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Algorithm for the Direct Enumeration of Chiral and Achiral Skeletons of a Homosubstituted Derivative of a Monocyclic Cycloalkane with a Large and Factorizable Ring Size *n*

Robert M. Nemba*,† and Alexandru T. Balaban‡

Faculty of Science, Laboratory of Physical Chemistry, Section of Molecular Topology, University of Yaounde I, P.O. Box 812 YDE, Cameroon, and Polytechnic University, Department of Organic Chemistry, Splaiul Independentei 313, 77207 Bucharest, Romania

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An algorithm with combinatorial formulas is derived for the direct enumeration of chiral and achiral skeletons of stereo and position isomers of homopolysubstituted monocyclic cycloalkanes ($C_nH_{2n-m}X_m$) with any large ring size n. Some developments are given when n is factorizable into the forms $n = \alpha^j$ or $n = 2^p\alpha^j$ where j, p, and α are integer numbers while α is odd prime. Some illustrations are given for $n = 27$ and 36 with $0 \le m \le 9$.

1. INTRODUCTION

In some previous papers,[1−3] it was shown that numbers of stereo and position isomers of cycloalkanes where one or more hydrogen atoms have been substituted can be calculated by means of Pólya's counting theorem.[4−9] Such calculations have been limited to systems with small ring size because of the unwieldiness of the expressions involved and the difficulty of expanding those expressions. Our purpose is to circumvent this limitation and present an algorithm for the direct determination of the numbers of chiral and achiral skeletons of stereo and position isomers of homopolysubstituted cycloalkanes ($C_nH_{2n-m}X_m$) with a higher ring size n factorizable into the two forms previously indicated. We assume ring flip to be fast enough to equilibrate conformers.

2. MATHEMATICAL FORMULATION

Let us consider the system $C_nH_{2n-m}X_m = (n,2n,m)$. The three non-negative integers n, $2n$, and m denote, respectively, the ring size, the number of available substitution sites, and the degree of substitution. The tridimensional graph or stereograph G of its parent monocyclic cycloalkane C_nH_{2n} shown in Figure 1 belongs to the symmetry point group D_{nh} which includes $4n$ symmetry operations. The n labeled vertices symbolize the carbon atoms, and the unlabeled vertices indicate the locations of the $2n$ hydrogen atoms which constitute the substitution sites. These latter collected in two subsets $E = \{1,2,3,...,n\}$ and $E' = \{1',2', 3',...,n'\}$ are permutable under the action of the $4n$ symmetry operations of D_{nh}. The elements of E and E' joined as indicated in Figure 2 constitute the vertices of an orthogonal prism which contains two regular n-gons as parallel faces. Some considerations and rules can be made from the spatial distribution of the substitution sites and the symmetry properties of the point group D_{nh} acting on the molecular

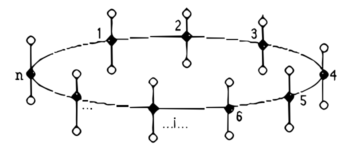

Figure 1. Molecular stereograph G of a monocyclic cycloalkane.

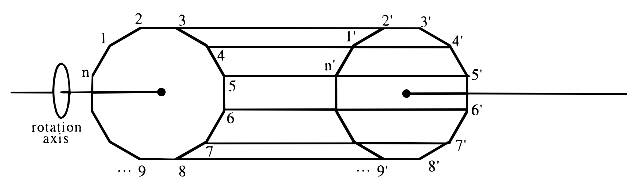

Figure 2. Orthogonal prism symbolizing the locations of the $2n$ hydrogen atoms (substitution sites) at the vertices of the two parallel n-gons.

stereograph G. If n is factorizable, each divisor d of n gives rise to a d-fold rotation axis which generates proper rotations C_d^r ($r \le d - 1$) and improper rotations $S_d^{r'}$ ($r' \le d - 1$ if d odd or $r' \le 2d - 1$ if d even). According to the parity of n one may notice the following.

Rule 1: *For d odd or even, each proper rotation C_d^r of D_{nh} permutes some elements of the subset E and produces $^n/_d$ d-cycles of permutations. This operation is simultaneously undertaken on the subset E′ and gives the same results. Therefore each proper rotation C_d^r permuting in parallel some elements of the subsets E and E′ produces $^{2n}/_d$ d-cycles of permutations noted $f_d^{2n/d}$.*

To exemplify this situation we consider the stereograph G of cyclohexane which belongs to the symmetry point group D_{6h}. If we set up $d = 3$ and $r = 1$, the proper rotation C_3 produces on $E = \{1,2,3,4,5,6\}$ two three-cycles of permutations noted (135) (246) and on $E' = \{1',2',3',4',5',6'\}$ the other two three-cycles (1′3′5′) (2′4′6′). This symmetry operation gives rise to the term (135) (246) (1′3′5′) (2′4′6′) also noted as f_3^4 which is a product of four disjoint permutation cycles of length 3.

† University of Yaounde I.
‡ Polytechnic, University of Bucharest.

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Table 1. Permutations Generated by Binary Axes and Reflections of D_{nh}

n (odd)	n (even)
$\sigma_h \to f_2^n$	$\sigma_h \to f_2^n$; $\frac{n}{2}\sigma_d \to \frac{n}{2} f_2^n$
$n\sigma_v \to n f_1^2 f_2^{n-1}$	$\frac{n}{2}\sigma_v \to \frac{n}{2} f_1^4 f_2^{n-2}$
$nC_2' \to n f_2^n$	$\frac{n}{2}C_2' \to \frac{n}{2} f_2^n$; $\frac{n}{2}C_2'' \to \frac{n}{2} f_2^n$

Rule 2: *For d odd, each improper rotation $S_d^{r'}$ of D_{nh} merges together into a single 2d-cycle, one d-cycle of the elements of E and another d-cycle of the elements of E′. Such permutations of length 2d applied to the sequence of 2n elements generate a product of $^n/_d$ permutations cycles of length 2d which produce the term $f_{2d}^{n/d}$.*

For instance the action of the improper rotation S_3 on the subsets E and E' with the same cardinality $n = 6$ as in the preceding example gives the cycle structure (13′51′35′)-(24′62′46′) which is the product of two disjoint permutation cycles of length 6 noted f_6^2.

Rule 3: *For d even, each improper rotation $S_d^{r'}$ of D_{nh} permuting the elements of the subsets E and E′ of G generates a product of $^{2n}/_d$ d-cycles of disjoint permutations noted $f_d^{2n/d}$.*

For $n = 6$ and $d = 2$, the preceding rule applied to $S_2 \equiv i$ generates the term f_2^6 which corresponds to the product of six disjoint transpositions (or two-cycle permutations) explicitly noted as follows: (14′) (25′) (36′) (1′4) (2′5) (3′6).

The permutations generated by the other symmetry elements of D_{nh} including the horizontal binary axes C_2', C_2'' and the reflections σ_h, σ_v, and σ_d are reported in Table 1 according to the parity of n.

The application of Pólya's theorem on the molecular stereograph G which belongs to the symmetry point group D_{nh} requires all the $4n$ symmetry operations to be expressed according to the parity of n, as the cycle indices $Z_T(n_-)$ and $Z_T(n_+)$ given in eqs 1 and 3 usually used for the topological enumeration which gives the figure inventory of geometrical isomers. The cycle indices $Z_E(n_-)$ and $Z_E(n_+)$ given in eqs 2 and 4 are obtained after eliminating with respect to the principle of Parks and Hendrickson[10] all the terms generated by reflections and improper rotations in eqs 1 and 3, respectively. Equations 2 and 4 apply to the remaining $2n$ symmetry operations and hold for enantiomeric enumeration in order to count all stereoisomers (including chiral pairs and achiral forms) of substituted derivatives of monocyclic cycloalkanes. Similarly, the cycle indices obtained from the $2n$ symmetry operations of D_{nh} including only reflections and improper rotations lead to the enumeration of achiral skeletons. It is to be noticed throughout this paper that the notation (n_-), (n_+), and $(n_\pm)$ is assigned to the integer numbers n odd, n even, and n odd or even, respectively. If n odd, then

$$Z_T(n_-) = \frac{1}{4n}\Big[\sum_{(d\neq 2)|2n} \varphi(d)(f_d^{2n/d}) + (n+1)f_2^n + n(f_1^2 f_2^{n-1})\Big] \quad (1)$$

$$Z_E(n_-) = \frac{1}{2n}\Big[\sum_{(d\neq 2)|n} \varphi'(d)(f_d^{2n/d}) + n f_2^n\Big] \quad (2)$$

and if n even, then

$$Z_T(n_+) = \frac{1}{4n}\left[\sum_{(d\neq 2)|n} \varphi(d)(f_d^{2n/d}) + \frac{3}{2}(n+2)f_2^n + \frac{n}{2}(f_1^4 f_2^{n-2})\right] \quad (3)$$

$$Z_E(n_+) = \frac{1}{2n}\Big[\sum_{(d\neq 2)|n} \varphi'(d)(f_d^{2n/d}) + (n+1)f_2^n\Big] \quad (4)$$

where the summation is over all the integers $d \neq 2$ that divide $2n$ in eq 1 or n in eqs 2−4. The number $\varphi(d)$ of symmetry operations (proper or improper rotations) that induce permutations of length d is obtained from eqs 5−7:

$$\varphi(d) = \varphi'(d)_{pr} \quad \text{if } d \text{ odd} \quad (5)$$

$$\varphi(d) = \varphi'(d)_{pr} + \varphi'(d)_{ir} + \varphi'(P_i)_{ir} \quad \text{if } d(\text{even}) = 2P_i \text{ and } P_i \text{ (odd prime integer)} \quad (6)$$

$$\varphi(d) = \varphi'(d)_{pr} + \varphi'(d)_{ir} \quad \text{if } d(\text{even}) \neq 2P_i \quad (7)$$

while $\varphi'(d)$ the number of proper rotations that generate permutations of length d is given by (8)

$$\varphi'(d) = \varphi'(d)_{pr} \quad (8)$$

The terms $\varphi'(d)_{pr}$ and $\varphi'(d)_{ir}$ are the Euler totient function[11] for the integer d (odd or even), and the indices (pr) and (ir) refer to proper and improper rotations induced by the d-fold rotation axis. The substitution in eqs 1−4 of the terms f_a^b by the corresponding figure counting series $(1 + x^a)^b$ and the expansion of the resulting algebraic expression then lead to the polynomials 9 and 10:

$$P_T(n_\pm,m_\pm) = \sum_{m=0}^{2n} A_T(n_\pm,m_\pm)(x^m) \quad (9)$$

$$P_E(n_\pm,m_\pm) = \sum_{m=0}^{2n} A_E(n_\pm,m_\pm)(x^m) \quad (10)$$

the coefficients of which satisfy the following relations

$$A_T(n_\pm,m_\pm) = A_c(n_\pm,m_\pm) + A_{ac}(n_\pm,m_\pm) \quad (11)$$

$$A_E(n_\pm,m_\pm) = 2A_c(n_\pm,m_\pm) + A_{ac}(n_\pm,m_\pm) \quad (12)$$

where $A_c(n_\pm,m_\pm)$ and $A_{ac}(n_\pm,m_\pm)$ denote respectively the numbers of chiral and achiral skeletons of stereo and position isomers of a homopolysubstituted monocyclic cycloalkane $C_nH_{2n-m}X_m$. It should be observed that the coefficient of the term x^m and that of the term x^{2n-m} in the generating functions 9 and 10 obey the following conditions:

$$A_T(n_\pm,m_\pm) = A_T(n_\pm,2n_\pm - m_\pm) \quad \text{and} \quad A_E(n_\pm,m_\pm) = A_E(n_\pm,2n - m_\pm)$$

These equivalences are due to the complementarity of the degrees of substitution m and $2n - m$. These conditions induce also the equivalences:

$$A_c(n_\pm,m_\pm) = A_c(n_\pm,2n_\pm - m_\pm) \quad \text{and} \quad A_{ac}(n_\pm,m_\pm) = A_{ac}(n_\pm,2n_\pm - m_\pm)$$

The derivation of the numerical sequences $A_c(n_\pm,m_\pm)$ and $A_{ac}(n_\pm,m_\pm)$ through the determination of $A_T(n_\pm,m_\pm)$ and $A_E(n_\pm,m_\pm)$ by the classical Pólya method is laborious for large ring size n and higher values of m. A direct and convenient way to circumvent this difficulty and compute these coefficients for singular values (n, m) is an everlasting problem for chemists. The emphasis in this work has been to set up a general pattern inventory of stereo and position isomers for a single system $C_nH_{2n-m}X_m$. A long time ago, related results for monocyclic aromatics had been published in Roumanian language. Obviously, no chirality was present.[12] The algorithm begins as follows: consider the system $C_nH_{2n-m}X_m$ and its triade of numbers (n, $2n$, m). Let us define for n odd, and m odd or even, the sets $F_{2n_-} = \{1,2,...,d,...,n,2n\}$ and $F_{m_\pm} = \{1,...,d',...,m,\}$ containing the divisors of $2n$ and m. We extract from these sets the subsets $F_{2n_-} \cap F_{m_-}$, $F_{2n_-} \cap F_{m_+}$ which contain the common divisors $\{d\}$ of the integer numbers ($2n$, m). Then the enantiomer-pairs and achiral skeletons inventories are given by (13)−(16).

If $(d \neq 2) \in F_{2n_-} \cap F_{m_-}$ and $\mu' = (m-1)/2$, then

$$A_c(n_-,m_-) = \frac{1}{4n}\left[\sum_{(d\neq 2)} (2\varphi'(d) - \varphi(d))\binom{2n/d}{m/d} - 2n\binom{n-1}{\mu'}\right] \quad (13)$$

$$A_{ac}(n_-,m_-) = \frac{1}{2n}\left[\sum_{(d\neq 2)} (\varphi(d) - \varphi'(d))\binom{2n/d}{m/d} + 2n\binom{n-1}{\mu'}\right] \quad (14)$$

If $(d \neq 2) \in F_{2n_-} \cap Fm_+$, then

$$A_c(n_-,m_+) = \frac{1}{4n}\left[\sum_{(d\neq 2)} (2\varphi'(d) - \varphi(d))\binom{2n/d}{m/d} - \binom{n}{m/2}\right] \quad (15)$$

$$A_{ac}(n_-,m_+) = \frac{1}{2n}\left[\sum_{(d\neq 2)} (\varphi(d) - \varphi'(d))\binom{2n/d}{m/d} + (n+1)\binom{n}{m/2}\right] \quad (16)$$

But if n is even, and m odd or even, we define this time the sets $F_{n_+} = \{1,2,...,d,...,n\}$ and $F_{m_\pm} = \{1,...,d',...,m\}$ containing the divisors of the integer numbers n and m and extract from these sets and according to the parities of both n and m one of the following subsets $F_{n_+} \cap F_{m_-}$ or $F_{n_+} \cap F_{m_+}$ which contain the common divisors $\{d\}$ of the integer numbers (n, m). Then the enantiomer-pairs and achiral skeletons inventories are given by eqs 17−20, respectively.

If $(d \neq 2) \in F_{n_+} \cap F_{m_-}$ and $\mu' = (m-1)/2$, then

$$A_c(n_+,m_-) = \frac{1}{4n}\left[\sum_{(d\neq 2)} (2\varphi'(d) - \varphi(d))\binom{2n/d}{m/d} - 2n\binom{n-1}{\mu'}\right] \quad (17)$$

$$A_{ac}(n_+,m_-) = \frac{1}{2n}\left[\sum_{(d\neq 2)} (\varphi(d) - \varphi'(d))\binom{2n/d}{m/d} + 2n\binom{n-1}{\mu'}\right] \quad (18)$$

If $(d \neq 2) \in F_{n_+} \cap F_{m_+}$, then

$$A_c(n_+,m_+) = \frac{1}{4n}\left[\sum_{(d\neq 2)} (2\varphi'(d) - \varphi(d))\binom{2n/d}{m/d} + \frac{1}{n-1}\left(\frac{m^2}{2} - n(m+1) + 1\right)\binom{n}{m/2}\right] \quad (19)$$

$$A_{ac}(n_+,m_+) = \frac{1}{2n}\left[\sum_{(d\neq 2)} (\varphi(d) - \varphi'(d))\binom{2n/d}{m/d} + \frac{1}{n-1}\left(n^2 + n(m+1) - \frac{m^2}{2} - 2\right)\binom{n}{m/2}\right] \quad (20)$$

In eqs 13−20 $\varphi(d)$ and $\varphi'(d)$ have the same definitions as previously given and the notation of type (r/s) refers to binomial coefficients. We illustrate the preceding developments by the following applications.

3. APPLICATIONS

Case 1. Enantiomer-pairs and achiral skeletons of $C_nH_{2n-m}X_m$ where n (odd) $= \alpha^j$ (α and j are integer numbers and α is prime).

Let $F_{2\alpha^j} = \{1,2,...,\alpha^k,...\alpha^j,2\alpha,...2\alpha^k,...,2\alpha^j\}$ be the set of divisors of $2\alpha^j$ and $1 \le k \le j$. The coefficient $\varphi'(\alpha)_{ir} = \varphi'(\alpha)_{pr} = (\alpha^k - \alpha^{k-1})$. According to eqs 1 and 2 the cycle indices $Z_T(\alpha^j)$ and $Z_E(\alpha^j)$ are given by (21) and (22).

$$Z_T(\alpha^j) = \frac{1}{4n}\Big[f_1^{2n} + (n+1)f_2^{n} + nf_1^{2}f_2^{n-1} + \sum_{k=1}^{j}(\alpha^k - \alpha^{k-1})(f_{\alpha^k}^{2\alpha^{j-k}} + f_{2\alpha^k}^{\alpha^{j-k}})\Big] \quad (21)$$

$$Z_E(\alpha^j) = \frac{1}{2n}\Big[f_1^{2n} + nf_2^{n} + \sum_{k=1}^{j}(\alpha^k - \alpha^{k-1})(f_{\alpha^k}^{2\alpha^{j-k}})\Big] \quad (22)$$

The generating functions for topological and enantiomeric enumerations can be obtained by replacing f_a^b by $(1 + x^a)^b$ and the expansion of the algebraic expressions depends upon the magnitude of the integers a and b. To avoid this difficult task and compute directly the numbers $A_c(\alpha^j,m_\pm)$ and $A_{ac}(\alpha^j,m_\pm)$ we shall deduce some recurrence formulas and generalizations depending on the factorization and parity of m. Let $m_- = \alpha^k$ and $F_{2\alpha^j} \cap F_{\alpha^k} = 1,\alpha,...,\alpha^i,...,\alpha^k$. Thus eqs 13 and 14 become

$$A_c(\alpha^j,\alpha^k) = \frac{1}{4n}\left[\binom{2n}{m} + \sum_{k}^{i=1}(\alpha^i - \alpha^{i-1})\binom{2\alpha^{j-i}}{\alpha^{k-i}} - 2n\binom{n-1}{(m-1)/2}\right] \quad (23)$$

$$A_{ac}(\alpha^j,\alpha^k) = \frac{1}{2n}\left[2n\binom{n-1}{(m-1)/2}\right] \quad (24)$$

Example 1. Enantiomer-pairs and achiral skeletons of $C_{27}H_{45}X_9$. Let $n = 3^3$ and $m = 3^2$ and $F_{54} \cap F_9 = \{1,3,3^2\}$, then

$$A_c(27,9) = \frac{1}{108}\left[\binom{54}{9} + (3^1 - 3^0)\binom{2\cdot 3^{3-1}}{3^{2-1}} + (3^2 - 3^1)\binom{2\cdot 3^{3-2}}{3^{2-2}} - 2\cdot 27\binom{(27-1)}{(9-1)/2}\right] = 49\ 232\ 691$$

$$A_{ac}(27,9) = \frac{1}{54}\left[54\cdot\binom{(27-1)}{(9-1)/2}\right] = 14\ 950$$

If $m_+ = 2\alpha^k$, then

$$A_c(\alpha^j,2\alpha^k) = \frac{1}{4n}\left[\binom{2n}{m} + \sum_{i=1}^{k}(\alpha^i - \alpha^{i-1})\left[\binom{2\alpha^{j-i}}{2\alpha^{k-i}} - \binom{\alpha^{j-i}}{\alpha^{k-i}}\right] - \binom{n}{m/2}\right] \quad (25)$$

$$A_{ac}(\alpha^j,2\alpha^k) = \frac{1}{2n}\left[\sum_{i=1}^{k}(\alpha^i - \alpha^{i-1})\binom{\alpha^{j-i}}{\alpha^{k-i}} + (n+1)\binom{n}{m/2}\right] \quad (26)$$

Example 2. Enantiomer-pairs and achiral skeletons of $C_{27}H_{48}X_6$. Let $n = 3^3$, $m = 2\alpha = 6$, $\alpha = 3$, $j = 3$, $k = 1$ and $F_{54} \cap F_6 = \{1,2,3,6\}$

$$A_c(27,6) = \frac{1}{108}\left[\binom{54}{6} + (3^1 - 3^0)\binom{2\cdot 3^{3-1}}{2\cdot 3^{1-1}} - (3^1 - 3^0)\binom{3^{3-1}}{3^{1-1}} - \binom{27}{3}\right] = 239\ 116$$

$$A_{ac}(27,6) = \frac{1}{54}\left[(3^1 - 3^0)\binom{3^3-1}{3^1-1} + (27+1)\binom{27}{3}\right] = 1517$$

If there is no common factor between $2\alpha^j$ and m except 1 or 2, i.e., $F_{2\alpha^j} \cap F_m = \{1,2\}$ or $F_{2\alpha^j} \cap F_m = \{1\}$, the eqs 25 and 26 become

$$A_c(\alpha^j,m) = \frac{1}{4n}\left[\binom{2n}{m} - \binom{n}{m/2}\right] \quad (27)$$

$$A_{ac}(\alpha^j,m) = \frac{1}{2n}\left[(n+1)\binom{n}{m/2}\right] \quad (28)$$

Example 3. Enantiomer-pairs and achiral skeletons of $C_{27}H_{50}X_4$. Let $n = 3^3$, $m = 2^2$, $F_{54} \cap F_4 = \{1,2\}$.

$$A_c(27,4) = \frac{1}{108}\left[\binom{54}{4} - \binom{27}{2}\right] = 2925$$

$$A_{ac}(27,4) = \frac{1}{54}\left[(28)\binom{27}{2}\right] = 182$$

Case 2. Enumeration of enantiomer-pairs and achiral skeletons when $n = 2^p\alpha^j$.

The divisors d of $n = 2^p\alpha^j$ are deduced from the relation $d = 2^{p-q}\alpha^k$ under the conditions $0 \le q \le p$, $0 \le k \le j$. The couples of integer values (q,k) needed for the computation of d and the determination of the cycle indices $Z_T(2^p\alpha^j)$ and $Z_E(2^p\alpha^j)$ are developed as shown in the following grid:

k→ q↓	0	1	2	....	j
0	0,0	0,1	0,2	....	0,j
1	1,0	1,1	1,2	....	1,j
2	2,0	2,1	2,2		2,j
....	....	....	....	....	....
p-1	p-1,0	p-1,1	p-1,2	....	p-1,j
p	p,0	p,1	p,2	....	p,j

Therefore for the even integer $n = 2^p\alpha^j$, eqs 3 and 4 become, respectively

$$Z_T(2^p\alpha^j) = \frac{1}{4n}\left[f_1^{2n} + \left(\frac{3}{2}n + 1\right)f_2^{n} + \frac{n}{2}f_1^4 f_2^{n-2} + \sum_{k=1}^{j}(\alpha^k - \alpha^{k-1})\left(f_{(\alpha^k)}^{(2^{p+1})(\alpha^{j-k})} + f_{(2\alpha^k)}^{(2^p)(\alpha^{j-k})}\right) + \sum_{q=0}^{p-1}2^{(p-q)}f_{(2^{p-q})}^{(2^{q+1})(\alpha^j)} + \sum_{q=0}^{p-1}\sum_{k=1}^{j}2^{(p-q)}(\alpha^k - \alpha^{k-1})\left(f_{(2^{p-q})(\alpha^k)}^{(2^{q+1})(\alpha^{j-k})}\right)\right] \quad (29)$$

and

$$Z_E(2^p\alpha^j) = \frac{1}{2n}\left[f_1^{2n} + nf_2^{n} + \sum_{k=1}^{j}(\alpha^k - \alpha^{k-1})\left(f_{(\alpha^k)}^{(2^{p+1})(\alpha^{j-k})}\right) + \sum_{q=0}^{p-1}2^{(p-q-1)}\left(f_{(2^{p-q})}^{(2^{q+1})(\alpha^j)}\right) + \sum_{q=0}^{p-1}\sum_{k=1}^{j}2^{(p-q-1)}(\alpha^k - \alpha^{k-1})\left(f_{(2^{p-q})(\alpha^k)}^{(2^{q+1})(\alpha^{j-k})}\right)\right] \quad (30)$$

To obtain the global solution of our enumeration problem, the classical method requires transforming of these cycle indices into Pólya counting polynomials of order $2n$. To circumvent such a procedure which cannot be done by hand and needs computer assistance for higher values of the ring size n and the degree of substitution m we shall use eqs 17–20. Let us illustrate this case by enumerating the stereoisomers of a system $C_nH_{2n-m}X_m$ where $n_+ = 2^p\alpha^j$ and $m_+ = 2^{p-q}\alpha^k$.

Table 2. Numbers of Enantiomer-Pairs and Achiral Skeletons of Homopolysubstituted Cycloalkanes ($C_nH_{2n-m}X_m$) Where the Degree of Substitution $0 \le m \le 9$ and the Ring Size n = 6, 7, 8, 9 , 12 , 27, and 36

	n													
	6		7		8		9		12		27		36	
m	$A_c(m,n)$	$A_{ac}(m,n)$	$A_c(m,n)$	$A_{ac}(m,n)$	$A_c(m,n)$	$A_{ac}(m,n)$	$A_c(m,n)$	$A_{ac}(m,n)$	$A_c(m,n)$	$A_{ac}(m,n)$	$A_c(m,n)$	$A_{ac}(m,n)$	$A_c(m,n)$	$A_{ac}(m,n)$
0	0	1	0	1	0	1	0	1	0	1	0	1	0	1
1	0	1	0	1	0	1	0	1	0	1	0	1	0	1
2	2	5	3	4	3	6	4	5	5	8	13	14	17	20
3	7	5	10	6	14	7	19	8	37	11	217	26	397	35
4	18	14	35	12	53	24	84	20	215	49	2925	182	7123	367
5	28	10	64	15	126	21	226	24	858	55	29120	325	96866	595
6	35	20	106	20	241	50	514	47	2778	174	239116	1517	1084666	4330
7			113	20	340	35	856	56	7128	165	1638520	2600	10226656	6545
8					390	65	1212	70	15252	410	9633780	9100	83114768	37077
9							1317	70	27077	330	49232691	14950	591036384	52360

The subset of common divisors is $F_{n_+} \cap F_{m_+} = 1,...\{2^{p-q}\},...\{\alpha^k\}...,\{2^{p-q}\alpha^k\}$ and the transformation of eqs 17 and 18 gives the following recurrence formulas 31 and 32 for the determination of enantiomeric pairs and achiral skeletons, respectively.

$$A_c(2^p\alpha^j,2^{p-q}\alpha^k) = \frac{1}{4n}\Bigg[\binom{2n}{m} + \sum_{i=1}^{k}(\alpha^i - \alpha^{i-1})\binom{2n/\alpha^i}{m/\alpha^i} + \frac{1}{n-1}\left(\frac{m^2}{2} - n(m+1) + 1\right)\binom{n}{m/2} - \sum_{i=1}^{k}(\alpha^i - \alpha^{i-1})\binom{2n/2\alpha^i}{m/2\alpha^i}\Bigg] \quad (31)$$

$$A_{ac}(2^p\alpha^j,2^{p-q}\alpha^k) = \frac{1}{2n}\Bigg[\sum_{q=0}^{p-2} 2^{p-q-1}\binom{2n/2^{p-q}}{m/2^{p-q}} + \sum_{q=0}^{p-2}\sum_{i=1}^{k}2^{p-q-1}(\alpha^i - \alpha^{i-1})\binom{2n/2^{p-q}\alpha^i}{m/2^{p-q}\alpha^i} + \frac{1}{n-1}\left(n^2 + n(m+1) - \frac{m^2}{2} - 2\right)\binom{n}{m/2}\Bigg] \quad (32)$$

Example 4. Enantiomer-pairs and achiral skeletons of homopolysubstituted cyclohexatriacontane $C_{36}H_{72-m}X_m$. For $C_{36}H_{72-m}X_m$, let $n = 36 = 2^2 3^2$, $m = 12 = 2^2 3$, $p = q = 2$, $k = 1$, $F_{36} \cap F_{12} = (1,2,3,4,6,12)$, $\varphi(1) = 1$, $\varphi'(1) = 1$; $\varphi(3) = 2$, $\varphi'(3) = 2$; $\varphi(4) = 4$, $\varphi'(4) = 2$; $\varphi(6) = 6$, $\varphi'(6) = 2$; $\varphi(12) = 8$, $\varphi'(12) = 4$.

$$A_c(36,12) = \frac{1}{144}\Bigg[\binom{72}{12} + (3^1 - 3^{1-1})\binom{72/3}{12/3} + \frac{1}{36-1}\left(\frac{12^2}{2} - 36(12+1) + 1\right)\binom{36}{12/2} - (3^1 - 3^{1-1})\binom{72/6}{12/6}\Bigg] = 106\,689\,321\,808$$

$$A_{ac}(36,12) = \frac{1}{72}\Bigg[2^{2-0-1}\binom{72/4}{12/4} + 2(3^1 - 3^0)\binom{72/6}{12/6} + 2^{2-0-1}(3^1 - 3^0)\binom{72/12}{12/12} + \frac{1}{36-1}\left(36^2 + 36(12+1) - \frac{12^2}{2} - 2\right)\binom{36}{6}\Bigg] = 1\,306\,284$$

If $m_+ = 2^{p-q}$, then

$$A_c(2^p\alpha^j,2^{p-q}) = \frac{1}{4n}\left[\binom{2n}{m} + \frac{1}{n-1}\left(\frac{m^2}{2} - n(m+1) + 1\right)\binom{n}{m/2}\right] \quad (33)$$

$$A_{ac}(2^p\alpha^j,2^{p-q}) = \frac{1}{2n}\Bigg[\sum_{q=0}^{p-2}2^{p-q-1}\binom{2n/2^{p-q}}{m/2^{p-q}} + \frac{1}{n-1}\left(n^2 + n(m+1) - \frac{m^2}{2} - 2\right)\binom{n}{m/2}\Bigg] \quad (34)$$

Example 5. Enantiomer-pairs and achiral skeletons of $C_{36}H_{68}X_4$. Let $n = 36 = 2^2 3^2$, $m = 4 = 2^2$, $p = 2$, $q = 0$, $F_{36} \cap F_4 = (1,2,4)$, $\varphi(1) = 1$, $\varphi'(1) = 1$; $\varphi(4) = 4$, $\varphi'(4) = 2$.

$$A_c(36,4) = \frac{1}{144}\left[\binom{72}{4} + \frac{1}{36-1}\left(\frac{4^2}{2} - 36(4+1) + 1\right)\binom{36}{2}\right] = 7123$$

$$A_{ac}(36,4) = \frac{1}{72}\left[2^{2-0-1}\binom{72/4}{4/4} + \frac{1}{36-1}\left(36^2 + 36(4+1) - \frac{4^2}{2}\right)\binom{36}{2}\right] = 367$$

If the common factors between $2^p\alpha^j$ and m_+ are 1 or 2 i.e., $F_{2^p\alpha^j} \cap F_{m^+} = \{1\}$ or $\{1,2\}$ then

$$A_c(2^p\alpha^j,m_+) = \frac{1}{4n}\left[\binom{2n}{m} + \frac{1}{n-1}\left(\frac{m^2}{2} - n(m+1) + 1\right)\binom{n}{m/2}\right] \quad (35)$$

$$A_{ac}(2^p\alpha^j,m_+) = \frac{1}{2n}\left[\frac{1}{n-1}\left(n^2 + n(m+1) - \frac{m^2}{2} - 2\right)\binom{n}{m/2}\right] \quad (36)$$

Example 6. Enantiomer-pairs and achiral skeletons of $C_{36}H_{62}X_{10}$. Let $n = 36 = 2^2 3^2$, $m = 10$, $F_{36} \cap F_{10} = (1,2)$. According to eqs 35 and 36

$$A_c(36,10) = \frac{1}{144}\left[\binom{72}{10} + \frac{1}{36-1}\left(\frac{10^2}{2} - 36(10+1) + 1\right)\binom{36}{10/2}\right] = 3\,723\,668\,168$$

$$A_{ac}(36,10) = \frac{1}{72}\left[\frac{1}{36-1}\left(36^2 + 36(10+1) - \frac{10^2}{2} - 2\right)\binom{36}{10/2}\right] = 245\,344$$

The numbers obtained from this counting procedure are given for illustration in Table 2 for $n = 27$ and 36 and the degrees of substitution $0 \leq m \leq 9$.

4. CONCLUSION

As it is assumed to be known so far from the chemical literature[13] the series of monocyclic cycloalkanes C_nH_{2n} have ring size $3 \leq n \leq 288$. This wide range of ring sizes leads to distinct applications of Pólya's theorem. Pólya's classical procedure requires first to obtain the cycle index according to the parity and divisibility character of the ring size n and the transformation of the cycle index into a polynomial function of order $2n$ the coefficients of which are solutions of our enumeration problem. The emphasis in this paper has been to set up an algorithm that circumvents these difficulties and multiple calculations and allows a direct determination of enantiomer-pairs and achiral skeletons of stereo and position isomers of any homopolysubstituted monocyclic cycloalkane $C_nH_{2n-m}X_m$.

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