Industrial-Scale Enantioselective Hydrogenation using Pfaltz-Type Catalysts: Chemical Development and Academic Collaborations

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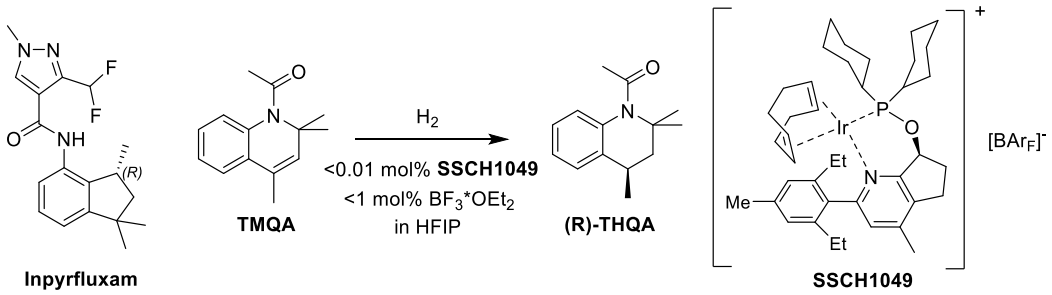
The use of modern catalytic methods, such as enantioselective hydrogenation in multi-hundred metric ton scale, still offers many challenges and is accordingly relatively rare. A robust and economical process demands identification of the right catalytic system and conditions that allow for full conversion and high stereo- and chemoselectivity at very low catalyst loadings.

Crabtree/Pfaltz-Type iridium complexes are one of the very few options to achieve high enantioselectivity in the hydrogenation of non-functionalized olefins. However, the high price of iridium demands substrate to catalyst ratios in the order of 10000:1 for attractive use cases in CropScience, which has been out of reach so far.

In search of a new production process for the novel fungicide Inpyrfluxam, we identified a single promising Crabtree/Pfaltz-Type Iridium complex using plate screening technology. Though only 25 turnovers were achieved initially, our labs succeeded in increasing this number to >10000 turnovers in collaboration with partners in both industry and academia. Moreover, we achieved not only excellent enantioselectivities of >97% ee, but also very attractive space-time yields.

Research activities included optimization of the catalyst structure, reaction solvent, and additives,[1,2] as well the large-scale procedure for preparing the chiral ligand backbone of catalyst SSCH1049.[3]



[1] Schneekönig, J.; Liu, W.; Leischner, T.; Junge, K.; Schotes, C.; Beier, C.; Beller*, M., *Organic Process Research & Development* **2020**, *24*, 443.

[2] Schotes*, C.; Müller, M., *ACS Sustain. Chem. Eng.* **2022**, *10*, 13244.

[3] Jones, M.; Harris, D.; Struble, J.; Hayes, M.; Koeller, K.; Chepiga Özgün, K.; Schirmer, H.; Heinrich, J.; Baechle, F.; Goudedranche, S.; Schotes*, C., *Organic Process Research & Development* **2022**, *26*, 2407.