

# In Kaisten, Syngenta Operates the World's Largest Plant in which an Enantioselective Catalytic Hydrogenation is Performed. How Did This Come About?

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**Abstract:** This article provides a short overview of the successful industrial-scale introduction of a new and demanding chemical process at Kaisten (Switzerland). A list of probably the most important criteria that prompted management to decide in favour of this location at that time is given.

**Keywords:** Competitiveness in production · Enantioselective hydrogenation · Large-scale manufacturing · Loop reactor

The success story began in 1970 with the discovery of the biological activity of metolachlor in the laboratories of what was then Ciba-Geigy AG in Basel. Metolachlor is the active ingredient of Dual<sup>®</sup>, one of the world's most important grass herbicides for the cultivation of corn and other crops.

The first industrial plant for the manufacture of *rac*-metolachlor (Scheme 1) started operations in 1978 (capacity >10,000 tonnes per annum). The first two synthesis steps were introduced in the company's own plant, which was opened in Kaisten in 1972. For technological reasons, the third synthesis step (chloroacetylation) went to what was then the Säurefabrik in Schweizerhalle.

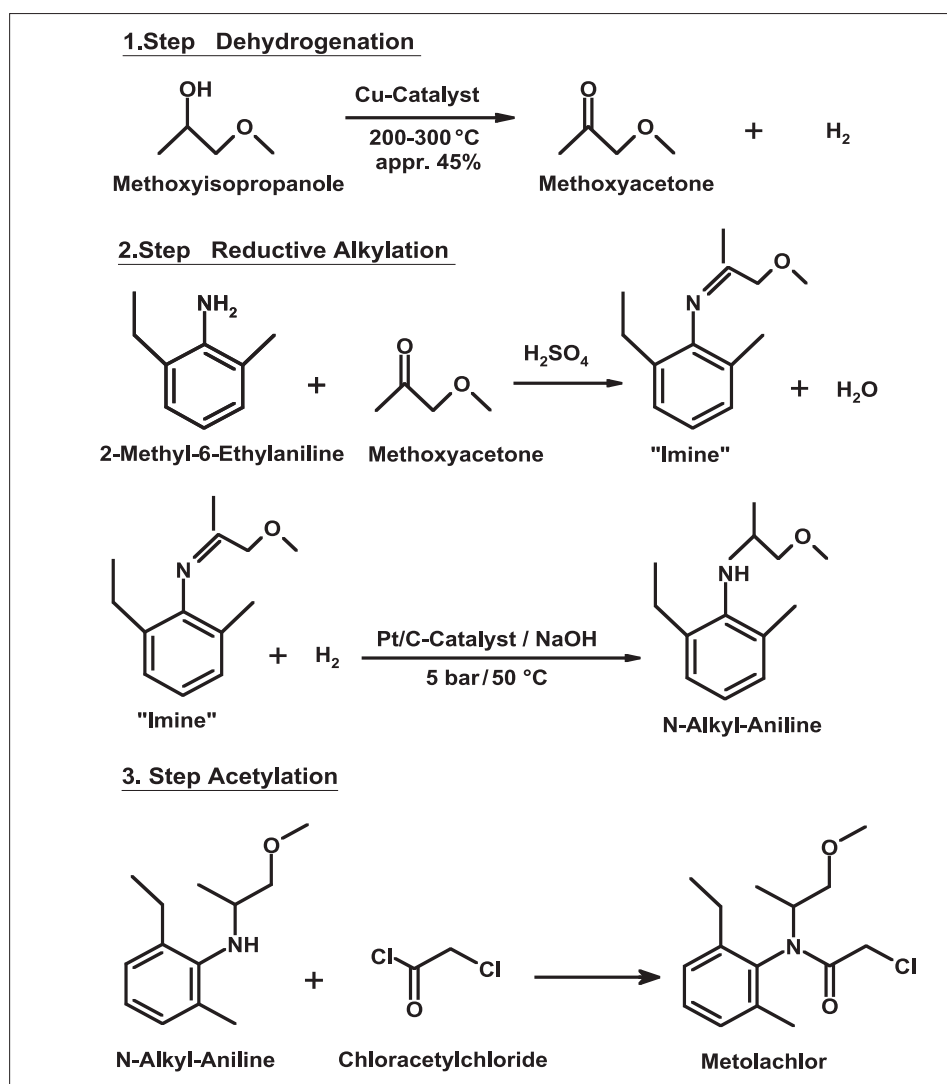
The unusual functionalization pattern results in extreme steric hindrance of the amino function. As a consequence, metolachlor has two chiral elements (Fig. 1): a chiral axis (atropisomerism, due to hindered rotation around the C–N axis) and a



stereogenic centre, leading to four stereoisomers. In 1982, when it became clear that the two (*1S*)-enantiomers of metolachlor were responsible for most of the biological activity, there was the obvious challenge of finding a chemically and economically feasible production process for the active

stereoisomers (for detailed information see [1]). However, the selective preparation of (*S*)-metolachlor was a formidable task, due to the very special structure and properties of this molecule and also because of the extremely efficient production process for the racemic product.

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Scheme 1. Synthesis of metolachlor

It took more than ten years' research and development work to find a suitable catalyst for the enantioselective imine hydrogenation which provides both a good substrate-to-catalyst ratio as well as a reasonable turnover frequency.

The breakthrough (Scheme 2) was achieved in 1994, just at the time when the patent of the *rac*-metolachlor expired. The key step in the new process is the homo-

geneous enantioselective catalytic hydrogenation at a pressure of 80 bar. To achieve optimum substance and heat transport in the reaction, it was decided to opt for a loop reactor (Fig. 2). In this technology, the reaction mixture is pumped *via* a heat exchanger through a nozzle where hydrogen is fed into the reaction solution, allowing both very good mixing and the use of the appropriate exchange surface (Fig. 2).

In view of the enormous importance of the new process for the company, plans for the industrial-scale plant were initiated in parallel with the development of the process. After a brief and intensive evaluation phase, it was decided to invest about CHF 80 million in the new production plant in Kaisten. The successful start-up of this industrial plant took place back in November 1996. What were probably the most important criteria for management at that time, which prompted the decision in favour of this location? In a discussion with those involved at the time, including Dr. Franz Weibel (Project Manager), the following points were considered which played an important part in the decision-making process.

- Far-sighted planning allowed the site to be continuously developed. Generous investments in infrastructure installations such as energy supplies or wastewater treatment systems were made at the very beginning of construction work on the production site (Master Plan). This allowed expansion projects afterwards to be handled quickly and at low cost. This was especially important in the project described here, because it had to be handled under considerable pressure of time because of the strategic importance.
- A stable political environment and good relations with the authorities in Switzerland mean that projects of this order of magnitude can be dealt with quickly and without any unforeseeable surprises. Thanks to a proactive information policy in respect of the surrounding communities no opposition was to be expected, which would have unnecessarily prolonged the approval procedure.
- An extensive logistical infrastructure and good integration into the public road and rail system are essential to ensure efficient movement of goods. The process described here involves a total turnover of about 40,000 tonnes of chemicals a year. The site in Kaisten already had numerous tank farms from

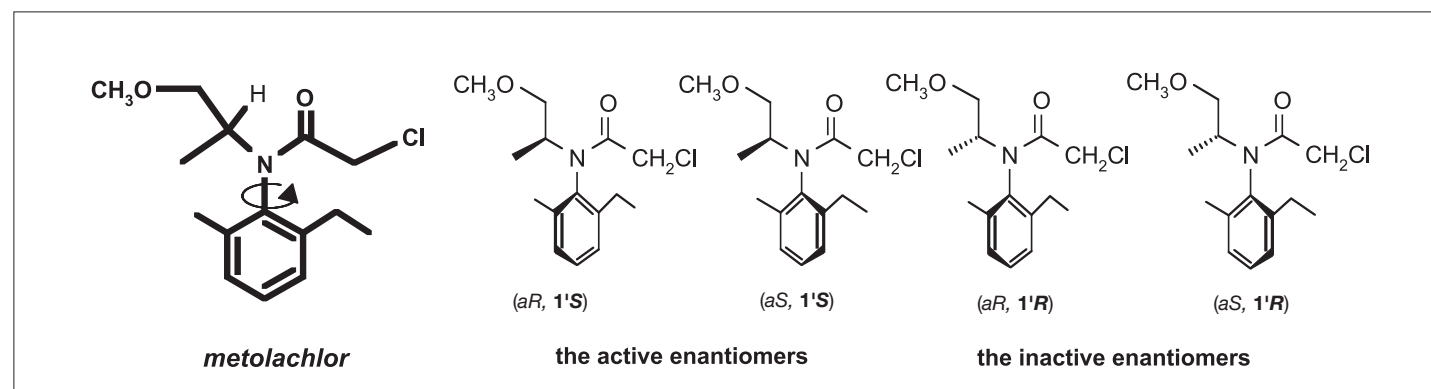
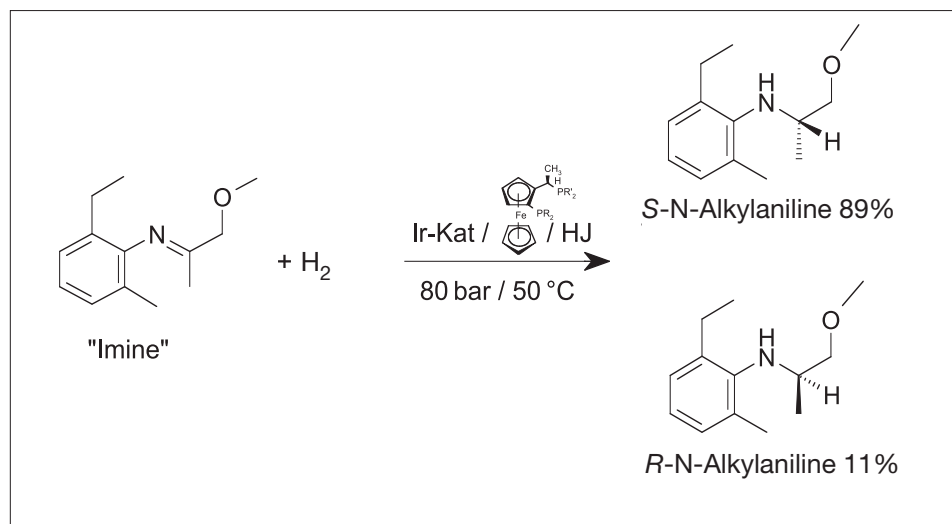


Fig. 1. Structure of metolachlor and its individual stereoisomers



Scheme 2. Enantioselective hydrogenation



Fig. 2. Loop reactor with circulation pump and heat exchanger

Kaisten (Münchwilen/Schweizerhalle) the critical process steps were developed in the company's own pilot plants. This enabled the future operators of the industrial plant to familiarize themselves with the new process for the first time.

- The new plant was conceived for uninterrupted operation and featured a high degree of automation. Monitoring was conducted in a central control room. The plant is operated around the clock in small teams. The personnel costs thus make up a relatively small proportion of the total manufacturing costs of the product.
- The chemical steps 1 and 3 of the synthesis of metolachlor remained unchanged in the introduction of the new process. Step 2 (reductive alkylation) was replaced in the new process, with alkylation and hydrogenation now taking place in two separate steps with a purification step in between. A transfer of the entire synthesis closer to the main market for this product, namely to the USA, would have been associated with substantially higher investment costs. The two key raw materials are supplied from Germany, which also poses no logistical problems. The hydrogen obtained from step 1 (dehydrogenation) in the new process can also be re-used after it has been purified.
- Finally, it has to be pointed out that the decision in favour of Kaisten was the lowest-cost option and, with regard to project risks, was also supported throughout the supply chain because of the limited changes it entailed.

The production team in Kaisten is making its contribution to the success story of (S)-metolachlor – and a success story that looks set to continue – thanks to its professional approach to work and its constant efforts to seek improvement.

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- [1] H.-U. Blaser, 'The Chiral Switch of (S)-Metolachlor: A Personal Account of an Industrial Odyssey in Asymmetric Catalysis', *Adv. Synth. Catal.* **2002**, *344*, 17–31.

the old process providing a total volume of 6000 m<sup>3</sup>, which it was possible to continue to use for the new process.

- Reliable and low-cost energy supplies were established at the site and did not have to be extended with the realization of this project. Directly adjacent to the site is an electricity producer who offers electrical power at competitive prices. Steam is produced in the site's own incinerators, amongst other things also with liquid waste from production.
- The geographical proximity to Process Development and Engineering proved very useful in the course of handling this project because the planning and construction of the industrial plant had already begun in parallel with the process development (concurrent engineering). In the new process, technologically very challenging process steps were involved which did not allow a direct scale-up from laboratory scale to the industrial-scale plant. In the vicinity of