

Structural Definition of Chemical Templates and the Prediction of New and Unusual Materials[#]

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Abstract. Synthetic applications of chemical templates have yielded, in succession, macrocycles, cage compounds, interlocking rings and a trefoil knot. The known kinds of templates are analyzed and used to provide a broad definition of a chemical template, which, in turn, leads to the prediction of exciting new forms of matter based on orderly molecular entanglements.

Key words. Chemical templates, molecular entanglements, molecular organization, template definition.

1. Retrospect

On the basis of the dates of a number of events, I believe I first met Charles Pedersen either late in 1965 or in 1966. At the time I was spending a week at the Experimental Station of du Pont for the purpose of consulting with chemists in various departments. I was asked to talk with Charlie and I clearly recall certain aspects of that rather special visit. He sought me out because we were both interested in macrocyclic ligands and he enthusiastically described his new family of crown ethers and their interactions with alkali metal ions. I recall how he used the old Fischer–Hirschfelder models in presenting his work; it was clear that he recognized the role of complementarity in the metal ion/ligand interaction. He wanted to know if this was significant and if any other alkali metal complexes were known. I explained to him that alkali metal ion complexes were indeed rare but not unknown, and, in fact, his cesium complexes were probably the first claimed for that element. I quickly became enthusiastic about his work and encouraged him to publish promptly. Further, I realized that the Nikko meeting of the International Conference on Coordination Chemistry was being planned and I volunteered to contact the organizing committee and suggest they invite him. That committee was receptive and he made his celebrated disclosure at Nikko. I met with Charlie and with his collaborator in solution studies, Dr. Frensdorf, on a number of subsequent consulting visits. Eventually I helped his supervisor nominate Charlie for the Delaware Section Award which I believe was the first recognition he received for his seminal works on alkali metal complexes of macrocyclic polyethers.

2. Introduction

Chemical templates are the basis of genetics and lie at the foundation of biology and, in recent decades, they have been used extensively in both inorganic and organic

[#] This paper is dedicated to the memory of the late Dr C. J. Pedersen.

chemistry, particularly in synthesis [1, 2, 3]. Chemical templates were first conceived and demonstrated for the field of synthetic chemistry many years ago [4], and they played a major role in the development of macrocyclic ligand and inclusion chemistry [1–3, 5]. More recently extraordinary new examples have been devised, producing interlocking rings and a molecular knot [2]. Despite the extensive activity in this area, the term *template* has not been adequately defined in the past and various processes have been dubbed template reactions without sharing common critical characteristics. By analyzing the structural relationship associated with molecular organization [3], it is now possible to provide a precise definition of a *chemical template* that brings order to the subject and gives promise of opening new vistas in chemistry, including the possibility of entirely new kinds of molecular materials.

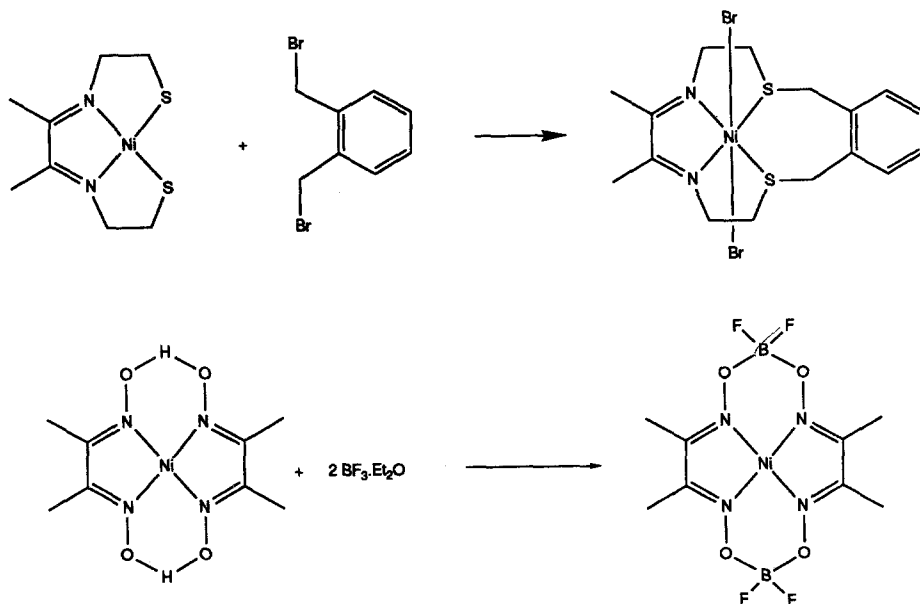
3. Discussion

Chemical templates are defined in terms of the basic elements of molecular organization [6].

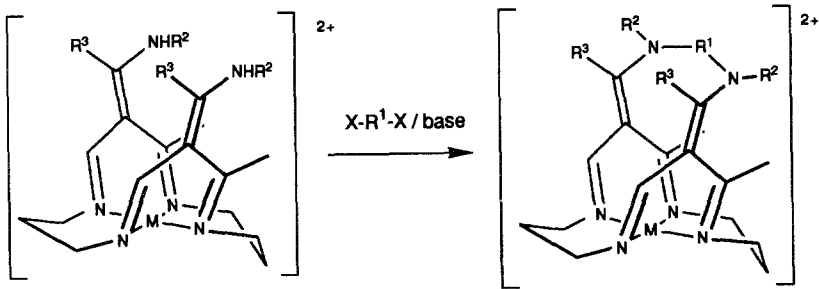
A chemical template organizes an assembly of atoms, with respect to one or more geometric loci, in order to achieve a particular linking of atoms [7].

In synthetic applications, the goals have been topological until relatively recently [8], although the most obvious natural templates have sequencing as their goal.

The simplest goal of a chemical template was and remains the synthesis of macrocyclic rings, and this has been accomplished by the closing of individual chelate rings by reactions carried out on ligands that are bound to metal ions. In such a case, it is necessary to organize the reacting ligands with respect to one or more edges of a coordination polygon or polyhedron, depending on the nature of the reactive ligand. As Scheme 1 shows, when a single tetradentate ligand is the



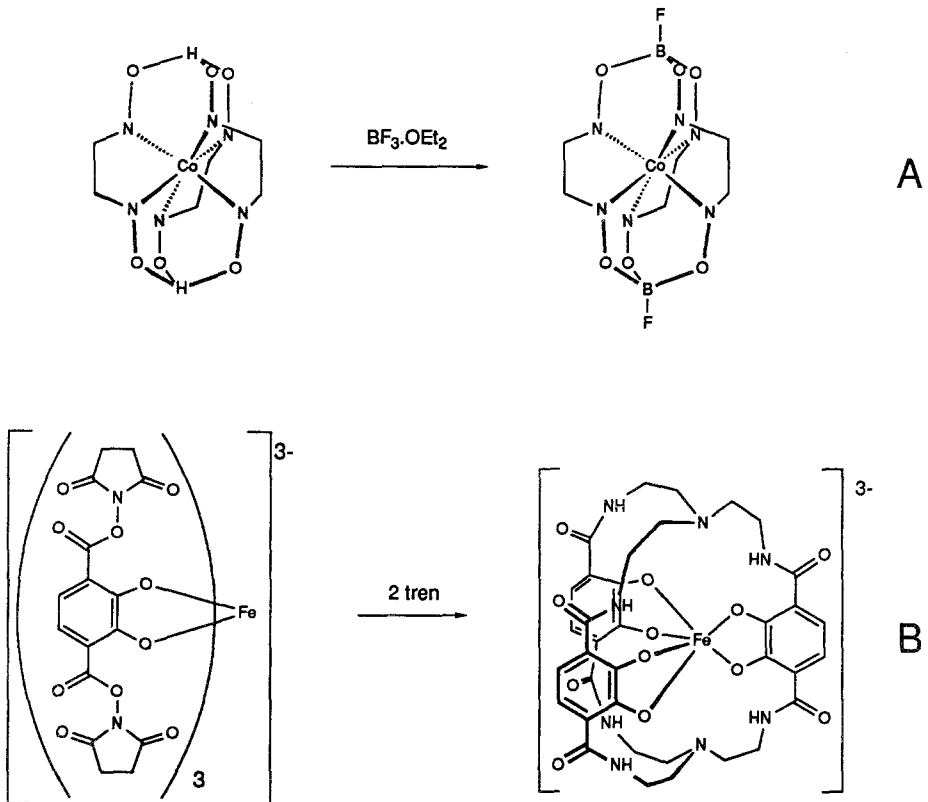
Scheme 1.



Scheme 2.

reactant, the organization is with respect to a single polyhedral edge, but when the reacting system is a pair of bidentate ligands then organization is required with respect to two edges [9]. Scheme 2 shows that the simple edge in question need not be a part of a *coordination polyhedron*, so long as it conforms to a sufficiently rigid orientation that is equivalent to the edge of a hypothetical polyhedron.

Macrobicyclization, and the concomitant enclosure of metal ions in bicyclic cages, was the second topological class of chemical templates to be recognized and exploited [10]. As Scheme 3A (in which methyl substituents and double bonds

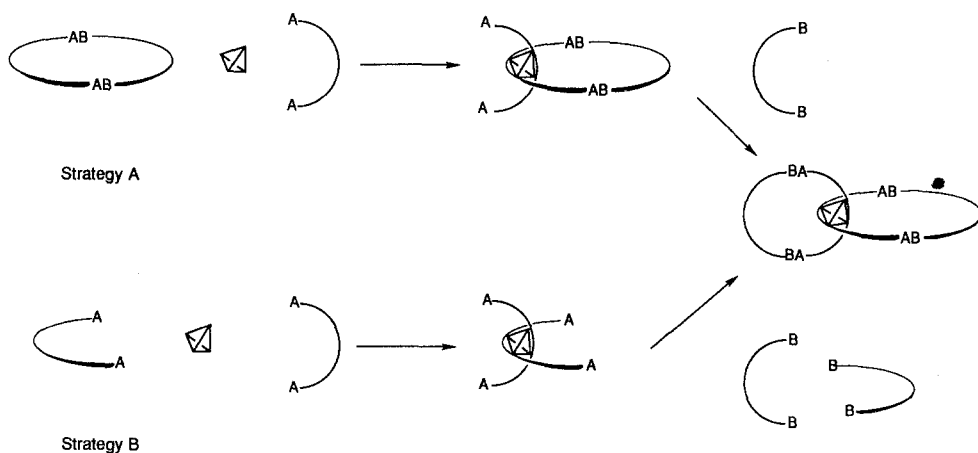


Scheme 3.

omitted for clarity) shows, this is accomplished by organization of the reacting bound ligands with respect to one face of a coordination polyhedron. As with simple macrocyclization, the atoms ligated to the metal ion may be those involved in the bicyclization reaction [11], but this need not be the case. The first example of a template bicyclization reaction used atoms α to the donor atoms [12] and studies on siderophore models [13] have used functional groups quite remote from the metal atoms (Scheme 3B). The key feature remains the organization of those reaction centers with respect to the polyhedral face. For these examples the polyhedral face has three corners and three strands are organized in the template process. Higher order faces, e.g. a square or pentagon, would organize corresponding numbers of strands.

Understanding the chemical templates in macrocyclization and macrobicyclization reactions is a simple exercise, but it is the analysis of the new topological types of chemical templates leading to catenanes and trefoil knots that makes the formal definition of a chemical template necessary and significant. In the template synthesis of interlocking molecular rings (catenanes) Dietrich-Buchecker and Sauvage [3] utilized two very similar templates. The simplest involves the positioning of the organized moiety within the compass of a previously formed and simultaneously coordinated ring. As Strategy A of Scheme 4 shows, the reactive ligand is organized with respect to a single tetrahedral edge that is orthogonal to the edge to which the preformed ring is bound.

It is simpler to state the case for the second and more basic template reaction used by those investigators to produce catenanes (Strategy B, Scheme 4). In this case the two reactive moieties that are precursors to the interlocking rings are organized with respect to mutually orthogonal tetrahedral edges. In general the four points involved in this template could be associated with structures other than a tetrahedral one and the edges need not be precisely orthogonal. For example two tridentate ligands, each of which occupies a pair of mutually planar octahedral edges (Figure 1), organize their ligands with respect to two mutually orthogonal octahedral four fold axes and this is a suitable template for the synthesis of



Scheme 4.

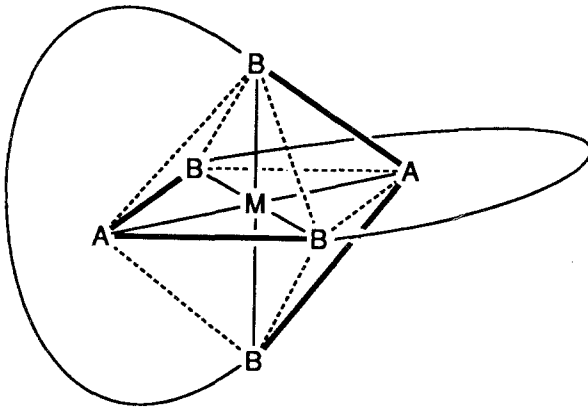
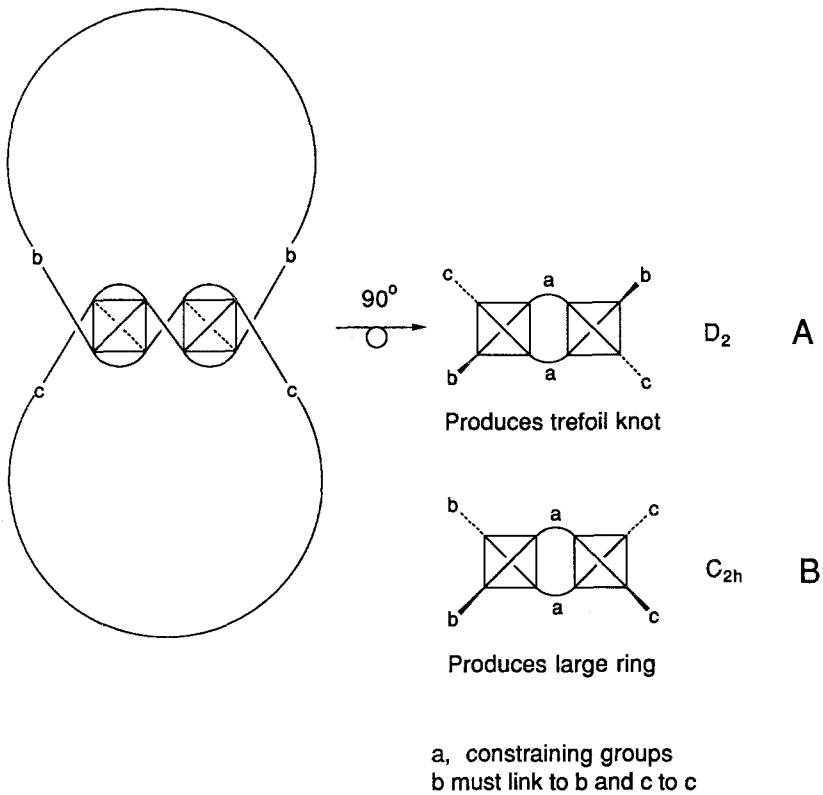


Fig. 1. An octahedral template designed to produce catenanes.

interlocking rings, although it has not yet been used. Similarly, trans-spanning pairs of bidentate ligands might be used in a square planar coordination sphere for the same topological purpose.

The template reaction leading to the trefoil knot (Scheme 5) breaks new ground as it extends organization to two metal centers and the 'assembly of atoms'



Scheme 5.

undergoing organization includes pairs of donors that chelate to each of the two templating centers [14]. Like the catenane template, two pairs of bridging bis(didentate) ligands are simultaneously bound with didentate groups from the different ligands occupying orthogonal tetrahedral edges. Further, the two templating centers must exhibit the same chiralities; otherwise the product of the template reaction would be a simple ring having no knot (Scheme 5B). This can be concisely stated:

for the trefoil knot, the 'assembly of atoms' is organized with respect to pairs of orthogonal edges on two mutually constrained and cochiral (tetrahedral) centers.

It should be noted that the template illustrated at the right in Scheme 5A is related to the structure shown (as its left) for the trefoil knot by rotation through 90° about an axis lying in the plane of the picture and passing through both metal atoms. Ring closure requires the joining of the two points marked C to each other below the plane of the paper and the two points marked B, above the plane of the paper.

4. Conclusions

Whereas the enormous impact of the processes leading to simple macrocyclization and to macrobicyclization is well known, the ultimate significance of the ingenious new template types devised by Sauvage and associates remains unclear. Here we predict that complicated templates may eventually produce entirely new forms of matter based on *orderly entanglements*. Further, these novel materials may have exceptional properties. Elastomers illustrate that *random molecular entanglements* have properties of great value. It is intriguing to reflect on the possibility of producing highly ordered molecular entanglements.

If template reactions can produce chains and knots, then they should be capable of producing molecular braids. And, if braiding is possible then so should be molecular knitting and even molecular weaving. Consider the properties of such intermolecular entanglements. Unusual strengths, uncommon flexibilities and fascinating anisotropies are obvious possibilities. The successful applications of the more obvious, but still subtle *chiral* templates in organometallic chemistry [15] gives promise that the further application of chemical templates to transition metal catalysis of polymerization processes can be expected to produce a variety of such ordered molecular entanglements, ultimately yielding the components of 'a *molecular macrame*'.

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References and notes

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5. Template macrocyclization and macrobicyclization reactions contributed heavily to the founding and developing of the fields of macrocyclic ligand chemistry and inclusion chemistry. Many symposia, journals, meetings and books have been devoted to these subjects.
6. The five fundamental factors that underlie molecular organization are so basic that they seem almost trivial; however, their proper consideration is essential in all molecular designs focused on problems involving molecular organization. Indeed this is probably why their essential mutual interdependence has only recently been articulated and demonstrated in analyzing such familiar 'effects' as the chelate effect, the macrocyclic effect and the template effect. They are geometry, size, topology, rigidity and complementarity.
7. The word 'organizes' (with respect to a geometric element; i.e. an edge or face) is used rather than the word 'orientation' because the group must be both propitiously located and capable of reaction. For example, if the atom or group of atoms in question is acting as a donor and is to serve as a nucleophile, then it must have the requisite potent lone pair of electrons. If the reactive site undergoing organization is a remote acyl carbon, then it must be sufficiently flexible to reach the critical transition state. Further, the definition says '...with respect to...' (a geometric locus) instead of 'in conformity with' because template relationships at the collection of points describing a geometric element require a vector sense as well as a positional one. This will be apparent as the discussion proceeds.
8. (a) T. R. Kelly, C. Zhao and G. J. Bridger: *J. Am. Chem. Soc.* **111**, 3744 (1989); (b) T. Tjivkua, P. Ballester and J. Rebek, Jr.: *J. Am. Chem. Soc.* **112**, 1249 (1990).
9. In the latter case it is particularly obvious that misorganization leads to failure. If the two bidentate ligands are chelated in an octahedral structure so that two of their ends are *trans* rather than *cis* to each other, then template ring closure is disfavored.
10. The first example of such a process was due to Boston and Rose and involved the case chosen as Scheme 3 (Ref. [12]). This was followed by examples from Parks, Wagner, and Holm (*Inorg. Chem.* **10**, 2472 (1971)) and from Goedken and Peng (*J. Chem. Soc., Chem. Commun.* 62 (1973)).
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