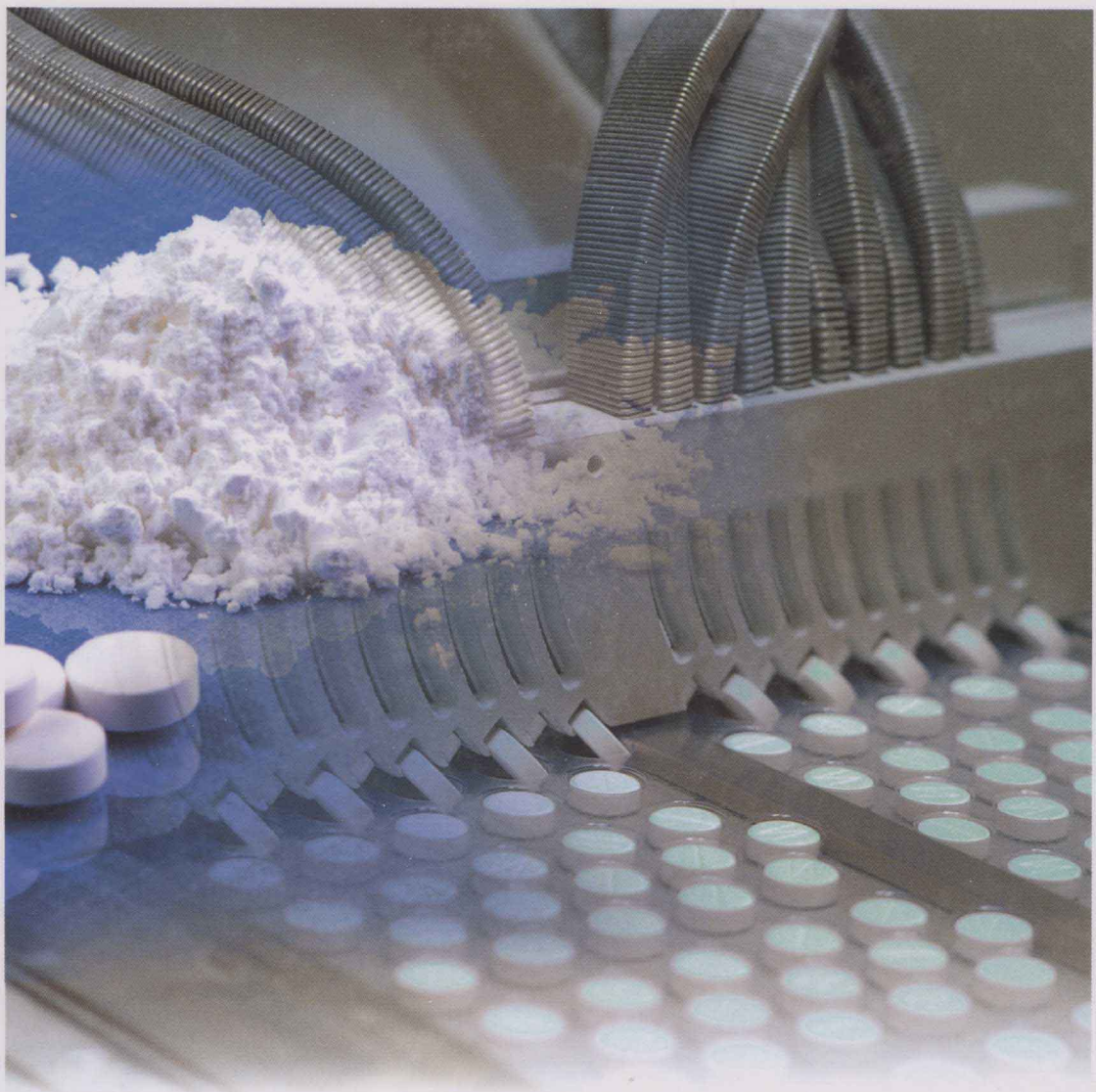


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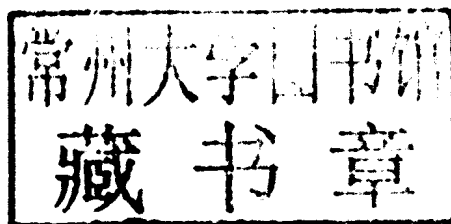
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Pharmaceutical Process Chemistry



*Edited by Takayuki Shioiri, Kunisuke Izawa,
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Pharmaceutical Process Chemistry



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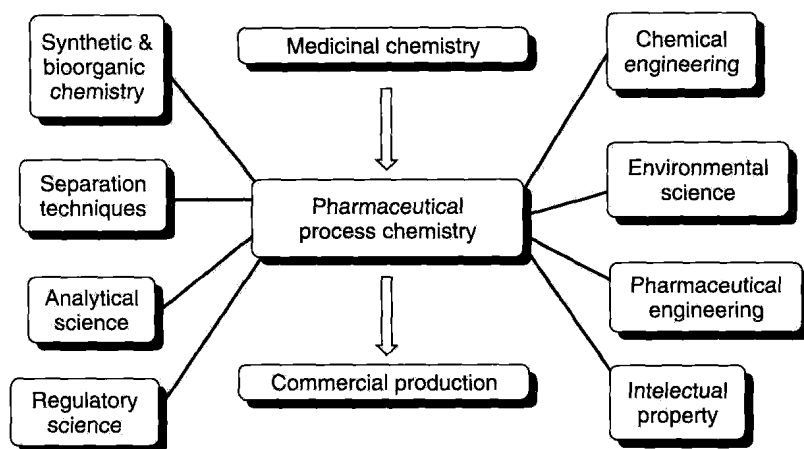
Preface

Pharmaceutical Process Chemistry is a very important field bridging medicinal chemistry and the industrial and commercial production of medicines. Although medicinal chemistry research is essential for finding novel innovative medicines and active pharmaceutical ingredients (APIs), neither medicines nor API can be made available to the world without active progress in pharmaceutical process chemistry. Further growth in this field should promote rapid progress in the development of new medicines.

The main purpose of medicinal chemistry is the discovery of pharmacologically active molecules at even a milligram scale while pharmaceutical process chemistry is concerned with the scale-up process for the production of useful molecules from milligrams to kilograms or even tons. Thus, pharmaceutical process chemistry has the following notable features:

- 1) selection of inexpensive and easily available starting materials in large quantities;
- 2) utilization of inexpensive catalysts and/or reagents and solvents;
- 3) establishment of robust and speedy procedures for producing drug candidates and API with high quality;
- 4) development of methods to produce drug candidates and API in an economical, convenient, and efficient manner;
- 5) avoidance of dangerous procedures and hazardous reagents;
- 6) selection of safer and environmentally friendly processes;
- 7) reduction of wastes.

Although synthetic & bioorganic chemistry currently plays a central role in pharmaceutical process chemistry, pharmaceutical process chemistry holds the hub position in relation to various other sciences including separation techniques, analytical science, chemical engineering, environmental science, pharmaceutical engineering, regulatory science, intellectual property, and so on, as shown in the figure.



This book intends to cover the broad area of pharmaceutical process chemistry, and should be useful not only for process chemists but also for academics and students. Although there has been a recent tendency in medicines to proceed “From Small Molecules to Macromolecules,” small synthetic molecules still have an important role in therapeutics. Thus, the introductory chapter addresses the importance of pharmaceutical process chemistry based on synthetic organic chemistry in the development of new small-molecule API. Various forefront synthetic methodologies that will be useful in the future growth of pharmaceutical process chemistry are then discussed. These methods may be applicable to process chemistry and may be useful for the production of new drug candidates and API, either as they stand or after the development of a suitable device for large-scale synthesis. The third part of this book addresses useful industrial synthetic and biochemical technologies and the fourth part discusses practical processes for the production of new medicines and API. The methods discussed should provide useful information for both process and academic chemists who are working on their own problems. The final part addresses aspects of this field, other than synthesis, that are useful for the production of new medicines: treatment of explosive reactions, crystal engineering, use of biomembranes, safety and environmental considerations, and so on.

All of the authors were selected from among the leaders in each area of specialization, and many of them have been invited to speak at symposia organized by the Japanese Society for Process Chemistry (JSPC) (<http://www.jspc-home.com/process/index.html>).

JSPC was founded in 2001 after several symposia and discussions between process chemistry directors in industry and university professors. JSPC aims to promote and encourage the development of process chemistry in various directions among members. JSPC has regular symposia twice a year in the summer and winter. Members of JSPC are affiliated with industry, especially the pharmaceutical industry, manufacturers of intermediates, universities, and so on. The number of participants in symposia continues to increase yearly. JSPC believes that it can play an important role in advancing and improving process chemistry.

Finally, we would like to express our gratitude to all of the contributors to this volume for their hard and ingenious work, and the reviewers of each chapter for their valuable comments and critical feedback. We want to thank the members of JSPC for their support and encouragement. We also want to thank the staff at Wiley for their outstanding editorial management.

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