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Enumeration of stereoisomers of chiral and achiral derivatives of monocyclic cycloalkanes having heteromorphous alkyl substituents with the same length k

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Abstract

A combinatorial method based on the determination of the averaged weight of permutations controlling the chirality/achirality fittingness of 2n substitution sites of the monocyclic cycloalkane allows to obtain generalized functional equations for direct enumeration of enantiomers pairs and achiral skeletons of any derivatives of monocyclic cycloalkanes having heteromorphous alkyl substituents of the same length or order k with the empirical formula $C_nH_{m_0}(R_k^1)_{m_1}\cdots(R_k^\gamma)_{m_\gamma}\cdots(R_k^{s_k})_{m_{s_k}}$, wherein at least two alkyl substituents of the same size k have each a distinct steric configuration γ ($1\leq\gamma\leq s_k$),s_k is the total number of chiral and achiral alkyl radicals sterically different of same order k. m_γ is the number of alkyl radicals of steric configuration γ of the system verifying the relation $\sum_{\gamma=1}^{s_k} m_\gamma + m_0 = 2n$. The integer sequences of enantiomer pairs and achiral skeletons are established for substituted derivatives of monocyclic cycloalkane for n=3, 4 and k=3, 4, 5. The composite stereoisomerisms of this particular compounds is also highlighted.

Keywords: enumeration, stereoisomer, chirality, chirality, monocyclic cycloalkanes, steric configuration, heteromorphous polyalkylation

1. Introduction

Up to 1870, the enumeration of isomers in chemistry was done through manual enumeration of drawing and counting of all the possible molecular structures of a given two-dimensional or plane organic compound. The so called "draw and count method" was a tedious work entailed by risks of repetition and / or omission of structures, especially for large molecules [1].

Facing these difficulties in counting chemical isomers and stereoisomers, researchers, to date, have developed methods and models of enumeration using not only mathematical theories (group theory, graph theory, etc.) but also information technology tools (computers, software's, etc.). These generated several enumeration methods based on the enumeration of isomers of constitution or function [2-6], of substitution isomers and then of stereoisomers. This latter is done nowadays using formulas for the direct quantitative determination [7-14]. Specifically, the computation of the number of stereoisomers of the homopolysubstituted and heteropolysubstituted monocyclic cycloalkane has been the subject of several studies [15-22]. In this regard, Nemba *et al.* have solved the problem of the enumeration of substituted monocycloalkanes with homomorphous alkyl substituents [21].

In this work, we are interested in determining the number of enantiomeric pairs and achiral skeletons of cycloalkanes with heteromorphous alkyl substituents. To simplify the language, we will speak of heteropolyalkylation of monocyclic cycloalkane with alkyl radicals of identical k size having sterically distinct configurations. Beyond the direct formulas of computation established, this work highlights a composite stereoisomerism due to the intrinsic chirality of the alkylated trees and the extrinsic chirality induced by their positioning or placement on the monocycloalkane. We highlight as well the concepts of pseudochirality, of pseudosymmetry and of enantiomeric mirror in this family of saturated or olefinic hydrocarbon compounds.

2. Definitions and mathematical formulation

2.1 Stereograph composition of G_k^γ

Let us consider the system $C_nH_{m_0}(R_k^1)_{m_1}\cdots(R_k^\gamma)_{m_\gamma}\cdots(R_k^{s_k})_{m_{s_k}}$, the empirical formula of the heteropolyalkylated monocyclic cycloalkane having heteromorphous alkyl substituents including at least two alkyl groups noted $R_k^\gamma = C_kH_{2k+1}$, having the same order, size or length *k*, with distinct sterically configuration γ($1\leq\gamma\leq s_k$). s_k being the total number of distinct chiral and achiral alkyl radicals of order k as defined below. m_γ is the number of alkyl radicals of steric configuration γ connected on the cycloalkane monocycle to generate the system $C_nH_{m_0}(R_k^1)_{m_1}\cdots(R_k^\gamma)_{m_\gamma}\cdots(R_k^{s_k})_{m_{s_k}}$ where $\sum_{\gamma=1}^{s_k} m_\gamma + m_0 = 2n$.

The molecular composite stereograph G_k^γ of the system $C_nH_{m_0}(R_k^1)_{m_1}\cdots(R_k^\gamma)_{m_\gamma}\cdots(R_k^{s_k})_{m_{s_k}}$ is obtained by connecting the roots of the graphs of the distinct planted steric trees R_k^γ to the sites or positions of substitution of the stereograph G of the parent molecule of the monocyclic cycloalkane C_nH_{2n} described in our previous work [22]. The mathematical and graphical interpretations of this composition of the graph *G* and the graphs R_k^γ to obtain G_k^γ are given respectively by the relation (1) and figure 1.

G_k^γ =G o R_k^γ ($1\leq\gamma\leq s_k$)= $C_nH_{m_0}(R_k^1)_{m_1}\cdots(R_k^\gamma)_{m_\gamma}\cdots(R_k^{s_k})_{m_{s_k}}$ (1)

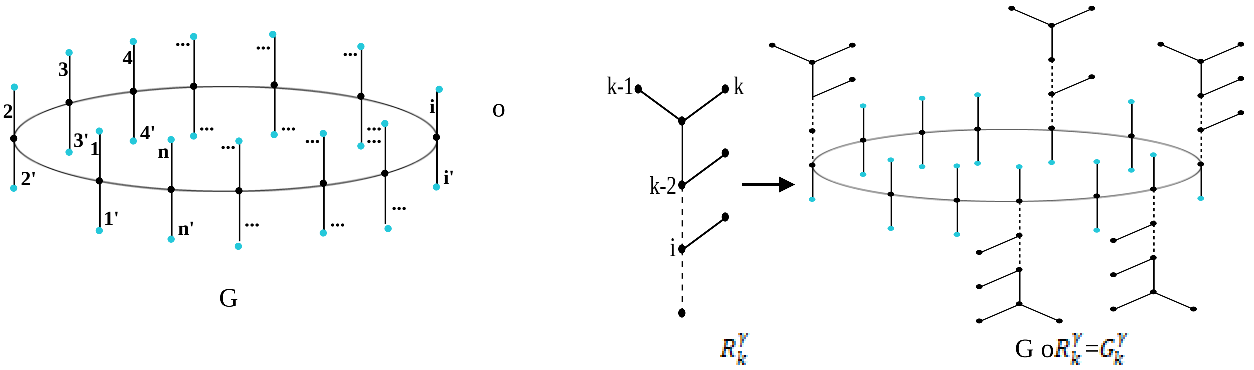


Fig 1: Composition of graph G with distinct planted heteromorphous steric treesR_k^γ

G_k^γ is the stereograph of a monocyclic cycloalkane heteropolyalkylated by alkyl radicals $R_k^\gamma$of identical size *k* having sterically distinct configurations γ.

2.2 Calculation of the number of combinations of heteromorphous alkyl radicals of same size k

According to graph theory, any alkyl radical C_kH_{2k+1} is equivalent to a planted steric tree which may have one or more isomers or stereoisomers including the chiral and achiral forms. s_k and p_k respectively give the total number and the number of steric trees planted of order *k*. We recall that the generating functions which give these numbers were established by Robinson *et al.* [23] in polynomials' series: $s(x) = \sum_k s_k x^k$ et $p(x) = \sum_k p_k x^k$ for $0\leq k\leq 14$. Values of s_k, p_k and s_k-p_k for $0\leq k\leq 18$ are computed and compiled in table 1.

Table 1: Value of s_k, p_k, and et s_k-p_k for $k\leq 18$

k	s_k	p_k	s_k-p_k
0	1	1	0
1	1	1	0
2	1	1	0
3	2	2	0
4	5	3	2
5	11	5	6
6	28	8	20
7	74	14	60
8	199	23	176
9	551	41	510
10	1533	69	1464
11	4436	122	4314
12	12832	208	12624
13	37496	370	37126
14	110500	636	109864
15	327420	1134	326286
16	979819	1963	977856
17	2944873	3505	2941368
18	8896515	6099	8890416

Graphs of planted steric trees (C_kH_{2k+1}) can be combined in three sets whose elements are equivalent to stereoisomers of sterically distinct alkyl radicals, namely:

- E_{a+c} is the set of chiral and achiral trees of cardinality s_k. Elements of E_{a+c} are pairs of enantiomers and achiral skeletons.
- E_a is the set of achiral trees of cardinality p_k. Elements of E_a are achiral skeletons.
- E_c is the set pairs enantiomers of cardinality s_k - p_k.

From these definitions, we can write the following relations:

$$|E_{c+a}| = s_k, |E_a| = p_k \Rightarrow \begin{cases} E_{c+a} = E_c \cup E_a \\ E_c \cap E_a = \varphi \end{cases} \quad (2)$$

Considering (2), we have:

$$|E_{c+a}| = |E_c| + |E_a| \Rightarrow |E_c| = |E_{c+a}| - |E_a| \quad (3)$$

And consequently $|E_c| = s_k\text{-}p_k$ (4)

Table 2 gives us the graphic representation of some distinct sterical trees of size *k* identified by letters, $1\leq k\leq 5$.

Note that a pair of enantiomers is represented by the same letter whose two stereoisomers are differentiated by the apostrophe.

To count the stereoisomers of the system $C_nH_{m_0}(R_k^1)_{m_1}\cdots(R_k^\gamma)_{m_\gamma}\cdots(R_k^{s_k})_{m_{s_k}}$, we will firstly determine the number of heteromorphous combinations of the different alkyl radicals of the same order k and secondly realize the product of the latter by the different results of the enumeration of the stereoisomers of the homopolysubstituted and / or heteropolysubstituted monocyclic cycloalkane obtained in our previous work [22].

We define beforehand some terms used in the rest of this work.

- *One type of substituent or alkyl radical* is symbolized by a letter of the alphabet which uniquely represents an alkyl radical of Table 2.
  Example: the substituent or type *A* radical of Table 2 represents n-propyl if $k = 3$ or n-butyl if $k = 4$; similarly, type *B* represents isopropyl if $k = 3$ or isobutyl if $k = 4$.
- *A group of substituents or alkyl radicals* denotes a combination of at least two types of alkyl radicals of distinct steric configuration having the same size or order *k* and which participates in a substitution.
  Example: AB, AC, ABC, BDE, AD'H ', etc. are some groups of substituents or alkyl radicals of order $k = 5$ selected from Table 2.
- *γ* is the number of types of sterically distinct substituents i.e. having the same order or size and different steric configuration in a group of substituents.
- A substituent group consisting of *i* letters of the alphabet i.e. several types of substituents of distinct steric

configuration and having the same order is also called i-uples.

Example: Considering the alkyl radicals of order *k* = *5*: the groups of substituents *AB, AC, BD,* etc. correspond to $\gamma=2$, they are *2-uples* of letters and groups *ADC, BDA, BCA,* etc. correspond to $\gamma=3$ and are called *3*-uples.

- IR_k is a set constituted of chiral and achiral alkyl radicals having the same order *k*.
  Example: IR_3^c={}, IR_4^c={*sec-butyl1, sec-butyl2*} or IR_3^c={} and IR_4^c={*D,D'*}.
- The number of elements of an *IR* set is called cardinal of a set and is noted *CardIR*. Ainsi, $CardIR_k=s_k$, $CardIR_k^a=p_k$ and $CardIR_k^c=s_k-p_k$.

Table 2: Graphical representation of some planted trees identified by letters of the alphabet

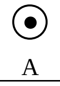
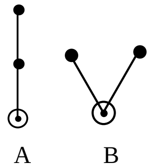
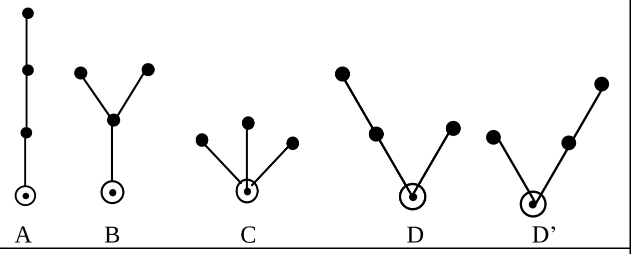
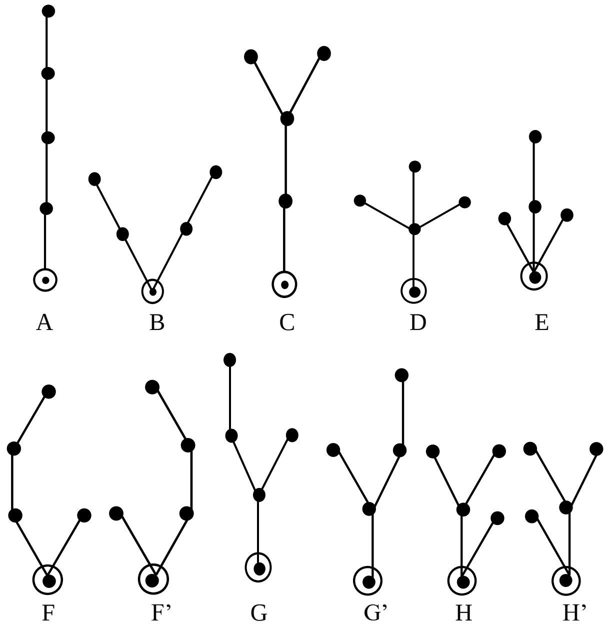
Size k	Alkyl radicals or planted trees
1	
2	
3	
4	
5	

Table 3 lists the sets E_{a+c}, E_a and E_c whose elements consist of the letters of the alphabet representing the alkyl radicals of Table 2.

Table 3: Sets E_{a+c}, E_a and E_c for alkyl radicals of size k with $1 \leq k \leq 5$

R_k	$E_{a+c}= IR_k$	$E_a=IR_k^a$	$E_c=IR_k^c$
CH_3	{A}	{A}	{Ø}
C_2H_5	{A}	{A}	{Ø}
C_3H_7	{A,B}	{A,B}	{Ø}
C_4H_9	{A,B,C,D,D'}	{A,B,C}	{D,D'}
C_5H_{11}	{A,B,C,D,E,F,F',G,G',H,H'}	{A,B,C,D,E}	{F,F',G,G',H,H'}

Following these definitions, we can roll out our algorithm as follows, first demonstrating the method of calculating the number of groups of substituents.

The number of groups of substituents or the number of i-uples of different letters without repetition taken in IR_k, IR_k^a or IR_k^c and composing a substitution is given by respectively by $N_k = \binom{s_k}{i}$, $N_k^a = \binom{p_k}{i}$ and $N_k^c = \binom{s_k - p_k}{i}$.

The number of mixed-letters representing combinations of chiral and achiral alkyl radicals is given by $N_k^{a+c} = N_k - N_k^a + N_k^c$.

2.3 Calculation of the number of chiral and achiral skeletons of the system

$$C_nH_{m_0}(R_k^1)_{m_1}\cdots(R_k^\gamma)_{m_\gamma}\cdots(R_k^{s_k})_{m_{s_k}}$$

The "stereoisomeric" composition of the system $C_nH_{m_0}(R_k^1)_{m_1}\cdots(R_k^\gamma)_{m_\gamma}\cdots(R_k^{s_k})_{m_{s_k}}$ results from (i) the nature of the steric configuration of the alkyl radicals (chiral or achiral tree) and (ii) the manner of attaching or implanting them to the monocycle (chiral or achiral location on the monocycle).

Unlike the polyalkylation of the monocyclic cycloalkane treated by Nemba *et al.* [21] where we had combinations of alkyl groups of the same order and same steric configuration that is to say homomorphous trees, we perform in this work combinations of heteromorphous alkyl trees having distinct configurations and same order *k*, chiral (c), achiral (a), or mixed (a + c) which will be planted on the monocyclic cycloalkane. In summary and at the risk of repeating ourselves, we observe that once again we have a composite stereoisomerism due to the intrinsic chirality of the alkylated trees and the extrinsic chirality induced by their position or placement on the monocyclic cycloalkane.

The composite stereoisomerism resulting from the present exercise of heteropolyalkylation of the monocyclic cycloalkane is summarized in Table 4 below.

Table 4: Composite stereoisomerism in heteropolyalkylated monocyclic cycloalkanes [21]

Chirality or achirality of the heteropolyalkylated monocycloalkane	**Combinations of steric configurations of alkyl radicals**		
Characteristics of placements m_1, …, m_γ, …, m_{sk} alkyl trees	*All the radicals combined i to i are chiral*	*All the radicals combined i to i are achiral*	*All the radicals combined i to i are achiral and chiral*
Chiral placements	Chiral radicals - Chiral placement (A_c^c)	Achiral radicals - Chiral placement (A_c^a)	Achiral and chiral radicals - Chiral placement (A_c^{a+c})
Achiral placements	Chiral radicals - Achiral placement (A_a^c)	Achiral radicals - Achiral placement (A_a^a)	Achiral and chiral radicals - Achiral placement (A_a^{a+c})

The different entities of Table 4 integrating the stereospecificity of the heteropolyalkylated monocyclic cycloalkane skeletons are defined as follows:

$A_c^c(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}; k)$: is the number of chiral stereoisomers composed from chiral alkyls (Chiral Radicals - Chiral Placements);

$A_a^c(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}; k)$: is the number of achiral stereoisomers compounded from chiral alkyls (Chiral Radicals - Achiral Placements);

$A_c^a(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}; k)$: is the number of chiral stereoisomers composed of achiral alkyl trees (Achiral Radicals - Chiral Placements);

$A_a^a(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}; k)$: is the number of achiral stereoisomers compounded from achiral alkyl trees (Achiral Radicals - Achiral Placements);

$A_c^{a+c}(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}; k)$: is the number of chiral stereoisomers composed of achiral and chiral alkyl trees (Achiral and chiral radicals - chiral Placements);

$A_a^{a+c}(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}; k)$: is the number of achiral stereoisomers composed of achiral and chiral alkyl trees (Achiral and chiral radicals - Achiral Placements).

The number of chiral and achiral stereoisomers of a monocyclic cycloalkane heteropolysubstituted by alkyl groups of the same order *k* and of distinct steric configurations □ is directly obtained from the product of the number of groups of substituents. N_k^c,N_k^a,N_k^{a+c} by the number of chiral placements $A_c(n, m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k})$ and achiral placements $A_a(n, m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k})$ of alkyl trees on the monocyclic cycloalkane of size n.

For this purpose, we recall the recurrence formulas established in our previous papers [24] which gives respectively the numbers of chiral and achiral skeletons $A_c(n,m)$ and $A_a(n,m)$ of the system $C_nH_{2n-m}X_m$ and also $A_c(n,m_1,m_2,\ldots,m_i,\ldots m_q)$ and $A_a(n,m_1,m_2,\ldots,m_i,\ldots m_q)$ of the system $C_nX_{m_1}\ldots Y_{m_i}\ldots Z_{m_q}$. By matching their variables to those of the present paper, i.e *$(n,m_1,\ldots,m_\gamma,\ldots m_{sk})$ corresponds $(n,m_1,m_2,\ldots,m_i,\ldots m_q)$*, we generate relations (5) - (10) which give an inventory of the different varieties of stereoisomers resulting from the heteromorphous polyalkylation of the monocyclic cycloalkane with alkyl trees of different steric configurations and of the same order k.

$$A_c^c(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}; k) = N_k^c \times A_c(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}) \quad (5)$$

$$A_a^c(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}; k) = N_k^c \times A_a(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}) \quad (6)$$

$$A_c^a(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}; k) = N_k^a \times A_c(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}) \quad (7)$$

$$A_a^a(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}; k) = N_k^a \times A_a(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}) \quad (8)$$

$$A_c^{a+c}(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}; k) = N_k^{a+c} \times A_c(n; m_0, m_1, \ldots, m_\gamma, \ldots, m_{s_k}) \quad (9)$$

$$A_a^{a+c}(n; m_0, m_1, \dots, m_\gamma, \dots, m_{s_k}; k)$$
$$= N_k^{a+c} \times A_a(n; m_0, m_1, \dots, m_\gamma, \dots, m_{s_k}) \qquad (10)$$

Therefore, the total number of chiral skeletons of the system $C_nH_{m_0}(R_k^1)_{m_1} \cdots (R_k^\gamma)_{m_\gamma} \cdots (R_k^{s_k})_{m_{s_k}}$ is:

$$\begin{aligned} A_c(n; m_0, m_1, \dots, m_\gamma, \dots, m_{s_k}; k) &= A_c^a(n; m_0, m_1, \dots, m_\gamma, \dots, m_{s_k}; k) \\ &+ A_a^c(n; m_0, m_1, \dots, m_\gamma, \dots, m_{s_k}; k) \\ &+ A_c^a(n; m_0, m_1, \dots, m_\gamma, \dots, m_{s_k}; k) \\ &+ A_c^{a+c}(n; m_0, m_1, \dots, m_\gamma, \dots, m_{s_k}; k) \\ &+ A_a^{a+c}(n; m_0, m_1, \dots, m_\gamma, \dots, m_{s_k}; k) \qquad (11) \end{aligned}$$

And the total number of achiral skeletons is:

$$A_a(n; m_0, m_1, \dots, m_\gamma, \dots, m_{s_k}; k) = A_a^a(n; m_0, m_1, \dots, m_\gamma, \dots, m_{s_k}; k) \qquad (12)$$

3. Some examples of application, results and graphical representations

3.1 Number of stereoisomers of the heteropolyalkylated cyclopropane having two types of heteromorphous propyl radicals

We have $IR_3=\{A,B\}$, $IR_3^a=\{A,B\}$, $IR_3^c=\{\}$, $s_3=2$, $p_3=2$, s_3-$p_3=0$, $i=2$ then $N_3 = \binom{2}{2} = 1$;$N_3^c = 0$; $N_3^a = \binom{2}{2} = 1$ which corresponds to the group of substituents AB and $N_3^{a+c} = 0$.

The group of substituents induces heteropolyalkylation of type $C_3H_{m_0}X_{m_1}Y_{m_2}$ with $X=A$, $Y=B$ or $X=B$, $Y=A$ and $m_0+m_1+m_2=6$. The numbers of stereoisomers A_a^a, A_c^a, A_a^c, A_c^c, A_a^{a+c} and A_c^{a+c} are respectively obtained from the following formulas:

$$A_a^a = N_3^a \times A_a, A_c^a = N_3^a \times A_c, A_a^c = N_3^c \times A_a,$$
$$A_c^c = N_3^c \times A_c, \qquad A_a^{a+c} = N_3^{a+c} \times A_a \qquad \text{and}$$
$$A_c^{a+c} = N_3^{a+c} \times A_c.$$

The numbers of stereoisomers corresponding to placements or positions A_a and A_c of $C_3H_{m_0}X_{m_1}Y_{m_2}$ having $m_0 \neq 0$, $m_1 \neq 0$, $m_2 \neq 0$ are the same with those of the system $C_nX_{m_1}Y_{m_2}Z_{m_3}$ which have been calculated in our previous paper for $n=3$ [19-22]. They are recalled in the present paper.

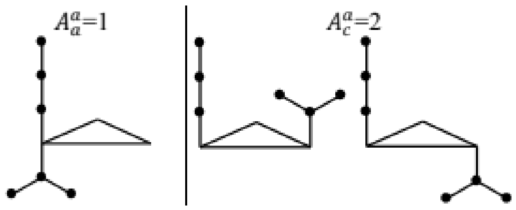
The numbers of stereoisomers corresponding to placements or positions A_a and A_c of $C_3H_{m_0}X_{m_1}Y_{m_2}$ having $m_0=0$, $m_1 \neq 0$, $m_2 \neq 0$ are equivalent to those of the system $C_nH_{2n-m}X_m$ given in our previous paper for $n=3$ [19-22].

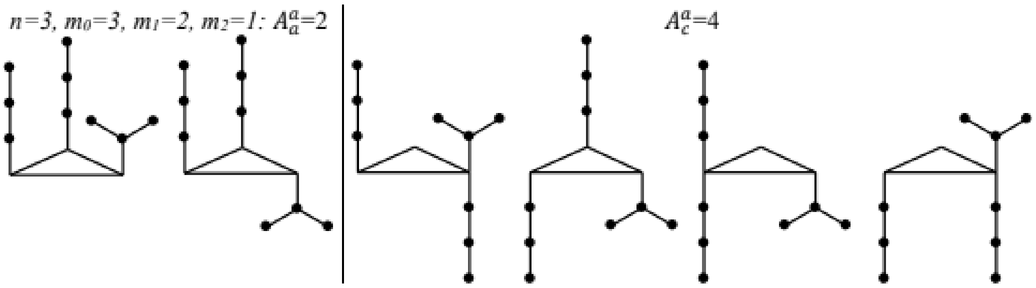
Using all these data, the inventory of stereoisomers of the heteropolyalkylated cyclopropane having two distinct alkyl trees or types of order $k = 3$ is summarized in Table 5.

Table 5: Number of stereoisomers of heteropolyalkylated cyclopropane having two types of distinct alkyl radicals of order $k = 3$

m_0	m_1	m_2	A_a	A_c	A_a^a	A_c^a	A_a^c	A_c^c	A_a^{a+c}	A_c^{a+c}
1	1	4	1	2	1	2	0	0	0	0
1	4	1	1	2	1	2	0	0	0	0
4	1	1	1	2	1	2	0	0	0	0
1	2	3	2	4	2	4	0		0	0
1	3	2	2	4	2	4	0	0	0	0
2	1	3	2	4	2	4	0	0	0	0
2	3	1	2	4	2	4	0	0	0	0
3	2	1	2	4	2	4	0	0	0	0
3	1	2	2	4	2	4	0	0	0	0
2	2	2	4	7	4	7	0	0	0	0
0	1	5	1	0	1	0	0	0	0	0
0	5	1	1	0	1	0	0	0	0	0
0	2	4	2	1	2	1	0	0	0	0
0	4	2	2	1	2	1	0	0	0	0
0	3	3	2	1	2	1	0	0	0	0

Depiction of some graphs: $n=3$, $m_0=4$, $m_1=1$, $m_2=1$:





3.2 Number of stereoisomers of heteropolyalkylated cyclobutane having two types of heteromorphous propyl radicals

We have $IR_3=\{A,B\}$, $IR_3^a=\{A,B\}$, $IR_3^c=\{\}$, $s_3=2$, $p_3=2$, $s_3-p_3=0$, $i=2$ then $N_3=\binom{2}{2}=1$; $N_3^c=0$; $N_3^a=\binom{2}{2}=1$ which corresponds to the group of substituents AB and $N_3^{a+c}=0$.

The group of substituents induces heteropolyalkylation of type $C_4H_{m_0}X_{m_1}Y_{m_2}$ with $X=A$, $Y=B$ or $X=B$, $Y=A$ and $m_0+m_1+m_2=8$. The numbers of stereoisomers A_a^a, A_c^a, A_a^c, A_c^c, A_a^{a+c} and A_c^{a+c} are respectively obtained from the following formulas:

$$A_a^a = N_3^a \times A_a, A_c^a = N_3^a \times A_c, A_a^c = N_3^c \times A_a,$$
$$A_c^c = N_3^c \times A_c, A_a^{a+c} = N_3^{a+c} \times A_a \text{ and } A_c^{a+c} = N_3^{a+c} \times A_c.$$

The numbers of stereoisomers corresponding to placements or positions A_a and A_c of $C_4H_{m_0}X_{m_1}Y_{m_2}$ having $m_0\neq0$, $m_1\neq0$, $m_2\neq0$ are the same with those of the system $C_nX_{m_1}Y_{m_2}Z_{m_3}$ which have been calculated in our previous paper for $n=4$ [19-22]. They are recalled and used in the present paper.

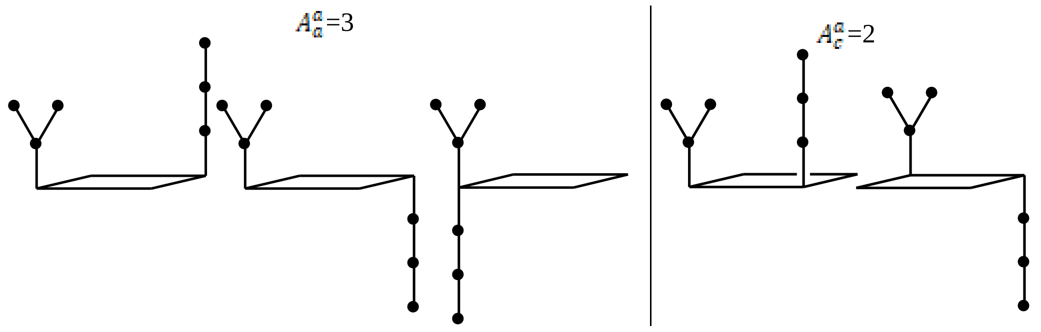
The numbers of stereoisomers corresponding to placements or positions A_a and A_c of $C_4H_{m_0}X_{m_1}Y_{m_2}$ having $m_0=0$, $m_1\neq0$, $m_2\neq0$ are equivalent to those of the system $C_nH_{2n-m}X_m$ given in our previous paper for $n=4$ [19-22].

Using all these data, the inventory of stereoisomers of the heteropolyalkylated cyclobutane having two distinct alkyl trees or types of order k = 3 is summarized in Table 6.

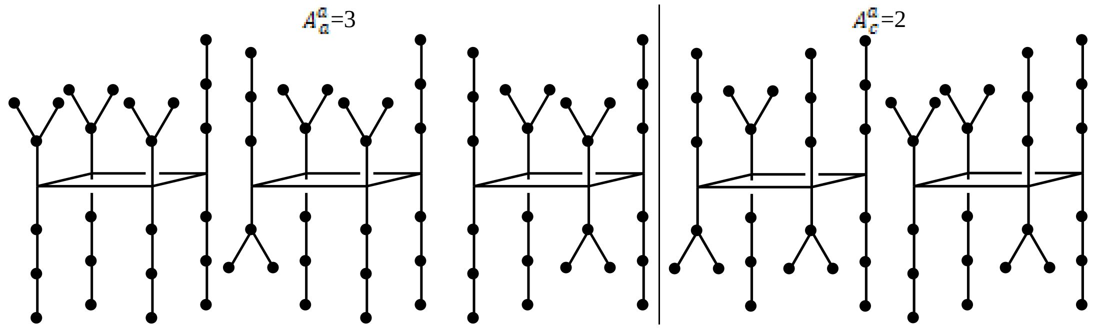
Table 6: Number of stereoisomers of heteropolyalkylated cyclobutane having two types of distinct alkyl radicals of order $k = 3$

m_0	m_1	m_2	A_a	A_c	A_a^a	A_c^a	A_a^c	A_c^c	A_a^{a+c}	A_c^{a+c}
6	1	1	3	2	3	2	0	0	0	0
1	6	1	3	2	3	2	0	0	0	0
1	1	6	3	2	3	2	0	0	0	0
5	2	1	5	8	5	8	0		0	0
5	1	2	5	8	5	8	0	0	0	0
2	5	1	5	8	5	8	0	0	0	0
2	1	5	5	8	5	8	0	0	0	0
1	5	2	5	8	5	8	0	0	0	0
1	2	5	5	8	5	8	0	0	0	0
4	2	2	14	23	14	23	0	0	0	0
2	4	2	14	23	14	23	0	0	0	0
2	2	4	14	23	14	23	0	0	0	0
4	3	1	7	14	7	14	0	0	0	0
4	1	3	7	14	7	14	0	0	0	0
3	4	1	7	14	7	14	0	0	0	0
3	1	4	7	14	7	14	0	0	0	0
1	3	4	7	14	7	14	0	0	0	0
1	4	3	7	14	7	14	0	0	0	0
3	3	2	10	30	10	30	0	0	0	0
3	2	3	10	30	10	30	0	0	0	0
2	3	3	10	30	10	30	0	0	0	0
0	7	1	1	0	1	0	0	0	0	0
0	1	7	1	0	1	0	0	0	0	0
0	6	2	4	1	4	1	0	0	0	0
0	2	6	4	1	4	1	0	0	0	0
0	5	3	3	2	3	2	0	0	0	0
0	3	5	3	2	3	2	0	0	0	0
0	4	4	7	3	7	3	0	0	0	0

Representation of some graphs:
$n=4$, $m_0=6$, $m_1=1$, $m_2=1$:



$n=4$, $m_0=0$, $m_1=3$, $m_2=5$:



3.3 Number of stereoisomers of heteropolyalkylated cyclopropane having two types of heteromorphous butyl radicals

We have $IR_4=\{A,B,C,D,D'\}$, $IR_4^a=\{A,B,C\}$, $IR_4^c=\{D,D'\}$, $s_4=5$, $p_4=3$, $s_4-p_4=2$, $i=2$ then $N_4=\binom{5}{2}=10$ which corresponds to groups of substituents *AB, AC, AD, AD', BC, BD, BD', CD, CD', DD'*; $N_4^c=\binom{2}{2}=1$ which corresponds to the group of substituents *DD'*; $N_4^a=\binom{3}{2}=3$ which corresponds to the group of substituents *AB, AC, BC*. $N_4^{a+c}=10-3-1=6$ which corresponds to groups of substituents *AD, AD', BD, BD', CD, CD'*.

All groups of substituents give heteropolyalkylations of type $C_3H_{m_0}X_{m_1}Y_{m_2}$ such as $m_0+m_1+m_2=6$; with the group de substituents *AB* for example, we can make the assignment *X=A, Y=B* or *X=B, Y=A*. Numbers of stereoisomers A_a^a, A_c^a, A_a^c, A_c^c, A_a^{a+c} and A_c^{a+c} are respectively obtained from the following formulas:

$A_a^a=N_4^a\times A_a$, $A_c^a=N_4^a\times A_c$, $A_a^c=N_4^c\times A_a$, $A_c^c=N_4^c\times A_c$, $A_a^{a+c}=N_4^{a+c}\times A_a$ and $A_c^{a+c}=N_4^{a+c}\times A_c$ with $N_4^a=3$, $N_4^c=1$ and $N_4^{a+c}=6$.

The numbers of stereoisomers corresponding to placements or positions A_a and A_c of $C_3H_{m_0}X_{m_1}Y_{m_2}$ having $m_0\neq0$, $m_1\neq0$, $m_2\neq0$ are the same with those of the system $C_nX_{m_1}Y_{m_2}Z_{m_3}$ which have been calculated in our previous paper for $n=3$ [19-22]. They are recalled in the present paper.

The numbers of stereoisomers corresponding to placements or positions A_a and A_c of $C_3H_{m_0}X_{m_1}Y_{m_2}$ having $m_0=0$, $m_1\neq0$, $m_2\neq0$ are equivalent to those of the system $C_nH_{2n-m}X_m$ given in our previous paper for $n=3$ [19-22].

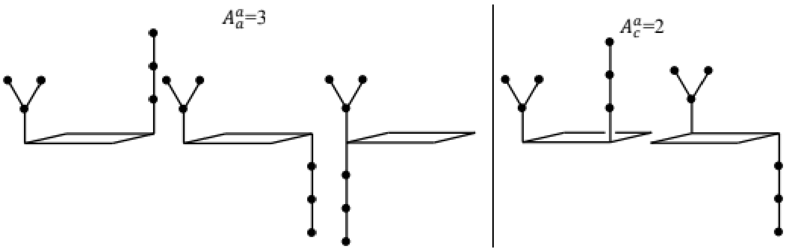
Using all these data, the inventory of stereoisomers of the heteropolyalkylated cyclopropane having two distinct alkyl trees or types of order k = 4 is summarized in Table 7.

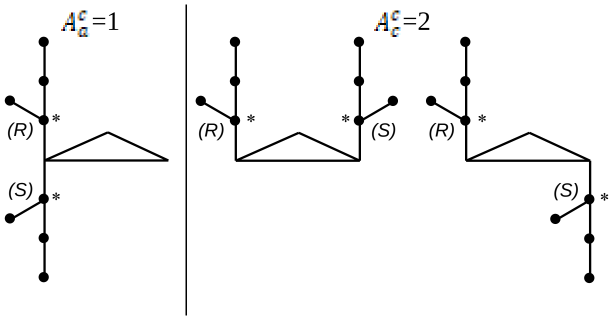
Table 7: Number of stereoisomers of heteropolyalkylated cyclopropane having two types of heteremorphous alkyl radicals of order *k* = 4

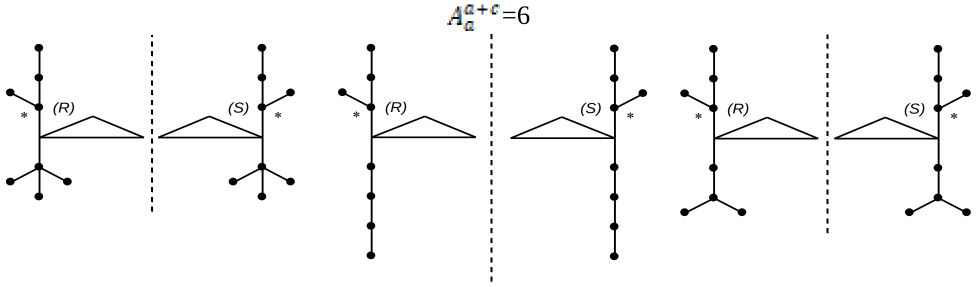
m_0	m_1	m_2	A_a	A_c	A_a^a	A_c^a	A_a^c	A_c^c	A_a^{a+c}	A_c^{a+c}
1	1	4	1	2	3	6	1	2	6	12
1	4	1	1	2	3	6	1	2	6	12
4	1	1	1	2	3	6	1	2	6	12
1	2	3	2	4	6	12	2	4	12	24
1	3	2	2	4	6	12	2	4	12	24
2	1	3	2	4	6	12	2	4	12	24
2	3	1	2	4	6	12	2	4	12	24
3	2	1	2	4	6	12	2	4	12	24
3	1	2	2	4	6	12	2	4	12	24
2	2	2	4	7	12	21	4	7	24	42
0	1	5	1	0	3	0	1	0	6	0
0	5	1	1	0	3	0	1	0	6	0
0	2	4	2	1	6	3	2	1	12	6
0	4	2	2	1	6	3	2	1	12	6
0	3	3	2	1	6	3	2	1	12	6

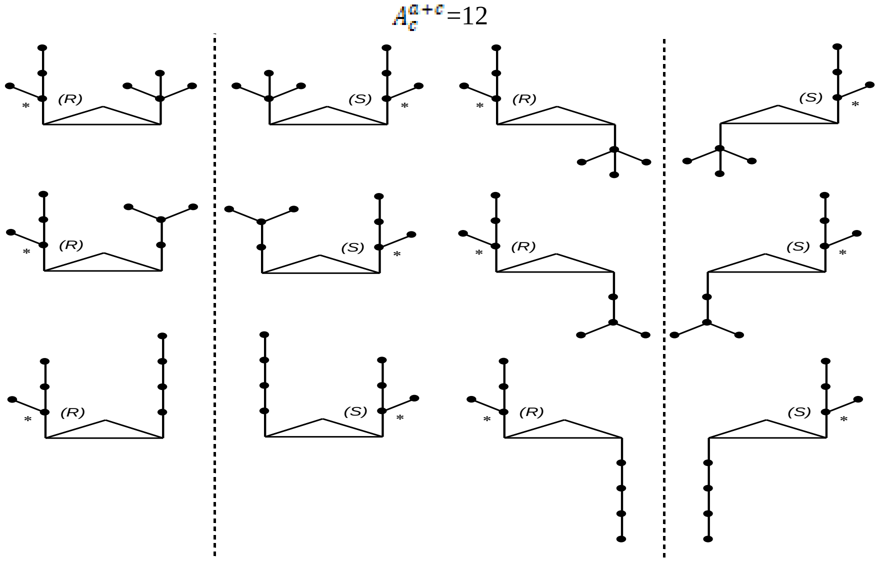
Some graphical representations:

$n=3$, $m_0=4$, $m_1=1$, $m_2=1$:









3.4 Number of stereoisomers of heteropolyalkylated cyclobutane having two types of heteromorphous butyl radicals

We have IR_4={A,B,C,D,D'}, IR_4^a={A,B,C}, IR_4^c={D,D'}, $s_4=5$, $p_4=3$, s_4-$p_4=2$, $i=2$ then $N_4 = \binom{5}{2} = 10$ which corresponds to groups of substituents *AB, AC, AD, AD', BC, BD, BD', CD, CD', DD'*; $N_4^c = \binom{2}{2} = 1$ which corresponds to the group of substituents *DD'*; $N_4^a = \binom{3}{2} = 3$ which corresponds to groups of substituents *AB, AC, BC.* $N_4^{a+c} = 10 - 3 - 1 = 6$ which corresponds to groups of substituents *AD, AD', BD, BD', CD, CD'.*

The groups of substituents induce heteropolyalkylation of type $C_4H_{m_0}X_{m_1}Y_{m_2}$ with *X=A, Y=B* or *X=B, Y=A* and $m_0+m_1+m_2=8$.

The numbers of stereoisomers A_a^a,A_c^a,A_a^c,A_c^c,A_a^{a+c} and A_c^{a+c} are respectively obtained from the following formulas:

$A_a^a = N_4^a \times A_a$, $A_c^a = N_4^a \times A_c$, $A_a^c = N_4^c \times A_a$, $A_c^c = N_4^c \times A_c$, $A_a^{a+c} = N_4^{a+c} \times A_a$ and $A_c^{a+c} = N_4^{a+c} \times A_c$ with $N_4^a = 3$, $N_4^c = 1$ et $N_4^{a+c} = 6$.

The numbers of stereoisomers corresponding to placements or positions A_a and $A_c$of $C_4H_{m_0}X_{m_1}Y_{m_2}$ having $m_0 \neq 0$, $m_1 \neq 0$, $m_2 \neq 0$ are the same with those of the system $C_nX_{m_1}Y_{m_2}Z_{m_3}$ which have been calculated in our previous paper for *n=4* [19-22]. They are recalled and used in the present paper.

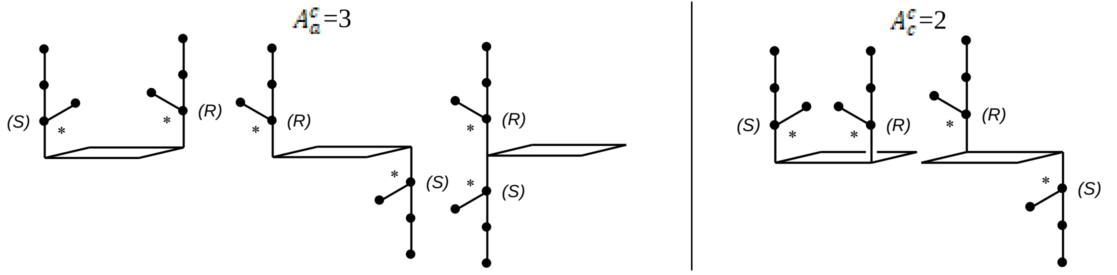
The numbers of stereoisomers corresponding to placements or positions A_a and $A_c$of $C_4H_{m_0}X_{m_1}Y_{m_2}$ having $m_0=0$, $m_1 \neq 0$, $m_2 \neq 0$ are equivalent to those of the system $C_nH_{2n-m}X_m$ given in our previous paper for *n=4* [19-22].

Using all these data, the inventory of stereoisomers of the heteropolyalkylated cyclobutane having two distinct alkyl trees or types of order k = 4 is summarized in Table 8.

Table 8: Number of stereoisomers of heteropolyalkylated cyclobutane having two types of distinct alkyl radicals of order $k = 4$

m_0	m_1	m_2	A_a	A_c	A_a^a	A_c^a	A_a^c	A_c^c	A_a^{a+c}	A_c^{a+c}
6	1	1	3	2	9	6	3	2	18	12
1	6	1	3	2	9	6	3	2	18	12
1	1	6	3	2	9	6	3	2	18	12
5	2	1	5	8	15	24	5	8	30	48
5	1	2	5	8	15	24	5	8	30	48
2	5	1	5	8	15	24	5	8	30	48
2	1	5	5	8	15	24	5	8	30	48
1	5	2	5	8	15	24	5	8	30	48
1	2	5	5	8	15	24	5	8	30	48
4	2	2	14	23	42	69	14	23	84	138
2	4	2	14	23	42	69	14	23	84	138
2	2	4	14	23	42	69	14	23	84	138
4	3	1	7	14	21	42	7	14	42	84
4	1	3	7	14	21	42	7	14	42	84
3	4	1	7	14	21	42	7	14	42	84
3	1	4	7	14	21	42	7	14	42	84
1	3	4	7	14	21	42	7	14	42	84
1	4	3	7	14	21	42	7	14	42	84
3	3	2	10	30	30	90	10	30	60	180
3	2	3	10	30	30	90	10	30	60	180
2	3	3	10	30	30	90	10	30	60	180
0	7	1	1	0	3	0	1	0	6	0
0	1	7	1	0	3	0	1	0	6	0
0	6	2	4	1	12	3	4	1	24	6
0	2	6	4	1	12	3	4	1	24	6
0	5	3	3	2	9	6	3	2	18	12
0	3	5	3	2	9	6	3	2	18	12
0	4	4	7	3	21	9	7	3	42	18

Some representation of graphs:
$n=4$, $m_0=6$, $m_1=1$, $m_2=1$:

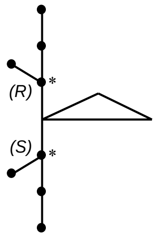


4. Discussions

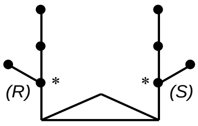
The enumeration method developed in this work makes it possible to enumerate directly the stereoisomers of the monocyclic hydrocarbon molecular system

$$C_nH_{m_0}(R_k^1)_{m_1}\cdots(R_k^\gamma)_{m_\gamma}\cdots(R_k^{s_k})_{m_{s_k}}.$$

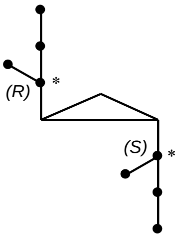
The stereoisomers obtained from the heteropolyalkylation of the monocyclic cycloalkane by heteromorphous alkyl radicals of different configurations and of the same order also induce complex stereochemical description problems.



A



B



C

If we make an interpretation of the stereochemistry of stereoisomers A, B, and C for example, we will say with Eliel *et al.* [25] that A is achiral because it contains a mirror plane which we will describe as enantiomeric mirror (σ_{ve}) which inverts the configurations of the two alkyl trees in geminate position by making them enantiotopic. Any compound that contains enatiotopic ligands are achiral. We consider that the chirality of these two alkyl radicals should lead us to notice this statement of Eliel *et al*. Therefore, we will say that A comes from a case of pseudochirality because the carbon bearing the two radicals is pseudoasymmetric.

As for compounds B and C, although both are considered in our computational model to be chiral, B is achiral according to Eliel *et al.* because containing a plane mirror σ_{ve} which reverses the R or S configuration of the trees fixed in cis position in S or R, B manifests, in our opinion, a pseudoachirality while C is chiral, conclusion identical with Eliel *et al.*, because containing no mirror plane and its ligands are diastereotopic. In addition, C has an extrinsic chirality (RR or SS), due to the position of the two alkyl trees fixed in trans position on the cycle, which induces a perfect chirality.

Furthermore, the compounds whose graphs are shown below are all pseudoachiral, because they all contain a mirror plane either enantiomeric (σ_{ve}) or real (σ_{vr}). σ_{vr} does not transform R into S and vice versa while σ_{ve} transforms R to S and vice versa.

5. Conclusion

The combinatorial method developed makes it possible to directly enumerate enantiomeric pairs and achiral skeletons of cycloalkanes having heteromorphous alkyl substituents or steric planted trees comprising the same number of carbon atoms k ($3 \leq k \leq \infty$) and empirical formula $C_nH_{m_0}(R_k^1)_{m_1}\cdots(R_k^{\gamma})_{m_\gamma}\cdots(R_k^{s_k})_{m_{s_k}}$ where at least two alkyl groups noted $R_k^{\gamma} = C_kH_{2k+1}$, of same order k, have each a distinct steric configuration γ ($1 \leq \gamma \leq s_k$). s_k being the total number of chiral and achiral alkyl radicals of order k. m_γ is the number of alkyl radicals of steric configuration γ of the system $C_nH_{m_0}(R_k^1)_{m_1}\cdots(R_k^{\gamma})_{m_\gamma}\cdots(R_k^{s_k})_{m_{s_k}}$ with $\sum_{\gamma=1}^{s_k} m_\gamma + m_0 = 2n$. This procedure has already been successfully applied by Nemba and Balaban for the case of homomorphic heteropolyalkylation [21] and its advantage is to bypass the Polya method [3] which first requires deriving the cycle index in accordance with symmetry and permutation group of the molecular system and then transform the cycle index into a generating function of the order 2n before continuing with the composition of the graphs to obtain the results of the system $C_nH_{m_0}(R_k^1)_{m_1}\cdots(R_k^{\gamma})_{m_\gamma}\cdots(R_k^{s_k})_{m_{s_k}}$.

In this work, we have used the basic concepts of permutation group theory and algebraic combinatorics as tools for mathematically expressing the chirality and adequacy of achirality induced by substitution sites of composite molecular system of heteromorphous polyalkylation. It is worth remembering that the compounds of this family of hydrocarbons serve as starting materials for extensive kinetic and mechanistic studies, while others are used successfully for important applications such as the manufacture of hydrocarbon resins and other chemicals. Hence the interest of the present scientific contribution.

Acknowledgements

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