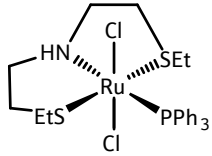
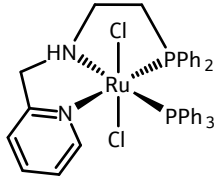
JM

Gusev technology for hydrogenation of esters, ketones and aldehydes

Johnson Matthey
Inspiring science, enhancing life

Catalog ID	Structure	CAS Number
C1-750 (Ru-SNS)		1462397-86-9
C1-850 (Ru-PNN)		1388712-91-1

Catalysts C1-750 and C1-850 ('Gusev technology') have been exclusively licenced to Johnson Matthey by GreenCentreCanada. Some transformations have been the subject of patents and patent applications. It is the User's responsibility to ensure freedom of operation for any commercial, industrial application, and no warranty is given in this respect.

Technology overview

Homogeneous ester hydrogenation has evolved into an efficient and cost-effective transformation. It provides a greener alternative to the use of hydrides for the reduction of esters and other carbonyl compounds. Highly chemoselective reductions are achieved at low catalyst loadings without the cryogenic conditions, complex work up and waste generation associated with the use of hydrides. Homogeneous ester hydrogenation catalysts work under reaction conditions milder than those required by heterogeneous catalysts.

Catalyst activity occurs under basic conditions, preferably using strong bases (alkoxides). Higher reaction rates and higher catalyst turn over numbers can generally be achieved at higher hydrogen pressure (molar substrate to catalyst ratio, S/C, >10,000/1) but operating at 5-10 bar is possible at good catalyst loadings (e.g. S/C 1,000-5,000/1).

Recommendation
Ru complex: C1-750 and C1-850.

Solvents
Neat, MeTHF, THF, PhMe, EtOH (and mixtures).

Additives
Basic additives required (e.g. 1-10% mol NaOMe, NaOEt, KOEt, KO*t*Bu).

Pressure
5 to 50 bar H_2 (loadings of S/C 1,000-5,000 are achievable at 5 bar; loadings of S/C >10,000/1 are achievable at higher pressure).

Reaction temperature
40 – 65 °C for C1-750 and 40 – 100 °C for C1-850.

Test conditions
We recommend initial test reactions carried out at 0.4 mol% (S/C 250/1) catalyst in MeTHF, 10 mol% KOEt (24% wt./wt. in EtOH), 5 to 50 bar H_2, 60 °C.

Recommendations are for proof of concept on small scale only.

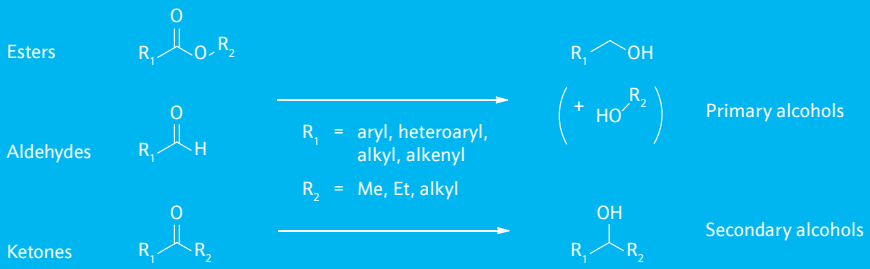
Substrate scope

1 Methyl and ethyl esters, aliphatic and aromatic.
Target catalyst loadings upon optimisation: S/C 10,000/1 to 50,000/1. Higher activity is generally expected for ethyl esters. Anhydrous conditions are preferred; increasing the amount of base and/or catalyst loadings can overcome activity reduction due to the presence of water.

2 Ketones, aliphatic and aromatic.
Very high activity expected. Target catalyst loadings upon optimisation: S/C 100,000/1. The highly chemoselective reduction of C=O groups is usually achieved without reduction of C=C bonds, although terminal alkenes and α,β-unsaturated ketones can be more susceptible to C=C bond hydrogenation.

3 Aldehydes, aliphatic and aromatic.
Target catalyst loadings upon optimisation: S/C 20,000/1 to 100,000/1. Reaction conditions can be optimised to minimise potential side products due to basic reaction conditions. The presence of water in small amounts (e.g. 1-5 vol%) can have beneficial effects on activity and/or selectivity, especially in the hydrogenation of α,β-unsaturated aldehydes.

4 Chiral substrates: esters, aldehydes, ketones.
The stereospecific reduction of chiral substrates, although complicated by the basic reaction conditions, is achieveable with no or minimal degradation of enantiopurity by appropriate choice of reaction conditions (e.g. EtOH, 10% KOEt, 40 °C, 30 bar H_2).



Target catalyst loadings: S/C 1,000/1 to 10,000/1.

5 Other transformations.
Catalysts C1-750 and C1-850 have been demonstrated to efficiently catalyse other reactions that are mechanistically related to ester hydrogenation.

- Hydrogenation of imines to amines (C1-850: 5% NaOEt, THF, S/C 50,000/1)
- Acceptorless dehydrogenative coupling (alcohol to ester, alcohol to amide; e.g. C1-850: EtOH to AcOEt, 1% NaOEt, EtOH, S/C 10,000/1).
- Transfer hydrogenation via ester metathesis (e.g. C1-750: benzyl formate to benzyl alcohol in toluene, EtOH excess, 5% KOtBu, 80 °C. S/C 100/1).

Recommendations are for proof of concept on small scale only.

Literature

Reviews (ester hydrogenation):

1 Blaser, H. U.; Pugin, B.; Spindler, F.; Saudan, L. A. *Applied Homogeneous Catalysis with Organometallic Compounds;* Wiley-Blackwell, **2017;** pp 621–690.

2 Pritchard, J.; Filonenko, G. A.; van Putten, R.; Hensen, E. J. M.; Pidko, E. A. *Chem. Soc. Rev.* **2015,** 44, 3808.

3 Werkmeister, S.; Junge, K.; Beller, M. *Org. Process Res. Dev.* **2014,** 18, 289.

4 Dub, P. A.; Ikariya, T. *ACS Catalysis* **2012,** 2, 1718.

5 Clarke, M. L. *Catal. Sci. Technol.* **2012,** 2, 2418.

Applications of C1-750:

6 Spasyuk, D.; Smith, S.; Gusev, D. G. *Angew. Chem. Int. Ed.* **2013,** 52, 2538.

Applications of C1-850:

7 Spasyuk, D.; Gusev, D. G *Organometallics* **2012,** 31, 5239

Hydrogenation of fatty esters:

8 Fairweather, N. T.; Gibson, M. S.; Guan, H. *Organometallics* **2015,** 34, 335.

Ester metathesis and application to transfer hydrogenation of esters:

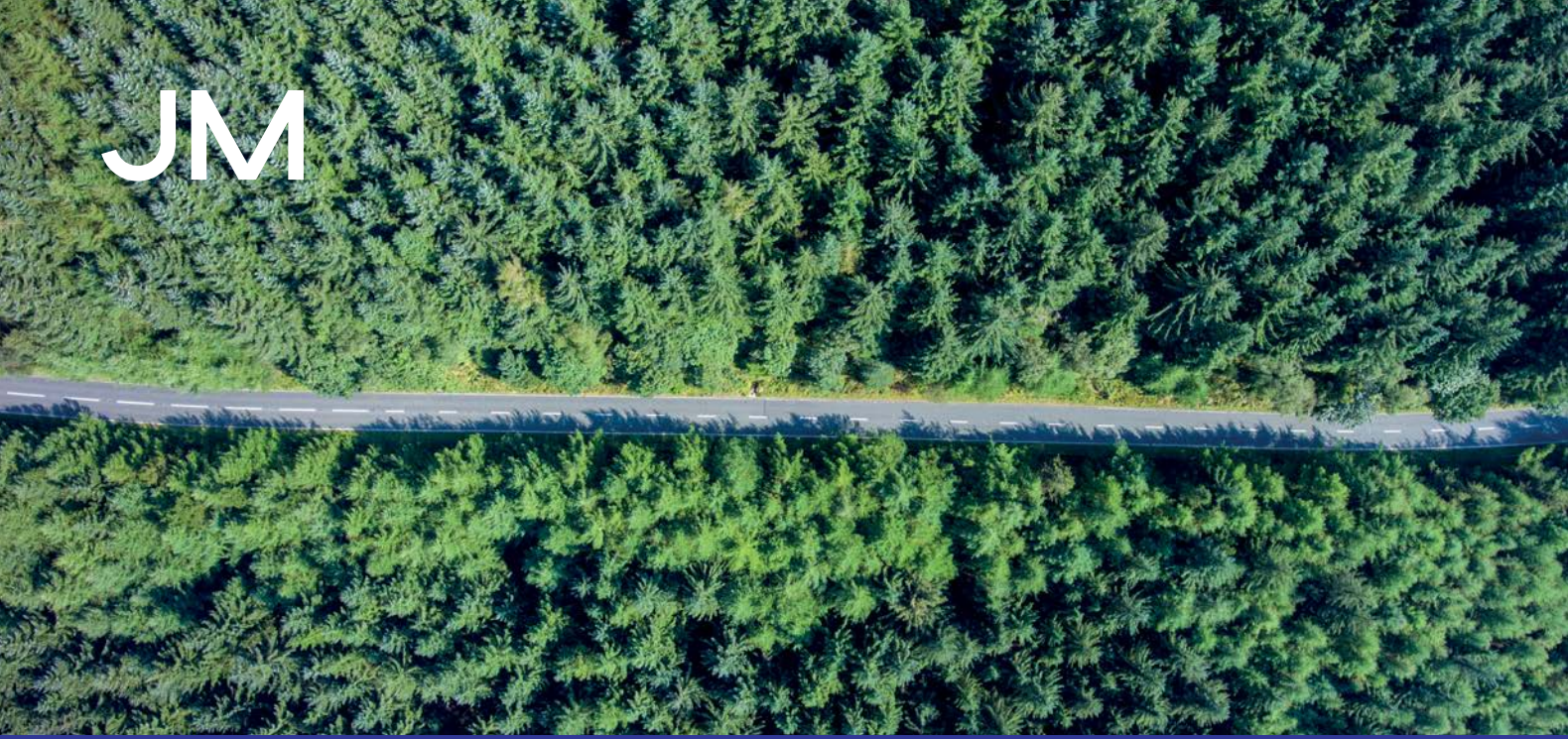
9 Dubey, A.; Khaskin, E. *ACS Catalysis* **2016,** 6, 3998

Acceptorless dehydrogenative coupling of alcohols:

10 Vicent, C.; Gusev, D. *ACS Catalysis* **2016,** 6, 3301

The coming of age of homogeneous ester hydrogenation - Gusev catalysts: why, how and when to use them:

11 Zanotti-Gerosa, A.; Grainger, D.; Todd, L.; Grasa, G.; Milner, L.; Boddie, E.; Browne, L.; Egerton, I.; Wong, L. *Chimica Oggi Catalysis & Biocatalysis* **2019**, 37(4), 10



Johnson Matthey
Inspiring science, enhancing life

To find out more search Gusev technology on matthey.com
or email pharma@matthey.com