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Topological Isomerism : Should Rotaxanes, Endohedral Fullerene Complexes and In-Out Isomers of Hydrogenated Fullerenes Be Considered as Such ?

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Abstract Rotaxanes are not considered to be topological isomers of their separated fragments. However, due to their similarity to catenanes, they are often discussed within the realm of topological chemistry. Similarly, "in" fullerene isomers (endohedral complexes, nested fullerenes, and the isomers of hydrogenated fullerenes) have not, until recently, been treated as topological isomers of the corresponding "out" isomers. In this paper the problem of topological isomerism is analysed departing from the standard topological notions of arbitrary continuous deformations imposed on the system under investigation as a sufficient condition for topological isomerism. Similarly to the isomer classification into conformational and configurational isomers, the energy barrier between the trivial (e. g., separated rings) and non-trivial (e. g., catenated) topological structures should be invoked into such classifications to limit allowed deformations of the systems under investigation. A precise mathematical model of the classification, based on topological invariants, is presented in an Appendix.

Introduction

For more than 100 years Möbius strips, links modelling catenanes, knots (Fig. 1), and other topological objects had been considered mathematicians' toys by chemists and the first paper discussing the possibility of syntheses of this kind of objects was not accepted for publishing in 1960. It circulated, was widely cited as preprint, and finally appeared more than 30 years later [1a]. The synthesis of a first molecule with unusual topological properties, [2]catenane **1a**, was published as early as 1960 [1b] followed by those of higher catenanes [2], Möbius strip **2a, b** [3], and trefoil knot **3a, b** [4]. At first catenanes have been obtained by means of the statistical approach. However, obtaining more complicated higher catenanes (such as doubly intertwined catenane 4, [5] olympiadane **5** [6], and multicatenane **6** with bicyclic core [7]) as well as trefoil knot **3** [4] was made possible only by directed syntheses taking advantage of preorganization phenomenon. On the other hand, catenated and knotted structures were found to be common in circular DNA **7** [8a] that, even in its simplest form

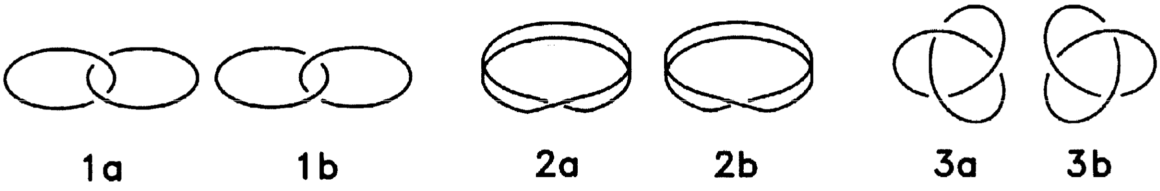

Fig. 1. Models of some non-trivial topological molecules.

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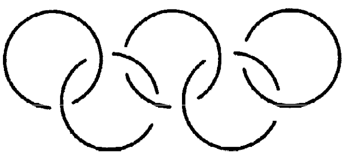

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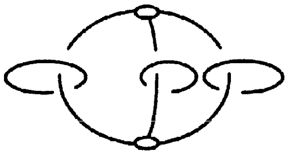

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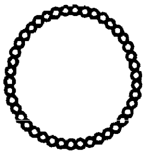

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of the cycle, models a non-trivial topological object. Moreover [8b], specific enzymes, topoisomerases, executing interconversions between circular and knotted (or catenated) DNAs have been identified.

The topological isomers can be represented by simple models to which precise topological definitions involving unusual deformations can be applied [9]. This is not the case for rotaxanes **8** [1c]. They represent the dumbbell systems consisting of a linear chain, threaded through a ring, with voluminous substituents at its ends preventing slipping out of the ring. Theoretically, by applying a nonphysical stretching to the ring, one could separate a rotaxane into two separate components (Fig. 2). Thus, they have not been included into the realm of topological molecules [1d - 1h]. However, in view of their similarity to catenanes, they are often discussed together with topologically distinct molecules [see, for instance, 1c, 1j, 10].

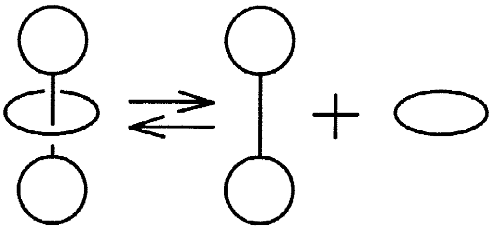

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Fig. 2. The equilibrium between a rotaxane and its separated fragments.

As will be discussed below, we believe that rotaxanes can be included into this group if only physically admissible deformations are taken into account. Similarly, endo- [11] and exohedral fullerene complexes, nested fullerenes [12] as opposed to separated ones, and "in" and "out" isomers of hydrogenated fullerenes with CH bonds pointing inside the C_{60} cage [13] have not, until recently [14], been considered as topological isomers since they interconvert upon application of nonphysical deformations.

In continuation of our work on classification of organic molecules [15] and that on "in-out" isomerism in perhydrogenated fullerenes [14], in this report we would like to analyse the problem of topological isomerism departing from the standard topological notions of arbitrary continuous deformations imposed on the system under investigation as a sufficient condition for topological isomerism. We believe that similarly to the isomer classification into conformational and configurational isomers [16], the energy barrier between the trivial (e. g., separated rings) and non-trivial (e. g., catenated) topological structures should be invoked into such classification.

Keeping in mind the difference between a real molecule and its mathematical model discussed by Mislow and Bickart [17], we believe that by analysing whether molecules are topological isomers the energy barrier for interconversion between the isomers should be taken into account. Let us consider an internal rotation around a CC bond. Depending on the barrier to this rotation, in this case there is a practically continuous change from conformers to atropisomers and geometrical isomers. In full analogy, by increasing the ring size, one can go from a well-defined rotaxane structure through a dynamic equilibrium depicted in Fig. 2 to two separate fragments.

As discussed below, the situation with endohedral fullerene complexes, nested fullerenes, and "in" isomers of hydrogenated fullerenes is similar and their topology should be discussed taking into account the corresponding barriers. Then, as shown in Appendix, their topological classification can be discussed in terms of well-established theory of topological invariants [9].

The Definitions and Their Implications

Topology is a branch of mathematics investigating relations among objects and object properties pertinent to continuous transformations of one object into another [9] like the one shown in Fig. 3. These transformations may involve considerable deformations of the objects. However, no cutting of them or gluing their distinct points together are allowed by the transformations. Thus, from topological point of view a circle and a triangle are equivalent while a circle and a line interval are distinct (Fig. 4). Similarly, two circles of different size are also topologically equivalent. Topological singularity of such molecules as those modelling links (catenanes) **1a** [1a - 1c], Möbius strip **2a, b** [1e], and knots **3a, b** [1f] was defined applying precise topological definitions allowing for considerable (sometimes unrealistic in terms of molecular stability) deformations applied to a standard molecular model. To include rotaxanes **8** and "in" isomers of hydrogenated fullerenes such as **9** into the realm of topologically distinguishable molecules, we have to put some semiquantitative physical restrictions on the allowed deformations. Fortunately, it is possible to incorporate these physical restrictions into the language of topological models.

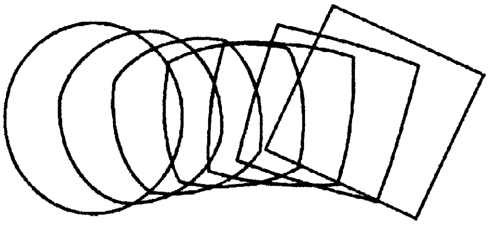
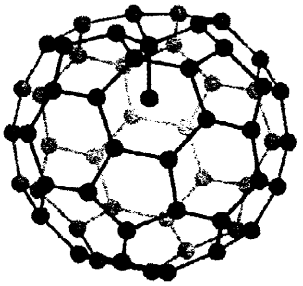


Fig. 3. An example of a continuous deformation of a circle into a square.



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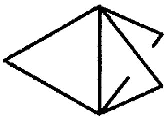
In the following a molecule will be represented basically by a set of point masses connected by linear bonds of definite length that can be represented by a molecular graph. The problem whether between the atoms in question there is a bond or not is gaining significance in view of (i) the rapid development of supramolecular chemistry involving noncovalent bonds [1i] and (ii) the anomalous bond order in [1.1.1]propellane **10**. Mislow [17b] proposed weighing graph wedges to describe such bonds. This idea lies beyond our discussion of molecular topology. For the obvious reason we will consider all objects in three-dimensional (3-D) Euclidean space and we admit only transformations of these objects coming from continuous transformations of 3D space.

Fig. 4. Topologically equivalent (left) and topologically distinct (right) objects.



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In his fundamental article on molecular topology [1e], Walba claims that he is analysing molecular properties in terms of low-dimensional molecular topology. However, as a matter of fact his discussion is limited to one-dimensional graphs, *i. e.* he deals only with one-dimensional topology. In this article, we propose to go beyond this limitation and consider some objects that can be better described including also two-dimensional surfaces. Similarly to Walba's approach, we focus our attention on qualitative rather than quantitative presentation with a clear description of the process of extraction of qualitative differences from quantitative ones. By the latter we understand geometrical and energy parameters of the system under discussion. To analyse the specificity of topological isomers, let us start from the definition of stereoisomers to show the differences between these two classes of isomerism. Two molecules are called *stereoismers* if they have identical connectivity schemes but differ in the space arrangement of their constituent atoms. As commonly accepted in organic stereochemistry, a molecule can assume only a finite number of such spatial arrangements. If one considers *geometrical, conformational* or *configurational isomerism* (Fig. 5) then one can see that :

1. The number of interconversion paths between these stereoisomers is strictly limited.
2. The height of the barrier to these processes defines the type of isomerism we deal with. However, the barriers change continuously and there are no strict quantitative limits defining conformational or configurational isomers and the ill-defined region between them is occupied by atropisomers.

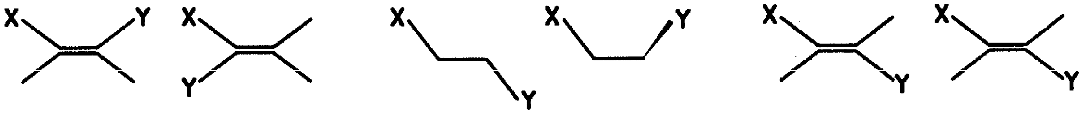


Fig. 5. Examples of geometrical (left), conformational (middle) and configurational (right) isomers.

On the other hand, the interconversions between *topological isomers* can, at least theoretically, be realized in a multitude of the bond breaking places. Thus, contrary to interconversions between other types of stereoisomers, there exist much more than one or two possible interconversion paths between topological isomers.

Concerning the barrier heights, in our approach, the situation with topological isomers is similar to that with stereoisomers, for which the barrier height defines the type of isomerism (geometrical, conformational, etc.). In the Walba presentation, the barriers involving interconversions between the topological isomers are infinite since there is no restriction to admissible deformations of the molecules under discussion whereas, in agreement with physical notions, we impose limitations on these barriers.

Let us note that the interconversions between such stereoisomers as geometrical, conformational or configurational ones implicate radical geometrical changes within well-defined small regions involving one or a couple of bonds. In other words, these changes are restricted to a local region consisting of neighbours and neighbours of neighbours of an atom. The situation with topological isomers is more complicated. Interconversions may involve only small local geometry changes spread over large regions. Such a situation is typical of [2]catenane in which, after breaking of any bond and dethreading, this bond is restored with its original geometry. Also in case of a (sufficiently large) knot and rotaxane the local geometry of their topological isomers is very close.

From the energy point of view, to execute the separation of two interlocked rings forming [2]catenane either one of its rings has to be cut or (equivalent to the cutting) at a certain moment they must intersect in a point. Thus, a stretching of at least one bond to such an extent that it breaks is a condition of the separation. Similarly, in the case of a non-trivially knotted ring molecule (in topology, a circle is a trivially knotted ring), the only possibility to convert it into the unknotted form requires bond breaking involving high energy barrier. In both cases, the energy required for the breaking has to be supplied to very small distinct, but arbitrarily chosen points of the system. Therefore, due to this high energy barrier, there is a clear-cut difference between topologically distinct objects (like knots or Möbius strips) and their corresponding counterparts (*i.e.* a ring) validating a classical linear model as a basis for topological analysis.

From a topological point of view Möbius-type molecules are very specific since they fall into two distinct categories depending on the parity of their winding number. Namely, those of one, 3, 5, *etc.* twists are constitutional isomers of the ones with an even number of twists. For instance, the isomer with one twist **2a** and the one with no twist, *e. i.* a simple ring, are constitutional isomers whereas those with left and right twists like **2a** and **2b** as well as those with the same parity of the winding number are topological isomers.

For rotaxanes **8**, endohedral fullerene complexes, nested fullerenes (as opposed to their separated fragments) and "in" isomers of hydrogenated fullerenes, the situation is much more complicated. If a continuous stretching is applied to a mathematical model representing the rotaxane structure, then there is a possibility of the disintegration of the system. However, if we pass from an ideal model to real molecules then for **8** with small central ring and bulky terminal groups there is no possibility for the separation of the systems into their constituent parts without at least one bond breaking. Therefore, in the real world there are three possibilities :

a. If the relative size of the ring as compared to the size of the voluminous substituents is small, then the rotaxane **8**, once formed, is stable since there is a high barrier for its decomposition.

b. If on the other hand the relative ring size is large, then the rotaxane structure is unstable. Even if it is formed, it decomposes into separate fragments due to the small barrier to the process.

c. In the intermediate case, there would be a coexistence of the two types of the systems.

It should be stressed that similarly to conformational and configurational isomers, there is no clear-cut quantitative distinction between the above categories. Indeed, by varying the ring size, one can span all three situations. Moreover, due to so-called "residual isomerism" [18], in some cases one can pass from one of the above categories to another by, for instance, changing the temperature. As a matter of fact, a few rotaxanes have been obtained by "slippage" of a ring through a substituent of intermediate volume at elevated temperatures. The rotaxanes synthesized in this way are stable at lower temperatures [19].

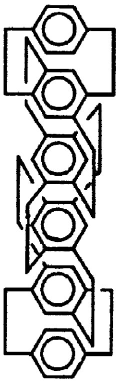
To conclude, the barrier to the decomposition process is an important factor determining the possibility of existence of a particular rotaxane structure in given conditions. Therefore, we believe that for large barriers towards unthreading, this group of compounds has distinct topological properties and belongs to the class of topological molecules.

Exactly the same reasoning can be applied to endohedral fullerene complexes [11], nested fullerenes [12], and "in" isomers of hydrogenated fullerenes [13, 14, 20]. They can all be called "in" fullerene isomers as opposed to the corresponding "out" isomers. In an ideal model situation of the endohedral fullerene complex one can enlarge a ring to allow the ion out of the cage. However, this would be a physically inadmissible deformation. In reality one has to break some bonds in the fullerene cage (leading to wider openings in the cage "surface") to allow for the complex decomposition. Also in this case the process involves a high energy barrier and endohedral fullerene complexes are topological isomers as well. Even larger "openings" are necessary in case of nested fullerenes to let a smaller inner fullerene out from the outer cage.

The hypothetical fully hydrogenated fullerene $C_{60}H_{60}$ (and some of its simple alkyl derivatives) has been shown to be considerably more stable with ten hydrogen atoms (or a methyl group) pointing inside the cavity than the all-out analogues [13, 14]. Also in this case the interconversion is impossible without bond breaking if only physically admissible deformations are taken into account. Thus, in-out isomerism in fulleranes also belongs to the class of topological isomerisms.

To be able to define precisely topological invariance allowing us to distinguish rotaxanes **8** from their separated fragments (and "in" and "out" fullerene isomers), we have to extend our simplified molecular model by adding surface membranes spanned on ring structures. In this model, fullerene cage can be represented by a polyhedral surface (mimicking a soccer ball) consisting of penta- and hexagons spanned over the five- and six-membered rings. Physically, each such penta- or hexagonal membrane stands here for a barrier impenetrable for ions, atoms or molecules (as is the case in nested fullerenes). This surface allows for the differentiation between the inner and outer space fragments and, consequently, between the "in" and "out" isomers. For rotaxanes, one can add an analogous infinite membrane, that does not hinder the movement along the chain until the terminal groups are involved) on the central ring. By such an enrichment of topological molecular structure, we are able to introduce new topological invariants that will allow us to include rotaxanes **8** and "in" and "out" fullerene isomers into the realm of topologically distinguishable molecules. A precise mathematical model is presented in Appendix.

Liang and Mislow [1h] discussed classification of topologically chiral molecules, that is of molecules that have topologically chiral graphs. They speak of geometrical and topological chirality. The former one is the usual chirality of molecules that cannot be superimposed on their mirror images. The latter refers to the chirality of the molecular graph. It should be stressed that a chiral molecule can be topologically achiral [6]. Chochin **11** [21] represents such an example.



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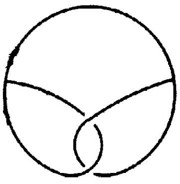
Topological non-trivialities in molecular world

Topological chemistry or some its aspects have been reviewed often [1]. The most comprehensive is the article on interlocked and intertwined structures and superstructures published by Amabilino and Stoddart [1i]. This review to a great extent covers the domain of topological chemistry. However, this area is rapidly developing. Therefore, a brief survey of novel topologically nontrivial molecules or the ones not included in the review will be given in the following in an attempt to put them into a framework of geometric topology outlined in the Appendix. Following the Amabilino and Stoddart example, in addition to known structures several hypothetical ones will be briefly discussed, too.

Syntheses of a "pretzel" molecule, *i. e.* linked catenane, **12** [22] and coupled [2]rotaxane **13** [23] have been recently reported by Vögtle's group while that of branched [7]catenane **14** was achieved by Stoddart et al. [24]. The resolution of a knot into enantiomers [25] and the synthesis of a composite knot **15** was published by the Dietrich-Buchecker and Sauvage group [26].



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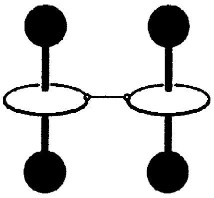

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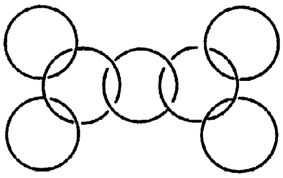

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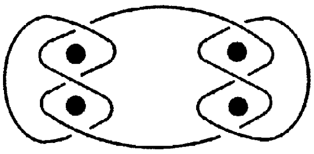

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Several topologically non-trivial DNA structures mimicking cube, knots and other topologically distinct structures [27] and a network of catenated DNAs (Fig. 6) have been obtained [28]. Borromean rings like **16** have been presented as exciting synthetic targets in Ref. 1i. The synthesis of DNA structures of this type followed [29].

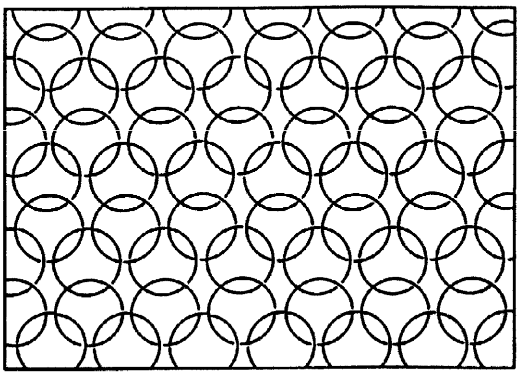
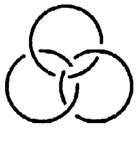


Fig. 6. A network of catenated DNA structures.

Interesting hypothetical cycloacenes **17**, related cycloacenes having Möbius strip-type structure with two twists and hypothetical knots with dualist graphs **18 - 20** composed of the appropriately linked aromatic rings have been proposed by Balaban [30]. These molecules seem too strained to be stable. However, larger systems of this type could be prospective synthetic targets.



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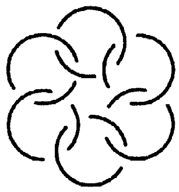

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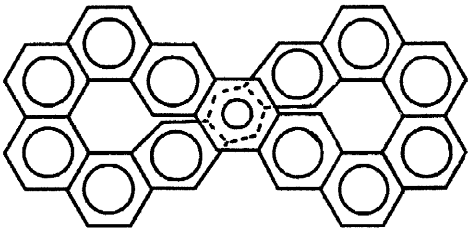

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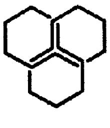

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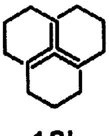

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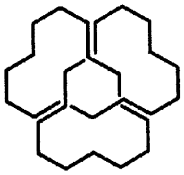

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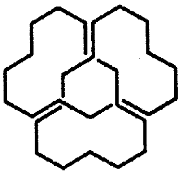

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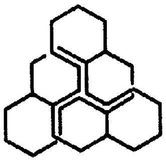

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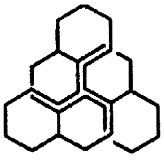

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A detailed study of in-out isomerism in hypothetical fulleranes $C_{60}H_{58}R_1R_2$ (R_1, R_2 = H, Me) exploring all constitutional and configurational isomers was recently carried out [20].

Other hypothetical structures of more complicated closed surfaces that can be mimicked by organic molecules are torii [31] or surfaces of higher genus (see Appendix). Torus-type molecules formed as closed nanotubes have been recently observed [32]. More complicated topological structures could be obtained by inserting an atom, an ion, or a ring into the tire-like torus.

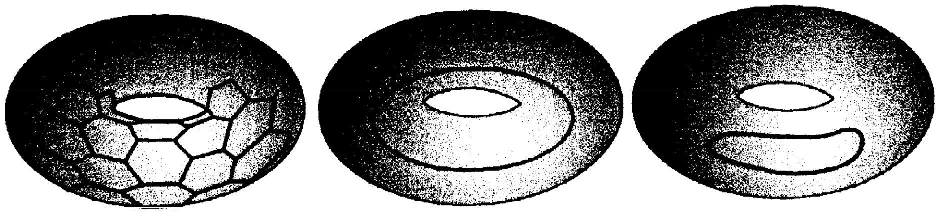
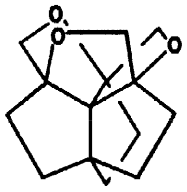


Fig. 7. A torus and its two "in" isomers with inserted ring.

Another recently recognized group of molecules with topologically nontrivial properties consists of molecules with nonplanar graphs. In addition to catenanes, knots and Möbius strip discussed earlier, to our knowledge only few molecules of this kind have been synthesized. Centrally annelated heterocyclic polyquinane **21** [33] and centrohexaindane **22** [34], [6]cochin **11** [21] (and its lower analogues as well as its analogues involving naphthalene units), "Kuratowski cyclophane" **23** [35] are the first examples of this type paving the avenues to new exciting chemistry. These molecules could be also interesting for prospective applications since they should exhibit unusual electric and magnetic properties.



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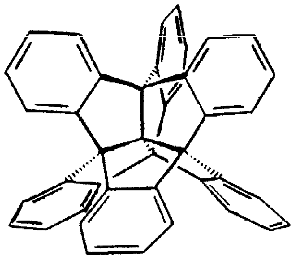

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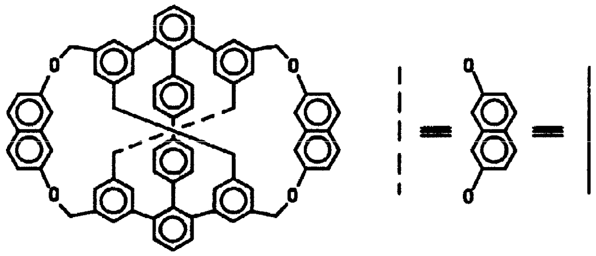

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Conclusions

Topological chemistry is booming due to the recent development in synthetic methods allowing the syntheses of organic molecules mimicking complicated topological objects. In this report a systematic approach to the classification of such molecules is presented on the basis of the height of energy barriers to interconversion between isomers in full analogy with the differentiation between conformational and configurational isomers in classical organic chemistry. The resulting topological classification of molecules can then be based on the well-established theory of topological invariants. According to this classification, rotaxanes and in-out fullerene isomers do belong to the realm of organic molecules with unusual topological structure. On the other hand, DNA helices, helicates and pseudorotaxanes also discussed by Amabilino and Stoddart [1i] should not be included into this group.

Appendix: Topology of polyhedra in Euclidean 3-space ;

Polyhedral complexes and polyhedra

A simplex in the three-dimensional Euclidean space is a point (0-simplex), a line interval (1-simplex), a triangle (2-simplex) or a tetrahedron (3-simplex). Each simplex is composed from its interior and its faces: in the case of a 0-simplex, the interior is composed from the only point and there are no faces, the faces of a 1-simplex are its endpoints, the faces of a 2-simplex are its edges and the faces of a 3-simplex are its triangular faces. For a given simplex, its subsimplices are faces, faces of its faces etc. down to the vertex level.

A collection C of simplices is a complex if and only if:

(1) if a simplex belongs to C then all its faces belong to C;

(2) the interiors of distinct simplices do not intersect;

(3) The intersections of simplices are sums of common subsimplices.

The maximum dimension of all simplices in C is called the dimension of C.

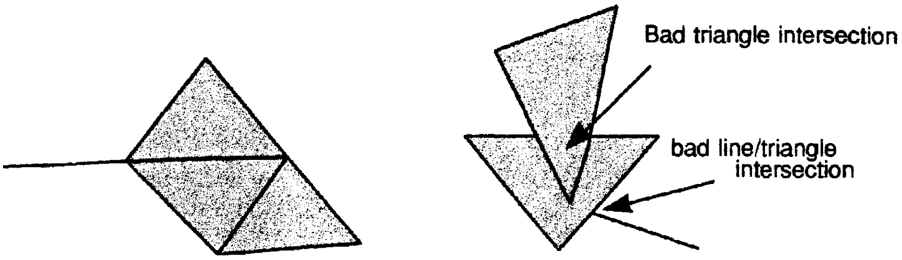

Fig. 8. Examples of a triangulation (left) and simplices not forming a triangulation (right).

A subset P of the Euclidean space is called a polyhedron if there exists a polyhedral complex C such that P is the set of all points of simplices of C. Then C is called a triangulation of P. Note that a polyhedron P can have different triangulations - for example any subdivision of an interval by a series of points gives a triangulation of this interval. The standard model of a chemical molecule consisting of atoms as points in the Euclidean space and bonds symbolized by the edges joining the atoms is clearly an example of a one-dimensional polyhedral complex. It should be emphasized that we do not analyse precisely the identities of points and edges of our complex - we are interested only in an overall shape of the resulting polyhedron. We will call two polyhedra P and Q in the Euclidean space topologically equivalent if there exists a continuous deformation of the space starting from the identity and ending with a mapping that carries P over Q.

A continuous deformation (like the one schematically shown in Fig. 3) is a family of homeomorphisms, that is of mappings that neither break apart nor glue the points in the space, indexed by a time-like parameter t and such that there are no sudden jumps as t changes from 0 to 1. For example, if P and Q differ only by a translation by a vector v then the family of translations by t^*v is the required deformation. In general, it is hard to determine whether two polyhedra are, or are not, topologically equivalent. There exists a variety of so-called topological invariants, that is, simple (or less simple) algebraic objects such as integer numbers, polynomials or groups that can be used for distinguishing topological objects. For example, the number of connected components (that is, parts of a polyhedron that cannot be joined by paths lying entirely in the polyhedron) is such an invariant. A single interval cannot be deformed into a sum of more than one disjoint intervals. With the apparatus of the topological invariants one can in many cases prove that two given polyhedra are not topologically equivalent in the Euclidean space. For a general reference to the topology of polyhedra and simplicial complexes see Ref. 9.

We will now outline one example of such an invariant for a polyhedron consisting of two components A and B, each equivalent to a closed curve. Suppose we have fixed the orientation (a "direction") of each of these curves and let us regard a vertex v of one curve and a vertex w of the other, since the orientations of both curves are fixed, there are vertices v' and w' next to v and w with respect to this orientation. We will now call the pair (v,w) positive if the three vectors $[v,w]$, $[v,v']$ and $[w,w']$ form a positively oriented basis and negative if this vector triple is negatively oriented.

Let us fix now a vector u in the space and let us count all the pairs (v,w) with the vertex v belonging to the first curve, w belonging to the second one and such that there are points p and q in the intervals vv' and ww' with the vector [p, q] parallel to u and with the same orientation. If we subtract the number of negative pairs (v, w) from that of the positive ones, then the resulting number does not depend on the choice of u, but only on the curves forming the polyhedron and their orientations. We call this number the linking number of A and B. It

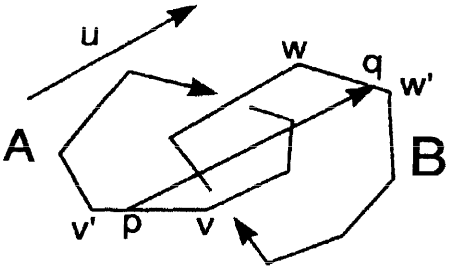

Fig. 9. A scheme of a summand in the linking index formula.

should be stressed that it can be interpreted in terms of electromagnetic induction in a wire B around the magnetic kernel A. It can be verified that if A and B can be separated by a deformation of the polyhedron then the linking number is 0 and that for the two simple planar polyhedral curves linked as the ordinary chain links the linking number is 1 or -1, depending on the orientation of both curves.

A very productive method of introduction of topological invariants for knots and links (that is, polyhedra equivalent to closed simple curves or disjoint sums of such curves in the space) is a careful analysis of the so-called diagrams, that is, plane images (projections) of the polyhedra with some indication which branch of the curve passes above the other branch at a crossing.

One can easily prove that for any given polyhedral link there exist regular projections, that is such projections that:

(1) the projection of every interval (one-dimensional simplex) is a nondegenerate interval;

(2) no triple crossing occurs and there are only finitely many crossings;

(3) there are no crossings involving the vertices of the polyhedron.

For each non-trivial diagram $D = D_+$ one can find a crossing in D such that two diagrams D_- and D_0 formed from D by the modifications shown in Fig. 10 can be simplified to the diagrams with less crossings than the original one. Therefore, it makes sense to use formulae relating invariants of D_+, D_- and D_0 to compute recursively these invariants for arbitrary diagrams.

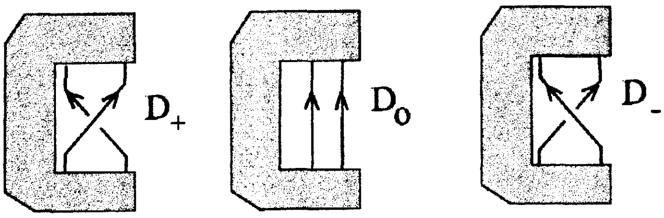

Fig. 10. Modifications of a diagram crossing. The shaded areas symbolize identical parts of the diagrams.

An important easily computable invariant enabling us to distinguish many non-equivalent links with great precision known as the Jones polynomial VD is defined for a diagram D by the following conditions :

(0) VD is a Laurent polynomial in $\sqrt{t}$ that is a finite sum of positive and negative powers of $\sqrt{t}$ with t being an independent variable and with integer coefficients:

$$VD(t) = \sum_{i=-k}^{k} a_i(\sqrt{t})^k$$

(1) "normalization condition" VT(t)=1 for a trivial (circle-like) diagram;

(2) recursion formula

$$VD_+(t)/t - VD_-(t) * t = (\sqrt{t} - 1/\sqrt{t})VD_0(t)$$

A non-trivial theorem states that for any two diagrams representing a link L the resulting Jones polynomials will be the same. Therefore it makes sense to call V a link invariant. This invariant, together with some generalizations assisted a rapid development of the knot theory in the last years. For a general reference to the modern knot theory, see Ref. 36.

The concept of a graph is well established as a model of a molecule. From the topological point of view a graph is a one-dimensional polyhedron. For the reason of broadening the scope of topological framework to include more complicated examples of isomerism we have to make our modelling machinery a little more precise.

As the topological notions are of more quantitative nature than the geometric or physical ones (defined in the terms of energy and other physical variables), the topological modelling involves some quantization procedures. A simple example of such a procedure is the introduction of a bond joining two atoms as an edge. For our purpose, this is only a symbol that the two atoms linked cannot be separated to a great distance without application of a relatively large energy that will change fundamentally the nature of the molecule in question (bond breaking).

Moreover, one can easily estimate that each transformation of the molecular system that would involve a crossing of two such bonds should also involve very high energetic barrier equivalent to the breaking of at least one of these bonds. These two facts allow us to state that all physically viable geometric transformations of molecules are topological equivalencies in the Euclidean 3-space and therefore the invariants outlined above can be used to distinguish topological isomers of a molecule under investigation.

We are now going a step further. Let us regard a simple example of an aromatic ring and any atom or ion outside of this ring. It can be easily observed that pushing this atom/ion through the ring should require again an amount of energy sufficient to break at least one bond. Therefore we can again state that from the "point of view" of this atom the ring can be regarded as a piece of surface and not only as a closed hexagonal curve. This in turn means that from that we can legitimately represent a fullerene molecule as a polyhedral surface topologically equivalent to the sphere and distinguish regions "inside" and "outside" of this sphere. This has actually been indirectly assumed in studies of endohedral fullerene complexes and in our works on "in-out" isomerism in perhydrogenated fullerenes [14, 20].

The construction of the linking index outlined above can be generalized to include such notions as the distinction between points "inside" and "outside" of a closed curve in the plane or points "inside" or "outside" a closed, two-sided surface. In the last case, one defines the orientation of a polyhedral triangulated surface as a selection of the "outwardly normal" vectors over the surface, that is unit vectors orthogonal to the triangular faces and such that for any two adjoined faces the vectors indicate the same side of the quadrilateral.

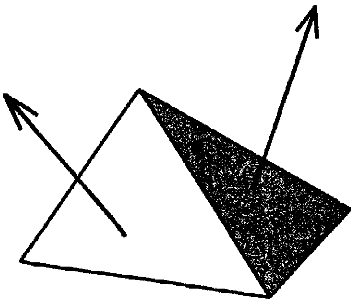

Fig. 11. Compatible orientations of two neighbouring triangles of a surface.

The index of a point p with respect to such an oriented surface can be now defined by selection of a vector *v* and count of intersections of the half-line starting from p in the direction of *v*. Again, an intersection is counted as positive if the vector normal to the intersected triangle forms an acute angle with the direction *v*.

The last type of topological isomers discussed in this paper, that of rotaxanes and their separated fragments, involves a similar reasoning. One can estimate the minimum diameter of the bulky groups of these molecules from the values of bond lengths and van der Waals radii. One can also estimate the maximum diameter of the empty space within the ring in the similar way. Again, if the bulky substituents are large enough, it is physically impossible to extend the ring so that the substituents would pass through its opening. Thus, in a somehow dual manner, the bulky groups can be regarded as infinitely large and our topological model of the rotaxane can be simplified to a curve (the backbone) linking two infinite planes (the bulky substituents) with the ring structure wrapped around the backbone in contrast to the ring separated from the backbone in the case of separable topological isomer.

The linking index defined above can be generalized to describe topological isomerism of rotaxanes and their separated fragments.

Fig. 12. An abstract topological model of a rotaxane **8** and its separated fragments.

For an example of a more mathematical treatment of the topological properties of DNA molecules, see Ref. 37.

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