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# Mechanostereochemistry*

Mark A. Olson[1], Youssry Y. Botros[2,3], and J. Fraser Stoddart[1,‡]

*[1]Department of Chemistry and Department of Materials Science and Engineering, Northwestern University, 2145 Sheridan Road, Evanston, IL 60208, USA; [2]Intel Labs/KACST, Building RNB-6-61, 2200 Mission College Boulevard, Santa Clara, CA 95054, USA; [3]National Center for Nano Technology Research, King Abdulaziz City for Science and Technology (KACST), P.O. Box 6086, Riyadh 11442, Kingdom of Saudi Arabia*

*Abstract*: Stereochemistry—in both its static and dynamic variants—has progressed apace now for more than a century to incorporate all aspects of covalent, coordinative, and noncovalent bonding at levels of structure which encompass constitution, configuration, and conformation. The advent of the mechanical bond in more recent times is now providing opportunities for the emergence of new stereochemical tenets and concepts, some of which bear close analogies with those of days gone by in chemistry. Since terminology helps to define and disseminate a discipline, we advocate that the term “mechanostereochemistry” be used to describe the chemistry of molecules with mechanical bonds.

*Keywords*: catenanes; mechanical bonds; mechanically interlocked molecules; molecular recognition; molecular switches; rotaxanes; self-assembly; template-directed synthesis.

## INTRODUCTION

The emergence of the mechanical bond (Fig. 1) during the past 25 years is giving chemistry a fillip in more ways than one. While its arrival on the scene is already impacting materials science and molecular nanotechnology, it is also providing a new lease of life to chemical synthesis where the formation of a mechanical bond [1] occurs as a consequence of the all-important templation orchestrated by molecular recognition and self-assembly processes [2]. The way in which covalent bond formation actuates noncovalent bonding interactions, switching on molecular recognition that leads to self-assembly and the template-directed synthesis [3] of mechanically interlocked molecules [4] (MIMs)—of which the so-called catenanes and rotaxanes [5] may be regarded as the prototypes—has introduced a level of integration into chemical synthesis that has not previously been obtained jointly at the supramolecular and molecular levels. The challenge now is to carry this level of integration, already achieved during the molecular synthesis of MIMs, beyond relatively small molecules into the realm of precisely functionalized extended molecular structures and aggregated superstructures that perform functions, according to an architectural, albeit molecular blueprint, in a collective manner by making use of the translational isomerism—namely, circumrotation in bistable catenanes, and translation in bistable rotaxanes—inherent to these MIMs as the key sources of instruction, as well as reversible activation and performance in multi-component integrated devices. The opportunity now exists to employ smart MIMs in molecular electronic devices (MEDs) and nanoelectromechanical systems (NEMS).

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‡Corresponding author: E-mail: stoddart@northwestern.edu

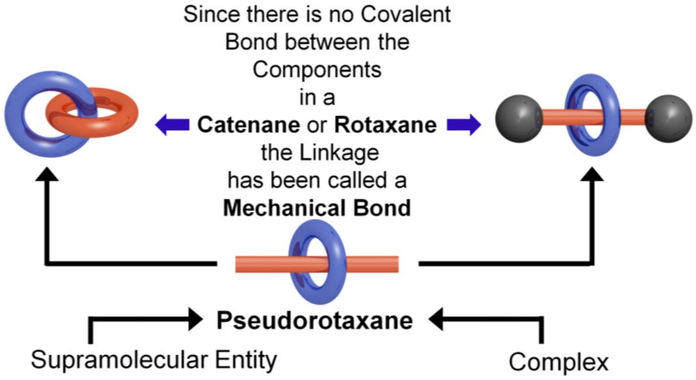

**Fig. 1** Defining the mechanical bond in the context of a catenane and a rotaxane. A catenane is a mechanically interlocked molecular architecture consisting of two or more interlocked macrocycles. A rotaxane is a mechanically interlocked molecular architecture consisting of a dumbbell-shaped component threaded through one or more macrocycles.

## A DEFINING MOMENT

The use of the term "mechanostereochemistry" to encompass all aspects of the mechanical bond is proposed. In a nutshell, mechanostereochemistry [6] is the stereochemistry of molecules with mechanical bonds. Just as "supramolecular chemistry may be defined [7] as 'chemistry beyond the molecule' bearing on the organized entities of higher complexity that result from the association of two or more chemical species held together by intermolecular forces", mechanostereochemistry may be defined as "chemistry beyond the supermolecule" related to robust mechanically interlocked components of precise form and predetermined function that results from the intramolecular forces between the matching components in molecules. In essence, mechanostereochemistry describes the rapidly emerging area of chemical science where components of molecules and extended structures are mechanically interlocked or sterically encumbered in such a manner that the components interact dynamically with one another as a result of a panoply of weak noncovalent bonds and/or as a consequence of dynamic coordinative or covalent bonds [8].

## TWO WORLDS APART YET FOREVER OVERLAPPING

The field of mechanostereochemistry is very clearly distinguishable from both conventional molecular chemistry and contemporary supramolecular chemistry [9]. Although MIMs and extended solid-state structures—for example, metal organic frameworks [10] (MOFs), where the crystal is the molecule and the molecule is the crystal—depend upon noncovalent and coordination chemistry for their synthesis, during this act of making, the intermolecular stabilizing forces are transformed into intramolecular ones just as soon as a mechanical bond is made and a new molecule is formed (Fig. 2). If making is one part, and a very important part at that, of mechanostereochemistry, then the other part, which is of equal importance, relates to the weak forces that are accumulated during the synthesis of catenanes and rotaxanes and which "live on" in the molecules and extended structures afterwards, making it possible to program them to carry out specific tasks by using our considerable experience to fine tune and even eradicate the noncovalent bonding interactions temporarily, such that we can drive molecules away from their equilibrium (ground) states into non-equilibrium (metastable) states and thus harness their potential as switches, motors, and machines [11]. Hence, this somewhat delicate and diverse practice of mechanostereochemistry can be seen to have both a creative aspect (molecular recognition, self-assembly, templation, etc.) and a functional role (relative movements of components, switching, self-emerg-

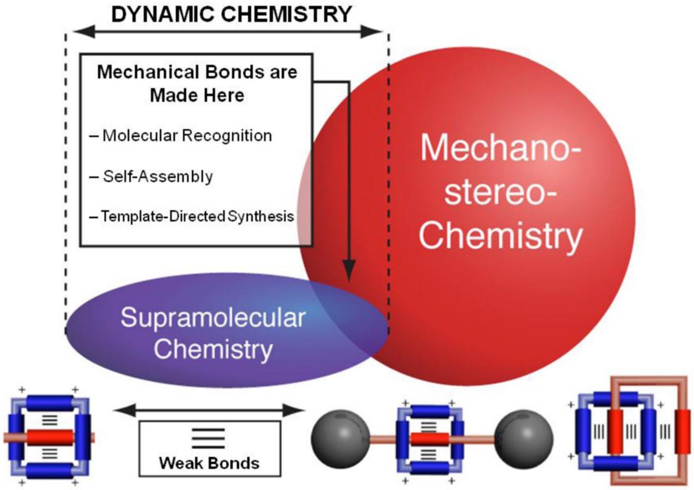

**Fig. 2** Chemistry is never (rarely!) black and white but many shades of gray. The merging of supramolecular chemistry with mechanostereochemistry illustrates this point extremely well.

ing, etc.) associated with its territory. Both the creative aspect and the functional role are dynamic in nature and ultimately molecular in context.

Since the vast majority of these MIMs [4] are products of templation [3] expressed during their synthesis—in which self-assembly [2] responds to molecular recognition motifs between components that are caught in the act of becoming interlocked—these catenanes and rotaxanes [5] have preferred relative geometries adopted by their components. In those situations with only one kind of recognition motif, the relative geometries between their highly symmetrical components express themselves in a highly degenerate fashion, much akin to the chair–chair inversion process [12] exhibited by cyclohexane. The first donor–acceptor [2]catenane [13] and [2]rotaxane [14] we made 20 years ago now are good examples of molecules where the degeneracy associated with the relative movements—circumrotation, pirouetting, and rocking [15] in the case of the degenerate [2]catenane [13] and shuttling in the case of the degenerate [2]rotaxane [14]—can be probed most straightforwardly by dynamic NMR spectroscopy [16] just like the chair–chair inversion process exhibited by cyclohexane. The stereochemical analogies involving all these degenerate mechanisms are shown in Fig. 3.

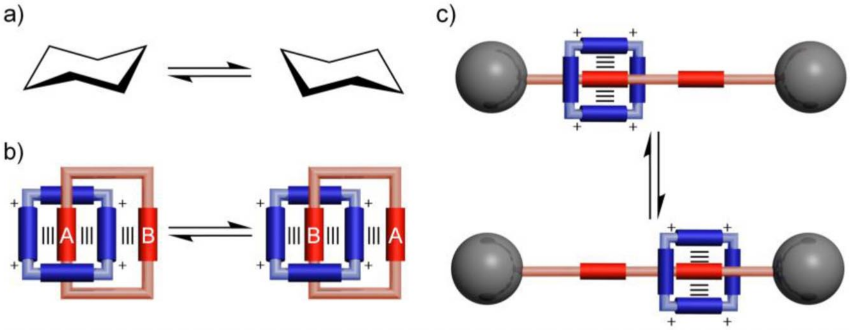

**Fig. 3** Structural formulas and graphical representations illustrating the stereochemical analogy between the highly degenerate chair–chair inversion process exhibited by cyclohexane (a) and the degeneracy associated with relative motions of circumrotation and shuttling, exhibited, respectively, by degenerate donor–acceptor [2]catenanes (b) and [2]rotaxanes (c).

## HISTORY HAS A HABIT OF REPEATING ITSELF

History has a habit of repeating itself in chemistry on a generational cycle [17]. Just as 40 years ago, stereochemists turned their attention to the investigation [18] of monosubstituted cyclohexanes (Fig. 4a) by $^1$H NMR spectroscopy in solution at low temperatures to identify conformational diastereoisomers (axial or equatorial), so mechanostereochemists of the past decade have used analogous $^1$H NMR spectroscopic techniques to study the translational isomerism [19] in bistable donor–acceptor [2]catenanes [20] and [2]rotaxanes [21]. The first really robust and efficient switchable [2]catenane [20] incorporating a tetrathiafulvalene (TTF) unit and a 1,5-dioxynaphthalene (DNP) one was employed subsequently to good effect in molecular switch tunnel junctions (MSTJs) in two-dimensional molecular electronic devices (2D MEDs) with crossbar architectures [22]. On account of the much stronger binding [23] of TTF to cyclobis(paraquat-*p*-phenylene) (CBPQT$^{4+}$) compared with 1,5-dimethoxynaphthalene, the bistable [2]catenane (Fig. 4b) exists preferentially (>9:1) as the translational isomer in which the TTF unit is included inside the CBPQT$^{4+}$ ring in the so-called [24] ground-state co-conformation (GSCC) rather than in the metastable state co-conformation (MSCC) where the DNP unit occupies the cavity inside the CBPQT$^{4+}$ ring. Oxidation of the TTF unit, however, alters the GSCC:MSCC ratio exclusively in favor of the DNP unit residing inside the cavity of the CBPQT$^{4+}$ ring. To date, however, we have not been able to isolate and characterize the MSCC after the fashion achieved with chlorocyclohexane [18c] where one (the Cl equatorial isomer) of its conformational diastereoisomers [25] has been isolated in pure crystalline form from the other one (the Cl axial isomer) which remains behind in the mother liquor. The same scenario holds true for many [21] but not all [26] the bistable [2]rotaxanes that have been designed and synthesized for incorporation [27] into MSTJs in 2D-MEDs, and more recently at metal [28] nanoparticle- and silica [29] nanoparticle–solvent interfaces.

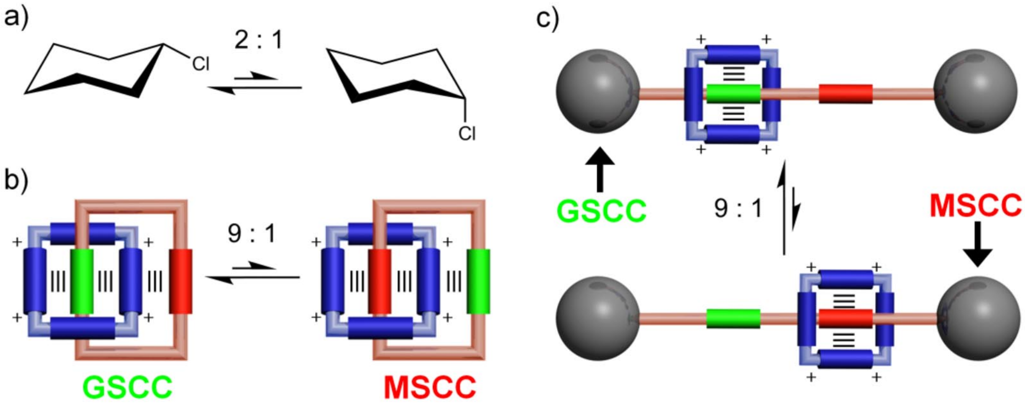

**Fig. 4** Structural formulas and graphical representations illustrating the stereochemical analogy relating the interconversion process between conformational diastereoisomers of chlorocyclohexane (a)—which exist in a 2:1 ratio at equilibrium, in favor of the equatorial isomer—and the translational isomerism of a donor–acceptor bistable [2]catenane (b) and [2]rotaxane (c)—which exist in an approximately 9:1 ratio at equilibrium, in favor of the translational isomer in which the TTF unit (green), rather than the DNP unit (red), is encircled by the CBPQT$^{4+}$ ring (blue).

## CONCLUSION

Whither mechanostereochemistry? As has been stated in another context elsewhere [9], "we need to forsake embracing routine projects that we know will yield results and lead to answers that are largely expected, so as to face challenges that are function-oriented and applications-driven, requiring the design of integrated systems whose complexity is such that (perhaps unexpected) emergent behavior is likely to be the end result. The time has come to design and craft a systems chemistry in which processes, including chemical reactions, are compartmentalized in a highly interconnected and ʽtalkative' manner so that they can be orchestrated in tune in an orderly and rhythmic fashion by the hundreds and thousands in space and time."

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