

## More Dead Ends and Detours

The path to a successful total synthesis is seldom an orderly endeavor. In spite of over a century of development, total synthesis remains a delightfully unpredictable experimental science with venerable reactions failing within complex settings. Physicist Ivar Giaever said in his Nobel Lecture “the greatest moment in an experiment is always just before I learn whether the particular idea is a good or a bad one. Thus even a failure is exciting, and most of my ideas have of course been wrong. But this time it worked!” This new book by Sierra, de la Torre, and Cossío captures these ecstasies of triumph through vignettes of overcoming failed strategy, crafting instructive stories on pitfalls in total synthesis.

*More Dead Ends and Detours*' unassuming title does not do justice to the significant improvements the authors have made on the original *Dead Ends and Detours*. Most noteworthy is the vastly improved focus on mechanistic understanding and learning from the detours. Whereas previously each section concluded with a brief summary of the key problems overcome, now the authors conclude each synthesis with a detailed mechanistic discussion of the key transformations and original DFT calculations performed by the authors. While in some instances they arrive at only a post-hoc rationalization based on calculated energetics, the authors more often probe well-known reactions in complex settings to arrive at a better understanding. As Roald Hoffmann describes in the Foreword: “in this way, [this book] makes a gentle case for the necessity of such calculations to enter the toolkit of the synthetic chemist.”

Each chapter presents two or three syntheses centered on an overarching theme. The issues range from “The Inertia of Conventional Functional Groups” to “When Metathesis Fails” and cover problems of relevance to modern organic synthesis. The book covers 22 prominent, contemporary total

syntheses. Importantly, the syntheses discussed are not examined in other well-known textbooks (with the exception of Brevetoxin A and Vannusals A and B). Each section opens with the background of the molecule and retrosynthetic analysis. The authors then delve into the execution and present the major issues encountered in the synthesis and their solutions. Successful strategies range from a simple change in protecting groups to complete revision of the synthetic plan. Each story is presented well and really conveys the intense struggle to overcome unexpected hurdles. Although some obstacles are unpredictable, readers will likely benefit from the numerous instructive instances where a calculation or stereoelectronic analysis could either lead directly to success or more fully rationalize a failure.

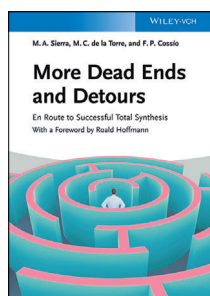
From a more critical perspective, there are quite a few grammatical and spelling errors, although they do not generally detract from the experience. A few minor quirks and organizational issues with a few figures are also hardly noticeable. Most significantly, the presentation of a few of the computed energies is overly confusing and takes away from the discussion when the reader is most attentive. This is especially disappointing because the discussion sections are otherwise fantastic and a wonderful addition to the series. Nevertheless, the authors accomplish their goal of creating a book that is fascinating to read and instructive.

The *Dead Ends and Detours* series occupies a unique position amongst total syntheses textbooks. While there are numerous books and series that highlight beautiful retrosynthetic logic and powerful reaction design, *More Dead Ends and Detours* pays tribute to the grit and determination that fuels every great total synthesis. In this new addition the authors have expanded an already excellent framework to create a book that will excite and educate readers at any level.

Steve McKerrall, Phil Baran

The Scripps Research Institute, La Jolla (USA)

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