

Continuous Enantioselective Hydrogenation in Supercritical CO₂

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Continuous catalytic hydrogenations utilising Supercritical Fluids (SCFs), particularly Supercritical CO₂ (scCO₂), have several advantages over traditional batch hydrogenation methodologies [1]. These advantages include the complete miscibility of H₂ in scCO₂ that can lead to enhancement of reaction rates due to the minimization of mass transport limitations. Also facile product recovery by depressurisation and increased safety due to reduced reactor volume when compared to batch methods.

A small continuous flow apparatus for the hydrogenation of substrates in scCO₂ has been developed. Calculations and gas analysis have been performed to establish the reliability and reproducibility of hydrogenation reactions. This apparatus allows the use of smaller amounts of experimental catalysts (~10 mg) and reaction conditions can be altered more rapidly due to the reduced reactor volume.

The use of supported homogeneous catalysts has been investigated looking at supported [Rh(COD)(Skewphos)]⁺BF₄⁻ and [Rh(COD)(Josiphos)]⁺BF₄⁻ catalysts. (Figure 1) The catalyst is supported on alumina via phosphotungstic acid (PTA). (Figure 2). It is synthesized from an achiral catalyst precursor [Rh(COD)₂]⁺BF₄⁻/(PTA)/Alumina.

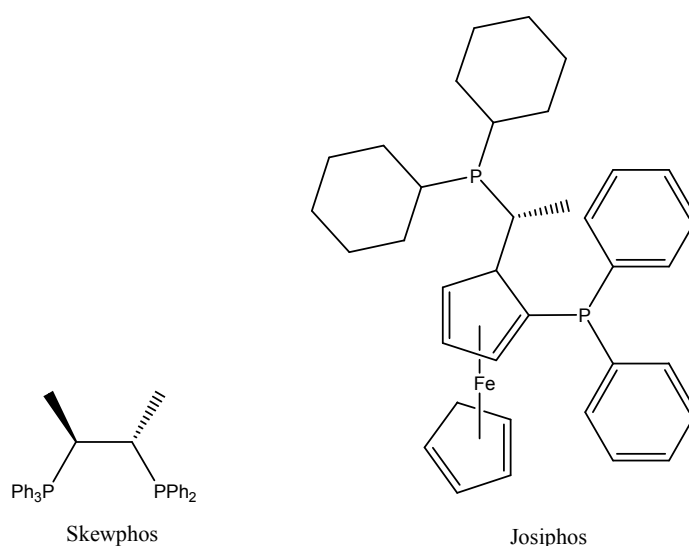


Figure 1: Chiral phosphine ligands investigated

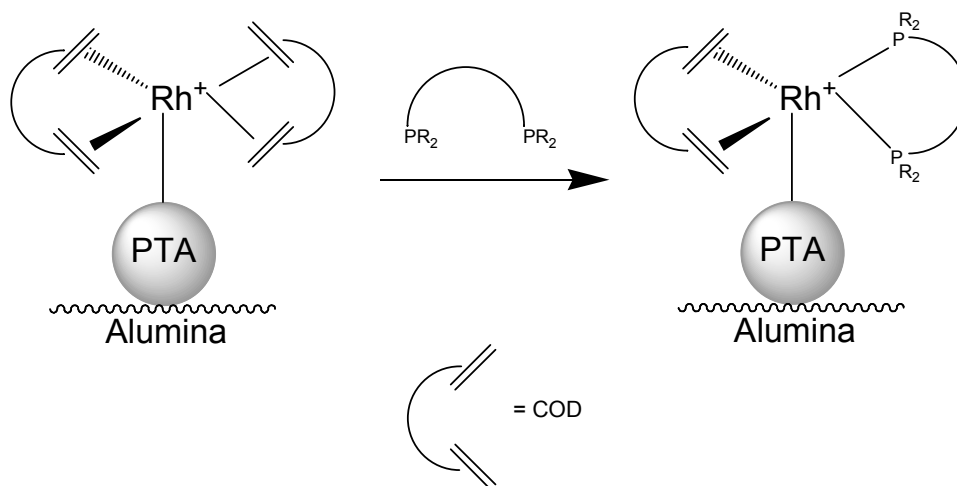


Figure 2: Preparation of the supported homogeneous catalyst.

The prototypical reaction was the hydrogenation of dimethyl itaconate (DMIT), often used as a substrate for enantioselective reactions. (Figure 3).

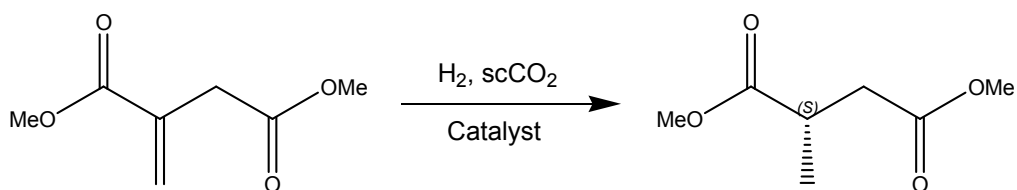


Figure 3: Enantioselective hydrogenation of DMIT using the supported homogeneous catalyst.

As a result of these investigations one of the first examples of an enantioselective hydrogenation in a continuous flow scCO_2 system has been reported [2], importantly without the need of a co-eluting chiral modifier. The larger Josiphos ligand gives a consistently higher ee than Skewphos.

REFERENCES:

- [1] Hitzler, M. G., Smail, F., Ross, S. K., Poliakoff, M., *Org. Process Res. Dev.*, Vol. 2, **1998**, p.137.
- [2] Stephenson, P., Licence, P., Ross, S. K., Poliakoff, M., *Green Chem.*, Vol. 6, **2004**, p.521.