

*Book Review*

**Templated Organic Synthesis.** Edited by F. Diederich (diederich@org.chem.ethz.ch) and Peter J. Stang (stang@chemistry.chem.utah.edu). Wiley-VCH: Weinheim. 1999. XX+411 pp. 268 DM. ISBN 3-527-29666-2

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Physicochemical theoretical development has been dwarfed by the abundant experimental achievements in molecular recognition studies, including the template effects reported in this book [1-3]. The traditional thermodynamics of the steam engine deals with molecules without any molecular discrimination: their kinetic energy is of the sole concern. Whether the steam is made of normal water, H<sub>2</sub>O, or expensive deuterated water, D<sub>2</sub>O, or the working gas is composed of some other molecules, it does not matter. The piston in the engine recognizes the gas molecules in the same way that a peasant in a remote Chinese village might recognize the laborers he would like to employ. He might concern himself only with whether the laborers are strong enough to drag a plough in his fields. He might even not want to distinguish if the power is provided by a man or a horse. However, now suppose a professor (e.g., one of the editors, Diederich [2a], from ETH Zurich) wants to accept somebody to work with him in his group. He would not take a horse, or even a lay person. Even most chemists might not be good enough candidates. Diederich's recognition is much more specific.

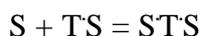
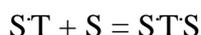
In the examples provided in this book the piston or the peasant are replaced by a professor-like template. Here, the thermodynamics that describes a "peasant and animal power" relationship becomes inadequate to explain many phenomena concerning the attractive interactions of molecules: sometimes these are the same, such as the case of hydrophobic molecules; sometime they are of contrasting properties, such as donor or ligand and acceptor, or substrate and enzyme. For example, both the similarity rule and the complementarity rule are still empirical rules. A natural guess would be that information-

theoretical methods be considered or developed in addition to the existing thermodynamic methods.

The present reviewer, as a long-time student of experimental chemistry, has been trying to find a theory supporting these empirical rules and all the related fundamental conceptual relationships, mainly the relation of the five parameters: higher symmetry, higher similarity, higher entropy, less information and less diversity; and they are all related to higher stability (as the present reviewer found). Information loss, entropy and symmetry are the most important concepts. Entropy defined as information loss has a broader meaning than thermodynamic entropy. Information theoretical entropy is independent of thermodynamic entropy. E.g., after the attractive interaction based on complementarity between two molecules of certain contrasting properties (one is a donor, the other is an acceptor), their properties are offset and the combined chemical species is more symmetric and consequently more stable.

I started to read this book when I brought it with me to Paris during the last two days of 1999 and the first days of celebrating the year 2000. I learned that Busch was the first who intentionally used templates in synthesis and articulated the concept "template effect" in the 1960s.

In chapter 1, for linear templates, on page 23, I wonder if the ternary complex S'T'S is formed in the following bimolecular manner:



both with the same binding constant  $K$ . It should be much more probable than the trimolecular equilibrium:



In chapter 2, the author Günther Wulff describes his elegant studies on "transfer of structural information" from template to polymer" (p38, p45). The relationship of the template to the imprinted cavity corresponds to the key/lock relation proposed by Emil Fischer for enzyme catalysis more than 100 years ago (p46).

Chapter 3 gives examples of templated formation of mechanical bonds. The first efficient synthesis of a [2]catenane using the template effect was accomplished by Sauvage et al. in France in 1983 (p76). The statement that: "... the information used to template their formation lives on in the molecules thereafter" (p95) is fascinating. Chapter 4 continues with the templates as the entrapped guest molecules or ions.

In Chapter 5 the authors mentioned "the molecular skeletons capable of storing sequence information into ones that can be read into complementary materials." (p134). The concept of specificity or fidelity is defined (p.134). As indicated before, very useful entropy effect considerations cannot be of much help because, according to thermodynamics alone, association is always entropically disfavored. There are only two states: associated and dissociated. The thermodynamic entropy concept cannot be

applied to differentiate between many ways of association, so far. Information and entropy defined as information loss are very important concepts in our further theoretical considerations.

Excellent examples of templates in organic synthesis are described in the final chapters (chapters 6-10). Chapter 6 is Breslow's famous organic synthesis of enzyme analogue structures and biomimetic reactions. The very large molecules of fullerene derivatives are covered in chapter 7. Tethered monomers form oligomers with expected structures (chapter 8). Chapter 9 starts with a more precise definition that a template is a molecular device which shapes a given substrate and thereby provides bias for a certain pathway over a competing one, and which is removed once it has exerted its function (p249). "By increasing the proximity between reacting centers, activation entropy is reduced" (chapter 10, p275). Chapter 10 is a book-sized report of the temporary (intramolecular) connection in organic synthesis by Liam R. Cox and Steven Ley.

The following two paragraphs are adapted from the books' website [3]:

Template-controlled reactions allow the synthesis of complex molecules which would hardly be achievable through classical methods. This handbook offers authoritative information on how noncovalent and covalent templates can be effectively applied to control reaction rates as well as regio- and stereoselectivity. From the concepts of template control such as molecular imprinting, self-replication, and reversible tether-directed remote functionalization, the reader is led to template-based ring-closing reactions, oligomerizations, and multiple functionalizations and their application in the synthesis of supramolecular scaffolds and natural products.

The editors and authors (J. F. Stoddart, G. Wulf, D. Lynn, R. Breslow, F. Diederich, just to name a few), all internationally recognized experts in their area, succeed in presenting the manifold aspects of template-controlled synthesis in a didactic way, making this methodology accessible to a broad readership of organic synthetic chemists. Well-selected, reliable key experimental protocols and an up-to-date reference list underline the practical approach of this valuable handbook. Being the first book of its kind, it will serve as a pace-setter and stimulate future research.

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## References and Notes

1. The homepage of Wiley-VCH is <http://www.wiley-vch.de/>.
2. (a) Diederich's homepage: <http://www.verw.ethz.ch/cgi-win/Who.exe?ID=468&lang=engl;>  
(b) Peter J. Stang's homepage: <http://courses.chem.utah.edu/facultyandstaff/stang/stang.html>
3. This book's website is <http://www.wiley-vch.de/books/tis/eng/3-527-29666-2.html>