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ON THE ENUMERATION OF CHIRAL AND ACHIRAL SKELETONS OF POSITION ISOMERS OF HOMOSUBSTITUTED MONOCYCLIC CYCLOALKANES WITH A RING SIZE n (odd or even).

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Abstract: Topological and enantiomeric enumerations have been carried out for counting chiral and achiral skeletons of position isomers of homosubstituted derivatives of monocyclic cycloalkanes ($C_nH_{2n-k}X_k$) with a ring size n (odd)= α, α^2, $\alpha\beta$ and n (even) = 2α, $2\alpha^2$, 2^p, $2^p\alpha$ (where α and β are prime integers and the exponent $p \geq 2$). Applications are shown for α = 3,5,7 ; α^2 = 9; $\alpha\beta$ = 15 ; 2α = 6; $2\alpha^2$ = 18, 2^p = 4, 8,16 and $2^p\alpha$ = 12.

1.INTRODUCTION

Monocyclic cycloalkanes briefly called cycloalkanes or cyclanes are constituted by a chain of multiple CH_2 groups and their molecular formula is $(CH_2)_n$. One may find in the Chemical Abstracts Service (CAS) Ring System Handbook that the largest single ring system actually known in this family of chemical compounds is the cyclooctaoctacontadictane which contains 288 carbon atoms.[1] The results of conformational analysis have shown that $(CH_2)_n$ systems with a ring size $n \geq 4$ have a non planar cycle and the conformers arising from the non planarity are not separable.But if one considers the geometric structure of polysubstituted derivatives of monocyclic cycloalkanes one may find the coexistence of stereo and position isomerisms. HASSEL[2] in 1950 using the schemata of homodisubstituted derivatives of cyclohexane ($C_6H_{10}X_2$) has graphically shown that to solve this problem one may reason in terms of a planar cycle. We have used this basic assumption and the theorem of POLYA[3] to set up topological and enantiomeric enumerations for counting chiral and achiral skeletons of homosubstituted derivatives of monocyclic cycloalkanes ($C_nH_{2n-k}X_k$) with a ring size n (odd) = α, α^2, $\alpha\beta$ and n (even)= 2α, $2\alpha^2$, 2^p, $2^p\alpha$. The applications are shown for α =3,5, 7; α^2 = 9; $\alpha\beta$ = 15 ; 2α = 6; $2\alpha^2$ = 18, 2^p =4, 8,16 and $2^p\alpha$= 12.

2.FORMULATION OF THE PROBLEM

Let us represent in figure 1 a tridimensional skeleton of a monocyclic cycloalkane by a tridimensional graph or stereograph which contains one planar n-membered ring shaped as a regular polygon with n vertices of degree 4 (see black knots) joined by n horizontal edges. From each vertex of the regular n-gon are originated a pair of colinear and antiparallel edges perpendicular to the plane of the cycle and bearing at their respective extremity a vertex of degree 1(see blank knots).Let us collect all the vertices of the stereograph into two sets. Firstly the set G_4 which contains all unspecified vertices of degree 4 and secondly the set G_1 which contains 2n labeled vertices of degree 1 (or 2n substitution sites). Hence . $G_1=\{1, 1', 2, 2', 3, 3', \ldots, n, n'\}$.

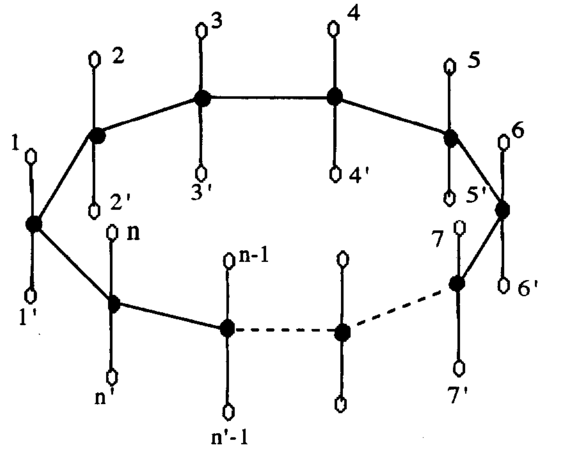

Figure 1 : Stereograph of a monocyclic cycloalkane $(CH2)_n$

To solve the problem of counting chiral and achiral skeletons of homosubstituted derivatives of monocyclic cycloalkanes ($C_nH_{2n-k}X_k$) we have considered the permutations of k substituents **X** among the 2n sites. This consideration allows to determine the cycle indices for topological and enantiomeric enumerations and to derive the corresponding generating functions. Any molecular system $(CH_2)_n$ represented by the stereograph shown in figure 1, belongs to the symmetry point group $\mathbf{D_{nh}}$ and its associated dihedral permutation group acting on G_1 is $\mathbf{D_n}$.According to POLYA's enumeration theorem the cycle index of a permutation group $\mathbf{D_n}$ with 4n elements is :

$$Z_t(D_n,G_1) = \frac{1}{4n}\left(\lambda_d S_d^{2n/d} + (n+1)S_2^n + nS_1^2S_2^{n-1}\right) \quad \text{if n (odd)} \tag{1a}$$

$$Z_t(D_n,G_1) = \frac{1}{4n}\left(\lambda_d S_d^{2n/d} + \frac{3}{2}(n+2)S_2^n + nS_1^4S_2^{n-2}\right) \quad \text{if n (even)} \tag{1b}$$

In the expressions 1a and 1b the symbols $(s_i)^j$ correspond to j permutation cycles of length i, the coefficient λ_d is the Euler-totient function[4] which represents the number of symmetry operations that generate 2n/d permutation cycles of length d among the 2n elements of G_1 and give rise to the term $(s_d)^{2n/d}$; and the summation is over all integers $d \neq 2$ that are factors of 2n.The symmetry operations that belong to the point group $\mathbf{D_{nh}}$ are : E, nC_2, $n\sigma_v$, σ_h, $(n-1)C_n^r$, $(n-1)S_n^{r'}$ when n is odd ,with the restrictions : $1 \leq r \leq n-1$ and $1 \leq r'(\text{odd}) \leq 2n-1$; and E, C_2, i, $n/2C'_2$, $n/2C''_2$, $n/2\sigma_v$, $n/2\sigma_d$, σ_h, $(n-2)C_n^r$, $(n-2)S_n^{r'}$ when n is even, with the restrictions : $1 \leq r \leq n-1$ and $1 \leq r'(\text{odd}) \leq n-1$.These symmetry operations are equivalent to permutations which contribute the terms to the cycle index as indicated in Table 1.

Table-1 : Contributions of Symmetry Operations to the Cycle Index.

n (odd)		n (even)	
symmetry operations	cycle index terms	symmetry operations	cycle index terms
$E=(C_n)^n$	$(s_1)^{2n}$	$E=(C_n)^n$	$(s_1)^{2n}$
σ_v	$(s_1)^2(s_1)^{n-1}$	σ_v	$(s_1)^4(s_1)^{n-2}$
σ_h, C'_2	$(s_2)^n$	$\sigma_h, \sigma_d, C_2, C'_2, C''_2$	$(s_2)^n$
C_n^r (r prime to n)	$(s_n)^2$	C_n^r (r prime to n)	$(s_n)^2$
$S_n^{r'}$ (r' prime to n)	(s_{2n})	$S_n^{r'}$ (r' prime to n)	(s_{2n})
$C_n^r=(C_{\alpha\beta})^{\alpha k'}=C_\beta^{k'}$	$(s_\beta)^{2\alpha}$ $(1\le k' \le\beta-1;\ a\le\beta)$	$C_n^r=(C_{\alpha\beta})^{\alpha k'}=C_\beta^{k'}$	$(s_\beta)^{2\alpha}$ $(1\le k'\le\beta-1)$ (β even)
$S_n^{r'}=(S_{\alpha\beta})^{\alpha k''}=S_\beta^{k''}$	$(s_{2\beta})^{\alpha}$ $(1\le k''(\text{odd})\le 2\beta-1)$	$S_n^{r'}=(S_{\alpha\beta})^{\alpha k''}=S_\beta^{k''}$	$(s_\beta)^{2\alpha}$ $(1\le k''(\text{odd})\le\beta-1)$ (β even)
		$S_n^{r'}=(S_{\alpha\beta})^{\alpha k''}=S_\beta^{k''}$	$(s_{2\beta})^{\alpha}$ $(1\le k''(\text{odd})\le 2\beta-1)$ (β odd)

Therefore taking into account the divisibility character of n and replacing in equation-1 the appropriate expressions of λ_d and $(s_d)^{2n/d}$ one may obtain the cycle index $Z_t(D_n,G_1)$ used for topological enumeration as indicated in equations 2 and 3.

$$Z_t(D_n,G_1)=\frac{1}{4n}\left[s_1^{2n}+(n+1)s_2^n+ns_1^2s_2^{n-1}+(n-1)(s_n^2+s_{2n})\right]\quad \text{if n is any prime integer} \tag{2a}$$

$$Z_t(D_n,G_1)=\frac{1}{4n}\Big[s_1^{2n}+(n+1)s_2^n+ns_1^2s_2^{n-1}+(\alpha-1)(s_\alpha^{2\beta}+s_{2\alpha}^{\beta})+(\beta-1)(s_\beta^{2\alpha}+s_{2\beta}^{\alpha})+ +(n-\alpha-\beta+1)(s_n^2+s_{2n})\Big]\quad \text{if } n=\alpha\beta \text{ and } \alpha<\beta \tag{2b}$$

$$Z_t(D_n,G_1)=\frac{1}{4n}\left[s_1^{2n}+(n+1)s_2^n+ns_1^2s_2^{n-1}+(\alpha-1)(s_\alpha^{2\alpha}+s_{2\alpha}^{\alpha})+(n-\alpha)(s_n^2+s_{2n})\right]\quad \text{if } n=\alpha^2 \tag{2c}$$

$$Z_t(D_n,G_1)=\frac{1}{4n}\left[s_1^{2n}+\frac{3}{2}(n+2)s_2^n+\frac{n}{2}s_1^4s_2^{n-2}+(\alpha-1)(s_\alpha^4+3s_n^2)\right]\quad \text{if } n=2\alpha \tag{3a}$$

$$Z_t(D_n,G_1)=\frac{1}{4n}\left[s_1^{2n}+\frac{3}{2}(n+2)s_2^n+\frac{n}{2}s_1^4s_2^{n-2}+(\alpha-1)(s_\alpha^{4\alpha}+3s_{2\alpha}^{2\alpha})+(\frac{n}{2}-\alpha)(s_{n/2}^4+3s_n^2)\right]\quad \text{if } n=2\alpha^2 \tag{3b}$$

$$Z_t(D_n,G_1)=\frac{1}{4n}\left[s_1^{2n}+\frac{3}{2}(n+2)s_2^n+\frac{n}{2}s_1^4s_2^{n-2}+\sum_{q=0}^{p-2}2^{(p-q)}s_{2^{(p-q)}}^{2^{(q+1)}}\right]\quad \text{if } n=2^p \tag{3c}$$

$$Z_t(D_n,G_1) = \frac{1}{4n}\Big[s_1^{2n} + \frac{3}{2}(n+2)s_2^n + \frac{n}{2}s_1^4 s_2^{n-2} + \sum_{q=0}^{p-2} 2^{(p-q)}[s_{2^{(p-q)}}^{\alpha.2^{(q+1)}} + (\alpha-1)s_{\alpha.2^{(p-q)}}^{2^{(q+1)}}] + (\alpha-1)(s_\alpha^{2^{(p+1)}} + 3s_{2\alpha}^{2^p})\Big] \quad \text{if } n = 2^p\alpha \tag{3d}$$

The method for finding the cycle index used for enantiomeric enumeration of graphs described by PARKS and HENDRICKSON[5] is comprised of four steps. The first step is to find the point group for a system considered as a tridimensional object. The second step is to eliminate the symmetry operations that do not produce whole body permutations. The third step is to find the contribution of each of the remaining operations to the cycle index making sure to eliminate equivalent permutations and the final step is to collect these contributions together into the cycle index. To demonstrate this we again take the cases where n (odd) = α, α^2,$\alpha\beta$ and n (even) = 2α, $2\alpha^2$, 2^p and $2^p\alpha$. The symmetry point group is as found above $\mathbf{D_{nh}}$ and the symmetry operations to be eliminated are: σ_h and $n\sigma_v$ when n is odd and σ_h, $n/2\sigma_v$, $n/2\sigma_d$ when n is even and all the improper rotations $S_n{}^{r'}$ in both cases. The permutation group for the system without those symmetry operations is also $\mathbf{D_n}$. The cycle index derived from this permutation group and used for enantiomeric enumeration is :

$$Z_e(D_n,G_1) = \frac{1}{2n}\left[s_1^{2n} + ns_2^n + (n-1)s_n^2\right] \quad \text{if n is any prime integer} \tag{4a}$$

$$Z_e(D_n,G_1) = \frac{1}{2n}\left[s_1^{2n} + ns_2^n + (\alpha-1)s_\alpha^{2\beta} + (\beta-1)s_\beta^{2\alpha} + (n-\alpha-\beta+1)s_n^2\right] \quad \text{if } n = \alpha\beta \text{ and } \alpha < \beta \tag{4b}$$

$$Z_e(D_n,G_1) = \frac{1}{2n}\left[s_1^{2n} + ns_2^n + (\alpha-1)s_\alpha^{2\alpha} + (n-\alpha)s_n^2\right] \quad \text{if } n = \alpha^2 \tag{4c}$$

$$Z_e(D_n,G_1) = \frac{1}{2n}\left[s_1^{2n} + (n+1)s_2^n + (\alpha-1)(s_\alpha^4 + s_n^2)\right] \quad \text{if } n = 2\alpha \tag{5a}$$

$$Z_e(D_n,G_1) = \frac{1}{2n}\left[s_1^{2n} + (n+1)s_2^n + (\alpha-1)[s_\alpha^{4\alpha} + s_{2\alpha}^{2\alpha} + (s_{n/2}^4 + s_n^2)]\right] \quad \text{if } n = 2\alpha^2 \tag{5b}$$

$$Z_e(D_n,G_1) = \frac{1}{2n}\left[s_1^{2n} + (n+1)s_2^n + \sum_{q=0}^{p-2} 2^{(p-q-1)} s_{2^{(p-q)}}^{2^{(q+1)}}\right] \quad \text{if } n = 2^p \tag{5c}$$

$$Z_e(D_n,G_1) = \frac{1}{2n}\Big[s_1^{2n} + (n+1)s_2^n + \sum_{q=0}^{p-2} 2^{(p-q-1)}[s_{2^{(p-q)}}^{\alpha.2^{(q+1)}} + (\alpha-1)s_{\alpha.2^{(p-q)}}^{2^{(q+1)}}] + (\alpha-1)(s_\alpha^{2^{(p+1)}} + s_{2\alpha}^{2^p})\Big] \quad \text{if } n = 2^p\alpha \tag{5d}$$

Let

$$g_t(k,x) = \sum_{k=0}^{2n} a_{k,t} x^k \tag{6}$$

and

$$g_e(k,x) = \sum_{k=0}^{2n} a_{k,e} x^k \tag{7}$$

be the generating functions for topological and enantiomeric enumerations respectively. These polynomials are obtained by replacing in the equations 2-5 each occurence $(s_i)^j$ by the term $(1+x^i)^j$ which is the figure counting series of j permutations of order i in the case of homogeneous substitution and by expanding the resulting algebraic expression. Therefore for a given ring size n and the degrees of substitution $0 \leq k \leq 2n$, one may obtain two associated generating functions the coefficients of which are defined hereafter.

Let $a_{k,c}$ and $a_{k,ac}$ be respectively the numbers of chiral and achiral skeletons of position isomers of the system $C_nH_{2n-k}X_k$. Given n and k and for any x^k, the coefficient $a_{k,t}$ in equation 6 is obtained by summing up the numbers $a_{k,c}$ and $a_{k,ac}$ while $a_{k,e}$ in equation 7 which takes into account the achiral forms and the duplication of chiral skeletons into enantiomeric pairs is also obtained by the addition of $a_{k,ac}$ and $2a_{k,c}$.Therefore:

$$a_{k,t} = a_{k,ac} + a_{k,c} \tag{8}$$

and

$$a_{k,e} = a_{k,ac} + 2a_{k,c} \tag{9}$$

The relations (8) and (9) induce two other generating functions :

$$g_c(k,x) = g_e(k,x) - g_t(k,x) = \sum_{k=0}^{2n} a_{k,c} x^k \tag{10}$$

$$g_{ac}(k,x) = g_t(k,x) - g_c(k,x) = \sum_{k=0}^{2n} a_{k,ac} x^k \tag{11}$$

which are respectively the counting polynomials indicating the number of chiral and achiral skeletons for each degree of homosubstitution in the system $C_nH_{2n-k}X_k$. One may notice that the coefficients of the generating functions 6), (7) ,(10) and (11) have respectively the following property :

$$a_k = a_{2n-k} \tag{12}$$

due to the complementarity of the substitution of degrees k and 2n-k .According to equation-12 the figure inventory is reduced to the computation of the coefficients a_k ranking from k=0 to n.The numbers of chiral and achiral position isomers determined from this counting procedure are given in Table 2 for n =3,4,5,6,7, 8, 9, 12, 15,16 and 18.The significance of these results is as follows : if we consider for instance the case of chlorocyclohexanes ($C_6H_{12-k}Cl_k$), for k = 2, $a_{k,t} = 7$ $a_{k,c} = 2$ and $a_{k,ac} = 5$ (see Table 2) ; these figures mean that among the seven distinct skeletons of position isomers of dichlorocyclohexane ($C_6H_{10}Cl_2$), two are

Table 2.The numbers $a_{k,c}$, $a_{k,ac}$, $a_{k,t}$ and $a_{k,e}$ of skeletons of position isomers of homosubstituted derivatives of monocyclic cycloalkanes ($C_nH_{2n-k}X_k$) with a ring size n=3,4,5,6,7,8,9,12,15,16 and 18.

n	3				4				5			
k	$a_{k,c}$	$a_{k,ac}$	$a_{k,t}$	$a_{k,e}$	$a_{k,c}$	$a_{k,ac}$	$a_{k,t}$	$a_{k,e}$	$a_{k,c}$	$a_{k,ac}$	$a_{k,t}$	$a_{k,e}$
0	0	1	1	1	0	1	1	1	0	1	1	1
1	0	1	1	1	0	1	1	1	0	1	1	1
2	1	2	3	4	1	4	5	6	2	3	5	7
3	1	2	3	4	2	3	5	7	4	4	8	12
4					3	7	10	13	10	6	16	26
5									10	6	16	26

n	6				7				8			
k	$a_{k,c}$	$a_{k,ac}$	$a_{k,t}$	$a_{k,e}$	$a_{k,c}$	$a_{k,ac}$	$a_{k,t}$	$a_{k,e}$	$a_{k,c}$	$a_{k,ac}$	$a_{k,t}$	$a_{k,e}$
0	0	1	1	1	0	1	1	1	0	1	1	1
1	0	1	1	1	0	1	1	1	0	1	1	1
2	2	5	7	9	3	4	7	10	3	6	9	12
3	7	5	12	19	10	6	16	26	14	7	21	35
4	18	14	32	50	35	12	47	82	53	24	77	130
5	28	10	38	66	64	15	79	143	126	21	147	273
6	35	20	55	90	106	20	126	232	241	50	291	532
7					113	20	133	246	340	35	375	715
8									390	65	455	845

n	9				12				15			
k	$a_{k,c}$	$a_{k,ac}$	$a_{k,t}$	$a_{k,e}$	$a_{k,c}$	$a_{k,ac}$	$a_{k,t}$	$a_{k,e}$	$a_{k,c}$	$a_{k,ac}$	$a_{k,t}$	$a_{k,e}$
0	0	1	1	1	0	1	1	1	0	1	1	1
1	0	1	1	1	0	1	1	1	0	1	1	1
2	4	5	9	13	5	8	13	18	7	8	15	22
3	19	8	27	46	37	11	48	85	61	14	75	136
4	84	20	104	188	215	49	264	479	455	56	511	966
5	226	24	250	476	858	55	913	1771	2330	91	2421	4751
6	514	47	561	1075	2778	174	2952	5730	9890	243	10133	20023
7	856	56	912	1768	7128	165	7293	14421	33748	364	34112	67860
8	1212	70	1282	2494	15252	410	15662	30914	97526	728	98254	195780
9	1317	70	1387	2704	27077	330	27407	54484	237956	1001	238957	476913
10					40738	672	41410	82148	500701	1602	502303	1003004
11					51772	462	52234	104006	909454	2002	911456	1820910
12					56194	794	56988	113182	1441477	2670	1444147	2885624
13									1994496	3003	1997499	3991995
14									2423604	3432	2427036	4850640
15									2583586	3432	2587018	5170604

Table 2. (Continued)

n	16				18			
k	$a_{k,c}$	$a_{k,ac}$	$a_{k,t}$	$a_{k,e}$	$a_{k,c}$	$a_{k,ac}$	$a_{k,t}$	$a_{k,e}$
0	0	1	1	1	0	1	1	1
1	0	1	1	1	0	1	1	1
2	7	10	17	24	8	11	19	27
3	70	15	85	155	91	17	108	199
4	553	82	635	1188	808	101	909	1717
5	3094	105	3199	6293	5168	136	5304	10472
6	14105	406	14511	28616	26983	574	27557	54540
7	52364	455	52819	105183	115600	680	116280	231880
8	164138	1390	165528	329666	419690	2260	422220	842180
9	437580	1365	438945	876525	1306362	2380	1308742	2615104
10	1007435	3458	1010893	2018328	3529344	6580	3535924	7065268
11	2014506	3003	2017509	4032015	8341424	6188	8347612	16689036
12	3526887	6510	3533397	7060284	17381984	14683	17396667	34778651
13	5425210	5005	5430215	10855425	32088112	12376	32100488	64188600
14	7364501	9438	7373939	14738440	52721904	25688	52747592	105469496
15	8836200	6435	8842635	17678835	77322278	19448	77341726	154664004
16	9389964	10677	9400641	18790605	101491896	35750	101527646	203019542
17					119397520	24310	119421830	238819350
18					126036461	39884	126076345	252112806

constitutionally chiral while the other five are constitutionally achiral and the integer value $a_{k,e} = 9$ represents the sum of enantiomeric pairs and achiral forms. But as no consideration is made for ring deformations in this pattern inventory, one must recall in mind that each skeleton of these position isomers gives rise to numerous conformers.In comparison with the chemical literature data our numbers $a_{k,t}$,$a_{k,e}$ and $a_{k,c}$ reported on the enumeration of position isomers of homosubstituted derivatives of cyclopropane, cyclobutane, cyclopentane and cyclohexane (see Table 2) are in agreement with the numerical values of the coefficients of the counting polynomials obtained earlier by BALABAN[6] in the same series of chemical compounds.

3.CONCLUSION

The focus of this paper has been to develop a general method for counting chiral and achiral skeletons of position isomers in the series of homopolysubstituted monocyclic cycloalkanes ($C_nH_{2n-k}X_k$) with a ring size n factorizable into the form n(odd)=$\alpha,\alpha^2,\alpha\beta$ and n (even) =$2\alpha,2\alpha^2,2P,2P\alpha$. The counting procedure directly and simply gives the numbers of chiral and achiral skeletons that match the numbers obtained by the empirical method of generation of polysubstituted skeletons . In the latter case, one must check among numerous skeletons the non redundancy of structures and then undertake the difficult task of identification of enantiomeric pairs and achiral forms.

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