

Asymmetric Catalysis on Industrial Scale

Challenges, Approaches and Solutions

Edited by

H. U. Blaser, E. Schmidt



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Introduction

HANS-ULRICH BLASER and ELKE SCHMIDT

1

Background and Motivation

After some soul searching we agreed to collaborate with Wiley-VCH on this book project on the technical application of enantioselective chemo- and biocatalysis. Some of the reasons for our positive decision were the following:

- While there are quite a number of recent books and monographs on the science of enantioselective catalysis using homogeneous, heterogeneous or biocatalysts, no good reference book exists focusing on relevant aspects of the large-scale application of these technologies.
- It is generally very difficult to obtain reliable information on industrial processes, on the one hand due to secrecy concerns and on the other hand because writing publications is not a central aspect of industrial work. In addition, the existing reports are often found in congress proceedings or scattered in monographs and thus not easily accessible.
- An additional incentive was of course the awarding of the Nobel Prize 2001 to W.S. Knowles, R. Noyori, and K.B. Sharpless for their work in the area of enantioselective catalysis. From the point of view of the industrial chemist, it was especially gratifying that the development of a technical process for L-dopa was the basis for the award to W.S. Knowles, a very rare event indeed! And to our great satisfaction, he agreed to let us include his Nobel lecture in our book.

2

Goals and Concept

When we contacted prospective authors for the planned monograph, we defined the central goal as follows: *“To show the organic chemist working in process development that enantioselective catalysis is not just an academic toy but is really a suitable tool for large-scale production of enantioenriched intermediates. To serve as a source of information and maybe also inspiration for academic research and last but not least strengthen the position of the industrial catalyst specialists working in the exciting but sometimes frustrating field of enantioselective catalysis”*.

For this purpose we decided to collect case studies on the development of industrial scale enantioselective processes written exclusively by the specialists who were very closely involved with the work described in their contribution. In this context, technical-scale can be anything from a few hundred kilograms of a complex chiral intermediate for a pharmaceutical to several thousand tons for a herbicide or an amino acid. Because up to now there were no similar books available, it was less important whether a particular process had been described previously but rather that interesting and useful information be collected and discussed in a context where it can be found easily.

We asked the authors to illustrate important aspects of development work, such as:

- the environment and situation for carrying out process development in industry such as time pressures, the fit of the catalytic step into the over-all synthesis or the competition with other synthetic approaches and so on;
- the typical problems that are encountered in the various phases of the development of a technical enantioselective process such as finding/developing the catalyst, optimization of the process or choice of the equipment etc.;
- the successful (and also the unsuccessful!) approaches to solve the problem(s) at hand.

In addition, and we realized that due to problems of confidentiality this would not always be possible, we suggested that the authors also address frequently asked questions such as

- which is the preferred catalyst (homogeneous, heterogeneous, biocatalyst)
- how to separate soluble catalysts from the reaction mixture
- how to handle the sometimes very sensitive catalysts (impurities, air sensitivity, temperature sensitivity, etc.)
- the need for catalyst recycling (is it feasible or to be avoided?)
- where to get the enzyme/chiral catalyst/ligand/auxiliary in commercial quantities
- what are the critical parameters to optimize an enantioselective catalytic reaction
- questions of special equipment (pressure, high/low temperature)
- which were the success factors and which the critical factors during process development.

3

Our (the Editors) Assessment of the Resulting Monograph

Originally, we contacted 41 potential authors we knew to be involved in the technical application of asymmetric catalysis, 27 agreed to write a chapter, a surprisingly high “yield” of almost 70%, and in fact we can present 25 contributions. Major reasons for declining the invitation were on the one hand confidentiality, se-