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Isomers and Chemical Graphs of Substituted Cycloalkanes

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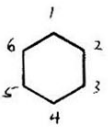
Abstract

Using Pólya's theorem and point group symmetry operations, procedures for determining the number of stereoisomers, enantiomers, and positional isomers of substituted cycloalkanes are summarized. A simple noncomputer method for determining the number of geometrical isomers and enantiomers of polysubstituted cycloalkanes having an identical substituent on each ring carbon is presented for the first time.

A very common stereochemical question posed by numerous organic chemistry textbooks is one requesting the student reader to enumerate all the possible stereoisomers of benzenehexachloride or inositol which possess seven geometrical isomers and one d,ℓ-pair. Although graph theoretical methods for enumerating the structural isomers of cycloalkanes having various degrees of substitution have been reported,[1-4] this author is unaware of any publication that specifically solves the above problem by graph theoretical methods. Herein is reported the graph theoretical solution of this very common student stereochemical problem.[5]

Table 1. All the Characteristic Symmetries of Benzene.

Structure	Permutations	Operations	Cycles
	(1)(2)(3)(4)(5)(6)	Identity	$j_1=6$
	(123456)	C_6-rotation	$j_6=1$
	(135)(246)	C_3-rotation	$j_3=2$
	(14)(25)(36)	C_2-rotation	$j_2=3$
	(153)(264)	C_3-rotation	$j_3=2$
	(165432)	C_6-rotation	$j_6=1$
	(1)(4)(26)(35)	C_2-rotation	$j_1=2$, $j_2=2$
	(2)(5)(13)(46)	C_2-rotation	$j_1=2$, $j_2=2$
	(3)(6)(15)(24)	C_2-rotation	$j_1=2$, $j_2=2$
	(12)(36)(45)	C_2-rotation	$j_2=3$
	(23)(14)(56)	C_2-rotation	$j_2=3$
	(34)(25)(16)	C_2-rotation	$j_2=3$

Cycle Index = $Z(D_6) = 1/12[S_1^6+2S_6+2S_3^2+S_2^3+3S_1^2S_2^2+3S_2^3]$

Configuration Counting Series = $Z(D_6, 1+x) = 1+x+3x^2+3x^3+3x^4+x^5+x^6$

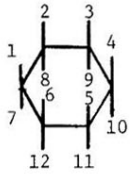
Pólya's Theorem employs the following cycle index of A which gives the average of terms over the whole permutation group

$$Z(A) = \frac{1}{|A|} \sum_{\alpha \in A} \prod_r S_r^{\,j_r(\alpha)} \qquad (1)$$

For benzene, Equation (1) translates to

$$Z(D_6) = \frac{1}{12}\,[S_1{}^6 + 2S_6 + 2S_3{}^2 + S_2{}^3 + 3S_1{}^2S_2 + 3S_2{}^3] \qquad (2)$$

Table 2. Enumeration of Polychlorinated Cyclohexanes.

Structure	Permutations	Operation	Cycles
	(1)(2)(3)(4)(5)(6)(7)(8)(9)(10)(11)(12)	Identity	$j_1 = 12$
	(1 2 3 4 5 6)(7 8 9 10 11 12)	C_6-rotation	$j_6 = 2$
	(1 3 5)(2 4 6)(7 9 11)(8 10 12)	C_3-rotation	$j_3 = 4$
	(1 4)(2 6)(3 5)(7 10)(8 12)(9 11)	C_2-rotation	$j_2 = 6$
	(1 5 3)(6 4 2)(7 11 9)(12 10 8)	C_3-rotation	$j_3 = 4$
	(1 6 5 4 3 2)(7 12 11 10 9 8)	C_6-rotation	$j_6 = 2$
	((1 7)(4 10)(2 12)(6 8)(3 11)(5 9)	C_2-rotation	$j_2 = 6$
	(2 7)(1 8)(3 12)(6 9)(4 11)(5 10)	C_2-rotation	$j_2 = 6$
	(2 8)(3 7)(1 9)(4 12)(6 10)(5 11)	C_2-rotation	$j_2 = 6$
	(2 9)(3 8)(1 10)(4 7)(5 12)(6 11)	C_2-rotation	$j_2 = 6$
	(3 9)(4 8)(2 10)(1 11)(5 7)(6 12)	C_2-rotation	$j_2 = 6$
	(3 10)(4 9)(5 8)(2 11)(1 12)(6 7)	C_2-rotation	$j_2 = 6$

$$\text{Cycle Index} = Z(D_{6_h}) = \frac{1}{12}\left[S_1^{12} + 2S_6^2 + 2S_3^4 + 7S_2^6\right]$$

$$\text{Configuration Counting Series} = C(x) = Z(D_{6_h}, 1 + x) =$$

$$1 + x + 9x^2 + 19x^3 + 50x^4 + 66x^5 + 90x^6 + 66x^7 + 50x^8 + 19x^9 + 9x^{10} + x^{11} + x^{12}$$

Pólya's theorem states that the generating function (configuration counting series) C(x) which enumerates equivalence classes of function determined by the permutation group A is obtained by substituting the figure counting series c(x) = 1 + x (where for polychlorobenzenes the 1 means no chlorine and the x means one chlorine may be present at a ring position) into the cycle index Z(x) as follows. Each variable S_r in Z(A) is replaced by $c(x^r)$ so that C(x) = Z[A,c(x)].

Thus Equation (2) becomes

$$C(x) = Z(D_6,\ 1 + x) = \frac{1}{12}\ [(1 + x)^6 + 2(1 + x^6) + 2(1 + x^3)^2 + (1 + x^2)^3 + 3(1 + x)^2(1 + x^2)^2 + 3(1 + x^2)^3] = 1 + x + 3x^2 + 3x^3 + 3x^4 + x^5 + x^6 \qquad (3)$$

of which the coefficients give the number isomers of the various chlorobenzenes (Table 1). Comparing this result with that of the nonsymmetrical case [$Z(S_1) = {S_1}^6$], one can see that Equation (2) contains five additional terms as a result of symmetry which because of averaging produces reduced coefficients and thereby enumerates a lower number of equivalent classes. From the coefficients of Equation (3), one may deduce that for benzene there is 1 isomer having no or one chlorine substituent, 3 isomers having two, three or four substituted chlorine atoms, and 1 isomer for either five or six substituted chlorine atoms. Note that the configuration counting series has end symmetry since the number of isomers with one chlorine substitutent and five hydrogens is the same as the number of isomers with five chlorine substituents and one hydrogen atom (which is one), etc. This solution for the number of isomers of poly-

chlorobenzene also gives the number of different six-beaded necklaces having only two possible colors.

The enumeration of polychlorinated cyclohexanes is given in Table 2. Polychlorinated cyclohexane isomer enumeration is illustrative of a system which can possess stereoisomers; reflection permutations must be excluded. Since two chlorine atoms can be substituted on a single ring carbon atom, there are 90 possible isomers just for hexachlorocyclohexane. A chemically germane but restricted case is the determination of the number of isomers of hexachlorocyclohexane (i.e., benzenehexachloride) where each ring carbon atom is guaranteed to contain only one chlorine substituent. The model used to obtain the solution to this latter system is as follows. Presume that the benzenehexachloride molecules are being viewed from a top view as shown in Figure 1. The first structure in Figure 1 has all the chlorine atoms on the same side which is located furthest from view, the second structure has one chlorine located on the top and the rest below, the third structure has two chlorine atoms on top and the rest below, and so forth. The solution of this model is precisely the same solution as for polychlorinated benzenes in Table 1. Thus all the geometrical isomers are given by the first four terms in the configuration counting series of Table 1 since this model has end symmetry (e.g., in having all the Cℓ atoms on the same side, they can either be all on the bottom or all on top which are equivalent). However, one of these geometrical isomers is also one enantiomer of a d,ℓ-pair. If the lower symmetry group classification (C_6) that excludes the C_2-axes of rotation which put both enantiomers into same class is used one obtains Table 3. Since the C_n group classification gives all the stereoisomers, both

Figure 1. Top View of Various Isomers of Benzenehexachloride (1,2,3,4,5,6-hexachlorocyclohexane).

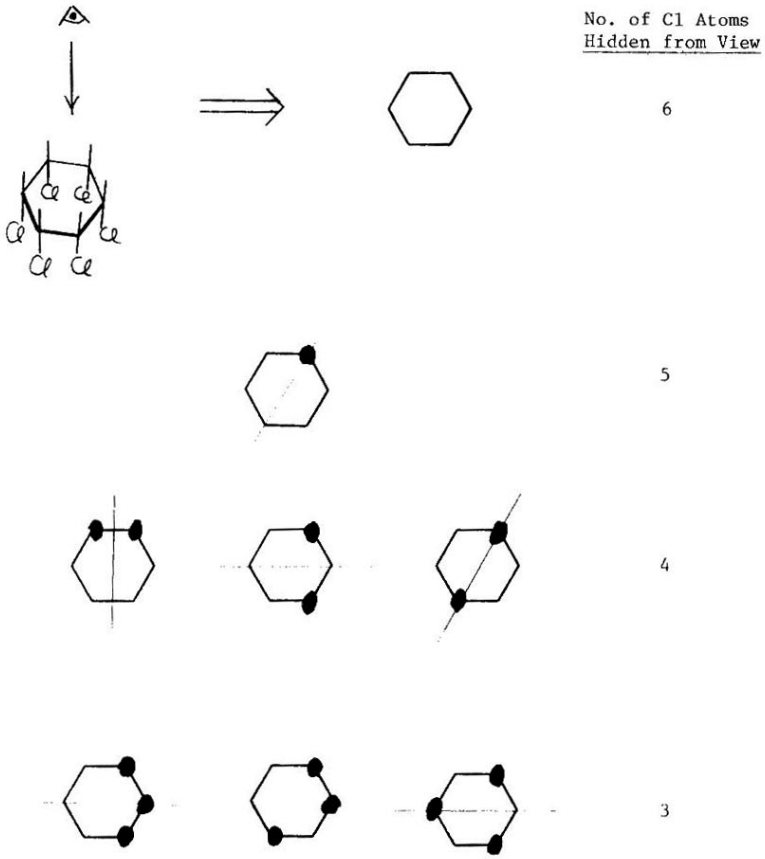
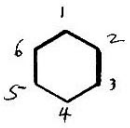


Table 3. C_6 Symmetries

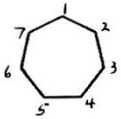
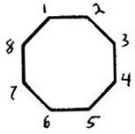
Structure	Permutations	Operations	Cycles
	(1)(2)(3)(4)(5)(6)	Identity	$j_1=6$
	(123456)	C_6-rotation	$j_6=1$
	(135)(246)	C_3-rotation	$j_3=2$
	(14)(25)(36)	C_2-rotation	$j_2=3$
	(153)(264)	C_3-rotation	$j_3=2$
	(165432)	C_6-rotation	$j_6=1$

Cycle Index = $Z(C_6) = 1/6[S_1^6+2S_6+2S_3^2+S_2^3]$

Configuration Counting Series = $Z(C_6,1+x) = 1+x+3x^2+4x^3+3x^4+x^5+x^6$

geometrical and optical isomers, and the D_n group classification gives only the geometrical isomers, subtracting the coefficients of the first terms in the configuration counting series from the D_n symmetry group from those obtained from the C_n symmetry group gives the number of d,ℓ-pairs for the corresponding cycloalkane having identical substituents on each ring carbon. Table 4 summarizes these results for several poly-substituted cycloalkanes of varying ring size from three to eight. From Table 4, one can see that for identically 1,2,3-trisubstituted cyclo-propane, 1,2,3,4-tetrasubstituted cyclobutane, and 1,2,3,4,5-pentasub-stituted cyclopentane no optical isomers are possible. Also, 1,2,3,4,5,6-hexachlorocyclohexane (or other identically 1,2,3,4,5,6-hexasubstituted cyclohexanes) exhibits optical isomerization only for one geometrical

Table 4. Computation of d,ℓ-Pairs of Cycloalkanes Having one Identical Substituent on Each Ring Carbon.

Structure	Configuration Counting Series	No. of d,ℓ-Pairs
	$Z(C_3,1+x) = 1+x+x^2+x^3$ $Z(D_3,1+x) = 1+x+x^2+x^3$	0
	$Z(C_4,1+x) = 1+x+2x^2+x^3+x^4$ $Z(D_4,1+x) = 1+x+2x^2+x^3+x^4$	0
	$Z(C_5,1+x) = 1+x+2x^2+2x^3+x^4+x^5$ $Z(D_5,1+x) = 1+x+2x^2+2x^3+x^4+x^5$	0
	$Z(C_6,1+x) = 1+x+3x^2+4x^3+3x^4+x^5+x^6$ $Z(D_6,1+x) = 1+x+3x^2+3x^3+3x^4+x^5+x^6$	1
	$Z(C_7,1+x) = 1+x+3x^2+5x^3+5x^4+3x^5+x^6+x^7$ $Z(D_7,1+x) = 1+x+3x^2+4x^3+4x^4+3x^5+x^6+x^7$	1
	$Z(C_8,1+x) = 1+x+4x^2+7x^3+10x^4+7x^5+4x^6+x^7+x^8$ $Z(D_8,1+x) = 1+x+4x^2+5x^3+8x^4+5x^5+4x^6+x^7+x^8$	4

isomer in which three chlorine substituents are above and three chlorine substituents are below the plane of the cyclohexane ring; Figure 1 shows that for these geometrical isomers there is at least one vertical plane-of-symmetry (e.g., parallel to the line shown) except for one of the geometrical isomers having three chlorine atoms located below (out-of-view) and three chlorine atoms located above (in-view) the cyclohexane ring plane. Similarly 1,2,3,4,5,6,7-heptachlorocycloheptane has only one optical pair of isomers for the case where three chlorine atoms are above and four chlorine atoms are below (or equivalently for the case where four chlorine atoms above and three chlorine atoms below) the ring plane. 1,2,3,4,5,6,7,8-Octachlorocyclooctane has two d,ℓ-pairs of isomers for the set of geometrical isomers having three chlorine substituents above (or below) the ring plane and two d,ℓ-pairs of isomers for the set of geometrical isomers having four chlorine substituents above (or/and below) the ring plane, i.e., a total of four d,ℓ-pairs of isomers.

Conclusion

A method for determining stereoisomers, geometrical isomers, and positional isomers has been reviewed. An adaptation of the method for enumerating the number of possible necklaces having two different colored beads allows one to compute the number optical isomers of cycloalkanes having identical substituents on each ring carbon; thus, $Z(C_6, 1+x)-Z(D_6, 1+x)$ = No. of d,ℓ-pairs. These procedures are useful in teaching students how to solve stereoisomer problems that traditionally have been solved by trial and error.

References

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2. A. T. Balaban, *Croat. Chem. Acta, 51,* 35 (1978).
3. B. Alspach and S. Aronoff, *Can. J. Chem., 55,* 2773 (1977).
4. T. L. Hill, *J. Chem. Phys., 11,* 294 (1943).
5. A preliminary account of this work was presented at the 17th Midwest Regional Meeting, American Chemical Society, Columbia, MO, Nov. 5-6, 1981, Abstract No. 648.