Table I

atom	orbital	H_{ii} (eV)	ζ_1	ζ_2	$c_1{}^a$	c_2
B	2s	−15.2	1.30			
	2p	−8.5	1.30			
C	2s	−21.4	1.625			
	2p	−11.4	1.625			
N	2s	−26.0	1.95			
	2p	−13.4	1.95			
La[24]	6s	−7.67	2.14			
	6p	−5.01	2.08			
	5d	−8.21	3.78	1.38	0.7766	0.4587

[a] Contraction coefficients used in the double-ζ expansion.

sets of points (both in the squares *and* octagons) are created. The possibility of creating two independent and electronically equivalent sets of orbitals near the Fermi level (at the HOMO) level is the common link between the cyclobutadiene, boron nitride, and MB_2C_2 problems.

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Appendix

The calculations are of the Extended Hückel type[23,24] with the parameters and exponents of Table I. The modified Wolfsberg–Helmholz formula[25] was used. The results for the ideal nets for I and II reported in Figures 2 and 3 were obtained with use of a common distance of 1.62 Å, exponents ζ_{2s} and ζ_{2p} of 1.30, and the H_{ii} values for B and C (Table I). Calculations for the ideal 6^3 net were carried out with use of a common distance of 1.42 Å, exponents ζ_{2s} and ζ_{2p} of 1.625, and the H_{ii} values for B and N. *k*-point meshes used in the calculations were as follows: 64 k-points for type I net; 55 k-points for type II net; 40 k-points for **18**; 55 k-points for **22**; and 64 k-points for **23** and **24**. Each of the k-points meshes are referred to the number of points computed in the irreducible wedge of the appropriate Brillouin zone. The DOS curves of Figure 1 were smoothed with Gaussian functions with a standard deviation of 0.08 eV.

Registry No. CaB_2C_2, 69106-69-0; B_2C_2La, 12678-10-3; boron nitride, 10043-11-5.

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Tying Knots around Chiral Centers: Chirality Polynomials and Conformational Invariants for Molecules

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Abstract: A method is proposed for the description and analysis of chirality properties of molecules with any number of chiral carbon centers. By using a simple algorithm, chirality information of molecules can be transferred to various knots which are in turn described by polynomials. These polynomials are remarkably simple, and they are invariant to conformational changes and provide an easy test for various types of chirality properties even for molecules of a large number of chiral centers. Several examples are discussed in some detail.

There have been several approaches to provide simple algebraic models for the description of molecular chirality; most recent works include various group theoretical approaches[1–6] which have given new insight and new methodology for such analyses. In this study we shall describe an intuitively simple (one may be tempted to say, playful) approach that, nonetheless, leads to a rigorous algebraic description of chirality in terms of simple polynomials.

A recent discovery of a set of polynomials describing the shapes, and, in particular, the chirality properties of knots of various types[7,8] is expected to have important implications in a variety of applied fields. Whereas the full development of these polynomials has required rather sophisticated mathematical techniques, nonetheless, their appreciation and intuitive understanding requires no more than high school mathematics and their application is extremely simple. In fact, their actual generation and application to the chirality problems of chemistry, addressed in this study, require no more than an understanding of what is polynomial and some practical skills in handling a string when tying knots around ball-and-stick molecular models.

In chemistry, chirality is of fundamental importance, appreciated by both chemists and mathematicians. This is well-illustrated by the fact that the very first chemical application of these new polynomials has already been described by one of the original discoverers of the new polynomials.[9] This application has led to a description of chirality of *cyclic chain molecules which themselves form loops, knots, and links* such as the molecules recently synthetized by Walba.[10] Although these molecules occur rarely in nature, they are of special theoretical interest. The same technique is also expected to find applications in processing electron

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(10) Walba, D. M. *Stereochemical Topology*; King, R. B., In Chemical Applications of Topology and Graph Theory, Elsevier: Amsterdam, 1983. A related early study on similar molecules is described by Wasserman (Wasserman, E. *J. Am. Chem. Soc.* **1960**, *82*, 4433) and by Frisch and Wasserman (Frisch, H. L.; Wasserman, E. *J. Am. Chem. Soc.* **1961**, *83*, 3789).

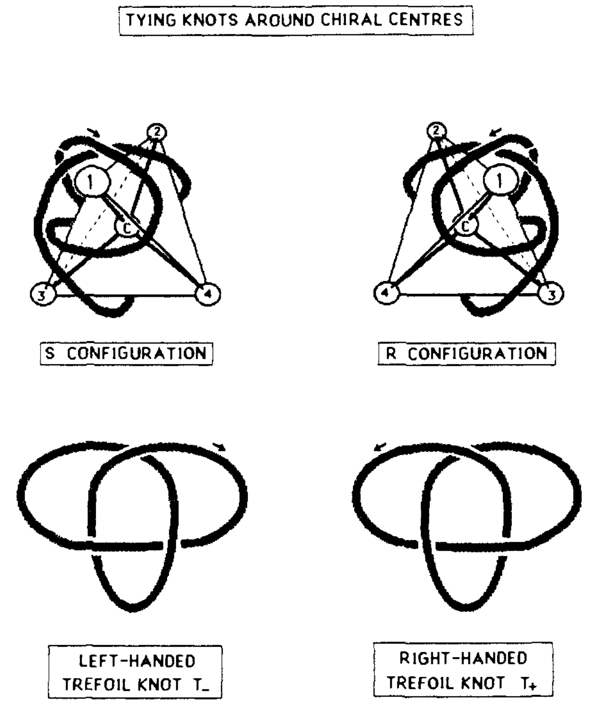

Figure 1. The left-handed and righ-handed trefoil knots obtained by applying the knot-generation algorithm to chiral carbon centers of *S* and *R* configurations, respectively.

microscopic images of folded and/or knotted polymer chains such as DNA.[11]

In this study we propose a simple method that allows one to apply the knot theoretical polynomials to a much larger family of molecules which family contains *all those molecules in which chirality is a consequence of one or several chiral carbon centers.* In a formal sense, we shall not apply the knot theoretical polynomial method directly to the description of chiral molecules, rather, we shall use these polynomials to describe the chirality of the *space surrounding the molecules.* We shall do this by "tying knots" around chiral (as well as achiral) carbon centers in a specified way. An algorithm, in fact, a set of practical instructions will be given, how to produce unique knots around such molecules, each of which knots is then characterized by a pair of chirality polynomials as its topological invariants. Then, these chirality polynomials can be used as a concise representation for the analysis and comparison of topological chirality properties of different molecules.

The main objective of this paper is to develop a knot-theoretical polynomial description of the chirality of molecules containing an *arbitrary large number of chiral and achiral carbon centers.* If the number of centers is large, then the recognition of various chirality properties and that of the overall effects of configuration inversion at selected centers become a rather complicated task when one is restricted to the manipulation of three dimensional models and plane drawings. On the other hand, the polynomials provide a simple computational method that can be implemented easily on a personal computer.

By a combination of a few simple knots as basic entities the knots of large molecules can be generated rather easily. For example, if the chirality is a result of chiral carbon centers, then a "knot bank" of *three* formal knots is sufficient to build the actual knot for the molecule. In fact, by knowing the polynomials for these three knots and knowing the rules of how to combine them, *no actual generation of the knots is required*, and the corresponding chirality polynomials can be generated by a few lines of algebra or by using the simplest of personal computers.

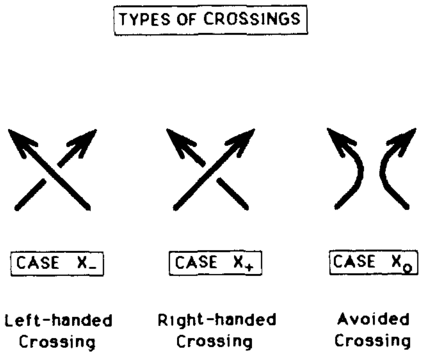

Figure 2. The three possible crossing types for plane projections of oriented strings.

From Chiral Centers to Knots and to Polynomials. We shall illustrate the main idea of the proposed model by a simple example. In Figure 1 an enantiomeric pair of chiral methane derivatives is shown. On the basis of the stereochemical priority and spatial distribution of the substituents, a set of simple instructions can be given, how to tie a string around each carbon atom (vide infra). By joining the beginning (marked with an arrow) and the end of the string, a knotted loop is obtained for each molecule. By removing these loops from the molecule, the two simple knots, the left-handed trefoil, and the right-handed trefoil are obtained, as shown in Figure 1. These two trefoil knots are *chiral*, and they reflect the chirality of the corresponding carbon centers used for their construction.

The essential point is that these knots describe the chirality of the *space surrounding the chiral center* and not that of the chiral center directly. If one imagines the molecule being a sculpture, then this model describes the chirality of the hollow casting shell. This is the very reason why the knot-theoretical description of chirality is now applicable to molecules which themselves do not form knots.

Note, that we shall assume that these knots are given an orientation, as shown by the arrow in Figure 1. Following the usual classification of knots[7-9] in terms of crossings in their two-dimensional projected images, we shall distinguish three crossing types, X_+, X_-, and X_0, shown in Figure 2. Case X_+ may be regarded as a "right-handed" crossing: when pointing the right thumb along either one of the arrows while holding it in one's right hand, the fingers point along the other arrow. Note that this remains true if the orientations of *both* arrows are reversed, e.g., if the orientation is reversed along the entire string in a single twisted loop.

Similarly, X_- can be regarded as a left-handed crossing with the same invariance properties. Case X_0 corresponds to "no crossing", or "avoided crossing".

Note that no matter how we produce a projection of the left-handed trefoil of Figure 1, as long as there are no tangential contacts between projections of string segments nor overlapping crossings, three crossings will be of type X_-. Similarly, the right-handed trefoil has all three of its crossings of type X_+ that does not depend on the particular way the trefoil is drawn, as long as there are no tangential contacts nor overlapping crossings.

The two chiral carbon centers can be characterized by the knots, hence, by the sets of crossing symbols (X_-, X_-, X_-) and (X_+, X_+, X_+), respectively. For knots of three crossings the possibilities are rather limited, and for trefoils a list of the crossing symbols (in fact, a single crossing symbol) is sufficient for characterization. However, if one wishes to extend this model to molecules with several chiral centers, hence, to more complicated knots and links, then a list of crossing symbols may conceal the possibilities for a simpler representation of the same knot or link and its topological and chiral properties. There is, however, a more concise description of the chirality of even complicated knots and links by generating topologically invariant polynomials which are defined in terms of these crossing types. These polynomials are rather simple and

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[11] Michels, J. P. J.; Wiegel, F. W. *Phys. Lett. A* **1982**, *90A*, 381. Dean, F. B.; Stasiak, A.; Koller, T.; Cozzarelli, N. R. *J. Biol. Chem.* **1985**, *260*, 4795. Wang, J. C. *Ann. Rev. Biochem.* **1985**, *54*, 665. Wasserman, S. A.; Cozzarelli, N. R. *Proc. Natl. Acad. Sci. U.S.A.* **1985**, *82*, 1079. Simon, J. *Topological Chirality of Certain Molecules*; to be published. Sumners, D. W. *The Role of Knot Theory in DNA Research*; to be published. Kikuchi, T.; Nêmethy, G.; Scheraga, H. A. *J. Comput. Chem.* **1986**, *7*, 67.

have some intriguing properties which are suitable for detecting and analyzing various types of topologically chiral molecules even in rather complicated cases.

In the following section we shall describe an actual algorithm which leads to unique knots for various combinations of chiral (and achiral) carbon centers. Subsequently, we shall describe the polynomials obtained for these knots and illustrate their chemical applications with simple examples. For sake of simplicity, we shall often use the term "knot" in a general sense for all objects obtained by manipulating strings and their crossings, that is, for proper knots as well as for links and for "unknotted" simple loops.

An Algorithm for Knot Generation. As has been pointed out by Mislow and Siegel,[5] within the Cahn-Ingold-Prelog (CIP) system for the characterization of chiral centers[12] by symbols R and S it is possible that the mirror image of an R center is also R (as is the case, e.g., for product of an achiral diastereomer of 2,3,4-trihydroxyglutaric acid with (S)-lactic acid[5]). This possibility, although uncommon, is inconsistent with the knot theoretical model and the relevant polynomials, where the behavior of objects with respect to *reflection planes* is the main tool for characterization. Since global chirality is equivalent to nonsuperimposibility of mirror images, the forthcoming analysis requires that the characterization of carbon centers is also based on the relations between the substituents and their mirror images. Following the distinction of *chirotopicity* and *stereogenicity* by Mislow and Siegel,[5] in this study we shall consider a tetrahedral carbon center C a *chirogenic center* (or in short, chiral center, wherever this term does not lead to ambiguity) if and only if *no two substituents of C are mirror images of one another.* Two substituents that are mirror images of one another will be considered *equivalent by reflection* (or in short, equivalent whenever this term does not lead to ambiguity), and we shall use the CIP system with identity of substituents replaced by equivalence of substituents. In particular, invoking equivalence by reflection instead of identity restricts the R and S classification to chirogenic centers. Within this framework no chirality label R or S is attached to the abovementioned (achirogenic) center in the example of Mislow and Siegel.[5] The concept of chirogenicity is distinct from both chirotopicity and stereogenicity; the carbon atom of a methyl group in a chiral molecule is chirotopic but achirogenic, whereas the carbon atom in a molecule CABRR having two *identical* chiral substituents R and two different achiral substituents A and B of the central carbon atom C is nonstereogenic but chirogenic.[13] Chirogenicity is directly linked to reflection properties and serves as a more convenient basis for our present studies.

In this and in the following sections it is necessary to define an ordering within sequences of pairs of numbers or in sequences of triplets of numbers, etc. We shall do this by the symmetric lexicographic ordering. Considering, e.g., triplets of numbers, first we write each triplet such that the three numbers are monotonically nondecreasing, e.g., instead of (3,1,3) we write (1,3,3,). In fact, we consider triplet (1,3,3) as the standard form that is symmetrically equivalent to all of its permutations. Then, we apply the lexicographic ordering to the standard forms, much the same way as alphabetic order is used in dictionaries, e.g., (1,7,8) comes before (2,2,3), that is, (1,7,8) is "smaller" than (2,2,3).

Consider first the simple case of a single carbon atom having four different substituents denoted by 1, 2, 3, and 4 as shown in Figure 1. We assume that these numerical labels follow the standard stereochemical rules for the priority of substituents, e.g., for the compound CHBrClI, bromochloroiodomethane, the labels 1, 2, 3, and 4 stand for I, Br, Cl, and H, respectively. This example illustrates the steps of the algorithm taken at each center.

The general rules for the generation of a unique knot are as follows: (i) Following the standard IUPAC numbering of atoms, order the chiral and achiral centers of the molecule. Choose the first such center. Mark one end of the string as the "origin" that defines an orientation for the string. (ii) Take all the k atoms of the molecule that are linked to the current chiral (or achiral) center. These atoms define the vertices of a convex polyhedron P. (Most commonly, P is a tetrahedron). (iii) Assign a number of priority, 1, 2, ... etc. to each vertex atom, based on the CIP rules of stereochemistry where identity of substituents is replaced by equivalence by reflection (see also note 13, concerning a previous example). If two substituents are equivalent, they are assigned identical numbers. (iv) Choose a face of the polyhedron P that has the set of lowest possible numbers assigned to its vertices. Attach the current position of the string to the middle of this face. (v) To lead the string from one face to the next face take first all number pairs (i,j) occurring on the edges of the current face, and for each pair (i,j) count the number $m(i,j)$ that is the number of times the string has passed between *numbers* i and j on the *current polyhedron* P. Take all those edges of P for which the number $m(i,j)$ is minimum. From this set choose and traverse an edge which bears the *smallest pair of numbers* at its vertices, as defined by the symmetric lexicographic ordering. It is possible that a chosen edge has already been crossed by the string segment between the starting face of P and the current location. We refer to such a case as multiple edge crossing. If the current occurrence of multiple edge crossing in the nth *on this polyhedron* P, then lead the string through the edge *under* the other string segment(s) if n is odd and *above* the other string segment(s) if n is even. (vi) Repeat step (v) until each edge has been crossed at least once and the string returns to the starting face. To ensure that no additional "knottedness" results from loose segments, tighten up each knotted segment at the centers. (vii) Move to the next center if there is any left and repeat steps (ii)–(vi). If there is no more center left, then remove the *molecular model.* We may view the resulting string in two ways: (a) in "high resolution", i.e., considering each knotted segment in full detail or (b) in "low resolution", i.e., considering each tightly knotted segment at the chiral centers as mere imperfections of the string. Join the two ends of the string so that in "low resolution" it should appear as a simple, unknotted loop. (viii) If there are equivalent substituents, then it is possible that the choice of starting face or the choice of the edge to be crossed is not unique. In such a case choose the alternative which generates the smallest pair of edge numbers at the earliest occasion where a difference occurs in the sequence of edges crossed. If two alternatives result in exactly the same pair sequence, then the knots are identical as it can be verified for all carbon centers by direct construction of these knots.

This algorithm generates a unique knot for the given set of chiral and achiral carbon centers. The information on the *topological chirality* of the chiral centers, i.e., on chirality properties that do not depend on the precise relative location and chemical identity of chiral centers, is retained in the knot even though the string is removed from the molecular model. Each knot defines a pair of polynomials that are *conformational invariants.* These polynomials provide a simple test for topological chirality, hence for chirality of the molecule in *any* conformation that preserves the chiral properties of individual centers. Whereas these polynomials are already powerful enough to give a *sufficient condition for molecular chirality*, they can be suitably modified for the description of colored knots that allows them to retain additional information on the chemical identities of individual chiral centers. As discussed in a subsequent section, these modified polynomials

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(12) Cahn, R. S.; Ingold, C. K.; Prelog, V. *Angew. Chem.* **1966**, *78*, 413.

(13) Since an interchange of the two R substituents does not lead to a new isomer, the carbon atom C is nonstereogenic. Note that in spite of the identity of two substituents, R and R, no mirror plane passes through C; hence, it is natural to regard this chirogenic carbon atom as a chiral center, that is, indeed the center of a chiral molecule. There are two choices for the ordering of the two R substituents; we adopt the one that is consistent with assigning label R to C. In general, we shall assign the label of the highest (CIP) priority pair of identical chiral substituents to the central C atom. For example, the labels of the central carbon atoms of molecules CABRR, CABSS, and CRRS′S′ are R, S, and S, respectively, where in CRRS′S′ it is assumed that the two identical S′ substituents have higher CIP priority number than that of the two identical R substituents. In the mirror image CSSR′R′ of CRRS′S′ the same rule implies a label R assigned to C. For a consistent generation of knots we need to prioritize substituents in such cases as well. In all instances, the actual priority numbers assigned to such identical chiral substituents are chosen so that the assignment is consistent with the given label R or S of the central carbon atom C. Note that the chemical relation "equivalent by reflection" (mirror image relation) is nontransitive and nonreflexive, hence not a mathematical equivalence relation.

Table I. Application of the Knot-Generating Algorithm to the Molecule Bromochloroiodomethane of Figure 1

face	edges crossed fewest times[a]	edge selctd	countr of multple crossngs	string passes with respct to itslf
(1,2,3)	(1,2), (1,3), (2,3)	(1,2)		
(1,2,4)	(1,4), (2,4)	(1,4)		
(1,3,4)	(1,3), (3,4)	(1,3)		
(1,2,3)	(2,3)	(2,3)		
(2,3,4)	(2,4), (3,4)	(2,4)		
(1,2,4)	(1,2), (1,4), (2,4)	(1,2)	1	under
(1,2,3)	(1,3), (2,3)	(1,3)	2	over
(1,3,4)	(3,4)	(3,4)		
(2,3,4)	(2,3), (2,4), (3,4)	(2,3)	3	under

[a] Since all substituents (I, Br, Cl, and H) are unique, there is a one-to-one assignment between pairs and edges.

Table II. Application of the Knot-Generating Algorithm to Achiral Derivatives I–VI

substitd species	substitutes postn				starting face	sequence of prs of edge nos. along string	knot
	1	2	3	4			
I	1	1	3	4	(1,1,3)	(1,1)(1,4)(1,3)(1,1)(1,4)(3,4)-(1,3)	U
II	1	2	2	4	(1,2,2)	(1,2)(1,4)(2,4)(2,2)	U
III	1	2	3	3	(1,2,3)	(1,2)(1,3)(3,3)(2,3)	U
IV	1	1	1	4	(1,1,1)	(1,1)(1,4)(1,1)	U
V	1	2	2	2	(1,2,2)	(1,2)(2,2)(2,2)	U
VI	1	1	1	1	(1,1,1)	(1,1)(1,1)(1,1)	U

provide both *sufficient and necessary conditions for chirality*. Before discussing the properties of these polynomials, we shall consider examples for knot generation.

As shown in Figure 1 the *S* configuration of bromochloroiodomethane generates the left-handed trefoil knot if one follows the steps of the algorithm. Note that no two substituents are equivalent by reflection, hence, there is a one-to-one assignment between number pairs and edges. The actual steps required are listed in Table I. Starting with face (1,2,3) the first edge crossed in edge (1,2) leading to face (1,2,4). On this face there are two edges, (2,4) and (1,4), which have been crossed the *fewest* times, actually, zero times, from which edge (1,4) bears the smaller pair of numbers; hence, this edge is chosen. Through this edge the string is led to the next face, face (1,3,4); the next edge is (1,3), etc. A complete list of faces and edges, in the order of their occurrences along the string, is given in Table I. The first multiple crossing occurs when leading the string from face (1,2,4) through edge (1,2). This is the first such occurrence ($n = 1$, an *odd* number); hence, the string is led *under* the string segment already there: the string segment from the starting face (1,2,3) to face (1,2,4). The next such occurrence ($n = 2$, an *even* number) is at edge (1,3), where the string is lead *over* itself. The third (and last) such occurrence is at edge (2,3) at the far side of tetrahedron P (where $n = 3$, an odd number) implying that the string is led *under* itself, as shown in Figure 1.

Note that the same sequence of face and edge symbols and over-and-under passes of the string occur for *both* enantiomers of Figure 1, but the resulting knots are *different*: they are enantiomeric images of one another. Furthermore, the orientation of the arrows on the two *completed* knots is *not* significant: the handedness of the trefoils is *not* affected by the reversal of the orientation of the arrows shown over them.

Whenever two or more substituents of either tetrahedra of Figure 1 are equivalent, then the algorithm generates a simple "unknotted" loop (the "unknot", U). Starting, e.g., with the S configuration of Figure 1, this can be tested by direct construction of these loops. In Table II the sequence of edge number pairs are given for six different achiral types obtained from the *S* form of Figure 1 by substituting equivalent groups. In each case the achiral "unknot" U is obtained; hence, for carbon centers the algorithm generates a chiral knot if and only if the center itself is chiral.

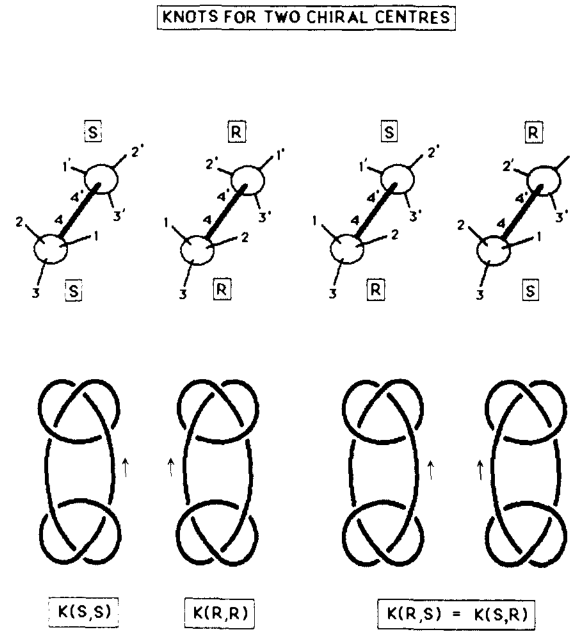

Figure 3. The three distinct knots obtained for the *S,S*, the *R,R*, and the *R,S* = *S,R* (meso) forms of two chiral centers of the same constitution.

In Figure 3 the simplest case of two chiral centers and the associated knots are shown. For simplicity we assume that substituents differing only by a prime in our notation are equivalent. The first two molecules are optically active enantiomers having chiral centers *S,S* and *R,R*, respectively, whereas the third and fourth molecules are identical meso forms with chiral centers *S,R*. The corresponding knots K(*S,S*), K(*R,R*), and K(*R,S*) = K(*S,R*) obtained by the algorithm described above possess the appropriate chirality properties. These knots have been drawn in a symmetric manner to facilitate the recognition of various chirality relations among them.

A rather trivial, nevertheless important observation: these knots preserve the chirality information independently of their actual representation or the way they are drawn in the plane, e.g., if they are drawn completely asymmetrically, as long as the string is not cut anywhere and there are no tangential contacts between string segments nor two or more crossings drawn on top of one another.

All that matters is the *pattern of crossings* in each knot that suggests that a simpler representation of molecular chirality is possible by making use of this "crossing information".

Chirality Polynomials $V(t)$ and $P(l,m)$. We shall use two recently discovered families of polynomials for the description of chirality: the Jones polynomial $V(t)$ and the two-variable polynomial $P(l,m)$ of Lickorish and Millett.[7-9] Here we shall follow the sign and exponent conventions employed by Millett.[14]

The rules for the generation of these polynomials are very simple and are summarized in Figure 4. We assume that the projections of the knots investigated are drawn in the plane without tangential contacts or two or more crossings above one another.

For the "unknot" U (a single loop with no crossings) shown in Figure 4, both polynomials are equal to unity, by definition

$$V_U(t) = 1 \qquad (1)$$

$$P_U(l,m) = 1 \qquad (2)$$

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(14) Whereas it has no effect on our present study, note that there is as yet no uniformity in the sign and exponent conventions employed for the definition of $V(t)$ in the recursive formula for the polynomial. The reader should be aware of this fact when making comparisons among polynomials published by different authors [7–9]. Note, that a recursive formula in which the sign of the last term in eq 3 is reversed can be obtained by a $t^{1/4} \rightarrow t^{1/4}e^{i\pi/2} = it^{1/4}$ substitution, suggesting an underlying generating formula

$$-s^{-4}S_{-}(s) + s^{4}S_{+}(s) + (s^{2} - s^{-2})S_{0}(s) = 0$$

By taking $s = t^{1/4}e^{i\pi/2}$ and $V(t) = S(t^{1/4}e^{i\pi/2})$, the recursive formula 3 is obtained, whereas the choice of $s = t^{1/4}$ and $V(t) = S(t^{1/4})$ leads to the alternative recursive formula.

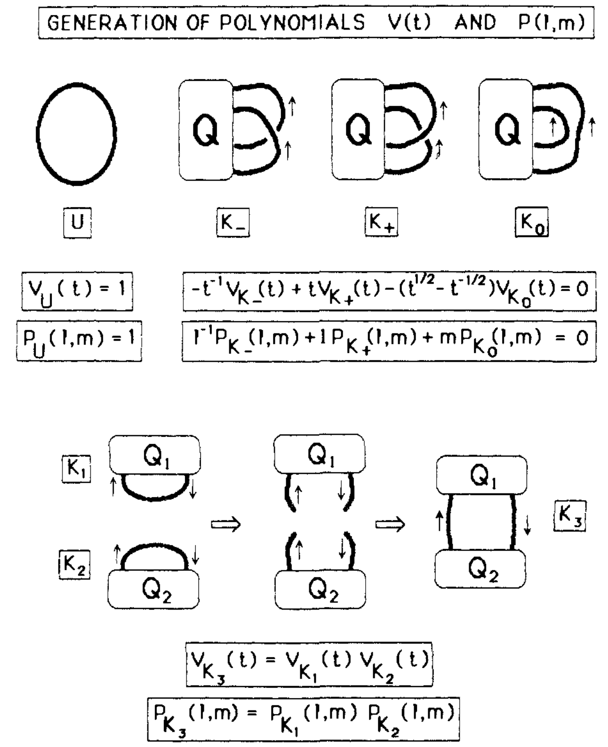

Figure 4. Rules for the generation of chirality polynomials $V(t)$ and $P(l,m)$. Both polynomials are identically 1 for the simple loop ("unknot") U. For any three knots K_-, K_+, and K_0, which are identical under the cover Q and differ only in their exposed parts, the corresponding polynomials are interrelated by the simple rules shown. If one cuts the string in two knots, K_1 and K_2, and joins them in a parallel fashion to obtain a new knot K_3, then the new polynomial of K_3 is the product of those of knots K_1 and K_2. This latter "product rule" provides a simple shortcut for the generation of chirality polynomials for larger molecules or for products of chemical reactions.

Consider now three knots, K_-, K_+, and K_0 which have *identical* projections on the plane except for a small neighborhood containing at most one crossing. In Figure 4 identical parts of the projections are denoted by Q, and the remaining parts are exactly the crossings X_- (left-handed crossing), X_+ (right-handed crossing) and X_0 ("avoided crossing") shown in Figure 2. Then for the polynomials of such three knots the following two relations are valid

$$-t^{-1}V_{K_-}(t) + tV_{K_+}(t) - (t^{1/2} - t^{-1/2})V_{K_0}(t) = 0 \qquad (3)$$

and

$$l^{-1}P_{K_-}(l,m) + lP_{K_+}(l,m) + mP_{K_0}(l,m) = 0 \qquad (4)$$

In fact, these two polynomials are interrelated: by substituting $l = it$, and $m = i(t^{1/2} - t^{-1/2})$ the polynomial $P_K(l,m)$ becomes $V_K(t)$. We shall use the simpler polynomial $V(t)$ in most of our examples; however, one should note that for a more general shape characterization of certain knots of a large number of crossings $P(l,m)$ is a more powerful distinguishing tool than $V(t)$.[8] As far as chirality is concerned, both $P(l,m)$ and $V(t)$ perform equally well.

By repeated applications of relations 1–4, one can generate the polynomial of the knot under study.[14]

For example, the polynomial V for the right-handed trefoil knot T_+ can be obtained by applying these rules in three subsequent steps for the triplets of knots shown in Figure 5. (For simplicity, we use the same term, "knot", for the proper knot T_+ as well as for the "unknot" U, "U^2", and link "L".) Under each knot the corresponding $V(t)$ polynomial is shown. In each step two of the three polynomials are known, either from earlier steps or from definition 1; hence, the third polynomial (placed in a heavy-line frame in Figure 5) can be obtained by using relation 3. (A similar method can be applied for the two-variable polynomial $P(l,m)$).

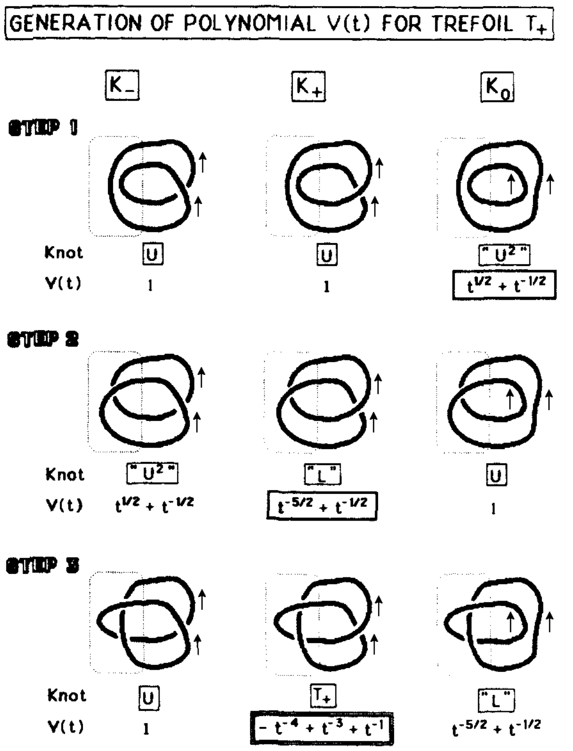

Figure 5. The three steps required for the direct generation of the chirality polynomial $V_{T_+}(t)$ of the right-handed trefoil knot, representing a chiral center of configuration *R*. Note that in each step the three planar projections differ only in precisely one crossing; hence, they are interrelated by the equation shown in Figure 4. In each step two of the polynomials are known, either from the definition $V_U(t) = 1$ or from an earlier step; hence, the third polynomial (shown in the heavy rectangular frame) can be calculated. In the last step, the chirality polynomial $V_{T_+}(t) = -t^{-4} + t^{-3} + t^{-1}$ is obtained for the right-handed trefoil T_+, that is, for the chiral carbon center of configuration *R*.

By using this method one easily finds that for the right-handed trefoil knot T_+ of chiral center R the two polynomials are

$$V_{T_+}(t) = -t^{-4} + t^{-3} + t^{-1} \qquad (5)$$

and

$$P_{T_+}(l,m) = -l^{-4} - 2l^{-2} + l^{-2}m^2 \qquad (6)$$

whereas for the left-handed trefoil knot T_- of chiral center S the polynomials are

$$V_{T_-}(t) = -t^4 + t^3 + t \qquad (7)$$

and

$$P_{T_-}(l,m) = -l^4 - 2l^2 + l^2m^2 \qquad (8)$$

A fundamental property of polynomials $V(t)$ and $P(l,m)$ is that any two topologically equivalent placements have exactly the same polynomials. For our purposes the most important additional property of these polynomials is the following relation:

If $V(t)$ and $P(l,m)$ are the polynomials of knot K of molecule M, and if $\bar{V}(t)$ and $\bar{P}(l,m)$ *are the polynomials of knot $\bar{K}$ of the mirror image $\bar{M}$ of molecule M, then*

$$\bar{V}(t) = V(t^{-1}) \qquad (9)$$

and

$$\bar{P}(l,m) = P(l^{-1},m) \qquad (10)$$

Since conformational changes (in the strict sense, that is, bond rotations) in any molecule M do not alter the chirality of various centers, hence, do not alter the knots or knot fragments associated with these centers, *these polynomials are conformational invariants of the molecules.* Consequently, if by conformational changes it is possible to generate a pair of mirror image molecules

M and M̄, then the same polynomials of eq 9 and 10 apply for any other conformations of these molecules. In particular, if a conformation of M is identical with (superimposable on) a conformation of M̄, then

$$\bar{V}(t) = V(t) \tag{11}$$

and

$$\bar{P}(l,m) = P(l,m) \tag{12}$$

hence

$$V(t) = V(t^{-1}) \tag{13}$$

and

$$P(l,m) = P(l^{-1},m) \tag{14}$$

Of course, if these conformations are identical, then the molecule M is achiral. *This chemical property is reflected in the chirality polynomials in a peculiar way: for achiral molecules polynomials $V(t)$ and $P(l,m)$ do not change if variables t and l are replaced by their reciprocals, $1/t$ and $1/l$, respectively.* We shall refer to relations 13 and 14 as *chirality conditions* (more precisely, achirality conditions).

Each of the relations 13 and 14 is a necessary condition (and for the actual knots also a sufficient condition, vide infra) *for the achirality of molecule M. Conversely, whenever $V(t)$ and $V(t^{-1})$ (and equivalently, whenever $P(l,m)$ and $P(l^{-1},m)$) do not agree, then molecule M is chiral in all of its possible conformations.*

The mere existence of a chiral conformation of M does not necessarily exclude the fulfillment of equivalent conditions 13 and 14. These conditions are necessarily fulfilled if conformational changes can bring about an interconversion of any pair of enantiomeric conformations of M. *Conformational changes do not affect the topological chirality of molecules and also leave the knottedness of the corresponding knots invariant. This latter invariance implies that of chirality polynomials $V(t)$ and $P(l,m)$; and this is the reason why these polynomials are conformational invariants of molecules.*

Achirality conditions 13 and 14 are somewhat counter intuitive. Whereas for large molecules chirality is more the rule than the exception, for most of the common, smaller molecules chirality and not achirality is regarded by most chemists as a special feature. For example, chiral carbon centers are marked by special asterisks and not the achiral ones, partly as a result of the traditional two-dimensional textbook representation of molecules. On the other hand, polynomials with properties 13 and 14 are rather exceptional, since most commonly a replacement of the variable with its reciprocal *does not* leave an arbitrary polynomial invariant. That is, achirality, a chemical property perceived by most chemists as rather common, is reflected by a rather unusual mathematical property of the polynomials. Conversely, the "less common" chemical property of chirality is reflected in a very common mathematical property: replacing the variable with its reciprocal usually does alter a polynomial.

The Case of Several Chiral Centers, Product Rule, and Polynomials for Colored Knots. In Figure 3 we have seen the example of two chiral centers, composed from two identical sets of substituents. The corresponding knots K(*S*,*S*), K(*R*,*R*), and K(*R*,*S*) = K(*S*,*R*) are generated by the algorithm described in a previous section. The polynomials of these knots can be obtained directly by repeated applications of relations 1–4. However, there is a useful shortcut that can be applied in the case of more complicated knots.

This shortcut is based on an intriguing *product rule* of the polynomials. Consider two knots, K_1 and K_2, cut both at some location, and join the two knots with orientations matching, as shown in Figure 4. *For the resulting knot K_3 the polynomials are the products of the respective polynomials of knots K_1 and K_2*

$$V_{K_3}(t) = V_{K_1}(t)V_{K_2}(t) \tag{15}$$

$$P_{K_3}(l,m) = P_{K_1}(l,m)P_{K_2}(l,m) \tag{16}$$

The result is independent of the locations where the cuts are made.

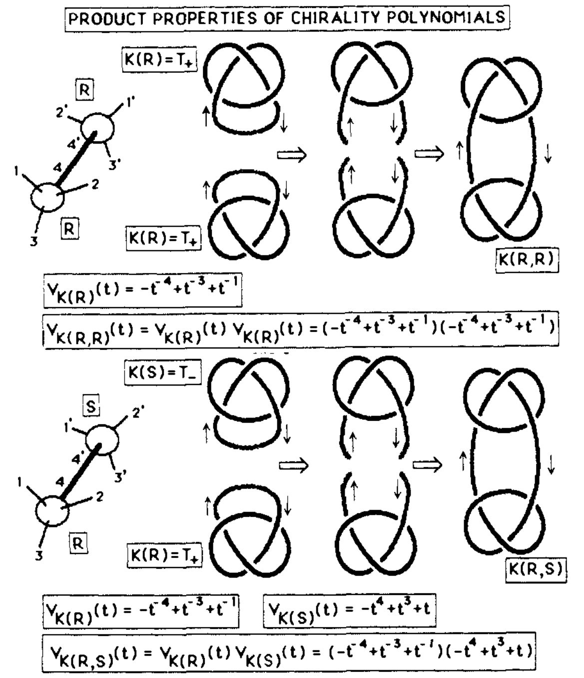

Figure 6. An illustration of the "product rule" of Figure 4, for the *R*,*R* and *R*,*S* configurations of a pair of chiral centers of the same constitution. The knot K(*R*,*R*) is *chiral*, since for its polynomial $V_{K(R,R)}(t)$ a replacement of t by t^{-1} results in a *different* polynomial

$$(-t^{-4} + t^{-3} + t^{-1})(-t^{-4} + t^{-3} + t^{-1}) \neq (-t^4 + t^3 + t)(-t^4 + t^3 + t)$$

On the other hand, for the product polynomial $V_{K(R,S)}(t)$ obtained for the *achiral meso* from *R*,*S*, the condition of achirality holds, since substitution of t^{-1} for t yields the *same* polynomial

$$(-t^{-4} + t^{-3} + t^{-1})\,(-t^4 + t^3 + t) = (-t^4 + t^3 + t)(-t^{-4} + t^{-3} + t^{-1})$$

The product rule specifies how to generate knots and chirality polynomials for a molecule obtained from a reaction of two reactants, if the knots of the reactants are known, and if the reaction procedes with retention of configurations. Note, that an achiral center in a given molecule or an addition reaction with an achiral reactant, if this addition does not change the chirality of other centers, adds only an "unknot" U to the knot; hence, neither the knot nor its polynomials will change. Also note that generating a *single* bond, i.e., a formal "*single connection*" between two chiral fragments, corresponds to generating *two* connecting string segments between the knots. This observation and the fact that the two connecting string segments are of opposite orientation, brings to mind some intriguing formal analogies with electron pairs of opposite spins forming a single covalent bond.

Two examples are shown in Figure 6. Consider the R,R configurations. Regarding the two chiral centers separately, each corresponds to a right-handed trefoil knot, K(*R*) = T_+, with the polynomial

$$V_{K(R)}(t) = -t^{-4} + t^{-3} + t^{-1} \tag{17}$$

as given by eq 5. For the complete molecule of configuration R,R the polynomial

$$V_{K(R,R)}(t) = V_{K(R)}(t)V_{K(R)}(t) = (-t^{-4} + t^{-3} + t^{-1})(-t^{-4} + t^{-3} + t^{-1}) \tag{18}$$

is implied by relation 5 that is identical with the polynomial obtained by a direct derivation using relations 1–4.

We may test chirality of this molecule by using relation 13. Evidently,

$$V_{K(R,R)}(t) \neq V_{K(R,R)}(t^{-1}) \tag{19}$$

that is,

$$(-t^{-4} + t^{-3} + t^{-1})(-t^{-4} + t^{-3} + t^{-1}) \neq (-t^4 + t^3 + t)(-t^4 + t^3 + t) \tag{20}$$

The right hand side of inequality 20 is in fact the V polynomial for the S,S configuration

$$V_{K(S,S)}(t) = (-t^4 + t^3 + t)(-t^4 + t^3 + t) \qquad (21)$$

that is, evidently, also chiral, as born out by the same condition 20.

The second example of Figure 6 is the R,S configuration, having the same substituents. For these two chiral centers the knots are the right-handed trefoil $K(R) = T_+$ and the left-handed trefoil $K(S) = T_-$, the latter having the polynomial as given by eq 7

$$V_{K(S)}(t) = -t^4 + t^3 + t \qquad (22)$$

Direct construction of the polynomial of the complete knot K(R,S) for this configuration gives the same result as the *product rule* 15

$$V_{K(R,S)}(t) = V_{K(R)}(t)V_{K(S)}(t) = (-t^{-4} + t^{-3} + t^{-1})(-t^4 + t^3 + t) \qquad (23)$$

This molecule, a *meso* form, is evidently achiral. This is born out by direct substitution into relation 13

$$V_{K(R,S)}(t) = V_{K(R,S)}(t^{-1}) \qquad (24)$$

That is, for the *meso* form of Figure 6 a replacement of variable t with t^{-1} does not change the polynomial, and this is the very condition for a molecule being achiral.

More possibilities and more interesting polynomials arise if the sets of substituents of the two or more chiral centers of the molecules do not agree in their constituents. The knot theoretical polynomials can be modified to provide a description and a more revealing chirality test for such cases. We shall use the following convention: if the set of four substituents of a center C_1 is the same as the set of four substituents of center C_2, or, if one set consists of the mirror images of substituents in the other set, then we use the *same color for the string* when generating individual knots for C_1 and C_2. Otherwise *strings of different colors* are used. Evidently, if C_1 and C_2 have substituents of different chemical constitution, then an R configuration at C_1 is *not* the mirror image of an S configuration at C_2, and a $K(R,S)$ knot does not represent an achiral *meso* form. This fact is reflected in the color difference of the two parts of knot $K(R,S)$ if this knot $K(R,S)$ is obtained by joining the colored $K(R)$ and $K(S)$ knots according to the "product rule". Whereas a shift of knotted segments along the string of $K(R,S)$ cannot change the knot theoretical identity of $K(R,S)$; nonetheless, it leads to ambiguities concerning the color assignment. However, no such ambiguity arises for the *polynomials*, if they are generated by the product rule from polynomials of colored knots of individual centers, having different variables. It appears natural to distinguish the variables of the polynomials of knots, for example, of $K(R)$ and $K(S)$, if these knots are of different colors. If *different variables* are used when applying the product rule for the polynomials, then chirality tests 13 and 14 to apply even if the centers C_1 and C_2 are substituted differently. Whereas in the final knot there is no correspondence between the chemical identities and chirality properties of centers, this correspondence *is* maintained in the final polynomials. Hence, the polynomials obtained by the product rule for colored knots carry more stereochemical information in addition to topological chirality carried by the resulting knot.

An example is shown in Figure 7. Let us suppose that substituents 1 and 1′ are different in the two chiral centers R and S; 1 ≠ 1′, but 2 = 2′ and 3 = 3′. A right-handed trefoil knot T_+ of a *blue string* is generated around center R, and a left-handed trefoil knot T_- of a *red string* is generated around center S. Taking two different variables, t_b and t_r, for the respective knots, the V polynomials are

$$V_{K(R)}(t_b) = -t_b^{-4} + t_b^{-3} + t_b^{-1} \qquad (25)$$

and

$$V_{K(S)}(t_r) = -t_r^4 + t_r^3 + t_r \qquad (26)$$

The product rule 15 for K(R,S) gives

$$V_{K(R,S)}(t_b,t_r) = (-t_b^{-4} + t_b^{-3} + t_b^{-1})(-t_r^4 + t_r^3 + t_r) \qquad (27)$$

By generalizing rule 13 and replacing *all t* type variables with their reciprocals, one obtains

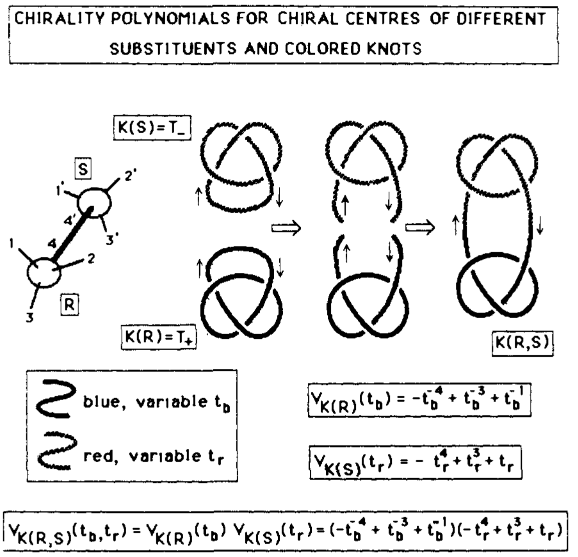

Figure 7. An illustration of the "product rule" for a pair of R and S chiral centers of different composition. The fact that the compositions are different can be represented by different colors (blue and red) of the strings for the knots and different variables (t_b and t_r) for the chirality polynomials. The condition of achirality for the product polynomial $V_{K(R,S)}(t_b,t_r)$ no longer holds, since the $t_b,t_r \rightarrow t_b^{-1},t_r^{-1}$ replacement results in

$$(-t_b^{-4} + t_b^{-3} + t_b^{-1})(-t_r^4 + t_r^3 + t_r) \neq (-t_b^4 + t_b^3 + t_b)(-t_r^{-4} + t_r^{-3} + t_r^{-1})$$

i.e., in a *different* polynomial. Hence the molecule is chiral. If, however, a change of substituents results in equivalent compositions for the two centers, R and S, then the colors and variables match, and by omitting the distinguishing b and r indices from t_b and t_r one obtains *equality* for the two polynomials, as required for an *achiral meso* form.

$$V_{K(R,S)}(t_b^{-1}, t_r^{-1}) = (-t_b^4 + t_b^3 + t_b)(-t_r^{-4} + t_r^{-3} + t_r^{-1}) \qquad (28)$$

Evidently,

$$V_{K(R,S)}(t_b^{-1},t_r^{-1}) \neq V_{K(R,S)}(t_b,t_r) \qquad (29)$$

hence the molecule is *chiral*. In fact, we obtain the polynomial for the S,R configuration

$$V_{K(R,S)}(t_b^{-1},t_r^{-1}) = V_{K(S,R)}(t_b,t_r) \qquad (30)$$

This result is consistent with the application of chirality rule 13 to the polynomials $V_{K(R)}(t_b)$ and $V_{K(S)}(t_r)$ of the colored knots $K(R)$ and $K(S)$, followed by the application of the product rule for the mirror images of knots $K(R)$ and $K(S)$.

A Sufficient and Necessary Condition for Chirality. The modified polynomials, depending on several variables, provide not only a sufficient condition but also a *sufficient and necessary* condition for chirality, for all molecules where chirality, if it exists, is a consequence of chiral (chirogenic) carbon centers. We shall show now, that in addition to being a sufficient condition, the inequality

$$V_K(t_1,t_2,...t_N) \neq V_{\bar{K}}(t_1,t_2,...t_N) \qquad (31)$$

is also a necessary condition for chirality. Take an enantiomeric pair of chiral molecules, M and $\bar{M}$,

$$M \neq \bar{M} \qquad (32)$$

and, contrary to the above, assume that the modified polynomials of relation 31 agree

$$V_K(t_1,t_2,...t_N) = V_{\bar{K}}(t_1,t_2,...t_N) \qquad (33)$$

We shall show that this is impossible; that proves (31).

By writing these polynomials in the form obtained by the product rule from polynomials of individual colored knots, K_i, eq 33 implies

$$V_K(t_1,...t_N) = \prod_{i=1}^{N} V_{K_i}(t_i) = \prod_{i=1}^{N} V_{\bar{K}_i}(t_i) \qquad (34)$$

For carbon centers each K_i is either a trefoil or an unknot. By omitting all $V_{\mathrm{U}} = 1$ polynomials of unknots, we are left with N' factors V_{K_i}, $N' \leq N$, each factor V_{K_i} belonging to a colored chiral knot K_i. Without loss of generality we may assume that these are the first N' factors in the original product 34

$$V_{\mathrm{K}}(t_1,...t_N) = \prod_{i=1}^{N'} V_{\mathrm{K}_i}(t_i) = \prod_{i=1}^{N'} V_{\bar{\mathrm{K}}_i}(t_i) \tag{35}$$

Since M and $\bar{\mathrm{M}}$ are chiral, $N' \geq 1$ follows. By exploiting property 9 on the right hand side, one finds that

$$\prod_{i=1}^{N'} V_{\mathrm{K}_i}(t_i) = \prod_{i=1}^{N'} V_{\mathrm{K}_i}(t_i^{-1}) \tag{36}$$

However, for trefoils

$$V_{\mathrm{K}_i}(t_i) \neq V_{\mathrm{K}_i}(t_i^{-1}) \tag{37}$$

Hence, eq 36 and the actual form of trefoil polynomials imply that for each index i there must exist an index j, $j \neq i$, such that

$$V_{\mathrm{K}_i}(t_i) = V_{\mathrm{K}_j}(t_j^{-1}) \tag{38}$$

that is

$$V_{\mathrm{K}_j}(t_j) = V_{\bar{\mathrm{K}}_i}(t_i) \tag{39}$$

For trefoils this is possible only if

$$t_j = t_i \tag{40}$$

Since the above pair assignment applies to all trefoils, N' must be even, and by using eq 39 one may write

$$V_{\mathrm{K}}(t_1,...t_{\mathrm{N}}) = \prod_{i=1}^{N'/2} [V_{\mathrm{K}_i}(t_i) V_{\bar{\mathrm{K}}_i}(t_i)] \tag{41}$$

Each square bracket depends on a single variable t_i; hence, by definition of t_i it refers to two chiral centers C and $\bar{\mathrm{C}}$ having either the same set of four substituents or two different sets where one set consists of the mirror images of the substituents in the other set. However, the two sets of substituents X, Y, Z, and W of C and $\bar{\mathrm{X}}$, $\bar{\mathrm{Y}}$, $\bar{\mathrm{Z}}$, and $\bar{\mathrm{W}}$ of $\bar{\mathrm{C}}$ cannot be the same. The pairing in eq 41 implies that the family of substituents $\bar{\mathrm{X}}$, $\bar{\mathrm{Y}}$, $\bar{\mathrm{Z}}$, and $\bar{\mathrm{W}}$ at $\bar{\mathrm{C}}$ must contain precisely one unpaired center of type $\mathrm{K}(t_i)$ that is the pair of the $\bar{\mathrm{K}}(t_i)$ type center $\bar{\mathrm{C}}$, whereas the family X, Y, Z, and W must contain precisely one unpaired center of type $\bar{\mathrm{K}}(t_i)$ that is the pair of $\mathrm{K}(t_i)$ at C. Since these unpaired centers $\bar{\mathrm{K}}(t_i)$ and $\mathrm{K}(t_i)$ are different, the two sets of substituents, {X,Y,Z,W} and {$\bar{\mathrm{X}}$,$\bar{\mathrm{Y}}$,$\bar{\mathrm{Z}}$,$\bar{\mathrm{W}}$}, cannot be the same.

Hence, substituents X, Y, Z, and W are the mirror images of $\bar{\mathrm{X}}$, $\bar{\mathrm{Y}}$, $\bar{\mathrm{Z}}$, and $\bar{\mathrm{W}}$, respectively. Furthermore, these substituents are arranged so that they form a $\mathrm{K}(t_i)$ type center at C and a $\bar{\mathrm{K}}(t_i)$ type center at $\bar{\mathrm{C}}$. Hence, center C with its substituents X, Y, Z, and W (that is, the entire molecule) is the mirror image of center $\bar{\mathrm{C}}$ with its substituents $\bar{\mathrm{X}}$, $\bar{\mathrm{Y}}$, $\bar{\mathrm{Z}}$, and $\bar{\mathrm{W}}$ (that is also the entire molecule). That is, the molecule is the mirror image of itself; hence, it is achiral that contradicts condition 32. Consequently, relation 33 is impossible for a chiral molecule, and *condition* 31 *is both sufficient and necessary condition for chirality.*

Comment on a Possible Generalization. All our above examples referred to chiral carbon centers, which do represent the majority of chirality problems of chemistry. However, the model can be extended easily to other chiral centers as well as to chirality problems involving no chiral centers at all. One may notice that the central carbon atoms in our examples have no direct role in the construction of the knots and polynomials; in fact, only the polyhedron defined by the substituents is of importance.

The simplest generalization is based on the above observation. For a general molecule composed from more than three atoms one may consider all possible quadruplets of nuclei. Each of these quadruplets defines a (usually distorted) tetrahedron, that in the coplanar case becomes a quadrilaterial, or a triangle, or a single line.

A serial number is assigned to each atom, and the quadruplets (hence, the corresponding geometrical objects) are ordered into a sequence according to the symmetric lexicographic order (e.g., (1,7,8,9) comes before (2,3,4,5)). A string of the *same* color is used for two quadruplets if and only if the two are composed from the same set of four nuclei, and the corresponding atom pair distances are the same in the two quadruplets. That is, the same color is used if and only if the two quadruplets are either superimposable on each other or are the mirror images of each other. Achiral nuclear configurations may contain chiral quadruplets, but in such a case to each chiral quadruplet one may assign another one that is its mirror image. The above color assignment ensures that this fact is reflected in the knots generated.

In the noncoplanar case the knot is generated exactly as described in the previous sections. If the nuclei are coplanar, then in the quadrilaterial and triangle cases the algorithm yields the unknot U, whereas in the collinear case there is no face, and no knot is generated. By considering all quadruplets of nuclei in the symmetric lexicographic order, the algorithm results in a unique (possibly colored) knot that carries all chirality information of the molecule. The corresponding polynomials $V(t)$ and $P(l,m)$ provide a concise description of this chirality information. Note, however, that this technique does not take into account the actual location of chemical bonds in the molecule, and, as a result, these polynomials are specific for the given nuclear configuration and are no longer in general conformational invariants.

However, a somewhat different "conformational" invariance property still can be shown to exist. The knots hence the polynomials are evidently invariant to any conformational motion of the nuclei that (i) leaves the color assignment unchanged, (ii) leaves each nondegenerate tetrahedron nondegenerate, and (iii) leaves each degenerate tetrahedron (i.e., coplanar quadruplet of nuclei) degenerate (i.e., coplanar). Such "tetrahedron-preserving", hence "polynomial-preserving", internal motions may include actual chemical reactions, e.g., addition reactions along specific reaction paths; hence, they are not restricted to internal rearrangements and conformational changes.

Summary

Chirality properties of molecules can be described in terms of a set of polynomials deduced from the topological properties of knots tied around chiral centers. An algorithm is proposed for the construction of a unique knot for any sequence of chiral and achiral carbon atoms. These knots have the remarkable property that they carry all the topological chirality information of the molecules. In particular, the addition or deletion of achiral centers do not alter these knots.

For every knot K two chirality polynomials, $V_{\mathrm{K}}(t)$ and $P_{\mathrm{K}}(l,m)$ can be constructed. The knots and their polynomials are invariant to conformational changes of the molecules. Joining two chiral molecular fragments corresponds to joining their knots to form a single knot that in turn corresponds to generating the *product* of the chirality polynomials of the two chiral molecular fragments. Using this method, one can easily generate the knots and chirality polynomials of molecules of a large number of chiral fragments. A change in substituents can be represented by a color change in the string of the knot that in turn corresponds to a change of variable of the polynomial.

In chemical applications the actual generation of knots is not required. Using the known polynomials for U, T_+, and T_- all the necessary polynomials can be generated by the product rule.

These polynomials provide a simple test for the chirality of molecules: the molecule is necessarily chiral if the replacement of variables t and l by t^{-1} and l^{-1}, respectively, does alter these polynomials

$$V_{\mathrm{K}}(t^{-1}) \neq V_{\mathrm{K}}(t)$$

and

$$P_{\mathrm{K}}(l,m) \neq P_{\mathrm{K}}(l^{-1},m)$$

In the case of several chiral centers and polynomials involving several variables, the analogous condition 31 is a sufficient and necessary condition for chirality. These polynomials are conformational invariants and provide a simple means for computer manipulations of chirality properties of large molecules of many chiral centers. The remarkable properties of the new, multivariable chirality polynomials underline the importance of the concept of *chirogenic center* used for their definition. This concept circumvents some of the difficulties in the conventional CIP characterization of chirality and provides a natural tool for the analysis of chirality associated with tetrahedral centers.

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Coupling between the Rotation of the Methyl Group and the Proton Exchange in 5-Methyl-9-hydroxyphenalen-1-one

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Abstract: Introduction of a methyl group in the symmetric position in 9-hydroxyphenalen-1-one couples the rotation of the methyl group with the oscillation of the intramolecularly hydrogen bonded proton if the frequencies of the two motions are of the same order of magnitude. This coupling produces two apparently paradoxical effects. On the one hand, the barrier splitting increases; on the other hand, the proton flux through the barrier decreases. If the motions of the methyl group and the proton were uncoupled, the energy levels would be a superposition of the gerade–ungerade eigenvalues of the double-minimum potential and the rotational manifold of the methyl group. However, the coupling between the two motions is observed to split those levels of the methyl rotation which are multiples of three, producing two manifolds, each consisting of six closely spaced energy levels with D_{3d} symmetry, which is that of the two-dimensional potential energy levels for the coupled motion. The calculated average separation between the two manifolds is in good agreement with the assigned experimental value. The fact that with the methyl in position five two closely spaced manifolds are obtained would explain the increase observed in the relaxation of the excited vibrational state in 5-methyl-9-hydroxyphenalen-1-one.

Laser-induced fluorescence (LIF) of 9-hydroxyphenalen-1-one (9-HPLN, Figure 1, I and its 5-methyl derivative (5-M-9-HPLN, Figure 1, II) in a neon matrix at 4 K shows[1] fully relaxed vibrational transitions; this allows the determination of the barrier splitting for the proton exchange in both the ground and the excited states. A barrier splitting of 92 cm^{-1} for 5-M-9-HPLN was found for the ground state, an increase from 69 cm^{-1} for 9-HPLN, the parent compound. In the excited states the splittings were of 311 cm^{-1} for the parent compound and 431 cm^{-1} for the 5-methyl derivative.

If the methyl group in position five rotated freely, the double-minimum potential for the proton exchange would remain symmetric, and the increase in the barrier splitting would denote a decrease in barrier height both in the ground and in the excited states.[1] This barrier reduction could have been caused by the inductive effect of the methyl group through the π-electron system in the molecule or by the proximity of the neon atoms.

The possibility of barrier reduction as the reason for the increase in the barrier splitting seems to be challenged by the NMR spectra as their interpretation seems to indicate a reduced barrier penetration with the addition of a methyl group.[2]

Increased splitting indicates barrier reduction only if the double-minimum potential remains symmetric. It was recently shown[3] that the introduction of a slight asymmetry in a symmetric double-minimum potential increases the splitting of the gerade–ungerade pair and at the same time decreases drastically the penetration through the barrier.

Restricted rotation of a methyl group, if it is in the symmetric position five, will be coupled with the large-amplitude nonharmonic oscillation of the intramolecularly hydrogen bonded proton. As was proposed in a previous publication,[4] when one of the C–H bonds of the methyl group is perpendicular to the plane of the molecule, the double-minimum potential remains symmetric. Rotation of the methyl group from this position destroys the symmetry, thus reducing drastically the tunneling rate.[5] This effect couples the motion of the hydrogen bonded proton with the rotation of the methyl group. The potential energy surface for the coupled motion is now two-dimensional, and, as proposed previously, the eigenstates will belong to the D_{3d} symmetry group, to which the Hamiltonian belongs. A similar Hamiltonian was successfully used to calculate the energy levels for the coupled motion in 2-methyl-3-hydroxyacrolein.

To determine why the barrier splitting increases when the methyl group is attached, the extent of the coupling between the proton exchange and the methyl rotation was evaluated from the potential energy surface.

Calculations

Ab initio SCF molecular orbital calculations were performed for the electronic energy[6] at the STO-3G level[7] with convergence on the density matrix set at 10^{-7} au.

The five geometries pertinent to the system (Figure 2) were optimized with the proper geometrical constraints until all analytical nuclear cartesian forces[8] were less than 0.0005 au/Bohr. As in the case of the parent compound, all atoms, except two or three hydrogens of the methyl group, are in a plane. The structure with minimum energy, an absolute minimum, is represented by structure A (Figure 2). In this structure one C–H bond of the methyl group is in the plane of the molecule and cis with respect to the O–H. There is another absolute minimum, 1.05 kJ/mol above the previous one, in which again one methyl C–H is in the plane but now trans with respect to the O–H (structure C, Figure

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