



# *Strategies and Tactics in Organic Synthesis*

Edited by  
**MICHAEL HARMATA**

## *Volume 6*

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# STRATEGIES AND TACTICS IN ORGANIC SYNTHESIS

## Volume 6

*Edited by*

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*With a foreword by*

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**STRATEGIES AND TACTICS  
IN ORGANIC SYNTHESIS**

**Volume 6**

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## Foreword

Synthesis is evolving in many dramatic ways. Since its genesis in the seminal work of Wöhler, whose one-step synthesis of urea marked a transition from the 19<sup>th</sup> century belief that natural products could not be made in the laboratory, the field has successfully addressed a dazzling array of natural and non-natural compounds, profoundly impacting chemistry, medicine, biology, materials, and most disciplines whose future is inexorably coupled to understanding processes at the molecular level. As we enter the 21<sup>st</sup> century with approximately one total synthesis being reported per day, it is clear that we can make many types of molecules. The challenges now are increasingly related to which molecules merit attention and whether those molecules could be made in a practical fashion. These challenges and the current state of the field are brilliantly addressed by Mike Harmata and the superb group of contributors to this outstanding volume of *Strategies and Tactics in Organic Synthesis*.

This volume offers the *unique* perspective on the evolution of synthesis that only those involved directly in the science can give: the vision, ideas, plans, insights, setbacks, troubleshooting, discoveries and, with hard work and creativity, the successes that attend the process. From the dramatic start of the first chapter – “The story you are about to read began to unfold in 1987” – to the always hoped for ending – “...the total synthesis of (+)-dactylol was successfully executed”, this collection of organic syntheses is rich with information, insights, and inspiration that only those involved with the work can present. The student of the field is exposed to the many factors that motivate an interest in synthesis from targets of profound medical potential or value to materials and molecules of functional interest on to opportunities to advance methods, reactions, strategies, and our fundamental understanding of structure and mechanism.

The range of synthetic problems in this volume is also impressive; including alkaloids, heterocycles, macrolides, terpenoids, polyketides, designed targets, sensors and many other systems that defy easy description. Infused in these analyses is the preeminent importance of step economy as it is becoming increasingly clear that the length of a synthesis influences if not determines most other economies and measures. This is clearly addressed by several contributors and perhaps

most poignantly in a contribution from the process sector, another bonus of this volume, where in one accounting an estimated 33,000 kilograms of solvent are used to produce 60 grams of final product. One often overlooks this measure of atom loss and its direct connection to synthesis length.

*Strategies and Tactics in Organic Synthesis* originated over two decades ago from the desire to capture the creative process of synthesis and the excitement of the field from the unique, behind-the-scenes perspectives of those innovators involved in its advancement. This richness of insight and information is generally neither available in the primary literature due to space constraints nor in secondary sources due mostly to the lack of input from those who actually designed and executed the work. Mike Harmata and his contributing authors use the powerful impact of this format to advantage in chronicling their beautiful and varied contributions to synthesis. The reader will be richly rewarded with exciting science, analyses, and even art. This is at once a great scholarly analysis of this exciting field and an inspiration for its future.

*Paul A. Wender*  
*Stanford University, CA*  
*March 2005*

## *Preface*

Proofreading and editing are time-consuming and it is not easy to do things both quickly and well at the same time. I hope I have done better than in the past to avoid typographical errors.

I want to thank all the contributors for their efforts and patience. It was a pleasure to be exposed to so much great science and art.

Thanks to the folks at Elsevier for their support of this series.

I am at the end of my contractual obligations with respect to this series. It is not clear at this writing that more volumes will appear. I hope they do and I stand ready to edit them, but market forces will determine whether any more of this series appear. To be not at all subtle: Buy the books: for yourself, friends and loved ones!

Finally and quite importantly, I have an active research program and without it, there would not likely be time to invest in "synergistic activities" like book editing. My thanks go out to the National Institutes of Health, the National Science Foundation and the Petroleum Research Fund for their continuing support of our work.

Michael Harmata

## **Dedication**

This volume is dedicated to my wonderful wife, Judy L. Snyder.

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