REVIEW

Chemical Graphs. IX. Isotope-Isomerism*
of Multiply-Labelled Compounds [1]

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Summary

Generalizations of previous figure-counting series used in Pólya's enumeration theorem are exploited to enable us to predict the number of isomers of multiply-labelled compounds. Nomenclature problems for such isotope-isomers are reviewed.

Introduction

Chemical phenomena originate in the electronic shells of atoms. The nature of their nuclei exerts an influence mainly through the nuclear charge. For isotopic atoms, with the same numbers of electrons and the same nuclear charges but differing in their nuclear masses, chemical behaviour is very similar, differences being manifest only through isotopic effects. Thus the numbers of neutrons in the nuclei have little influence on the chemical properties of isotopic atoms, but determine their nuclear properties such as stability, radioactive half-life***, isotopic spin, etc.

The replacement of an atom in a molecule by another one with a different isotopic composition from that encountered in nature (i.e. isotopic labelling) has become an increasingly important tool of chemical research since the early experiments of Paneth and von Hevesy [3].

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* "Isotope-isomerism" is preferred to "isotopic isomerism" because of derivation of adjectives (isotope-isomeric) and nouns (isotope-isomerization).
*** The so-called "stable" isotopes have radioactive half-lives longer than ca. 10^{11} years; half-lives of up to 10^{20} years (as for ^{130}Te) can be determined by indirect techniques[2].

In labelled molecules a new kind of isomerism appears : isotope-isomerism. Two molecules which contain different isotopes of the same element are called isotopic molecules [4]. *Isotope-isomers* [4] are molecules of the same structure labelled with the same isotope(s) but differing in the position of the label(s), for example D_2CH-CH_3 and DCH_2-CH_2D, or $^{13}CH_3-CH_2-CH_3$ and $CH_3-^{13}CH_2-CH_3$. Compounds containing two or more different types of isotope-isomeric molecules are named isotope-isomeric mixtures. The number of positions in a molecule which are labelled with one and the same isotope is called *isotopic multiplicity*, e.g. in the case of the above two examples, isotopic multiplicities are 2 for ethane ($^2H_2$) and 1 for propane (^{13}C). A molecule labelled with two different isotopes of the same element, or with nuclides of two different elements (again, "labelling" is by definition equivalent to "changing the natural isotopic composition") is termed a *doubly-labelled molecule*.

Mass spectrometry, radioactivity measurements, magnetic resonance and Mössbauer spectra, as well as degradative methods followed by isotopic analyses [5], can distinguish among isotope-isomeric molecules.

DEFINITION OF A LABELLED COMPOUND

Though there exist numerous laboratories and monographs, as well as a journal dedicated to labelled compounds, the definition of a labelled compound still has some obscure points. In fact, the difficulty lies in defining the non-labelled compounds.

One possibility would be to consider for each element one standard isotope (the most abundant in nature), and define unlabelled compounds as containing exclusively these nuclides. In this case the usual organic compounds would have to be considered as labelled molecules, owing to the natural ^{13}C, ^2H, ^{18}O, ^{15}N, etc.

A more satisfactory and widely accepted definition considers that in a non-labelled molecule the average isotopic composition of each atom is that encountered in nature. In this case the non-labelled compounds is a statistical [6] mixture of isotope-isomeric molecules. This is illustrated by the isotopic composition of the atmosphere [7]. As another example, non-labelled propane contains

   96.6 % $^{12}C_3H_8$, 2.2 % $^{13}CH_3-^{12}C_2H_5$, 1.1 % $(^{12}CH_3)_2$ $^{13}CH_2$

and small amounts (less than 0.2 %) of $^{12}C^{13}C_2H_8$, $^{13}C_3H_8$ and deuterium-containing molecules. A mixture containing

   96.6 % $^{12}C_3H_8$, 2.2 % $(^{12}CH_3)_2\,^{13}CH_2$ and 1.1 % $^{13}CH_3-^{12}C_2H_5$

would have to be considered as labelled propane (enriched in ^{13}C in position 2,

and in ^{12}C in positions 1 and 3) though the overall isotopic composition does not differ from that of non-labelled propane.

The small amounts of natural radioisotopes such as ^{3}H or ^{14}C with half-lives considerably shorter than 10^6 years, which are generated continuously by various non-equilibrium processes, should better be ignored. When the natural isotopic composition has slight fluctuations (as for the stable isotopes of hydrogen or oxygen), a standard value [2] should be taken as reference.

According to the latter definition, a single molecule is always labelled (except for the cases when it consists only of monoisotopic elements such as $^{19}F_2$, $^{127}I_2$, $^{19}F^{127}I$ or $^{31}P^{19}F_5$, when it is unlabelled).

NUMBERS OF ISOTOPE-ISOMERIC MOLECULES OF GIVEN TYPES

After earlier attempts to find formulas for the number of istope-isomeric molecules [8], H. Hübner [9] applied Pólya's enumeration theorem [10] to this problem for the case of a single C-isotopic label in acyclic (n-heptane and n-octane as examples) or cyclic (benzene, toluene, ethylbenzene and xylenes) hydrocarbons. In the present paper we generalize to several isotopic labels by making constant use of group theory.

A molecule may be regarded as a graph where the atoms are the vertices, and the covalent bonds are the edges of the graph. Unless otherwise stated, hydrogen and other univalent atoms are left out and only polyvalent atoms are indicated in the graph.

Given a graph G, its symmetry mappings must first be determined. This can be done by determining the (point) group Γ (G) of this graph and then finding the symmetry axes from character tables [11]. Then the cycle index Z is calculated for the respective permutation group (symmetric group S, alternating group A, cyclic group C, dihedral group D, or identity group E), either by making use of the symmetry operations around the symmetry axes [8], or by employing the available formulas [12–14] for the corresponding permutation groups which obviate the need of considering all symmetry operations. Both procedures are illustrated in the examples below.

Pólya's enumeration theorem [10,13] states that by substituting for each indeterminate variable c_k in the cycle index the appropriate figure-counting series, a polynomial configuration counting series $b(x)$ is obtained whose coefficients indicate the numbers of configurations, i.e. in the present case the numbers of isotope-isomers. For one isotopic label, the figure-counting

series is : $c_k = 1 + x^k$ (in the previous paper [12], this counting series was presented in a different notation : $y_k = r^k + s^k$).

Thus, in a given graph G with p points, the number of different subsets of n points (i.e. the number of singly-labelled isotope-isomers with isotopic multiplicity n) is the coefficient of x^n in the polynomial configuration counting series $b(x) = Z [\Gamma (G), 1 + x]$. The same formula applies for calculating numbers of isomers for n-substituted hydrocarbon derivatives in which n hydrogen atoms were replaced by n identical univalent substituents, e.g. chlorine atoms.

As the first example we will discuss toluene, which can be considered in standard graphical notation [14] as the graph $K_2 . C_6$ resulting by identifying one point of the complete graph K_2 of order 2 with one point of the cyclic graph C_6 with 6 points. The group of this graph is easily seen to be $\Gamma (K_2 . C_6) = E_3 + S_2 [E_2]$ again using standard notation [14] for operations on permutation groups, and its cycle index is

$$Z(E_3 + S_2[E_2]) = Z(E_3).Z(S_2[E_2]) = c_1^3.\tfrac{1}{2}(c_1^4 + c_2^2) = \tfrac{1}{2}(c_1^7 + c_1^3 c_2^2)$$

Alternatively, the same cycle index results from the point group C_{2v} with symmetry elements (excluding inversion centres or axes, and symmetry planes) E and C_{2v} as indicated in the character tables [10]. By the former operation the 7 vertices are unaffected (c_1^7); by the second operation, 3 vertices are unaffected and 2 pairs of vertices are exchanged pairwise ($c_1^3 c_2^2$).

Toluene : $Z(C_{2v}) = \tfrac{1}{2}(c_1^7 + c_1^3 c_2^2)$

Its configuration counting series is, according to Polya's theorem [10]

$$Z(\Gamma(G), 1 + x) = \tfrac{1}{2}[(1 + x)^7 + (1 + x)^3(1 + x^2)^2] =$$
$$= 1 + 5x + 13x^2 + 21x^3 + 21x^4 + 13x^5 + 5x^6 + x^7$$

The coefficient of x, for example, indicates that there exist five isotope-isomers of singly carbon-labelled toluene with isotopic multiplicity one ($^{12}C_6^{13}C H_8$); the coefficient of x^3 indicates that there are 21 isotope-isomers of singly carbon-labelled toluene with isotopic multiplicity three ($^{12}C_4 {}^{13}C_3 H_8$), etc. Their formulas are given in ref. [8].

Similarly one finds the following cycle indices [8] :

ortho-Xylene : $Z(C_{2v}) = \tfrac{1}{2}(c_1^8 + c_2^4)$

meta-Xylene : $Z(C_{2v}) = \tfrac{1}{2}(c_1^8 + c_1^2 c_3^2)$

para-Xylene : $Z(D_{2h}) = \tfrac{1}{4}(c_1^8 + c_1^4 c_2^2 + 2c_2^4)$

n-Heptane : $Z(D_{\infty h}) = \tfrac{1}{2}(c_1^7 + c_1 c_2^3)$

n-Octane : $Z(D_{\infty h}) = \tfrac{1}{2}(c_1^8 + c_2^4)$

Benzene : $Z(D_{6h}) = \tfrac{1}{12}(c_1^6 + 3c_1^2 c_2^2 + 4c_2^3 + 2c_3^2 + 2c_6)$

One can extend this treatment for double labelling (either with two distinct isotopes of the same element, or of different elements), by substituting in the cycle index the modified figure-counting series $c_k = 1 + x_1^k + x_2^k$ when the two labels cannot be attached to the same atom, or $c_k = 1 + x_1^k + x_2^k + x_1^k x_2^k$ when they can. The former figure-counting series also applies to counting substituted hydrocarbon derivatives with two different univalent substituents, e.g. chlorine and bromine.

As a second example we shall illustrate the isotope-isomers of doubly-labelled benzene. For benzene labelled with ^{13}C and ^{14}C for instance, we have (the two labels cannot involve the same atom) :
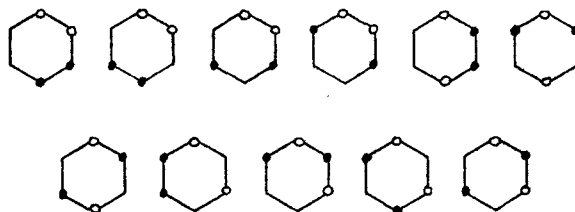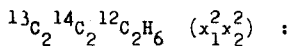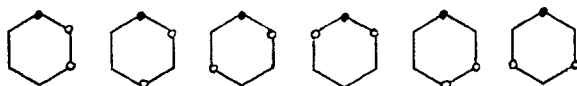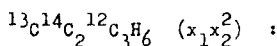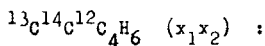
$$Z(D_{6h}, 1 + x_1 + x_2) = \tfrac{1}{12}[(1 + x_1 + x_2)^6 + 3(1 + x_1 + x_2)^2(1 + x_1^2 + x_2^2)^2 +$$
$$+ 4(1 + x_1^2 + x_2^2)^3 + 2(1 + x_1^3 + x_2^3)^2 + 2(1 + x_1^6 + x_2^6)] =$$
$$= 1 + x_1 + x_2 + x_1^5 + x_2^5 + x_1 x_2^5 + x_1^5 x_2 + x_1^6 + x_2^6 +$$
$$+ 3(x_1 x_2 + x_1^2 + x_2^2 + x_1^3 + x_2^3 + x_1^4 + x_2^4 + x_1 x_2^4 + x_1^4 x_2 + x_1^3 x_2^3 +$$
$$+ x_1^2 x_2^4 + x_1^4 x_2^2) + 6(x_1 x_2^2 + x_1^2 x_2 + x_1 x_2^3 + x_1^3 x_2 + x_1^2 x_2^3 + x_1^3 x_2^2) + 11 x_1^2 x_2^2$$

This indicates that there exist : one isomer for $^{12}C_6H_6$ or $^{13}C^{12}C_5H_6$, three isomers for $^{13}C^{14}C^{12}C_4H_6$, $^{13}C_2{}^{12}C_4H_6$ or $^{13}C_3{}^{12}C_3H_6$, six isomers for $^{14}C^{13}C_2{}^{12}C_3H_6$, and eleven isomers for $^{14}C_2{}^{13}C_2{}^{12}C_2H_6$. Some of these isomers are presented in Table 1, where ^{13}C and ^{14}C are indicated by black and open circles, and ^{12}C is not indicated*.

For a carbon- and deuterium-labelled benzene, the two labels can involve the same carbon atom, hence we have to include also the term $x_1 x_2$ in the figure-counting series :

$$Z(D_{6h}, 1 + x_1 + x_2 + x_1 x_2) = \tfrac{1}{12}[(1 + x_1 + x_2 + x_1 x_2)^6 + 3(1 + x_1 + x_2 +$$
$$+ x_1 x_2)^2(1 + x_1^2 + x_2^2 + x_1^2 x_2^2)^2 + 4(1 + x_1^2 + x_2^2 + x_1^2 x_2^2)^3 +$$
$$+ 2(1 + x_1^3 + x_2^3 + x_1^3 x_2^3)^2 + 2(1 + x_1^6 + x_2^6 + x_1^6 x_2^6)] =$$
$$= (1 + x_1^6 + x_2^6 + x_1^6 x_2^6 + x_1 + x_2 + x_1^5 + x_2^5 + x_1 x_2^6 + x_1^6 x_2 + x_1^5 x_2^6 + x_1^6 x_2^5) +$$
$$+ 3(x_1^2 + x_2^2 + x_1^4 + x_2^4 + x_1^2 x_2^6 + x_1^6 x_2^2 + x_1^4 x_2^6 + x_1^6 x_2^4 + x_1^3 + x_2^3 +$$
$$+ x_1^3 x_2^6 + x_1^6 x_2^3) + 4(x_1 x_2 + x_1 x_2^5 + x_1^5 x_2 + x_1^5 x_2^5) + 9(x_1 x_2^2 + x_1^2 x_2 +$$
$$+ x_1 x_2^4 + x_1^4 x_2 + x_1^2 x_2^5 + x_1^5 x_2^2 + x_1^4 x_2^5 + x_1^5 x_2^4) + 12(x_1 x_2^3 + x_1^3 x_2 +$$
$$+ x_1^3 x_2^5 + x_1^5 x_2^3) + 24(x_1^2 x_2^2 + x_1^2 x_2^4 + x_1^4 x_2^2 + x_1^4 x_2^4) +$$
$$+ 28(x_1^2 x_2^3 + x_1^3 x_2^2 + x_1^3 x_2^4 + x_1^4 x_2^3) + 38 x_1^3 x_2^3$$

* For clarity, molecular formulas in the text and in Tables do not respect the order of increasing mass numbers for isotopes of the same element.

TABLE 1. Isotope-isomers of doubly ^{13}C and ^{14}C labelled benzene

$$^{13}C^{14}C^{12}C_4H_6 \quad (x_1 x_2) \quad :$$

$$^{13}C^{14}C_2{}^{12}C_3H_6 \quad (x_1 x_2^2) \quad :$$

$$^{13}C_2{}^{14}C_2{}^{12}C_2H_6 \quad (x_1^2 x_2^2) \quad :$$

This formula shows that there exist : one isomer for $^{12}C_6H_6$, $^{12}C_6H_5D$ or $^{13}C^{12}C_5H_6$, three isomers for $^{12}C_6H_4D_2$, $^{12}C_6H_3D_3$, $^{13}C_2{}^{12}C_4H_6$ or $^{13}C_3{}^{12}C_3H_6$, four isomers for $^{13}C^{12}C_5H_5D$, nine isomers for $^{13}C_2{}^{12}C_4H_5D$ or $^{13}C^{12}C_5H_4D_2$, twelve isomers for $^{13}C^{12}C_5H_3D_3$ or $^{13}C_3{}^{12}C_3H_5D$, twenty-four isomers for $^{13}C_2{}^{12}C_4H_4D_2$, twenty-eight isomers for $^{13}C_2{}^{12}C_4H_3D_3$ or $^{13}C_3{}^{12}C_3H_4D_2$, and thirty-eight isomers for $^{13}C_3{}^{12}C_3H_3D_3$. These isomers are shown in Table 2.

To generalize for an arbitrary number of labels, the number of isomers of a multiply-labelled molecule with a_1 labels of species 1, a_2 labels of species 2, ..., a_n labels of species n, can be found as the coefficient of the term

$$x_1^{a1} x_2^{a2} ... x_n^{an}$$

in the polynomial configuration counting series obtained by substituting into the cycle index the following figure-counting series :

$$c_k = 1 + \sum_{i=1}^{n} x_i^k \text{ if a point can bear up to one label;}$$

$$c_k = 1 + \sum_{i=1}^{n} x_i^k + (1\text{-}\delta_{ij}) \sum_{i=1}^{n}\sum_{j=1}^{n} x_i^k x^k \text{ for up to two labels attached to one atom;}$$

$$c_k = 1 + \sum_{i=1}^{n} x_i^k + (1\text{-}\delta_{ij}) \sum_{i=1}^{n}\sum_{j=1}^{n} x_i^k x_j^k + (1\text{-}\delta_{hij}) \sum_{h=i}^{n}\sum_{i=1}^{n}\sum_{j=1}^{n} x_h^k x_i^k x_j^k \text{ for up to three}$$

labels and so on. The Kronecker delta functions are $\delta_{ij} = 1$ for $i = j$, $\delta_{ij} = 0$ for $i \neq j$.

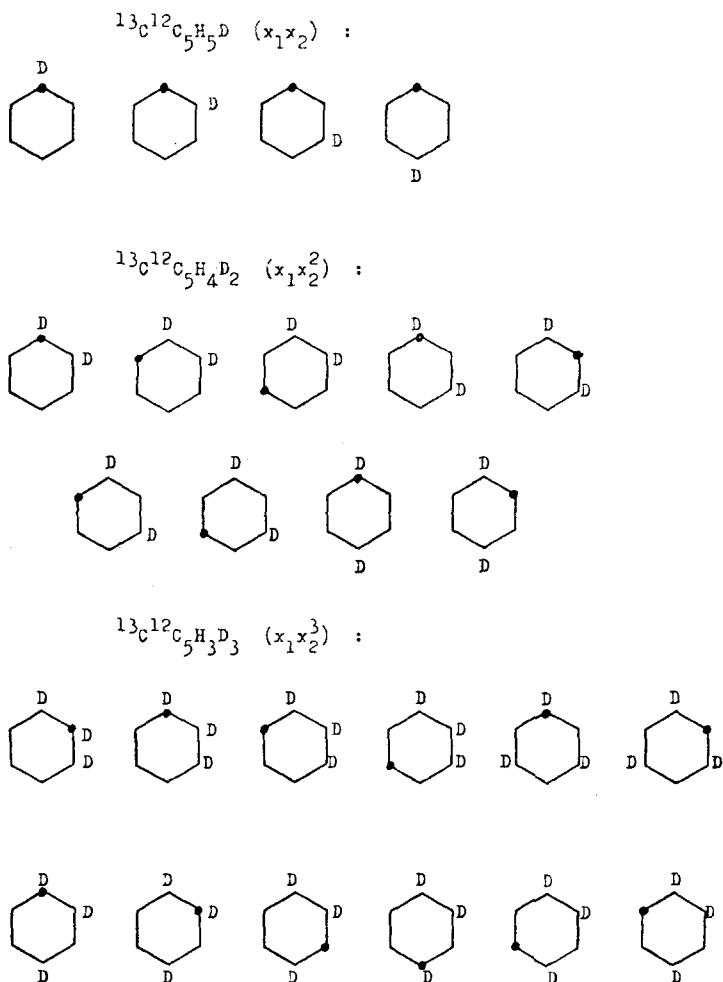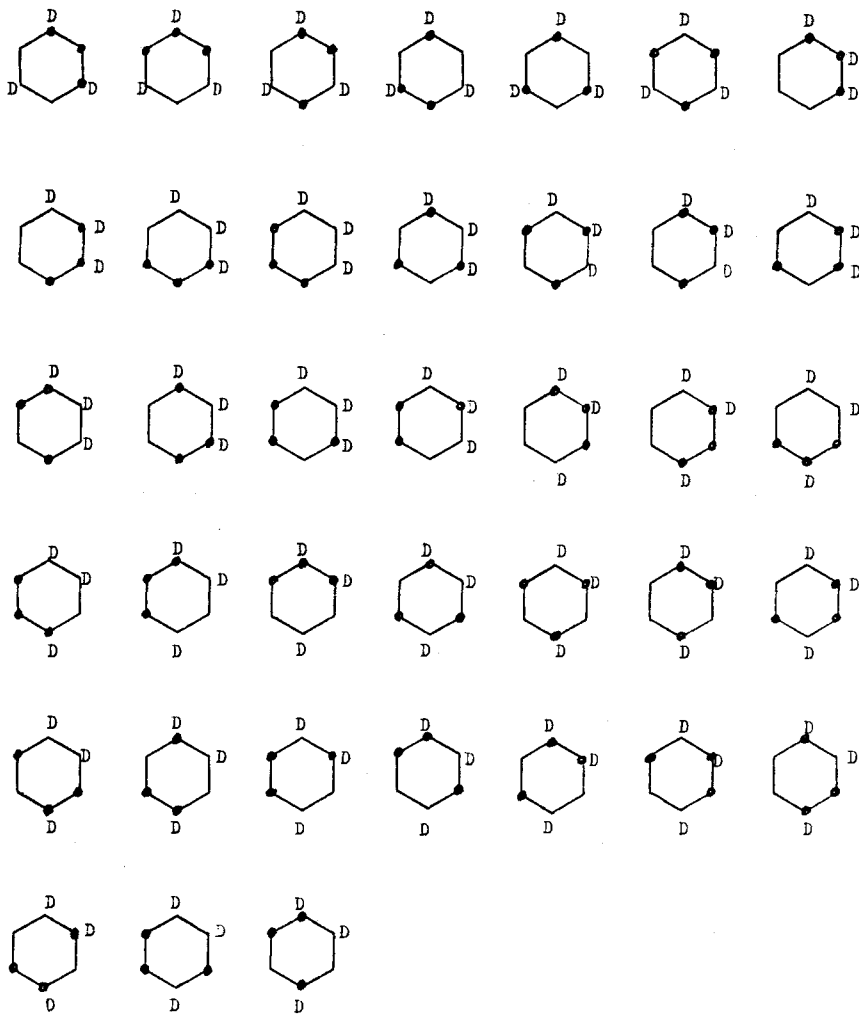TABLE 2. Isotope isomers of doubly carbon- and deuterium-labelled benzene

$^{13}C^{12}C_5H_5D \quad (x_1 x_2) :$

$^{13}C^{12}C_5H_4D_2 \quad (x_1 x_2^2) :$

$^{13}C^{12}C_5H_3D_3 \quad (x_1 x_2^3) :$

TABLE 2. *(continued)*

$$^{13}C_3{}^{12}C_3H_3D_3 \quad (x_1^3 x_2^3) \quad :$$

$$^{13}C_2{}^{12}C_4H_4D_2 \quad (x_1^2 x_2^2) \quad :$$

$$^{13}C_2{}^{12}C_4H_3D_3 \quad (x_1^2 x_2^3) \quad :$$
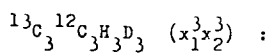
We shall illustrate, as the third and last example, the configuration counting series for the hydrocarbons $(CH)_p$, $p = 4$, 5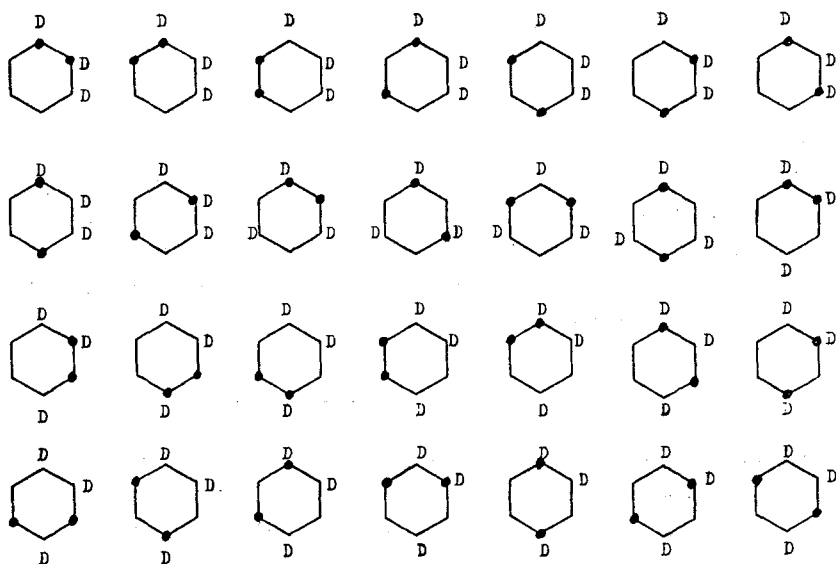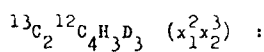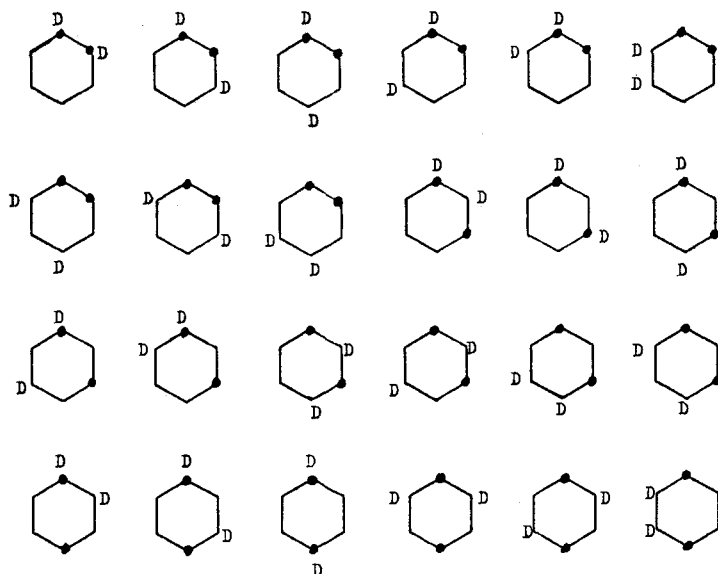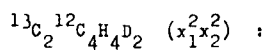, 6, 7, and 8 in the regular planar configurations corresponding to the dihedral groups D_4, D_5, D_6, D_7, and D_8 obtained with the first figure-counting series above. Since the potentials (or numbers of partitions*) of the numbers 4, 5, 6, 7, and 8 are 5, 7, 11, 15, and 22, respectively, for these groups we will have the corresponding numbers of terms. In the following, the partitions and coefficients of the configuration counting series b_p ($p = 4$ to 8) are given; to link up with our previous data [12], one should bear in mind that variables x_1, x_2, x_3,... were there noted r, s, t...

$$b_4 : x_1^4,\ x_1^3x_2,\ 2x_1^2x_2^2,\ 2x_1^2x_2x_3,\ x_1x_2x_3x_4$$

$$b_5 : x_1^5,\ x_1^4x_2,\ 2x_1^3x_2^2,\ 2x_1^3x_2x_3,\ 4x_1^2x_2^2x_3,\ 6x_1^2x_2x_3x_4,\ 12x_1x_2x_3x_4x_5$$

$$b_6 : x_1^6,\ x_1^5x_2,\ 3x_1^3x_2^3,\ 3x_1^4x_2^2,\ 10x_1^3x_2x_3x_4,\ 6x_1^3x_2^2x_3,\ 3x_1^4x_2x_3,\ 11x_1^2x_2^2x_3^2,$$
$$16x_1^2x_2^2x_3x_4,\ 30x_1^2x_2x_3x_4x_5,\ 60x_1x_2x_3x_4x_5x_6$$

$$b_7 : x_1^7,\ x_1^6x_2,\ 3x_1^5x_2^2,\ 4x_1^4x_2^3,\ 3x_1^5x_2x_3,\ 9x_1^4x_2^2x_3,\ 15x_1^4x_2x_3x_4,\ 10x_1^3x_2^3x_3,\ 18x_1^3x_2^2x_3^2,$$
$$30x_1^3x_2^2x_3x_4,\ 60x_1^3x_2x_3x_4x_5,\ 48x_1^2x_2^2x_3^2x_4,\ 90x_1^2x_2^2x_3x_4x_5,\ 180x_1^2x_2x_3x_4x_5x_6,$$
$$360x_1x_2x_3x_4x_5x_6x_7$$

$$b_8 : x_1^8,\ x_1^7x_2,\ 4x_1^6x_2^2,\ 5x_1^5x_2^3,\ 8x_1^4x_2^4,\ 4x_1^6x_2x_3,\ 12x_1^5x_2^2x_3,\ 21x_1^5x_2x_3x_4,\ 19x_1^4x_2^3x_3,$$
$$33x_1^4x_2^2x_3^2,\ 54x_1^4x_2^2x_3x_4,\ 105x_1^4x_2x_3x_4x_5,\ 70x_1^3x_2^3x_3x_4,\ 38x_1^3x_2^3x_3^2,\ 108x_1^3x_2^2x_3^2x_4,$$
$$210x_1^3x_2^2x_3x_4x_5,\ 420x_1^3x_2x_3x_4x_5x_6,\ 171x_1^2x_2^2x_3^2x_4^2,\ 318x_1^2x_2^2x_3^2x_4x_5,$$
$$630x_1^2x_2^2x_3x_4x_5x_6,\ 1260x_1^2x_2x_3x_4x_5x_6x_7,\ 2520x_1x_2x_3x_4x_5x_6x_7x_8.$$

The coefficient of each term again indicates the number of isomers; each x_i in the term represents one isotopic species (or one type of substituent, or one colour of beads in the necklace problem [12]; an upper limit of three different colours had been set earlier [12]), while its exponent represents the isotopic multiplicity (or the number of substituents of the same type, or the number of beads with the same colour).

NOMENCLATURE OF ISOTOPE-ISOMERS

The proposal of W. A. Boughton reported by Crane [17] for the nomenclature of hydrogen-labelled molecules, adopted by Chemical Abstracts [18,19], is based on the special names of ^2H (deuterium, noted by d) and ^3H (tritium,
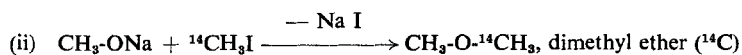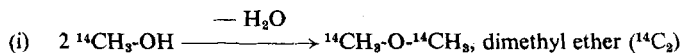
* The partitions of n are the different ways of representing the given positive integer n as sums of positive integers ([15],[16]).

noted by t). This system cannot be extended to other nuclides because no other element has different names for different mass numbers. Accordingly, various other nomenclature proposals were advocated by individuals or national committees [20-37], by multinational [38] or international organizations [39]. The Definitive Rules for the Nomenclature adopted by IUPAC [40] indicate the mass numbers of nuclides as upper left superscripts. With the recommendations provisionally adopted by the International Commission for Nomenclature of the IUPAC [39], a workable system for the nomenclature of labelled organic compounds was achieved, and most of the disputed questions raised previously [22,23,30,32,24] were settled.

Thus the name of a labelled compound indicates: (i) the chemical structure by its usual chemical name, and (ii) the qualitative isotopic composition by the addition of informations concerning the nature and the position in the molecule of the isotopes. It is agreed that no quantitative indication on the amount of labelling, that is to what extent the isotopic composition of the respective position differs from the natural one, is to be given in the name.

There are two points, however, which deserve a comment.

In practice, a chemical substance always involves large numbers of molecules. Accordingly, statistical considerations based on the history of the substance, i.e. its method of preparation, should be taken into account [34]. If it is agreed that one should name a labelled compound after the molecules with the highest isotopic multiplicity achieved during the preparation, then this should only apply to isotope-isomeric mixtures of chemically identical molecules possessing a statistical distribution of isotopic composition. For instance, starting with barium carbonate 50 % enriched in ^{13}C one can prepare calcium carbide and hence acetylene, whose molar composition would be the following: 25 % $^{12}C_2H_2$, 50 % $^{12}C^{13}CH_2$, 25 % $^{13}C_2H_2$ (isotopic effects being ignored); this statistical isotope-isomeric mixture should be collectively named as acetylene ($^{13}C_2$). A theoretical mixture consisting in $^{12}C_2H_2$ (50 mole %) and $^{13}C_2H_2$ (50 mole %) should not be named as one compound, but as a mixture. An acetylene prepared from CH_3-$^{13}COOH$ by halogenation, reduction, dehydrohalogenation and dehydration should be named acetylene (^{13}C). As a further example, consider ^{14}C-labelled dimethyl ether. It can be obtained by two routes:

(i) $2\ ^{14}CH_3\text{-OH} \xrightarrow{\ -\ H_2O\ } \ ^{14}CH_3\text{-O-}^{14}CH_3$, dimethyl ether ($^{14}C_2$)

(ii) $CH_3\text{-ONa} + \ ^{14}CH_3I \xrightarrow{\ -\ Na\ I\ } CH_3\text{-O-}^{14}CH_3$, dimethyl ether ($^{14}C$)

At low specific activities, in both cases most molecules will have no label, and a small number of molecules will have one label; in the former case only, a very small number of molecules will have an isotopic multiplicity of two ^{14}C atoms per molecule. Though rather academic, this distinction should be reflected in the name, as indicated above.

Secondly, there is the problem of multiply-labelled compounds. The provisional rules [39] only state that the symbols of the nuclides should be placed in alphabetical order. To be more precise, one should have to add that this applies to the alphabetical order of the symbols (not of the names since these differ in various languages), that hydrogen, deuterium and tritium should be listed under H even though D and T may be used, and that in molecular formulas and names of compounds multiply labelled with several isotopes of the same element, the symbols of these nuclides with the respective locant indications should be arranged in the order of increasing mass numbers.

BIBLIOGRAPHY

1. Part VIII, BALABAN, A. T. — *Rev. Roumaine Chim*, **15** : 463 (1970).
2. LEDERER, C. M., HOLLANDER, J. M. and PERLMAN, I. — "Table of Isotopes", 6th Edition, Wiley, New York, 1967, table I.
3. HEVESY, G. and PANETH, F. — *Z. anorg. Chem.*, **82** : 322 (1913); PANETH, F. and HEVESY, G. — *Monatsh.*, **36** : 75 (1915); HEVESY, G. and PANETH, F. — " Lehrbuch der Radioaktivität ", 2. Aufl., Leipzig, 1931; English translation, 2nd Ed., Oxford Univ. Press, 1938; PANETH, F. — "Radioactive Elements as Indicators", McGraw-Hill Inc., New York, 1928; HEVESY, G. — "Radioactive Indicators", Interscience, New York, 1948; "Adventures in Radioisotope Research", Pergamon Press, New York, 1962.
4. CLUSIUS, K. — *Z. Elektrochem.*, **58** : 586 (1954).
5. UNCUTA, C. and BALABAN, A.T. — *Studii si Cercetàri Chim. Acad. R. S. Romània*, (in press).
6. MARTALOGU, N., MUMUIANU, D., MAGDA, M. and BALABAN, A. T. — *ibid.*, **8** : 329 (1960).
7. ECK, C. F. — *J. Chem. Educ.*, **46** : 706 (1969).
8. PINKUS, A. G. — *J. Chem. Educ.*, **34** : 299 (1957); PINKUS, A. G. and McLACHLAN, E. K. — *Chem. and Ind.*, **1960** : 1106; MAI, L. A. — *Zhurn. Obshchei Khim.*, **28** : 2887 (1958).
9. HÜBNER H., — *Abh. Dtsch. Akad. Wiss. zu Berlin, Kl. Chem., Geol., Biol., Sonderband Stabile Isotope*, **1964** : 701.
10. PÓLYA, G. — *Z. Kristallogr.*, **93** : 415 (1936); *Acta Math.*, **68** : 145 (1937).
11. COTTON, F. A. — "Chemical Applications of Group Theory", Wiley, New York, 1963; JAFFÉ, H. H. and ORCHIN, M. — "Symmetry in Chemistry", Wiley, New York, 1965. FERRARO, J. R. and ZIOMEK, J. S. (editors) — "Introductory Group Theory and Its Application to Molecular Structure", Plenum Press, New York, 1969.
12. BALABAN, A. T. and HARARY, F. — *Rev. Roumaine Chim.*, **12** : 1511 (1967).
13. HARARY, F. — chapters 1-5 in "Graph Theory and Theoretical Physics", (F. HARARY, editor), Academic Press, London, 1967. HARARY, F. — chapters 1-6 in "A Seminar on Graph Theory" (F. HARARY, editor), Holt, Rinehart and Winston, New York, 1967; HARARY, F. — *Pacific J. Math.*, **6** : 57 (1956).

14. HARARY, F. — "Graph Theory", Addison-Wesley Publ. Comp., Reading, Mass., 1969.
15. HARDY, G. H. and WRIGHT, E. M. — "An Introduction to the Theory of Numbers", 3rd Edition, Oxford Univ. Press, chapter 19, 1954.
16. ABRAMOWITZ, M. A. and STEGUN, I. A. — "Handbook of Mathematical Functions", Natl. Bureau of Standards, Washington, D. C., 1964.
17. CRANE, E. J. — *Ind Eng. Chem., News Ed.*, **13** : 200 (1934); *Science*, **80** : 86 (1934).
18. PATTERSON, A. M., CAPELL, L. T. and MAGILL M. A. — *Chem. Abstr.*, **39** : 5874 (1945).
19. Subject Index, *Chem. Abstr.*, **66** (1967), paragraphs 53-61.
20. OTVOS, J. V. and WAGNER, C. D. — *Science*, **106** : 409 (1947).
21. COLLINS, C. J. — *J. Amer. Chem. Soc.*, **70** : 2418, footnote 3 (1948).
22. COLLINS, C. J., CROMPTON, C. E., RONZIO, A. R. and TOLBERT, B. M. — ORNL-1084 (1951).
23. ANDERSON, R. C. — BNL-44, p. 110 (1950); *Nucl. Sci. Abstr.*, **4** : 4853 (1950).
24. CALVIN, M., HEIDELBERGER, C., REID, J. C., TOLBERT, B. M. and YANKWICH, P. E. — "Isotopic Carbon", Wiley, New York, pp. x-xii, 1949.
25. ARNSTEIN, H. R. V. and BENTLEY, R. — *Quart. Rev.*, **4**, : 172 (1950).
26. THOMAS, S. L. and TURNER, H. S. — *Quart. Rev.*, **7** : 407 (1953).
27. NEVENZEL, J. C., RILEY, R. F., HOWTON, D. R. and STEINBERG, G. — UCLA-316, p. 8 (1954).
28. WEYGAND, F. and SIMON H. — "Houben-Weyl's Methoden der Organischen Chemie", vol. 4, part 2, p. 539. G. Thieme Verlag, Stuttgart, 1955.
29. KERSAINT, G. — *Bull. Soc. Chim. France*, **1957** : 53.
30. MURRAY, A., III and WILLIAMS, D. L. — "Organic Syntheses with Isotopes", part I, chapter 1, pp. 2-9. Interscience Publ., New York, 1958.
31. SEGAL, H. H. — *J. prakt. Chem.*, [4], **7** : 299 (1959).
32. CATCH, J. R. — "Carbon-14 Compounds", pp. 72-78. Butterworths, London, 1961.
33. PARKANYI, C. — *Chem. listy*, **58** : 1283 (1964).
34. HÜBNER, H. — *Chem. listy*, **58** : 1273 (1964); *Abh. Dtsch. Akad. Wiss. zu Berlin, Kl. Chem., Geol., Biol., Sonderband Stabile Isotope*, **1964**, 709.
35. GUSEV, G. G. and KAPUSTIN, Yu. M. — "Tritii v organicheskii khimii", p. 8. Atomizdat, Moscow, 1964.
36. BUBNER, M. and SCHMIDT, L. — " Die Synthese Kohlenstoff-14 markierter organischer Verbindungen ", p. 31. Verlag Georg Thieme, Leipzig, 1966.
37. RAAEN, V. F., ROPP, G. A. and RAAEN, H. P. — "Carbon-14", p. 363. McGraw-Hill, New York, 1968.
38. "Labelled Compounds. Rules for the Nomenclature of Labelled Organic Compounds", Recommendation for standardization, Council of Mutual Economic Assistance (accepted by the Permanent Commission for Peaceful Uses of Nuclear Energy, Moscow, June 1968).
39. IUPAC, " Règles de Nomenclature pour la Chimie Organique (Règles 1965) ", Butterworths, p. 303; *Bull. Soc. Chim. France*, **1967** : 3581.
40. IUPAC, "Definitive Rules for the Nomenclature of Organic Chemistry (1957 Rules)", Butterworths; *J. Amer. Chem. Soc.*, **82** : 5545 (1960).