**Welcome and Introduction**

To celebrate the 100th birthday of LONZA, the Industrial Chemistry Section of the New Swiss Chemical Society organized together with the research management of LONZA a symposium on ‘Industrial Asymmetric Synthesis’. For a company to exist for one hundred years is nowadays no small feat. In the name of our society, I sincerely wish to congratulate all LONZA chemists and their coworkers. The foresight of LONZA’s former President Dr. Hans Jucker, who encouraged steadfastly innovation in chemistry and technology, helped LONZA flourish even in today’s difficult times.

Since Pasteur, chirality has fascinated chemists, and many have speculated about its origin. According to a recent Science article [1], chirality may have existed before the origin of life!

Today, asymmetric synthesis, particularly when performed by catalysis, has become very important also for chemical production. We all understand why asymmetric synthesis is important, we want the bioactive molecule, the stereospecific entity, and not the racemate. In medicine, the wrong enantiomer may have undesired side effects, in farming, we want to be effective and friendly to the environment and avoid to spray useless molecules into the fields, in flavor and fragrances, we want the correct odor and taste. (S)-Limonene, for example, has a lime-type odor, while the (R)-isomer has an orange-type odor.

Asymmetric synthesis usually promises a shorter route to the desired material, but not always! A shorter route is usually more efficient, therefore cheaper and for the environment much friendlier. Efficiency, cost, safety, and care for the environment, these are production priorities.

To me, the prime example of this is the Dopa story. In the early seventies, as a young production chemist, I had the chance to participate in a gigantic effort by Hoffmann-La Roche USA to build a Dopa factory in record time. We were all fired up by the hope to help Parkinson patients. The Roche synthesis was a classic one, making use of classical resolving technology and, if I remember correctly, subsequent racemization of the undesired enantiomer.

Only a few years later, in 1973, Monsanto invented the now famous direct route. In only three steps, they obtained the desired (S)-isomer in 95% enantiomeric excess. Use of the Wilkinson catalyst, a chiral rhodium complex, made this possible. At once the Roche process was obsolete, and a short while later the expensive installations were quiet and empty. This episode had a great impact on the thinking of all chemists and particularly on the production chemists. It emphasized the point that resolution and racemization of the unwanted enantiomer need extra equipment, perhaps even a special production plant, and that may mean crystallizers, distillation columns, reactors, holding tanks, etc. To the company’s profit and loss sheet, it may mean millions of dollars or francs.

However, the case is not always so clear cut, as can be seen in the Menthol story.

Since 1973, Haarman & Reimer has been producing (–)-menthol from thymol in a highly efficient five-step synthesis. The diffcult part of the process is the separation of (±)-menthol from other isomers and then to separate the two enantiomers. The crucial step of this process is the enantioselective crystallization of (–)–(+)-menthol benzate. The (–)-menthol has to be recycled. I do not know how many steps are involved in the recycling process or what type of installations are needed, but, I think, that they are not inexpensive.

In 1980, Noyori discovered BINAP and developed for Takasago a four-step (–)-menthol synthesis from myrcene. The key step is the BINAP-catalyzed enantioselective isomerization of the allylic amine to (R)-citronellalamine in 99% yield. Hydrolysis of the amine gives the chiral aldehyde, which is then transformed by a highly stereoselective cyclization to isopulegol. The hydrogenation of isopulegol in a last step gives the desired (–)-menthol. This scheme has actually an interesting twist to it. Myrcene, the starting material for this synthesis is achiral, it is made from chiral β-pinene, then converted back to a chiral intermediate before being transformed to the final chiral product.

How can the classical Haarman & Reimer process still be competitive with the shorter asymmetric Takasago process? That’s a question I cannot answer, but I know that they are competitive. It is, of course, obvious that the catalyst turnover number is crucial to the economic viability of such a process, and this particularly so if the cost of its production is high. In Takasago’s case, this number, according to literature, is 400 000.

This example may show another route of production which does not please our research colleagues who have just invented a new cheaper route. Your process may be cheaper, more elegant and efficient, but, the production chemist says, we have a plant which is running well, has been paid off, so let’s run it until tight capacity calls for a new one.

But enough of old stories, let’s see what’s happening today and perhaps what will be happening tomorrow.