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Chemical Graphs. XXXII.[1] Constitutional and Steric Isomers of Substituted Cycloalkanes

A. T. Balaban

Department of Organic Chemistry, The Polytechnic, Bucharest, Roumania

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Pólya's theorem was applied to cycloalkanes in order to obtain the numbers of stereoisomers, enantiomers, and constitutional isomers of substituted derivatives. Whereas the stereoisomers result from the actual constitutional graphs of the flexible cycloalkanes, special graphs must be devised for ignoring stereoisomerism or enantiomerism.

INTRODUCTION

Preceding papers in this series,[2–5] as well as other publications[6–10] were concerned with calculating the numbers of isomers of chemical compounds by making use of Pólya's counting theorem (Hauptsatz).[11–15]

It was shown[16] that the numbers of stereoisomers in cycloalkanes where one or more hydrogen atoms had been substituted can be calculated by means of Pólya's theorem, as applied to a time-averaged conformation of the flexible cycloalkane, i. e. to a planar conformation.

In a previous paper,[3] it was demonstrated for adamantane that Pólya's theorem can be applied to constitional graphs which had been suitably modified in order to ignore enantiomerism (affording only the numbers of constitutional and *cis-trans* isomers), or to ignore all stereoisomers (affordings therefore only the numbers of constitutional isomers). These modified graphs need not respect the normal valency rules. The present paper develops a similar approach for cycloalkanes.

PÓLYA'S COUNTING THEOREM

As it is assumed to be known (otherwise the literature[2–16] should be consulted), the application of Pólya's theorem requires all symmetry operations on the chemical graph to be expressed as a cycle index:

$$Z(A) = \frac{1}{|A|} \sum_{\alpha \in A} \prod_{k} y_k^{i} \qquad (1)$$

where k indicates a k-nary axis, and $|A|$ is the order of the symmetry group.

The numbers of isomers result as a »configuration counting series« $Z(1+x)$ by substituting the »figure counting series«

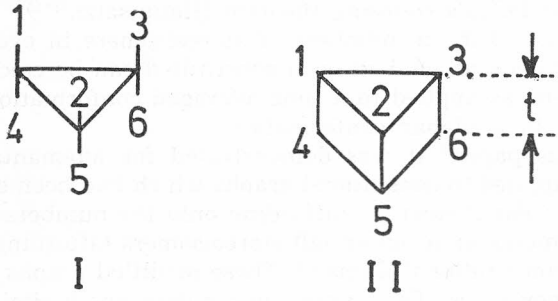
$$y_k = 1 + x^k \qquad (2)$$

into the cycle index, and developing the polynomial in x: the coefficient of

x^m gives the numbers of isomers where m sites were replaced by the same type of substituents (labels). By appropriate modification of the figure counting series y_k, i. e. by adding various terms to expression (2), it is possible to take into account various other, more complicated, modes of substitution,[5] e. g. with several types of substituents (labels). In the present paper, only expression (2) will be used, however.

ALL ISOMERS (INCLUDING STEREOISOMERS) OF CYCLOALKANES

In agreement with literature data,[16] the chemical graph whose cycle index is to be taken as a basis for applying Pólya's theorem is the planar cycloalkane itself C_nH_{2n}. The $2n$ hydrogen atoms which are to be partly substituted may be imagined as the vertices of an orthogonal prism with regular n-gons as the parallel faces. The symmetry operations involve 1-, 2-, and n-nary axes when n is a prime number, as well as further axes when n is not prime. The number of symmetry operations is easily found by visual inspection of the molecular graph: for cyclopropane, this graph is I and is equivalent to the trigonal prism II. A more rigorous treatment is by writing all permutations as indicated in the first part of Table I; this immediately gives the cycle index presented in Table II, and by substituting the figure counting series (2), one obtains the configuration counting series presented in Table II. The four di- and tri-substituted stereoisomers of cyclopropane are depicted in the upper row of Figure 1.



A similar procedure gives the numbers of stereoisomers for cyclobutane (Table II and upper row of Figure), as well as for cyclopentane and cyclohexane (Table II).

GEOMETRICAL ISOMERS OF CYCLOALKANES

In order to leave out enantiomerism, i. e. to count only geometrical isomers, one has to start from a graph with appropriate symmetry: this is the limit of graph II when the prism thickness t tends to zero. The second part of Table I illustrates the resulting symmetry operations for cyclopropane, and Table II gives the cycle indices and the configuration counting series for cyclopropane through cyclohexane. The second row of Figures 1 and 2 illustrates the numbers of geometrical isomers for cyclopropane and cyclobutane, respectively.

By substracting the configuration counting series presented in Tables II and III for corresponding cycloalkanes, one finds the configuration counting

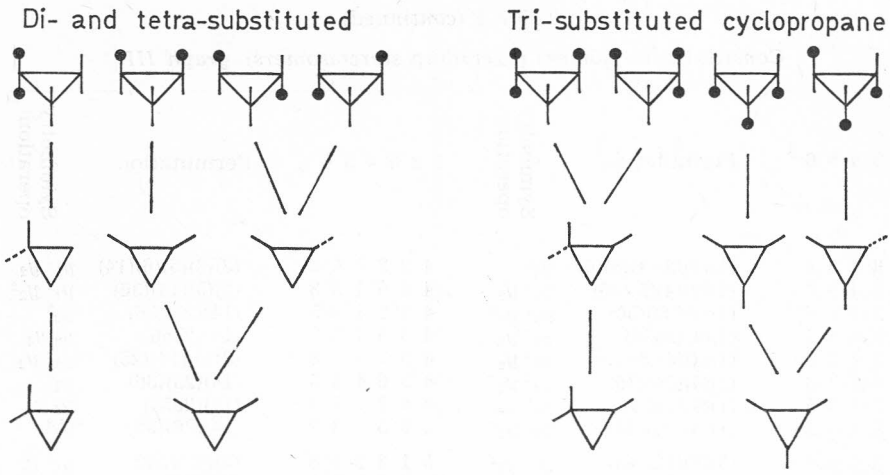


Figure 1. Isomers of substituted cyclopropanes: upper row, all stereoisomers (including enantiomers); middle row, geometrical isomers (ignoring enantiomerism); lower row, constitutional isomers (ignoring stereoisomers).

TABLE I

Permutations and Corresponding Symmetry Operations for the Molecular Graphs Associated with Cyclopropane

Stereoisomers (including enantiomers), graphs I, or II with finite t:

1 2 3 4 5 6	Permutation	Symmetry operation
1 2 3 4 5 6	(1)(2)(3)(4)(5)(6)	y_1^6
2 3 1 5 6 4	(123)(456)	y_3^2
3 1 2 6 4 5	(132)(465)	y_3^2
4 6 5 1 3 2	(14)(26)(53)	y_2^3
5 4 6 2 1 3	(15)(24)(36)	y_2^3
6 5 4 3 2 1	(16)(25)(34)	y_2^3

Geometrical isomers (excluding enantiomerism), graph II with $t \to 0$:

1 2 3 4 5 6	Permutation	Symmetry operation
1 2 3 4 5 6	(1)(2)(3)(4)(5)(6)	y_1^6
1 3 2 4 6 5	(1)(4)(23)(56)	$y_1^2 y_2^2$
2 3 1 5 6 4	(123)(456)	y_3^2
2 1 3 5 4 6	(3)(6)(12)(45)	$y_1^2 y_2^2$
3 2 1 6 5 4	(2)(5)(13)(46)	$y_1^2 y_2^2$
3 1 2 6 4 5	(132)(465)	y_3^2
4 5 6 1 2 3	(14)(25)(36)	y_2^3
4 6 5 1 3 2	(14)(26)(35)	y_2^3
5 4 6 2 1 3	(15)(24)(36)	y_2^3
5 6 4 2 3 1	(153426)	y_6
6 4 5 3 1 2	(162435)	y_6
6 5 4 3 2 1	(16)(25)(34)	y_2^3

Table I (continued)

Constitutional isomers (excluding stereoisomers), graph III:

1 2 3 4 5 6	Permutation	Symmetry operation	1 2 3 4 5 6	Permutation	Symmetry operation
1 2 3 4 5 6	(1)(2)(3)(4)(5)(6)	y_1^6	4 2 3 1 5 6	(2)(3)(5)(6)(14)	$y_1^4 y_2$
1 2 6 4 5 3	(1)(2)(4)(5)(36)	$y_1^4 y_2$	4 2 6 1 5 3	(2)(5)(14)(36)	$y_1^2 y_2^2$
1 3 2 4 6 5	(1)(4)(23)(56)	$y_1^2 y_2^2$	4 3 2 1 6 5	(14)(23)(56)	y_2^3
1 3 5 4 6 2	(1)(4)(2356)	$y_1^2 y_4$	4 3 5 1 6 2	(14)(2356)	$y_2 y_4$
1 5 3 4 2 6	(1)(3)(4)(6)(25)	$y_1^4 y_2$	4 5 3 1 2 6	(3)(6)(14)(25)	$y_1^2 y_2^2$
1 5 6 4 2 3	(1)(4)(25)(36)	$y_1^2 y_2^2$	4 5 6 1 2 3	(14)(25)(36)	y_2^3
1 6 2 4 3 5	(1)(4)(2653)	$y_1^2 y_4$	4 6 2 1 3 5	(14)(2653)	$y_2 y_4$
1 6 5 4 3 2	(1)(4)(26)(35)	$y_1^2 y_2^2$	4 6 5 1 3 2	(14)(26)(35)	y_2^3
2 1 3 5 4 6	(3)(6)(12)(45)	$y_1^2 y_2^2$	5 1 3 2 4 6	(3)(6)(1542)	$y_1^2 y_4$
2 1 6 5 4 3	(12)(36)(45)	y_3^2	5 1 6 2 4 3	(36)(1542)	$y_2 y_4$
2 3 1 5 6 4	(123)(456)	y_3^2	5 3 1 2 6 4	(156423)	y_6
2 3 4 5 6 1	(123456)	y_6	5 3 4 2 6 1	(156)(234)	y_3^2
2 4 3 5 1 6	(3)(6)(1245)	$y_1^2 y_4$	5 4 3 2 1 6	(3)(6)(15)(24)	$y_1^2 y_2^2$
2 4 6 5 1 3	(36)(1245)	$y_2 y_4$	5 4 6 2 1 3	(15)(24)(36)	y_2^3
2 6 4 5 3 1	(126)(345)	y_3^2	5 6 1 2 3 4	(153)(264)	y_3^2
2 6 1 5 3 4	(126543)	y_6	5 6 4 2 3 1	(153426)	y_6
3 1 2 6 4 5	(132)(465)	y_3^2	6 1 2 3 4 5	(165432)	y_6
3 1 5 6 4 2	(135462)	y_6	6 1 5 3 4 2	(162)(354)	y_3^2
3 2 1 6 5 4	(2)(5)(13)(46)	$y_1^2 y_2^2$	6 2 1 3 5 4	(2)(5)(1643)	$y_1^2 y_4$
3 2 4 6 5 1	(2)(5)(1346)	$y_1^2 y_4$	6 2 4 3 5 1	(2)(5)(16)(34)	$y_1^2 y_2^2$
3 4 2 6 1 5	(132465)	y_6	6 4 2 3 1 5	(165)(243)	y_3^2
3 4 5 6 1 2	(135)(246)	y_3^2	6 4 5 3 1 2	(162435)	y_6
3 5 1 6 2 4	(13)(25)(46)	y_2^3	6 5 1 3 2 4	(25)(1643)	$y_2 y_4$
3 5 4 6 2 1	(25)(1346)	$y_2 y_4$	6 5 4 3 2 1	(16)(25)(34)	y_2^3

TABLE II

Cycle Indices Z and Configuration Counting Series Z(1 + x) for the Numbers of All Isomers (Including Stereoisomers) of Cycloalkanes where Hydrogens are Substituted by One Type of Substituent

Cyclopropane:

$$Z = (y_1^6 + 2y_3^2 + 3y_2^3)/6$$

$$Z(1 + x) = 1 + x + 4x^2 + 4x^3 + 4x^4 + x^5 + x^6$$

Cyclobutane:

$$Z = (y_1^8 + 2y_4^2 + 5y_2^4)/8$$

$$Z(1 + x) = 1 + x + 6x^2 + 7x^3 + 13x^4 + 7x^5 + 6x^6 + x^7 + x^8$$

Cyclopentane:

$$Z = (y_1^{10} + 4y_5^2 + 5y_2^5)/10$$

$$Z(1 + x) = 1 + x + 7x^2 + 12x^3 + 26x^4 + 26x^5 + 26x^6 + 12x^7 + 7x^8 + x^9 + x^{10}$$

Cyclohexane:

$$Z = (y_1^{12} + 2y_6^2 + 2y_3^4 + 7y_2^6)/12$$

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

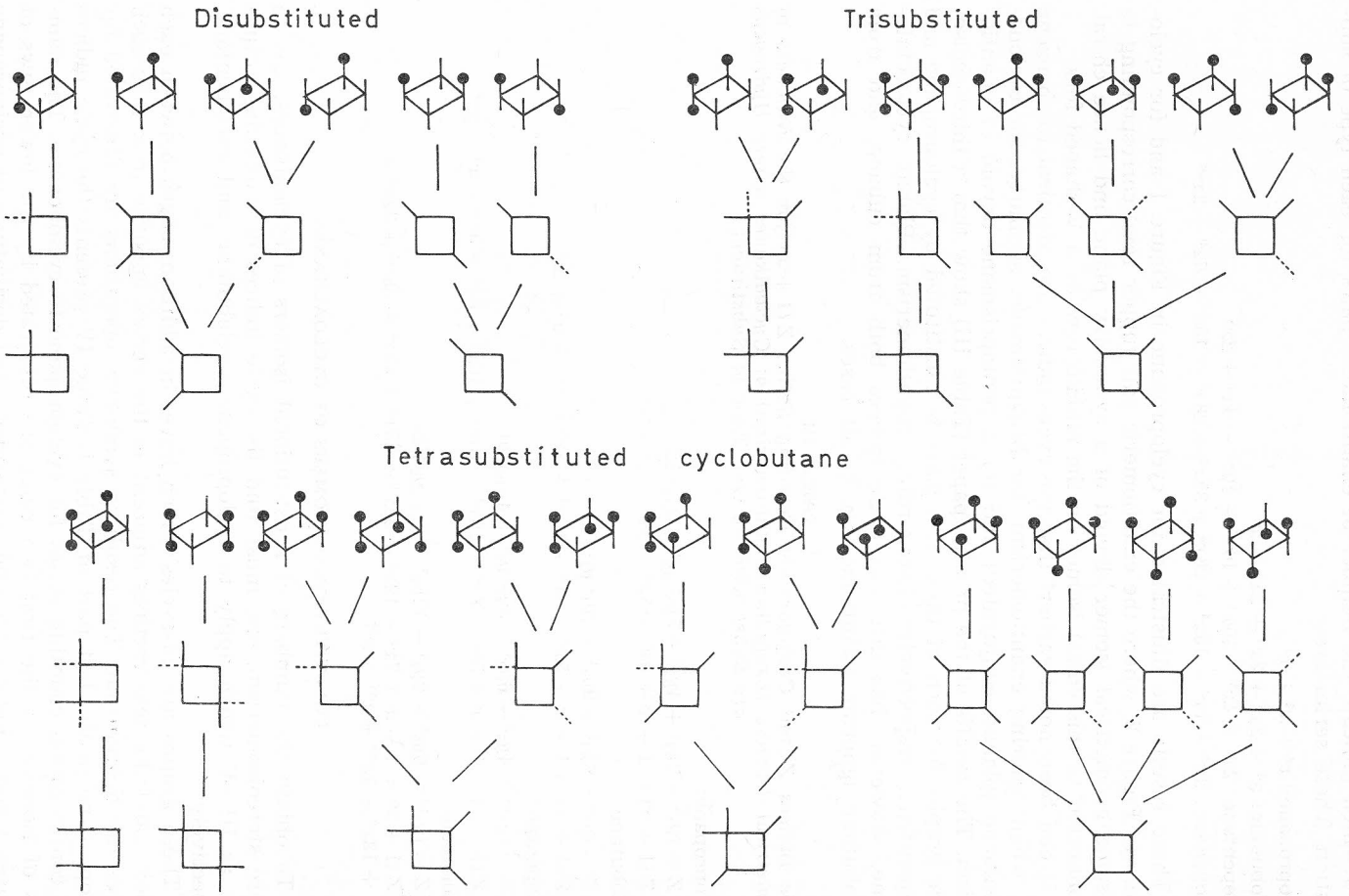


Figure 2. Isomers of substituted cyclobutanes: upper row, all stereoisomers (including enantiomers); middle row, geometrical isomers (ignoring enantiomerism); lower row, constitutional isomers (ignoring stereoisomerism).

series which indicate the number of enantiomeric pairs for each type of substitution. These series are:

Cyclopropane: $x^2 + x^3 + x^4$
Cyclobutane: $x^2 + 2x^3 + 3x^4 + 2x^5 + x^6$
Cyclopentane: $2x^2 + 4x^3 + 10x^4 + 10x^5 + 10x^6 + 4x^7 + 2x^8$
Cyclohexane: $2x^2 + 7x^3 + 18x^4 + 28x^5 + 35x^6 + 28x^7 + 18x^8 + 7x^9 + 2x^{10}$

These results are illustrated for cyclopropane in Figure 1 and for cyclobutane in Figure 2, where the enantiomeric pair (upper row) corresponding to the same geometrical isomer devoid of a symmetry plane and hence chiral, is connected to this chiral isomer on the middle row by a V-shaped fork.

It had been noted earlier[2] that the cycle indices are identical for benzene and, when ignoring enantiomerism, for benzprismane; similarly, for cyclodecapentaene (planar, conjugated) and for a pentaprismane devoid of enantiomerism. The results of the present paper (Table III) show that a third »coisomeric graph« for each of these two pairs is constituted by cyclopropane and cyclopentane, respectively, disregarding enantiomerism. Planar cycloöctatetraene,[5] however, has different cycle indices both from cubane, and from cyclobutane ignoring enantiomerism in all cases.

TABLE III

Cycle Indices Z and Configuration Counting Series $Z(1 + x)$ for the Numbers of Geometrical Isomers (Excluding Enantiomerism) of Cycloalkanes where Hydrogens are Substituted by One Type of Substituent

Cyclopropane:

$$Z = (y_1^6 + 2y_3^2 + 4y_2^3 + 3y_1^2 y_2^2 + 2y_6)/12$$

$$Z(1 + x) = 1 + x + 3x^2 + 3x^3 + 3x^4 + x^5 + x^6$$

Cyclobutane:

$$Z = (y_1^8 + 4y_4^2 + 9y_2^4 + 2y_1^4 y_2^2)/16$$

$$Z(1 + x) = 1 + x + 5x^2 + 5x^3 + 10x^4 + 5x^5 + 5x^6 + x^7 + x^8$$

Cyclopentane:

$$Z = (y_1^{10} + 4y_5^2 + 6y_2^5 + 5y_1^2 y_2^4 + 4y_{10})/20$$

$$Z(1 + x) = 1 + x + 5x^2 + 8x^3 + 16x^4 + 16x^5 + 16x^6 + 8x^7 + 5x^8 + x^9 + x^{10}$$

Cyclohexane:

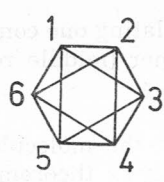
$$Z = (y_1^{12} + 6y_6^2 + 2y_3^4 + 12y_2^6 + 3y_1^4 y_2^4)/24$$

$$Z(1 + x) = 1 + x + 7x^2 + 12x^3 + 32x^4 + 38x^5 + 55x^6 + 38x^7 + 32x^8 + 12x^9 + 7x^{10} + x^{11} + x^{12}$$

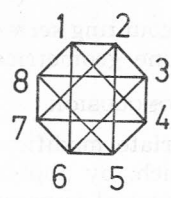
CONSTITUTIONAL ISOMERS OF CYCLOALKANES

To obtain the numbers of constitutional isomers of cycloalkanes, i. e. to ignore stereoisomerism, one must find the cycle indices of molecular graphs such as III—V which apply to cyclopropane, cyclobutane, and cyclopentane, respectively.

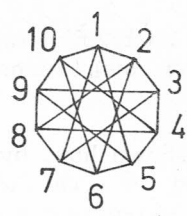
These graphs are $2n$-cycles which have, in addition, edges between each vertex i and the two vertices adjacent to the vertex opposite to i: thus each vertex has degree four. The resulting symmetry operations are illustrated for cyclopropane in the last part of Table I. Table IV presents the cycle indices and configuration counting series for cyclopropane to cyclohexane. The numbers of isomers for the first two rings are illustrated by the lower rows of Figures 1 and 2 for di-, tri, and tetra-substituted derivatives of cyclopropane and cyclobutane.



III



IV



V

For higher cycloakanes, the number of symmetry operations, i. e. the order $|A|$ of the symmetry group in (1), increases exponentially: for cycloalkanes with n carbon atoms and $2n$ hydrogen atoms,

$$|A| = 2n \cdot 2^0 = h \cdot 2^{n+1}$$

TABLE IV

Cycle Indices Z and Configuration Counting Series $Z(1+x)$ for the Numbers of Constitutional Isomers (Ignoring Stereoisomerism) of Cycloalkanes Where Hydrogens are Substituted by One Type of Substituent

Cyclopropane:

$$Z = (y_1^6 + 8y_3^2 + 7y_2^3 + 9y_1^2 y_2^2 + 8y_6 + 3y_1^4 y_2 + 6y_1^2 y_4)/48$$

$$Z(1+x) = 1 + x + 2x^2 + 2x^3 + 2x^4 + x^5 + x^6$$

Cyclobutane:

$$Z = (y_1^8 + 28y_4^2 + 17y_2^4 + 10y_1^4 y_2^2 + 4y_1^6 y_2 + 12y_1^2 y_2^3 + 4y_1^4 y_4 + 8y_1^2 y_2 y_4 + 28y_2^2 y_4 + 16y_8)/128$$

$$Z(1+x) = 1 + x + 3x^2 + 3x^3 + 5x^4 + 3x^5 + 3x^6 + x^7 + x^8$$

$$Z = (y_1^8 + 28y_4^2 + 17y_2^4 + 10y_1^4 y_2^2 + 4y_1^6 y + 12y_1^2 y_2^3 + 4y_1^4 y_4$$

Cyclopentane:

$$Z = (y_1^{10} + 5y_1^8 y_2 + 10y_1^6 y_2^2 + 10y_1^4 y_2^3 + 25y_1^2 y_2^4 + 40y_1^2 y_2^2 y_4 + 40y_2^3 y_4 + 21y_2^5 + 20y_1^2 y_4^2 + 20y_2 y_4^2 + 64y_5^2 + 64y_{10})/320$$

$$Z(1+x) = 1 + x + 3x^2 + 4x^3 + 7x^4 + 7x^5 + 7x^6 + 4x^7 + 3x^8 + x^9 + x^{10}$$

Cyclohexane:

$$Z = (y_1^{12} + 6y_1^{10} y_2 + 15y_1^8 y_2^2 + 20y_1^6 y_2^3 + 27y_1^4 y_2^4 + 30y_1^2 y_2^5 + 24y_1^4 y_2^2 y_4 + 12y_1^4 y_4^2 + 48y_1^2 y_2^3 y_4 + 24y_1^2 y_2 y_4^2 + 45y_2^6 + 120y_2^4 y_4 + 108y_2^2 y_4^2 + 96y_6^2 + 32y_3^4 + 32y_4^3 + 64y_3^2 y_6 + 64y_{12})/768$$

$$Z(1+x) = 1 + x + 4x^2 + 6x^3 + 12x^4 + 13x^5 + 18x^6 + 13x^7 + 12x^8 + 6x^9 + 4x^{10} + x^{11} + x^{12}$$

By subtracting the configuration counting series presented in Tables III and IV for corresponding cycloalkanes, one finds the configuration counting series which indicate the numbers of geometrical isomers related to one and the same constitutional isomer, i. e. the numerical difference between geometrical and constitutional isomers; these series are:

Cyclopropane: $x^2 + x^3 + x^4$

Cyclobutane: $2x^2 + 2x^3 + 5x^4 + 2x^5 + 2x^6$

Cyclopentane: $2x^2 + 4x^3 + 9x^4 + 9x^5 + 9x^6 + 4x^7 + 2x^8$

Cyclohexane: $3x^2 + 6x^3 + 20x^4 + 25x^5 + 37x^6 + 25x^7 + 20x^8 + 6x^9 + 3x^{10}$

Figures 1 and 2 illustrate these counting series by relating one constitutional isomer (lower row) to more than one geometrical isomer (middle row).

CONCLUSION

It was shown how, by appropriate modification of the molecular graphs, one can find the cycle indices which, by applying Pólya's theorem, give the numbers of stereoisomers, of geometrical isomers, or of constitutional isomers of cycloalkanes. This procedure is useful in teaching students of organic chemistry, as a test for mastering approaches to traditional problems which used to be solved by visual, or by trial and error, methods.

Acknowledgement. I am indebted to my son, Teodor-Silviu Balaban, for having originated this problem.

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SAŽETAK

Kemijski grafovi. XXXII. Konstitucijski i sterički izomeri supstituiranih cikloalkana

A. T. Balaban

Određen je broj stereoizomera, enantiomera i konstitucijskih izomera supstituiranih cikloalkana s pomoću teorema Polye. Broj stereoizomera određen je iz stvarnih konstitucijskih grafova fleksibilnih cikloalkana. Broj geometrijskih i konstitucijskih izomera određen je s pomoću specijalnih grafova, koji zanemaruju enantiomere ili stereoizomere.

ODJEL ZA ORGANSKU KEMIJU POLITEHNIKE
U BUKUREŠTU, BUKUREŠT, RUMUNJSKA

Prispjelo 15 studenoga 1977.