

Roger Arthur Sheldon, Herman van Bekkum

# Fine Chemicals through Heterogeneous Catalysis

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R. A. Sheldon, H. van Bekkum

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# Preface

The subject of this book is the application of heterogeneous catalysis in organic synthesis with emphasis on transformations of relevance to fine chemicals manufacture. Both gas and liquid phase reactions are included although the latter are more numerous, analogous to fine chemicals manufacture where substrates and products often have low volatility and/or thermal stability, necessitating operation in the liquid phase. The subject is divided on the basis of the major types of catalytic conversions employed in organic synthesis: acid and base catalysis, hydrogenation and dehydrogenation, oxidation and C-C bond formation.

Heterogeneous catalysis has a long history, dating back to the early studies of alcohol dehydration over alumina and alcohol oxidation over platinum metal in the nineteenth century. Another milestone was the discovery, by the organic chemists Sabatier and Senderens, of catalytic hydrogenations at the beginning of the twentieth century. The high potential of catalysts as „molecular marriage brokers and divorce lawyers“ gradually became apparent and, following the advent of petrochemicals in the nineteen twenties, heterogeneous catalysis by solid acids and supported metals was widely applied in oil refining and petrochemicals. In contrast, fine chemicals manufacture was dominated by synthetic organic chemists who adhered to „stoichiometric“ methodologies. But „times are a changing“. The pressure of environmental legislation has, in the last decade, provided an important stimulus for the development of clean, catalytic methodologies. And heterogeneous catalysts have the added benefit of ease of separation and reuse.

This book is directed towards chemists engaged in organic synthesis, and catalysis, both in industrial and academic laboratories, who are concerned with research and development as well as education. Our primary aim is to cultivate a deeper understanding and, hence, promote a greater utilization of heterogeneous catalysis in organic synthesis. To this end, an international group of recognized authorities in the field of heterogeneous catalysis has been gathered together.

A general introduction to the subject is followed by a discussion of basic principles regarding types of catalyst and their preparation and characterization and types of catalytic reactors. Chapter 3 deals with the different types of solid acids. In the following chapters (4-6) various (solid) acid-catalyzed transforma-

tions are reviewed, *e. g.* aromatic substitutions and rearrangements and isomerizations. Solid base-catalyzed processes, *e. g.* aldol and related condensations are discussed in Chapter 7. Subsequent chapters deal with catalytic hydrogenation and dehydrogenation (Chapter 8), catalytic oxidation (Chapter 9) and catalytic C-C bond formation (Chapter 10), culminating in a future outlook (Chapter 11).

Each chapter contains an extensive bibliography covering the principal literature through the end of 1999.

Finally, the editors would like to express their sincere thanks to their friends and colleagues who have contributed such fine chapters to this book. We gratefully acknowledge the invaluable assistance of Mrs. Mieke van der Kooij in coordinating the traffic of manuscripts between contributors, editors and publisher. We also thank Wim Jongeleen for the cover illustration. Finally, we thank Dr. Anette Eckerle and Dr. Roland Kessinger of Wiley-VCH for their help in preparing this book.

Summer 2000

*Roger Sheldon*  
*Herman van Bekkum*



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# 1 Introduction

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## 1.1 What are Fine Chemicals?

There are no universally accepted definitions of bulk, fine, and specialty chemicals, nor are these classifications based on any intrinsic properties. A substance that is currently viewed as a bulk chemical might well have been classified as a fine chemical at an earlier stage in its development. A useful working definition of a fine chemical is one with a price of more than 10 US dollars  $\text{kg}^{-1}$  and a volume of less than 10 000 tons per annum on a worldwide basis. We make no distinction between fine chemicals, that are often intermediates, and specialty chemicals such as pharmaceuticals, pesticides, and flavors and fragrances. The type of technology used to manufacture these products is dictated more by volume than by product application.

From a chemical viewpoint fine chemicals are generally complex, multifunctional molecules and, consequently, are often of low volatility and limited thermal stability. This means that processes are generally performed in the liquid phase. Fine chemicals manufacture often involves multistep syntheses and is generally performed in a multipurpose equipment. This contrasts with the manufacture of bulk chemicals which usually involves continuous processing in dedicated plants. Hence, the emphasis in fine chemicals manufacture is on the development of processes that have broad scope and can be implemented in standard multipurpose equipment.

## 1.2 The Environmental Factor

It is now widely accepted that there is an urgent need for more environmentally acceptable processes in the chemical industry [1]. This trend towards what has become known as green chemistry [2,3] or sustainable technology necessitates a paradigm shift from traditional concepts of process efficiency, that focus exclusively on chemical yield, to one that assigns economic value to eliminating waste and avoiding the use of toxic and/or hazardous substances. Green chemistry eliminates waste at the source, i. e. it is primary pollution prevention rather than waste remediation (end-of-pipe solutions).

The sheer magnitude of the waste problem in the manufacture of chemicals is readily apparent from a consideration of the amount of waste produced per kg product, the so-called 'E factor' [4,5], in different segments of the chemical industry (Table 1).

These enormous quantities of waste consist primarily of inorganic salts, such as sodium chloride, sodium sulfate, and ammonium sulfate, formed in the reaction or in subsequent neutralization steps. The *E* factor increases dramatically on going downstream from bulk to fine chemicals and pharmaceuticals, partly because the production of the latter involves multistep syntheses and partly because of the use of stoichiometric (inorganic) reagents rather than catalytic methodologies. Although the absolute quantities are much smaller than in the synthesis of bulk chemicals, the need for greener, low-salt technologies is clearly more urgent in fine chemicals manufacture.

Comparisons of alternative processes solely on the basis of the amount of waste is obviously a gross oversimplification. An assessment of the environmental impact of a process should take both the amount and the nature of the waste into account. To this end the environmental quotient (*EQ*) was introduced [4]. It is obtained by multiplying the *E* factor by an arbitrarily assigned unfriendliness quotient, *Q*. For example, if an innocuous salt such as NaCl is assigned a *Q* value of 1 then heavy metal salts could be given a factor of, say, 100–1000 depending on their toxicity, ease of recycling, etc. The magnitude of *Q* is obviously debatable but it is clear that a quantitative assessment of the environmental impact of waste streams is, in principle, possible.

**Table 1.** E factors in the chemical industry.

Industry segment	Product tonnage <sup>a</sup>	<i>E</i> (kg waste/kg product)
Bulk chemicals	$< 10^4$ – $10^6$	$< 1 \rightarrow 5$
Fine chemicals	$10^2$ – $10^4$	$5 \rightarrow > 50$
Pharmaceuticals	$10$ – $10^3$	$25 \rightarrow > 100$

<sup>a</sup>Depending on the product this could be the capacity of a single plant or the world-wide production.