

It is better to travel hopefully . . .

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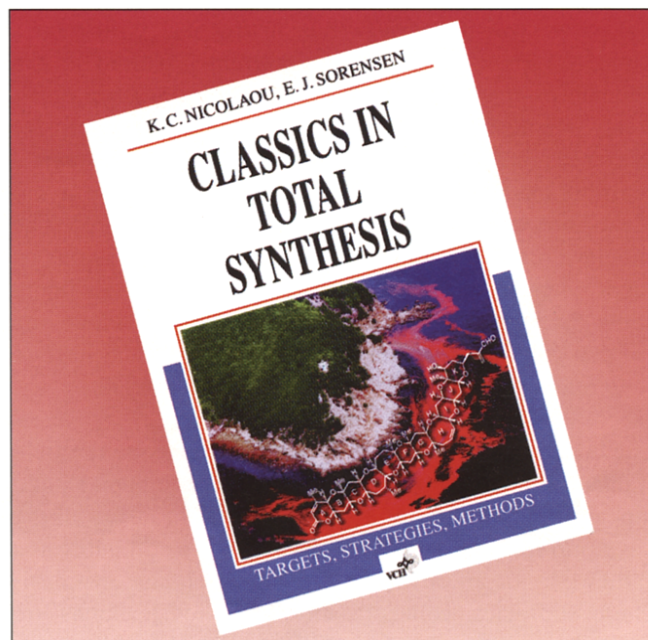
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Classics in Total Synthesis. Targets, Strategies, Methods by KC Nicolaou and EJ Sorensen, VCH Publishers Inc., 1996, 798 pages. \$49.95 softcover (ISBN 3-527-29231-4); \$80.00 hardcover (ISBN 3-527-29284-5).

This book sets out to do nothing less than provide a historical record of the “greatest syntheses of all time”, and to do this it catalogs a selection of classic total syntheses spanning the last four decades. From Woodward’s strychnine synthesis in 1954 up through Nicolaou’s brevetoxin B synthesis in 1995, the book chronicles in considerable depth 36 headline total syntheses of natural products. Using this framework, the authors skillfully weave a path for the reader through the progress and evolution of the science of total synthesis, conveying emotions of excitement, wonderment, surprise and disappointment, and ultimately evoking an awe for the collective achievements of the field and those who work in it.

The first chapter sets forth the philosophy, purpose and use of the field of organic synthesis in broad strokes, supplemented by informative and entertaining quotes from some of the ‘great masters’. It concludes with an entertaining poem entitled ‘Ithaca’ by C.P. Cavafy that sets up a metaphor comparing the total synthesis of natural products to a long journey in which it is the voyage and not the destination that counts. The travel log then begins.

Each of the next 36 chapters is organized in one way or another around a classic total synthesis of one or more molecules. Strychnine (Woodward and Overman), the prostaglandins (Corey and Stork), monensin (Kishi and Still), periplanone B (Still and Schreiber), steroids (Johnson and Vollhardt) and beta-lactams (Sheehan and Merck) are each visited twice, with solo stops at reserpine (Woodward), carpanone (Chapman), vitamin B12 (Woodward and Eschenmoser), erythronolide B (Corey), isocomene (Pirrung), biotin (Hoffmann-La Roche), L-hexoses (Masamune and Sharpless), asteltoxin (Schreiber), menthol (Takasago), hirsutene and capnellene (Curran), ginkgolide (Corey), methyl homosecodaphniphyllate (Heathcock), indolizomycin (Danishefsky), cytovaricin (Evans), gilvocarcin (Suzuki), paeoniflorigenin and paeoniflorin (Corey), and palytoxin (Kishi). The remaining destinations, which comprise about a third of the book, are the syntheses



which have helped to define Nicolaou as one of the current masters of the field. These are endiandric acids, amphoteronolide B and amphotericin B, calicheamicin, rapamycin, taxol, zaragozic acid, and brevetoxin B.

The chapters are as diverse as the target molecules themselves. They range from short glimpses of syntheses that are simply to be admired — carpanone is only three pages (but then again the synthesis is only two steps) — up to fifty page excursions through the syntheses of complicated molecules like brevetoxin and rapamycin. Each chapter opens with an ‘Introduction’ that puts the problem in perspective, and this is followed by sections on ‘Retrosynthetic analysis and strategy’ and ‘Total synthesis’. A short ‘Conclusion’ brings home the high points of the synthesis.

Like the journey to Ithaca, the book departs from the main road of the synthesis under discussion often and liberally, and it is these departures that differentiate the book from many other compilations on natural products total synthesis. The side trips lead the reader through an instructive and pleasurable tour of many of the most important developments in the field of organic synthesis. Sights along the way include the Woodward-Hoffmann rules, asymmetric catalysis, chiral auxiliaries, and a long list of key reactions that have been used time and again in natural products synthesis. Indeed, many of the syntheses are chosen as prime examples of the strategy or reaction that they represent. Furthermore, several of the chapters

take detours through other important total syntheses, so the book presents many more syntheses than it would appear to do at first glance.

Also like the journey to Ithaca, the book is long — almost 800 pages. But it doesn't really matter if you stop for a while along the way — I have currently paused at the Phoenician markets — because each of the chapters is nicely organized in a stand-alone fashion. The extensive references provide a detailed road map back to the original contributions that are summarized in the book. The layout of the book is beautiful and it is remarkably error-free. The judicious placement of repeat structures in the margins on pages where text is separated from the scheme or figure under discussion is an innovative feature. This allows you to keep going forward on your journey; you don't have to keep turning the pages back to see schemes passed.

The book is not easily accessible to those outside the field of organic chemistry, but within the field the book should appeal to everyone from new or occasional tourists all the way up to lifelong travelers. It should serve admirably as a framework for an advanced course on organic synthesis where strategies, concepts and important reactions are introduced in the context of their actual use. In many respects, *Classics in Total Synthesis* is the perfect complement to Corey and Cheng's *The Logic of Chemical Synthesis*. The Corey and Cheng book is an organized and analytical approach in which experience is reduced to retrosynthetic principles for synthetic planning. In contrast, the Nicolaou and Sorensen book is a free-wheeling tour guide to total synthesis — how it was and is. If your personal library has the Corey and Cheng book, you will surely want to add the Nicolaou and Sorensen book.

Like any 'greatest of all time' list, the authors' 'top-36' hit parade is likely to disappoint some. Fans of the classics might maintain that some of the modern music on the list will never stand the test of time. And if you don't like music originating from the United States, you may also be disappointed. For those who are feeling let down that their favorite synthesis was not included, the authors hint at a second volume. So we may eventually end up with some sort of 'All-Star Team' (elected by the fans? or by the players?) or perhaps even a total synthesis 'Hall of Fame'. And why not? Like a subjective list of any kind, this book is a celebration of what was and is exciting about the topic. But the 'journey to Ithaca' metaphor reminds us that all of this subjective evaluation is really beside the point. The synthetic leaders and the natural products that they have made are indeed the destinations of the book, but it is the journey that counts and this journey is nothing less than a pilgrimage through modern synthetic organic chemistry. I recommend that you buy a copy of this book, and I bid you Bon Voyage!