Recent combinatorial chemistry books

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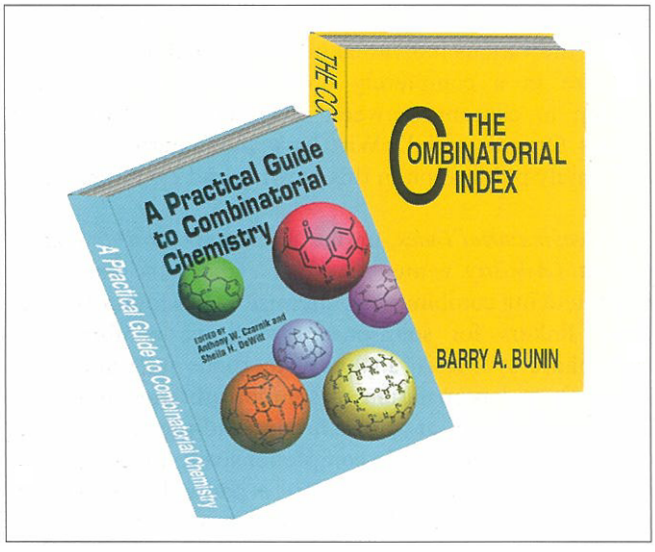
Two good introductions to a new field, *A Practical Guide to Combinatorial Chemistry* edited by Anthony Czarnik and Sheila DeWitt (American Chemical Society) and *The Combinatorial Index* by Barry Bunin (Academic Press), have recently been published. They are very different yet complementary books intended for the practicing combinatorial chemist.



A Practical Guide to Combinatorial Chemistry consists of 13 chapters, excluding the introduction and summary, organized into five sections (counting chapter 2 as one section). The book starts with a discussion of chemical similarity and the tools available to aid in the design of a library optimized for chemical diversity and auxiliary properties such as MWt and CLOGP. The chemist is then walked through synthesis methods, both solid-phase and solution-phase, pool deconvolution strategies, synthesis equipment, screening and information or data management. Section one provides a comprehensive basis for assessing chemical similarity, both from the point of view of maximizing diversity between library members and of selecting for similarity to a known binder. Good references are provided, both to the scientific literature and to commercial sources of software and methods. I would have liked to see some discussion of the 'diluting' effect of the inherent or preserved structure dictated by the common chemistry used to assemble the library on the measurement of diversity, but altogether this section represents a good overview of the design of chemical libraries.

Section two starts with a chapter giving the rationale for solid-phase synthesis, surveys the available bead supports, provides a good selection of the diverse linkers that make up the combinatorial chemist's tool box and ends with a very short section on analytical methods. One omission is a failure to reference the grafted surfaces that are extensively used for solid-phase synthesis. Additionally, the text does not provide the reader with reaction context for which the various tabulated linkers could be appropriate. The next chapter provides a little more of the same overall rationale for combinatorial chemistry but biased towards solution- phase synthesis. This is followed in the next chapter by a brief overview of the few analytical tools available for monitoring the reaction while the components are still attached to the solid phase. The last chapter in this section briefly discusses iterative deconvolution as applied to pooling strategies, followed by the more common encoding methods applicable to the split-and-pool synthesis procedures. Section three then parallels section two, but in the context of the important, but less used, solution-phase synthesis of chemical libraries.

Section four starts off with a description of various items of equipment that are available, or have been described in the literature, to support library synthesis. This is followed by a discussion of reaction optimization, which, as many a combinatorial chemist will testify, is usually the most time-consuming step in the overall process of preparing a new chemical library. An omission from this section is any discussion of the effects that different monomers can have on the reaction conditions, a topic that often goes under the title of 'monomer rehearsal'. The last chapter deals with examples of the parallel synthesis of discrete compounds often referred to in the context of focused libraries often associated with the rounding out of the structure–activity relationship around the more active or interesting molecules obtained from screening a primary library.

Section five contains two chapters dealing with very different topics. First is a discussion on the very important issue of data management, focused primarily on capturing the important elements of the synthesis strategy and the composition of the resulting library members. A brief look at the problems associated with the storing and processing of the results obtained from screening a library against a biological target follows.

Overall, *A Practical Guide to Combinatorial Chemistry* represents a good basis for anyone thinking about entering the field. For practicing combinatorial chemists, the book is a good source of insights and references to this growing field. Readers should recognize that any book assembled from the contributions of many different authors will reflect the various individual biases and will be difficult to organize in a completely ordered way without some overlap in content between chapters. Given that, the editors Czarnik and DeWitt have put together a useful and timely publication in this growing and exciting field.

The Combinatorial Index, unlike *A Practical Guide to Combinatorial Chemistry*, is much more of a laboratory manual for the practicing combinatorial chemist. It has four main sections: linkers for solid-phase synthesis; combinatorial solid-phase synthesis; analytical methods for solid-phase synthesis and preparation of solution libraries and combined approaches at the solution/solid-phase interface. Although each section is comprehensively indexed, it is, at first glance, difficult to locate a particular subject by searching in the index. Luckily, this does not detract from the overall value of the book because topics covered in each section are well organized in a consistent manner, making it very easy to look up relevant information once one is familiar with the book's structure. Comprehensive references to supporting literature are appended to each section rather than combined at the end of the chapter. I particularly found the information summarized in appendices 1 (Summary of functional group transformations) and 2 (Classification of heterocyclization reactions) to be a very valuable reference and I continue to use it day to day. Overall, *The Combinatorial Index* is an excellent compilation of source material about linkers and chemical strategies as used in combinatorial chemistry today.