

Asymmetric Hydrogenation: A Sustainable Technology for Pharmaceutical Manufacture

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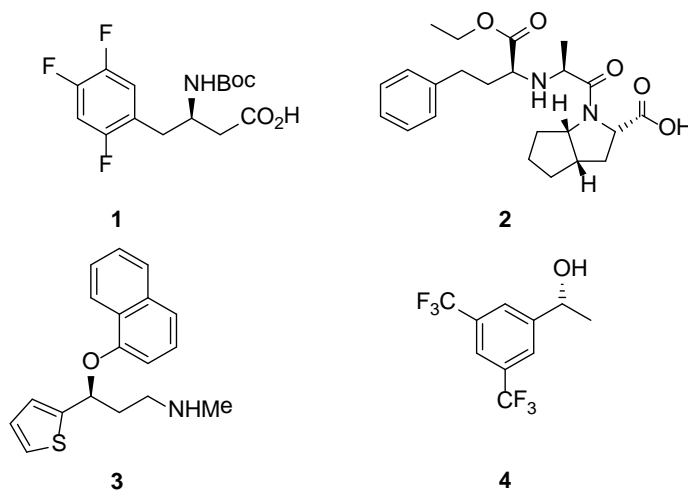
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Abstract

Asymmetric hydrogenation is routinely applied for the manufacture of intermediates and active pharmaceutical ingredients (API's), as well as some applications for agrochemicals and bulk chemical production. Chiral Quest has over 15 years' experience in the application of asymmetric hydrogenation processes, and has developed some highly active and selective catalyst systems.^{1,2} Catalyst loadings of 10,000/1 to 120,000/1 molar have been achieved, which means that very little precious metals are utilised, which can be recovered and used to make fresh catalyst.

This presentation will demonstrate how such technology can be used in the commercial manufacture of α - and β -amino acids, such as an intermediate (1) for Sitagliptin³ and a highly efficient route to and Ramipril (2).⁴ For alcohol intermediates, routes to Duloxetine (3)⁵ and Aprepitant (4) intermediates will be presented, both operating on 5-30 MT scale, using efficient catalyst loadings.



References:-

1. Zhang, W.; Chi, Y.; Zhang, X. *Acc. Chem. Res.* 2007, *40*, 1278-1290.
2. Versatility and broad applications of TangPhos and DuanPhos catalysts. Lennon, I. C.; *Chimica Oggi; Chemistry Today.* 2010, *28*, 46-47.
3. Process and intermediates for the preparation of *n*-acylated-4-aryl beta-amino acid derivatives. Wu, S.; Yu, B.; Wang, Y.; Delice, A.; Zhu, J. US2010280245
4. Enantioselective synthesis of cycloalkenyl-substituted alanines. Liu, Z.; Lin, S.; Li, W.; Zhu, J.; Liu, X.; Zhang, X.; Lu, H.; Xiong, F.; Tian, Z. US2011257408
5. Liu, D.; Gao, W.; Wang, C.; Zhang, X. *Angew. Chem. Int. Ed.* 2005, *44*, 1687-1689.