Theoret. Chim. Acta (Berl.) 51, 37–54 (1979)

THEORETICA CHIMICA ACTA

A Generalized Wreath Product Method for the Enumeration of Stereo and Position Isomers of Polysubstituted Organic Compounds

K. Balasubramanian*

Birla Institute of Technology and Science, Pilani, Rajasthan 333031, India

A *generalized* wreath product group is developed in the root-to-root product formalism for the enumeration of stereo and position isomers of polysubstituted organic compounds. The methods expounded here are used for enumerating the NMR signals of polysubstituted organic compounds.

Key words: Generalized wreath product – Root-to-root product – Isomer enumeration – NMR signals

1. Introduction

Extensive expositions of the isomer enumeration methods can be found in the review papers of Rouvray [1, 2]. The problem of enumerating isomers essentially reduces to finding what is known as the cycle index of a permutation group [3] and then obtaining a generating function for isomers using a theorem of Polya [3]. Read [4] stated that a method is yet to be developed for the enumeration of stereo-isomers of polysubstituted organic compounds. Read [5] recently enumerated the stereoisomers of certain specific compounds like $C_nH_{2n}XY$, where X and Y are attached to the end carbons. We report here a general method for the enumeration of stereo and position isomers of polysubstituted organic compounds containing any number of functional groups. The group of permutations for the enumeration of isomers at room temperature should contain the point group operations and the permutations induced by any additional internal degrees of freedom. Leonard [6, 7] enumerated the isomers of nonrigid cyclohexane molecules by including the permutations induced by a ring-flip operator in the permutation group of the rigid molecule. Davidson [8] investigated the three-fold rotors in alkanes, two-fold rotors in polyphenyls and certain higher-fold rotors in metal complexes from the standpoint

---

* Present address: Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218, USA.

0040-5744/79/0051/0037/$03.60

of their cycle indices with what is known as the wreath product also referred to as the Kranz group. The Kranz group or wreath product is a special case of the generalized wreath product that we develop here. Robinson *et al.* [9] enumerated the chiral, achiral and the monosubstituted alkanes. Balaban *et al.* [10] obtained the cycle index of *H*-labelled adamantanes using Polya's result [3] for the cycle index of the wreath product group.

In Sect. 2 we formulate a method for the enumeration of isomers of polysubstituted organic compounds. In Sect. 3 the generalized wreath product method in the molecular stereo product or root-to-root product formalism is used for enumerating the NMR signals of polysubstituted organic compounds. In the ensuing sections we assume an acquaintanceship with the elementary concepts related to Polya's theorem [3]. However, we give sufficient definitions to make this a self-contained paper. The paper is fortified with a number of examples with the object of smoothening one's encounter with the generalized wreath product.

2. Isomers of Polysubstituted Organic Compounds

2.1. Mathematical Formulation

Every molecule can be assigned a graph, the vertices of the graph representing the atoms, and the edges representing the bonds. The vertices that correspond to the five carbon atoms of the graph shown in Fig. 1, are distinguishable from the other vertices in the sense that these vertices are chemically specified. In this example they are specified as carbon atoms. The other vertices of degree 1 (valency 1) are unspecified. Such distinguishable vertices of a graph are called the *roots*. Thus, the vertices corresponding to the five carbon atoms are the roots of the chemical graph. Usually a graph does not imply any spatial symmetry; it depicts how the various atoms in the molecule are connected. Here we extend this concept to encompass the spatial symmetry. The *molecular stereograph* is defined as the graph that corresponds to the given molecule and which also includes all the chemical information as regards to the spatial symmetry of the molecule. Then, enumerating stereoisomers will correspond to the non-equivalent ways of mapping the unspecified vertices of the molecular stereograph into a certain set of atoms or functional groups under a group action.

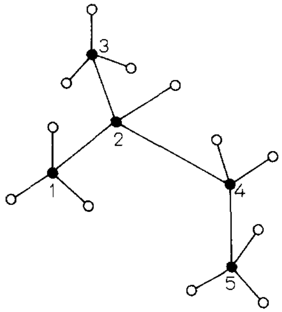


Fig. 1. A molecular stereograph. The vertices that bear the numbers 1, 2, 3, 4, and 5 are the roots. The other vertices are chemically unspecified

Let Γ be the molecular stereograph of the given molecule M. Let the induced subgraph of the roots of Γ be Q. All the vertices of the same degree in Q will be grouped in the same set. Thus, the vertices of Q can be partitioned into mutually exclusive sets. For example, the roots of the molecular stereograph shown in Fig. 1, can be partitioned into the sets $Y_1 = \{1, 3, 5\}$, $Y_2 = \{4\}$ and $Y_3 = \{2\}$. Every vertex in Q is assigned an unlabelled diagram which we shall call a *type*. We can assign to each primary carbon in the stereograph Q, a type consisting of three chemically unspecified vertices and a specified root; with a secondary carbon atom a type consisting of two unspecified vertices and a root can be associated; to a tertiary carbon a type with a single vertex and a root can be assigned. Let the type assigned to the elements of the set Y_i be T_i. For the molecular stereograph shown in Fig. 1, Q, T_1, T_2 and T_3 are shown in Fig. 2.

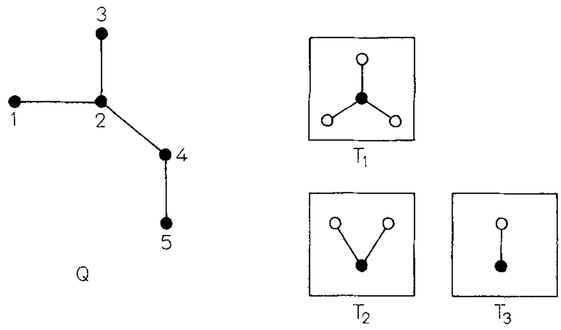


Fig. 2. The Quotient graph Q and the various types of the molecular stereograph shown in Fig. 1

Even though types are *unlabelled diagrams*, in order to realize the transformations of group operations let us label the vertices of a type in a particular standard way. In the latter portion of the paper, we will give a precise definition of a type. Now, any molecular stereograph Γ can be constructed by *attaching* each of the elements of Y_i and the root of a copy of the type T_i. Symbolically,

$$\Gamma = Q(y_{ir} \rightarrow T_{ir})$$

where the symbol $y_{ir} \rightarrow T_{ir}$ denotes the root-to-root isomorphism between an element $y_{ir} \in Y_i$ and the root of a copy of the tape T_i. The product thus formulated between the roots of Γ and the types can be called a *molecular stereo-product* or *root-to-root product*.

To enumerate the stereo-position isomers at room temperature, we look at the group G of all *proper rotations* of the point group corresponding to the stereograph Q. At room temperature the carbon–carbon internal rotations are present. Such internal rotations permute the chemically unspecified vertices of the primary carbon atom. However, they do *not* permute the chemically unspecified vertices of the secondary and tertiary carbon atoms. Consequently, while constructing the molecular stereo-product, we need not attach an identical copy of the type T_1 to the elements of the set Y_1; rather we may attach an *isomorphic copy* (a copy of T_1, that is a permutation of the chemically unspecified vertices of T_1 induced by certain isomorphisms) to the elements of Y_1 in Q. Such isomorphic copies of a type that will be used in the construction of the molecular stereo-product will be called the *representatives* of the corresponding type. Let us observe that in the preceding example, however, we have to attach *identical copies* of T_2 and T_3 to the elements of Y_2 and Y_3 respectively. Hence, we envisage, in general, a group H_i acting on the type T_i. Indeed, the objects that isomorphisms generate as a result of their action on T_i are the various representatives that we use in the construction of the molecular stereo-product. For example, in the process of enumerating the stereo-position isomers, the group H_1 acting on T_1 is $\boldsymbol{C}_3$, consisting of three elements. The group H_2, acting on T_2 is $\boldsymbol{E}_2$. (Hereafter, let $\boldsymbol{E}_n$ stand for the identity group acting on n elements.) The group H_3 acting on T_3 is $\boldsymbol{E}_1$. To enumerate the position isomers one considers the *graph* Γ (instead of the molecular stereograph) of the molecule. The group G acting on the quotient graph Q of the root-to-root product, is the *automorphism group* of the graph Q which is defined as the set of those permutations of the vertices of the graph Q that preserve the adjacency. Alternatively, the automorphism group of the graph Q consists of those permutations of the vertices of Q, whose permutation matrices $\boldsymbol{P}$'s satisfy the following property:

$$\boldsymbol{P}\boldsymbol{A}\boldsymbol{P}^{-1}=\boldsymbol{A}$$

where $\boldsymbol{A}$ is the adjacency matrix of the graph Q. For example, the automorphism group of the graph Q, shown in Fig. 2, is $\boldsymbol{S}_2(5)$ which denotes the symmetric group consisting of 2! permutations acting on 5 elements. (In general, let $\boldsymbol{S}_n(m)$ denote the symmetric group consisting of $n!$ elements, acting on m elements.) The permutations are (1)(2)(3)(4)(5) and (13)(2)(4)(5). It is interesting that Quintas and Yarmish [11, 12] used the carbon automorphism group to enumerate the chiral alkanes. Now, since in the position isomer formulation stereo-isomers are equivalent, we allow all the possible permutations of the chemically unspecified vertices attached to the same carbon atom. This can be expressed as groups $H_1 = \boldsymbol{S}_3(3)$, $H_2 = \boldsymbol{S}_2(2)$ and $H_3 = \boldsymbol{E}_1$. Subsequently, we transfer the group actions G on Q, H_1 on T_1, etc., into a single group H acting on Γ. The group of all such permutations acting on Γ that includes all the "internal permutations" can be obtained by composing the group G with the groups $H_1, H_2 \ldots$ in a generalized manner. A special case of such a composition, namely, the composition of a group G with a group H_1 is the well-known Kranz group or wreath product. Therefore, it is appropriate to call the generalized composition of the group G with several groups $H_1, H_2 \ldots$ the *generalized wreath product*. It may be denoted as

$$H = G[H_1, H_2, H_3 \ldots].$$

In the next section we obtain a theorem for the cycle index of H. Before we do that, let us investigate the nature of H. We start with certain notations and terminologies. Let X_{ir} be a representative that is isomorphic to T_i and which will also be attached to the element $y_{ir} \in Y_i \cdot (r = 1, 2, \ldots |Y_i|)$. Thus, another convenient way of looking at the set Y_i is a set Y_i' of all representatives that are in one-to-one correspondence with the elements of the set Y_i. Let us observe that $|Y_i| = |Y_i'|$. Now, the root-to-root isomorphism defined between an element y_{ir} in Y_i and T_{ir} can be transferred to various representatives. Thus, we conceive of an isomorphism P_{ir} between an X_{ir} and T_i. In symbols,

$$P_{ir}: X_{ir} \rightarrow T_i.$$

It can be seen that the isomorphism thus defined is an equivalence relation. The *isomorphism equivalence class* is referred to as a type. This is the definition of a type that we promised to give.

Lemma 1: For any element h in H if $hX_{ir} = X_{jr'}$ then $i = j$.

Proof: This is a consequence of the fact that either G is the point group of the stereograph Q or G is the automorphism group of the graph Q. In the former case, the elements of G being symmetry operations, they do not permute the vertices of different degrees into each other. In the latter case, the automorphism group, by definition, preserves the adjacency; consequently, the elements of G, and therefore those of H do not permute the elements of different degrees in Q.

Lemma 2: Every element h in H induces a permutation on Q.

Proof: H consists of the generalized composition of all the permutations of Q and those of various types. As a result, in particular, every element in H induces a permutation on the elements of Q.

To every representative X_{ir} let a group G_i be assigned akin to the group associated with every type. Then, it follows that $G_i \simeq H_i$. This is a direct consequence of the isomorphism between X_{ir} and T_i.

Lemma 3: Let $g \in G$, $g_{ir} \in G_i$ and let $m_i = |Y_i|$. Then, there exists a 1-1 correspondence between an element $h \in H$ and an ordered $(t+1)$-tuple s of the form (where t is the number of types)

$$s = (g; g_{11}, g_{12}, \ldots, g_{1m_1}; g_{21}, g_{22} \ldots g_{2m_2}; \ldots ; g_{t1}, g_{t2} \ldots g_{tm_t}).$$

Proof: The lemma will be proved by constructing an s given an h and vice versa. A given $h \in H$ induces a $g \in G$ by Lemma 2. Hence the first component of s is determined. We define g_{ir} for each i and $r = 1, 2, \ldots m_i$ as

$$g_{ir} = p_{ir'} \cdot (h\,|_{X_{ir}}) \cdot p_{ir}^{-1}$$

where $h\,|_{X_{ir}}$ denotes h restricted to X_{ir}. By lemma 1 $hX_{ir} = X_{ir'}$. This construction of g_{ir} can be pictorially depicted as follows:

$$\begin{tikzcd} X_{ir} \arrow[rr, "h"] \arrow[dr, "p_{ir}"'] & & X_{ir'} = hX_{ir} \arrow[dl, "p_{ir'}"] \\ & T_i \arrow[loop above, "g_{ir}"] & \end{tikzcd}$$

Therefore, every $(t+1)$-tuple, s of the form $(g; g_{11}, g_{12} \ldots g_{1m_1}; \ldots; g_{t1}, g_{t2} \ldots g_{tm_t})$ is determined. Conversely, given an s we can construct an h by finding that y_{ir}, which is gy_{ir} and defining.

$$h|_{X_{ir}} = (P_{ir'}^{-1})\cdot(g_{ir})\cdot(P_{ir}).$$

Thus the correspondence is one-to-one.

Example. Let us illustrate the preceding construction by the nonrigid ethane molecule, shown in Fig. 3.

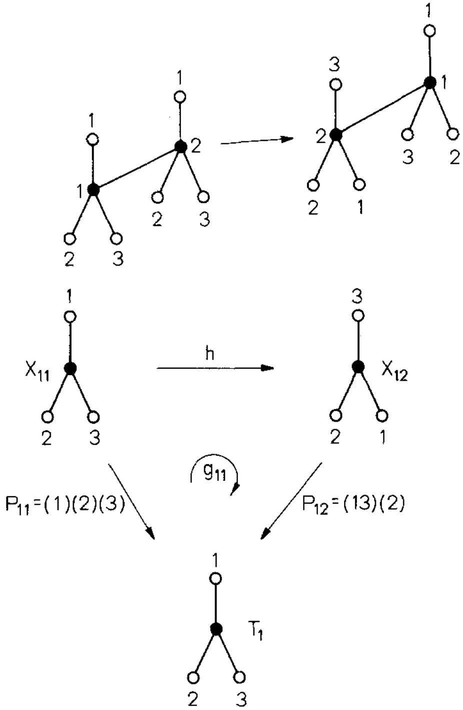


Fig. 3. The nonrigid ethane molecule. Construction of an element of the corresponding wreath product

It can be seen from Fig. 3 that $h|_{X_{11}}=(13)(2)$ and $h|_{X_{12}}=(1)(23)$. Therefore

$$g_{11}=P_{12}h\,|X_{11}\;P_{11}^{-1}=(1)(2)(3)=e'\in C_3.$$

Similarly,

$$g_{12}=P_{11}h\,|_{X_{12}}\;P_{12}^{-1}=(123)=c_3\in C_3.$$

Hence, s is determined as $(c_2; e', c_3)$. Conversely, given this s, it can be shown that $h|_{X_{11}}$ and $h|_{X_{12}}$ are the same as the ones that we started with.

2.2. *The Cycle Index of the Generalized Wreath Product*

The cycle index of a permutation group G is defined [3] as:

$$P_G(S_1, S_2 \ldots) = \frac{1}{|G|} \sum_{g\in G} S_1^{b_1} S_2^{b_2} \ldots$$

where $S_1^{b_1} S_2^{b_2} \ldots$ is a representation of the cycle structure of a typical permutation $g \in G$ having b_1 cycles of length 1, b_2 cycles of length 2 and so on. The S-variables are just dummy symbols. It is possible to express the cycle index of the generalized wreath product in terms of the cycle indices of the composing groups. Harary [13] obtained this using the Robinson–Harary generalized composition theorem [14]. However, following the Wright's procedure [15] which seems to be more fundamental, theorem 1 that we state below can be proved. Nevertheless, modifications have to be made in Wright's procedure since for our purpose the theorem has to be proved in the root-to-root product, whereas Wright proves it in the lexicographic product.

Define a polynomial Z_Q with the dummy variables S_{ij}'s as follows.

$$Z_Q=\frac{1}{|G|}\sum_{g\in G}\prod_{i}\prod_{j} S_{ij}^{c_{ij}(g)}$$

where $c_{ij}(g)$ denotes the number of j-cycles of g in the set Y_i. Z_Q can be called the *cycle index* of the (stereo) *graph* Q. Let $Z_i(S_1, S_2, \ldots)$ denote the cycle index of the group H_i. Define Z_{ij} as:

$$Z_{ij}=Z_i(S_k\to S_{kj})$$

where the symbol $S_k\to S_{kj}$ stands for the operation of replacing every cycle of length k by a cycle of length kj. (kj denotes the product.)

Theorem 1 [16]: The cycle index of H, the group for isomer enumeration, is

$$Z_H=Z_Q(S_{ij}\to Z_{ij}).$$

Z_H is obtained by *replacing* every S_{ij} in Z_Q by the cycle index Z_{ij}. For a proof in the molecular stereo product or root-to-root product see [16].

Example: We now illustrate the theorem by constructing the cycle index of the group for the stereo-position isomers and the position isomers of the molecule shown in Fig. 1. The point group which corresponds to Q is E_5 and $H_1=\boldsymbol{C}_3$, $H_2=\boldsymbol{E}_2$ and $H_3=\boldsymbol{E}_1$. By the definition of Z_Q,

$$Z_Q=S_{11}^3S_{21}S_{31}.$$

The various Z_{ij}'s are given as follows:

$$Z_{11}=\tfrac{1}{3}(S_1^3+2S_3);\qquad Z_{21}=S_1^2;\qquad Z_{31}=S_1.$$

Hence, by theorem 1, the cycle index of the group for isomer enumeration is:

$$Z_H=Z_Q(S_{ij}\to Z_{ij})=S_1^3\cdot\{\tfrac{1}{3}(S_1^3+2S_3)\}^3. \tag{1}$$

To enumerate the position isomers we let G be the automorphism group of Q, and as shown earlier it is $\boldsymbol{S}_2(5)$. Thus,

$$Z_Q=\tfrac{1}{2}(S_{11}^3S_{21}S_{31}+S_{11}S_{12}S_{21}S_{31}). \tag{2}$$

The groups H_1, H_2 and H_3 are $\boldsymbol{S}_3(3)$, $\boldsymbol{S}_2(2)$ and $\boldsymbol{E}_1$ respectively. As a result, it can be seen that

$$Z_{11}=\tfrac{1}{6}(S_1^3+2S_3+3S_1S_2);\qquad Z_{21}=\tfrac{1}{2}(S_1^2+S_2);$$
$$Z_{31}=S_1;\qquad Z_{12}=\tfrac{1}{6}(S_2^3+2S_6+3S_2S_4).$$

By theorem 1,

$$Z_H=\tfrac{1}{2}[\{\tfrac{1}{6}(S_1^3+2S_3+3S_1S_2)\}^3\{\tfrac{1}{2}(S_1^2+S_2)\}S_1$$
$$+\{\tfrac{1}{6}(S_2^3+2S_6+3S_2S_4)\}\{\tfrac{1}{6}(S_1^3+2S_3+3S_1S_2)\}\{\tfrac{1}{2}(S_1^2+S_2)\}S_1] \qquad (3)$$

Example: As a second example exemplifying the significance of theorem 1 and the flexibility of the generalized wreath product consider the molecule shown in Fig. 4. Suppose that one wishes to obtain the stereoisomers of the corresponding polysubstituted compounds, but with the restriction that the chemically unspecified vertices of the "ethyl-tail" are not to be projected in space. Then all that one has to do is to construct the cycle index of the generalized wreath product of the group $G = C_3$ with the groups $H_1 = C_3$, $H_2 = S_3(3)$ and $H_3 = S_2(2)$ in the appropriate root-to-root product. Z_Q for this problem is given by Eq. (4).

$$Z_Q=\tfrac{1}{3}(S_{11}^3S_{21}S_{31}+2S_{13}S_{21}S_{31}) \qquad (4)$$

By theorem 1

$$Z_H=\tfrac{1}{972}[(S_1^3+2S_3)^3(S_1^2+S_2)(S_1^3+3S_1S_2+2S_3)$$
$$+18(S_3^3+2S_9)(S_1^2+S_2)(S_1^3+3S_1S_2+2S_3)] \qquad (5)$$

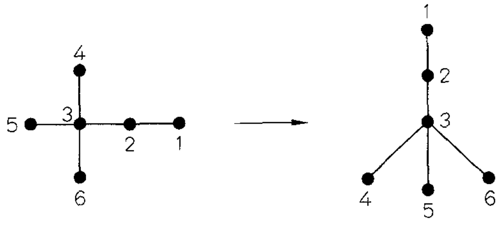


Fig. 4. A chemical graph on six vertices and its stereoprojection

2.3. Enumeration of Isomers

Let D be the set of chemically unspecified vertices of the (stereo) graph Γ. Let R be a set of l atoms or functional groups. Each element $\gamma_j \in R$ is assigned a weight α_j. The weights can be formal symbols but they must come from a commutative ring in order that the mathematical manipulation with the weights makes sense. Let $\mathscr{F}$ be the set of all maps from D to R. Two elements $f_1, f_2 \in \mathscr{F}$ are said to be *equivalent* if there exists a $\pi \in G[H_1, H_2 \ldots]$ such that

$$f_1(d)=f_2(\pi d)$$

for every $d \in D$. Clearly, the relation thus defined on the set of functions is an equivalence relation. Thus, the generalized wreath product divides the set $\mathscr{F}$ into equivalence classes. Let us define the weight of a function as the product of the weights of the corresponding images. Let the weight α_j be assigned to the functional group t_j; then the map corresponding to a molecule of the formula $C_n(t_1)_{b_1}(t_2)_{b_2} \ldots (t_l)_{b_l}$ will have the weight

$$w=\alpha_1^{b_1}\alpha_2^{b_2} \ldots \alpha_l^{b_l}.$$

Let $\mathscr{F}_w$ denote the subset of $\mathscr{F}$ containing all those maps with the same weight w.

Polya [3] called each equivalence class a *pattern*. Each pattern is in fact an isomer. The weight of a pattern is defined as the weight of any element in the pattern. The sum of the weights of the patterns is called the *pattern inventory*.

Theorem 2 [Polya]: The pattern inventory is given by

$$Z_H\left(S_k \rightarrow \sum_{i=1}^{l} \alpha_i^k\right).$$

Therefore, the coefficient of $\alpha_1^{b_1}\alpha_2^{b_2} \ldots \alpha_l^{b_l}$ in the pattern inventory gives the number of isomers of the molecule $C_n(t_1)_{b_1}(t_2)_{b_2} \ldots (t_1)_{b_l}$. Since in this paper, patterns and isomers are equivalent, we use the terminologies pattern inventory and *isomer inventory* equivalently. Let us denote the pattern inventory by $P(\alpha_1, \alpha_2 \ldots, \alpha_l)$ if α's are the weights of the elements of the set R. Let $N(\alpha_1^{b_1}\alpha_2^{b_2} \ldots \alpha_l^{b_l})$ stand for the coefficient of $\alpha_1^{b_1}\alpha_2^{b_2} \ldots \alpha_l^{b_l}$ in the pattern inventory. In many situations the pattern inventory changes depending upon the parity of certain variables. If u is the variable whose parity changes the pattern inventory, we indicate this by

$$P_{u^-}(\alpha_1, \alpha_2 \ldots) \quad \text{or} \quad P_{u^+}(\alpha_1, \alpha_2 \ldots)$$

where the negative sign is used if the parity is odd and the positive sign is used if the parity is even.

2.4. *Isomers of Linear Polysubstituted Alkanes*

In this section we outline a general method of the enumeration of stereo, optical and position isomers of polysubstituted linear alkanes. In 2.4.1 we enumerate the stereo-position isomers and enantiomers. In 2.4.2 the position isomers are enumerated.

2.4.1. Stereo-Position Isomers and Enantiomers

Let n be the number of carbon atoms. We assume here that the internal rotations are present. When n is odd the C_2 axis passes through the central carbon atom. The chemically unspecified vertices attached to this carbon transform into each other under the permutations induced by the C_2 axis. Accordingly, the central carbon should be treated as a special case. The cycle index of the corresponding generalized wreath product is therefore the same for both the parities of n. The cycle index is given by (6).

$$Z_H = \tfrac{1}{18}(S_1^{2n+2} + 4S_1^{2n-1}S_3 + 4S_1^{2n-4}S_3^2 + 3S_2^{n+1} + 6S_2^{n-2}S_6) \tag{6}$$

By theorem 2, the pattern inventory is given by (7).

$$\begin{aligned} P(\alpha_1, \alpha_2, \ldots, \alpha_l) = \tfrac{1}{18}\Bigg\{&\left(\sum_{i=1}^{l} \alpha_i\right)^{2n+2} + 4\left(\sum_{i=1}^{l} \alpha_i\right)^{2n-1}\left(\sum_{i=1}^{l} \alpha_i^3\right) \\ &+ 4\left(\sum_{i=1}^{l} \alpha_i\right)^{2n-4}\left(\sum_{i=1}^{l} \alpha_i^3\right)^2 + 3\left(\sum_{i=1}^{l} \alpha_i^2\right)^{n+1} \\ &+ 6\left(\sum_{i=1}^{l} \alpha_i^2\right)^{n-2}\left(\sum_{i=1}^{l} \alpha_i^6\right)\Bigg\} \end{aligned} \tag{7}$$

Example: Isomers of $C_3H_6X_2$.

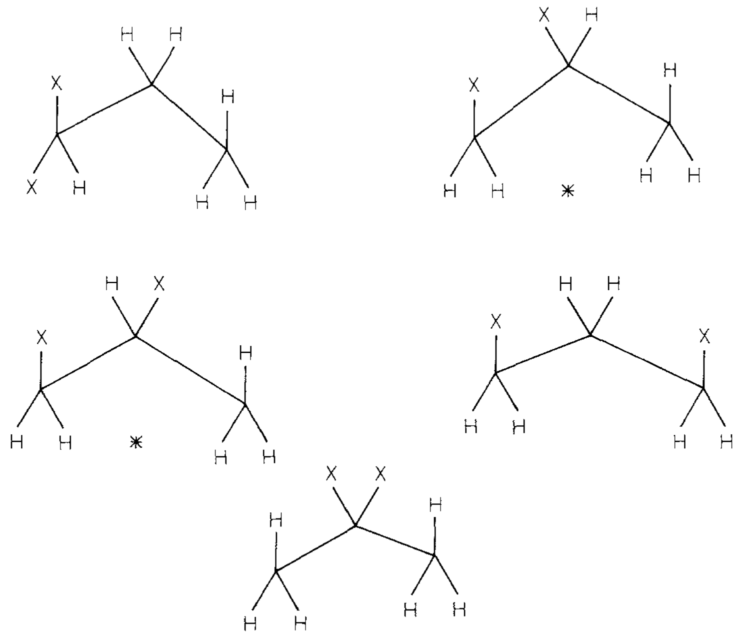


Fig. 5. The five isomers of $C_3H_6X_2$. The optically active isomers carry asterisks

The number of isomers of $C_3H_6X_2$ can be obtained by putting $n=3$ in (7) and collecting the coefficient of $\alpha_1^6\alpha_2^2$, which is

$$\frac{1}{18}\left\{\binom{8}{2}+4\binom{5}{2}+4\binom{2}{2}+3\binom{4}{1}+6\binom{1}{1}\right\}=5.$$

The five isomers are shown in Fig. 5.

In particular, when the set R has two elements, namely the hydrogen atom and a functional group X, and further if the weight of the hydrogen atom is 1 and that of X is α, (7) simplifies to (8).

$$\begin{aligned}P(1,\alpha)=\tfrac{1}{18}\{&(1+\alpha)^{2n+2}+4(1+\alpha)^{2n-1}(1+\alpha^3)+4(1+\alpha)^{2n-4}(1+\alpha^3)^2\\&+3(1+\alpha^2)^{n+1}+6(1+\alpha^2)^{n-2}(1+\alpha^6)\}\end{aligned}\tag{8}$$

The coefficient of α^k in (8), representing the number of isomers of $C_nH_{2n+2-k}X_k$ is given by (9) if k is odd and by (10) if k is even.

$$\begin{aligned}N_{k^-}(\alpha^k)=\frac{1}{18}\Bigg[&\binom{2n+2}{k}+4\binom{2n-1}{k}+4\binom{2n-1}{k-3}\\&+4\binom{2n-4}{k}+8\binom{2n-4}{k-3}+4\binom{2n-4}{k-6}\Bigg]\end{aligned}\tag{9}$$

$$N_{k^+}(\alpha^k)=\frac{1}{18}\left[18N_{k^-}(\alpha^k)+3\binom{n+1}{k/2}+6\binom{n-2}{k/2}+6\binom{n-2}{(k-6)/2}\right]\tag{10}$$

where $N_{k^-}(\alpha^k)$ in (10) is given by (9).

To enumerate the optical isomers, one includes a plane of symmetry in the generalized wreath product and subtracts the isomer inventory obtained with the plane from the isomer inventory obtained without the plane. The coefficient of $\alpha_1^{b_1}\alpha_2^{b_2}\dots\alpha_l^{b_l}$ gives the number of *dl*-pairs. When one includes a plane of symmetry, the cycle index of the resulting generalized wreath product is given by (11) if n is odd and by (12) if n is even.

$$Z_{n^-} = \tfrac{1}{36}(18Z_H + 12S_1^2S_2^n + 6S_1^2S_2^{n-3}S_6) \tag{11}$$

$$Z_{n^+} = \tfrac{1}{36}(18Z_H + 3S_2^{n+1} + 6S_6S_2^{n-2} + 9S_1^2S_2^n) \tag{12}$$

where Z_H is given by Eq. (6). Let $E(\alpha_1, \alpha_2 \dots \alpha_l)$ stand for the generating function for enantiomer pairs. Then enantiomer inventories are given by (13) and (14) for odd and even parities of n respectively.

$$E_{n^-}(\alpha_1, \alpha_2 \dots, \alpha_l) = \frac{1}{36}\left[18P(\alpha_1, \alpha_2 \dots, \alpha_l) - 12\left(\sum_i \alpha_i\right)^2\left(\sum_i \alpha_i^2\right)^n - 6\left(\sum_i \alpha_i\right)^2\left(\sum_i \alpha_i^2\right)^{n-3}\left(\sum_i \alpha_i^6\right)\right] \tag{13}$$

$$E_{n^+}(\alpha_1, \alpha_2 \dots \alpha_l) = \frac{1}{36}\left[18P(\alpha_1, \alpha_2, \dots \alpha_l) - 3\left(\sum_i \alpha_i^2\right)^{n+1} - 9\left(\sum_i \alpha_i\right)^2\left(\sum_i \alpha_i^2\right)^n - 6\left(\sum_i \alpha_i^2\right)^{n-2}\left(\sum_i \alpha_i^6\right)\right] \tag{14}$$

where $P(\alpha_1, \alpha_2 \dots \alpha_l)$ is given by Eq. (7).

Example: Enantiomer-pairs of $C_3H_6X_2$.

Let $n = 3$ in (13) and collect the coefficient of $\alpha_1^6\alpha_2^2$. This is

$$\frac{1}{36}\left[90 - 12 - 12\binom{3}{2\ \ 1} - 6\right] = 1.$$

This *dl*-pair is shown in Fig. 5 with asterisks. In the special case when the set R has two elements, namely, the hydrogen atom and a group X, the coefficient of α^k in (13) or (14) is shown below. There are four cases depending upon the parities of both n and k. They are indicated by appropriate suffixes.

$$N_{n^-k^-}(\alpha^k) = \frac{1}{36}\left[18N_{k^-}(\alpha^k) - 24\binom{n}{(k-1)/2} - 12\binom{n-3}{(k-1)/2} - 12\binom{n-3}{(k-7)/2}\right] \tag{15}$$

$$N_{n^-k^+}(\alpha^k) = \frac{1}{36}\left[18N_{k^+}(\alpha^k) - 12\binom{n}{(k-2)/2} - 12\binom{n}{k/2} - 6\binom{n-3}{k/2} - 6\binom{n-3}{(k-2)/2} - 6\binom{n-3}{(k-6)/2} - 6\binom{n-3}{(k-8)/2}\right] \tag{16}$$

$$N_{n+k^-}(\alpha^k)=\frac{1}{36}\left[18N_{k^-}(\alpha^k)-18\binom{n}{(k-1)/2}\right] \tag{17}$$

$$\begin{aligned}N_{n+k^+}(\alpha^k)=\frac{1}{36}\Bigg[&18N_{k^+}(\alpha^k)-9\binom{n}{k/2}-9\binom{n}{(k-2)/2}\\&-3\binom{n+1}{k/2}-6\binom{n-2}{k/2}-6\binom{n-2}{(k-6)/2}\Bigg]\end{aligned} \tag{18}$$

where $N_{k^-}(\alpha^k)$ and $N_{k^+}(\alpha^k)$ are given by (9) and (10) respectively.

2.4.2. Position Isomers

To enumerate the position isomers let $H_1=\boldsymbol{S}_3(3)$, $H_2=\boldsymbol{S}_2(2)$ and $H_3=\boldsymbol{E}_1$. The automorphism group for a linear n-carbon chain is $\boldsymbol{S}_2(\mathrm{n})$.

Let Z_c be

$$\begin{aligned}Z_c=\sum_{m=0}^{n-2}\binom{n-2}{m}\{&S_1^{2m+6}S_2^{n-2-m}+4S_1^{2m}S_2^{n-2-m}S_3^2+9S_1^{2m+2}S_2^{n-m}\\&+4S_1^{2m+3}S_2^{n-2-m}S_3+12S_1^{2m+1}S_2^{n-1-m}S_3+6S_1^{2m+4}S_2^{n-1-m}\}.\end{aligned} \tag{19}$$

Then the cycle index for position isomers is given by (20) if n is even and by (21) if n is odd.

$$\begin{aligned}Z_{n^+}=\frac{1}{72\cdot 2^{n-2}}\Bigg[&Z_c+6\cdot 2^{(n-2)/2}\cdot\sum_{p=0}^{(n-2)/2}\binom{(n-2)/2}{p}\\&\times\{S_2^{2p+3}S_4^{((n-2)/2)-p}+2S_2^{2p}S_4^{((n-2)/2)-p}S_6+3S_2^{(2p+1)}S_4^{((n-2)/2)-p+1}\}\Bigg]\end{aligned} \tag{20}$$

$$\begin{aligned}Z_{n^-}=\frac{1}{72\cdot 2^{n-2}}\Bigg[&Z_c+6\cdot 2^{(n-3)/2}\sum_{p=0}^{(n-3)/2}\binom{(n-3)/2}{p}\\&\times\{S_1^2S_2^{2p+3}S_4^{((n-3)/2)-p}+2S_1^2S_2^{2p}S_4^{((n-3)/2)-p}S_6+S_2^{2p+4}S_4^{((n-3)/2)-p}\\&+3S_1^2S_2^{2p+1}S_4^{((n-3)/2)-p+1}+2S_2^{(2p+1)}S_4^{((n-3)/2)-p}S_6\\&+3S_2^{2p+2}S_4^{((n-3)/2)-p+1}\}\Bigg]\end{aligned} \tag{21}$$

The generating functions for position isomers can be obtained by replacing S_k by $\sum_i \alpha_i^k$ in (20) and (21) depending upon the parity of n.

Example: Position Isomers of C_3H_7Br.

Let $n=3$ and let $S_k\to\sum_i\alpha_i^k$ in (21). The coefficient of $\alpha_1^7\alpha_2$ in the resulting expression is

$$\begin{aligned}\frac{1}{144}\Bigg\{&\binom{8}{7\ \ 1}+4\binom{5}{4\ \ 1}+7\binom{6}{5\ \ 1}+16\binom{3}{2\ \ 1}+15\binom{4}{3\ \ 1}+4\binom{2}{1\ \ 1}\\&+12+15\binom{2}{1\ \ 1}+12\binom{2}{1\ \ 1}+18\binom{2}{1\ \ 1}\Bigg\}=\frac{288}{144}=2.\end{aligned}$$

The result can easily be verified.

2.5. Isomers of Polysubstituted Hydrocarbons

In the section we use Read's result [4] for structural isomers for counting the stereoisomers. For a compound with the formula $C_n(t_1)_{b_1}(t_2)_{b_2} \ldots (t_l)_{b_l}$, the number of double bonds and triple bonds is dependent on the factor $2n+2-\sum_{i=1}^{l} b_i v_i$, where v_i is the valency of the functional group t_i. It can be easily seen that the maximum number of double bonds is $[(2n+2-\sum_i v_i b_i)/2]$ ($[x]$ denotes the greatest integer contained in x). The maximum number of triple bonds will be $[(2n+2-\sum_i v_i b_i)/4]$. The various combinations of double and triple bonds can be obtained by decreasing the number of double bonds from $[(2n+2-\sum_i v_i b_i)/2]$ to 0 or 1 in steps of 2 and simultaneously increasing the number of triple bonds in steps of 1 from 0. Read [4] enumerated the structures with a given combination of double and triple bonds. We obtain the stereo-graph for each structure taking into account the spatial symmetry of the constituting orbitals. For example, a chemical graph and its stereo-projection are shown in Fig. 4. The internal rotations are observed only around carbon–carbon single bonds as a consequence of the high energy barrier to rotation around double bonds. We emphiasize that the structure should be projected in all possible non-equivalent ways. For an enantiomeric graph there can be more than one stereo-projection. The isomers are enumerated analogous to the treatment given in Sect. 2.4.

Example. Isomers of $C_6H_{10}Br_2Cl_2$.

We illustrate the preceding discussion by enumerating the stereo-position isomers of $C_6H_{10}Br_2Cl_2$. It can be seen that

$$2n+2-\sum_i v_i b_i = 0.$$

Thus, we first enumerate the saturated graphs containing six vertices. Each of them is projected in space and the corresponding point group is identified. Fig. 4 shows the graph of the structure 5 in Table 1 and its stereo-projection. To enumerate the stereo-position isomers of the corresponding polysubstituted compounds, we let $G=C_3$, $H_1=C_3$, and $H_2=E_2$. The cycle index of the resulting wreath product is given by (22).

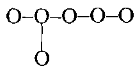
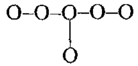
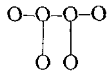
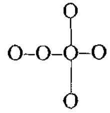
$$\begin{aligned} Z_H = \tfrac{1}{243}(&S_1^{14}+8S_1^{11}S_3+24S_1^{8}S_3^{2}+32S_1^{5}S_3^{3}+16S_3^{4}S_1^{2}\\ &+18S_1^{5}S_3^{3}+36S_1^{2}S_3^{4}+36S_1^{5}S_9+72S_1^{2}S_3S_9) \end{aligned} \tag{22}$$

The coefficient of $\alpha_1^{10}\alpha_2^{2}\alpha_3^{2}$ in the appropriate pattern inventory, which is the number of isomers of $C_6H_{10}Br_2Cl_2$, can be seen to be 142. If we let $G=C_{3v}$ the coefficient of $\alpha_1^{10}\alpha_2^{2}\alpha_3^{2}$ becomes 110. Thus the number of enantiomer pairs is

$$142-110=32.$$

The results for the isomers of $C_6H_{10}Br_2Cl_2$ and $C_6H_{13}Br$ as obtained from the same pattern inventory are given in Table 1. The results on the isomers of $C_6H_{13}Br$ can be easily verified.

Table 1. Isomers of $C_6H_{10}Br_2Cl_2$ and $C_6H_{13}Br$

Compound				$C_6H_{10}Br_2Cl_2$		$C_6H_{13}Br$	
		Point Group					
S. No.	Type	stereo-position	*dl*-pairs	No. of stereo-position isomers	No. of *dl*-pairs	No. of stereo-position isomers	No. of *dl*-pairs
1.	O-O-O-O-O-O	C_2	C_{2v}	882	424	5	2
2.		E	σ	858	418	8	3
3.		E	σ	858	418	8	3
4.		C_2	C_{2h}	208	99	3	1
5.		C_3	C_{3v}	142	32	4	1

3. Application to NMR spectroscopy

We devote this section to the application of the generalized wreath product method to NMR spectroscopy.

3.1. Mathematical Formulation of the Problem

We give a method here for partitioning the protons (or in general any nuclei) into equivalence classes induced by the generalized wreath product. Consider the molecule $CH_3 \cdot CHCl \cdot CH_2Cl$ whose stereo-projection is shown in Fig. 6. All the *vertices other than* the *protons* are considered to be *specified* chemically, while proton resonance is under consideration. Thus the vertices that correspond to the carbon and chlorine atoms are specified in the molecule $CH_3 \cdot CHCl \cdot CH_2Cl$.

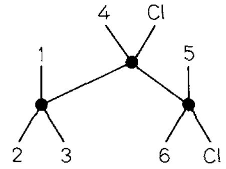


Fig. 6. The molecular stereograph of $CH_3 \cdot CHCl \cdot CH_2Cl$. The vertices which correspond to the protons are treated as unspecified and they carry the labels 1, 2, 3, 4, 5 and 6

The molecular stereograph of the given molecule is expressed as the root-to-root product, the carbon atoms being the roots. Thus, for the molecule $CH_3 \cdot CHCl \cdot CH_2Cl$, the quotient stereograph Q and the various types are shown in Fig. 7. Let G be the point group of the stereograph Q. Let the permutations induced by the carbon–carbon internal rotations be expressed as the groups $H_1, H_2 \ldots$

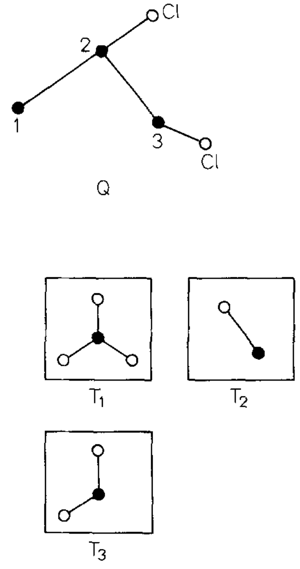


Fig. 7. The Quotient graph Q and the various types of the molecular stereo-product of $CH_3 \cdot CHCl \cdot CH_2Cl$

acting on the types $T_1, T_2 \ldots$ respectively. Note that all *improper rotations* are also *included* in $G[H_1, H_2 \ldots]$ since *enantiotopic protons cannot be distinguished* in NMR spectra. Let D be the set of chemically unspecified vertices of the root-to-root product. Let R be a set consisting of two elements, namely the proton and a group Z. Let us define a map f_i from the set D to R as follows:

$$f_i(d_k) = \begin{cases} \mathrm{Z} \text{ if } k = i \\ \mathrm{H} \text{ if } k \neq i \end{cases}$$

where $d_k \in D$. Let the weights α_1 and α_2 be assigned to the proton and the group Z respectively. Then the weight of the map, as defined above, is

$$w = \alpha_1^{m-1}\alpha_2$$

where $m = |D|$. Let $\mathscr{F}_w$ denote the set of all such maps from D to R. Note that

$$|\mathscr{F}_w| = |D| = m.$$

In the above set-up two protons H_i and H_j (where the labels i and j refer to the labels of the corresponding chemically unspecified vertices of the root-to-root product) are magnetically equivalent if there exists a $\pi \in \mathrm{G}[\mathrm{H}_1, \mathrm{H}_2 \ldots]$ such that

$$f_i(d_k) = f_j(\pi d_k)$$

for every d_k in D.

The relation thus defined on $\mathscr{F}_w$ is clearly an equivalence relation. Therefore, $G[H_1, H_2 \ldots]$ divides $\mathscr{F}_w$ into equivalence classes.

Theorem 3: The wreath product equivalence classes of $\mathscr{F}_w$ are the partitions of the magnetically non-equivalent protons. Thus, the number of classes into which the protons are partitioned is the cardinality of the wreath product equivalence classes of $\mathscr{F}_w$.

Proof: Given two functions f_i and f_j we can determine the protons H_i and H_j. This is a consequence of the fact that f_i takes all d_k's in D to H excepting the vertex d_i. This indeed corresponds to H_i of the given molecule. Thus H_i is determined. Conversely, given an H_i and an H_j we can find those functions in $\mathscr{F}_w$ that take d_i and d_j to Z. Thus, the correspondence is one-to-one. Further, by the very definition of the equivalence relation on the set of functions, if the functions are equivalent then the protons are also magnetically equivalent. Hence, the result follows.

In this sense the six protons of the molecule $\mathrm{CH_3 \cdot CHCl \cdot CH_2Cl}$ (see Fig. 6) are partitioned into the following wreath product equivalent classes.

$$\{1, 2, 3\}, \{4\}, \{5\}, \{6\}.$$

Theorem 4: The number of classes into which the protons are partitioned is given by the coefficient of $\alpha_1^{m-1}\alpha_2$ in the pattern inventory.

Theorem 4 is a direct consequence of Polya's theorem, since the coefficient of $\alpha_1^{m-1}\alpha_2$ in the pattern inventory gives the number of patterns with the weight $\alpha_1^{m-1}\alpha_2$.

Example. Consider the molecule $CH_3 \cdot CHCl \cdot CH_2Cl$.

It can be seen that $G = \boldsymbol{E}_5$, $H_1 = \boldsymbol{C}_3$, $H_2 = \boldsymbol{E}_1$ and $H_3 = \boldsymbol{E}_2$. Hence the cycle index is given by Eq. (23)

$$Z_{G[H_1, H_2, H_3]} = \tfrac{1}{3}(S_1^6 + 2S_1^3 S_3) \tag{23}$$

The inventory of NMR signals or NMR inventory is given by (24).

$$P(\alpha_1, \alpha_2) = \tfrac{1}{3}[(\alpha_1 + \alpha_2)^6 + 2(\alpha_1 + \alpha_2)^3(\alpha_1^3 + \alpha_2^3)] \tag{24}$$

The coefficient of $\alpha_1^5 \alpha_2$ in (24) is

$$\frac{1}{3}\left[\binom{6}{5\quad 1} + 2\binom{3}{2\quad 1}\right] = 4.$$

The fact that the NMR spectrum of the molecule $CH_3 \cdot CHCl \cdot CH_2Cl$ contains four signals is well known to chemists but here we have an elegant and general approach to any compound. This method has the additional advantage that it has eliminated the enantiotopic protons and identified them as equivalent. However, the *diastereotopic protons* are considered *non-equivalent* which corresponds to reality too!

4. Conclusion

In this paper I gave a rigorous mathematical approach for enumerating stereo isomers, and subsequently, for enumerating NMR signals. Even though the generalized wreath product group was developed in this paper in the context of isomer enumeration, it is interesting to note that it is a generalization of the results of Longuet-Higgins [17] and Woodman [18] for the groups of non-rigid molecules. The author [19] recently applied the generalized wreath product method further to the enumeration of stable stereo and position isomers of polysubstituted alcohols by incorporating the principle of inclusion and exclusion. A collection of a few open problems in isomer enumeration can be found in [20]. The representation theory of generalized wreath product groups was recently developed by the author. The manuscript is being submitted for publication. Further applications of the methods developed here to the enumeration of internal rotation reactions and spontaneous generation of optical activity can be found in [21].

Acknowledgements. The author is indebted to Prof. Dr. V. Krishnamurthy for his invaluable guidance. A course entitled combinatorial mathematics taught by Prof. V. Krishnamurthy motivated the author to carry out this investigation. The author is also indebted to Dr. Robert A. Davidson, Prof. A. T. Balaban, Dr. P. C. Hariharan and the referees for their invaluable comments on the manuscript.

References

1. Rouvray, D. H.: Chem. Soc. Rev. **3**, 355 (1974)
2. Rouvray, D. H.: Endeavour **34**, 28 (1975)
3. Polya, G.: Acta Math. **68**, 145 (1937)
4. Read, R. C., in: Graph theory and applications, Y. Alavi *et al.* eds., Lecture notes in mathematics **303**, pp. 243–259. Berlin: Springer-Verlag 1972

5. Read, R. C., in: Chemical applications of graph theory, Balaban, A. T, ed., pp. 25–53. New York: Academic Press 1976
6. Leonard, J. E., Hammond, G. S., Simmons, H. E.: J. Am. Chem. Soc. **97**, 5052 (1975)
7. Leonard, J. E.: J. Phys. Chem. **81**, 2212 (1977)
8. Davidson, R. A.: Unified combinatorial molecular stereo analysis. Ph.D. thesis, The Pennsylvania State University, USA (1977)
9. Robinson, R. W., Harary, F., Balaban, A. T.: Tetrahedron **32**, 355 (1976)
10. Balaban, A. T., Palmer, E. M., Harary, F.: Rev. Roum. Chim. **22**, 517 (1977)
11. Quintas, L. V., Yarmish, J.: Proc. 2nd. Caribbean Conf. on combinatorics and computing, Read, R. C., Cadogan, C., eds., pp. 160–190. University of West Indies, Barbados, W.I. 1977
12. Quintas, L. V., Yarmish, J., in: Proc. 2nd. intern. conf. on combinatorial mathematics, Klein, B., ed. New York Academy of Sciences 1978 (in press)
13. Harary, F., Palmer, E. M.: Graphical enumeration. New York: Academic Press 1973
14. Robinson, R. W.: J. Combinatorial Theory **9**, 327 (1970)
15. Wright, J. A.: Cycle indices of certain types of quasi orders. Doctoral dissertation, University of Rochester, New York (1972)
16. Balasubramanian, K.: Combinatorial enumeration of chemical isomers. Master's Thesis, Birla Institute of Technology and Science, Pilani (Rajasthan) India (1977)
17. Longuet-Higgins, H. C.: Mol. Phys. **6**, 445 (1963)
18. Woodman, C. M.: Mol. Phys. **11**, 109 (1966); **19**, 753 (1970)
19. Balasubramanian, K., in: Proc. 2nd intern. conf. on combinatorial mathematics, Klein, B., ed. New York Academy of Sciences 1978 (in press)
20. Balasubramanian, K.: Open problem collection. Proc. 2nd international conf. on combinatorial mathematics, Capobianco, M., Mauver, S., McCarthy, D., Molluzzo, J. C., eds. New York Academy of Sciences 1978 (in press)
21. Balasubramanian, K.: Submitted for publication

Received November 11, 1977/July 13, 1978