogenisation of Rh–MeDuPHOS, chosen as a typical representative of the class of catalysts reported by Burk *et al.*<sup>2–8</sup> Immobilisation was realized by occluding the catalyst in a polydimethylsiloxane membrane. This easy approach to heterogenisation was earlier applied already for several transition metal complexes.<sup>10–12</sup> The hydrogenation of MAA was selected as a test reaction (Scheme 1). A PDMS solution was prepared by mixing 0.075 g of crosslinker [tetrakis-(dimethylsiloxy)silane, United Chemical Technologies], 22  $\mu$ l of Pt catalyst [*cis*-dichlorobis(diethyl sulfide)platinum(II), Aldrich, applied as a 2 wt% solution in toluene], 2.25 g of the vinylterminated silicone polymer ( $M_n = 5350$  with a polydispersity = 2.27, obtained after stripping the polymer under vacuum till constant weight, United Chemical Technologies), and 0.465 g of the silica (Hi-sil 233, pretreated at 120 °C, PPG Industries) in 11.5 g of dichloromethane (Fig. 1). The catalyst was prepared by dissolving the Rh salt [bis(cycloocta-1,5-diene)rhodium(I) trifluoromethanesulfonate, 99%, Strem] and the ligand {(–)-1,2-bis[(2*R*,5*R*)-2,5-dimethylphospholano]benzene, 99%, Strem} separately in methanol (Fig. 2). An amount of 0.0397 g of Rh salt and 0.0264 g of ligand were dissolved in 2.1 and 0.7 g of methanol, respectively. The ligand solution was then added dropwise to the Rh salt solution under constant stirring. Further stirring for 15 min turned the yellow solution into dark orange. A portion of 0.174 g of this solution, corresponding to 5  $\mu$ mol



Scheme 1 Asymmetric hydrogenation of MAA.

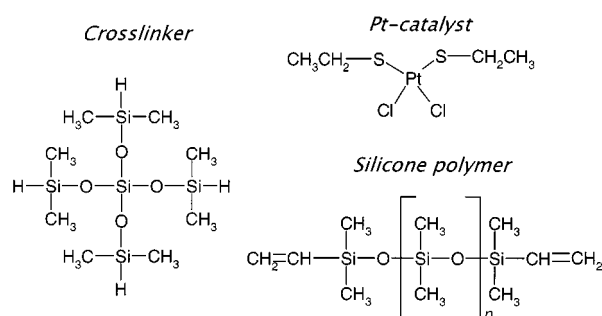


Fig. 1 PDMS constituents.

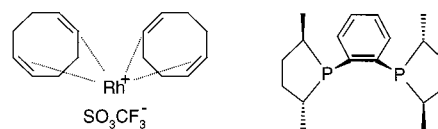


Fig. 2 Rh salt and ligand for Rh–MeDuPHOS synthesis.

of the Rh complex, was poured in a Petri dish and after removal of the methanol, 1.5 g of the PDMS solution was added. After complete dissolution of the complex in this mixture, the solvent was allowed to evaporate. Approximately 3 h later, the curing of the PDMS was finished and the resulting membrane was stored under nitrogen prior to use in the reactor. A typical TEM image of such a composite membrane is shown in Fig. 3, proving the good dispersion of the silica particles in the membrane matrix. A 20 ml reactor with magnetic stirring was used in which the membrane was clamped between two porous stainless steel disks. A volume of 18 ml of methanol was added to the reactor, together with 2 g of MAA. Reaction took place at 60 °C at a pressure of 40 bar during 24 h for the membrane reaction and 2 h for the homogeneous reference reaction. The reaction mixture was analysed with gas chromatography (Chiraldex G-TA column, Astec).

A homogeneous reaction (Table 1) was performed in order to test the activity of the prepared catalyst and its ability to reduce MAA. Even though attempts to utilize Rh–MeDuPHOS in enantioselective ketone hydrogenations were reported to be unavailing<sup>5</sup> and in spite of the fact that Burk *et al.* found other DuPHOS and BPE related catalysts performing better than Ru-BINAP,<sup>3,4</sup> we found for Rh–MeDuPHOS an activity in the MAA hydrogenation at 60 °C that was even superior to that of Ru-BINAP, a catalyst commonly used for this reaction.<sup>9,13,14</sup> The membrane occluded catalyst (membrane thickness 452  $\mu$ m) was first tested in ethylene glycol (EG), the solvent preferentially used for the analogous Ru–BINAP/PDMS system.<sup>15</sup> The activity of the catalyst was lower than in the homogeneous reaction but remained constant in a second run, in which the same enantioselectivity was maintained. No reactivity was

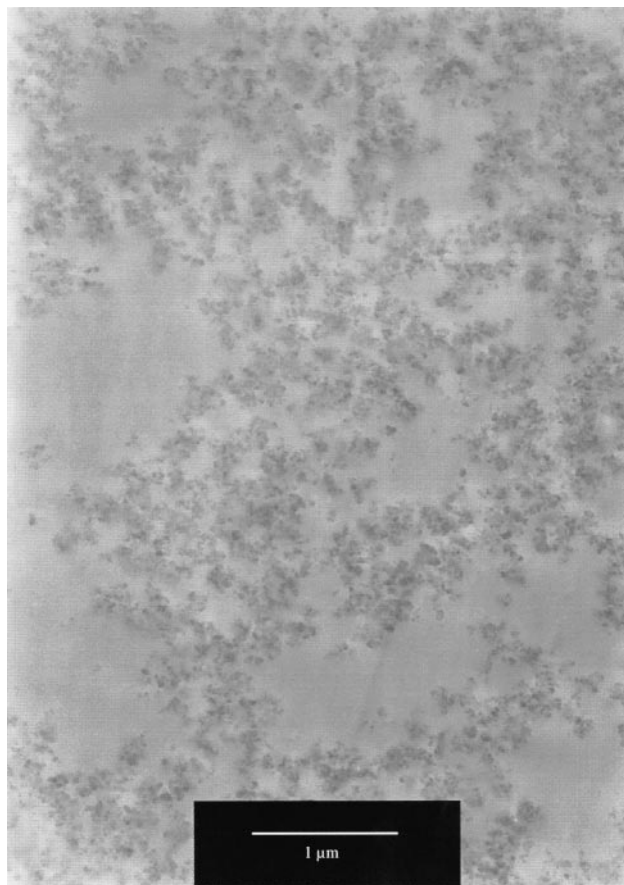


Fig. 3 TEM photograph of a PDMS membrane containing 10 wt% silica.

**Table 1** Turnover frequency and enantioselectivity in the hydrogenation of MAA. (H = homogeneous reaction; 1 = first membrane reaction; 2 = second membrane reaction). All reaction selectivities were 100%. Reaction time: 2 h (for homogeneous reactions) or 24 h (for heterogeneous reactions)

Catalyst	Solvent	TOF/h <sup>-1</sup>	ee(%)
Rh–MeDuPHOS (H)	MeOH	482	99
Ru–BINAP (H)	MeOH	135	90
Rh–MeDuPHOS/PDMS (1)	EG	7	93
Rh–MeDuPHOS/PDMS (2)	EG	7	93
Rh–MeDuPHOS/PDMS (1)	MeOH	28	90
Rh–MeDuPHOS/PDMS (2)	MeOH	28	90

found when only the reaction mixture from the first membrane catalysed reaction was used in another run after adding new

substrate to the reactor. This proved that the reported system was a truly heterogeneous version of the catalyst. By performing the reaction in methanol, the membrane activity (thickness 578 μm) could be increased fourfold, while leaving enantioselectivity quasi-unaffected. Exactly the same results were found in a second run. This is remarkable because methanol is a good solvent for the catalyst and it was found earlier that the use of such solvents generally causes leaching of the catalyst from PDMS membranes.<sup>11</sup> Also the mixture of this reaction proved to be completely inactive in a subsequent run with new substrate added. The absence of Rh in all reaction mixtures was also confirmed subsequently with ICP-MS.

The reported heterogenisation allows facile recycling of this versatile catalyst and should enable the development of continuous processes. Experiments to improve the activity of the reported membrane system by optimizing the membrane properties and to expand it further to other reactions and catalysts of this class are planned. In particular, the complete absence of leaching in methanol opens interesting perspectives in this respect.

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