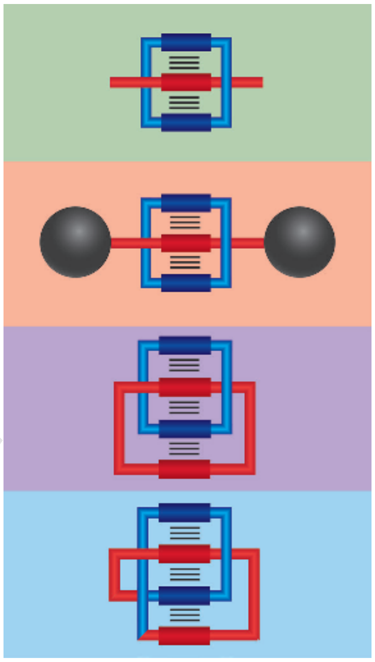
Chapter 1 An Introduction to the Mechanical Bond



Conspectus

Mechanical bonds are omnipresent and all pervasive. They occupy every nook and cranny of human experience in both static and dynamic settings that range from being close to infinitesimally small to those which can be described as large by comparison. In the domain of the molecular world, the mechanical bond emerges as an additional expression of the nature of the chemical bond in all its manifestations. This emergent phenomenon takes place in the lower reaches of the nanometer length scale as a special architectural feature. It emerges just as soon as it becomes spatially possible to entangle the *component parts* of molecules, the sizes of which are governed in part by the subnanometer distances between their constituent atoms.

The production of chemical compounds composed of *mechanically interlocked molecules* (MIMs) by acts of *templation*, be they passive or active in their origins, are hand-me-downs from the science of (supramolecular) chemistry beyond the molecule, which affords *molecular recognition* free rein to exercise its special powers of organization in marshaling the component parts of the MIMs prior to their being transported back into the molecular world by the formation of chemical bonds. This relatively recent extension of bonding in molecules opens the door on a yet little explored field of chemistry—namely that of *chemical topology*, which leads to the concept of *topological isomerism*, where two or more molecular ensembles may contain the same atoms and chemical bonds, yet cannot be interconverted by any deformations that do not involve the breaking and making of chemical bonds.

Intersecting the fields of *supramolecular chemistry* and *chemical topology* is the discipline of *mechanostereochemistry*. Just as stereochemistry is the study of the relative spatial arrangements of atoms in molecules, mechanostereochemistry is the stereochemistry of molecules with mechanical bonds. Catenanes and rotaxanes are a subset of MIMs that possess mechanical bonds. A *catenane* is a molecule with two or more interlocking ring-shaped component parts. The simplest of catenanes with two interlocked rings is a *topological isomer* of the two rings separated from each other. A *rotaxane* comprises (a) ring(s) threaded by (a) dumbbell(s) possessing stoppers that are too bulky for the ring(s) to transgress. The simplest of the rotaxanes with one ring and one dumbbell is not a topological isomer of the ring and dumbbell separated from one another since expansion of the ring or compression of the stoppers (without the breaking of chemical bonds) can lead to the separation of the component parts by a process known as *slippage*.

A *mechanical bond* is an entanglement in space between two or more component parts, such that they cannot be separated without breaking or distorting chemical bonds between atoms. It follows that a mechanical bond is as strong as the weakest participating chemical bond. Hence, catenanes and rotaxanes are most appropriately described as molecules, or more precisely, as *mechanomolecules*. Since entanglements are possible in molecules—for example, knots—that lack component parts, not all MIMs possess mechanical bonds. While catenanes and knots fall under the aegis of chemical topology, rotaxanes are considered to be topologically trivial because their component parts may be separated by the continuous deformation of chemical bonds. It is this dichotomy that exists between catenanes and knots on the one hand and rotaxanes on the other that has led to the adoption of the term mechanical bond when describing catenanes and rotaxanes in preference to topological bonds, which are present in catenanes and knots, but *not* in rotaxanes. One of the endearing charms of chemistry is that it defies repeatedly attempts at clear-cut descriptions of phenomena under its guard. In this particular instance, the much higher promise of wider applicability on the part of rotaxanes makes the case for promoting the chemistry of the mechanical bond.

Although the mechanical bond has been exploited and revered in society, art and Nature from time immemorial, it has proved to be immensely challenging to introduce synthetically into molecules and hence chemistry. Nothing of much significance had been recorded in the scientific literature up until the 1960s. This decade and the succeeding one witnessed simultaneously the advent of a painstaking classical approach, under the guidance of covalent-directed synthesis alongside statistical forays based on little more than the chance events of the threading of large-sized rings by suitably long molecular chains. With the emergence of host-guest and supramolecular chemistry in the 1970s, however, the stage was set for molecular recognition to lead to the *directed synthesis* of mechanomolecules through the acts of templation with coordinative, followed by noncovalent, bonds of many different persuasions. The result has been an exponential growth these past 35 years in *molecular nanotechnology*, coupled to a paradigm shift in molecular structure and function. While mechanomolecules have found their way, both singly and collectively, into switches and motors, the molecules themselves have led to a renaissance in *molecular aesthetics*. Introducing mechanical bonds into molecules can only assist in garnering support for the growing initiative to widen aesthetic considerations in chemistry.

The Nature of the Mechanical Bond: From Molecules to Machines, First Edition. Carson J. Bruns and J. Fraser Stoddart.

Introduction

A scientist wakes up in the morning, rubs her eyes, draws back the curtains and pulls up the window blinds. She goes through her morning ablutions and gets dressed; she buttons up her blouse, puts on her earrings, and ties her shoes. She plaits her hair into a braid before opening her door and hopping on a bicycle for her morning commute. As she rides in to work, she barely notices the other bicycles, cars, buses, and trains that carry the other morning commuters on their ways, or the swinging French doors, chain-link fences, and flagpole pulleys that decorate various home fronts on her route. On reaching work, she locks up her bicycle on a rack and takes an elevator up a few floors to her laboratory, where she opens up her computer and begins to think about something that has already pervaded her morning without even entering her consciousness. The window blinds, the blouse and buttons, the braids and earrings, the bicycles and automobiles, the fences and flagpoles, the bike lock and the elevator, not to mention the computer sitting in front of her, all share at least one thing in common—namely, the mechanical bond.

Although chemistry[1] has often been hailed[2–6] as "the central science", we must remember that chemists do not have a monopoly on the definition of a bond. In finance, a bond is an instrument of indebtedness. Biologists speak of pair bonding as a strong affinity between two individuals—often a breeding male and female—of a species. Social scientists speak of maternal bonds, paternal bonds, affectional bonds, male bonding, female bonding, and so on. Anthropologists classify acephalous societies, which lack political leaders and hierarchies, as land-bonded, village-bonded, or lineage-bonded societies. Indeed, bonds describe relationships, associations, and connectivity. A mechanical bond can therefore be understood as the connection between two objects that are held together by mechanical forces, meaning physical forces or contact forces, as a result of their entanglement in space. The mechanical bond is not at all exclusive to chemistry. In fact, the mechanical bond appears to be far more prevalent in our everyday lives—in art, technology, and nature, for example—than it is in synthetic molecules. Nevertheless, the study of the molecular mechanical bond has transitioned in little more than 50 years from being (i) a mere curiosity in the minds of a few forward-thinking intellectuals in the first half of the 20th century, to becoming (ii) a rather esoteric subfield of synthetic organic chemistry, practiced only by a handful of academic and industrial researchers in the 1950s, 60s, and 70s, to (iii) entering a phase of rapid and steady growth near the end of the 1980s on the back of new synthetic protocols which made the synthesis of molecules with mechanical bonds much more facile, to (iv) flourishing into the increasingly diverse and interdisciplinary field of chemistry that it is today.

Defining the Mechanical Bond

Arguably the most influential chemistry book ever to have been written—one which shaped profoundly our modern understanding of bonding in molecules—is Linus Pauling's 1939 monograph[1] on *The Nature of the Chemical Bond*. This classic treatise summarizes the pioneering work carried out by himself and others during the 1920s and 1930s. Pauling classifies chemical bonding into three categories—electrostatic, covalent, and metallic bonds—representing extremes between which many intermediate types of bonds (e.g., hydrogen and halogen bonding) may exist. According to Pauling –

> *…there is a chemical bond between two atoms or groups of atoms in case that the forces acting between them are such as to lead to the formation of an aggregate with sufficient stability to make it convenient for the chemist to consider it as an independent molecular species.*[1]

It was not until more than two decades later that the newest bond in chemistry—namely, the mechanical bond—emerged on the scene. In Pauling-inspired prose, we might say that there is a mechanical bond between two objects in case that their ability to be separated is obstructed by an entanglement in three-dimensional space. This definition encompasses mechanical bonds at all scales, not only the molecular one. In chemistry, the mechanical bond is an emergent[A] type of bond that arises only when groups of atoms become large enough to permit the formation of entanglements in space. Whereas chemical bonds are typically shared between atoms, mechanical bonds are shared between groups of atoms, or molecular entities, which we will call component parts. In this volume we will refer to molecules with mechanical bonds as mechanomolecules.

Mechanical bond – An entanglement in space between two or more molecular entities (component parts) such that they cannot be separated without breaking or distorting chemical bonds between atoms.

Component part – A group of atoms, or 'molecular entity', comprised of chemical bonds, which is mutually engaged in mechanical bonding with another molecular entity.

Mechanomolecule – A molecule possessing one or more mechanical bonds.

The two quintessential types of mechanomolecules (**Figure 1.1**) are catenanes and rotaxanes. A catenane—its name derived from the Latin word *catena*, meaning 'chain'—is a molecule with two or more interlocking ring-shaped component parts. A rotaxane—derived from the Latin words *rota* (wheel) and *axis* (axle)—comprises a ring threaded by an axle-like molecular entity, or 'dumbbell', with endgroups (stoppers) that are too bulky for the ring to transgress. Some mechanomolecules, such as rotacatenanes,[7] suitanes,[8] double-lassos,[9] helix-rod assemblies,[10] mechanically self-locked ring-in-ring assemblies,[11] and Gemini catenanes[12] do not fit cleanly into either category—see **Section 4.3**.

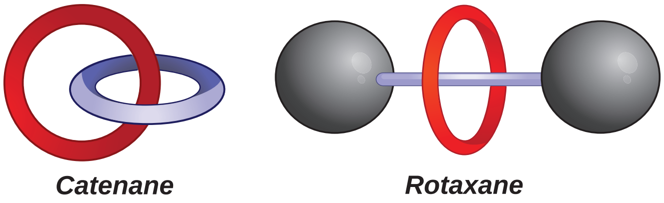


Figure 1.1 Graphical representations of a catenane (left) and a rotaxane (right), which comprise the two main classes of mechanomolecules.

Mechanomolecules belong to several intersecting fields (**Figure 1.2**) of chemical research. Catenanes and rotaxanes are a subset of a family of molecules known[13–17] as Mechanically Interlocked Molecules, or MIMs, for short. Not all MIMs necessarily possess mechanical bonds because entanglements are possible in molecules that lack distinguishable component parts, such as molecular knots. Another intersecting field of research is chemical topology,[18–25] which deals with the aspects of structure that are preserved throughout any process of continuous deformation—i.e., stretching, compressing, or bending of bonds without allowing them to cross or break. Discussions of chemical topology are featured in **Sections 1.2.1** and **1.3.2**, as well as the **Chapter 2** Introduction, **Section 4.1**, and **Section 5.2.4**. Some MIMs, such as knots and catenanes, fall under the umbrella of chemical topology, while other MIMs, such as rotaxanes and suitanes, are considered topologically trivial because their component parts may be separated by continuous deformation. The identification of rotaxanes as molecules with topological bonds is a common misnomer in the literature. Another common misnomer identifies catenanes and rotaxanes as supramolecular entities, or supermolecules. We do not consider most mechanomolecules to be supermolecules, at least when

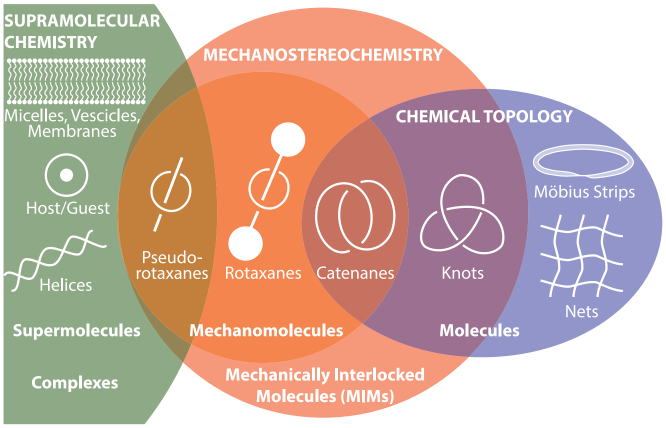


Figure 1.2 A Venn diagram illustrating how different types of molecular species fit into the intersecting fields of supramolecular chemistry, mechanostereochemistry, and chemical topology.

[A] The term 'emergent' is muddled with ambiguity in the literature. In our view, new properties that arise as a result of an increase in the complexity of a system may be considered emergent. See **Section 1.3.5**.

the mechanical bond is sealed by strong covalent bonds, because the component parts cannot dissociate and exchange as supramolecular complexes do. In the case of complexes known[26] as pseudorotaxanes, which lack stoppers that are sufficiently bulky to prevent the dissociation of component parts, the boundary between mechanomolecules and supermolecules is blurred. This grey area in between the supramolecular and the 'mechanomolecular' is discussed in **Section 3.1.1**.

It is clear to us that the boundaries and relationships between mechanical and chemical bonds are not always straightforward. Is the mechanical bond a chemical bond? Yes and no.

Yes, because…	**No**, because…
…mechanically interlocked molecular entities are engaged in a situation that fully satisfies Pauling's definition (also the IUPAC Gold Book definition[27]) of a chemical bond.	…the mechanical bond can exist between many types of objects other than discrete molecular entities – it is much more than a chemical bond!
…the mechanical bond can be identified in molecules.	…a mechanical bond cannot exist between atoms.
…like chemical bonds, mechanical bonds carry an entropic penalty[B].	…unlike chemical bonds, there is no enthalpy of a mechanical bond[B].

Table 1.1 Different types of bonds and typical ranges for their associated energies.

Bond Type	**Energy Range[a] / kcal·mol^{-1}**
'*Weak' Chemical Bonds – Intermolecular & van der Waals*	
Dispersion Forces	≤1
Dipole–Dipole Interactions	0.5–2
Hydrogen Bonds	1–10
Halogen Bonds	1–40
Ion-Pairing[b]	2–50
Strong Chemical Bonds – Covalent and Ionic	
Coordinate/Dative Bonds (M–X)	10–100
Organic Covalent Bonds (C–X)	60–100
Ionic Lattice[b]	250–4000
Mechanical Bond	≈ weakest participating chemical bond[c]

[a] Energy ranges are estimated on an atom-to-atom basis. Many van der Waals interactions, especially dispersion forces, are typically multivalent, increasing in strength with increasing molecular size.

[b] Ionic lattice energies reflect crystallization from the gas phase, while ion-pairing reflects the formation of contact, solvent-shared, or solvent-separated ion pairs in solution. The much weaker ion-pair interaction depends heavily on the dielectric constant, according to Debye-Hückel theory.

[c] The strength of a mechanical bond is approximately equal to, or greater than, the weakest chemical bond that 'participates' such that its cleavage would allow component parts to dissociate.

Mechanical bonds seem to be in a grey area when it comes to chemical bonding, arising from the fact that they are indeed stable bonds in molecules, yet maintained only by the physical forces that prevent bonds from passing through one another. A mechanical bond is therefore approximately as strong as the weakest participating chemical bond (**Table 1.1**) in the constitution of its component parts. A 'participating' chemical bond is one that is critical to maintaining a mechanical bond—i.e., cleavage of a participating chemical bond would cause the mechanical bond to break. The vast majority of synthetic mechanical bonds in the molecular world are sealed by covalent or coordinate (dative) bonds, owing to their high thermodynamic and kinetic stabilities. We reiterate that most rotaxanes and catenanes are better described as *molecules*, rather than *supermolecules*, when their molecular pieces cannot be separated without breaking strong chemical bonds. There are examples of mechanical bonds, however, that rely on weaker interactions, such as hydrogen bonding in biomolecular (**Section 2.3.12**) assemblies.

One can understand a lot about the chemistry of mechanical bonds by means of analogy with the chemistry of covalent bonds. In order to facilitate our discussion of molecules with mechanical bonds, it will be convenient to introduce terminology as a matter of comparison with counterpart terms involving chemical bonds—these definitions come either from our Glossary or the IUPAC Gold Book.[27] For example, since stereochemistry encompasses chemical bonding at all levels of structure in both dynamic and static contexts, we advocate the term 'mechanostereochemistry' for describing all aspects of mechanical bonding in molecules.[16]

Stereochemistry[27] – the study of the relative spatial arrangements of atoms that form the structure of molecules and their manipulation.

Mechanostereochemistry[16] – the stereochemistry of molecules with mechanical bonds.

Generalizing beyond chemistry the concept of the mechanical bond as a situation in which the physical separation of two objects is obstructed by an entanglement in space, it becomes apparent that life as we know it is deeply

---

[B] Any enthalpic gains or losses associated with breaking or making mechanical bonds are attributable to covalent, dative, and/or noncovalent (electrostatic) interactions between atoms that are gained or lost as a consequence of mechanical bonding, rather than to the mechanical bond itself. Since the mechanical bond limits the translational and conformational freedom of its component parts, however, the corresponding entropic penalty can be attributed directly to the mechanical bond.

entrenched in mechanical bonds. The prototypical mechanical bond is that of a chain link: two rings interlocked such that they cannot be separated, each of them able to move independently within the constraints of the other. This (constrained) freedom of motion is one of the enduring attributes of the mechanical bond. The ability of mechanically linked objects to move relative to one another serves as the basis for most machinery—take the spinning wheels of a bicycle as an archetypal example. Note, however, that objects can share a mechanical bond without freedom of motion as well. For example, the mechanically bonded bolt that constrains a street sign to a post is intended to prevent motion. The advantage of a mechanical bond in this context is modularity, since it is easier to change a sign that is screwed into a post than one that is welded onto it. Thus, the mechanical bond is conceptually different from a seal involving welding or glue, for example, or from containment,[28–31] where one object is encased completely within another.[C]

It is clear to us that the mechanical bond is everywhere and its role in our everyday lives is indispensable. Therefore, this book begins with an examination (**Section 1.1**) of the mechanical bond in contexts other than chemistry. Later, we survey how molecules with mechanical bonds, which cannot be seen by the naked eye, are represented (**Section 1.2**) in the scientific literature in the form of images. We give pride of place in this Chapter to a topic that is rarely covered in formal chemical literature—namely, beauty. There is a deep connection between chemistry and art, rendering both disciplines fair game for a branch of philosophy known as aesthetics—a field that deals with art, beauty, and taste. We are committed to the notion that the mechanical bond is a thing of immense beauty in addition to its all-pervasive functional diversity. Following an introduction to the mechanical bond across a variety of different settings, communities, and length scales, we will preview the range of this book's contents in the context of molecular aesthetics (**Section 1.3**), before finally offering a perspective (**Section 1.4**) on the evolution of mechanostereochemistry. The discussion in **Sections 1.1–1.3**, which is driven by the concept of beauty in chemistry,[32] is expanded upon and borrowed from, in part, our review[33] of mechanical bonds in the context of beauty, with permission from the publisher (copyright 2012 Springer-Verlag).

1.1 The Ubiquity of the Mechanical Bond

The unique connection between chemistry and art has been recognized since at least 1860, when French chemist Marcellin Berthelot wrote, "*La Chimie crée son objet. Cette faculté créatrice semblable à celle de l'art lui-même, la distingue essentiellement des sciences naturelles et historiques,*" which translates in English to:

> *"Chemistry creates its own object. This creative quality, resembling that of art itself, distinguishes it essentially from natural and historical sciences."*

Berthelot recognized that the creative component of chemistry is not only unlike other sciences, but also similar to that of art. But what is art? To attempt to define it is to enter a realm that chemists, naïve as we are in these matters, had best avoid. We note, nevertheless, that the former Wikipedia[34] definition, "the process or product of deliberately arranging elements in a way to affect the senses or emotions," can be truncated into a reasonably suitable definition for (synthetic) chemistry—the process or product of deliberately arranging elements. The essence of creativity is indeed inherent to both disciplines.

The similarities and differences between art and science have been long deliberated.[35] Foremost among these deliberations is the issue of beauty. Rather than attempting to summarize or evaluate the numerous angles on the relationship between science and art, let us simply draw attention to the philosophy that has profoundly shaped modern perceptions on the subject of beauty in science, which stems from the notion that science and art are different forms of symbolic activities. Werner Heisenberg, a Nobel Prize winner in Physics and proponent of this perspective, defined[36] beauty as "the proper conformity of the parts to one another and to the whole." He crowned mathematical beauty—unification through abstraction—as the prevailing flavor of beauty in science. This ideal is noble but it is unfortunate that it has reigned so exclusively; others have noted[37] the irony that chemistry, for all its sensory content—its colors, odors, textures—is much less associated with beauty than mathematical physics. Whence the beauty of empirical science? As Roald Hoffman and Pierre Laszlo[38] have commented, "*our discipline is a curious mix of empirical observation and abstract reasoning. This is not unlike music—but it parts chemistry from the pure rigor of mathematics.*" We hope this Chapter will garner support for the growing initiative[39–44] to widen aesthetic considerations in chemistry, even as a basis for research.[45]

A discussion of beauty in chemistry might consider the beauty of materials[46]—the color and texture of a pigment, or the shape and clarity of a crystal, for example—or refer to the molecules themselves. Both have an obvious connection with the visual arts; chemistry is largely responsible for the ever-growing diversity of materials artists manipulate, but there is beauty in the structures of molecules as well. In this Chapter, we will leave materials aside and focus on the beauty of molecular structures, or more accurately their representations in which chemists engage with pride and prejudice. The topic of molecular beauty is largely eschewed from the literature, residing instead primarily in the informal discussions, meetings, and conferences between colleagues. Nobel laureate Roald Hoffman,[47] who

---

[C] Examples of containment in the molecular world include carceplexes,[28] endohedral fullerenes[29] and molecular peapods,[30] and many kinds of self-assembled 'molecular flasks' and cages.[31] Our perspective is that these types of molecules and assemblies are fundamentally different than MIMs because they involve complete enclosure rather than entanglement.

recognized that chemistry's rich and visual symbolic language is an important contributor to beauty in science, spearheaded[48–51] a more formal discussion in 1988.

The roots of molecular beauty can be traced back to the Platonic tradition. To Plato, "the most beautiful bodies in the whole realm of bodies" were the tiny polyhedra, now deemed the Platonic solids, which he proposed comprise the universe: the four elements—earth (cube), fire (tetrahedron), air (octahedron), water (icosahedron)—and the ether (dodecahedron) (**Figure 1.3**). Joachim Schummer, who has written[41] extensively on chemical aesthetics, reflects:

> *"Modern chemistry is exactly the art that provides creative access to what Plato considered the realm of the most beautiful bodies. Therefore, it is no surprise that chemists put their creative activity also in the service of beauty."*

Of course, the 'realm of the most beautiful bodies' is too small to see, but there is something charming about the way a molecule is physically crafted, like sculpture, through diligent labor, yet is only perceived mentally, like poetical imagery, with the aid of symbols. Here, we engage these symbols—our imperfect and incomplete representations of molecules—as artwork. We will not hazard straying into the complex territory of contention on this issue, which has been discussed[41] superbly elsewhere, for we understand beauty as that which provides one with a sense of personal pleasure more than in the context of rigorous aesthetic formalisms. We take for granted that beauty has a place in chemistry because we know, as such, that chemists are passionate in their vocation and take great pleasure in their work. The same may be said of people in countless other occupations, from farmers to cyber hackers, who also undoubtedly find beauty in their work. Moreover, despite a lack of formal aesthetic training among most chemists—and the longstanding stigma associated with discussing beauty in the scientific literature—at least 2% of chemistry papers mention[52] aesthetic values as a justification for studying a molecule. Classic examples include a variety of synthetic Platonic and Archimedean objects[53] such as cubane,[54] dodecahedrane,[55,56] buckminsterfullerene,[57] and many metal-ligand coordination complexes and cages[58,59] that have been lauded[42] for their symmetry, simplicity, uniformity, and harmony—"simply beautiful and beautifully simple." On the other hand, natural products and their corresponding organic transformations have been admired[60–62] for the beauty in their elegance, complexity, and sophistication. Woodward, arguably the most preeminent organic chemist of the 20th century, recognized the art of organic synthesis—an art acknowledged even by the Nobel Prize committee—as an act of beauty.[63]

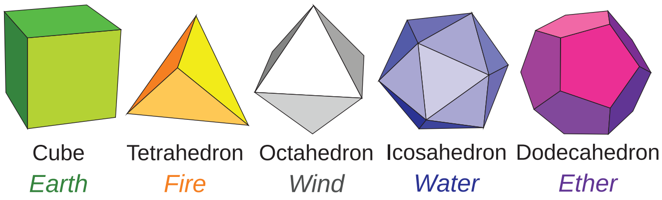


Figure 1.3 The Platonic solids were the most beautiful bodies according to Plato. Like molecules, these imperceptibly small objects were thought to compose the physical world.

Molecular nanotechnology has uncovered yet another way to address beauty in chemistry: miniaturization. Chemists now frequently "miniaturize" everyday objects by constructing them, to varying and sometimes quite liberal degrees of approximation, using molecules as their building blocks. Our affinity for miniaturization is a consequence of (i) the development of supramolecular chemistry,[64] which has made this kind of miniaturization possible, and (ii) the emergence of a paradigm shift in molecular representations, in which molecules are portrayed more ambiguously so as to resemble their macroscopic analogues. In other words, the vision of a miniaturized world has been catalyzed in part by the beautiful new ways of representing molecules, which deliberately blur the lines between the molecular world and the macroscopic one. We have referred to these graphical representations as cartoons, as well as illustrations, and—in this Chapter—art. In this regard, mechanically interlocked molecules are of particular interest because they have played a central role in molecular nanotechnology and the aforementioned paradigm shift to more artistically disposed figures and schemes in the literature. Moreover, the mechanical bond is ubiquitous in the macroscopic world, but has been, until relatively recently, challenging to introduce into molecules.

There is no question that beauty is subjective—even if chemistry is not *about* beauty, few who practice it would argue that it is devoid of beauty. In this Section, we will use images to highlight, support, and substantiate claims on the beauty of mechanostereochemistry. Insofar as beauty is derived from our surroundings, the mechanical bond cannot be ignored. It is applied and admired in society, art, and Nature alike, and its beauty is held as both an ancient and modern sentiment. The ubiquity of the mechanical bond is apparent in everyday life (**Section 1.1.3**) because of modern tools and machinery, many of which we consider beautiful—think of a sporty car or a delicate Rube Goldberg (Heath Robinson) machine. Likewise, interlocked rings can be found in thousands of works of art (**Section 1.1.2**) dating through antiquity. Perhaps most surprising to the casual reader will be the predominance of mechanical bonds in Nature (**Section 1.1.1**), even within the cells of our own bodies.

1.1.1 Mechanical Bonds in Nature

Perhaps the most incontrovertible source from which we derive beauty is Nature. In terms of molecular beauty, Nature has perfected its brand of chemistry over billions of years and is an endless source of inspiration for chemists. For all our efforts, the number of chemicals and reactions we have discovered and created seem diminished by the bewildering complexity and sheer abundance of those present in Nature. In particular, the diversity and intricacy of

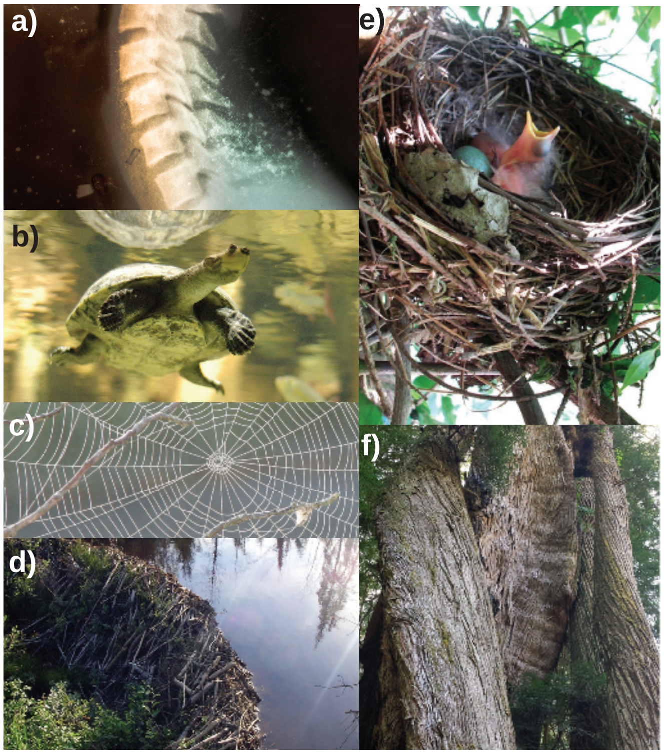


Figure 1.4 Examples of mechanical bonds in Nature. (a) X-Ray image of human vertebrae, which protect the spinal cord with rotaxane-like mechanical bonds. (b) A turtle forms a type of mechanical bond with its protective shell that is known in the molecular world as a suitane. (c) The mechanically criss-crossed network of a spider's web is what traps the spider's prey. (d) The structural integrity of a beaver dam is attributable, in large part, to a mechanically interlocked network of branches and logs. Photo: Lars Lindahl. (e) The mechanically bonded twigs which support the structure of a bird's nest provide a safe space for eggs and hatchlings. (f) If one of the entangled trunks of California Red-wood National Park's corkscrew trees were to be uprooted, the mechanical bond would prevent it from falling. Photo: Paul Herrig

systems and cycles in the chemistry of life processes are still far beyond our total comprehension. Even so, in a world where structure and function are so intrinsically linked, it should come as no surprise that Nature started dabbling with mechanical bonds long before humans came onto the scene. Our very bones form mechanical bonds with other tissues and organs, such as the rotaxane-like mammalian spine (**Figure 1.4a**). Just as the vertebrae offer protection for the fragile spinal cord, the suitane-like[8] mechanical bond of a turtle's shell (**Figure 1.4b**) helps protect the turtle's body. A number of animals rely on mechanical bonds for survival—spiders (**Figure 1.4c**) employ mechanical bonds to capture prey, while beavers (**Figure 1.4d**) and birds (**Figure 1.4e**) use them to build homes. Even trees (**Figure 1.4f**) occasionally tangle themselves into mechanically interlocked situations.

Although mechanical bonds can be identified in Nature across the macroscale, mechanical bonds are being made and broken incessantly within the microscopic world of cells. Contrary to modern industry, where technology utilizes the mechanical bond far more ubiquitously on the macroscale than on the nanoscale, Nature depends more vitally on mechanical interlocking at the molecular level. DNA is foremost among the players in biological MIMs. DNA catenanes[65] and knots[66] are intermediate structures in basic biological processes such as DNA recombination and replication, as mediated by various enzymes.[67] Many natural topological DNA structures have now been imaged[68] quite beautifully by electron microscopy (**Figure 1.5a**).

Not only does DNA form itself into catenated and knotted structures, it also rotaxanates itself with pseudo-macrocyclic enzymes.[69,70] λ-Exonuclease is an enzyme that participates (**Figure 1.5b**) in DNA replication and repair by encircling DNA fully as it sequentially hydrolyzes nucleotides—a biomolecular rotaxane! T4 DNA Polymerase holoenzyme[71] is an analogous example; its protein subunits clamp around a DNA strand to form a toroid in what chemists of the mechanical bond would call a 'clipping' process. It should be noted that chemists have been able to mimic this concept of a mechanically linked catalyst on a polymer[72–74] using traditional organic catalytic reactions. See **Section 6.15.3.1**.

DNA is not the only entity that can serve as component of biological MIMs—a continually growing number of mechanically interlocked protein structures have also been discovered –

- The extraordinary interlocked structure[75] of the bacteriophage HK97 capsid involves an icosahedral shell of topologically linked protein macrocycles (**Figure 1.5c**) which resemble the netting of chainmail. The 420 isopeptide crosslinks of this topological net strengthen[76] the mechanical properties of the capsid and may prevent it from bursting prematurely under the very high internal pressure (up to 40 atm) of its densely packed DNA cargo.
- *E. coli* Class Ia ribonuclease reductase[77] is another enzyme which forms a ring assembly that was found to be concatenated in the crystal.
- An enzyme known as CS$_2$ hydrolase, which converts carbon disulfide rapidly into carbon dioxide and hydrogen sulfide, has evolved in extremophilic life-forms—namely, acid-loving (acidophilic) and heat-loving (thermophilic) archaea living in harsh volcanic areas. The protein monomers of CS$_2$ hydrolase assemble into two different forms—one of them (**Figure 1.5d**) is a hexadecamer in which two octameric protein macrorings are catenated, while the other form is a non-catenated square-shaped octameric ring.[78,79] Measurements of the enzyme kinetics suggest that the hexadecameric catenane is more active than the octameric ring, most likely because it can accommodate a higher density of active sites per assembly.[80]
- The crystal structure (**Figure 1.5e**) of a C168S mutant of a typical Cys-2 peroxiredoxin III enzyme from bovine mitochondria was discovered[81] to be a [2]catenane comprising two interlocked dodecameric protein toroids. The protein-protein contacts within each ring are driven by

hydrophobic forces, while the ring-ring protein contacts arise from dipolar interactions.
- RecR, a protein involved in DNA repair in prokaryotes, assembles into a tetrameric protein complex with a central hole of over 3 nm in diameter. Two of these tetramers are concatenated in the crystal,[82] which implies that the tetramer can be easily opened and closed in the cell, since DNA occupies this cavity during repair.[83]
- Extremophiles that are adapted to survive in harsh conditions such as highly acidic environments and temperatures exceeding 100 °C must have evolved special strategies to prevent their cellular proteins from denaturation. Another thermophilic archaeon known as Pyrobaculum aerophilum relies on topologically linked proteins (**Figure 1.5f**) to stabilize its citrate synthase enzyme. The enzyme exists as a homodimer in which intramolecular disulfide bonds create a topological link—i.e., a catenane—which renders the monomers inseparable, imparting the protein with extra thermal stability.[84]
- During gene replication, the separation of sister chromatids (two identical copies of a chromosome) is regulated by the protein cohesin, which has been found[85] to entrap circular DNA loops in topologically catenated structures using chemical crosslinks, which influence the kinetics of cell division processes.
- Various proteins are recruited to the surface of mitochondria to form a nanotube around the entire organelle. The mechanical bond between this nanotube and the mitochondria is responsible for mitochondrial replication because it provides the contractile force for membrane scission.[86,87] The phenomenon of a ring contracting as it encircles a rod in order to sever it is not unlike certain digestive processes or a common method of bovine castration! It is intriguing that this mechanical pinching process happens at the scale of intracellular processes as well.

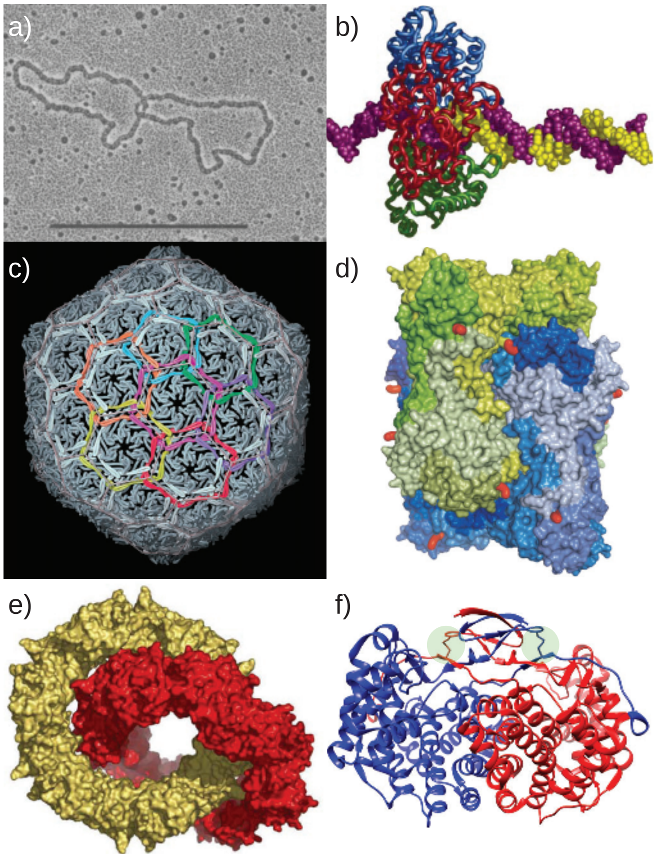


Figure 1.5 Examples of mechanical bonds in molecular biology. (a) Electron micrograph of a DNA catenane.[68] Scale bar: 1 μm. (b) The crystal structure of λ-exonuclease, paired with a model depicting how it encircles DNA while catalyzing its hydrolysis.[69] (c) 'Protein chainmail': The crystal structure of the bacteriophage HK97 capsid, highlighting catenated protein macrocycles.[75] (d) The crystal structure of the catenated enzyme CS_2 hydrolase.[80] (e) The crystal structure of the catenated peroxiredoxin III enzyme C168S mutant.[81] (f) Disulfide crosslinks (green circles) stabilize the citrate synthase enzyme of Pyrobaculum aerophilum.[84] (a)–(e) reproduced with permission from refs. 68 (copyright 1980 Elsevier), 69 (copyright 2003 Oxford Univesity Press), 75 (copyright 2000 AAAS), 80 (copyright 2014 Royal Society of Chemistry), 81 (Copyright 2005 Elsevier)

Although we feel that the beauty of this biomolecular machinery speaks for itself, Nature does not create art deliberately—the mechanical bond plays a vital functional role in these systems, which ranges from added stability to precise spatial organization of proteins and nucleic acids. It is apparent that our achievements as chemists in harnessing the chemistry of mechanical bonds have been surpassed as usual by Nature, who executes her particular brand of chemistry with a level of elegance, complexity, and beauty that we can only hold in awe, yet will surely use as a source of inspiration for many years to come.

1.1.2 Mechanical Bonds in Art

If anything can speak to the aesthetics of the mechanical bond, it is the art that portrays it. Nowhere is the beauty of the mechanical bond more validated than in the world of art—indeed, artists have been drawing, painting, carving, and sculpting mechanical bonds for thousands of years!

The mechanical bond may be celebrated (**Figure 1.6–1.7**) with many art forms, including (but not limited to) prints and carvings (**Figure 1.6c–d, 1.7a**), sculpture (**Figure 1.7b–c**), textiles (**Figure 1.7d–e**), stained glass (**Figure 1.7f**), origami (**Figure 1.7g**), body art (**Figure 1.7h**), mosaics (**Figure 1.7i**), architecture (**Figure 1.7j**), and even performance art (**Figure 1.7k**).

Borromean rings, such as those portrayed in **Figure 1.6** and **Figure 1.7e-f**, are a class of mechanically interlocked objects that deserve special attention in this Section on account of their prevalence in art, spanning across many cultures and thousands of years.[88] Their name originates from the aristocratic Borromeo family of what is now northern Italy, on whose crest (**Figure 1.6b**) and estate edifices the rings appear frequently. They have been associated with the Borromeo family from at least the 15th century, though recorded use of the symbols date back to at least the 13th century in Christian iconography (**Figure 1.6c**), the 12th century in Japanese emblems, and the 9th century in

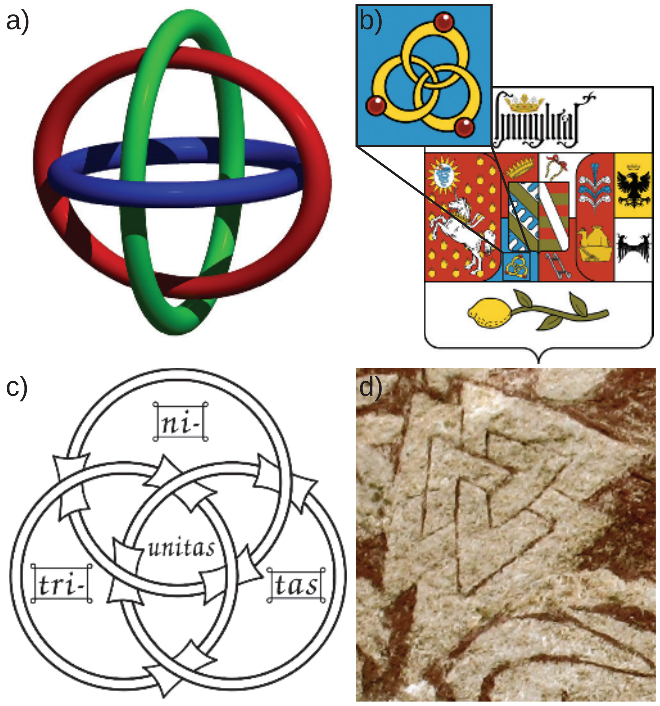


Figure 1.6 The Borromean Rings (BRs). (a) An orthogonal perspective of BRs visualizes the three inseparable rings, where breaking any one ring unlinks the other rings. (b) BRs as they appear on the Borromeo family crest. (c) The use of BRs to symbolize the Holy Trinity date back to the 13th century. (d) The Valknot is a Borromean Viking symbol found on ancient stone carvings from as early as the 9th century.

Viking symbols (**Figure 1.6d**), making them a remarkably universal icon.[D] Topologically speaking, the three rings are interlocked in such a way that breaking any one ring results in the dissociation of the other two intact rings (**Figure 1.6a**). This mutual dependence is what has made the rings such a powerful symbol for threefold unification, having been adopted to symbolize triads including Christianity's Holy Trinity (father, son, and holy spirit), Shintoism's three realms (heaven, earth, underworld), and even an advertising campaign (purity, body, flavor) for Ballantine Brewery's beer. The richness of symbolism, as well as the accompanying centuries of artwork associated with Borromean Rings, leaves little question as to their beauty. Molecular Borromean rings[89] are discussed in **Section 4.1.1.3**.

Solomon Knots have a similar history of predominance in art and history. The Solomon Knot is more accurately described as a link, since it consists of two rings that are doubly interlocked. The structure of the link, which has no obvious beginning or end, has made it a remarkably adaptable icon. It has been an important symbol in many cultures throughout history, including parts of Judaism, Christianity, and Islam, as well as with the Yoruba, Akan, and Kuba people of Africa.[90] The mosaic (**Figure 1.7i**) from the Byzantine Basilica beneath the Church of the Nativity in Bethlehem, Israel contains several examples of ancient artwork portraying the Solomon Knot. As the seal of the Biblical King Solomon, this symbol has represented wisdom and knowledge. In other contexts, it has signified eternity, beauty, and royalty. From ancient Roman mosaics to Celtic carvings to African headdresses to Middle Eastern relics and stained glass church windows, the Solomon Knot is a powerful symbol of beauty in art, religion, and culture. Seeing Solomon's Knot by Lois Rose Rose[91] is a recent and well-crafted exploration of the artwork of Solomon's Knot across time and cultures. Molecular Solomon Knots are discussed in **Section 4.1.1.1**.

Many artists employ links as symbols of unification, since their mechanical bonds bring together two or more otherwise unconnected objects. Particularly classic examples are the *Bonds of Friendship* statues (**Figure 1.7c**) by John Robinson in the sister cities of Sydney, Australia and Portsmouth, England depicting two linked rings,[92] as well as Ryoji Goto's 1978 *Intersecting Space Construction* (**Figure 1.7b**) symbolizing the beauty of human connections. One of the most famous artists to glorify the mechanical bond was M.C. Escher, whose math and science-based art has long encouraged discourse on the topic of beauty in science. His final print, *Snakes* (**Figure 1.7a**), portrays an array of interlocking rings that extends infinitely inwards, inhabited by a few mechanically interlocked serpents. We find this piece beautiful, not only for its rotational symmetry and mechanical bonds, but also because it points to the concept of infinitesimal smallness—foreshadowing the days when networks of interlocked rings almost too small to imagine are a reality—see **Section 4.1.3.5**. Minsuk Cho's Ring Dome Pavilion (**Figure 1.7j**) marks what must be one of the largest (and perhaps only) architectural structures comprising exclusively mechanically interlocked rings, while the attractive structure of Daniel Kwan's *Ten Interlocking Triangular Prisms* (**Figure 1.7g**) highlights the challenging complexity that can be attained among objects with mechanical bonds.

The mechanical bond is a focal point for human expression. With all sorts of different art forms celebrating the mechanical bond and the corresponding meaningful concepts and feelings which it symbolizes, it is not difficult to engender an eagerness to celebrate the beauty of the mechanical bond at the molecular level too.

1.1.3 Mechanical Bonds in Everyday Life

One cannot navigate the modern world without regularly encountering the mechanical bond. We typically take it for granted. So pervasive are interlocked structures in all things man-made, if we acknowledged consciously every mechanical bond we encountered, we might scarcely be able to accommodate any other mental processes! Here, we simply point (**Figure 1.8**) to fashion and technology as illustrative reminders of its omnipresence in society.

We all wear the mechanical bond day in and day out; those with body piercings even use it as a permanent

---

[D] For many more images of Borromean artwork, see ref. 88.

Figure 1.7 Examples of mechanical bonds in art. (a) In M.C. Escher's woodblock print, *Snakes*, a net of multiply interlocked rings extends infinitely inwards. © 2015 The M.C. Escher Company, The Netherlands. All rights reserved. www.mcescher.com (b) The *Intersecting Space Construction* statue at Hakone Open-Air Museum, Japan by Ryoji Goto presents an interlocked network of connected bodies. (c) Two copies of the *Bonds of Friendship* sculpture by John Robinson are located in Portsmouth, England and Sydney, Australia, commemorating a centuries-old relationship between these two sister cities. (d) Weaving is an art form that depends on mechanical bonds between enmeshed threads or reeds. (e) Borromean rings are portrayed in the textile artwork of Kirsten Griffiths. (f) Three interlocking rings are portrayed in the stained glass artwork within the Catedral de São Pedro de Alcântra in Petrópolis, Rio de Janeiro, Brazil. (g) Ten Interlocking Prisms origami design by Daniel Kwan (photo: Jakub Solovsk). (h) Permanent and semi-permanent mechanical bonds with the flesh represent a form of body art known as piercing. The earring ornament in this photo also contains hundreds of mechanical bonds comprising interlocked chains and beads. (i) Ancient mosaic of catenated objects and Solomon Knots in the Byzantine Basilica, Israel. (j) The Ring Dome Pavilion by architect Minsuk Cho is composed entirely of mechanically interlocked plastic rings—1500 hula hoops and 12000 zip-ties. Photo: Rory Hyde. (k) Performance arts such as trapeze also rely on mechanical bonds, such as transient ones between bodies in motion, as well as those which comprise the swing and its supporting structure.

decoration. This practice is not exclusive to Western society; note the mechanically bound objects around the headdress, ears, mouth, and neck of the Mursi woman of southern Ethiopia in **Figure 1.8a**, and the neck-extending rings of Northern Thailand's Kayan Lahwi woman (**Figure 1.8b**). These are perhaps extreme examples, but we all use the mechanical bond to a tremendous extent in the decoration of our bodies and clothing, from both a practical standpoint and an aesthetic one. Rings, necklaces, bracelets, belts, and even our shirts and trousers all form mechanical bonds with our bodies and with themselves. For example, compare a necklace with a rotaxane; the necklace is the ring, while the head, neck, and shoulders comprise the dumbbell. Meanwhile, the necklace itself is composed of mechanical bonds if it is beaded or has a clasp. Consider getting dressed in the morning—if you tie your shoes, strap a belt around your waist, button up your shirt, and clasp on a watch or some jewelry, you have already formed dozens of mechanical bonds around your body before breakfast!

The mechanical bond and technology have gone hand-in-hand since the advent of machinery. Indeed, many of the world's simplest and oldest machines, a wheel-and-axle or a pulley (**Figure 1.8j**), for example, are based on the mechanical bond. Interlocking parts have been especially important in transportation—imagine trying to sail without knots and pulleys or drive without wheels! The mechanical bond also appeared as early as 2700 BCE in the world's first calculator—the abacus (**Figure 1.8f**). Just as we find it near the beginning of human history, most of us meet the mechanical bond near the beginning of our lives, since it is essential to many toys such as rattles or the bead maze in **Figure 1.8g**.

It is obvious by now that few modern machines would be capable of existing without some kind of mechanical bond, whether it is the washer around a screw or the disc in a hard drive. Even more examples are given in **Figure 1.8**. Indeed, with every draw of a curtain (**Figure 1.8c**), turn of a doorknob (**Figure 1.8d**), or flip of a switch, the mechanical bond is at our service. Between fashion and technology, societies are irrevocably dependent on the mechanical bond. With mechanical bonds being such a necessary component in machinery, it is only fitting that they also represent a cornerstone of molecular machines—see **Sections 1.3.6** and **6.15**.

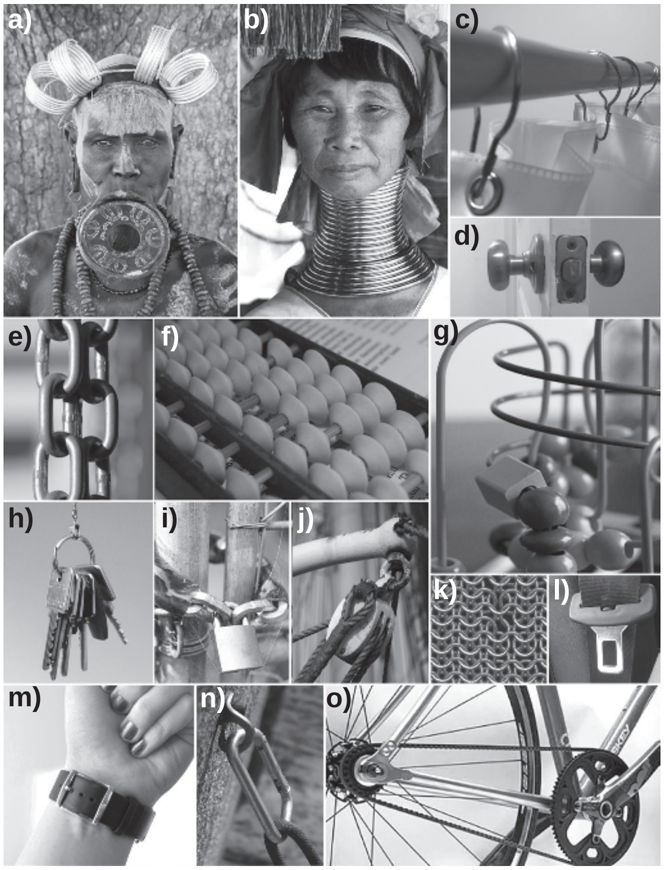


Figure 1.8 Examples of mechanical bonds in everyday life. (a) Decorative mechanical bonds of a Mursi woman. (b) A Khayan Lahwi woman with mechanically interlocked neck extenders. (c) A shower curtain. (d) A doorknob has the essence of the 'dumbbell' portion of a rotaxane, where the door is the ring! (e) A chain link. (f) Mechanically interlocked beads underpin the function of an abacus, as well as (g) a children's bead maze. (h) Keys catenated with a keychain ring. (i) A lock. (j) A pulley on a sailship. (k) Chainmail. (l) A seatbelt buckle. (m) A wristwatch makes a rotaxane with the hand and body as stoppers, while its clasp also relies on a mechanical bond to keep it fastened. (n) The mechanical bond of a carabiner helps climbers cling to rock faces. (o) Hundreds of mechanical bonds exist in the chain, crank, and wheels of a bicycle.

1.2 Representing Molecular Mechanical Bonds

Having established a background of beauty for the mechanical bond in art, nature, and society, we now consider beauty as the mechanical bond is miniaturized beyond our ability to perceive it directly. Since mechanomolecules are not available to our senses, their beauty is more associated with the wide variety of modes we use to represent them—e.g., symbols, drawings, models, and cartoons. Just as chemical signs and symbols have evolved over the centuries from primitive beginnings in alchemy,[93–95] the portrayal of MIMs have also evolved, even playing a vital role in modern notions of molecular representation in chemistry as a whole. In particular, as molecular structures have grown larger and more complex, it has become useful to represent them in ways that eliminate finer details, such as the bond order, atomic composition, and so on, especially when trying to convey a message that has more to do with self-assembly, intra- and intermolecular interactions, or secondary structure. Because it represents chemistry "beyond the molecule," supramolecular chemistry[64] has played a major role in this transition, but so has the chemistry of the mechanical bond, or as we call it, mechanostereochemistry.[16]

All sorts of everyday objects have been reconstructed as molecules by virtue of template-directed synthesis, from switches and buttons to rotors and elevators. The likeness of MIMs to macroscopic objects and machines has done much to advance molecular nanotechnology and is, as we shall see, another important aspect of their beauty.

1.2.1 A Historical Perspective

It is believed[18] that mechanical bonds were discussed hypothetically prior to 1912 by Willstätter at a seminar in Zürich, but the idea did not appear in the chemical literature[96] until 1953. A significant publication by Frisch and Wasserman[18] in 1961 was the first to articulate the connection between stereochemistry and topology. In chemistry, topology is concerned with the properties of a molecule that are independent of any spatial rearrangements and bond distortions that can be performed without allowing covalent bonds to break or pass through one another. Topologically speaking, catenanes and rotaxanes are very different. The linked rings of a [2]catenane (the bracketed term represents the number of component parts in a MIM) are topologically distinct from two rings that are not interlocked, i.e., they are topological isomers. On the other hand, a [2]rotaxane is topologically identical to its component parts because the ring can be separated from the dumbbell by stretching or compressing the appropriate bonds. The concept of chemical topology,[25] which has been expounded masterfully by David Walba[20] and Christopher Hunter,[97] among others, is also highly relevant to the study of molecular knots.[98,99] See **Section 1.3.2** for a discussion of topological beauty.

Following a noteworthy attempt[100] in 1958, the first claim to a successful MIM synthesis (**Figure 1.9a**) came in 1960, when Wasserman[101] reported that cyclization of a long polymethylene C_{32}-chain esterified at both ends in the presence of a large C_{34}-cycloalkane gave very low yields of a catenane, which was isolated by chromatography two years later.[102] Small improvements in the use of this statistical method were made—most notably, Harrison and Harrison's 6% yield of a rotaxane by repeating a statistical threading reaction on a resin-bound macrocycle 70 times,[103] and Zilkha's[104,105] two-step catenane synthesis that converted a statistical [2]rotaxane directly into a [2]catenane in 3% overall yield. Meanwhile, however, Schill was developing an important approach he called directed synthesis,[106] in which macrocycles are built up around an aromatic core such that severing a few bonds at the core in the final steps affords a catenane (**Figure 1.9b**). This approach was also applied to the directed synthesis of [3]catenanes,[107–110] and [2]rotaxanes.[111–114] Schill's 1971 monograph,[115] *Catenanes, Rotaxanes, and Knots*, is an indispensable reference on the early work in the chemistry of mechanical bonds.

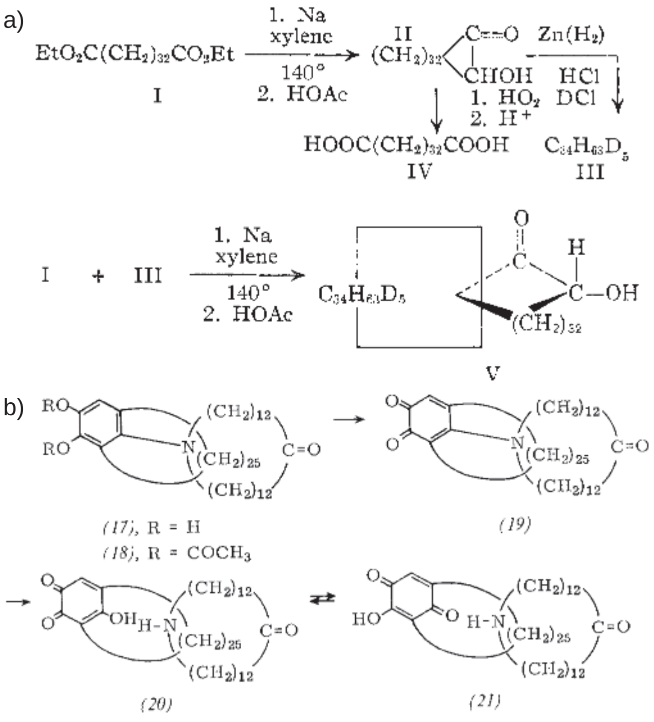


Figure 1.9 Historically significant synthetic schemes exemplifying the two applied approaches to catenane synthesis prior to 1983. (a) Wasserman's first statistical synthesis[101] relied on the macrocyclization of a linear compound (I) in the presence of a deuterated cycloalkane (III) to produce small amounts of the catenane V. (b) Schill's first example[106] of directed synthesis by covalent templation was a catenane that formed after cleaving the covalent bonds around the aromatic core in compound 16. Reproduced with permission from refs 101 (copyright 1960 American Chemical Society) and 106 (copyright 1964 Wiley-VCH)

Although the statistical and directed approaches were the only known routes to catenanes for decades, a Möbius strip approach (**Figure 1.10**) was proposed in the late 1950s independently by Frisch / Wasserman[18] and van Gulick.[116] These founders of molecular topology realized that molecules resembling Möbius strips could be cut (**Figure 1.10a**) into catenated and knotted structures, depending on the location of the cut and the number of half-twists in the strip. Walba[117–119] made this approach look more realistic in the early 1980s when he began synthesizing wreath-like macrocycles from tetrahydroxy-methylethylene (THYME) polyethers resembling a three-rung ladder. If the wreath with two half-twists could be isolated and its ladder rung crosslinks severed in half (**Figure 1.10b**), a [2]catenane would be the result. Walba synthesized[117] the zero-twist cylinder and subsequently also isolated[118] the molecular Möbius strip with one half-twist. He verified experimentally that two macrocycles are obtained by cutting the cylinder in half by ozonolysis of the THYME double bonds, while the same action on the Möbius strip leaves it in one piece as a larger macrocycle.[119] No double half-twist Möbius strip that would lead to the [2]catenane has been reported, however. See **Sections 2.1–2.2** for a more detailed discussion of these historical landmarks in mechanostereochemistry.

Sauvage's seminal publication[120] in 1983, which used a copper(I) ion to template the formation of mechanically interlocked ligands (catenates / catenands), breathed new life into the field of MIMs in relation to their accessibility, applicability, and even their structural portrayals. The early catenanes were portrayed (**Figure 1.9**) in condensed line formulas and represented for conceptual purposes by basic line drawings like those in **Figure 1.10**. The result was a picture that sufficiently communicated atomic and topological content, but bore little resemblance to what the actual structure might look like if we could set eyes on it. When Sauvage illustrated a structural diagram of his first

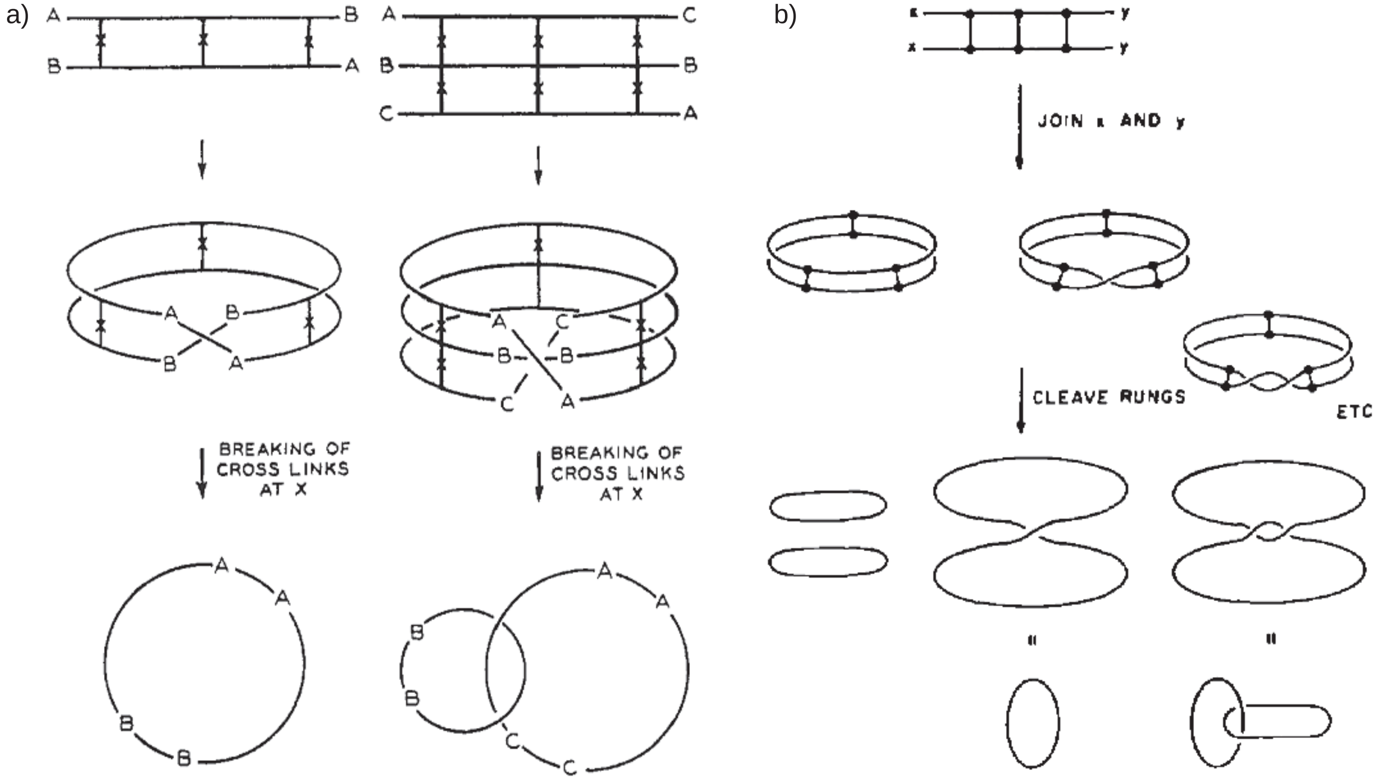


Figure 1.10 Historical strategies for synthesizing catenanes from Möbius strips. (a) Frisch and Wasserman[18] illustrated the results of cutting Möbius strips comprising grid-like bands. (b) Walba[20] outlined a strategy to produce three-rung molecules with different numbers of half-twists, where bisecting the one with two half-twists would afford a [2]catenane. Reproduced with permission from ref. 18 (copyright 1961 American Chemical Society) and ref. 20 (copyright 1985 Elsevier)

[2]catenate (**Figure 1.11**), the result was an image that was rich in beauty as well as topological and molecular information. This diagram—hand-drawn in India ink—expressed most elegantly the right information, while still hinting at the three-dimensional nature of the molecule. It has appeared[121] many times over the years in the literature from Sauvage's group and is a milestone in chemical representation. It is the gold standard of a MIM drawing, saturated with information and easy to interpret.

Sauvage's metal coordination template marked the beginning of the modern era for making mechanical bonds—namely, template-directed synthesis. Advances in this modern era have been associated with discovering new supramolecular template motifs (**Section 1.3.1**, **Section 2.3**) building new interlocked topologies and architectures (**Sections 1.3.2–1.3.3**, **Chapter 4**), discovering elegant protocols (**Section 1.3.4**, **Chapter 3**) and emergent properties (**Section 1.3.5**), crafting artificial molecular switches, machines, and motors (**Section 1.3.6**, **Chapter 6**), as well as featuring applications relying specifically on the mechanical bond. In **Sections 1.2.2–1.2.6**, we now examine how depictions of MIMs have changed alongside these many new developments of an evolutionary nature. With simple two- and three-component MIMs, it was possible to achieve Sauvage's gold standard of drawings, but as complexity and diversity grew in the field, it quickly became useful to turn to new tools that aided and abetted the depiction of MIMs in an eye-catching, easily discernable way—namely,

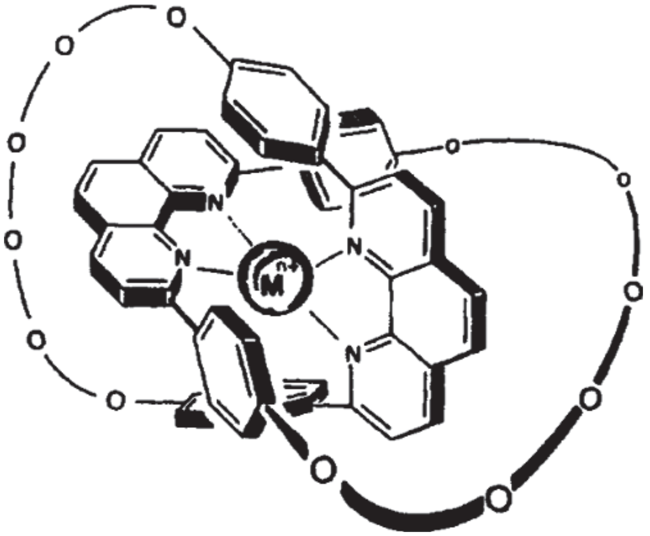


Figure 1.11 Sauvage's structural diagram of a catenand, a major breakthrough in 1983.[120] Reprinted with permission from ref. 121 (copyright 1986 American Chemical Society)

with the use of perspective stereoformulas (**Section 1.2.2**), depictions in color (**Section 1.2.3**), solid-state portrayals (**Section 1.2.4**), graphical representations (**Section 1.2.5**), and technomorphs (**Section 1.2.6**).

1.2.2 Perspective Stereoformulas

A stereoformula, also known as a projection formula, is defined in the IUPAC gold book[27] as a three-dimensional view of a molecule, either as such or in a projection. Examples of these projections include (i) Fischer, (ii) Newman, (iii) sawhorse, (iv) wedge, and (v) zig-zag projections. Sauvage's beautiful diagram (**Figure 1.11**) of his seminal [2]catenate is probably best classified as a type of projection known[27] as a perspective formula, which portrays the geometrical features of a molecule as a view from an appropriate direction. The perspective stereoformula will be our projection of choice for the majority of structural representation in this book.

In our perspective stereoformulas, we employ (**Figure 1.12**) 'full moons' to denote aromaticity in π-conjugated ring systems. This style of representation should not be mistaken for open circles, which are traditionally used to denote ring systems with precisely six π-electrons according to Clar's π-sextet rule.[122] Considering the example of anthracene, only one of Clar's π-sextets exists in any of its three major Kekulé resonance structures, meaning that the Clar structure of anthracene should be illustrated with only one open circle. By contrast, our full moons are placed in all three rings of anthracene to denote a fully unsaturated ring system without specifying a specific resonance structure. We feel that this slightly less detailed style of representation is not inappropriate in most cases involving mechanical bonds because the interactions of interest are between component parts rather than between atoms.

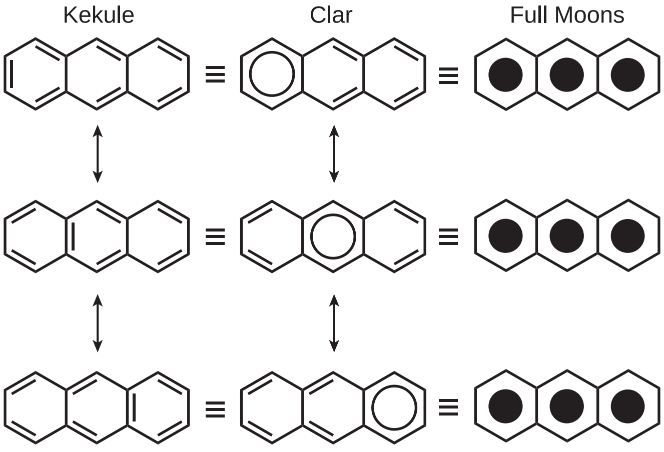


Figure 1.12 Three different representation styles for the structural formulas of aromatic molecules, exemplified by anthracene. When illustrated according to the conventions of Kekulé and Clar, the various resonance structures can be denoted unambiguously. The 'full moons' we employ in our structural formulas denote unsaturated ring systems more generally and do not offer an option for specifying resonance structures.

1.2.3 Depictions in Color

Color and MIMs go together like bread and butter. When journals began printing color in the mid-1980s, the mechanical bond made the perfect poster child because color dramatically clarified the portrayal of mechanically interlocked structures, which cannot be drawn without bonds crossing over and under one another. The first example in a primary publication[123] came in the form of the crystal structure (**Figure 1.13**) of a [3]catenate synthesized in the Sauvage laboratory. The carbon atoms in each macrocycle were uniquely colored, making each of the three component parts immediately and effortlessly discernable. This creative act represented a veritable leap forward in MIM portrayal and heralded the changes in structural depiction that would continue to evolve.

Figure 1.13 The solid-state structure of Sauvage's [3]catenate. The colors give unprecedented clarity (and beauty) to the image. Reprinted with permission from ref. 123 (copyright 1987 Wiley-VCH)

Gradually, color made its way past crystal structures and into different kinds of structural representation. Following the two initial communications[124,125] in 1988 describing in colorful detail the structure and host-guest properties of the tetracationic receptor, cyclobis(paraquat-*p*-phenylene) ($CBPQT^{4+}$), the donor-acceptor mechanomolecules based on $CBPQT^{4+}$ were among the earliest compounds to be depicted[126] in the form of colored stereoformulas (e.g., **Figure 1.14a**) and graphical representations. The π-donors were shaded in pillar-box red and the π-acceptors were shaded in royal blue, which is part of the reason[E] that $CBPQT^{4+}$ is known (**Section 2.3.3.8**) as the "little blue box".[127] This color palette has remained in use for more

---

[E] Another reason for the 'little blue box' nickname is that the compound is obtained on occasion as a blue-tinted solid. The blue color arises when a population of the viologen subunits becomes reduced to a radical cation.

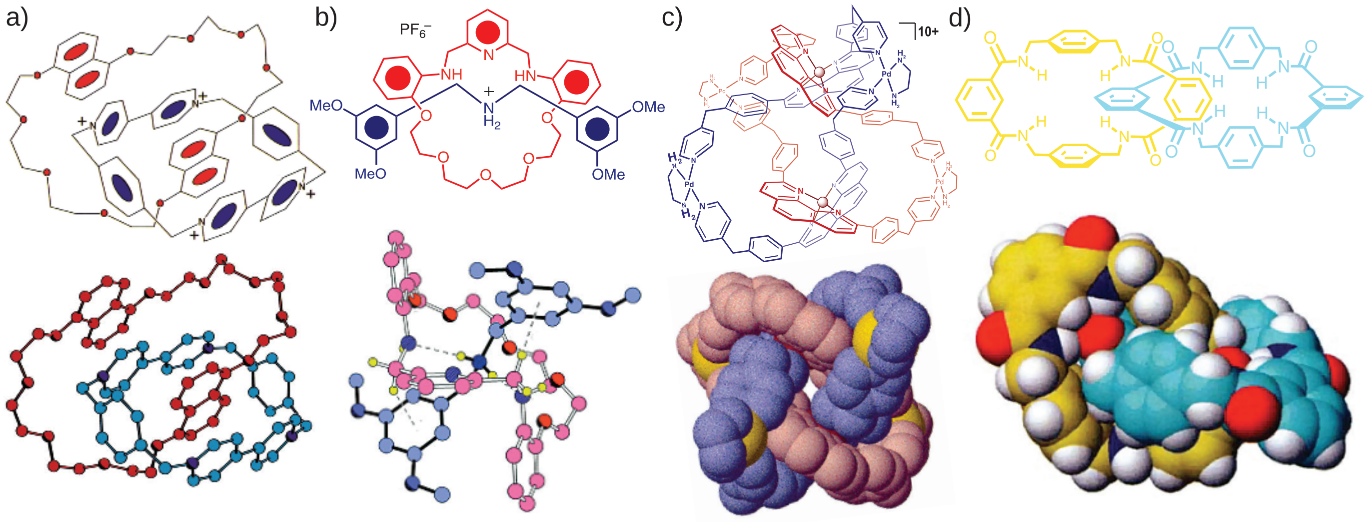


Figure 1.14 Examples of the use of color in depictions of various MIMs. Note how the colors and positions of component parts in the space-filling structures reflect those in the stereoformulas to unify different representations of (a) a donor-acceptor [2]catenane,[128] (b) a strong hydrogen-bonded [2]rotaxane,[129] (c) a transition metal-templated Solomon Knot,[130] and (d) a benzylic amide [2]catenane.[131] Reproduced with permission from refs 128 (copyright 1991 Royal Society of Chemistry), 129 (copyright 2000 Wiley-VCH), 130 (copyright 1999 Royal Society of Chemistry), and 131 (copyright 1995 Wiley-VCH)

than 25 years to the present day. Nowadays, the use of color has been embraced by many research groups and spread well beyond mechanostereochemistry—indeed, scientists in most fields of chemistry use color very effectively for the sake of bringing clarity to their representations.

Several examples of colored MIMs are shown in **Figure 1.14**. In particular these examples[128–131] illustrate how color-coding the constituents of a MIM can form a cohesive link between its various representations—two-dimensional, three-dimensional, graphical, or otherwise. The coherence and readability of these figures is what makes them beautiful, in addition to our natural proclivity for color. We will discuss shortly the use of graphical representations (cartoons) to represent MIMs, a context in which color can be employed to considerable advantage. To the scientifically minded person, the beauty that color gives to an image might have less to do with its aesthetic appeal than with the augmented intelligibility it imparts. We conclude that colors communicate molecular information more clearly, precisely, consistently, and in our minds, more beautifully as well.

1.2.4 Solid-State Portrayals

In the immortal words of John Keats, “beauty is truth, and truth beauty.” We understand truth as that which is in accordance with fact or reality. Crystal structures are arguably among the most beautiful ways to represent molecules because of their high content of truth. X-ray crystallography provides some measure of truth about structure because it provides information about the real positions of atoms in the crystal, albeit in a form that is averaged over time and space. Thus, nothing can be more accurate about the way a molecule “looks”—in the solid state at least—than an X-ray crystal structure, save perhaps for some very recent advances in single molecule imaging provided by atomic-resolution microscopy.[132] When it comes to visualizing mechanical bonds, a solid-state structure gives unique insight into how the component parts in a mechanomolecule are oriented relative to each other, whilst also revealing the presence of any noncovalent bonding interactions between them. The ability to rotate and examine the structure of a MIM from any angle in three dimensions supplies an immensely satisfying sense of connection with the molecular world.

Likewise, three-dimensional renderings of MIMs remind us instantly of some of the ordinary objects we encounter in our everyday lives (see **Section 1.1**). Take Olympiadane,[133] for example (**Figure 1.15**), with its five interlocked rings unmistakably sharing the same topology as that of the Olympic logo. Most catenanes bear resemblance at least to the links of a chain, as their name implies. Regardless of their resemblance to familiar objects, hundreds of crystal structures of MIMs have been produced since their debut in 1985, when Sauvage[134] published the first solid-state structure (**Figure 1.16a**) of a [2]catenane. It is impossible to do

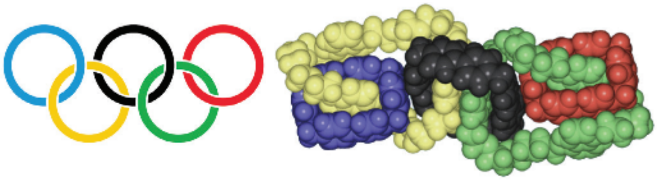


Figure 1.15 The solid-state structure of Olympiadane,[133] which shares its topology with the logo of the Olympic games.

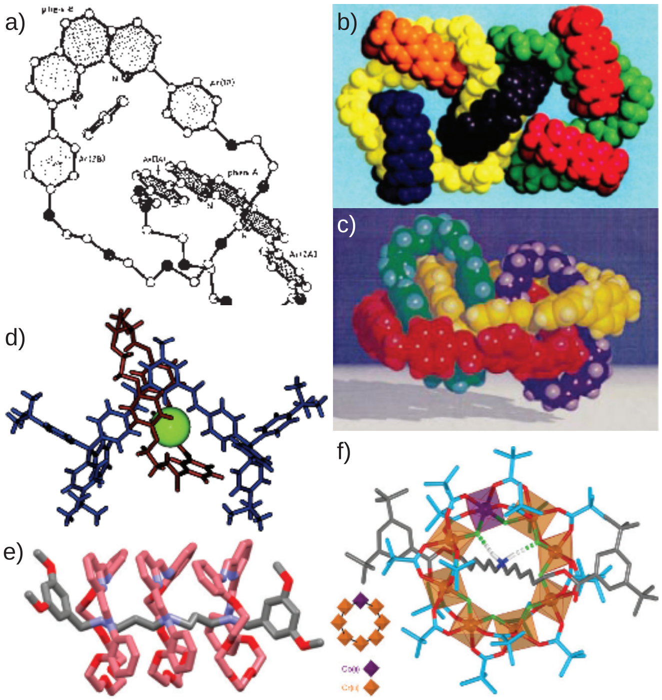


Figure 1.16 Examples of beautiful X-ray crystal structures of MIMs. (a) The first crystal structure of a MIM – Sauvage's [2]catenane.[134] (b) A branched heptacatenane[135] has a large number of interlocked rings for a discrete molecule. (c) Two identical catenanes embraced in a self-complexing dimeric assembly.[136] (d) Beer's first anion-binding rotaxane with its chloride template.[137] (e) A dynamically-assembled [4]rotaxane adopts a rigid rod shape by π–π stacking interactions.[138] (f) A simple and elegant inorganic-organic hybrid [2]rotaxane.[139] Reproduced with permission from refs. 134 (copyright 1985 Royal Society of Chemistry), 135 (copyright 1997 Wiley-VCH), 136 (copyright 2000 Wiley-VCH), 137 (copyright 2002 American Chemical Society), 138 (copyright 2010 Wiley-VCH), 139 (copyright 2009 Nature Publishing Group)

justice to all of the beauty contained in the databank of solid-state mechanically interlocked structures. In **Figure 1.16,** we simply present a few examples that we find noteworthy.[134–139] In **Section 1.3**, see **Figures 1.25**, **1.27**, and **1.29**, as well as **Scheme 1.3** to find more beautiful mechanically interlocked crystal structures.

It is convenient here to discuss a different kind of mechanically interlocked solid-state architecture made possible through the development of metal-organic frameworks[140–143] (MOFs) and coordination polymers. MOFs are infinite, robust, crystalline networks composed of organic struts coordinated to metals or metal clusters as secondary building units (SBUs) and have very high porosities on account of their rigid reticular architectures. The massive amount of void space in some kinds of MOFs oftentimes coaxes them into forming two or more interpenetrated networks in the same crystal, i.e., polyrotaxane[144] and catenated frameworks.[145–147] While researchers interested in high surface areas and porosities want to avoid catenated MOFs as much as possible, they are marvelous structures from the perspective of topology: these infinite catenated networks are the molecular cousins of the sculpture in **Figure 1.6b**. MIMs have also been introduced[148] into coordination polymers and MOFs as linkers by Kim,[149,150] Loeb,[151–159] our group in collaboration with Yaghi,[160,161] Sauvage,[162] and Hupp,[163,164] as well as Sessler,[165–167] Winpenny,[168] and Wang and Su.[169] The example illustrated in **Figure 1.17**, resulting from a collaboration with Yaghi,[160] incorporates a molecular catenane into a catenated MOF. The beauty of this framework lies in its unprecedented complexity, linker size, and topology—it is difficult to imagine a crystal any more jam-packed with mechanical bonds. The cartoon of the MOF in **Figure 1.17d**, which offers a more palatable depiction of its topology, testifies to the importance of the transition to graphical representations. Coordination networks with mechanical bonds are discussed in **Sections 4.1.3.5** and **4.2.3.8**.

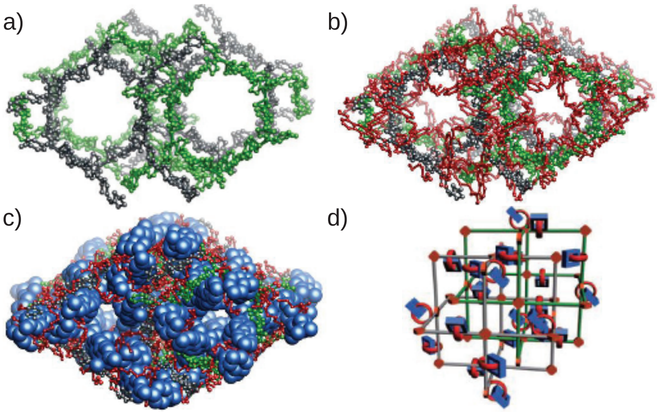


Figure 1.17 A catenated MOF with catenated linkers.[160] (a) A ball-and-stick representation of the X-ray crystal structure of the MOF with the pendent catenanes omitted in order to aid in the visualization of the interpenetrated networks, colored in green and grey. (b) The same MOF with pendant crown-10 macrocycles included in red – only the CBPQT^{4+} rings are omitted. (c) A complete view of the MOF structure, in which the CBPQT^{4+} cyclophanes are assigned space-filling representations in blue. (d) A graphical illustration of the catenated MOF topology. Adapted with permission from ref. 160 (copyright 2010 Wiley)

1.2.5 Graphical Representations

It will be recalled from **Section 1.2.1** that first-generation MIMs were represented primarily by primitive line drawings and line formulas. Although Sauvage took a refreshing step forward into stereoformulas and structural diagrams, there was still a need to find a compromise between the simple line drawings that convey only topology and the detailed structural formulas that detail every atom and bond. Again Sauvage was among the first to pioneer the next evolutionary step: graphical representations/cartoons. His 1985 report of a [3]catenate[170] included a graphically simplified reaction scheme with shading (**Figure 1.18a**) intended apparently for aesthetic purposes. Few, if any,

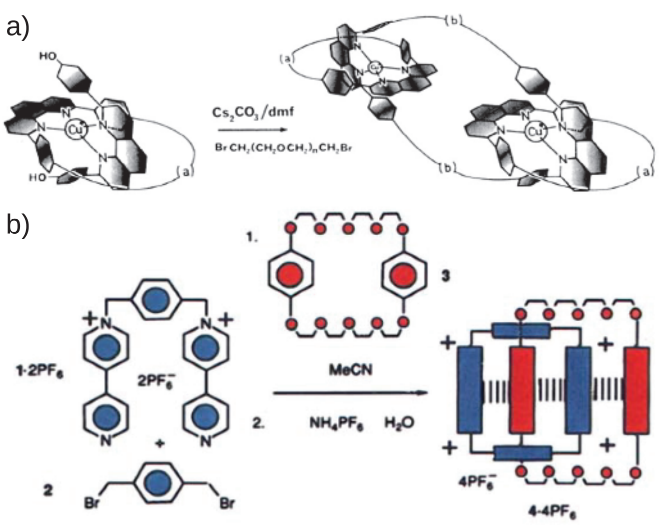


Figure 1.18 Early examples of MIM cartoons. (a) Sauvage's cartoon of a [3]catenate.[170] (b) A synthetic scheme depicting the synthesis of a donor-acceptor [2]catenane relies on abstraction, color, and hash marks in order to emphasize topology, noncovalent bonding interactions, and electronic properties.[171] Reproduced with permission from refs. 170 (copyright 1985 American Chemical Society) and 171 (copyright 1991 Wiley-VCH)

other cartoons existed in the literature until the first donor-acceptor [2]catenane was introduced[126] in 1989. The importance of this contribution is in the way the information about noncovalent bonding interactions is communicated through the use of simplified graphics.[171] Coloring in the rectangles, etc. with felt-tipped pens helped to clarify aspects of the molecular structure (**Figure 1.18b**) such as its topology, the electron density of its component parts (π-donor or π-acceptor), and the noncovalent bonds (thick hashed lines) involved in its formation.

Although graphical representations are an effective means of communication, they were met initially with a fair share of criticism. As the years passed by, we and others began taking the time to make them more aesthetically appealing, paying attention to details like size, shape, shading, and readability. The result is that our cartoons—and graphical representations more generally—have gone through an evolutionary process of their own, represented chronologically in **Figure 1.19**, which was more or less at the point it is today by the year 2000. Two-dimensional cartoons were displaced progressively by three-dimensional ones, which inherently aid in the visualization of mechanostereochemistry by their portrayal of perspective. Our first 3D cartoon was a branched heptacatenane (**Figure 1.19**), which was illustrated directly below the space-filling representation of the solid-state structure (**Figure 1.16b**) in the original paper[135] in 1997. A comparison between the two modes of depiction makes it obvious why there is utility in such cartoons; they do justice to the topology as well as the Euclidean shape of the molecule.

Figure 1.20 presents a number of the different ways that have been employed to represent the same catenane. It is apparent that venturing into cartoons has opened space for much more freedom and creativity in the representation of molecules. Note that every type of cartoon in

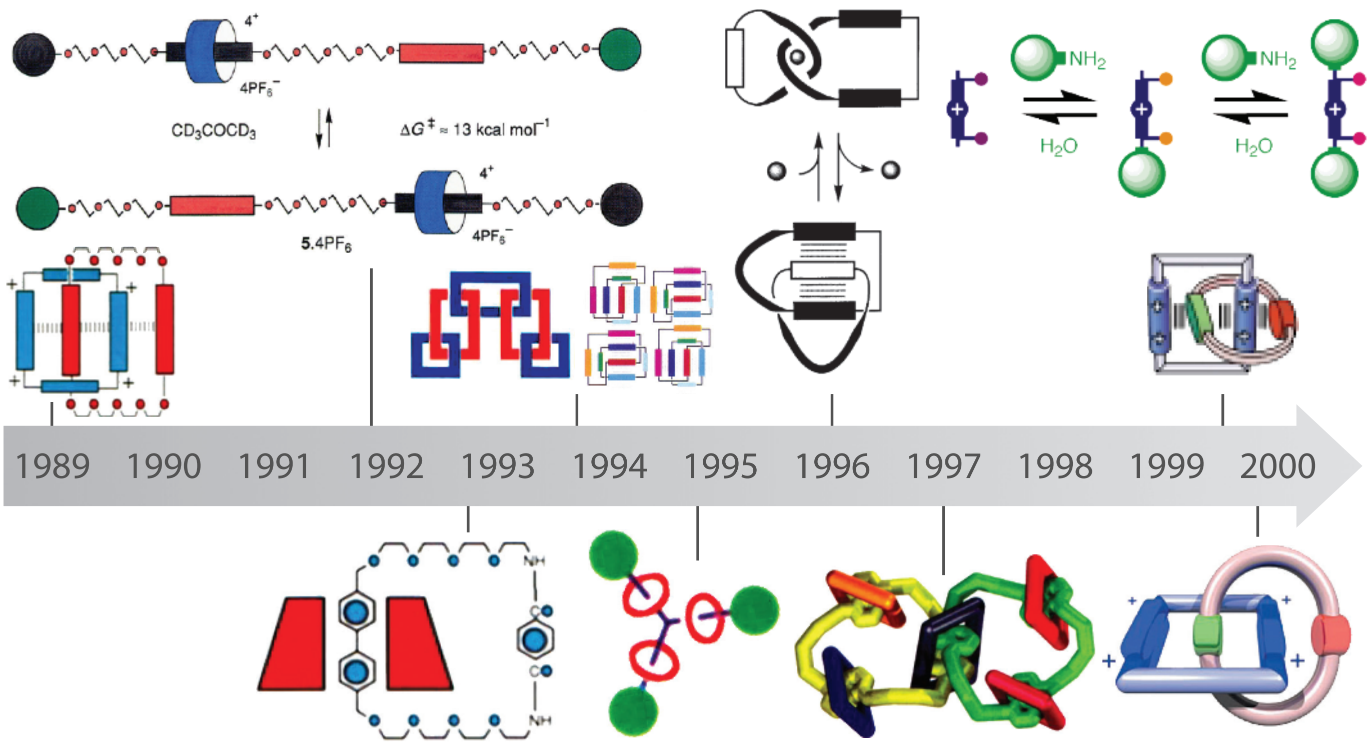


Figure 1.19 A timeline of selected MIM cartoons from our laboratory.

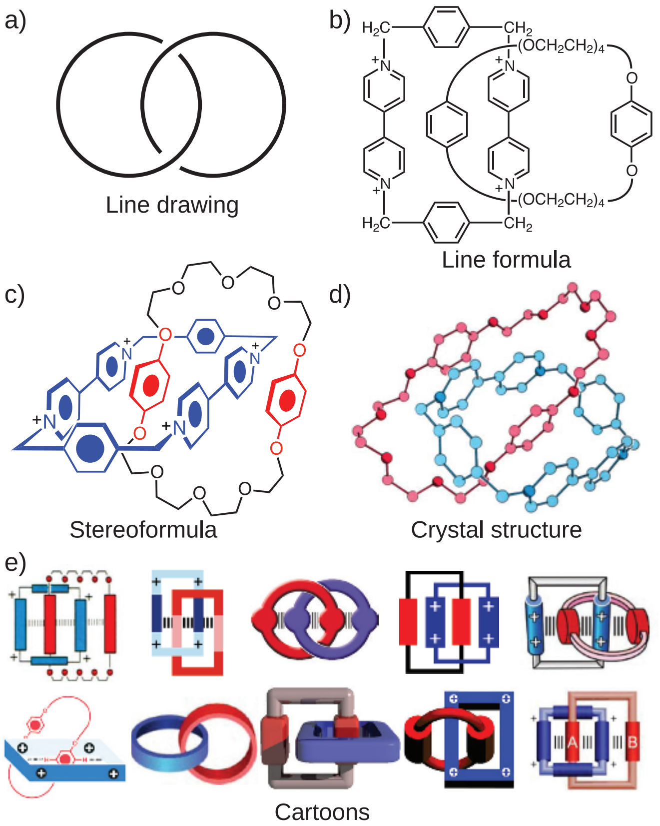


Figure 1.20 Different representations of the same donor–acceptor [2]catenane: (a) line drawings and (b) line formulas were the order of the day until the modern era of MIMs gave way to (c) perspective stereoformulas and (d) crystal structures, as well as (e) graphical representations. These cartoons (e) can be a helpful compromise between these representations when attempting to emphasize the topology, noncovalent bonding interactions, shape, beauty, or function of a MIM. Adapted with permission from ref 33 (copyright 2012 Springer)

Figure 1.20e has been published in the chemical literature. We conclude that the transition to cartoons has been a boon in the field simply because they (i) highlight topology by de-emphasizing atom and bond details, (ii) allow for the denotation of features that structural formulas lack—e.g., noncovalent bonding interactions, (iii) provide a more focused picture of a molecule's Euclidean shape, (iv) declutter and beautify figures and schemes, and (v) elicit creativity and inspire ideas for future research. The fifth and last point is related to the subject of **Section 1.2.6** on how MIMs have influenced the growth of molecular nanotechnology.

1.2.6 Technomorphs

In some cartoons, a MIM can look less like a molecule and more like a classical object, like a toy or LEGO set. Take the MIMs in **Figure 1.21** for example; these representations were drawn intentionally to look as though they were built from pipes, nuts, and bolts. Though they bear the same topology as the molecules they represent, they look more like the handiwork of a plumber than that of a synthetic chemist—chemically meaningless unless placed in the proper context. The objects in the figure hang in tension between the molecular world and the ordinary world, belonging ambiguously to both. The way in which these images refer at once to molecular and classical objects has been described by Joachim Schummer[172] as a "Gestalt Switch in Molecular Image Perception." Schummer's important thesis about "*an aesthetic phenomenon that symbolically linked the world of molecules and the world of ordinary objects, and…prompted the creation of a new sign language*" is embodied by images like those in **Figure 1.21**, for which he coined the term 'technomorphs.' Note that some cartoons in **Figure 1.20** are also technomorphs.

The technomorphic representations of supermolecules and mechanomolecules are truly valuable from both a practical and an aesthetic standpoint. Practically speaking, they played a role in inspiring chemists to think about molecules as classical objects and push back the frontiers of molecular nanotechnology. Because of technomorphism, suddenly a molecule that looks like a car should be driven as though it were a car,[173] those that look like cages should trap things inside,[31] and so on. This mode of thinking applies immensely to MIMs, where a frenzy of creative research accompanies imaginative project titles. Over the years, our own group has fabricated molecular shuttles,[174] switches,[175] push-buttons,[176] trains,[177] elevators,[178] pistons,[179] muscles,[180] abacuses,[181] motors,[182] and valves.[183] Other groups have reported MIMs as molecular necklaces,[184–186] locks,[187] rotors,[188] chameleons,[189] and charm bracelets[190]—the list goes on and on. These types of molecular nanostructures, whose names and representations are deliberately evocative, are known[191,192] also as technomimetic molecules. It is apparent that the visionary dream of nanotechnology is aided and abetted by the new symbols borne out of supramolecular chemistry[64,193] and mechanostereochemistry.[16]

Though we allow ourselves to talk freely about the beauty of molecular structures, technomorphic representations are among the few products of chemistry that can currently withstand a formal aesthetic philosophy. Schummer, a philosopher of science, has undertaken a systematic investigation[41] of chemical representations in the context of

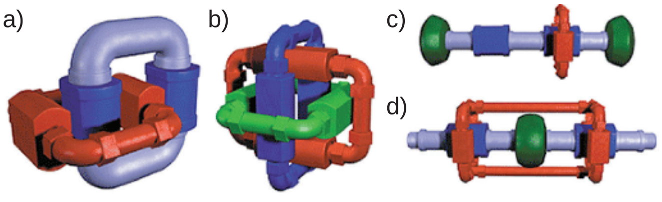


Figure 1.21 Technomorphic representations of (a) a [2]catenane, (b) Borromean rings, (c) a [2]rotaxane, and (d) a suit[2]ane. Adapted with permission from ref. 33 (copyright 2012 Springer)

idealistic aesthetics (Plato, Kant),[194] aesthetics of symbols (Goodman),[195] and Eco's semiotic theory,[196] concluding in the negative on all but Eco's theory. In brief, Umberto Eco's modern semiotic theory would recognize that technomorph symbols are rich in aesthetic content because they (i) can be interpreted ambiguously, (ii) challenge the interpreter to develop new interpretations, and (iii) redirect the interpreter's attention to the symbol itself. In other words, an individual's reflection on and interpretation of a technomorph is a *bona fide* aesthetic experience as well as a new, powerful driving force for ongoing research.

It is good news that cartoons, particularly the subset referred to as technomorphs, have been accepted by the chemical community as a new symbolic language. The result has been the formation of a symbolic link between molecular and classical objects, images that appeal to a broader audience—no background in chemistry is necessary!

1.3 Aesthetics of Mechanical Bonds

The various ways to represent MIMs on paper comprise, more often than not, a portrayal of beauty in their own right. In the previous Section, we have tried to engage you, the reader, in the beauty of printed molecular representations. There remain many other ways to perceive the beauty of molecular objects, some of them particularly unique to MIMs, but the situation becomes less well-defined when we depart from concrete illustrations and images and venture into even more subjective territory. Roald Hoffman,[197] a pioneer of molecular aesthetics, has approached beauty in chemistry from the perspective that "*beauty is built out of individual pleasure around an object or idea*." The aesthetic experience of molecular structures is therefore inexorably tied up with our subjective biases. Synthetically derived molecules are retroactively beautified out of a psychological need to associate pleasure with hard work. We find reasons to label a molecule beautiful and experiments elegant, because we experienced much work, time, and failure in order to achieve them. Nevertheless, these notions of beauty are common to the experiences of most, if not all, chemists, and are therefore very relevant to a more complete understanding of the discipline of chemistry. The words of Nobel Laureate Charles Pedersen,[198] whose serendipitous discovery of crown ethers eventually spawned the fields of host-guest chemistry,[199] supramolecular chemistry,[193] and mechanostereochemistry[16]—are a case in point:

> *"One of my first actions was motivated by esthetics more than science. I derived great esthetic pleasure from the three-dimensional structure of [the first crown ether]."* [198]

Pedersen's account demonstrates that molecular beauty is not just an interesting topic for discussion; it can also have a profound impact on scientific research. Here, we discuss aspects of beauty in MIMs that can be independent of their printed representations. In other words, this Section is about where chemists of the mechanical bond find pleasure in their research.

1.3.1 Beauty in Diversity

Molecular recognition motifs (**Section 2.3**) that are reported in the literature as templates for MIMs are continually growing more and more diverse. They include (**Figure 1.22**) molecules associating by dint of hydrophobic forces (**Section 2.3.1**), molecules assembling around cationic templates, such as transition metal (**Section 2.3.2**) and alkali, alkaline earth, and lanthanide metal ions (**Section 2.3.8**), π-associated donor-acceptor templates (**Section 2.3.3**), hydrogen (**Section 2.3.4**) and halogen (**Section 2.3.5**) bonding, anion binding (**Section 2.3.6**) and ion-pairing (**Section 2.3.7**) templates. Cyclophanes (**Section 2.3.9**), which often rely on a combination of these different types of noncovalent bonding interactions to encapsulate guests, radical pairs (**Section 2.3.10**), homophilic interactions (**Section 2.3.11**), and biomolecular self-assembly (**Section 2.3.12**) provide yet more territory for producing templation. The MIMs illustrated in **Figure 1.22** represent some of the seminal examples[120,126,137,139,200–230] of these motifs. The remarkable diversity of these interlocked structures is a source of beauty. To quote Donald Hicks,[231] "*there is no time of year when the trees are more beautiful than when they are different colors. Diversity adds beauty to our world.*" Although we can classify all of the supramolecular recognition motifs involved in mechanostereochemistry into only a handful of categories, there is ample diversity to create a potentially endless variety of beautiful molecules with mechanical bonds—an attitude captured by the ancient writings of Sun Tzu in The Art of War –

> *"There are not more than five musical notes, yet the combinations of these five give rise to more melodies than can ever be heard.*
> *There are not more than five primary colors, yet in combination they produce more hues than can ever be seen."*

1.3.2 Topological Beauty

Let us take a moment to clarify the difference between topography and topology. The aspects of a molecule relating to its geometry (tetrahedral, square planar, etc.), symmetry, size, and shape, are characterized by its topography. By contrast, the topology of a molecule relates to geometric properties and spatial relationships that remain invariant throughout continuous deformation, i.e., stretching, bending, and compressing bonds without breaking them). It is well accepted that the beauty of a molecular structure is often associated with its shape in Euclidean geometry (topography), but here we recognize that beauty can be associated with topology as well.

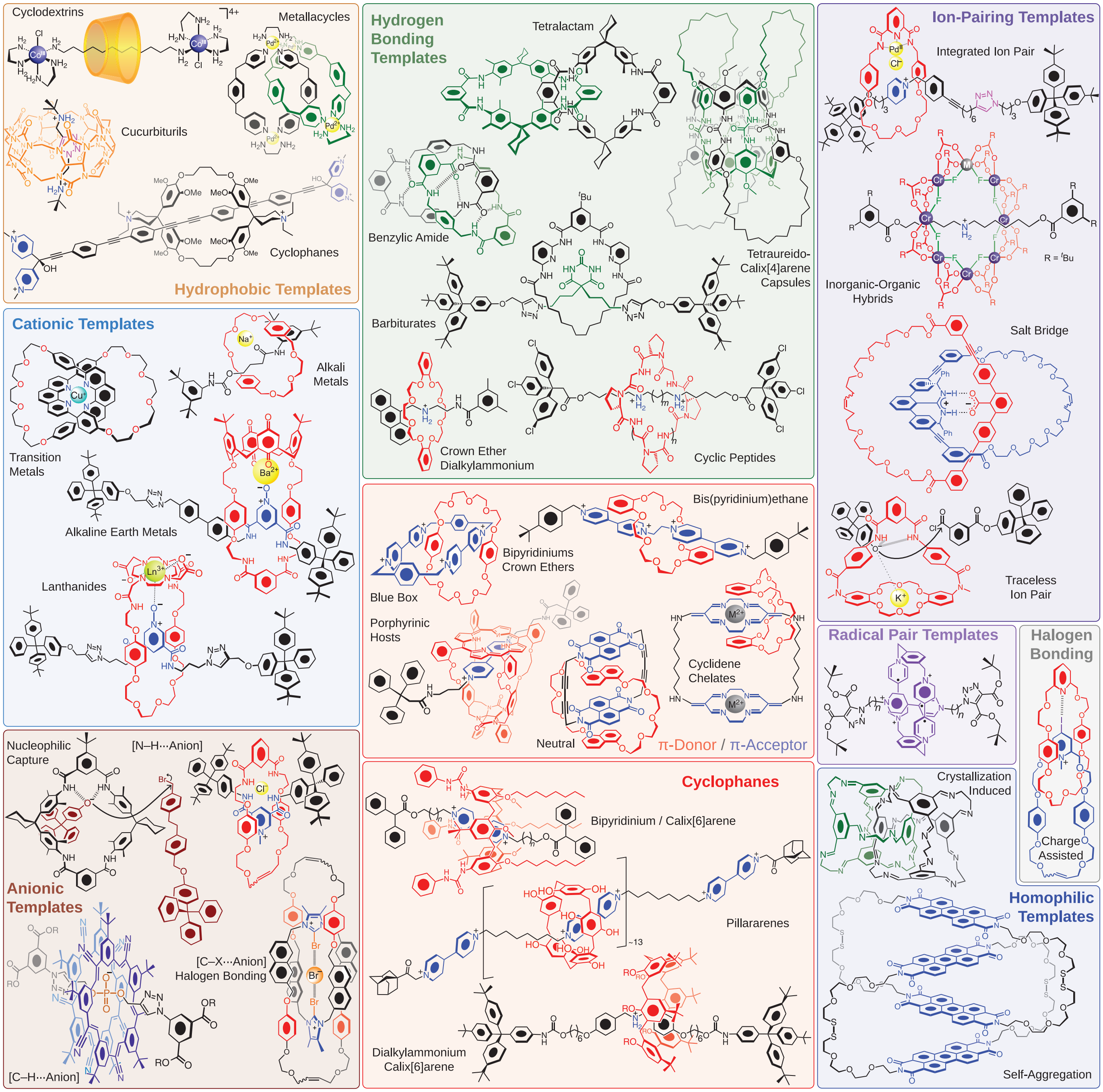


Figure 1.22 Beauty in diversity. Seminal examples of MIMs employing various types of supramolecular templates. Hydrophobic templates: cyclodextrins,[200] cucurbiturils,[201] metallacycles,[202] and other charged cyclophanes.[203] Cationic templates: transition metals,[120] alkali metals,[204] alkaline earth metals,[205] lanthanides.[206] π-Donor/π-Acceptor templates: bipyridinium derivatives (e.g., 'blue box') and crown ethers,[126] bis(pyridinium)ethane,[207] porphyrinic hosts,[208] neutral π-acceptors,[209] cyclidene chelates.[210] Hydrogen bonding: tetralactam rings,[211] benzylic amide rings,[212] tetraureidocalix[4]arene capsules,[213] barbiturates,[214] dialkylammonium⊂crown,[215] cyclic peptides.[216] Halogen Bonding: charge-assisted.[217] Anionic templates: nucleophilic capture,[218] [N–H···Anion] hydrogen bonding,[137] [C–H···Anion] interactions,[219] [C–X···Anion] halogen bonding.[220] Ion-pairing templates: integrated ion pairs,[221] inorganic-organic hybrids,[139] salt bridges,[222] traceless ion pairs.[223] Other cyclophanes: calix[6]arenes,[224,225] pillararenes.[226] Radical-pair templates.[227,228] Homophilic templates: self-aggregation,[229] crystallization-induced assembly.[230] See **Section 2.3**.

David Walba[20] in 1985 was among the first to discuss topological beauty in the primary literature, noting that "*topological stereochemistry is a unique field, esthetically and intellectually pleasing in the extreme.*" Two years later, Jean-Pierre Sauvage's first major review[232] of MIMs paid tribute to the aesthetic value of catenanes and catenands. He proposed that "*the beauty of some molecules might be independent of shape and rest only in [their] topological*

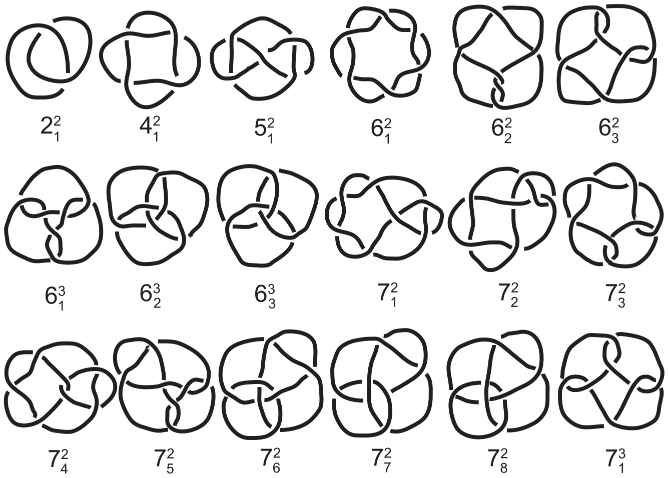


Figure 1.23 Projections of the 18 prime links with <8 crossings. Reprinted with permission from ref. 33 (copyright 2012 Springer)

properties." A review by Amabilino and Pérez-García[24] constitutes a delightful look at topological molecules in the context of how chemists represent them. Sauvage and Amabilino[233] have also engaged the beauty of molecular knots in a chapter in a monograph[32] on *Beauty in Chemistry*. We refer the reader to these articles for further discussion on topological beauty.

In the field of mathematical topology, all closed loops are called knots. Three-dimensional knots are often characterized by the minimal number of crossing points in their two-dimensional projections. In Alexander-Briggs[234] notation, prime knots are catalogued by their crossing number, with subscripts denoting an arbitrary order amongst other knots with equal crossing numbers. A circle with no entanglement is known as the unknot (crossing number 0), while the simplest non-trivial knot is the trefoil knot (crossing number 3). Two or more knots interlocked in space are known in mathematics as links. Links can be described[234] by an extension of the Alexander-Briggs notation, where each link is characterized by its crossing number, with a superscript denoting the number of component knots and a subscript denoting an (arbitrary) rank order. **Figure 1.23** shows the 18 prime links with less than eight crossings. Only 2^2_1 (a [2]catenane or 'Hopf link'),[101] 4^2_1 (a doubly interlocked [2]catenane or 'Solomon Link'),[235] 6^2_1 (a triply interlocked [2]catenane or 'Star of David' catenane),[236] 6^3_2 (Borromean Rings),[237] and 6^3_3 (cyclic [3]catenane)[238] have been reproduced (**Figure 1.24**) in the form of synthetic molecules—see **Section 4.1.1**.

Although unlinked knots lack any formal mechanical bonds because they lack component parts, they are nevertheless topologically non-trivial mechanically interlocked objects. The challenge of synthesizing knots in molecular form has been met (**Figure 1.25**) with considerable success. Importantly, molecular knots have also paved a pathway for chemists to follow, inspiring molecular designs that incorporate other types of mechanical bonds. For example, Sauvage's seminal synthesis of a trefoil knot[239,240] from a dinuclear metallohelicate was the conceptual progenitor of his Solomon Link synthesis[235] from a trinuclear metallohelicate. Likewise, Leigh's seminal pentafoil knot synthesis[241,242] from a cyclopentameric double helicate set the stage for the construction[236] of his Star of David catenane from a cyclohexameric double helicate. Other topologically non-trivial structures lacking mechanical bonds, such as composite knots[243] and ravels,[244,245] provide further inspiration for the rational design of mechanically interlocked molecular topologies.

Other types of catenane topologies include composite (**Section 4.1.2**), multi-annulated (**Section 4.1.3**), and covalently bridged (**Section 4.1.4**) links. Selected seminal examples (**Figure 1.26**) of several of these topologies

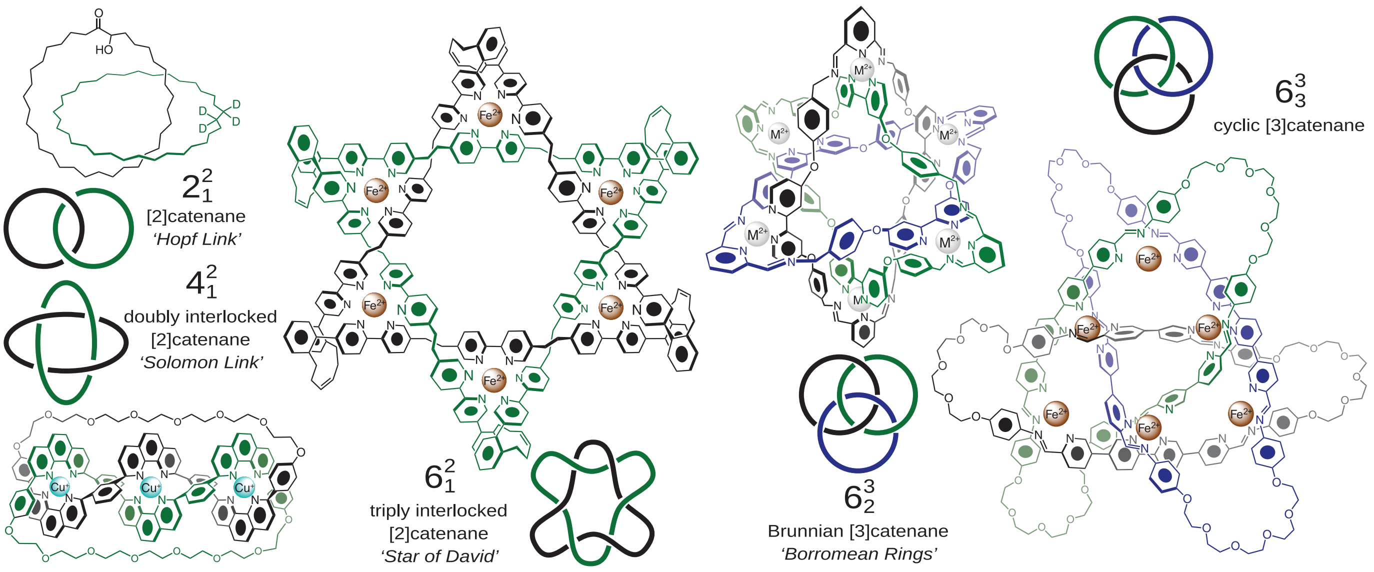


Figure 1.24 Seminal examples of synthetic prime links: 2^2_1 [2]catenane / Hopf link,[101] 4^2_1 doubly interlocked [2]catenane[235] / Solomon Link,[325] 6^2_1 triply interlocked [2]catenane / Star of David,[236] 6^2_2 Brunnian link / Borromean Rings,[237] 6^3_2 cyclic [3]catenane.[238]

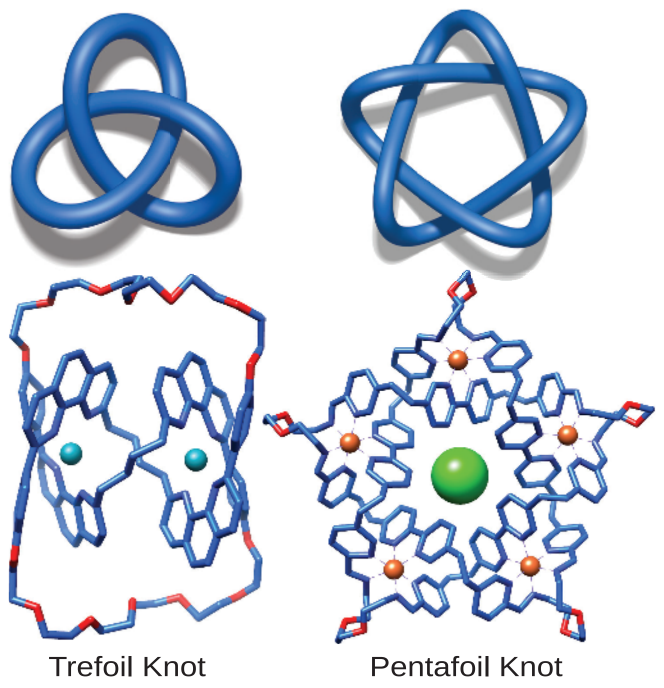


Figure 1.25 Knots, such as the seminal trefoil knot reported by Sauvage[239] and the pentafoil knot reported by Leigh,[241] are topologically non-trivial molecules which lack mechanical bonds, yet have laid the foundation for the synthesis of MIMs with exotic topologies and architectures.

include (i) Sauvage's radial [*n*]catenanes,[246] topologies also championed by Kimoon Kim[184,186,247] under the banner of 'molecular necklaces', (ii) Fujita's macrobicyclic homo[2]-catenane of triply interlocked cages,[248] (iii) Kuroda's macrotricyclic homo[2]catenane of quadruply interlocked cages,[249] (iv) a macrobicyclic [3]catenane, also known as a bis[2]catenane,[250] (v) a branched [6]catenane,[135] (vi) a side-chain poly[2]catenane,[251] (vii) a main-chain poly[2]catenane, which was originally introduced by Geerts,[252] (viii) a macrotricyclic hetero[2]catenane, introduced by Becher[253] (ix) a macrobicyclic hetero[4]catenane resulting from a collaboration between Vögtle and Sauvage,[254] (x) covalently bridged [2]catenanes, which originated[106] as precatenanes in Schill's directed syntheses, but later became known[255–257] as pretzelanes or [2]pseudocatenanes (xi) a doubly threaded macrobicyclic [2]catenane introduced by Becher[258] under the title of a [3]pseudocatenane, a topology also known[259–261] as a 'handcuff' catenane, (xii) a [4]pseudocatenane introduced by Chen,[262] (xiii) a macrotricyclic hetero[7]catenane arising from a Nitschke-Sanders collaboration,[263] (xiv) Vögtle's cyclic bis[2]-catenane,[264] and (xv) Chiu's cyclic tetrakis[2]catenane.[265]

The structures of many beautiful MIMs have also been elucidated in the solid state by X-ray crystallography. Space-filling representations of several of these novel topologies are presented in **Figure 1.27**. The collection includes examples of all of the synthetic prime links,[134,236–238,266] composite links such as a [3]catenane,[123] [5]catenanes—namely, Olympiadane[133] and Kimoon Kim's[186] appropriately titled 'molecular necklace'[184] radial [5]catenane—as well as a branched [7]catenane,[135] a pretzelane,[267] [3]- and [4] pseudocatenanes,[260,262] acyclic[268] and cyclic[265] bis[2]catenanes, and other topologies based on multi-annulated component parts[269] or molecular cages.[248,249,270] A more complete discussion of molecular topology is available **Section 5.2.4**, while the diversity of topologically linked molecules are summarized more comprehensively in **Section 4.1**. Topologically trivial architectures with mechanical bonds have also been prepared, and will be described in **Section 1.3.3** and **Sections 4.2–4.3**.

1.3.3 Architectural Beauty

A synthetic chemist has the opportunity to experience the same thrill that architects and artisans encounter when designing and building something new. We use the term 'architecture' to describe MIMs as we widen our scope from mathematical topology to include topologically trivial species such as rotaxanes. Mechanostereochemistry is full of opportunities to create new and exotic architectures. In **Figures 1.28–1.29** we feature the stereoformulas and solid-state structures, respectively, of a handful of MIMs with beautiful architectures.

A number of rotaxane-based architectures involve the installation of covalent bridges between mechanically bonded component parts. Recalling that covalently bridging the topological linkage of a [2]catenane results in a pretzelane (**Section 4.1.4.1**) and bridging two rings of a [3]catenane results in a handcuff catenane / pseudocatenane (**Section 4.2.3.4**), opportunities abound for linking various rotaxane component parts with covalent bonds, giving rise to a more diverse set of architectures—[1]rotaxanes, figures-of-eight, daisy chains, Bonnanes, bundles, elevators, suitanes, and others—depending on the nature of the covalent bridge(s). A [1]rotaxane[271,272] (**Figures 1.28b**, **1.29e**, **Section 4.2.3.1**) is the result of covalently linking the ring of a [2]rotaxane to its dumbbell. This architecture is also known as a molecular ouroboros,[273,274] a molecular lasso,[275–277] or a [c1]daisy chain.[278] A 'molecular 8'[279] or figure-of-eight[280,281] (**Figure 1.29j**, **Section 4.3.4**) arises from connecting the ring to the axle on both sides. Daisy chains[282] (**Section 4.2.3.2**) also comprise conjoined ring-rod component parts, yet they are cross threaded into acyclic or cyclic oligomers and polymers known[283] as [*a*n]daisy chains or [*c*n]daisy chains, respectively, where *n* is the number of ring-rod monomers in the assembly. Examples of [*c*2]daisy chains[284,285] (**Figures 1.28d**, **1.29f**) and [*c*3]daisy chains[286] (**Figure 1.28h**) are presented. Coutrot[9,287] has described macrocyclized [*c*2]daisy chains and nicknamed them 'rotamacrocycle' architectures (**Section 4.3.2**). Bistable daisy chains can express[180,288–291] muscle-like actuation properties—see **Section 6.13.1.1**.

Other covalently bridged rotaxane-like architectures involve bis-, tris-, or tetra-macrocyclic species. Linear rotaxanes with covalently bridged rings (**Section 4.2.3**) have been dubbed 'bonnanes' by Vögtle,[292] after the city of Bonn, Germany's former 'bridge capital'. Rotaxanes possessing a

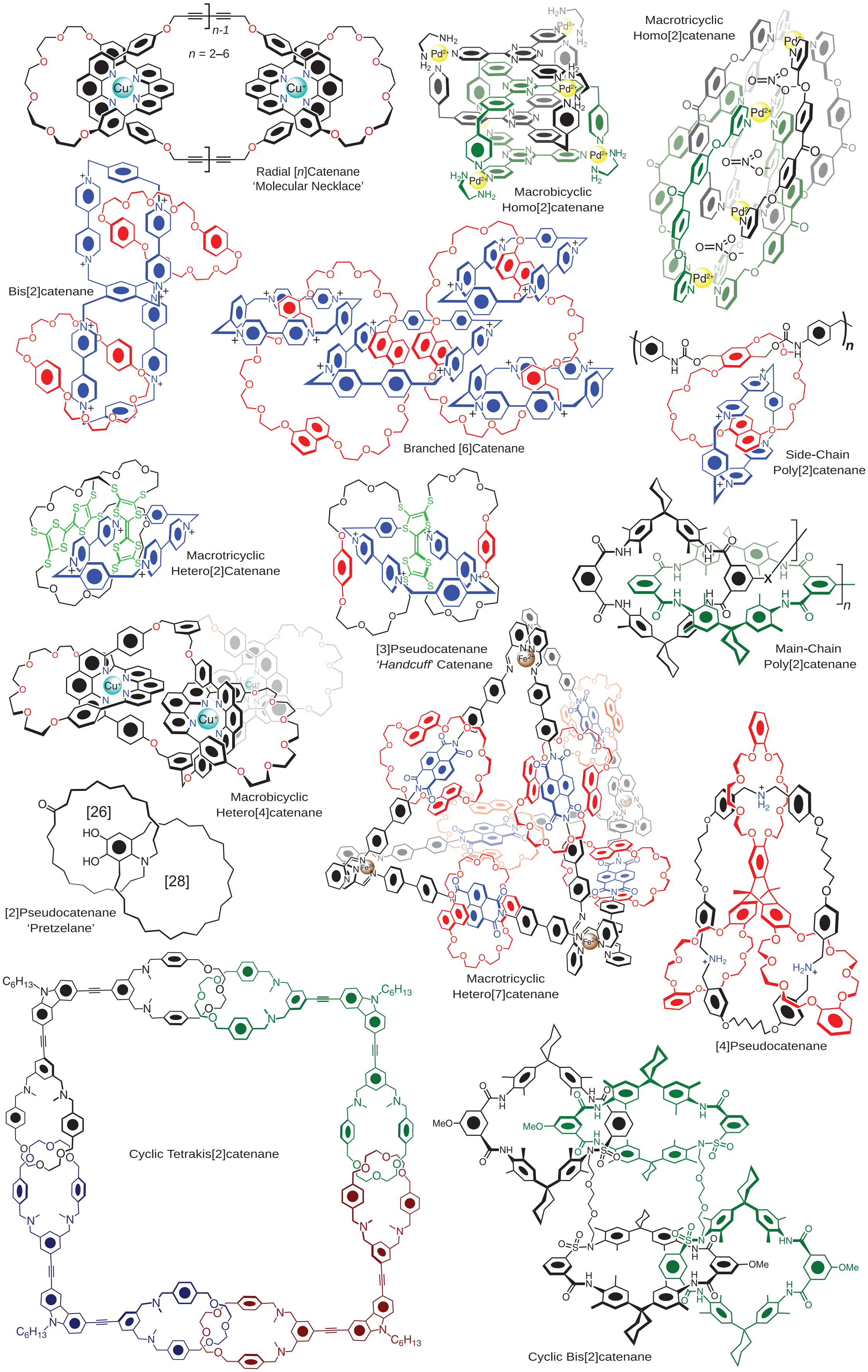


Figure 1.26 Seminal examples of selected molecular link topologies: Sauvage's radial [*n*]catenanes / 'molecular necklaces',[246] Fujita's macrobicyclic homo[2]catenane of triply interlocked cages,[248] Kuroda's macrotricyclic homo[2]catenane of quadruply interlocked cages,[249] bis[2]catenane,[250] branched [6]catenane,[135] side-chain poly[2]catenane,[251] main-chain poly[2]catenane,[252] macrotricyclic hetero[2]catenane,[253] macrobicyclic hetero[4]catenane,[254] [2]pseudocatenane / 'pretzelane',[106] [3]pseudocatenane / handcuff catenane,[258] [4]pseudocatenane,[262] macrotricyclic hetero[7]catenane,[263] cyclic bis[2]catenane,[264] cyclic tetrakis[2]catenane.[265]

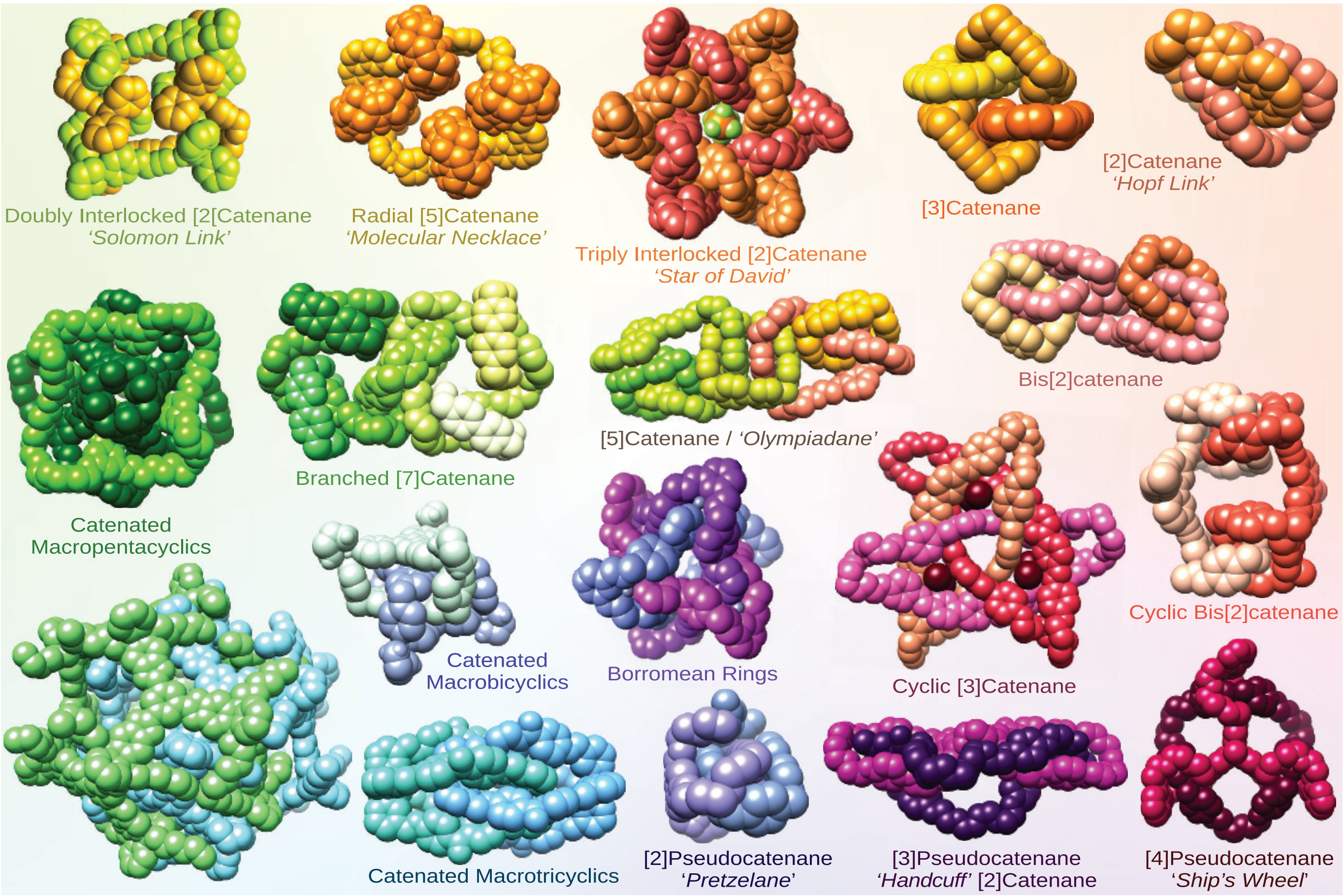


Figure 1.27 Space-filling representations of the solid-state structures of some beautiful MIM topologies: [2]catenane,[134] [3]catenane,[123] [5]catenane (Olympiadane),[133] [5]catenane 'molecular necklace',[184] branched [7]catenane,[135] eightfold interlocked multicatenane,[269] triply interlocked coordination cages,[248] quadruply interlocked coordination cages,[249,270] Solomon link,[266] Borromean Rings,[237] triply interlocked 'Star of David' [2]catenane,[236] cyclic [3]catenane,[238] pretzelane,[267] doubly threaded 'handcuff' [2]catenane or [3]pseudocatenane,[260] 'ship's wheel' [4]pseudocatenane,[262] bis[2]catenane,[268] cyclic bis[2]catenane.[265] Solvent molecules, counterions, and protons are omitted for the sake of clarity.

single bridge between two rings have also been called[293] handcuff rotaxanes, by analogy with handcuff catenanes. Cyclic [4]rotaxanes (**Figure 1.28c**) have been introduced[294] in which two bis-macrocycles are threaded by two dumbbells to give a ladder-like geometry. Sauvage[295] has obtained a crystal structure (**Figure 1.29i**) of a cyclic [4]rotaxane based on transition metal templates. Tris- and tetra-macrocyclic 'platforms', which are triply or quadruply interlocked with tripodal or tetrapodal 'rigs', respectively, have been described as mechanically interlocked 'bundles',[296] and 'molecular elevators',[178] the latter case pertaining to situations where a platform can be translocated under the influence of external stimuli—see **Section 6.13.1.3**. A triply interlocked bundle[296] is illustrated in **Figure 1.28g**, while the solid-state structure of a fourfold interlocked molecular elevator[297,298] is represented in **Figure 1.29d**. A suitane (**Section 4.3.5**) is a molecule that has been named[8,299] to reflect a molecular 'suit' which mechanically envelops a multi-limbed molecular 'body' (a suit[*n*]ane has *n* 'limbs'). A suit[2]ane (**Figure 1.29g**) thus involves a bulky molecular core bearing two appendages, all of which are encircled by a unibody macrotricyclic 'suit'.

There remain many architectures with mechanical bonds beyond simple two- or three-component rotaxanes that do not involve covalently bridged component parts. Polyrotaxanes, for example, are relatively commonplace in the literature—see **Section 4.2.1.1**. Recently, it has proven to be possible to control the secondary structure of oligorotaxanes, creating large, well-defined rigid-rods[138,300] (**Figure 1.28i**) and foldamers[301–303] (**Figure 1.28j**) based on the mechanical bond. Another type of multicomponent architecture is that of the rotacatenane (**Figure 1.28a**, **Section 4.3.1**), first introduced[7] in 1999, which comprises a [2]catenane threaded by a molecular dumbbell. More recently, the term rotacatenane has been expanded to describe[304] larger architectures possessing both rotaxane and catenane moieties. A similar concept involves two dumbbells encircled by a single ring—an architecture (**Figure 1.28e**, **Section 4.2.1.2**) first created by Anderson.[305] Sauvage[306] and Leigh[307] have also created examples of these doubly threaded architectures, the latter case, which was nicknamed a 'molecular sheaf', includes a crystal structure (**Figure 1.29c**) of the architecture. A larger

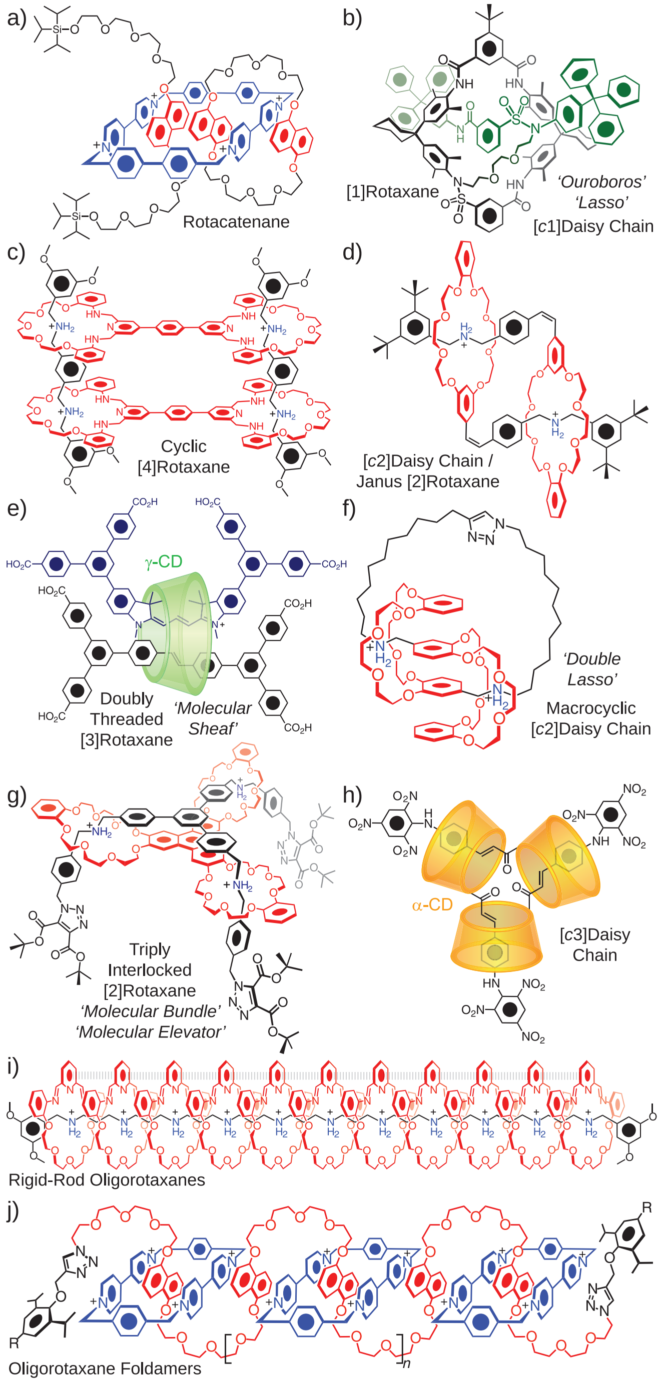


Figure 1.28 Seminal examples of MIM architectures. (a) Rotacatenane.[7] (b) [1]Rotaxane,[271] (c) Cyclic [4]rotaxane.[294] (d) [*c*2]-Daisy chain,[284] (e) Doubly threaded [3]rotaxane,[305] (f) Macrocyclic [*c*2]daisy chain double-lasso.[287] (g) Triply interlocked [2]rotaxane.[296] (h) [*c*3]Daisy chain.[286] (i) Rigid-rod oligorotaxanes.[138,300] (j) Oligorotaxane foldamers.[301,302]

molecular sheaf (**Figure 1.29h**) comprising two dumbbells, each encircled by two inorganic rings, has also been described by Leigh and Winpenny.[139]

The solid-state structures of two particularly unusual architectures are depicted in **Figure 1.29a–b**. Jiang and Huc[10] have produced a number of 'helix-rod' host-guest complexes, which resemble [2]rotaxanes wrapped (**Figure 1.29a**) in molecular helices instead of rings. The mechanical bond in this case lies in a grey area (see **Section 3.1.1**) since the rod and helix can dissociate, although the timescale of exchange is relatively slow, on the order of days, when the stoppers are sufficiently bulky. Stang and Chi[11] have reported the self-assembly of a rotaxane-like ring-in-ring architecture (**Figure 1.29b**) in which two bulky metallacycles are mechanically interlocked, yet not catenated.

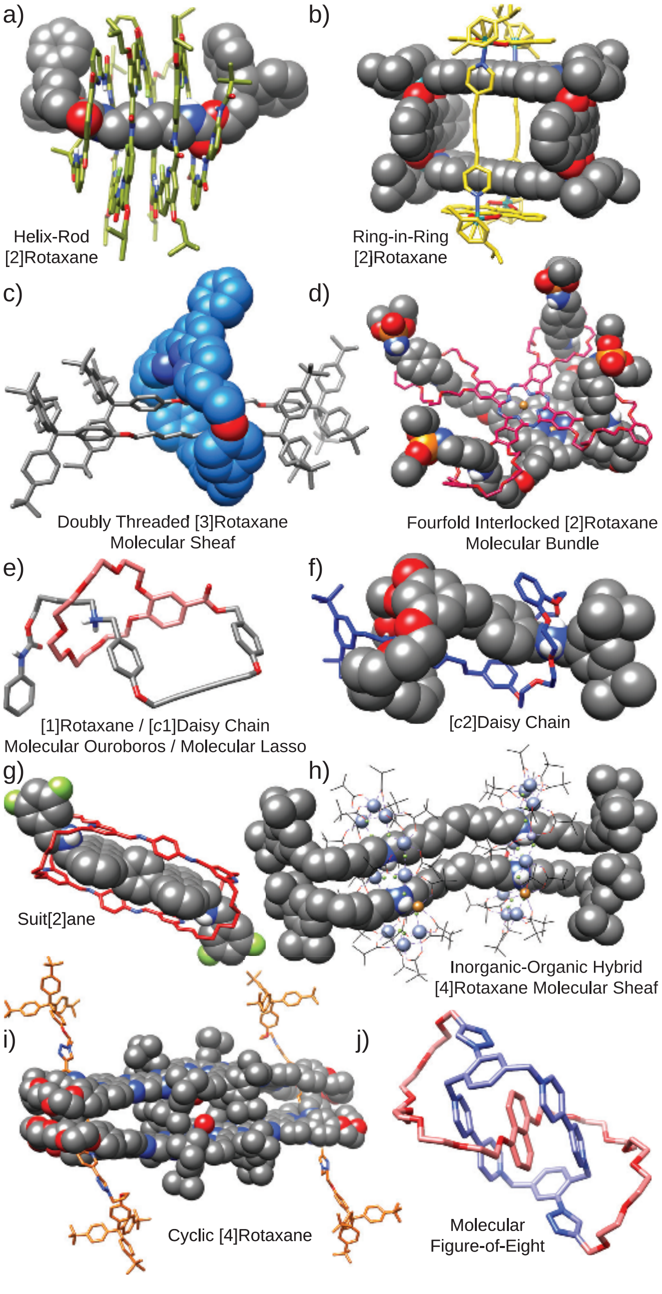


Figure 1.29 Solid-state structures of some beautiful MIM architectures. (a) Helix-rod rotaxane.[10] (b) Ring-in-ring rotaxane.[11] (c) Doubly-threaded [3]rotaxane.[307] (d) Fourfold interlocked [2]rotaxane.[298] (e) [1]Rotaxane.[272] (f) [*c*2]Daisy chain.[285] (g) Suit[2]ane.[8] (h) Organic-inorganic hybrid doubly threaded doubly encircled [4]rotaxane.[139] (i) Cyclic [4]rotaxane.[295] (j) Figure-of-eight.[281] Solvent/matrix molecules, counterions, and C–H protons are omitted for the sake of clarity.

Given all of the pleasure and beauty derived from creating new interlocked architectures, we have only scratched at the surface of what is possible. Many of the molecules shown in this Section were already framed in the context of beauty in the primary literature, and we expect that aesthetic considerations will continue to motivate new architectural developments.

1.3.4 Simplicity and Elegance

Simplicity is probably the least controversial trait that a molecule needs to be beautified in the minds of chemists, who have always been drawn to Platonic notions of beauty. Who could blame chemists for this kind of thinking? Simplicity is tied to the pleasing virtues of balance, symmetry, wholeness, and harmony. It is also tied to clarity and comprehension, which is tied to truth (**Section 1.2.4**), which is tied to beauty. When a chemist examines a simple molecule, a network of these related concepts inevitably leaves him or her with a sense of pleasure and satisfaction.

There is no lack of beautifully simple MIMs. The quintessential example is the all-hydrocarbon [2]catenane (**Figure 1.30**) prepared by Schill,[308] in which the simplest non-trivial topology is constituted only by methylene units. Other beautifully simple MIMs comprise highly symmetrical structures that make them "easy on the brain", such as many of the compounds in **Sections 1.3.2** and **1.3.3**. Although these molecules look relatively simple, it is clear that an IUPAC name would be far from simple, a testament to the growing importance of images and graphical representation in chemistry.

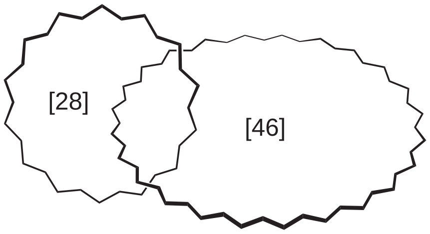


Figure 1.30 Stereoformula of an all-hydrocarbon [2]catenane introduced by Schill.[307] Bracketed numbers denote the number of carbon atoms constituting each ring.

Although we are, no doubt, aesthetically drawn to simple molecules—recall the Platonic solids from the introduction—experiments are where the beauty of simplicity truly shines. While we have chosen the word 'beauty' to describe the aesthetic value of structural representations, 'elegance' is a term that has been employed[61] to describe the aesthetic value of experiments. Here, we present some selected examples of experimental milestones that embody elegance in mechanostereochemistry. This case is our only foray into experimental beauty and the list is by no means exhaustive.

1. Templated Synthesis: Sauvage[120] revived an all but forsaken discipline by introducing (**Figure 1.31**) transition metal templates for synthesizing MIMs. His raison d'être for using coordination chemistry to position organic precursors appropriately to interlock them in subsequent reactions, which dramatically reduces the number of steps and increases the yield by orders of magnitude over those obtained for previous MIMs, was supremely elegant. **Figure 1.31** portrays his shorthand drawing of the original template strategies[120] for catenane synthesis. Sauvage's templated synthesis set the stage for the plethora of novel molecular recognition motifs (see **Figure 1.22** and **Section 2.3**) employed today in the making of mechanical bonds.

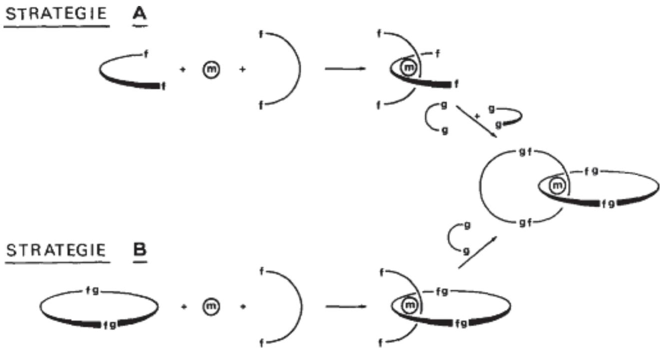


Figure 1.31 Sauvage's scheme depicting his seminal template-directed strategies for synthesizing MIMs. A tetrahedral center orients U-shaped species appropriately for subsequent ring-closure, resulting in a catenate. Reprinted with permission from ref. 120 (copyright 1983 Elsevier).

2. Thermodynamic Control: MIMs can now be synthesized routinely in near-quantitative yields—a convenience that can be attributed in large part to the advent of thermodynamically controlled protocols, although a number kinetically controlled reactions are also high yielding. See **Chapter 3** for a review of MIM synthesis under thermodynamic control. Seminal examples[129,202,309–314] of elegant thermodynamically controlled protocols for making mechanical bonds are illustrated in **Figure 1.32**. They include (in order of appearance) (i) slippage[309] (**Section 3.1**), which involves the passage of a ring over a size-complementary stopper that is sufficiently bulky to prevent deslipping, (ii) olefin metathesis[310] (**Section 3.4**), which involves a catalyst—typically Grubbs' Ru alkylidene catalysts—scrambling the constituents of double bonds, (iii) disulfide exchange (**Section 3.5.1**), which involves the oxidative coupling of thiols and reductive cleavage of disulfides, (iv) kinetically labile metal-ligand bonds (**Section 3.2**)—a revolution led by Makoto Fujita,[202] (v) reversible nucleophilic substitutions (**Section 3.5.2**), such competing S_N2 processes[312] in dynamic equilibrium, (vi) imine bonds[129,315] (**Section 3.3.1**) whose reversible nature facilitates the self-assembly of MIMs, (vii) boronic esters[313] (**Section 3.3.3**) formed reversibly from boronic acids and diols, and (viii) self-assembled monolayers[314] (SAMs) (**Section 3.6**).

We emphasize here that thermodynamically controlled reactions—especially olefin metathesis, metal coordination, and imine bonding—have been indispensible in orchestrating the self-assembly of many of the most exotic,

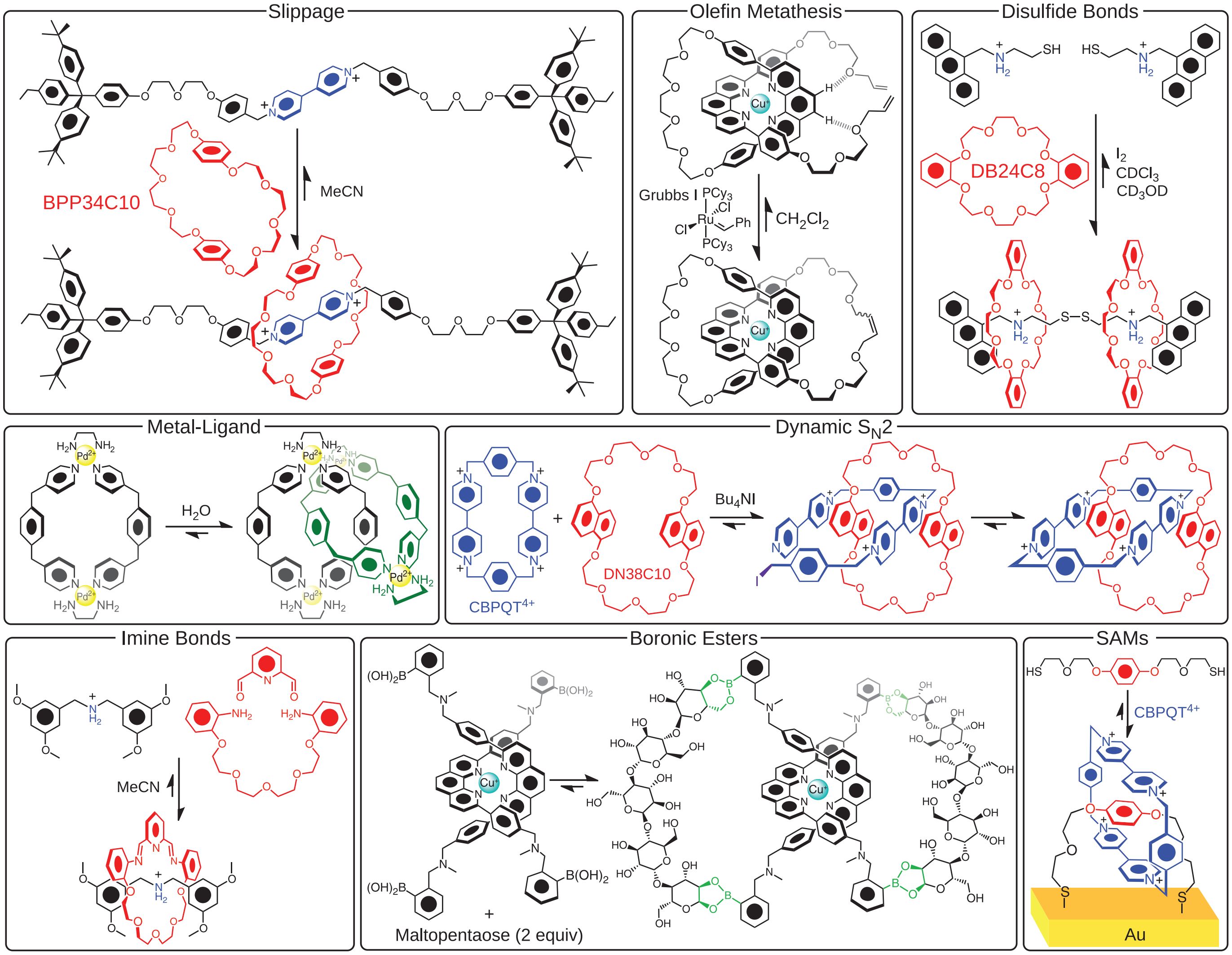
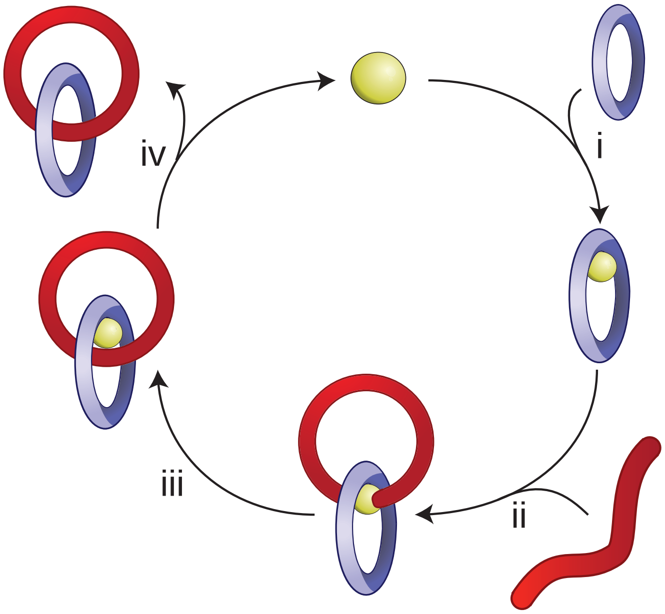


Figure 1.32 Examples of elegant thermodynamically-controlled reactions employed in the near-quantitative synthesis of MIMs. Slippage[309] involves the passage of a ring over a size-complimentary stopper that is sufficiently bulky to prevent deslipping. Grubbs' catalysts impart olefin-containing MIMs with dynamic properties by scrambling the constituents of double bonds via olefin metathesis.[310] Reversible disulfide bonds establish thermodynamic control by disulfide exchange.[311] Labile coordinative bonds are employed in the self-assembly of MIMs.[202] A weakly nucleophilic leaving group (I^-) competes with a nucleophilic macrocylization/catenation event in a reversible S_N2 reaction.[312] Reversible imine bonds facilitate the selection of MIMs from dynamic combinatorial libraries.[129] MIMs can be self-assembled from boronic acids and diols via the reversible formation of boronic esters.[313] Self-assembled monolayers (SAMs) provide a means to mount rotaxanes on surfaces under thermodynamic control.[314] See **Chapter 3**.

beautiful, and challenging topologies and architectures including molecular necklaces,[184,186,190,247,316,317] handcuff catenanes,[259,260,318] mechanically interlocked cages,[230,248,249,270,319] molecular trefoil knots,[320–323] pentafoil knots,[241,242] Solomon knots,[324–326] Borromean rings,[89,237,327,328] the Star of David catenane,[236] the cyclic [3]catenane,[238] daisy chains,[329,330] molecular bundles,[331] and very large discrete rigid-rod oligorotaxanes.[138,300]

3. Active Template Synthesis: A step beyond the template is the 'active template,' introduced in 2006 independently by the groups of Saito[332] and Leigh.[333] An active template is a moiety acting simultaneously as a template and a catalyst. It relies on the use of a macrocycle that is capable of immobilizing a template/catalyst within its cavity, such that it promotes an endotopic ring-closing reaction (for catenanes) or coupling (for rotaxanes), resulting in a mechanical bond. A cartoon depicting the concept of an active metal template is shown in **Scheme 1.1**. The elegant dual role of the template means that the metal ion can be used in sub-stoichiometric amounts without compromising yield, and permanent coordination sites need not be built into every component part of the corresponding MIM. Although they are relatively new to the scene, active templates have already been employed[334] in the synthesis of rotaxanes, catenanes, trefoil knots, shuttles, and switches, making use of copper-catalyzed Huisgen terminal azide-alkyne 1,3-cycloadditions,[333] Glaser terminal alkyne homo-couplings,[332] Ullmann-type



Scheme 1.1 Generalized mechanism of active template synthesis,[334] exemplified by the case of a [2]catenane. (i) A metal catalyst (gold) is bound within the cavity of a macrocycle (blue). (ii) A reagent (red) coordinates the metal within the macrocycle. (iii) A covalent bond is formed catalytically, resulting also in the topological and mechanical bond of a catenane. (iv) The catalyst is regenerated and the catenane is expelled. See **Section 2.4**.

C–S couplings,[332] Cadiot-Chodkiewicz alkyne heterocouplings,[335] as well as Pd- and Ni-mediated homocouplings,[336,337] Ni-catalyzed sp^3–sp^3 homocoupling of unactivated alkyl bromides,[307,338] oxidative Heck cross-couplings,[339] Michael additions,[340] Diels-Alder reactions,[341] and Goldberg amidations.[342] See **Section 2.4** for a review of active template strategies. This new method of making mechanical bonds is undeniably versatile and elegant.

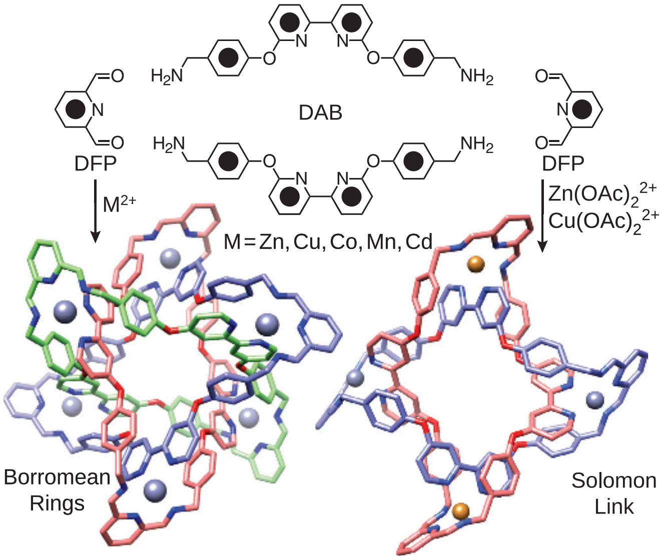
1.3.5 Complexity and Emergence

Opposite the pleasure of comprehension, harmony, and tidiness that goes with the topics of simplicity and elegance is the pleasure of surprise and learning that accompanies the related concepts of complexity[343,344] and emergence.[345–348] Since complex systems are inherently difficult to understand, beauty must be sought in tension and challenge rather than simplicity and harmony. Emergence, however, is immediately pleasing when we encounter it: the 'Eureka' moment, the recognition that the whole is greater than the sum of its parts, that the output could not be predicted by inspection of the input. Emergence arises out of complexity—it is the diamond at the bottom of a dark mine.

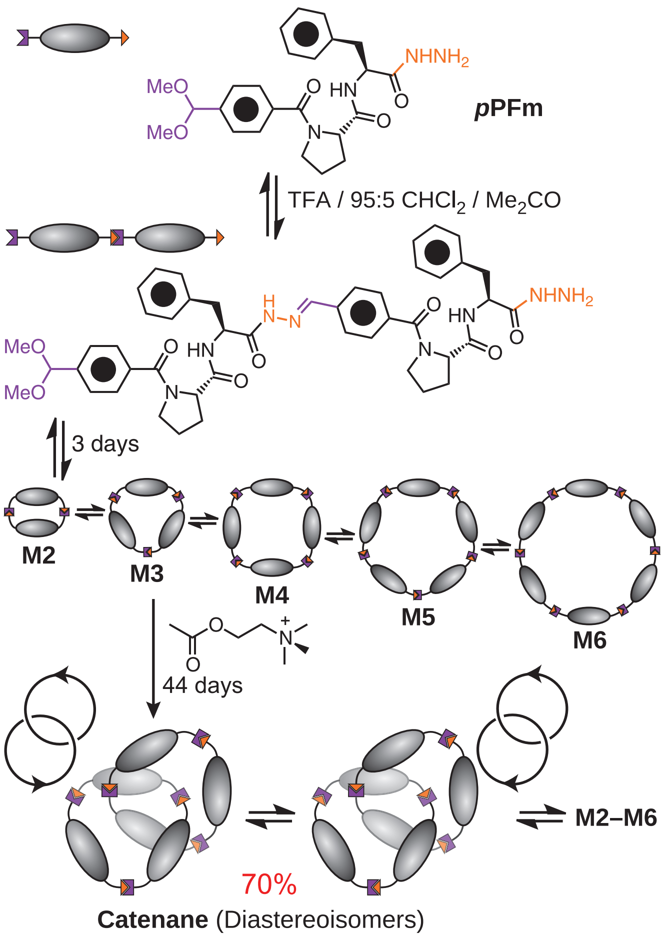
We are in danger of conflating 'complex' with 'complicated'. While there is undoubtedly beauty to be found in both, in science they have different meanings. Complexity is related to chaos—dynamic, non-equilibrium, and practically unpredictable phenomena. Chaos theory was borne out of meteorology and mathematics and is conceptually (and hypothetically) demonstrated by the famous "butterfly effect," a metaphor coined by Lorenz[349] which questioned if the flap of a butterfly's wings could trigger catastrophic weather weeks later and many miles away. Complexity and chaos is a growing and highly multidisciplinary field of research, characterized by systems that are highly sensitive to variations in initial conditions. By contrast, 'complicated' only refers to things that are, well…complicated—something with many parts or intricacies, perhaps. Again we find ourselves in muddy waters, where we must admit that there is a prominent subjective air to this business of complexity and emergence. What is complex to one person might seem only complicated to another, wiser person. What is emergent now will not be emergent in 100 years when it is more deeply understood. For example, the literature is sprinkled with tales of serendipity—unexpected discoveries of mechanical bonds in reactions that were intended for other purposes. Among the most famous of these allegories are the fortuitous discoveries of hydrogen-bonded catenanes of the neutral variety—see **Figure 1.22** and **Section 2.3.4.1**. Hunter's seminal synthesis[211] of a tetralactam [2]catenane was an unexpected result of an attempt to make a simple macrocycle. Likewise, Leigh's first benzylic amide catenane was isolated[131] serendipitously as the unexpected product of a reaction intended to prepare a macrocyclic host for CO_2. These stories reflect the subjective and temporal dependence of discovery and knowledge—although they were unexpected at the time of their discovery, these hydrogen-bonded molecular recognition systems are now well understood and employed with high frequency and success in mechanostereochemistry. Today, few would argue that they are extraordinary in terms of emergence and complexity. On the other hand, Whitesides[343] has noted that even the simplest organic reactions are complex when considered rigorously—substrates can adopt an unlimited number of conformations and reactants have an enormous variety of interactions with solvent molecules, ions, other reactants, and so on. Hence, chemistry is an empirical science. We understand these truly complex reactions by correlating structure and reactivity in the light of lots of data. In this sense, emergence might be an area of chemistry where our data is too incomplete to give us a reliable understanding of structure-response relationships. With this disclaimer, we share a few examples that we find of emergence in mechanostereochemistry.

A promising arena for observing emergent phenomena is dynamic combinatorial chemistry[350] (DCC), which involves a pool of molecules interacting through reversible covalent bonds. Often, preferred species in the dynamic combinatorial library (DCL) of these reactants can be selected and/or amplified under certain experimental conditions, such as the addition of a template or a change in solvent polarity or temperature. It can take days or weeks for a DCL to reach equilibrium and pass through an array of complex and emergent structures. Even at equilibrium, DCLs can easily be complicated, even complex or chaotic when they are highly sensitive to initial conditions. Sanders[351] demonstrated (**Scheme 1.2**) this idea beautifully in 2005, when he reported a DCL composed of a peptide (*p*PFm) that equilibrates over three days into a variety of macrocyclic oligomers ranging in size from a dimer (**M2**) up to a hexamer (**M6**), yet a more elaborate [2]catenane comprising two 42-membered **M3** rings is formed as the dominant species in the presence an acetylcholine additive, if given enough time to equilibrate—see **Section 3.3.2**.

Another possible case[325] of emergence (**Scheme 1.3**) is the fortuitous isolation of a Solomon Knot from the same pool of precursors employed in the self-assembly of the molecular Borromean Rings. Whereas a dynamic combinatorial library (DCL) of 2,6-diformylpyridine (DFP) and 2,2´-bipyridine derived diamine (DAB) ligands leads to the self-assembly[237,328] of molecular Borromean Rings in the presence of several metal templates, including Zn^{II} or Cu^{II}, the unexpected emergence[325] of a doubly-interlocked [2]catenane (Solomon Knot) is observed[325] upon crystallization of a DCL containing an equimolar mixture of Zn^{II} and Cu^{II} templates. The outcome's high sensitivity to subtle changes in initial conditions, with solvent, counterions, and templates all playing an important role in the (not yet well understood) crystallization process indicates a complex interplay of interactions. The crystallization of the Solomon Knot is most likely a kinetically controlled process, since the Borromean rings are the dominant species in solution, and indeed crystals of a Solomon knot possessing only Zn^{II} templates can be hand-separated from the crystals of Borromean rings under different crystallization conditions.[328] More recently, a subtle structural modification to the DAB ligand involving the addition of methylene spacers in between the amino and bipyridine moieties was found to lead to the simultaneous self-assembly[352] of a [2]catenane, trefoil knot, and Solomon knot in one pot, providing further evidence for the complexity of the equilibrium governing the formation of these molecular topologies.

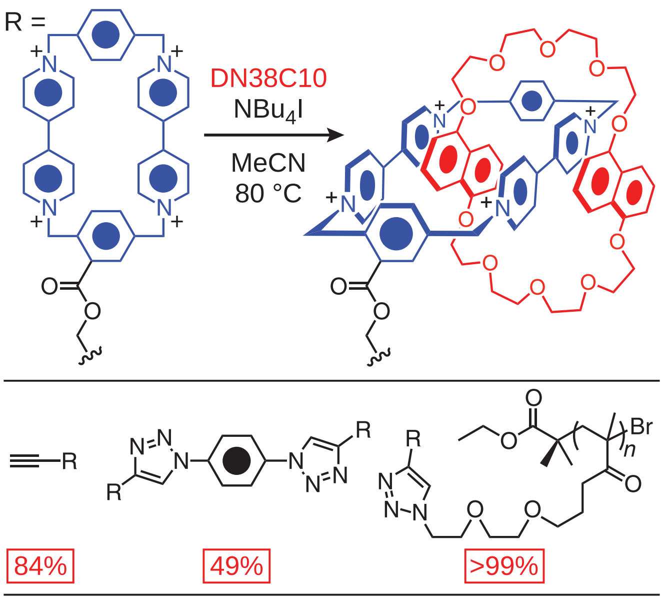


Scheme 1.3 The self-assembly of molecular Borromean Rings[237,328] from a dynamic combinatorial library (DCL) containing DFP and DAB ligands with divalent metal combinatorial library (DCL) of 2,6-diformylpyridine (DFP) and 2,2´-bipyridine derived diamine (DAB) ligands leads to the self-assembly[237,328] of templates, as well as the unexpected emergence of a Solomon Knot[325] upon crystallization of a DCL containing a 1:1 mixture of Zn^{II} and Cu^{II} templates. Tubular representations of solid-state structures are illustrated with protons, counterions, and solvent molecules omitted for the sake of clarity.



Scheme 1.2 Sanders' dynamic combinatorial library based on the reversible imine bonds of the dipeptide building block *p*PFm, which yields mainly oligomeric macrocycles (**M2–M6**) until an acetylcholine template is added, which selects and amplifies an exquisite hexameric [2]catenane.[351]

It has been discovered[353] that a polymer can demonstrate emergent phenomena when catenated under thermodynamic control. The previously-developed[312] iodide-catalyzed self-assembly of donor-acceptor [2]catenanes has been applied to a polymerizable monomer containing a derivative of cyclobis(paraquat-*p*-phenylene) (CBPQT^{4+}) in 84% yield. When dimerized, the catenation proceeds in an unsurprising 49% yield. However, when the catenation is performed on the poly-CBPQT^{4+} compound, the reaction unexpectedly proceeds (**Scheme 1.4**) to >99% completion. This result[353] has been rationalized by postulating a cooperative,



Scheme 1.4 A polymerized derivative of the tetracationic cyclophane CBPQT^{4+} displays the emergent property of quantitative thermodynamic catenation by iodide-catalyzed self-assembly with the DN38C10 crown ether macrocycle. The analogous monomeric and dimeric species do not react quantitatively.[353]

synergistic templating effect by nearby tetracationic cyclophanes on the backbone of the polymer that are not present in the monomeric and dimeric compounds.

Owing to the ambiguous meanings of complexity and emergence, spectacular examples of emergent phenomena in mechanostereochemisty may abound, or they may be exceedingly rare, depending heavily on one's opinion. Nevertheless, the chemistry of complexity is sure to become a busier and ever more pleasing avenue that chemists will continue to traverse.

1.3.6 Beautiful Machines with Mechanical Bonds

Humanity has beautified machines since at least the time of the European Renaissance—as exemplified by the fusion of art and natural philosophy (the forerunner to modern science) in the manuscripts of the one and only Leonardo da Vinci—and probably for almost as long as machines have existed. Countless modern marketing campaigns are aimed at portraying the beauty of machines—automobiles, timepieces, electronic devices, and so on—in order to gain business. Molecular machines, such as the protein-based enzymes and assemblies that carry out life-sustaining nanoscopic work inside of cells, are perhaps the most beautiful machines of all because they were crafted by Nature over billions of years of evolution to express astonishing feats of mechanical work and motion against the enormous chaotic thermal fluctuations that dominate objects on the nanoscale, embodied by the "wiggles and jiggles" known as Brownian motion.[354,355] One of the most compelling aspects of MIMs is that their architectures are well suited for designing artificial molecular switches and machines. See **Chapter 6**. The motion of one component part relative to another can often be controlled by an external stimulus in bistable and multistable MIMs. The fact that MIMs can express these mechanical motions in response to an influx of energy is the reason why they are often referred to as "molecular machines" or "motor molecules", though it would be more accurate to call most of them switches unless the motions are harnessed to do work.

The ring of a catenane or rotaxane can be shuttled (**Figure 1.33**) from one site to another under the influence of a wide variety of stimuli, including redox, light, pH, cations, anions, solvents, covalent reactions, temperature, molecular recognition, pressure, and mechanical force. Seminal examples[175,356–365] of molecular switches employing these stimuli are illustrated in **Figure 1.33**, representing another case of beauty in diversity. In more recent years, a number of important examples[188,366–369] of mechanically interlocked systems expressing biased, mechanostereoselective, or "unidirectional" motion have been described, as well as a number of molecular ratchets that exhibit[369–376] energetically demanding and entropically unfavorable transport—see **Section 6.15.2**. These molecules are setting the foundation for artificial molecular machines that can perform complex tasks more akin to biological molecular machines. Reviews and monographs on the subject of mechanically interlocked molecular machines, such as switches and motors, are abundant in the literature.[377–396]

A car that doesn't start or a computer that doesn't boot up are machines that many people would more likely describe as 'useless' rather than 'beautiful'. Likewise, molecular switches that simply bump around and tumble randomly in solution aren't very useful—they must carry out a functional task to be considered machines in the true sense of the word. Thus, the most beautiful molecular machines are those that we put to work for us. One of most promising strategies for garnering function from artificial molecular machines is to organize them at interfaces or in bulk.[397–400] See **Sections 6.14** and **Section 6.15.1**. Here we highlight several noteworthy examples of molecular machines that go beyond being simple switches.

Wouldn't it be amazing if the tiny nanomotions of artificial molecular machines could be cooperatively scaled up to do work on macroscopic objects? Nature has implemented this strategy in muscle tissue, where the chemically driven mechanical motions of molecular machines known as myosin are scaled over many orders of magnitude, courtesy of their integration within a hierarchically organized material comprising bundles of aligned filaments. Rotaxanes have been recognized[180,288–291] for their ability to express muscle-like extensile and contractile motions. Furthermore, some single-molecule investigations[401,402] of switchable rotaxanes by force spectroscopy have shown unequivocally that they are capable of generating force, even against an external load, an observation which bodes well for the future of artificial molecular machines.

An enticing demonstration[403–405] of the possibility of doing macroscopic work with mechanically interlocked artificial

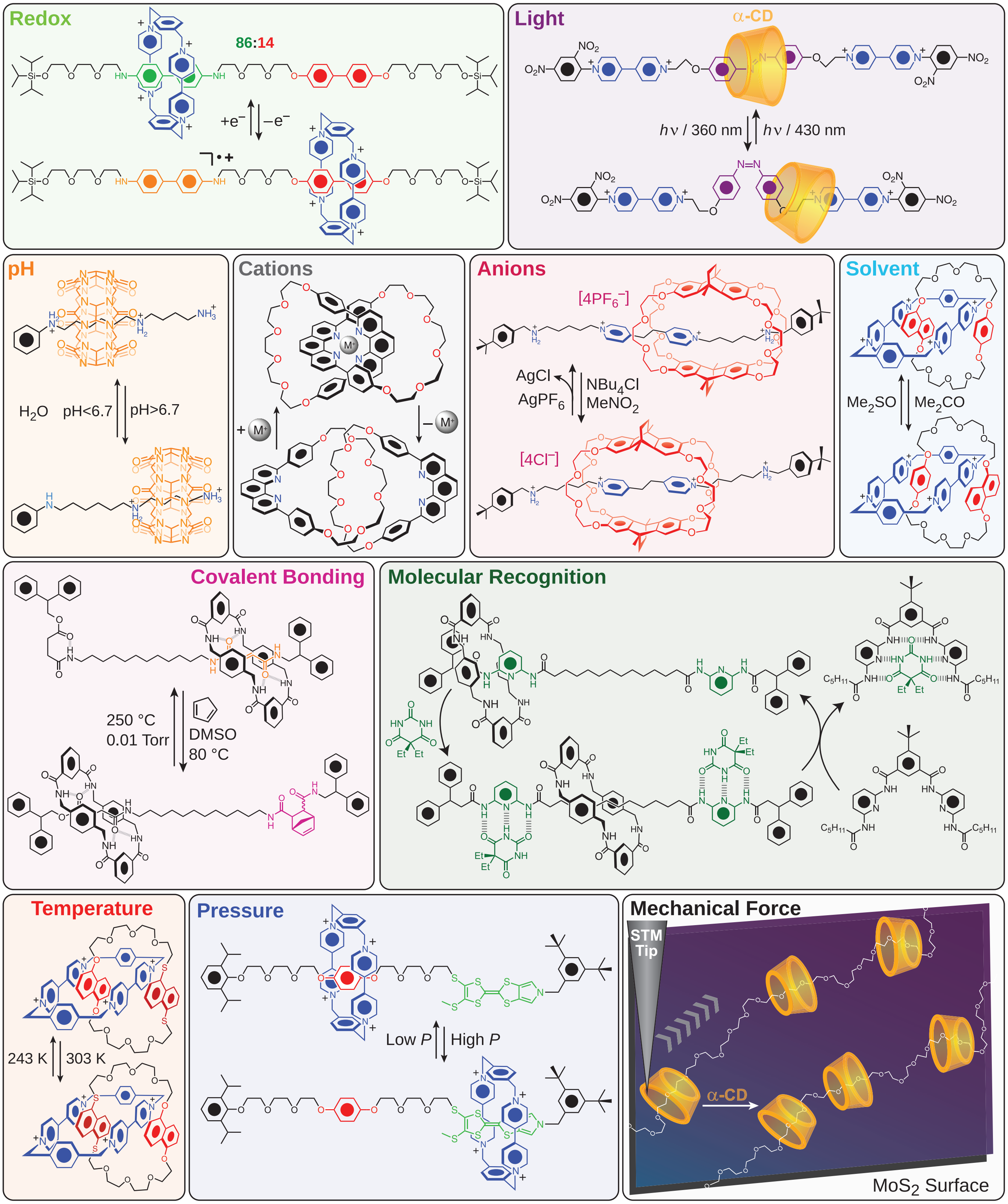


Figure 1.33 Beauty in diversity. Different types of stimuli that drive mechanically interlocked molecular switches include redox,[175] light,[356] pH,[357] cations,[358] anions,[359] solvent,[360] covalent bonding,[361] molecular recognition,[362] temperature,[363] pressure,[364] and mechanical force.[365]

molecular machines been devised by immobilizing zillions of redox-switchable, palindromic bistable [3]rotaxane 'molecular muscles' on the surface of a thin gold-coated microcantilever. Remarkably, the chemical or electrochemical redox actuation (**Figure 1.34**) of these anchored molecules bends the cantilever up and down, a movement that can be detected with a laser beam focused on its surface. Although it remains below the macroscopic scale, this experiment demonstrates that energy can be transduced and work can be done by molecular switches organized at an interface. More recently, Giuseppone[406,407] has demonstrated that the concerted acid/base actuation of bistable [*c*2]daisy chain monomers embedded in a long metallosupramolecular polymer can change its countour length by several microns—orders of magnitude greater in scale than the individual switches embedded in the backbone, and that aggregates of hydrogen-bonded [*c*2]daisy chain supramolecular polymers exhibit very different morphologies when the monomers are in the contracted and extended states. These experiments provide a strong proof-of-concept that rotaxanes are capable of serving as artificial muscles—see **Section 6.15.1.2**.

Leigh[408] described an experiment in 2005 that also utilizes molecular switches to transport (**Figure 1.35**) a macroscopic droplet across a surface. Bistable rotaxanes were physisorbed onto a surface and irradiated with UV light, which led to the photoisomerization of an olefin in a

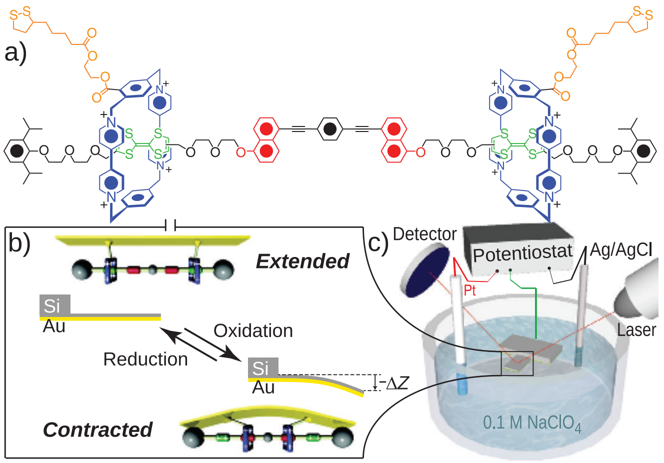


Figure 1.34 Electrochemically driven mechanical actuation of a gold-coated microcantilever by bistable [3]rotaxane 'molecular muscles.'[405] (a) Structural formula of a palindromic bistable [3]rotaxane with gold-binding dithiolanes attached to the rings. (b) Graphical representation of the reversible bending of a cantilever by actuation of a self-assembled monolayer (~8 billion molecules) of the rotaxanes on its surface. The rotaxanes 'contract' when stereoelectronic changes induced by redox stimuli cause them to glide in opposite directions. (c) Diagram of the electrochemical cell (Ag/AgCl, Pt, and the cantilever are the reference, counter, and working electrodes, respectively) and combined AFM device used to measure the bending by detecting a laser beam reflected off of the cantilever's surface. Adapted with permission from ref. 33 (copyright 2012 Springer)

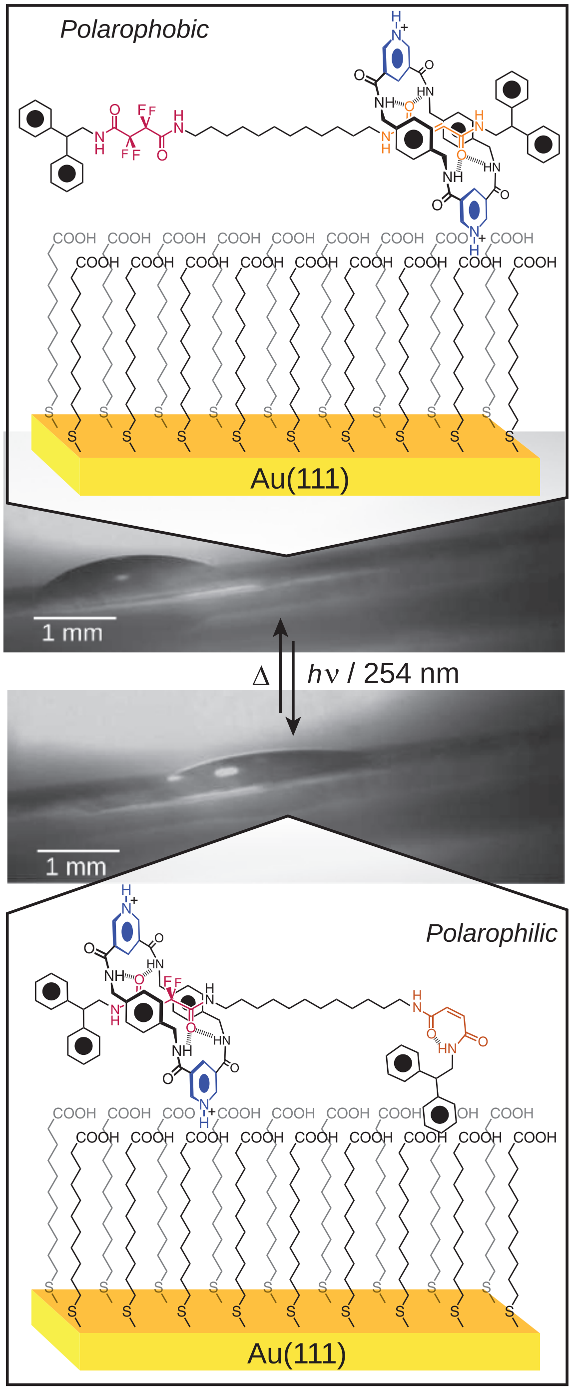


Figure 1.35 Light-driven transport of a diiodomethane droplet up a 12° incline on a Au(111) surface coated with a SAM of 11-mercaptoundecanoic acid and physisorbed, photoswitchable bistable [2]rotaxanes.[408] In the ground state (top), the ring preferentially encircles an unfluorinated fumaramide recognition site and the exposed tetrafluorosuccinamide recognition site contributes to the polarophobicity of the surface. When a light beam focused on one side of the droplet causes some of the fumaramide (*trans*-olefin) units to isomerize to maleamide (*cis*-olefin), the ring within this population of the photostationary state shuttles to encircle the fluorinated recognition unit (bottom), which decreases the surface polarophobicity and causes the droplet to move several millimeters uphill. Photographs reprinted with permission from ref. 408 (copyright 2005 Nature Publishing Group)

population of the rotaxanes and caused the ring to shuttle over to a fluorinated recognition site, which in turn changed the polarophobicity of the surface. Photoswitching the surface in this manner underneath one side of a diiodomethane droplet causes it to move several millimeters up a 12° incline.

Now for a bit of science fiction: what if single molecules could be utilized to perform logic operations or store information, like transistors? A joint effort toward this end between ourselves and Heath,[409–416] which addressed the organization and electrochemical actuation of bistable donor-acceptor MIMs as molecular monolayers within crossbar interfaces known as molecular switch tunnel junctions (MSTJs), culminated[416] after a decade in a high density memory device (**Figure 1.36**) in 2007. The monolayer of bistable rotaxanes was incorporated into a crossbar logic architecture (**Figure 1.36c**) in a size regime corresponding to little more than 100 molecules per junction. Actuation of the bistable switches in these MSTJs validated them as storage elements; about 25% of the bits had sufficient on/off ratios to be configured into a device. The resulting 160-kilobit memory circuit had a density of 10^{11} bits·cm^{-2}, for a total memory cell size of 0.0011 mm^2, which is approximately the cross-sectional area of a white blood cell (**Figure 1.36d**). A memory circuit of these dimensions is roughly on par with that of a storage density projected[417] to be available in 2020 if Moore's Law continues to be obeyed.

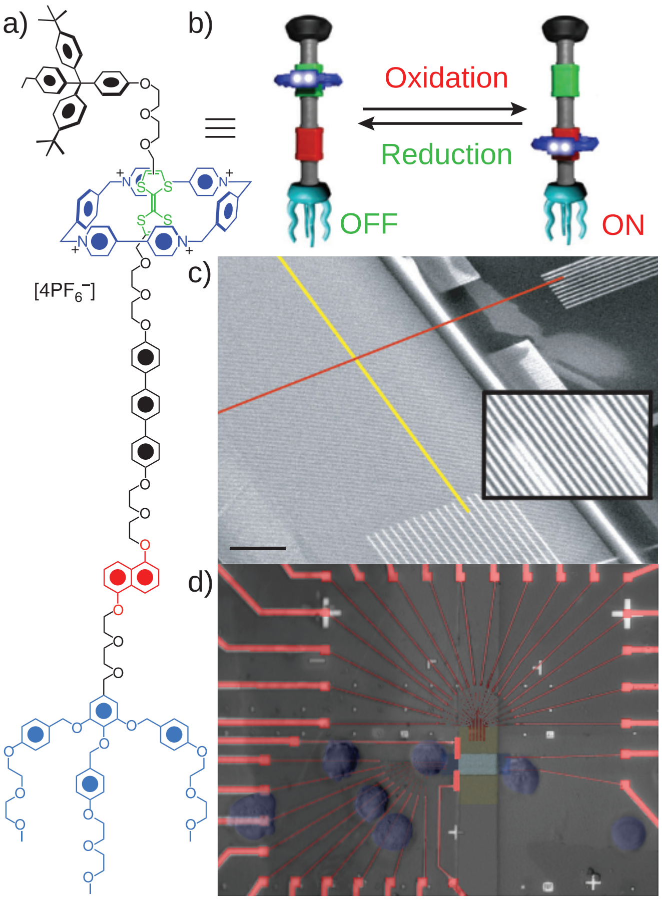


Figure 1.36 A 160-kbit molecular electronic memory device.[416] (a) Structural formula of the molecular switches used in the device. (b) Technomorph representations depicting how the molecular switches can be electrochemically toggled "on" and "off" in the device into co-conformational states with different conductivities. (c) SEM image of the intersection between top (red) and bottom (yellow) electrodes for the MSTJs. (d) Microscopic image of the memory device (blue area) and its electrical contacts (red) with white blood cells (green) as a reference of scale. Reprinted with permission from ref. 33 (copyright 2012 Springer)

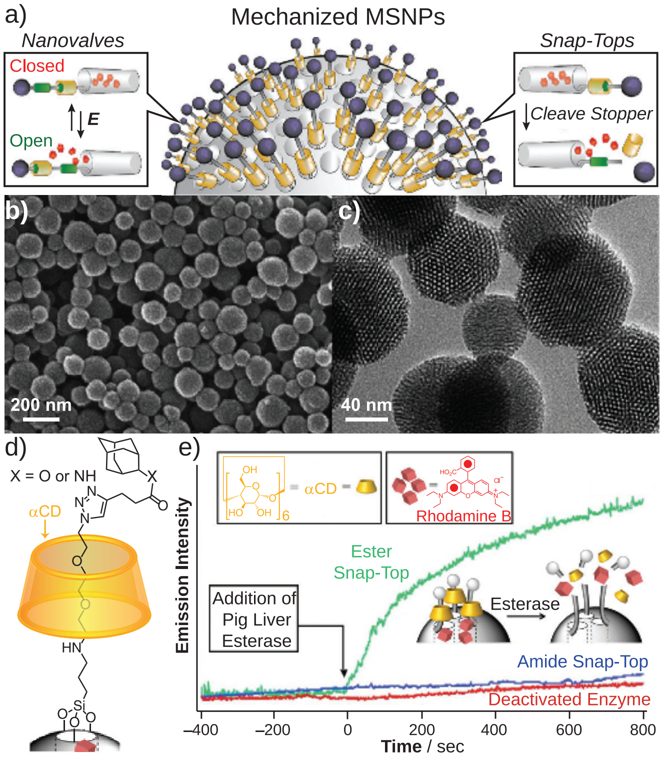
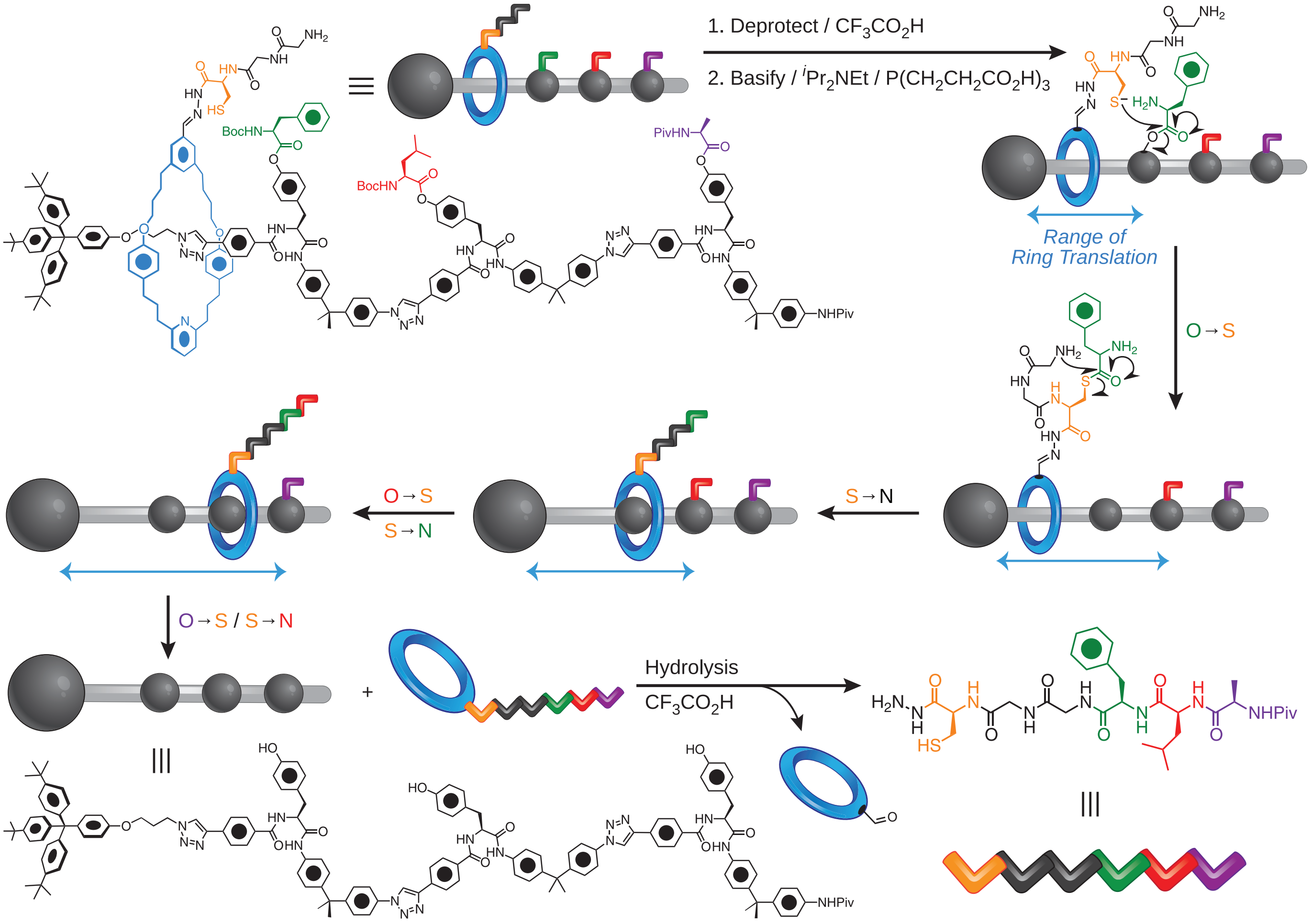


Figure 1.37 Examples of mechanized mesoporous silica nanoparticles (MSNPs).[418–420] (a) Illustrations of the functions of rotaxane nanovalve and snap-top mechanisms for controlled release of cargo.[394] (b) SEM image of MSNPs. (c) TEM image of MSNPs.[418] (d) Structural formula of an α-cyclodextrin (αCD)-based snap-top rotaxane blocking the pores of a MSNP. The stopper is connected to the axle by an amide bond or an enzyme-cleavable ester bond. (e) Release profile of rhodamine B from the snap-top MSNPs.[449] The addition of pig liver esterase decomposes the mechanical bond by cleavage of the ester-linked stopper, which releases αCD and hence the cargo from the nanoparticles, an outcome which is monitored by the fluorescence intensity of rhodamine B. Controls employing an amide bonded snap-top or deactivated enzyme do not release significant amounts of cargo from the MSNPs. SEM and TEM images reprinted with permission from ref. 418 (copyright 2009 Royal Society of Chemistry), release profile adapted with permission from ref. 449 (copyright 2008 American Chemical Society)

The question inevitably arises: can we build artificial molecular machines that are "smart" enough to respond to signals within our bodies, releasing therapeutic drugs or diagnostic contrast agents, for example, only at a localized and desired site? Once again, reality is not so far from the dream. A number of research groups are developing a variety of "mechanized nanoparticles"[418–420] (**Figure 1.37**)



Scheme 1.5 Sequence-specific peptide synthesis by a rotaxane artificial molecular machine.[454] The ring adds monomers to the end of its peptide sidechain by a series of native chemical ligation reactions, the sequence of which is defined by the sequence of monomers confining the ring to the rotaxane's dumbbell.

with these applications in mind. Efforts thus far have been associated chiefly with the covalent functionalization of supramolecular and molecular switches on the surfaces of mesoporous silica nanoparticles[421] (MSNPs, **Figure 1.37b–c**) that can act as stimulus-responsive (**Figure 1.37a**) gates to the nanopores.[422,423] Since 2004, bistable rotaxanes and pseudorotaxanes at the surface of these nanoparticles have been demonstrated over and over again to release cargo selectively from MSNPs in response to changes in pH,[179,424–434] light,[435–442] redox stimuli,[183,443–446] and salt concentration,[447] as well as in oscillating magnetic fields[448] and as a result of the introduction of specific enzymes[449,450] or small molecules.[451–453] **Figure 1.37d–e** provides one example[449] of how these mechanized nanoparticles operate, depicting the release profile of 'snap-top' rotaxane-gated MSNPs that are activated with an enzyme to release their internal cargo. One of the pH-responsive systems has been shown to work autonomously to release cargo *in vitro*,[429] making these materials highly promising candidates as drug delivery vehicles. The large number of examples produced in a relatively short time span signifies these nanocarriers as useful, beautiful applications of artificial molecular machinery. See **Section 6.15.1.1**.

With the exception of muscles, most of Nature's machines do their work on the nanoscale. A particularly important apparatus is the ribosome—the large, complex protein assembly responsible for reading the information encoded in messenger RNA and synthesizing the corresponding polypeptide chains that fold into proteins. Leigh[454] has constructed an artificial molecular machine that relies intimately on the mechanical bond to perform the ribosome-like task (**Scheme 1.5**) of synthesizing an oligopeptide chain in a sequence-specific manner. The machine is constructed by a combination of active template synthesis and Cu^I-catalyzed azide-alkyne cycloaddition (CuAAC) click chemistry to display a short cystine–glycine–glycine peptide sequence appended by a hydrazone linkage to a ring, which encircles a dumbbell possessing a pre-defined sequence of protected, phenolic ester-linked monomers, each separated by a rigid spacer. Once assembled, the machine is set into action by acidic deprotection of these reactive monomers, as well as by the addition of a non-nucleophilic base, which facilitates a reaction known as native chemical ligation[455] (NCL), wherein (i) the dumbbell's peptide monomer in closest proximity to the ring is captured by trans-acylation to the thiolate site of the ring's reactive cystine residue, resulting in a thioester, which (ii) undergoes S→N shift, transferring the peptide monomer to the *N*-terminal residue, or "elongation site", at the end of the ring's peptide chain. Sequence specificity arises from the fact that each monomer displayed by the dumbbell acts as a stopper, forbidding the passage of the ring until it is cleaved, thus preventing any amino acids from being transferred to the elongation site out-of-turn. After the ring has picked up all three of the dumbbell's monomers by this sequential O→S / S→N acyl transfer process, it is no longer constrained by a mechanical bond and is therefore free to diffuse away from the dumbbell. The oligopeptide chain can then be isolated by hydrolysis of the hydrazone bond. Several limitations prevent this machine from competing with solid-phase peptide synthesis or the ribosome—long timescales (~12 h / peptide), short sequences limited to only a few amino acids, and loss of sequence information after it is "read" and "written". Despite these limitations, this ingenious piece of exquisite chemistry, which has been praised for its likeness to a Turing machine,[456] an automated peptide synthesizer,[456,457] and indeed the ribosome,[457,458] represents a major landmark for molecular machines and the mechanical bond.

The beauty of employing controlled molecular mechanical motions to do work and perform technologically important functions is similar to that of technomorphic representations (**Section 1.2.6**) in the sense that it draws a connection between the molecular and macroscopic worlds. Artificial molecular machines remind us of the classical machines we know and use every day, although they operate under completely different principles on account of the enormous thermal fluctuations that lead to Brownian motion on the molecular size scale. The tension between these two worlds presents a challenge that has led chemists to respond with creative, often bio-inspired solutions to operating machines at low Reynolds number. At the same time, the awesome molecular machinery of the cell has provided inspiration for the first artificial molecular machines that can perform complex tasks on the nanoscale, building a beautiful bridge between the synthetic and natural worlds.

1.3.7 The Art of the Mechanical Bond

We consider many of the figures and schemes of MIMs in the primary literature to be artwork in and of themselves, yet even more deliberate artwork inspired by MIMs has been created for journal covers and graphical abstracts over the years, along with the occasional work of art for arts' sake. We have curated a collection of over 100 cover art images in **Appendix A** paying tribute to publications that have been featured on journal covers on topics related to the mechanical bond. The large number and diversity of these titles reflects the interdisciplinary nature of the field and the highly creative and immensely productive attributes of its practitioners. Paintings (**Figure 1.38**) by Mike Thompson, which decorate the walls of the Evanston laboratory, are inspired directly by the topological beauty of mechanomolecules.

We do not need any convincing that the mechanical bond is indeed "a work of art". Although it is framed mostly outside the bounds of any formal aesthetic framework, molecular beauty is very much a part of chemists' experience. At the end of the day, MIMs are beautiful because they are researched by hard-working, passionate people who cannot help but to take pleasure in their work. We find beauty in many aspects of the mechanical bond, from its prevalence in nature (**Section 1.1.1**), art (**Section 1.1.2**), and daily life (**Section 1.1.3**), to the pleasure of building new supramolecular (**Section 1.3.1**) and molecular topologies (**Section 1.3.2**) and architectures (**Section 1.3.3**), to the appeal of elegant new protocols (**Section 1.3.4**), the prospect of uncovering complex and emergent phenomena (**Section 1.3.5**), not to mention the remarkable potential and functional utility of molecular switches and

Figure 1.38 MIM-inspired paintings by Mike Thompson.

machines (**Section 1.3.6**). At the same time, many chemists are surely artists at heart, sculpting molecules instead of clay, synthesizing masterpieces instead of painting them, even demonstrating a knack for visual presentation as evidenced by the development of new graphical modes (**Section 1.2**) of communication, such as the cartoons and technomorphs that simultaneously aid in communication and stimulate innovation. Roald Hoffman[197] has commented, "*It never ceases to amaze me how a community of people who are not talented at drawing, nor trained to do so, manages to communicate faultlessly so much three-dimensional information.*" We add to this comment our amazement at the beauty such images can bear, and their ability to draw connections between molecules and classical objects. Whether we speak of images, topologies and architectures, experimental elegance, or functional novelty, the research associated with mechanical bonds is indeed a pleasing, beautiful, and rewarding line of work.

1.4 Evolution of Mechanostereochemistry

We close this introductory Chapter with a perspective and brief assessment of the growth and development of the field of chemistry that deals with mechanical bonds—or, as we call it—mechanostereochemistry.[16,17] Without a doubt, the mechanical bond will continue to evolve. We believe that the publication of this book is timely because the evolution of MIMs appears to be approaching a turning point. The evolutionary tree is no longer a sapling as it enters a new stage of life. Soon it will not be possible to consolidate the diverse aspects of the mechanical bond in chemistry into a single volume. Consider the degree to which the field is growing (**Figure 1.39**)—the histograms tracking the approximate number of publications[F] (**Figure 1.39a**) and literature citations (**Figure 1.39b–c**) on the topic of catenanes and rotaxanes on a year-by-year basis reveals that the number of articles published in this field each year has undergone steady and linear growth for over two decades, beginning around 1990. At the close of 2015, there were well over 3000 publications and almost 100,000 citations related to catenanes and rotaxanes in chemistry. The journals with 10 or more publications indexed under the keywords 'catenane' or 'rotaxane' at the close of 2015 are ranked in **Figure 1.40**, with general chemistry journals such as the *Journal of the American Chemocal Society*, *Angewandte Chemie*, and *Chemical Communications* dominating the spread, in a testament to the interdisciplinarity of the field. Geographically, the publications on mechanical bonds originate (**Figure 1.41**) from all around the world: Japan and the United States are in close contention to be the most active countries in this particular field of research, with the UK and China not far behind. In spite of this evidence for a remarkable worldwide interest in mechanical bonds at the molecular level, we note that the whole of mechanostereochemistry is underrepresented in our statistics, since mechanical bonds are prevalent in many synthetic compounds (**Section 4.3**) and biomolecules that lie beyond the scope of catenanes and rotaxanes.

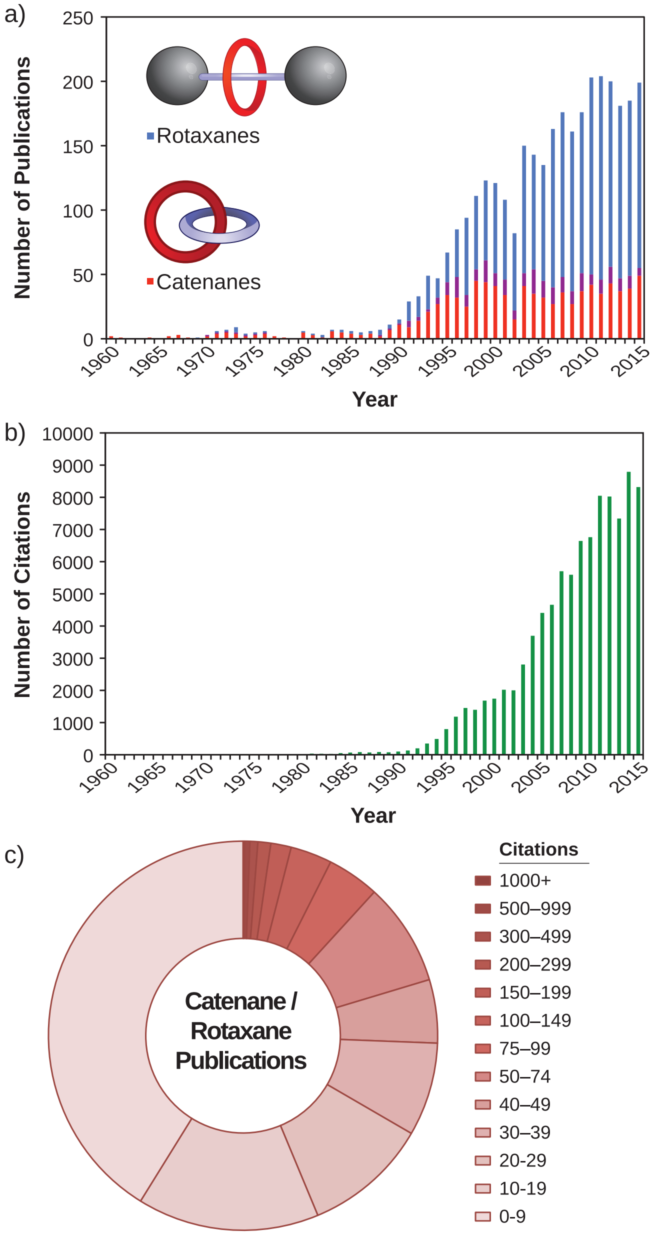


Figure 1.39 Statistics on journal publications indexed under the keywords, catenane or rotaxane. Histograms indicate the approximate number of (a) publications (total >3000) and (b) citations (total ~100,000) per year, from 1960 to 2015. Purple regions correspond to articles indexed under both keywords. The distribution of citations among these articles at the close of 2015 is represented by (c) a donut chart visualizing the proportionation of publications garnering different citation ranges. Citation counts are taken from Thomson Reuters Web of Science on 3 Jan 2016.

Another way to put perspective on the field is to look at the rhetoric of the literature in a time-resolved manner. The

---

[F] Publications were tabulated in Scifinder (www.scifinder.com) using the keywords 'catenane' and 'rotaxane'

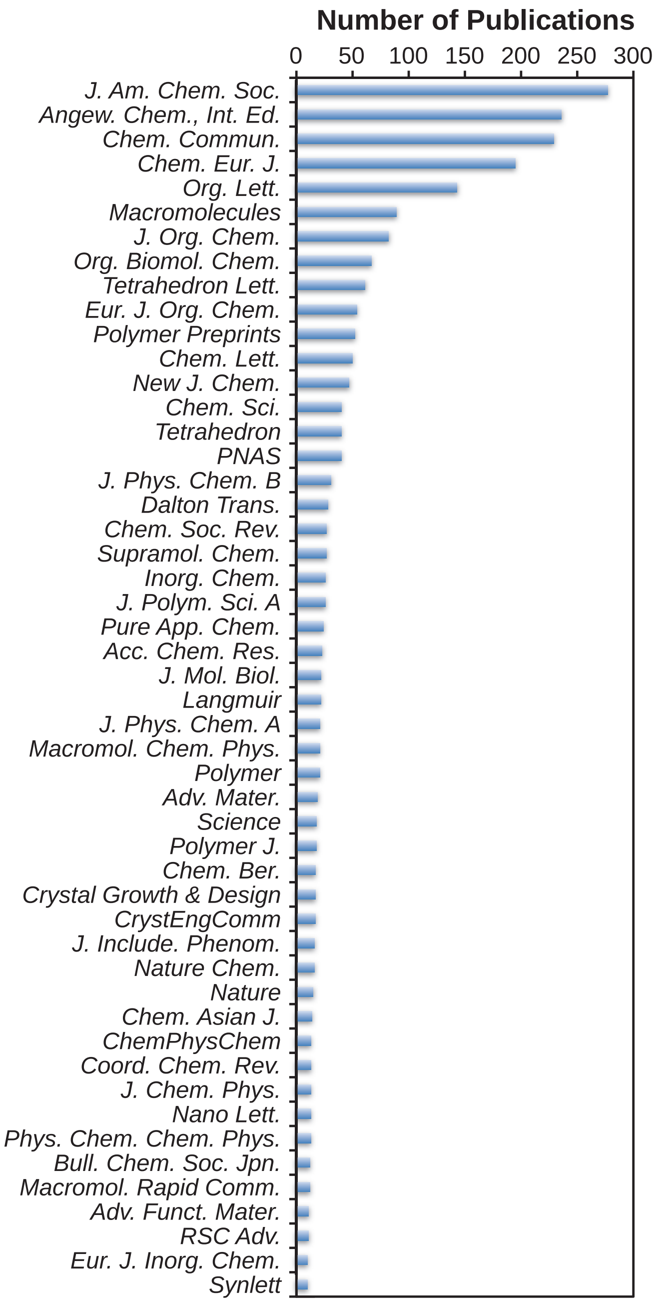


Figure 1.40 A comparison of international journals with 10 or more publications indexed under the keywords, catenane or rotaxane, at the end of 2015.

artwork[G] in **Figure 1.42** portrays words that are scaled according to their frequency of appearance in the abstracts of the most highly cited papers from different eras of the mechanical bond. These eras are divided into four time periods: Pre-1990, 1990–1999, 2000–2010, and 2010–2015. Some trends can be identified by careful inspection of the most frequently used words during these eras. Prior to 1990, the prominence of words such as copper, catenate, catenand, and ligand reveal that the early literature prior to the boom of research beginning in 1990 was dominated by Sauvage's work on metallo-catenanes and rotaxanes. In the 1990s, words such as assemble, self-assembly, complex, and supramolecular become much more visible, reflecting the novel template-directed synthetic methods based on supramolecular chemistry which became a high priority. In the 2000s, we can see words such as systems, control, machine, device, movement, and switch come into the limelight, suggesting

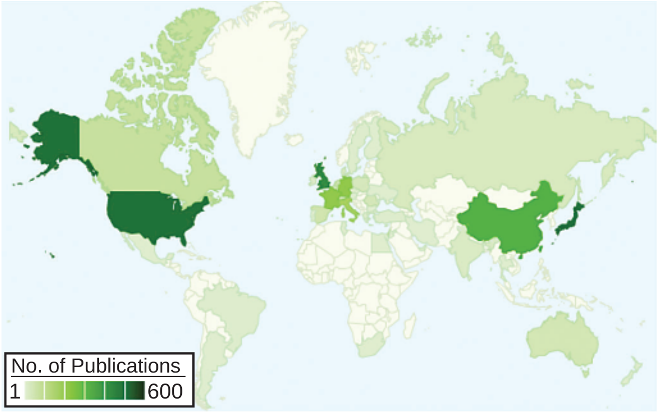


Figure 1.41 The distribution of publications indexed under the keywords, catenane or rotaxane, color-scaled on a world map according to country of origin.

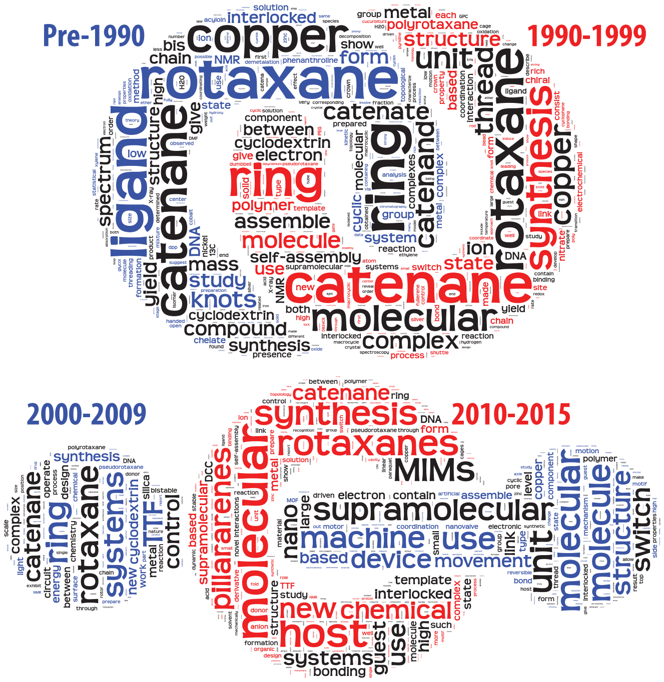


Figure 1.42 Word art based on abstracts from the most highly cited papers from various eras in the life of the mechanical bond. Each catenane or rotaxane component part is color-coded with respect to labels designating to which era the set of words belongs. Words are scaled according to the frequency with which they appear in the highly cited literature.

[G] These word art images are based on the first ~10,000 words to appear in abstracts, ranked in order of citation frequency for papers matching the keywords *rotaxane* or *catenane*.

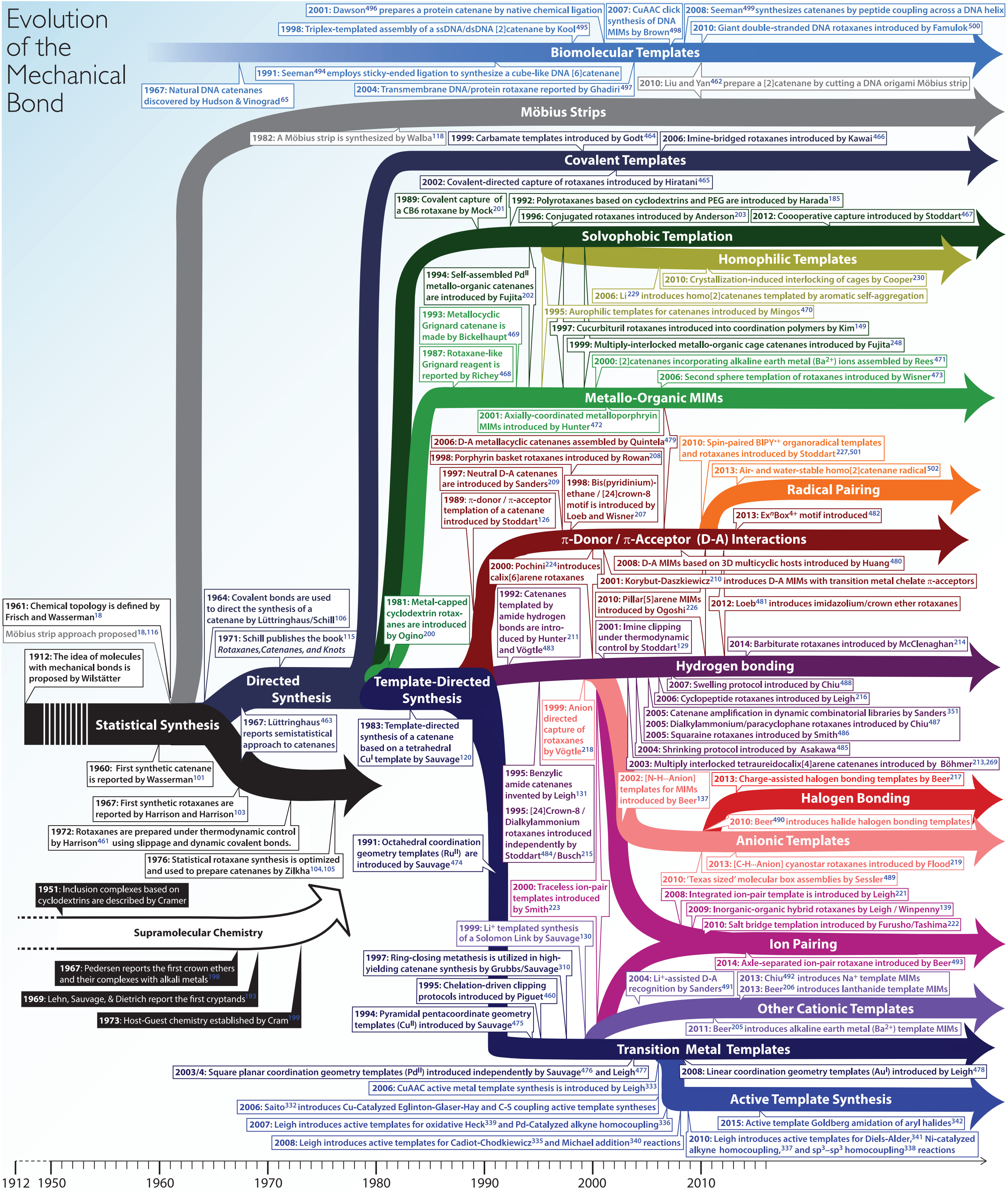


Figure 1.43 A time-resolved evolutionary tree, highlighting milestones and differentiation events in the synthesis of molecules with mechanical bonds and entanglements. See **Chapters 2–3**. A magnifying glass is prerequisite for readers who wish to explore the intricacies of the evolution of the mechanical bond in the molecular world.

that molecular switches were a heavy focus of this time period. Finally, a remarkable spike in research activity has placed pillararenes among the most frequent words in the highly cited abstracts of the current era, though we must wait at least another five years to find out which concepts will truly represent the hot topics of the present decade. An astute observer will notice from the information in the publication histogram (**Figure 1.39a**) and word art (**Figure 1.42**) that rotaxanes have been outcompeting catenanes in terms of research attention. Although much of the seminal work on mechanical bonds was done on catenanes, most of the growth of the field has been driven by rotaxane research. Catenane research, on the other hand, appears to have reached a plateau, at least for the time being. This inequality among the two main types of mechanically bonded molecules may be related to superior synthetic accessibility and potential applications of rotaxanes.

The evolution of the mechanical bond is not unlike Darwinian evolution by natural selection[459]—for example, events of differentiation can be identified in an evolutionary tree (**Figure 1.43**) describing milestones (see refs. 18,65, 101,103–106,115,116,118,120,126,129,131, 137,139,149,185,200–211,213–215,218,219,221–224, 226,227,229,230,248,269,307,310,324,332,333,335, 336,338–342,351,460–502) in the synthesis of mechanical bonds, where new strategies and template motifs have been introduced. An analogy to Darwin's 'survival of the fittest' mechanism for natural selection is also at play in mechanostereochemistry, since the majority of publications related to MIMs are attributable to only a handful of the 'fittest' types of recognition motifs: (i) hydrophobic forces (**Section 2.3.1**), especially those underpinning the supramolecular chemistry of the cyclodextrins and cucurbiturils, (ii) transition metal templates (**Section 2.3.2**), especially those based on copper, (iii) π-donor/π-acceptor templates (**Section 2.3.3**), especially those based on viologens, and (iv) hydrogen-bonded templates (**Section 2.3.4**), especially those based on macrocyclic lactams and crown ethers—which represent approximately 75% of the literature on mechanical bonds. See **Figure 2.87** in the conclusion of **Chapter 2** for a breakdown of the literature by template classification. Some of the newcomers to the field, such as anion binding (**Section 2.3.6**), active template synthesis (**Section 2.4**) and the host-guest chemistry of the pillararenes (**Section 2.3.9.2**), are proliferating rapidly.

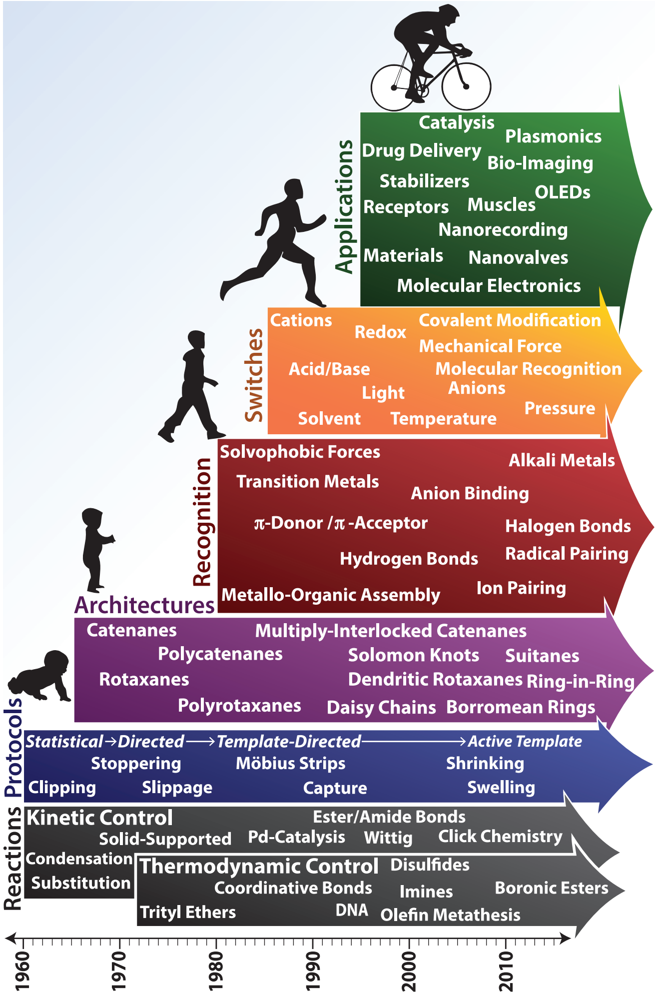


Figure 1.44 Timeline of research on the mechanical bond.

The evolution of the mechanical bond is also captured in a timeline (**Figure 1.44**) showing how molecules with mechanical bonds have 'grown up' from a foundation of synthetic reactions and protocols, through to contemporary devices and applications. In the beginning, synthetic reactions and protocols for making mechanical bonds represented the only kind of research in mechanostereochemistry. As synthetic techniques (**Chapters 2–3**) became more highly developed—the most significant of which was the advent of template-directed synthesis—making mechanical bonds became more and more routine. As MIM synthesis was being mastered, more time and resources became available for the development of new mechanically interlocked architectures (**Chapter 4**), novel types of dynamics, isomerism, and chirality (**Chapter 5**), as well as molecular switches (**Chapter 6**). This stage of research is also reaching maturity, clearing a path for the next stage, which will be associated with artificial molecular machines (**Chapter 6**) and practical applications for mechanical bonds in science and technology. Although progress will continue on all of these fronts, the time is now upon us to cast aside our complacency, forsake our muddling along in solution, and press on to new frontiers—e.g., integrated systems, materials, solid-state chemistry, genuine molecular machinery, non-equilibrium self-organization and dynamics, applications in energy and medicine, complexity and emergence, and so on. We expect that, as the field pushes back these frontiers and others, a compilation of the important discoveries of the past will help to set the stage for this next act.

It is clear to us that the mechanical bond represents a flourishing field of chemistry, to the extent that a completely comprehensive review of the entire body of literature would be next to impossible. We have tried to strike a balance between being as comprehensive as possible in our coverage of topics related to MIMs, with the goal of summarizing synthetic protocols, molecular design motifs, techniques, dynamics, applications, significance, and future directions for the field, yet we have been forced in many cases to select only what we consider to be the most influential research. In this regard, we would be the first to admit that we might have been blind to or ignorant of some pieces of research that will give momentum to the mechanical bond's rise to prominence in chemistry.

References

(1) Pauling, L. *The Nature of the Chemical Bond: An Introduction to Modern Structural Chemistry*; Cornell University Press: Ithaca, **1939**.

(2) Brown, T. E.; LeMay, H. E.; Bursten, B. E.; Murphy, C.; Woodward, P.; Stoltzfus, M. E. *Chemistry - The Central Science*; 13th Ed.; Prentice Hall: Upper Saddle River, NJ, **2014**.

(3) Balaban, A. T.; Klein, D. J. Is Chemistry "the Central Science?" How Are Different Sciences Related? Co-Citations, Reductionism, Emergence, and Posets. *Scientometrics* **2006**, *69*, 615–637.

(4) Venturi, M.; Marchi, E.; Balzani, V. The Beauty of Chemistry in the Words of Writers and in the Hands of Scientists. *Top. Curr. Chem.* **2012**, *323*, 73–106.

(5) Bertozzi, C. R. The Centrality of Chemistry. *ACS Cent. Sci.* **2015**, *1*, 1–2.

(6) Desiraju, G. R. Chemistry: The Middle Kingdom. Resonance **2007**, *12*, 44–60.

(7) Amabilino, D. B.; Ashton, P. R.; Bravo, J. A.; Raymo, F. M.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. Molecular Meccano 52. Template-Directed Synthesis of a Rotacatenane. *Eur. J. Org. Chem.* **1999**, 1295–1302.

(8) Williams, A. R.; Northrop, B. H.; Chang, T.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. Suitanes. *Angew. Chem., Int. Ed*. **2006**, *45*, 6665–6669.

(9) Romuald, C.; Arda, A.; Clavel, C.; Jimenez-Barbero, J.; Coutrot, F. Tightening or Loosening a pH-Sensitive Double-Lasso Molecular Machine Readily Synthesized From an Ends-Activated [*c*2]Daisy Chain. *Chem. Sci.* **2012**, *3*, 1851–1857.

(10) Gan, Q.; Ferrand, Y.; Bao, C.; Kauffmann, B.; Grélard, A.; Jiang, H.; Huc, I. Helix-Rod Host-Guest Complexes with Shuttling Rates Much Faster Than Disassembly. *Science* **2011**, *331*, 1172–1175.

(11) Vajpayee, V.; Song, Y. H.; Cook, T. R.; Kim, H.; Lee, Y.; Stang, P. J.; Chi, K. W. A Unique Non-Catenane Interlocked Self-Assembled Supramolecular Architecture and Its Photophysical Properties. *J. Am. Chem. Soc.* **2011**, *133*, 19646–19649.

(12) Li, S.-H.; Zhang, H. Y.; Xu, X.; Liu, Y. Mechanically Selflocked Chiral Gemini-Catenanes. *Nature Commun*. **2015**, *6*: 7590.

(13) Anelli, P. L.; Ashton, P. R.; Ballardini, R.; Balzani, V.; Delgado, M.; Gandolfi, M. T.; Goodnow, T. T.; Kaifer, A. E.; Philp, D.; Pietraszkiewicz, M.; Prodi, L.; Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Vicent, C.; Williams, D. J. Molecular Meccano 1. [2]Rotaxanes and a [2]Catenane Made to Order. *J. Am. Chem. Soc*. **1992**, *114*, 193–218.

(14) Amabilino, D. B.; Stoddart, J. F. Interlocked and Intertwined Structures and Superstructures. *Chem. Rev.* **1995**, *95*, 2725–2828.

(15) Stoddart, J. F. The Chemistry of the Mechanical Bond. *Chem. Soc. Rev.* **2009**, *38*, 1802–1820.

(16) Olson, M. A.; Botros, Y. Y.; Stoddart, J. F. Mechanostereochemistry. *Pure Appl. Chem*. **2010**, *82*, 1569–1574.

(17) Barin, G.; Forgan, R. S.; Stoddart, J. F. Mechanostereochemistry and the Mechanical Bond. *Proc. R. Soc. A* **2012**, *468*, 2849–2880.

(18) Frisch, H. L.; Wasserman, E. Chemical Topology. *J. Am. Chem. Soc.* **1961**, *83*, 3789–3795.

(19) Sokolov, V. I. Topological Ideas in Stereochemistry. *Russian Chem. Rev.* **1973**, *42*, 452–463.

(20) Walba, D. M. Topological Stereochemistry. *Tetrahedron* **1985**, *41*, 3161–3212.

(21) Dodziuk, H.; Nowiński, K. S. Topological Isomerism: Should Rotaxanes, Endohedral Fullerene Complexes and In-Out Isomers of Hydrogenated Fullerenes Be Considered as Such? *Tetrahedron* **1998**, *54*, 2917–2930.

(22) Siegel, J. S. Chemical Topology and Interlocking Molecules. *Science* **2004**, *304*, 1256–1258.

(23) Fenlon, E. E. Open Problems in Chemical Topology. *Eur. J. Org. Chem.* **2008**, 5023–5035.

(24) Amabilino, D. B.; Pérez-García, L. Topology in Molecules Inspired, Seen and Represented. *Chem. Soc. Rev*. **2009**, *38*, 1562–1571.

(25) Forgan, R. S.; Sauvage, J.-P.; Stoddart, J. F. Chemical Topology: Complex Molecular Knots, Links, and Entanglements. *Chem. Rev.* **2011**, *111*, 5434–5464.

(26) Ashton, P. R.; Philp, D.; Spencer, N.; Stoddart, J. F. The Self-Assembly of [*n*]Pseudorotaxanes. *J. Chem. Soc., Chem. Commun.* **1991**, 1677–1679.

(27) IUPAC. *Compendium of Chemical Terminology;* 2nd Ed. (the "Gold Book"); Compiled by A. D. McNaught and A. Wilkinson. Blackwell Scientific Publications: Oxford, **1997**. XML Online Corrected Version: http://Goldbook.Iupac.org Created by M. Nic, J. Jirat, B. Kosata; Updates Compiled by A. Jenkins. ISBN 0-9678550-9-8.DOI:10.1351/Goldbook.

(28) Jasat, A.; Sherman, J. C. Carceplexes and Hemicarceplexes. *Chem. Rev.* **1999**, *99*, 931–968.

(29) Popov, A. A.; Yang, S.; Dunsch, L. Endohedral Fullerenes. *Chem. Rev.* **2013**, *113*, 5989–6113.

(30) Vostrowsky, O.; Hirsch, A. Molecular Peapods as Supramolecular Carbon Allotropes. *Angew. Chem., Int. Ed*. **2004**, *43*, 2326–2329.

(31) Yoshizawa, M.; Klosterman, J. K.; Fujita, M. Functional Molecular Flasks: New Properties and Reactions Within Discrete, Self-Assembled Hosts. *Angew. Chem., Int. Ed*. **2009**, *48*, 3418–3438.

(32) *Topics in Current Chemistry: Beauty in Chemistry*; Fabbrizzi, L., Ed.; Springer: Berlin Heidelberg, **2012**; Vol. *323*.

(33) Bruns, C. J.; Stoddart, J. F. The Mechanical Bond: A Work of Art. *Top. Curr. Chem.* **2012**, *323*, 19–72.

(34) Wikipedia. *Art*. http://en.wikipedia.org/art (Accessed Dec **2010**).

(35) Pfenninger, K. H.; Shubik, V. R. *The Origins of Creativity*; Oxford University Press: New York, **2001**.

(36) Heisenberg, W. *The Meaning of Beauty in the Exact Sciences*; Anshen, R. N., Ed.; Harper & Row: New York, **1974**.

(37) Spector, T. I.; Schummer, J. Aesthetics and Visualization in Chemistry. *HYLE* **2003**, *9*, 3–6.

(38) Hoffmann, R.; Laszlo, P. Representation in Chemistry. *Angew. Chem., Int. Ed. Engl*. **1991**, *30*, 1–16.

(39) Kretzenbacher, H. L. The Aesthetics and Heuristics of Analogy: Model and Metaphor in Chemical Communication. *HYLE* **2003**, *9*, 191–218.

(40) Laszlo, P. Foundations of Chemical Aesthetics. *HYLE* **2003**, *9*, 11–32.

(41) Schummer, J. Aesthetics of Chemical Products: Materials, Molecules, and Molecular Models. *HYLE* **2003**, *9*, 73–104.

(42) Hoffmann, R. Molecular Beauty. *J. Aesthet. Art Critic.* **1990**, *48*, 191–204.

(43) University of Science and Technology of China; Tsinghua University Press. Beautiful Chemistry http://beautifulchemistry.net (Accessed May 2015).

(44) Jogalekar, A. Truth and Beauty in Chemistry http://blogs.scientificamerican.com/the-curious-wavefunction/2013/01/24/truth-and-beauty-in-chemistry/ (Accessed May 2015).

(45) Root-Bernstein, R. Sensual Chemistry: Aesthetics as a Motivation for Research. *HYLE* **2003**, *9*, 33–50.

(46) Miodownik, M. A. Toward Designing New Sensoaesthetic Materials. *Pure Appl. Chem*. **2007**, *79*, 1635–1641.

(47) Hoffmann, R. *Roald Hoffman on the Philosophy, Art, and Science of Chemistry*; Kovac, J.; Weisberg, M., Eds.; Oxford University Press: New York, **2012**.

(48) Hoffmann, R. Molecular Beauty. *Am. Sci.* **1988**, *76*, 389–391.

(49) Hoffmann, R. Molecular Beauty II: Frogs About to Be Kissed. *Am. Sci.* **1988**, *76*, 604–605.

(50) Hoffmann, R. Molecular Beauty III: As Rich as Need Be. *Am. Sci.* **1989**, *77*, 177–178.

(51) Hoffmann, R. Molecular Beauty IV: Toward an Aesthetic Theory of Six-Coordinate Carbon. *Am. Sci.* **1989**, *77*, 330–332.

(52) Schummer, J. Scientometric Studies on Chemistry II: Aims and Methods of Producing New Chemical Substances. *Scientometrics* **1997**, *39*, 125–140.

(53) MacGillivray, L. R.; Atwood, J. L. Structural Classification and General Principles for the Design of Spherical Molecular Hosts. *Angew. Chem., Int. Ed*. **1999**, *38*, 1018–1033.

(54) Eaton, P. E.; Cole, T. W. Cubane. *J. Am. Chem. Soc.* **1964**, *86*, 3157–3158.

(55) Ternansky, R. J.; Balogh, D. W.; Paquette, L. A. Dodecahedrane. *J. Am. Chem. Soc.* **1982**, *104*, 4503–4504.

(56) Paquette, L. A.; Ternansky, R. J.; Balogh, D. W.; Kentgen, G. Total Synthesis of Dodecahedrane. *J. Am. Chem. Soc.* **1983**, *105*, 5446–5450.

(57) Kroto, H. W.; Heath, J. R.; O'Brien, S. C.; Curl, R. F.; Smalley, R. E. C_{60}: Buckminsterfullerene. *Nature* **1985**, *318*, 162–163.

(58) Seidel, S. R.; Stang, P. J. High-Symmetry Coordination Cages via Self-Assembly. *Acc. Chem. Res.* **2002**, *35*, 972–983.

(59) Harris, K.; Fujita, D.; Fujita, M. Giant Hollow M_nL_{2n} Spherical Complexes: Structure, Functionalisation and Applications. *Chem. Commun.* **2013**, *49*, 6703–6712.

(60) Nicolaou, K. C. Inspirations, Discoveries, and Future Perspectives in Total Synthesis. *J. Org. Chem.* **2009**, *74*, 951–972.

(61) Ball, P. *Elegant Solutions: Ten Beautiful Experiments in Chemistry*; The Royal Society of Chemistry: Cambridge, **2005**.

(62) Hall, N. Creating Complexity – the Beauty and Logic of Synthesis. *Chem. Commun.* **2003**, 661–664.

(63) Woodward, C. E. Art and Elegance in the Synthesis of Organic Compounds: Robert Burns Woodward. In *Creative People at Work: Twelve Cognitive Case Studies*; Wallace, D. B.; Gruber, H. E., Eds.; Oxford University Press: New York, **1989**; pp. 227–254.

(64) Lehn, J.-M. *Supramolecular Chemistry: Concepts and Perspectives*; Wiley-VCH: Weinheim, **1995**.

(65) Hudson, B.; Vinograd, J. Catenated Circular DNA Molecules in HeLa Cell Mitochondria. *Nature* **1967**, *216*, 647–652.

(66) Krasnow, M. A.; Stasiak, A.; Spengler, S. J.; Dean, F.; Koller, T.; Cozzarelli, N. R. Determination of the Absolute Handedness of Knots and Catenanes of DNA. *Nature* **1983**, *304*, 559–560.

(67) Wasserman, S. A.; Cozzarelli, N. R. Biochemical Topology: Applications to DNA Recombination and Replication. *Science* **1986**, *232*, 951–960.

(68) Kreuzer, K. N.; Cozzarelli, N. R. Formation and Resolution of DNA Catenanes by DNA Gyrase. *Cell* **1980**, *20*, 245–254.

(69) Subramanian, K.; Rutvisuttinunt, W.; Scott, W.; Myers, R. S. The Enzymatic Basis of Processivity in λ-Exonuclease. *Nucleic Acids Res.* **2003**, *31*, 1585–1596.

(70) Kovall, R.; Matthews, B. W. Toroidal Structure of λ-Exonuclease. *Science* **1997**, *277*, 1824–1827.

(71) Trakselis, M. A.; Alley, S. C.; Abel-Santos, E.; Benkovic, S. J. Creating a Dynamic Picture of the Sliding Clamp During T4 DNA Polymerase Holoenzyme Assembly by Using Fluorescence Resonance Energy Transfer. *Proc. Natl. Acad. Sci. U.S.A.* **2001**, *98*, 8368–8375.

(72) Thordarson, P.; Bijsterveld, E. J. A.; Rowan, A. E.; Nolte, R. J. M. Epoxidation of Polybutadiene by a Topologically Linked Catalyst. *Nature* **2003**, *424*, 915–918.

(73) Coumans, R. G. E.; Elemans, J. A. A. W.; Nolte, R. J. M.; Rowan, A. E. Processive Enzyme Mimic: Kinetics and Thermodynamics of the Threading and Sliding Process. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 19647–19651.

(74) Monnereau, C.; Ramos, P. H.; Deutman, A. B. C.; Elemans, J. A. A. W.; Nolte, R. J. M.; Rowan, A. E. Porphyrin Macrocyclic Catalysts for the Processive Oxidation of Polymer Substrates. *J. Am. Chem. Soc.* **2010**, *132*, 1529–1531.

(75) Wikoff, W. R.; Liljas, L.; Duda, R. L.; Tsuruta, H.; Hendrix, R. W.; Johnson, J. E. Topologically Linked Protein Rings in the Bacteriophage HK97 Capsid. *Science* **2000**, *289*, 2129–2133.

(76) Roos, W. H.; Gertsman, I.; May, E. R.; Brooks, C. L., III; Johnson, J. E.; Wuite, G. J. L. Mechanics of Bacteriophage Maturation. *Proc. Natl. Acad. Sci. U.S.A.* **2012**, *109*, 2342–2347.

(77) Zimanyi, C. M.; Ando, N.; Brignole, E. J.; Asturias, F. J.; Stubbe, J.; Drennan, C. L. Tangled Up in Knots: Structures of Inactivated Forms of *E.coli* Class Ia Ribonucleotide Reductase. *Structure* **2012**, *20*, 1374–1383.

(78) Smeulders, M. J.; Barends, T. R. M.; Pol, A.; Scherer, A.; Zandvoort, M. H.; Udvarhelyi, A.; Khadem, A. F.; Menzel, A.; Hermans, J.; Shoeman, R. L.; Wessels, H. J. C. T.; van den Heuvel, L. P.; Russ, L.; Schlichting, I.; Jetten, M. S. M.; Op den Camp, H. J. M. Evolution of a New Enzyme for Carbon Disulphide Conversion by an Acidothermophilic Archaeon. *Nature* **2011**, *478*, 412–416.

(79) van Eldijk, M. B.; van Leeuwen, I.; Mikhailov, V. A.; Neijenhuis, L.; Harhangi, H. R.; van Hest, J. C. M.; Jetten, M. S. M.; Op den Camp, H. J. M.; Robinson, C. V.; Mecinović, J. Evidence That the Catenane Form of CS_2 Hydrolase Is Not an Artefact. *Chem. Commun*. **2013**, *49*, 7770–7772.

(80) van Eldijk, M. B.; Pieters, B. J.; Mikhailov, V. A.; Robinson, C. V.; van Hest, J. C. M.; Mecinović, J. Catenane Versus Ring: Do Both Assemblies of CS_2 Hydrolase Exhibit the Same Stability and Catalytic Activity? *Chem. Sci.* **2014**, *5*, 2879–2884.

(81) Cao, Z.; Roszak, A. W.; Gourlay, L. J.; Lindsay, J. G.; Isaacs, N. W. Bovine Mitochondrial Peroxiredoxin III Forms a Two-Ring Catenane. *Structure* **2005**, *13*, 1661–1664.

(82) Lee, B. I.; Kim, K. H.; Park, S. J.; Eom, S. H.; Song, H. K.; Suh, S. W. Ring-Shaped Architecture of RecR: Implications for Its Role in Homologous Recombinational DNA Repair. *EMBO J.* **2004**, *23*, 2029–2038.

(83) Honda, M.; Fujisawa, T.; Shibata, T.; Mikawa, T. RecR Forms a Ring-Like Tetramer That Encircles dsDNA by Forming a Complex with RecF. *Nucleic Acids Res*. **2008**, *36*, 5013–5020.

(84) Boutz, D. R.; Cascio, D.; Whitelegge, J.; Perry, L. J.; Yeates, T. O. Discovery of a Thermophilic Protein Complex Stabilized by Topologically Interlinked Chains. *J. Mol. Biol*. **2007**, *368*, 1332–1344.

(85) Farcas, A.-M.; Uluocak, P.; Helmhart, W.; Nasmyth, K. Cohesin's Concatenation of Sister DNAs Maintains Their Intertwining. *Molecular Cell* **2011**, *44*, 97–107.

(86) Youle, R. J.; Karbowski, M. Mitochondrial Fission in Apoptosis. *Nature Rev. Mol. Cell Bio*. **2005**, *6*, 657–663.

(87) Mears, J. A.; Lackner, L. L.; Fang, S.; Ingerman, E.; Nunnari, J.; Hinshaw, J. E. Conformational Changes in Dnm1 Support a Contractile Mechanism for Mitochondrial Fission. *Nature Struct. Mol. Biol*. **2011**, *18*, 20–26.

(88) Cromwell, P. R. The Borromean Rings http://www.liv.ac.uk/~spmr02/rings/index.html (Accessed Apr **2011**).

(89) Cantrill, S. J.; Chichak, K. S.; Peters, A. J.; Stoddart, J. F. Nanoscale Borromean Rings. *Acc. Chem. Res*. **2005**, *38*, 1–9.

(90) *African Art and Leadership*; Fraser, D.; Cole, H. M., Eds.; University of Wisconsin Press: Madison, **1972**.

(91) Rose, L. R. *Seeing Solomon's Knot*; Lois Rose Rose: Los Angeles, **2005**.

(92) Stoddart, J. F. Whither and Thither Molecular Machines. *Chem. Aust*. **1992**, *59*, 576–577.

(93) Greenberg, A. *The Art of Chemistry: Myths, Medicines, and Materials*; Wiley: Hoboken, **2003**.

(94) Obrist, B. Visualization in Medieval Alchemy. *HYLE* **2003**, *9*, 131–170.

(95) Weininger, S. J. Contemplating the Finger - Visuality and the Semiotics of Chemistry. *HYLE* **1998**, *4*, 3–27.

(96) Frisch, H.; Martin, I.; Mark, H. Zur Struktur der Polysiloxene. *I. Monatsh. Chem*. **1953**, *84*, 250–256.

(97) Breault, G. A.; Hunter, C. A.; Mayers, P. C. Supramolecular Topology. *Tetrahedron* **1999**, *55*, 5265–5293.

(98) Dietrich-Buchecker, C.; Colasson, B. X.; Sauvage, J.-P. Molecular Knots. *Top. Curr. Chem*. **2005**, *249*, 261–283.

(99) Lukin, O.; Vögtle, F. Knotting and Threading of Molecules: Chemistry and Chirality of Molecular Knots and Their Assemblies. *Angew. Chem., Int. Ed*. **2005**, *44*, 1456–1477.

(100) Lüttringhaus, A.; Cramer, F.; Prinzbach, H.; Henglein, F. M. Cyclisationen von Langkettigen Dithiolen. Versuche zur Darstellung sich umfassender Ringe mit Hilfe von Einschlußverbindungen. *Liebigs Ann. Chem*. **1958**, *613*, 185–198.

(101) Wasserman, E. The Preparation of Interlocking Rings: a Catenane. *J. Am. Chem. Soc*. **1960**, *82*, 4433–4434.

(102) Wasserman, E. Chemical Topology. *Sci. Am*. **1962**, *207*, 94–102.

(103) Harrison, I. T.; Harrison, S. The Synthesis of a Stable Complex of a Macrocycle and a Threaded Chain. *J. Am. Chem. Soc*. **1967**, *89*, 5723–5724.

(104) Agam, G.; Graiver, D.; Zilkha, A. Studies on the Formation of Topological Isomers by Statistical Methods. *J. Am. Chem. Soc*. **1976**, *98*, 5206–5214.

(105) Agam, G.; Zilkha, A. Synthesis of a Catenane by a Statistical Double-Stage Method. *J. Am. Chem. Soc*. **1976**, *98*, 5214–5216.

(106) Schill, G.; Lüttringhaus, A. Preparation of Catena Compounds by Directed Synthesis. *Angew. Chem., Int. Ed. Engl*. **1964**, *3*, 546–547.

(107) Schill, G.; Zürcher, C. [3]-Catenanes. *Angew. Chem., Int. Ed. Engl*. **1969**, *8*, 988.

(108) Schill, G.; Zürcher, C. [3]-Catenane durch gezeiete Synthese. *Chem. Ber*. **1977**, *110*, 2046–2066.

(109) Schill, G.; Rissler, K.; Fritz, H.; Vetter, W. Synthesis, Isolation, and Identification of Translationally Isomeric [3] Catenanes. *Angew. Chem., Int. Ed. Engl*. **1981**, *20*, 187–189.

(110) Riβler, K.; Schill, G.; Fritz, H.; Vetter, W. Gezielte Synthese von translationsisomeren [3]-Catenanen. *Chem. Ber*. **1986**, *119*, 1374–1399.

(111) Schill, G.; Zollenkopf, H. Rotaxane. *Nachr. Chem. Techn*. **1967**, *15*, 149–150.

(112) Schill, G.; Zollenkopf, H. Rotaxan-Verbindungen, I. *Liebigs Ann. Chem*. **1969**, *721*, 53–74.

(113) Schill, G.; Henschel, R. Rotaxan-Verbindungen , II. Eine Diansa-Verbindung des 5-Amino-6-methoxy-4.7-dimethyl-benzodioxols als Modell zur Synthese von Catenanen und Rotaxanen. *Liebigs Ann. Chem*. **1970**, *731*, 113–119.

(114) Schill, G.; Zürcher, C.; Vetter, W. Rotaxan-Verbindungen, III. Synthese eines Rotaxans mit Triphenylmethyl-Sperrgruppen und massenspextrometrische Untersuchungen. *Chem. Ber*. **1973**, *106*, 228–235.

(115) Schill, G. *Catenanes, Rotaxanes, and Knots*; Academic Press: New York, **1971**.

(116) van Gulick, N. Theoretical Aspects of the Linked Ring Problem. *New J. Chem*. **1993**, *17*, 619–625.

(117) Walba, D. M.; Richards, R. M.; Sherwood, S. P.; Haltiwanger, R. C. Strategy for the Synthesis of Cylindrical Macropolycyclic Hosts with Hydrophilic Interior Surfaces: Crown Ether Rings Fused by the Tetrahydroxymethylethylene (THYME) Unit. *J. Am. Chem. Soc*. **1981**, *103*, 6213–6215.

(118) Walba, D. M.; Richards, R. M.; Haltiwanger, R. C. Total Synthesis of the First Molecular Möbius Strip. *J. Am. Chem. Soc*. **1982**, *104*, 3219–3221.

(119) Walba, D. M.; Armstrong, J. D., III; Perry, A. E.; Richards, R. M.; Homan, T. C.; Haltiwanger, R. C. The Thyme Polyethers: An Approach to the Synthesis of a Molecular Knotted Ring. *Tetrahedron* **1986**, *42*, 1883–1894.

(120) Dietrich-Buchecker, C. O.; Sauvage, J. P.; Kintzinger, J. P. Une Nouvelle Famille de Molecules: Les Metallo-Catenanes. *Tetrahedron Lett*. **1983**, *24*, 5095–5098.

(121) Cesario, M.; Dietrich, C. O.; Edel, A.; Guilhem, J.; Kintzinger, J.-P.; Pascard, C.; Sauvage, J.-P. Topological Enhancement of Basicity: Molecular Structure and Solution Study of a Monoprotonated Catenand. *J. Am. Chem. Soc*. **1986**, *108*, 6250–6254.

(122) Solà, M. Forty Years of Clar's Aromatic π-Sextet Rule. *Front. Chem*. **2013**, *1*, Article 22.

(123) Dietrich-Buchecker, C. O.; Guilhem, J.; Khemiss, A. K.; Kintzinger, J.-P.; Pascard, C.; Sauvage, J.-P. Molecular Structure of a [3]-Catenate: Curling up of the Interlocked System by Interaction between the Two Copper Complex Subunits. *Angew. Chem., Int. Ed. Engl*. **1987**, *26*, 661–663.

(124) Odell, B.; Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. Cyclobis(paraquat-*p*-phenylene). A Tetracationic Multipurpose Receptor. *Angew. Chem., Int. Ed. Engl*. **1988**, *27*, 1547–1550.

(125) Ashton, P. R.; Odell, B.; Reddington, M. V.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J. Isostructural, Alternately-Charged Receptor Stacks. The Inclusion Complexes of Hydroquinone and Catechol Dimethyl Ethers with Cyclobis(paraquat-*p*-phenylene). *Angew. Chem., Int. Ed. Engl*. **1988**, *27*, 1550–1553.

(126) Ashton, P. R.; Goodnow, T. T.; Kaifer, A. E.; Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Vicent, C.; Williams, D. J. A [2]Catenane Made to Order. *Angew. Chem., Int. Ed. Engl*. **1989**, *28*, 1396–1399.

(127) Frasconi, M.; Fernando, I. R.; Wu, Y.; Liu, Z.; Liu, W.-G.; Dyar, S. M.; Barin, G.; Wasielewski, M. R.; Goddard, W. A., III; Stoddart, J. F. Redox Control of the Binding Modes of an Organic Receptor. *J. Am. Chem. Soc*. **2015**, *137*, 11057–11068.

(128) Ashton, P. R.; Brown, C. L.; Chrystal, E. J. T.; Goodnow, T. T.; Kaifer, A. E.; Parry, K. P.; Philp, D.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. The Self-Assembly of a Highly Ordered [2]Catenane. *J. Chem. Soc., Chem. Commun.* **1991**, 634–639.

(129) Glink, P. T.; Oliva, A. I.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. Template-Directed Synthesis of a [2]Rotaxane by the Clipping under Thermodynamic Control of a Crown Ether Like Macrocycle Around a Dialkylammonium Ion. *Angew. Chem., Int. Ed*. **2001**, *40*, 1870–1875.

(130) Ibukuro, F.; Fujita, M.; Yamaguchi, K.; Sauvage, J.-P. Quantitative and Spontaneous Formation of a Doubly Interlocking [2]Catenane Using Copper(I) and Palladium(II) as Templating and Assembling Centers. *J. Am. Chem. Soc*. **1999**, *121*, 11014–11015.

(131) Johnston, A. G.; Leigh, D. A.; Pritchard, R. J.; Deegan, M. D. Facile Synthesis and Solid-State Structure of a Benzylic Amide [2]Catenane. *Angew. Chem., Int. Ed. Engl*. **1995**, *34*, 1209–1212.

(132) Gross, L.; Mohn, F.; Moll, N.; Meyer, G.; Ebel, R.; Abdel-Mageed, W. M.; Jaspars, M. Organic Structure Determination Using Atomic-Resolution Scanning Probe Microscopy. *Nature Chem*. **2010**, *2*, 821–825.

(133) Amabilino, D. B.; Ashton, P. R.; Reder, A. S.; Spencer, N.; Stoddart, J. F. Olympiadane. *Angew. Chem., Int. Ed. Engl*. **1994**, *33*, 1286–1290.

(134) Cesario, M.; Dietrich-Buchecker, C. O.; Guilhem, J.; Pascard, C.; Sauvage, J.-P. Molecular Structure of a Catenand and Its Copper(I) Catenate: Complete Rearrangement of the Interlocked Macrocyclic Ligands by Complexation. *J. Chem. Soc., Chem. Commun*. **1985**, 244–247.

(135) Amabilino, D. B.; Ashton, P. R.; Boyd, S. E.; Lee, J. Y.; Menzer, S.; Stoddart, J. F.; Williams, D. J. The Five-Stage Self-Assembly of a Branched Heptacatenane. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 2070–2072.

(136) Cabezon, B.; Cao, J.; Raymo, F. M.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. A Self-Complexing [2]Catenane. *Angew. Chem., Int. Ed*. **2000**, *39*, 148–151.

(137) Wisner, J. A.; Beer, P. D.; Drew, M. G. B.; Sambrook, M. R. Anion-Templated Rotaxane Formation. *J. Am. Chem. Soc*. **2002**, *124*, 12469–12476.

(138) Belowich, M. E.; Valente, C.; Stoddart, J. F. Template-Directed Syntheses of Rigid Oligorotaxanes under Thermodynamic Control. *Angew. Chem., Int. Ed*. **2010**, *49*, 7208–7212.

(139) Lee, C. F.; Leigh, D. A.; Pritchard, R. G.; Schultz, D.; Teat, S. J.; Timco, G. A.; Winpenny, R. E. Hybrid Organic-Inorganic Rotaxanes and Molecular Shuttles. *Nature* **2009**, *458*, 314–318.

(140) Li, H.; Eddaoudi, M.; O'Keeffe, M.; Yaghi, O. M. Design and Synthesis of an Exceptionally Stable and Highly Porous Metal-Organic Framework. *Nature* **1999**, *402*, 276–279.

(141) Eddaoudi, M.; Kim, J.; Rosi, N.; Vodak, D.; Wachter, J.; O'Keeffe, M.; Yaghi, O. M. Systematic Design of Pore Size and Functionality in Isoreticular MOFs and Their Application in Methane Storage. *Science* **2002**, *295*, 469–472.

(142) Yaghi, O. M.; O'Keeffe, M.; Ockwig, N. W.; Chae, H. K.; Eddaoudi, M.; Kim, J. Reticular Synthesis and the Design of New Materials. *Nature* **2003**, *423*, 705–714.

(143) Chae, H. K.; Siberio-Pérez, D. Y.; Kim, J.; Go, Y.; Eddaoudi, M.; Matzger, A. J.; O'Keeffe, M.; Yaghi, O. M. A Route to High Surface Area, Porosity and Inclusion of Large Molecules in Crystals. *Nature* **2004**, *427*, 523–527.

(144) Yang, J.; Ma, J.-F.; Batten, S. R. Polyrotaxane Metal–Organic Frameworks (PMOFs). *Chem. Commun*. **2012**, *48*, 7899–7912.

(145) Batten, S. R.; Robson, R. Interpenetrating Nets: Ordered, Periodic Entanglement. *Angew. Chem., Int. Ed*. **1998**, *37*, 1460–1494.

(146) Reineke, T. M.; Eddaoudi, M.; Moler, D.; O'Keeffe, M.; Yaghi, O. M. Large Free Volume in Maximally Interpenetrating Networks: The Role of Secondary Building Units Exemplified by $Tb_2(ADB)_3[(CH_3)_2SO]_4$•$16[(CH_3)_2SO]$. *J. Am. Chem. Soc*. **2000**, *122*, 4843–4844.

(147) Chen, B.; Eddaoudi, M.; Hyde, S. T.; O'Keeffe, M.; Yaghi, O. M. Interwoven Metal-Organic Framework on a Periodic Minimal Surface with Extra-Large Pores. *Science* **2001**, *291*, 1021–1023.

(148) Loeb, S. J. Rotaxanes as Ligands: From Molecules to Materials. *Chem. Soc. Rev*. **2007**, *36*, 226–235.

(149) Whang, D.; Kim, K. Polycatenated Two-Dimensional Polyrotaxane Net. *J. Am. Chem. Soc*. **1997**, *119*, 451–452.

(150) Lee, E.; Kim, J.; Heo, J.; Whang, D.; Kim, K. A Two-Dimensional Polyrotaxane with Large Cavities and Channels: A Novel Approach to Metal–Organic Open-Frameworks by Using Supramolecular Building Blocks. *Angew. Chem., Int. Ed*. **2001**, *40*, 399–402.

(151) Hoffart, D. J.; Loeb, S. J. Metal-Organic Rotaxane Frameworks: Three-Dimensional Polyrotaxanes From Lanthanide-Ion Nodes, Pyridinium *N*-Oxide Axles, and Crown-Ether Wheels. *Angew. Chem., Int. Ed*. **2005**, *44*, 901–904.

(152) Loeb, S. J. Metal-Organic Rotaxane Frameworks; MORFs. *Chem. Commun.* **2005**, 1511–1518.

(153) Mercer, D. J.; Vukotic, V. N.; Loeb, S. J. Linking [2]Rotaxane Wheels to Create a New Type of Metal Organic Rotaxane Framework. *Chem. Commun*. **2010**, *47*, 896–898.

(154) Vukotic, V. N.; Loeb, S. J. One-, Two- and Three-Periodic Metal-Organic Rotaxane Frameworks (MORFs): Linking Cationic Transition-Metal Nodes with an Anionic Rotaxane Ligand. *Chem. Eur. J*. **2011**, *16*, 13630–13637.

(155) Mercer, D. J.; Yacoub, J.; Zhu, K.; Loeb, S. K. [2]Pseudorotaxanes, [2]Rotaxanes and Metal–Organic Rotaxane Frameworks Containing Tetra-Substituted Dibenzo[24]crown-8 Wheels. *Org. Biomol. Chem*. **2012**, *10*, 6094–6104.

(156) Vukotic, V. N.; Harris, K. J.; Zhu, K.; Schurko, R. W.; Loeb, S. J. Metal–Organic Frameworks with Dynamic Interlocked Components. *Nature Chem*. **2012**, *4*, 456–460.

(157) Frank, N. C.; Mercer, D. J.; Loeb, S. J. An Interwoven Metal-Organic Framework Combining Mechanically Interlocked Linkers and Interpenetrated Networks. *Chem. Eur. J*. **2013**, *19*, 14076–14080.

(158) Zhu, K.; Vukotic, V. N.; O'Keefe, C. A.; Schurko, R. W.; Loeb, S. J. Metal–Organic Frameworks with Mechanically Interlocked Pillars: Controlling Ring Dynamics in the Solid-State via a Reversible Phase Change. *J. Am. Chem. Soc*. **2014**, *136*, 7403–7409.

(159) Zhu, K.; O'Keefe, C. A.; Vukotic, V. N.; Schurko, R. W.; Loeb, S. J. A Molecular Shuttle That Operates Inside a Metal–Organic Framework. *Nature Chem*. **2015**, *7*, 514–519.

(160) Li, Q.; Sue, C.-H.; Basu, S.; Shveyd, A. K.; Zhang, W.; Barin, G.; Fang, L.; Sarjeant, A. A.; Stoddart, J. F.; Yaghi, O. M. A Catenated Strut in a Catenated Metal-Organic Framework. *Angew. Chem., Int. Ed*. **2010**, *49*, 6751–6755.

(161) Li, Q.; Zhang, W.; Miljanić, O. Š.; Knobler, C. B.; Stoddart, J. F.; Yaghi, O. M. A Metal–Organic Framework Replete with Ordered Donor–Acceptor Catenanes. *Chem. Commun*. **2010**, *46*, 380–382.

(162) Coskun, A.; Hmadeh, M.; Barin, G.; Gándara, F.; Li, Q.; Choi, E.; Strutt, N. L.; Cordes, D. B.; Slawin, A. M. Z.; Stoddart, J. F.; Sauvage, J.-P.; Yaghi, O. M. Metal-Organic Frameworks Incorporating Copper-Complexed Rotaxanes. *Angew. Chem., Int. Ed*. **2012**, *51*, 2160–2163.

(163) Cao, D.; Juríček, M.; Brown, Z. J.; Sue, A. C.-H.; Liu, Z.; Lei, J.; Blackburn, A. K.; Grunder, S.; Sarjeant, A. A.; Coskun, A.; Wang, C.; Farha, O. K.; Hupp, J. T.; Stoddart, J. F. Three-Dimensional Architectures Incorporating Stereoregular Donor-Acceptor Stacks. *Chem. Eur. J*. **2013**, *19*, 8457–8465.

(164) McGonigal, P. R.; Deria, P.; Hod, I.; Moghadam, P. Z.; Avestro, A.-J.; Horwitz, N. E.; Gibbs-Hall, I. C.; Blackburn, A. K.; Chen, D.; Botros, Y. Y.; Wasielewski, M. R.; Snurr, R. Q.; Hupp, J. T.; Farha, O. K.; Stoddart, J. F. Electrochemically Addressable Trisradical Rotaxanes Organized Within a Metal–Organic Framework. *Proc. Natl. Acad. Sci. U.S.A*. **2015**, *112*, 11161–11168.

(165) Gong, H.-Y.; Rambo, B. M.; Cho, W.; Lynch, V. M.; Oh, M.; Sessler, J. L. Anion-Directed Assembly of a Three-Dimensional Metal–Organic Rotaxane Framework. *Chem. Commun*. **2011**, *47*, 5973–5975.

(166) Gong, H.-Y.; Rambo, B. M.; Nelson, C. A.; Cho, W.; Lynch, V. M.; Zhu, X.; Oh, M.; Sessler, J. L. Multi Component Self-Assembly: Supramolecular Organic Frameworks Containing Metal–Rotaxane Subunits (RSOFs). *Dalton Trans*. **2012**, *41*, 1134–1137.

(167) Gong, H.-Y.; Rambo, B. M.; Nelson, C. A.; Lynch, V. M.; Zhu, X.; Sessler, J. L. Rare-Earth Cation Effects on Three-Dimensional Metal–Organic Rotaxane Framework (MORF) Self Assembly. *Chem. Commun*. **2012**, *48*, 10186–10188.

(168) Whitehead, G. F. S.; Cross, B.; Carthy, L.; Milway, V. A.; Rath, H.; Fernandez, A.; Heath, S. L.; Muryn, C. A.; Pritchard, R. G.; Teat, S. J.; Timco, G. A.; Winpenny, R. E. P. Rings and Threads as Linkers in Metal–Organic Frameworks and Poly-Rotaxanes. *Chem. Commun*. **2013**, *49*, 7195–7197.

(169) Liang, J.; Wang, X.-L.; Jiao, Y.-Q.; Qin, C.; Shao, K.-Z.; Su, Z.-M.; Wu, Q.-Y. Metal Ion Directed Metal–Organic Rotaxane Frameworks with Intrinsic Features of Self-Penetration and Interpenetration. *Chem. Commun*. **2013**, *49*, 8555–8557.

(170) Sauvage, J.-P.; Weiss, J. Synthesis of Dicopper(I) [3]Catenates: Multiring Interlocked Coordinating Systems. *J. Am. Chem. Soc*. **1985**, *107*, 6108–6110.

(171) Ashton, P. R.; Brown, C. L.; Chrystal, E. J. T.; Goodnow, T. T.; Kaifer, A. E.; Parry, K. P.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. Self-Assembling [3]Catenanes. *Angew. Chem., Int. Ed. Engl*. **1991**, *30*, 1039–1042.

(172) Schummer, J. Gestalt Switch in Molecular Image Perception: The Aesthetic Origin of Molecular Nanotechnology in Supramolecular Chemistry. *Found. Chem*. **2006**, *8*, 53–72.

(173) Shirai, Y.; Osgood, A. J.; Zhao, Y.; Kelly, K. F.; Tour, J. M. Directional Control in Thermally Driven Single-Molecule Nanocars. *Nano Lett*. **2005**, *5*, 2330–2334.

(174) Anelli, P. L.; Spencer, N.; Stoddart, J. F. A Molecular Shuttle. *J. Am. Chem. Soc*. **1991**, *113*, 5131–5133.

(175) Bissell, R. A.; Córdova, E.; Kaifer, A. E.; Stoddart, J. F. A Chemically and Electrochemically Switchable Molecular Shuttle. *Nature* **1994**, *369*, 133–137.

(176) Spruell, J. M.; Paxton, W. F.; Olsen, J. C.; Benítez, D.; Tkatchouk, E.; Stern, C. L.; Trabolsi, A.; Friedman, D. C.; Goddard, W. A., III; Stoddart, J. F. A Push-Button Molecular Switch. *J. Am. Chem. Soc*. **2009**, *131*, 11571–11580.

(177) Ashton, P. R.; Brown, C. L.; Chrystal, E. J. T.; Parry, K. P.; Pietraszkiewicz, M.; Spencer, N.; Stoddart, J. F. Molecular Trains: Self Association and Dynamic Properties of Two New Catenanes. *Angew. Chem., Int. Ed. Engl*. **1991**, *30*, 1042–1045.

(178) Badjić, J. D.; Balzani, V.; Credi, A.; Silvi, S.; Stoddart, J. F. A Molecular Elevator. *Science* **2004**, *303*, 1845–1849.

(179) Zhao, Y.-L.; Li, Z.; Kabehie, S.; Botros, Y. Y.; Stoddart, J. F.; Zink, J. I. pH-Operated Nanopistons on the Surfaces of Mesoporous Silica Nanoparticles. *J. Am. Chem. Soc*. **2010**, *132*, 13016–13025.

(180) Bruns, C. J.; Stoddart, J. F. Rotaxane-Based Molecular Muscles. *Acc. Chem. Res*. **2014**, *47*, 2186–2199.

(181) Ashton, P. R.; Ballardini, R.; Balzani, V.; Credi, A.; Dress, K. R.; Ishow, E.; Kleverlaan, C. J.; Kocian, O.; Preece, J. A.; Spencer, N.; Stoddart, J. F.; Venturi, M.; Wenger, S. Molecular Meccano 61. A Photochemically Driven Molecular-Level Abacus. *Chem. Eur. J*. **2000**, *6*, 3558–3574.

(182) Balzani, V.; Clemente-León, M.; Credi, A.; Ferrer, B.; Venturi, M.; Flood, A. H.; Stoddart, J. F. Autonomous Artificial Nanomotor Powered by Sunlight. *Proc. Natl. Acad. Sci. U.S.A*. **2006**, *103*, 1178–1183.

(183) Saha, S.; Leung, K. C.-F.; Nguyen, T. D.; Stoddart, J. F.; Zink, J. I. Nanovalves. *Adv. Funct. Mater*. **2007**, *17*, 685–693.

(184) Roh, S.-G.; Park, K.-M.; Park, G.-J.; Sakamoto, S.; Yamaguchi, K.; Kim, K. Synthesis of a Five-Membered Molecular Necklace: A 2+2 Approach. *Angew. Chem., Int. Ed*. **1999**, *38*, 637–641.

(185) Harada, A.; Li, J.; Kamachi, M. The Molecular Necklace: A Rotaxane Containing Many Threaded α-Cyclodextrins. *Nature* **1992**, *356*, 325–327.

(186) Whang, D.; Park, K.-M.; Heo, J.; Ashton, P.; Kim, K. Molecular Necklace: Quantitative Self-Assembly of a Cyclic Oligorotaxane From Nine Molecules. *J. Am. Chem. Soc*. **1998**, *120*, 4899–4900.

(187) Fujita, M.; Ibukuro, F.; Yamaguchi, K.; Ogura, K. A Molecular Lock. *J. Am. Chem. Soc*. **1995**, *117*, 4175–4176.

(188) Leigh, D. A.; Wong, J. K. Y.; Dehez, F.; Zerbetto, F. Unidirectional Rotation in a Mechanically Interlocked Molecular Rotor. *Nature* **2003**, *424*, 174–179.

(189) Leigh, D. A.; Moody, K.; Smart, J. P.; Watson, K. J.; Slawin, A. M. Z. Catenane Chameleons: Environment-Sensitive Translational Isomerism in Amphiphilic Benzylic Amide [2]Catenanes. *Angew. Chem., Int. Ed. Engl*. **1996**, *35*, 306–310.

(190) Clark, P. G.; Guidry, E. N.; Chan, W. Y.; Steinmetz, W. E.; Grubbs, R. H. Synthesis of a Molecular Charm Bracelet via Click Cyclization and Olefin Metathesis Clipping. *J. Am. Chem. Soc*. **2010**, *132*, 3405–3412.

(191) Jimenez-Bueno, G.; Rapenne, G. Technomimetic Molecules: Synthesis of a Molecular Wheelbarrow. *Tetrahedron Lett*. **2003**, *44*, 6261–6263.

(192) Rapenne, G. Synthesis of Technomimetic Molecules: Towards Rotation Control in Single-Molecular Machines and Motors. *Org. Biomol. Chem*. **2005**, *3*, 1165–1169.

(193) Lehn, J.-M. Supramolecular Chemistry—Scope and Perspectives Molecules, Supermolecules, and Molecular Devices (Nobel Lecture). *Angew. Chem., Int. Ed. Engl*. **1988**, *27*, 89–112.

(194) Kant, I. *Critique of Judgement*; Macmillan: London, **1892**.

(195) Goodman, N. *Languages of Art: an Approach to a Theory of Symbols*; Bobbs-Merrill: Indianapolis, **1968**.

(196) Eco, U. *A Theory of Semiotics*; Indiana University Press: Bloomington, **1976**.

(197) Hoffmann, R. Thoughts on Aesthetics and Visualization in Chemistry. *HYLE* **2003**, *9*, 7–10.

(198) Pedersen, C. J. The Discovery of Crown Ethers (Nobel Lecture). *Angew. Chem., Int. Ed. Engl*. **1988**, *27*, 1021–1027.

(199) Cram, D. J. The Design of Molecular Hosts, Guests, and Their Complexes (Nobel Lecture). *Angew. Chem., Int. Ed. Engl*. **1988**, *27*, 1009–1020.

(200) Ogino, H. Relatively High-Yield Synthesis of Rotaxanes. Synthesis and Properties of Compounds Consisting of Cyclodextrins Threaded by α,ω-Diaminoalkanes Coordinated to Cobalt(III) Complexes. *J. Am. Chem. Soc*. **1981**, *103*, 1303–1304.

(201) Mock, W. L.; Irra, T. A.; Wepsiec, J. P.; Adhya, M. Catalysis by Cucurbituril. The Significance of Bound-Substrate Destabilization for Induced Triazole Formation. *J. Org. Chem*. **1989**, *54*, 5302–5308.

(202) Fujita, M.; Ibukuro, F.; Hagihara, H.; Ogura, K. Quantitative Self-Assembly of a [2]Catenane From Two Preformed Molecular Rings. *Nature* **1994**, *367*, 720–723.

(203) Anderson, S.; Anderson, H. L. Synthesis of a Water-Soluble Conjugated [3]Rotaxane. *Angew. Chem., Int. Ed. Engl*. **1996**, *35*, 1956–1959.

(204) Lin, Y.-H.; Lai, C.-C.; Liu, Y.-H.; Peng, S.-M.; Chiu, S.-H. Sodium Ions Template the Formation of Rotaxanes From BPX26C6 and Nonconjugated Amide and Urea Functionalities. *Angew. Chem., Int. Ed*. **2013**, *52*, 10231–10236.

(205) Hancock, L. M.; Beer, P. D. Sodium and Barium Cation-Templated Synthesis and Cation-Induced Molecular Pirouetting of a Pyridine *N*-Oxide Containing [2]Rotaxane. *Chem. Commun*. **2011**, *47*, 6012–6014.

(206) Zapata, F.; Blackburn, O. A.; Langton, M. J.; Faulkner, S.; Beer, P. D. Lanthanide Cation-Templated Synthesis of Rotaxanes. *Chem. Commun*. **2013**, *49*, 8157–8159.

(207) Loeb, S. J.; Wisner, J. A. 1,2-Bis(4,4′-dipyridinium)ethane: A Versatile Dication for the Formation of [2]Rotaxanes with Dibenzo-24-Crown-8 Ether. *Chem. Commun*. **1998**, *2757–2758*.

(208) Rowan, A. E.; Aarts, P. P. M.; Koutstaal, K. W. M. Novel Porphyrin–Viologen Rotaxanes. *Chem. Commun*. **1998**, *611–612*.

(209) Hamilton, D. G.; Sanders, J. K. M.; Davies, J. E.; Clegg, W.; Teat, S. J. Neutral [2]Catenanes From Oxidative Coupling of π-Stacked Components. *Chem. Commun*. **1997**, *897–898*.

(210) Korybut-Daszkiewicz, B.; Więckowska, A.; Bilewicz, R.; Domagala, S.; Wozniak, K. Novel [2]Catenane Structures Introducing Communication Between Transition Metal Centers via π···π Interactions. *J. Am. Chem. Soc*. **2001**, *123*, 9356–9366.

(211) Hunter, C. A. Synthesis and Structure Elucidation of a New [2]-Catenane. *J. Am. Chem. Soc*. **1992**, *114*, 5303–5311.

(212) Johnston, A. G.; Leigh, D. A.; Nezhat, L.; Smart, J. P.; Deegan, M. D. Structurally Diverse and Dynamically Versatile Benzylic Amide [2]Catenanes Assembled Directly From Commercially Available Precursors. *Angew. Chem., Int. Ed. Engl*. **1995**, *34*, 1212–1216.

(213) Vysotsky, M. O.; Bolte, M.; Thondorf, I.; Böhmer, V. New Molecular Topologies by Fourfold Metathesis Reactions Within a Hydrogen-Bonded Calix[4]arene Dimer. *Chem. Eur. J*. **2003**, *9*, 3375–3382.

(214) Tron, A.; Thornton, P. J.; Rocher, M.; Jacquot de Rouville, H. P.; Desvergne, J. P.; Kauffmann, B.; Buffeteau, T.; Cavagnat, D.; Tucker, J. H.; McClenaghan, N. D. Formation of a Hydrogen-Bonded Barbiturate [2]-Rotaxane. *Org. Lett*. **2014**, *16*, 1358–1361.

(215) Kolchinski, A. G.; Busch, D. H.; Alcock, N. W. Gaining Control Over Molecular Threading: Benefits of Second Coordination Sites and Aqueous-Organic Interfaces in Rotaxane Synthesis. *J. Chem. Soc., Chem. Commun.* **1995**, 1289–1291.

(216) Aucagne, V.; Leigh, D. A.; Lock, J. S.; Thomson, A. R. Rotaxanes of Cyclic Peptides. *J. Am. Chem. Soc*. **2006**, *128*, 1784–1785.

(217) Gilday, L. C.; Lang, T.; Caballero, A.; Costa, P. J.; Félix, V.; Beer, P. D. A Catenane Assembled Through a Single

Charge-Assisted Halogen Bond. *Angew. Chem., Int. Ed*. **2013**, *52*, 4356–4360.

(218) Hübner, G. M.; Gläser, J.; Seel, C.; Vögtle, F. High-Yielding Rotaxane Synthesis with an Anion Template. *Angew. Chem., Int. Ed*. **1999**, *38*, 383–386.

(219) Lee, S.; Chen, C.-H.; Flood, A. H. A Pentagonal Cyanostar Macrocycle with Cyanostilbene CH Donors Binds Anions and Forms Dialkylphosphate [3]Rotaxanes. *Nature Chem*. **2013**, *5*, 704–710.

(220) Caballero, A.; Zapata, F.; White, N. G.; Costa, P. J.; Félix, V.; Beer, P. D. A Halogen-Bonding Catenane for Anion Recognition and Sensing. *Angew. Chem., Int. Ed*. **2012**, *51*, 1876–1880.

(221) Barrell, M. J.; Leigh, D. A.; Lusby, P. J.; Slawin, A. M. Z. An Ion-Pair Template for Rotaxane Formation and Its Exploitation in an Orthogonal Interaction Anion-Switchable Molecular Shuttle. *Angew. Chem., Int. Ed*. **2008**, *47*, 8036–8039.

(222) Nakatani, Y.; Furusho, Y.; Yashima, E. Amidinium Carboxylate Salt Bridges as a Recognition Motif for Mechanically Interlocked Molecules: Synthesis of an Optically Active [2]Catenane and Control of Its Structure. *Angew. Chem., Int. Ed*. **2010**, *49*, 5463–5467.

(223) Shukla, R.; Deetz, M. J.; Smith, B. D. [2]Rotaxane with a Cation-Binding Wheel. *Chem. Commun.* **2000**, 2397–2398.

(224) Arduini, A.; Ferdani, R.; Pochini, A.; Secchi, A.; Ugozzoli, F. Calix[6]arene as a Wheel for Rotaxane Synthesis. *Angew. Chem., Int. Ed*. **2000**, *39*, 3453–3456.

(225) Pierro, T.; Gaeta, C.; Talotta, C.; Casapullo, A.; Neri, P. Fixed or Invertible Calixarene-Based Directional Shuttles. *Org. Lett*. **2011**, *13*, 2650–2653.

(226) Ogoshi, T.; Nishida, Y.; Yamagishi, T.-A.; Nakamoto, Y. High Yield Synthesis of Polyrotaxane Constructed From Pillar[5]arene and Viologen Polymer and Stabilization of Its Radical Cation. *Macromolecules* **2010**, *43*, 7068–7072.

(227) Li, H.; Fahrenbach, A. C.; Dey, S. K.; Basu, S.; Trabolsi, A.; Zhu, Z.; Botros, Y. Y.; Stoddart, J. F. Mechanical Bond Formation by Radical Templation. *Angew. Chem., Int. Ed*. **2010**, *49*, 8260–8265.

(228) Li, H.; Zhu, Z.; Fahrenbach, A. C.; Savoie, B. M.; Ke, C.; Barnes, J. C.; Lei, J.; Zhao, Y.-L.; Lilley, L. M.; Marks, T. J.; Ratner, M. A.; Stoddart, J. F. Mechanical Bond-Induced Radical Stabilization. *J. Am. Chem. Soc*. **2013**, *135*, 456–467.

(229) Wang, W.; Wang, L.; Palmer, B. J.; Exarhos, G. J.; Li, A. D. Cyclization and Catenation Directed by Molecular Self-Assembly. *J. Am. Chem. Soc*. **2006**, *128*, 11150–11159.

(230) Hasell, T.; Wu, X.; Jones, J. T. A.; Bacsa, J.; Steiner, A.; Mitra, T.; Trewin, A.; Adams, D. J.; Cooper, A. I. Triply Interlocked Covalent Organic Cages. *Nature Chem*. **2010**, *2*, 750–755.

(231) Hicks, D. *Look Into the Stillness: A Spiritual Journey through Inspirational Quotes*. Nature's Path: Amelia Court House, Virginia, **2015**.

(232) Dietrich-Buchecker, C. O.; Sauvage, J.-P. Interlocking of Molecular Threads: From the Statistical Approach to the Templated Synthesis of Catenands. *Chem. Rev*. **1987**, *87*, 795–810.

(233) Sauvage, J.-P.; Amabilino, D. B. The Beauty of Knots at the Molecular Level. *Top. Curr. Chem.* **2012**, *323*, 107–125.

(234) Rolfsen, D. *Knots and Links*; Publish or Perish: Berkeley, **1976**.

(235) Nierengarten, J.-F.; Dietrich-Buchecker, C. O.; Sauvage, J.-P. Synthesis of a Doubly Interlocked [2]-Catenane. *J. Am. Chem. Soc*. **1994**, *116*, 375–376.

(236) Leigh, D. A.; Pritchard, R. G.; Stephens, A. J. A Star of David Catenane. *Nature Chem*. **2014**, *6*, 978–982.

(237) Chichak, K. S.; Cantrill, S. J.; Pease, A. R.; Chiu, S. H.; Cave, G. W. V.; Atwood, J. L.; Stoddart, J. F. Molecular Borromean Rings. *Science* **2004**, *304*, 1308–1312.

(238) Wood, C. S.; Ronson, T. K.; Belenguer, A. M.; Holstein, J. J.; Nitschke, J. R. Two-Stage Directed Self-Assembly of a Cyclic [3]Catenane. *Nature Chem*. **2015**, *7*, 354–358.

(239) Dietrich-Buchecker, C. O.; Sauvage, J.-P. A Synthetic Molecular Trefoil Knot. *Angew. Chem., Int. Ed. Engl*. **1989**, *28*, 189–192.

(240) Dietrich-Buchecker, C. O.; Guilhem, J.; Pascard, C.; Sauvage, J.-P. Structure of a Synthetic Trefoil Knot Coordinated to Two Copper(I) Centers. *Angew. Chem., Int. Ed. Engl*. **1990**, *29*, 1154–1156.

(241) Ayme, J.-F.; Beves, J. E.; Leigh, D. A.; McBurney, R. T.; Rissanen, K.; Schultz, D. A Synthetic Molecular Pentafoil Knot. *Nature Chem*. **2012**, *4*, 15–20.

(242) Ayme, J.-F.; Beves, J. E.; Leigh, D. A.; McBurney, R. T.; Rissanen, K.; Schultz, D. Pentameric Circular Iron(II) Double Helicates and a Molecular Pentafoil Knot. *J. Am. Chem. Soc*. **2012**, 9488–9497.

(243) Carina, R. F.; Dietrich-Buchecker, C.; Sauvage, J.-P. Molecular Composite Knots. *J. Am. Chem. Soc*. **1996**, *118*, 9110–9116.

(244) Castle, T.; Evans, M. E.; Hyde, S. T. Ravels: Knot-Free but Not Free. Novel Entanglements of Graphs in 3-Space. *New J. Chem*. **2008**, *32*, 1484–1492.

(245) Li, F.; Clegg, J. K.; Lindoy, L. F.; Macquart, R. B.; Meehan, G. V. Metallosupramolecular Self-Assembly of a Universal 3-Ravel. *Nature Commun*. **2011**, *2*: 205.

(246) Bitsch, F.; Dietrich-Buchecker, C. O.; Khemiss, A. K.; Sauvage, J.-P.; Van Dorsselaer, A. Multiring Interlocked Systems: Structure Elucidation by Electrospray Mass Spectrometry. *J. Am. Chem. Soc*. **1991**, *113*, 4023–4025.

(247) Park, K.-M.; Kim, S.-Y.; Heo, J.; Whang, D.; Sakamoto, S.; Yamaguchi, K.; Kim, K. Designed Self-Assembly of Molecular Necklaces. *J. Am. Chem. Soc*. **2002**, *124*, 2140–2147.

(248) Fujita, M.; Fujita, N.; Ogura, K.; Yamaguchi, K. Spontaneous Assembly of Ten Components Into Two Interlocked, Identical Coordination Cages. *Nature* **1999**, *400*, 52–55.

(249) Fukuda, M.; Sekiya, R.; Kuroda, R. A Quadruply Stranded Metallohelicate and Its Spontaneous Dimerization Into an Interlocked Metallohelicate. *Angew. Chem., Int. Ed*. **2008**, *47*, 706–710.

(250) Ashton, P. R.; Reder, A. S.; Spencer, N.; Stoddart, J. F. Self-Assembly of a Chiral Bis[2]catenane. *J. Am. Chem. Soc*. **1993**, *115*, 5286–5287.

(251) Hamers, C.; Raymo, F. M.; Stoddart, J. F. Molecular Meccano 42. Main-Chain and Pendant Poly([2]catenane)s Incorporating Complementary π-Electron-Rich and -Deficient Components. *Eur. J. Org. Chem.* **1998**, 2109–2117.

(252) Geerts, Y.; Muscat, D.; Müllen, K. Synthesis of Oligo[2]catenanes. *Macromol. Chem. Phys*. **1995**, *196*, 3425–3435.

(253) Nielsen, M. B.; Thorup, N.; Becher, J. Synthesis of a Criss-Cross Overlapped Tetrathiafulvalenophane and a Topologically New [2]Catenane. *J. Chem. Soc., Perkin Trans*. *1* **1998**, 1305–1308.

(254) Dietrich-Buchecker, C.; Frommberger, B.; Lüer, I.; Sauvage, J.-P.; Vögtle, F. Multiring Catenanes with a Macrobicyclic Core. *Angew. Chem., Int. Ed. Engl*. **1993**, *32*, 1434–1437.

(255) Vogtle, F.; Safarowsky, O.; Heim, C.; Affeld, A.; Braun, O.; Mohry, A. Catenanes, Rotaxanes and Pretzelanes-Template Synthesis and Chirality. *Pure Appl. Chem*. **1999**, *71*, 247–251.

(256) Safarowsky, O.; Windisch, B.; Mohry, A.; Vögtle, F. Nomenclature for Catenanes, Rotaxanes, Molecular Knots, and Assemblies Derived From These Structural Elements. *J. Prakt. Chem*. **2000**, *342*, 437–444.

(257) Reuter, C.; Mohry, A.; Sobanski, A.; Vögtle, F. [1]Rotaxanes and Pretzelanes: Synthesis, Chirality, and Absolute Configuration. *Chem. Eur. J*. **2000**, *6*, 1674–1682.

(258) Li, Z.-T.; Stein, P. C.; Svenstrup, N.; Lund, K. H.; Becher, J. Synthesis of Novel Tetrathiafulvalene-Based [3]Pseudocatenanes by Self-Assembly; Prevention of *Trans*/*Cis* Isomerization. *Angew. Chem., Int. Ed. Engl*. **1995**, *34*, 2524–2528.

(259) Frey, J.; Kraus, T.; Heitz, V.; Sauvage, J.-P. A Catenane Consisting of a Large Ring Threaded Through Both Cyclic Units of a Handcuff-Like Compound. *Chem. Commun.* **2005**, 5310–5312.

(260) Evans, N. H.; Serpell, C. J.; Beer, P. D. Chloride Anion Templated Synthesis and Crystal Structure of a Handcuff Catenane. *Angew. Chem., Int. Ed*. **2011**, *50*, 2507–2510.

(261) Hartlieb, K. J.; Blackburn, A. K.; Schneebeli, S. T.; Forgan, R. S.; Sarjeant, A. A.; Stern, C. L.; Cao, D.; Stoddart, J. F. Topological Isomerism in a Chiral Handcuff Catenane. *Chem. Sci*. **2014**, *5*, 90–100.

(262) Zhu, X.-Z.; Chen, C.-F. A Highly Efficient Approach to [4]Pseudocatenanes by Threefold Metathesis Reactions of a Triptycene-Based Tris[2]pseudorotaxane. *J. Am. Chem. Soc*. **2005**, *127*, 13158–13159.

(263) Black, S. P.; Stefankiewicz, A. R.; Smulders, M. M. J.; Sattler, D.; Schalley, C. A.; Nitschke, J. R.; Sanders, J. K. M. Generation of a Dynamic System of Three-Dimensional Tetrahedral Polycatenanes. *Angew. Chem., Int. Ed*. **2013**, *52*, 5749–5752.

(264) Jäger, R.; Schmidt, T.; Karbach, D.; Vögtle, F. The First Pretzel-Shaped Molecules. via Catenane Precursors. *Synlett* **1996**, 723–725.

(265) Wu, Y.-W.; Tung, S.-T.; Lai, C.-C.; Liu, Y.-H.; Peng, S.-M.; Chiu, S.-H. Cyclic [2]Catenane Dimers, Trimers, and Tetramers. *Angew. Chem., Int. Ed*. **2015**, *54*, 11745–11749.

(266) McArdle, C. P.; Vittal, J. J.; Puddephatt, R. J. Molecular Topology: Easy Self-Assembly of an Organometallic Doubly Braided [2]Catenane. *Angew. Chem., Int. Ed*. **2000**, *39*, 3819–3822.

(267) Liu, Y.; Bonvallet, P. A.; Vignon, S. A.; Khan, S. I.; Stoddart, J. F. Donor-Acceptor Pretzelanes and a Cyclic Bis[2]catenane Homologue. *Angew. Chem., Int. Ed*. **2005**, *44*, 3050–3055.

(268) Ashton, P. R.; Horn, T.; Menzer, S.; Preece, J. A.; Spencer, N.; Stoddart, J. F.; Williams, D. J. Towards a Molecular Anchor Chain. Synthesis and Catenations of Spiro Crown Ethers. *Synthesis* **1997**, 480–488.

(269) Wang, L.; Vysotsky, M. O.; Bogdan, A.; Bolte, M.; Böhmer, V. Multiple Catenanes Derived From Calix[4]arenes. *Science* **2004**, *304*, 1312–1314.

(270) Zhang, G.; Presly, O.; White, F.; Oppel, I. M.; Mastalerz, M. A Shape-Persistent Quadruply Interlocked Giant Cage Catenane with Two Distinct Pores in the Solid State. *Angew. Chem., Int. Ed*. **2014**, *53*, 5126–5130.

(271) Jäger, R.; Händel, M.; Harren, J.; Rissanen, K.; Vögtle, F.; Rissanen, K. Chemistry with Rotaxanes: Intra- and Intermolecularly Covalently Linked Rotaxanes. *Liebigs Ann*. **1996**, 1201–1207.

(272) Zhou, Q.; Wei, P.; Zhang, Y.; Yu, Y.; Yan, X. Benzo-21-crown-7-Based [1]Rotaxanes: Syntheses, X-Ray Crystal Structures, and Dynamic Characteristics. *Org. Lett*. **2013**, *15*, 5350–5353.

(273) Nygaard, S.; Liu, Y.; Stein, P C; Flood, A. H.; Jeppesen, J. O. Using Molecular Force to Overcome Steric Barriers in a Springlike Molecular Ouroboros. *Adv. Funct. Mater*. **2007**, *17*, 751–762.

(274) Nielsen, K. A.; Bähring, S.; Jeppesen, J. O. Acid/Base Controllable Molecular Recognition. *Chem. Eur. J*. **2011**, *17*, 11001–11007.

(275) Rosengren, K. J.; Clark, R. J.; Daly, N. L.; Göransson, U.; Jones, A.; Craik, D. J. Microcin J25 Has a Threaded Sidechain-to-Backbone Ring Structure and Not a Head-to-Tail Cyclized Backbone. *J. Am. Chem. Soc*. **2003**, *125*, 12464–12474.

(276) Wilson, K.-A.; Kalkum, M.; Ottesen, J.; Yuzenkova, J.; Chait, B. T.; Landick, R.; Muir, T.; Severinov, K.; Darst, S. A. Structure of Microcin J25, a Peptide Inhibitor of Bacterial RNA Polymerase, is a Lassoed Tail. *J. Am. Chem. Soc*. **2003**, *125*, 12475–12483.

(277) Clavel, C.; Romuald, C.; Brabet, E.; Coutrot, F. A pH-Sensitive Lasso-Based Rotaxane Molecular Switch. *Chem. Eur. J*. **2013**, *19*, 2982–2989.

(278) Bruns, C. J.; Frasconi, M.; Iehl, J.; Hartlieb, K. J.; Schneebeli, S. T.; Cheng, C.; Stupp, S. I.; Stoddart, J. F. Redox Switchable Daisy Chain Rotaxanes Driven by Radical–Radical Interactions. *J. Am. Chem. Soc*. **2014**, *136*, 4714–4723.

(279) Reuter, C.; Wienand, W.; Schmuck, C.; Vögtle, F. A Self-Threaded “Molecular 8.” *Chem. Eur. J*. **2001**, *7*, 1728–1733.

(280) Boyle, M. M.; Forgan, R. S.; Friedman, D. C.; Gassensmith, J. J.; Smaldone, R. A.; Stoddart, J. F.; Sauvage, J.-P. Donor–Acceptor Molecular Figures-of-Eight. *Chem. Commun*. **2011**, *47*, 11870–11872.

(281) Boyle, M. M.; Gassensmith, J. J.; Whalley, A. C.; Forgan, R. S.; Smaldone, R. A.; Hartlieb, K. J.; Blackburn, A. K.; Sauvage, J.-P.; Stoddart, J. F. Stereochemistry of Molecular Figures-of-Eight. *Chem. Eur. J*. **2012**, *18*, 10312–10323.

(282) Rotzler, J.; Mayor, M. Molecular Daisy Chains. *Chem. Soc. Rev*. **2013**, *42*, 44–62.

(283) Ashton, P. R.; Parsons, I. W.; Raymo, F. M.; Stoddart, J. F.; White, A. J. P.; Williams, D. J.; Wolf, R. Self-Assembling Supramolecular Daisy Chains. *Angew. Chem., Int. Ed*. **1998**, *37*, 1913–1916.

(284) Rowan, S. J.; Cantrill, S. J.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. Toward Daisy Chain Polymers: “Wittig Exchange” of Stoppers in [2]Rotaxane Monomers. *Org. Lett*. **2000**, *2*, 759–762.

(285) Chiu, S.-H.; Rowan, S. J.; Cantrill, S. J.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. An Hermaphroditic [*c*2]Daisy Chain. *Chem. Commun*. **2002**, *2948–2949*.

(286) Hoshino, T.; Miyauchi, M.; Kawaguchi, Y.; Yamaguchi, H.; Harada, A. Daisy Chain Necklace: Tri[2]rotaxane Containing Cyclodextrins. *J. Am. Chem. Soc*. **2000**, *122*, 9876–9877.

(287) Romuald, C.; Cazals, G.; Enjalbal, C.; Coutrot, F. Straightforward Synthesis of a Double-Lasso Macrocycle From a Nonsymmetrical [*c*2]Daisy Chain. *Org. Lett*. **2013**, *15*, 184–187.

(288) Jiménez, M. C.; Dietrich-Buchecker, C.; Sauvage, J.-P. Towards Synthetic Molecular Muscles: Contraction and Stretching of a Linear Rotaxane Dimer. *Angew. Chem., Int. Ed*. **2000**, *39*, 3284–3287.

(289) Collin, J.-P.; Dietrich-Buchecker, C.; Gaviña, P.; Jimenez-Molero, M. C.; Sauvage, J.-P. Shuttles and Muscles: Linear Molecular Machines Based on Transition Metals. *Acc. Chem. Res*. **2001**, *34*, 477–487.

(290) Jimenez-Molero, M. C.; Dietrich-Buchecker, C.; Sauvage, J.-P. Towards Artificial Muscles at the Nanometric Level. *Chem. Commun.* **2003**, 1613–1616.

(291) Niess, F.; Duplan, V.; Sauvage, J.-P. Molecular Muscles: From Species in Solution to Materials and Devices. *Chem. Lett*. **2014**, *43*, 964–974.

(292) Kishan, M. R.; Parham, A.; Schelhase, F.; Yoneva, A.; Silva, G.; Chen, X.; Okamoto, Y.; Vögtle, F. Bridging Rotaxanes’ Wheels—Cyclochiral Bonnanes. *Angew. Chem., Int. Ed*. **2006**, *45*, 7296–7299.

(293) Ciao, R.; Talotta, C.; Gaeta, C.; Margarucci, L.; Casapullo, A.; Neri, P. An Oriented Handcuff Rotaxane. *Org. Lett*. **2013**, *15*, 5694–5697.

(294) Aricó, F.; Chang, T.; Cantrill, S. J.; Khan, S. I.; Stoddart, J. F. Template-Directed Synthesis of Multiply Mechanically Interlocked Molecules Under Thermodynamic Control. *Chem. Eur. J*. **2005**, *11*, 4655–4666.

(295) Collin, J.-P.; Durola, F.; Frey, J.; Heitz, V.; Reviriego, F.; Sauvage, J.-P.; Trolez, Y.; Rissanen, K. Templated Synthesis of Cyclic [4]Rotaxanes Consisting of Two Stiff Rods Threaded Through Two Bis-Macrocycles with a Large and Rigid Central Plate as Spacer. *J. Am. Chem. Soc*. **2010**, *132*, 6840–6850.

(296) Badjić, J. D.; Balzani, V.; Credi, A.; Lowe, J. N.; Silvi, S.; Stoddart, J. F. A Mechanically Interlocked Bundle. *Chem. Eur. J*. **2004**, *10*, 1926–1935.

(297) Yamada, Y.; Okamoto, M.; Furukawa, K.; Kato, T.; Tanaka, K. Switchable Intermolecular Communication in a Four-Fold Rotaxane. *Angew. Chem., Int. Ed*. **2012**, *51*, 709–713.

(298) Yamada, Y.; Mihara, N.; Shibano, S.; Sugimoto, K.; Tanaka, K. Triply Stacked Heterogeneous Array of Porphyrins and Phthalocyanine Through Stepwise Formation of a Fourfold Rotaxane and an Ionic Complex. *J. Am. Chem. Soc*. **2013**, *135*, 11505–11508.

(299) Northrop, B. H.; Aricó, F.; Tangchiavang, N.; Badjić, J. D.; Stoddart, J. F. Template-Directed Synthesis of Mechanically Interlocked Molecular Bundles Using Dynamic Covalent Chemistry. *Org. Lett*. **2006**, *8*, 3899–3902.

(300) Belowich, M. E.; Valente, C.; Smaldone, R. A.; Friedman, D. C.; Thiel, J.; Cronin, L.; Stoddart, J. F. Positive Cooperativity in the Template-Directed Synthesis of Monodisperse Macromolecules. *J. Am. Chem. Soc*. **2012**, *134*, 5243–5261.

(301) Basu, S.; Coskun, A.; Friedman, D. C.; Olson, M. A.; Benítez, D.; Tkatchouk, E.; Barin, G.; Yang, J.; Fahrenbach, A. C.; Goddard, W. A. III; Stoddart, J. F. Donor-Acceptor Oligorotaxanes Made to Order. *Chem. Eur. J*. **2011**, *17*, 2107–2119.

(302) Zhu, Z.; Bruns, C. J.; Li, H.; Lei, J.; Ke, C.; Liu, Z.; Shafaie, S.; Colquhoun, H. M.; Stoddart, J. F. Synthesis and Solution-State Dynamics of Donor–Acceptor Oligorotaxane Foldamers. *Chem. Sci*. **2013**, *4*, 1470–1483.

(303) Bruns, C. J.; Stoddart, J. F. Mechanically Interlaced and Interlocked Donor–Acceptor Foldamers. *Adv. Polym. Sci*. **2013**, *261*, 271–294.

(304) Xue, W.; Li, Z.; Liu, G.; Chen, X.; Li, T.; Liu, S. H.; Yin, J. Construction of Rotacatenanes Using Rotaxane and Catenane Frameworks. *Org. Biomol. Chem*. **2014**, *12*, 4862–4871.

(305) Klotz, E. J. F.; Claridge, T. D. W.; Anderson, H. L. Homo- and Hetero-[3]Rotaxanes with Two π-Systems Clasped in a Single Macrocycle. *J. Am. Chem. Soc*. **2006**, *128*, 15374–15375.

(306) Prikhod'ko, A.; Sauvage, J.-P. Passing Two Strings Through the Same Ring Using an Octahedral Metal Center as Template: A New Synthesis of [3]Rotaxanes. *J. Am. Chem. Soc*. **2009**, *131*, 6794–6807.

(307) Chean, H. M.; Leigh, D. A.; Maffei, F.; McGonigal, P. R.; Slawin, A. M. Z.; Wu, J. En Route to a Molecular Sheaf: Active Metal Template Synthesis of a [3]Rotaxane with Two Axles Threaded Through One Ring. *J. Am. Chem. Soc*. **2011**, *133*, 12298–12303.

(308) Schill, G.; Schweickert, N.; Fritz, H.; Vetter, W. [2]-[Cyclohexatetraoctane][cyclooctacosane]catenane, the First Hydrocarbon Catenane. *Angew. Chem., Int. Ed. Engl*. **1983**, *22*, 889–891.

(309) Ashton, P. R.; Philp, D.; Spencer, N.; Stoddart, J. F. A New Design Strategy for the Self-Assembly of Molecular Shuttles. *J. Chem. Soc., Chem. Commun*. **1992**, 1124–1128.

(310) Mohr, B.; Sauvage, J.-P.; Grubbs, R. H.; Weck, M. High-Yield Synthesis of [2]Catenanes by Intramolecular Ring-Closing Metathesis. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 1308–1310.

(311) Kolchinski, A. G.; Alcock, N. W.; Roesner, R. A.; Busch, D. H. Molecular Riveting: High Yield Preparation of a [3]-Rotaxane. *Chem. Commun.* **1998**, 1437–1438.

(312) Miljanić, O. Š.; Stoddart, J. F. Dynamic Donor-Acceptor [2]Catenanes. *Proc. Natl. Acad. Sci. U.S.A*. **2007**, *104*, 12966–12970.

(313) Yamamoto, M.; Takeuchi, M.; Shinkai, S. Oligosaccharide Binding to a Boronic-Acid-Appended Phenanthroline-Cu(I) Complex Which Creates Superstructural Helicates and Catenates. *Tetrahedron* **2002**, *58*, 7251–7258.

(314) Lu, T.; Zhang, L.; Gokel, G. W.; Kaifer, A. E. The First Surface-Attached Catenane: Self-Assembly of a Two-Component Monolayer. *J. Am. Chem. Soc*. **1993**, *115*, 2542–2543.

(315) Rowan, S. J.; Stoddart, J. F. Thermodynamic Synthesis of Rotaxanes by Imine Exchange. *Org. Lett*. **1999**, *1*, 1913–1916.

(316) Ko, Y. H.; Kim, K.; Kang, J.-K.; Chun, H.; Lee, J. W.; Sakamoto, S.; Yamaguchi, K.; Fettinger, J. C.; Kim, K. Designed Self-Assembly of Molecular Necklaces Using Host-Stabilized Charge-Transfer Interactions. *J. Am. Chem. Soc*. **2004**, *126*, 1932–1933.

(317) Dasgupta, S.; Wu, J. Template-Directed Synthesis of Kinetically and Thermodynamically Stable Molecular Necklace Using Ring Closing Metathesis. *Org. Biomol. Chem*. **2011**, *9*, 3504–3515.

(318) Frey, J.; Kraus, T.; Heitz, V.; Sauvage, J.-P. Synthesis of a Bis-Macrocycle Containing Two Back-to-Back Rigidly Connected 1,10-Phenanthroline Units as a Central Core and Its Incorporation in a Handcuff-Like Catenane. *Chem. Eur. J*. **2007**, *13*, 7584–7594.

(319) Henkelis, J. J.; Ronson, T. K.; Harding, L. P.; Hardie, M. J. M_3L_2 Metallo-Cryptophanes: [2]Catenane and Simple Cages. *Chem. Commun*. **2011**, *47*, 6560–6562.

(320) Rapenne, G.; Dietrich-Buchecker, C.; Sauvage, J.-P. Copper(I)- or Iron(II)-Templated Synthesis of Molecular Knots Containing Two Tetrahedral or Octahedral Coordination Sites. *J. Am. Chem. Soc*. **1999**, *121*, 994–1001.

(321) Dietrich-Buchecker, C.; Rapenne, G.; Sauvage, J.-P. Synthesis of Catenanes and Molecular Knots by Copper(I)-Directed Formation of the Precursors Followed by Ruthenium(II)-Catalyzed Ring-Closing Metathesis. *Coord. Chem. Rev*. **1999**, *185-186*, 167–176.

(322) Guo, J.; Mayers, P. C.; Breault, G. A.; Hunter, C. A. Synthesis of a Molecular Trefoil Knot by Folding and Closing on an Octahedral Coordination Template. *Nature Chem*. **2010**, *2*, 218–222.

(323) Ayme, J.-F.; Gil-Ramírez, G.; Leigh, D. A.; Lemonnier, J.-F.; Markevicius, A.; Muryn, C. A.; Zhang, G. Lanthanide Template Synthesis of a Molecular Trefoil Knot. *J. Am. Chem. Soc*. **2014**, *136*, 13142–13145.

(324) Dietrich-Buchecker, C.; Sauvage, J.-P. Lithium Templated Synthesis of Catenanes: Efficient Synthesis of Doubly Interlocked [2]-Catenanes. *Chem. Commun.* **1999**, 615–616.

(325) Pentecost, C. D.; Chichak, K. S.; Peters, A. J.; Cave, G. W. V.; Cantrill, S. J.; Stoddart, J. F. A Molecular Solomon Link. *Angew. Chem., Int. Ed*. **2007**, *46*, 218–222.

(326) Peinador, C.; Blanco, V.; Quintela, J. M. A New Doubly Interlocked [2]Catenane. *J. Am. Chem. Soc*. **2009**, *131*, 920–921.

(327) Chichak, K. S.; Cantrill, S. J.; Stoddart, J. F. Dynamic Nanoscale Borromean Links. *Chem. Commun.* **2005**, 3391–3393.

(328) Meyer, C. D.; Forgan, R. S.; Chichak, K. S.; Peters, A. J.; Tangchaivang, N.; Cave, G. W. V.; Khan, S. I.; Cantrill, S. J.; Stoddart, J. F. The Dynamic Chemistry of Molecular Borromean Rings and Solomon Knots. *Chem. Eur. J*. **2010**, *16*, 12570–12581.

(329) Evans, N. H.; Beer, P. D. A Janus [2]Rotaxane Synthesized by Using an Anion-Templated Clipping Methodology. *Chem. Eur. J*. **2011**, *17*, 10542–10546.

(330) Bozdemir, O. A.; Barin, G.; Belowich, M. E.; Basuray, A. N.; Beuerle, F.; Stoddart, J. F. Dynamic Covalent Templated-Synthesis of [*c*2]Daisy Chains. *Chem. Commun*. **2012**, *48*, 10401–10403.

(331) Badjić, J. D.; Cantrill, S. J.; Grubbs, R. H.; Guidry, E. N.; Orenes, R.; Stoddart, J. F. The Exclusivity of Multivalency in Dynamic Covalent Processes. *Angew. Chem., Int. Ed*. **2004**, *43*, 3273–3278.

(332) Saito, S.; Takahashi, E.; Nakazono, K. Synthesis of [2]Rotaxanes by the Catalytic Reactions of a Macrocyclic Copper Complex. *Org. Lett*. **2006**, *8*, 5133–5136.

(333) Aucagne, V.; Hänni, K. D.; Leigh, D. A.; Lusby, P. J.; Walker, D. Catalytic "Click" Rotaxanes: A Substoichiometric Metal-Template Pathway to Mechanically Interlocked Architectures. *J. Am. Chem. Soc*. **2006**, *128*, 2186–2187.

(334) Crowley, J. D.; Goldup, S. M.; Lee, A.-L.; Leigh, D. A.; McBurney, R. T. Active Metal Template Synthesis of Rotaxanes, Catenanes and Molecular Shuttles. *Chem. Soc. Rev*. **2009**, *38*, 1530–1541.

(335) Berná, J.; Goldup, S. M.; Lee, A.-L.; Leigh, D. A.; Symes, M. D.; Teobaldi, G.; Zerbetto, F. Cadiot-Chodkiewicz Active Template Synthesis of Rotaxanes and Switchable Molecular Shuttles with Weak Intercomponent Interactions. *Angew. Chem., Int. Ed*. **2008**, *47*, 4392–4396.

(336) Berná, J.; Crowley, J. D.; Goldup, S. M.; Hänni, K. D.; Lee, A.-L.; Leigh, D. A. A Catalytic Palladium Active-Metal Template

Pathway to [2]Rotaxanes. *Angew. Chem., Int. Ed*. **2007**, *46*, 5709–5713.

(337) Crowley, J. D.; Goldup, S. M.; Gowans, N. D.; Leigh, D. A.; Ronaldson, V. E.; Slawin, A. M. Z. An Unusual Nickel-Copper-Mediated Alkyne Homocoupling Reaction for the Active-Template Synthesis of [2]Rotaxanes. *J. Am. Chem. Soc*. **2010**, *132*, 6243–6248.

(338) Goldup, S. M.; Leigh, D. A.; McBurney, R. T.; McGonigal, P. R.; Plant, A. Ligand-Assisted Nickel-Catalysed sp^3–sp^3 Homocoupling of Unactivated Alkyl Bromides and Its Application to the Active Template Synthesis of Rotaxanes. *Chem. Sci*. **2010**, *1*, 383–386.

(339) Crowley, J. D.; Hänni, K. D.; Lee, A.-L.; Leigh, D. A. [2]Rotaxanes Through Palladium Active-Template Oxidative Heck Cross-Couplings. *J. Am. Chem. Soc*. **2007**, *129*, 12092–12093.

(340) Goldup, S. M.; Leigh, D. A.; Lusby, P. J.; McBurney, R. T.; Slawin, A. M. Z. Active Template Synthesis of Rotaxanes and Molecular Shuttles with Switchable Dynamics by Four-Component Pd^{II}-Promoted Michael Additions. *Angew. Chem., Int. Ed*. **2008**, *47*, 3381–3384.

(341) Crowley, J. D.; Hänni, K. D.; Leigh, D. A.; Slawin, A. M. Z. Diels-Alder Active-Template Synthesis of Rotaxanes and Metal-Ion-Switchable Molecular Shuttles. *J. Am. Chem. Soc*. **2010**, *132*, 5309–5314.

(342) Hoekman, S.; Kitching, M. O.; Leigh, D. A.; Papmeyer, M.; Roke, D. Goldberg Active Template Synthesis of a [2]Rotaxane Ligand for Asymmetric Transition-Metal Catalysis. *J. Am. Chem. Soc*. **2015**, *137*, 7656–7659.

(343) Whitesides, G. M.; Ismagilov, R. F. Complexity in Chemistry. *Science* **1999**, *284*, 89–92.

(344) Whitesides, G. M. Reinventing Chemistry. *Angew. Chem., Int. Ed*. **2015**, *54*, 3196–3209.

(345) Balazs, A. C.; Epstein, I. R. Emergent or Just Complex? *Science* **2009**, *325*, 1632–1633.

(346) Gibb, B. C. The Emergence of Emergence. *Nature Chem*. **2011**, *3*, 3–4.

(347) Taylor, E. An Explication of Emergence. *Philos. Stud*. **2015**, *172*, 653–669.

(348) Stoddart, J. F. A Platform for Change. *Supramol. Chem*. **2015**, *27*, 567–570.

(349) Lorenz, E. N. *The Essence of Chaos*; University of Washington Press: Seattle, **1995**.

(350) Corbett, P. T.; Leclaire, J.; Vial, L.; West, K. R.; Wietor, J.-L.; Sanders, J. K. M.; Otto, S. Dynamic Combinatorial Chemistry. *Chem. Rev*. **2006**, *106*, 3652–3711.

(351) Lam, R. T. S.; Belenguer, A.; Roberts, S. L.; Naumann, C.; Jarrosson, T.; Otto, S.; Sanders, J. K. M. Amplification of Acetylcholine-Binding Catenanes From Dynamic Combinatorial Libraries. *Science* **2005**, *308*, 667–669.

(352) Prakasam, T.; Lusi, M.; Elhabiri, M.; Platas-Iglesias, C.; Olsen, J.-C.; Asfari, Z.; Cianférani-Sanglier, S.; Debaene, F.; Charbonnière, L. J.; Trabolsi, A. Simultaneous Self-Assembly of a [2]Catenane, a Trefoil Knot, and a Solomon Link From a Simple Pair of Ligands. *Angew. Chem., Int. Ed*. **2013**, *52*, 9956–9960.

(353) Olson, M. A.; Coskun, A.; Fang, L.; Basuray, A. N.; Stoddart, J. F. Polycatenation under Thermodynamic Control. *Angew. Chem., Int. Ed*. **2010**, *49*, 3151–3156.

(354) Astumian, R. D. Thermodynamics and Kinetics of a Brownian Motor. *Science* **1997**, *276*, 917–922.

(355) Astumian, R. D.; Hänggi, P. Brownian Motors. *Phys. Today* **2002**, *55*, 33–39.

(356) Murakami, H.; Kawabuchi, A.; Kotoo, K.; Kunitake, M.; Nakashima, N. A Light-Driven Molecular Shuttle Based on a Rotaxane. *J. Am. Chem. Soc*. **1997**, *119*, 7605–7606.

(357) Mock, W. L.; Pierpont, J. A Cucurbituril-Based Molecular Switch. *J. Chem. Soc., Chem. Commun.* **1990**, 1509–1511.

(358) Dietrich-Buchecker, C. O.; Sauvage, J.-P.; Kern, J.-M. Templated Synthesis of Interlocked Macrocyclic Ligands: The Catenands. *J. Am. Chem. Soc*. **1984**, *106*, 3043–3045.

(359) Lin, C.-F.; Lai, C.-C.; Liu, Y.-H.; Peng, S.-M.; Chiu, S.-H. Use of Anions to Allow Translational Isomerism of a [2]Rotaxane. *Chem. Eur. J*. **2007**, *13*, 4350–4355.

(360) Ashton, P. R.; Blower, M. A.; Philp, D.; Spencer, N.; Stoddart, J. F.; Tolley, M. S.; Ballardini, R.; Ciano, M.; Balzani, V.; Gandolfi, M. T.; Prodi, L.; McLean, C. H. The Control of Translational Isomerism in Catenated Structures. *New J. Chem*. **1993**, *17*, 689–695.

(361) Leigh, D. A.; Pérez, E. M. Shuttling Through Reversible Covalent Chemistry. *Chem. Commun.* **2004**, 2262–2263.

(362) Martinez-Cuezva, A.; Berná, J.; Orenes, R.-A.; Pastor, A.; Alajarín, M. Small-Molecule Recognition for Controlling Molecular Motion in Hydrogen-Bond-Assembled Rotaxanes. *Angew. Chem., Int. Ed*. **2014**, *53*, 6762–6767.

(363) Asakawa, M.; Ashton, P. R.; Dehaen, W.; L'abbé, G.; Menzer, S.; Nouwen, J.; Raymo, F. M.; Stoddart, J. F.; Tolley, M. S.; Toppet, S.; White, A. J. P.; Williams, D. J. Molecular Meccano 19. Self-Assembly of Novel [2]Catenanes and [2]Pseudorotaxanes Incorporating Thiacrown Ethers or Their Acyclic Analogs. *Chem. Eur. J*. **1997**, *3*, 772–787.

(364) Sørensen, A.; Andersen, S. S.; Flood, A. H.; Jeppesen, J. O. Pressure Effects in the Synthesis of Isomeric Rotaxanes. *Chem. Commun*. **2013**, *49*, 5936–5938.

(365) Shigekawa, H.; Miyake, K.; Sumaoka, J.; Harada, A.; Komiyama, M. The Molecular Abacus: STM Manipulation of Cyclodextrin Necklace. *J. Am. Chem. Soc*. **2000**, *122*, 5411–5412.

(366) Hernandez, J. V.; Kay, E. R.; Leigh, D. A. A Reversible Synthetic Rotary Molecular Motor. *Science* **2004**, *306*, 1532–1537.

(367) Arduini, A.; Bussolati, R.; Credi, A.; Monaco, S.; Secchi, A.; Silvi, S.; Venturi, M. Solvent- and Light-Controlled Unidirectional Transit of a Nonsymmetric Molecular Axle Through a Nonsymmetric Molecular Wheel. *Chem. Eur. J*. **2012**, *18*, 16203–16213.

(368) Li, H.; Cheng, C.; McGonigal, P. R.; Fahrenbach, A. C.; Frasconi, M.; Liu, W.-G.; Zhu, Z.; Zhao, Y.; Ke, C.; Lei, J.; Young, R. Y.; Dyar, S. M.; Co, D. T.; Yang, Y.-W.; Botros, Y. Y.; Goddard, W. A. III; Wasielewski, M. R.; Astumian, R. D.; Stoddart, J. F. Relative Unidirectional Translation in an Artificial Molecular Assembly Fueled by Light. *J. Am. Chem. Soc*. **2013**, *135*, 18609–18620.

(369) Ragazzon, G.; Baroncini, M.; Silvi, S.; Venturi, M.; Credi, A. Light-Powered Autonomous and Directional Molecular Motion of a Dissipative Self-Assembling System. *Nature Nanotechnol*. **2015**, *10*, 70–75.

(370) Chatterjee, M. N.; Kay, E. R.; Leigh, D. A. Beyond Switches: Ratcheting a Particle Energetically Uphill with a Compartmentalized Molecular Machine. *J. Am. Chem. Soc*. **2006**, *128*, 4058–4073.

(371) Serreli, V.; Lee, C.-F.; Kay, E. R.; Leigh, D. A. A Molecular Information Ratchet. *Nature* **2007**, *445*, 523–527.

(372) Alvarez-Pérez, M.; Goldup, S. M.; Leigh, D. A.; Slawin, A. M. Z. A Chemically-Driven Molecular Information Ratchet. *J. Am. Chem. Soc*. **2008**, *130*, 1836–1838.

(373) Carlone, A.; Goldup, S. M.; Lebrasseur, N.; Leigh, D. A.; Wilson, A. A Three-Compartment Chemically-Driven Molecular Information Ratchet. *J. Am. Chem. Soc*. **2012**, *134*, 8321–8323.

(374) Cheng, C.; McGonigal, P. R.; Liu, W.-G.; Li, H.; Vermeulen, N. A.; Ke, C.; Frasconi, M.; Stern, C. L.; Goddard, W. A., III; Stoddart, J. F. Energetically Demanding Transport in a Supramolecular Assembly. *J. Am. Chem. Soc*. **2014**, *136*, 14702–14705.

(375) Cheng, C.; McGonigal, P. R.; Schneebeli, S. T.; Li, H.; Vermeulen, N. A.; Ke, C.; Stoddart, J. F. An Artificial Molecular Pump. *Nature Nanotechnol*. **2015**, *10*, 547–553.

(376) Sevick, E. Nanomachines: A Light-Driven Molecular Pump. *Nature Nanotechnol*. **2015**, *10*, 18–19.

(377) Balzani, V.; Gómez-López, M.; Stoddart, J. F. Molecular Machines. *Acc. Chem. Res*. **1998**, *31*, 405–414.

(378) Sauvage, J.-P. Transition Metal-Containing Rotaxanes and Catenanes in Motion: Toward Molecular Machines and Motors. *Acc. Chem. Res*. **1998**, *31*, 611–619.
(379) Balzani, V.; Credi, A.; Raymo, F. M.; Stoddart, J. F. Artificial Molecular Machines. *Angew. Chem., Int. Ed*. **2000**, *39*, 3348–3391.
(380) Dietrich-Buchecker, C.; Jimenez-Molero, M. C.; Sartor, V.; Sauvage, J.-P. Rotaxanes and Catenanes as Prototypes of Molecular Machines and Motors. *Pure Appl. Chem*. **2003**, *75*, 1383–1393.
(381) Balzani, V.; Venturi, M.; Credi, A. *Molecular Devices and Machines: A Journey Into the Nanoworld*; 2nd ed.; Wiley-VCH: Weinheim, **2008**.
(382) Flood, A. H.; Ramirez, R. J. A.; Deng, W.-Q.; Muller, R. P.; Goddard, W. A., III; Stoddart, J. F. Meccano on the Nanoscale - A Blueprint for Making Some of the World's Tiniest Machines. *Aust. J. Chem*. **2004**, *57*, 301–322.
(383) Collin, J.-P.; Heitz, V.; Sauvage, J.-P. Transition-Metal-Complexed Catenanes and Rotaxanes in Motion: Towards Molecular Machines. *Top. Curr. Chem*. **2005**, *262*, 29–62.
(384) Balzani, V.; Credi, A.; Silvi, S.; Venturi, M. Artificial Nanomachines Based on Interlocked Molecular Species: Recent Advances. *Chem. Soc. Rev*. **2006**, *35*, 1135–1149.
(385) Credi, A. Artificial Nanomachines Based on Interlocked Molecules. *J. Phys.: Condens. Matter* **2006**, *18*, S1779–S1795.
(386) Kay, E. R.; Leigh, D. A.; Zerbetto, F. Synthetic Molecular Motors and Mechanical Machines. *Angew. Chem., Int. Ed*. **2007**, *46*, 72–191.
(387) Kay, E. R.; Leigh, D. A. Beyond Switches: Rotaxane- and Catenane-Based Synthetic Molecular Motors. *Pure Appl. Chem*. **2008**, *80*, 17–29.
(388) Fahrenbach, A. C.; Bruns, C. J.; Cao, D.; Stoddart, J. F. Ground-State Thermodynamics of Bistable Redox-Active Donor–Acceptor Mechanically Interlocked Molecules. *Acc. Chem. Res*. **2012**, *45*, 1581–1592.
(389) Yang, W.; Li, Y.; Liu, H.; Chi, L.; Li, Y. Design and Assembly of Rotaxane-Based Molecular Switches and Machines. *Small* **2012**, *8*, 504–516.
(390) Neal, E. A.; Goldup, S. M. Chemical Consequences of Mechanical Bonding in Catenanes and Rotaxanes: Isomerism, Modification, Catalysis and Molecular Machines for Synthesis. *Chem. Commun*. **2014**, *50*, 5128–5142.
(391) Fahrenbach, A. C.; Bruns, C. J.; Li, H.; Trabolsi, A.; Coskun, A.; Stoddart, J. F. Ground-State Kinetics of Bistable Redox-Active Donor–Acceptor Mechanically Interlocked Molecules. *Acc. Chem. Res*. **2014**, *47*, 482–493.
(392) Coskun, A.; Banaszak, M.; Astumian, R. D.; Stoddart, J. F.; Grzybowski, B. A. Great Expectations: Can Artificial Molecular Machines Deliver on Their Promise? *Chem. Soc. Rev*. **2012**, *41*, 19–30.
(393) Abendroth, J. M.; Bushuyev, O. S.; Weiss, P. S.; Barrett, C. J. Controlling Motion at the Nanoscale: Rise of the Molecular Machines. *ACS Nano* **2015**, *9*, 7746–7768.
(394) Cheng, C.; McGonigal, P. R.; Stoddart, J. F.; Astumian, R. D. Design and Synthesis of Nonequilibrium Systems. *ACS Nano* **2015**, *9*, 8672–8688.
(395) Kay, E. R.; Leigh, D. A. Rise of the Molecular Machines. *Angew. Chem., Int. Ed*. **2015**, *54*, 10080–10088.
(396) Erbas-Cakmak, S.; Leigh, D. A.; McTernan, C. T.; Nussbaumer, A. L. Artificial Molecular Machines. *Chem. Rev*. **2015**, *115*, 10081–10206.
(397) Browne, W. R.; Feringa, B. L. Making Molecular Machines Work. *Nature Nanotechnol*. **2006**, *1*, 25–35.
(398) Stoddart, J. F. Thither Supramolecular Chemistry? *Nature Chem*. **2009**, *1*, 14–15.
(399) Deng, H.; Olson, M. A.; Stoddart, J. F.; Yaghi, O. M. Robust Dynamics. *Nature Chem*. **2010**, *2*, 439–443.
(400) Boyle, M. M.; Smaldone, R. A.; Whalley, A. C.; Ambrogio, M. W.; Botros, Y. Y.; Stoddart, J. F. Mechanised Materials. *Chem. Sci*. **2011**, *2*, 204–210.
(401) Brough, B.; Northrop, B. H.; Schmidt, J. J.; Tseng, H.-R.; Houk, K. N.; Stoddart, J. F.; Ho, C.-M. Evaluation of Synthetic Linear Motor-Molecule Actuation Energetics. *Proc. Natl. Acad. Sci. U.S.A*. **2006**, *103*, 8583–8588.
(402) Lussis, P.; Svaldo-Lanero, T.; Bertocco, A.; Fustin, C.-A.; Leigh, D. A.; Duwez, A.-S. A Single Synthetic Small Molecule That Generates Force Against a Load. *Nature Nanotechnol*. **2011**, *6*, 553–557.
(403) Huang, T. J.; Brough, B.; Ho, C.-M.; Liu, Y.; Flood, A. H.; Bonvallet, P. A.; Tseng, H.-R.; Stoddart, J. F.; Baller, M.; Magonov, S. A Nanomechanical Device Based on Linear Molecular Motors. *Appl. Phys. Lett*. **2004**, *85*, 5391–5393.
(404) Liu, Y.; Flood, A. H.; Bonvallet, P. A.; Vignon, S. A.; Northrop, B. H.; Tseng, H.-R.; Jeppesen, J. O.; Huang, T. J.; Brough, B.; Baller, M.; Magonov, S.; Solares, S. D.; Goddard, W. A. III; Ho, C.-M.; Stoddart, J. F. Linear Artificial Molecular Muscles. *J. Am. Chem. Soc*. **2005**, *127*, 9745–9759.
(405) Juluri, B. K.; Kumar, A. S.; Liu, Y.; Ye, T.; Yang, Y.-W.; Flood, A. H.; Fang, L.; Stoddart, J. F.; Weiss, P. S.; Huang, T. J. A Mechanical Actuator Driven Electrochemically by Artificial Molecular Muscles. *ACS Nano* **2009**, *3*, 291–300.
(406) Du, G.; Moulin, E.; Jouault, N.; Buhler, E.; Giuseppone, N. Muscle-Like Supramolecular Polymers: Integrated Motion From Thousands of Molecular Machines. *Angew. Chem., Int. Ed*. **2012**, *51*, 12504–12508.
(407) Goujon, A.; Du, G.; Moulin, E.; Fuks, G.; Maaloum, M.; Buhler, E.; Giuseppone, N. Hierarchical Self-Assembly of Supramolecular Muscle-Like Fibers. *Angew. Chem., Int. Ed*. **2016**, *55*, 703–707.
(408) Berná, J.; Leigh, D. A.; Lubomska, M.; Mendoza, S. M.; Pérez, E. M.; Rudolf, P.; Teobaldi, G.; Zerbetto, F. Macroscopic Transport by Synthetic Molecular Machines. *Nature Mater*. **2005**, *4*, 704–710.
(409) Collier, C. P.; Wong, E. W.; Behloradský, M.; Raymo, F. M.; Stoddart, J. F.; Kuekes, P. J.; Williams, R. S.; Heath, J. R. Electronically Configurable Molecular-Based Logic Gates. *Science* **1999**, *285*, 391–394.
(410) Wong, E. W.; Collier, C. P.; Behloradský, M.; Raymo, F. M.; Stoddart, J. F.; Heath, J. R. Fabrication and Transport Properties of Single-Molecule-Thick Electrochemical Junctions. *J. Am. Chem. Soc*. **2000**, *122*, 5831–5840.
(411) Collier, C. P.; Mattersteig, G.; Wong, E. W.; Luo, Y.; Beverly, K.; Sampaio, J.; Raymo, F. M.; Stoddart, J. F.; Heath, J. R. A [2]Catenane-Based Solid State Electronically Reconfigurable Switch. *Science* **2000**, *289*, 1172–1175.
(412) Collier, C. P.; Jeppesen, J. O.; Luo, Y.; Perkins, J.; Wong, E. W.; Heath, J. R.; Stoddart, J. F. Molecular-Based Electronically Switchable Tunnel Junction Devices. *J. Am. Chem. Soc*. **2001**, *123*, 12632–12641.
(413) Luo, Y.; Collier, C. P.; Jeppesen, J. O.; Nielsen, K. A.; DeIonno, E.; Ho, G.; Perkins, J.; Tseng, H.-R.; Yamamoto, T.; Stoddart, J. F.; Heath, J. R. Two-Dimensional Molecular Electronics Circuits. *ChemPhysChem* **2002**, *3*, 519–525.
(414) DeIonno, E.; Tseng, H.-R.; Harvey, D. D.; Stoddart, J. F.; Heath, J. R. Infrared Spectroscopic Characterization of [2]Rotaxane Molecular Switch Tunnel Junction Devices. *J. Phys. Chem. B* **2006**, *110*, 7609–7612.
(415) Choi, J. W.; Flood, A. H.; Steuerman, D. W.; Nygaard, S.; Braunschweig, A. B.; Moonen, N. N. P.; Laursen, B. W.; Luo, Y.; DeIonno, E.; Peters, A. J.; Jeppesen, J. O.; Xu, K.; Stoddart, J. F.; Heath, J. R. Ground-State Equilibrium Thermodynamics and Switching Kinetics of Bistable [2]Rotaxanes Switched in Solution, Polymer Gels, and Molecular Electronic Devices. *Chem. Eur. J*. **2006**, *12*, 261–279.
(416) Green, J. E.; Choi, J. W.; Boukai, A.; Bunimovich, Y.; Johnston-Halperin, E.; DeIonno, E.; Luo, Y.; Sheriff, B. A.; Xu, K.; Shin, Y. S.; Tseng, H.-R.; Stoddart, J. F.; Heath, J. R. A 160-Kilobit Molecular Electronic Memory Patterned at 10^{11} Bits Per Square Centimetre. *Nature* **2007**, *445*, 414–417.

(417) Semiconductor Industry Association. The International Technology Roadmap for Semiconductors: Process Integration, Devices, and Structures. SIA, Washington D.C., **2005**. http://www.itrs2.net/itrs-reports.html. (Accessed 24 May 2016).

(418) Cotí, K. K.; Belowich, M. E.; Liong, M.; Ambrogio, M. W.; Lau, Y. A.; Khatib, H. A.; Zink, J. I.; Khashab, N. M.; Stoddart, J. F. Mechanised Nanoparticles for Drug Delivery. *Nanoscale* **2009**, *1*, 16–39.

(419) Ambrogio, M. W.; Thomas, C. R.; Zhao, Y.-L.; Zink, J. I.; Stoddart, J. F. Mechanized Silica Nanoparticles: A New Frontier in Theranostic Nanomedicine. *Acc. Chem. Res*. **2011**, *44*, 903–913.

(420) Li, Z.; Barnes, J. C.; Bosoy, A.; Stoddart, J. F.; Zink, J. I. Mesoporous Silica Nanoparticles in Biomedical Applications. *Chem. Soc. Rev*. **2012**, *41*, 2590–2605.

(421) Klichko, Y.; Liong, M.; Choi, E.; Angelos, S.; Nel, A. E.; Stoddart, J. F.; Tamanoi, F.; Zink, J. I. Mesostructured Silica for Optical Functionality, Nanomachines, and Drug Delivery. *J. Am. Ceram. Soc*. **2009**, *92*, S2–S10.

(422) Angelos, S.; Johansson, E.; Stoddart, J. F.; Zink, J. I. Mesostructured Silica Supports for Functional Materials and Molecular Machines. *Adv. Funct. Mater*. **2007**, *17*, 2261–2271.

(423) Liong, M.; Angelos, S.; Choi, E.; Patel, K.; Stoddart, J. F.; Zink, J. I. Mesostructured Multifunctional Nanoparticles for Imaging and Drug Delivery. *J. Mater. Chem*. **2009**, *19*, 6251–6257.

(424) Angelos, S.; Yang, Y.-W.; Patel, K.; Stoddart, J. F.; Zink, J. I. pH-Responsive Supramolecular Nanovalves Based on Cucurbit[6]uril Pseudorotaxanes. *Angew. Chem., Int. Ed*. **2008**, *47*, 2222–2226.

(425) Angelos, S.; Khashab, N. M.; Yang, Y.-W.; Trabolsi, A.; Khatib, H. A.; Stoddart, J. F.; Zink, J. I. pH Clock-Operated Mechanized Nanoparticles. *J. Am. Chem. Soc.* **2009**, *131*, 12912–12914.

(426) Du, L.; Liao, S.; Khatib, H. A.; Stoddart, J. F.; Zink, J. I. Controlled-Access Hollow Mechanized Silica Nanocontainers. *J. Am. Chem. Soc*. **2009**, *131*, 15136–15142.

(427) Khashab, N. M.; Belowich, M. E.; Trabolsi, A.; Friedman, D. C.; Valente, C.; Lau, Y.; Khatib, H. A.; Zink, J. I.; Stoddart, J. F. pH-Responsive Mechanised Nanoparticles Gated by Semirotaxanes. *Chem. Commun*. **2009**, 5371–5373.

(428) Park, C.; Oh, K.; Lee, S. C.; Kim, C. Controlled Release of Guest Molecules From Mesoporous Silica Particles Based on a pH-Responsive Polypseudorotaxane Motif. *Angew. Chem., Int. Ed*. **2007**, *46*, 1455–1457.

(429) Meng, H.; Xue, M.; Xia, T.; Zhao, Y.-L.; Tamanoi, F.; Stoddart, J. F.; Zink, J. I.; Nel, A. E. Autonomous in Vitro Anticancer Drug Release From Mesoporous Silica Nanoparticles by pH-Sensitive Nanovalves. *J. Am. Chem. Soc*. **2010**, *132*, 12690–12697.

(430) Wang, C.; Li, Z.; Cao, D.; Zhao, Y.-L.; Gaines, J. W.; Bozdemir, O. A.; Ambrogio, M. W.; Frasconi, M.; Botros, Y. Y.; Zink, J. I.; Stoddart, J. F. Stimulated Release of Size-Selected Cargos in Succession From Mesoporous Silica Nanoparticles. *Angew. Chem., Int. Ed*. **2012**, *51*, 5460–5465.

(431) Xue, M.; Cao, D.; Stoddart, J. F.; Zink, J. I. Size-Selective pH-Operated Megagates on Mesoporous Silica Materials. *Nanoscale* **2012**, *4*, 7569–7574.

(432) Chen, T.; Yang, N.; Fu, J. Controlled Release of Cargo Molecules From Hollow Mesoporous Silica Nanoparticles Based on Acid and Base Dual-Responsive Cucurbit[7]uril Pseudorotaxanes. *Chem. Commun*. **2013**, *49*, 6555–6557.

(433) Fu, J.; Chen, T.; Wang, M.; Yang, N.; Li, S.; Wang, Y.; Liu, X. Acid and Alkaline Dual Stimuli-Responsive Mechanized Hollow Mesoporous Silica Nanoparticles as Smart Nanocontainers for Intelligent Anticorrosion Coatings. *ACS Nano* **2013**, *7*, 11397–11408.

(434) Wang, M.; Chen, T.; Ding, C.; Fu, J. Mechanized Silica Nanoparticles Based on Reversible Bistable [2]Pseudorotaxanes as Supramolecular Nanovalves for Multistage pH-Controlled Release. *Chem. Commun*. **2014**, *50*, 5068–5071.

(435) Hernandez, R.; Tseng, H.-R.; Wong, J. W.; Stoddart, J. F.; Zink, J. I. An Operational Supramolecular Nanovalve. *J. Am. Chem. Soc*. **2004**, *126*, 3370–3371.

(436) Ferris, D. P.; Zhao, Y.-L.; Khashab, N. M.; Khatib, H.; Stoddart, J. F.; Zink, J. I. Light-Operated Mechanized Nanoparticles. *J. Am. Chem. Soc*. **2009**, *131*, 1686–1688.

(437) Park, C.; Lee, K.; Kim, C. Photoresponsive Cyclodextrin-Covered Nanocontainers and Their Sol-Gel Transition Induced by Molecular Recognition. *Angew. Chem., Int. Ed*. **2009**, *48*, 1275–1278.

(438) Yan, H.; Teh, C.; Sreejith, S.; Zhu, L.; Kwok, A.; Fang, W.; Ma, X.; Nguyen, K. T.; Korzh, V.; Zhao, Y. Functional Mesoporous Silica Nanoparticles for Photothermal-Controlled Drug Delivery In Vivo. *Angew. Chem., Int. Ed*. **2012**, *51*, 8373–8377.

(439) Sun, Y.-L.; Yang, B.-J.; Zhang, S. X.-A.; Yang, Y.-W. Cucurbit[7]uril Pseudorotaxane-Based Photoresponsive Supramolecular Nanovalve. *Chem. Eur. J*. **2012**, *18*, 9212–9216.

(440) Tarn, D.; Ferris, D. P.; Barnes, J. C.; Ambrogio, M. W.; Stoddart, J. F.; Zink, J. I. A Reversible Light-Operated Nanovalve on Mesoporous Silica Nanoparticles. *Nanoscale* **2014**, *6*, 3335–3343.

(441) Li, M.; Yan, H.; Teh, C.; Korzh, V.; Zhao, Y. NIR-Triggered Drug Release From Switchable Rotaxane-Functionalized Silica-Covered Au Nanorods. *Chem. Commun*. **2014**, *50*, 9745–9748.

(442) Wang, W.; Wen, Y.; Xu, L.; Du, H.; Zhou, Y.; Zhang, X. A Selective Release System Based on Dual-Drug-Loaded Mesoporous Silica for Nanoparticle-Assisted Combination Therapy. *Chem. Eur. J*. **2014**, *20*, 7796–7802.

(443) Nguyen, T. D.; Tseng, H.-R.; Celestre, P. C.; Flood, A. H.; Liu, Y.; Stoddart, J. F.; Zink, J. I. A Reversible Molecular Valve. *Proc. Natl. Acad. Sci. U.S.A*. **2005**, *102*, 10029–10034.

(444) Khashab, N. M.; Trabolsi, A.; Lau, Y. A.; Ambrogio, M. W.; Friedman, D. C.; Khatib, H. A.; Zink, J. I.; Stoddart, J. F. Redox- and pH-Controlled Mechanized Nanoparticles. *Eur. J. Org. Chem.* **2009**, 1669–1673.

(445) Luo, Z.; Ding, X.; Hu, Y.; Wu, S.; Xiang, Y.; Zeng, Y.; Zhang, B.; Yan, H.; Zhang, H.; Zhu, L.; Liu, J.; Li, J.; Cai, K.; Zhao, Y. Engineering a Hollow Nanocontainer Platform with Multifunctional Molecular Machines for Tumor-Targeted Therapy *in Vitro* and *in Vivo*. *ACS Nano* **2013**, *7*, 10271–10284.

(446) Gayam, S. R.; Wu, S.-P. Redox Responsive Pd(II) Templated Rotaxane Nanovalve Capped Mesoporous Silica Nanoparticles: A Folic Acid Mediated Biocompatible Cancer-Targeted Drug Delivery System. *J. Mater. Chem. B* **2014**, *2*, 7009–7016.

(447) Nguyen, T. D.; Leung, K. C.-F.; Liong, M.; Pentecost, C. D.; Stoddart, J. F.; Zink, J. I. Construction of a pH-Driven Supramolecular Nanovalve. *Org. Lett*. **2006**, *8*, 3363–3366.

(448) Thomas, C. R.; Ferris, D. P.; Lee, J.-H.; Choi, E.; Cho, M. H.; Kim, E. S.; Stoddart, J. F.; Shin, J.-S.; Cheon, J.; Zink, J. I. Noninvasive Remote-Controlled Release of Drug Molecules in Vitro Using Magnetic Actuation of Mechanized Nanoparticles. *J. Am. Chem. Soc*. **2010**, *132*, 10623–10625.

(449) Patel, K.; Angelos, S.; Dichtel, W. R.; Coskun, A.; Yang, Y.-W.; Zink, J. I.; Stoddart, J. F. Enzyme-Responsive Snap-Top Covered Silica Nanocontainers. *J. Am. Chem. Soc*. **2008**, *130*, 2382–2383.

(450) Liu, J.; Du, X.; Zhang, X. Enzyme-Inspired Controlled Release of Cucurbit[7]uril Nanovalves by Using Magnetic Mesoporous Silica. *Chem. Eur. J*. **2011**, *17*, 810–815.

(451) Ambrogio, M. W.; Pecorelli, T. A.; Patel, K.; Khashab, N. M.; Trabolsi, A.; Khatib, H. A.; Botros, Y. Y.; Zink, J. I.; Stoddart, J. F. Snap-Top Nanocarriers. *Org. Lett*. **2010**, *12*, 3304–3307.

(452) Liu, J.; Du, X. pH- and Competitor-Driven Nanovalves of Cucurbit[7]uril Pseudorotaxanes Based on Mesoporous Silica Supports for Controlled Release. *J. Mater. Chem*. **2010**, *20*, 3642–3649.

(453) Raju, M. V. R.; Lin, H.-C. A Cyanide-Responsive Supramolecular Nanovalve Based on Pd(II)-Templated Pseudo-Rotaxane. *J. Mater. Chem. A* **2015**, *3*, 6414–6422.

(454) Lewandowski, B.; De Bo, G.; Ward, J. W.; Papmeyer, M.; Kuschel, S.; Aldegunde, M. J.; Gramlich, P. M. E.; Heckmann, D.; Goldup, S. M.; D'Souza, D. M.; Fernandes, A. E.; Leigh, D. A. Sequence-Specific Peptide Synthesis by an Artificial Small-Molecule Machine. *Science* **2013**, *339*, 189–193.

(455) Dawson, P. E.; Muir, T. W.; Clark-Lewis, I.; Kent, S. B. Synthesis of Proteins by Native Chemical Ligation. *Science* **1994**, *266*, 776–779.

(456) Wilson, C. M.; Gualandi, A.; Cozzi, P. G. A Rotaxane Turing Machine for Peptides. *ChemBioChem* **2013**, *14*, 1185–1187.

(457) Bertran-Vicente, J.; Hackenberger, C. P. R. A Supramolecular Peptide Synthesizer. *Angew. Chem., Int. Ed*. **2013**, *52*, 6140–6142.

(458) McGonigal, P. R.; Stoddart, J. F. Interlocked Molecules: A Molecular Production Line. *Nature Chem*. **2013**, *5*, 260–262.

(459) Darwin, C. R. *On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life*; John Murray: London, **1859**.

(460) Piguet, C.; Bernardinelli, G.; Williams, A. F.; Bocquet, B. Formation of the First Isomeric [2]Catenates by Self-Assembly About Two Different Metal Ions. *Angew. Chem., Int. Ed*. **1995**, *34*, 582–584.

(461) Harrison, I. T. The Effect of Ring Size on Threading Reactions of Macrocycles. *J. Chem. Soc., Chem. Commun.* **1972**, 231–232.

(462) Han, D.; Pal, S.; Liu, Y.; Yan, H. Folding and Cutting DNA Into Reconfigurable Topological Nanostructures. *Nature Nanotechnol*. **2010**, *5*, 712–717.

(463) Lüttringhaus, A.; Isele, G. Synthesis of a Catena Compound by the Semistatistical Principle. *Angew. Chem., Int. Ed. Engl*. **1967**, *6*, 956–957.

(464) Ünsal, Ö.; Godt, A. Synthesis of a [2] Catenane with Functionalities and 87-Membered Rings. *Chem. Eur. J*. **1999**, *5*, 1728–1733.

(465) Hiratani, K.; Suga, J.-I.; Nagawa, Y.; Houjou, H.; Tokuhisa, H.; Numata, M.; Watanabe, K. A New Synthetic Method for Rotaxanes via Tandem Claisen Rearrangement, Diesterification, and Aminolysis. *Tetrahedron Lett*. **2002**, *43*, 5747–5750.

(466) Kawai, H.; Umehara, T.; Fujiwara, K.; Tsuji, T.; Suzuki, T. Dynamic Covalently Bonded Rotaxanes Cross-Linked by Imine Bonds Between the Axle and Ring: Inverse Temperature Dependence of Subunit Mobility. *Angew. Chem., Int. Ed*. **2006**, *45*, 4281–4286.

(467) Ke, C.; Smaldone, R. A.; Kikuchi, T.; Li, H.; Davis, A. P.; Stoddart, J. F. Quantitative Emergence of Hetero[4]rotaxanes by Template-Directed Click Chemistry. *Angew. Chem., Int. Ed*. **2012**, *52*, 381–387.

(468) Richey, H. G., Jr; Kushlan, D. M. Interactions of a Diarylmagnesium Compound with Cryptands and Crown Ethers: Formation of Ar_3Mg^-, $ArMg(cryptand)^+$, and Threaded Ar_2Mg(crown ether). *J. Am. Chem. Soc*. **1987**, *109*, 2510–2512.

(469) Gruter, G.-J. M.; de Kanter, F. J. J.; Markies, P. R.; Nomoto, T.; Akkerman, O. S.; Bickelhaupt, F. Formation of the First Organometallic Catenane. *J. Am. Chem. Soc*. **1993**, *115*, 12179–12180.

(470) Mingos, D. M. P.; Yau, J.; Menzer, S.; Williams, D. J. A Gold(I) [2]Catenane. *Angew. Chem., Int. Ed. Engl*. **1995**, *34*, 1894–1895.

(471) Castro, S. L.; Just, O.; Rees, W. S., Jr. A Quadruply Stranded, Alkaline Earth Metal Containing Helical Catenate: A Charge-Neutral Heterotopic Homodinuclear [2] Catenane. *Angew. Chem., Int. Ed*. **2000**, *39*, 933–935.

(472) Hunter, C. A.; Low, C. M. R.; Packer, M. J.; Spey, S. E.; Vinter, J. G.; Vysotsky, M. O.; Zonta, C. Noncovalent Assembly of [2]Rotaxane Architectures. *Angew. Chem., Int. Ed*. **2001**, *40*, 2678–2682.

(473) Blight, B. A.; Wisner, J. A.; Jennings, M. C. Synthesis of a [2]Rotaxane Through First- and Second-Sphere Coordination. *Chem. Commun.* **2006**, 4593–4595.

(474) Sauvage, J.-P.; Ward, M. A Bis(rerpyridine)ruthenium(II) Catenate. *Inorg. Chem*. **1991**, *30*, 3869–3874.

(475) Livoreil, A.; Dietrich-Buchecker, C. O.; Sauvage, J.-P. Electrochemically Triggered Swinging of a [2]-Catenate. *J. Am. Chem. Soc*. **1994**, *116*, 9399–9400.

(476) Hamann, C.; Kern, J.-M.; Sauvage, J.-P. Palladium(II)-Directed Formation of Pseudo-Rotaxanes: The 3 + 1 Approach to Threaded Species Using Square-Planar Geometries. *Dalton Trans.* **2003**, 3770–3775.

(477) Fuller, A.-M.; Leigh, D. A.; Lusby, P. J.; Oswald, I. D. H.; Parsons, S.; Walker, D. B. A 3D Interlocked Structure From a 2D Template: Structural Requirements for the Assembly of a Square-Planar Metal-Coordinated [2]Rotaxane. *Angew. Chem., Int. Ed*. **2004**, *43*, 3914–3918.

(478) Goldup, S. M.; Leigh, D. A.; Lusby, P. J.; McBurney, R. T.; Slawin, A. M. Z. Gold(I)-Template Catenane and Rotaxane Synthesis. *Angew. Chem., Int. Ed*. **2008**, *47*, 6999–7003.

(479) Chas, M.; Blanco, V.; Peinador, C.; Quintela, J. M. Synthesis of [3]Catenanes Based on Metal-Directed Self-Assembly and π-Donor/π-Acceptor Interactions. *Org. Lett*. **2007**, *9*, 675–678.

(480) Li, S.; Liu, M.; Zhang, J.; Zheng, B.; Zhang, C.; Wen, X.; Li, N.; Huang, F. High-Yield Preparation of [2]Rotaxanes Based on the Bis(*m*-phenylene)-32-crown-10-Based Cryptand/Paraquat Derivative Recognition Motif. *Org. Biomol. Chem*. **2008**, *6*, 2103.

(481) Zhu, K.; Vukotic, V. N.; Loeb, S. J. Molecular Shuttling of a Compact and Rigid H-Shaped [2]Rotaxane. *Angew. Chem., Int. Ed*. **2012**, *51*, 2168–2172.

(482) Barnes, J. C.; Juríček, M.; Strutt, N. L.; Frasconi, M.; Sampath, S.; Giesener, M. A.; McGrier, P. L.; Bruns, C. J.; Stern, C. L.; Sarjeant, A. A.; Stoddart, J. F. ExBox: A Polycyclic Aromatic Hydrocarbon Scavenger. *J. Am. Chem. Soc*. **2013**, *135*, 183–192.

(483) Vögtle, F.; Meier, S.; Hoss, R. One-Step Synthesis of a Fourfold Functionalized Catenane. *Angew. Chem., Int. Ed. Engl*. **1992**, *31*, 1619–1622.

(484) Ashton, P. R.; Campbell, P. J.; Chrystal, E. J. T.; Glink, P. T.; Menzer, S.; Philp, D.; Spencer, N.; Stoddart, J. F.; Tasker, P. A.; Williams, D. J. Dialkylammonium Ion/Crown Ether Complexes: The Forerunners of a New Family of Interlocked Molecules. *Angew. Chem., Int. Ed. Engl*. **1995**, *34*, 1865–1869.

(485) Yoon, I.; Narita, M.; Shimizu, T.; Asakawa, M. Threading-Followed-by-Shrinking Protocol for the Synthesis of a [2]Rotaxane Incorporating a Pd(II)–Salophen Moiety. *J. Am. Chem. Soc*. **2004**, *126*, 16740–16741.

(486) Arunkumar, E.; Forbes, C. C.; Noll, B. C.; Smith, B. D. Squaraine-Derived Rotaxanes: Sterically Protected Fluorescent Near-IR Dyes. *J. Am. Chem. Soc*. **2005**, *127*, 3288–3289.

(487) Cheng, P.-N.; Hung, W.-C.; Chiu, S.-H. A New Macrocycle That Forms Pseudorotaxane-Like Complexes with Dibenzylammonium Ions. *Tetrahedron Lett*. **2005**, *46*, 4239–4242.

(488) Chiu, C.-W.; Lai, C.-C.; Chiu, S.-H. "Threading-Followed-by-Swelling": A New Protocol for Rotaxane Synthesis. *J. Am. Chem. Soc*. **2007**, *129*, 3500–3501.

(489) Gong, H.-Y.; Rambo, B. M.; Karnas, E.; Lynch, V. M.; Sessler, J. L. A "Texas-Sized" Molecular Box That Forms an Anion-Induced Supramolecular Necklace. *Nature Chem*. **2010**, *2*, 406–409.

(490) Serpell, C. J.; Kilah, N. L.; Costa, P. J.; Félix, V.; Beer, P. D. Halogen Bond Anion Templated Assembly of an Imidazolium

Pseudorotaxane. *Angew. Chem., Int. Ed*. **2010**, *49*, 5322–5326.

(491) Kaiser, G.; Jarrosson, T.; Otto, S.; Ng, Y.-F.; Bond, A. D.; Sanders, J. K. M. Lithium-Templated Synthesis of a Donor-Acceptor Pseudorotaxane and Catenane. *Angew. Chem., Int. Ed*. **2004**, *43*, 1959–1962.

(492) Tung, S.-T.; Lai, C.-C.; Liu, Y.-H.; Peng, S.-M.; Chiu, S.-H. Synthesis of a [2]Catenane From the Sodium Ion Templated Orthogonal Arrangement of Two Diethylene Glycol Chains. *Angew. Chem., Int. Ed*. **2013**, *52*, 13269–13272.

(493) Knighton, R. C.; Beer, P. D. Axle Component Separated Ion-Pair Recognition by a Neutral Heteroditopic [2]Rotaxane. *Chem. Commun*. **2014**, *50*, 1540–1542.

(494) Chen, J.; Seeman, N. C. Synthesis From DNA of a Molecule with the Connectivity of a Cube. *Nature* **1991**, *350*, 631–633.

(495) Ryan, K.; Kool, E. T. Triplex-Directed Self-Assembly of an Artificial Sliding Clamp on Duplex DNA. *Chem. Biol*. **1998**, *5*, 59–67.

(496) Yan, L. Z.; Dawson, P. E. Design and Synthesis of a Protein Catenane. *Angew. Chem., Int. Ed*. **2001**, *40*, 3625–3627.

(497) Sánchez-Quesada, J.; Saghatelian, A.; Cheley, S.; Bayley, H.; Ghadiri, M. R. Single DNA Rotaxanes of a Transmembrane Pore Protein. *Angew. Chem., Int. Ed*. **2004**, *43*, 3063–3067.

(498) Kumar, R.; El-Sagheer, A.; Tumpane, J.; Lincoln, P.; Wilhelmsson, L. M.; Brown, T. Template-Directed Oligonucleotide Strand Ligation, Covalent Intramolecular DNA Circularization and Catenation Using Click Chemistry. *J. Am. Chem. Soc*. **2007**, *129*, 6859–6864.

(499) Liu, Y.; Kuzuya, A.; Sha, R.; Guillaume, J.; Wang, R.; Canary, J. W.; Seeman, N. C. Coupling Across a DNA Helical Turn Yields a Hybrid DNA/Organic Catenane Doubly Tailed with Functional Termini. *J. Am. Chem. Soc*. **2008**, *130*, 10882–10883.

(500) Ackermann, D.; Schmidt, T. L.; Hannam, J. S.; Purohit, C. S.; Heckel, A.; Famulok, M. A Double-Stranded DNA Rotaxane. *Nature Nanotechnol*. **2010**, *5*, 436–442.

(501) Trabolsi, A.; Khashab, N.; Fahrenbach, A. C.; Friedman, D. C.; Colvin, M. T.; Cotí, K. K.; Benítez, D.; Tkatchouk, E.; Olsen, J.-C.; Belowich, M. E.; Carmielli, R.; Khatib, H. A.; Goddard, W. A. III; Wasielewski, M. R.; Stoddart, J. F. Radically Enhanced Molecular Recognition. *Nature Chem*. **2010**, *2*, 42–49.

(502) Barnes, J. C.; Fahrenbach, A. C.; Cao, D.; Dyar, S. M.; Frasconi, M.; Giesener, M. A.; Benitez, D.; Tkatchouk, E.; Chernyashevskyy, O.; Shin, W. H.; Li, H.; Sampath, S.; Stern, C. L.; Sarjeant, A. A.; Hartlieb, K. J.; Liu, Z.; Carmieli, R.; Botros, Y. Y.; Choi, J. W.; Slawin, A. M. Z.; Ketterson, J. B.; Wasielewski, M. R.; Goddard, W. A. III; Stoddart, J. F. A Radically Configurable Six-State Compound. *Science* **2013**, *339*, 429–433.