

COULD HAVE BEEN CHEMICAL WORLD OF LIVING THINGS OTHER ?

ABSTRACT. At most four types (groups) of isomers have been revealed, in natural things or as envisaged structures: *meso*, *C₂ symmetrical*, *irrechi*, *constitutional*. In vertebrate almost exclusively *constitutional* isomers have been found. On the other hand, all fundamental natural combinations, found as *constitutional* isomers in vertebrates, are able to form symmetric isomers. (Hence, they keep symmetry as a possibility and not as a reality). Symmetric isomers of *constitutional* ones also possess functional groups. Therefore, a comparison could be made between a real and a possible situation, and an interesting and unique conclusion results from this comparison. A series of symmetric compounds, especially *C₂ symmetrical* ones, have been isolated from plants and microorganisms, however no counterparts of these combinations were ever found in vertebrates. However, a preliminary conclusion could be drawn: symmetry phenomenon is much better represented in plants and microorganisms than in vertebrates. Of symmetric isomers, the *meso* ones are characterized by a mirror plane of symmetry, i.e. an area capable to hide (mask) atoms or planar structures of polarized light.

Key words: isomers, *meso*, *C₂ symmetrical* (CTS), diastereomeric chiral (*irrechi*), *constitutional*, comparative chemistry, integrative, duality, mirror plane of symmetry

1. INTRODUCTION

In silico integrative approach of isomers generated by the same molecular formula has been applied to a large diversity of natural compounds and some synthetic ones (1-6). At most four groups (types) have been identified and defined within the same molecular formula.

(A) **Symmetric** based on a mirror plane of symmetry (A1), a center of symmetry (A2), an alternating axis of symmetry (A3) or devoid of a mirror plane of symmetry but specified in this way as a result of Cahn-Ingold-Prelog rules (7,8) (A4). (A1) are *meso* isomers, and also (A4) providing their molecule is formed of two enantiomeric halves. One can assert that molecules of (A4) group are formed of two imaginary enantiomeric halves separated by an imaginary mirror plane of symmetry. *Meso* isomers are optically inactive (optinactive) due to an internal compensation.

At the time when Fischer invented xylitol (9), an optinactive polyol, at least one *meso* isomer was known, i.e. *meso*-tartaric acid, discovered by Pasteur (10,11). *Meso*-tartaric acid has a homodimeric structure, and xylitol a heterodimeric one. Mirror plane of symmetry cuts a bond of *meso*-tartaric acid, and four atoms of xylitol (C, H, OH). One might theorize that mirror plane of symmetry hides (masks) the atoms cut by it from polarized light, and what remains, as evidenced by this physical instrument, is an entity containing an even number of atoms, i.e. a homodimer. Mirror plane of symmetry has to be regarded as an intrinsic property of *meso* compounds. It should be considered both a physical instrument and a natural phenomenon. *Meso* heterodimers constitute a chemical duality, the two opposed sides of duality are their heterodimeric character, on one hand, and their expression as homodimers, on the other hand. According to Kelvin and Prelog theory (12-14) *meso* compounds are internally heterochiral. There is a fundamental difference between the mirror plane of symmetry in macrocosmos and at physical-chemical level in microcosmos. In the first case, the mirror plane of symmetry just indicates the limit of the two enantiomeric halves. At physical-chemical level, it can cut atoms and hide them of polarized light. As will be evident of this paper, this spectacular property of mirror plane of symmetry plays an extremely important role in systematization of isomers emerging of the same molecular formula.

Imprecise breaking of identity of the the two halves of *meso* isomers leads to two enantiomers (15) i.e. the internal enantiomerism is externalized.

(B) C_2 **symmetrical (CTS)** compounds have been defined in relation with an axis and a rotation of 180° . After this maneuver the same atoms should be regained as initially (16-18), and all CTS compounds are chiral and optactive. Fischer demonstrated the existence of some chiral compounds with identical ends, that produced exclusively one derivative by reactions randomly affecting their ends. E. g. D- and L-mannitol, D- and L-iditol, and their aldaric acids, as well as D- and L-threitol and the enantiomers of tartaric acid. Besides these compounds whose molecule is formed exclusively of two identical chiral halves, there are CTS combinations where the two chiral halves are linked on a matrix. E. g. 3-keto- and 3-deoxyxylitol, 3-keto- and 3-deoxyribitol, etc. The chiral units of the third CTS group molecules can be recognized especially by Cahn-Ingold-Prelog rules (7,8). According to Kelvin and Prelog theory (12-14), CTS formed exclusively of two identical chiral halves are homochiral with each other and internally homochiral (18,19). Of this reason, they could be named also *twin* molecules (20). The exceptional properties of *twin* (CTS) compounds were also noticed by Vickery (21). Homodimeric CTS compounds constitute a chemical duality, the two opposed sides of duality are optical activity, on one hand, and their symmetry, on the other hand. There is one universal rule concerning CTS compounds: every member of this group possesses a real or imaginary, but plausible, *meso* isomer. Some more clearings are requisite. Compounds based on 1,2-diamino-cyclohexane (17,22-24) are CTS as long as they are trans. Their cis isomer should be *meso* only by adopting a planar cycle, as for allo-inositol. Of the six *meso* isomers of inositol (25,26), five are characterized by 1,4 mirror plane of symmetry, while allo-inositol is devoid of such a plane. Its *meso* nature can be explained only by a planar structure, hence the mirror plane of symmetry cuts two opposed bonds. (One can write a *meso* isomer of 1,2-diamino cyclohexane as 1,2-cyclobutane derivative).

The first CTS combinations, the two enantiomers of tartaric acid, have been separated by Pasteur (1848) by crystalization from a racemic mixture that had been prepared by Kestner (1822) (10,11,27). Pasteur noticed two types of crystals, that were enantiomorphic with one another. He separated the two types of crystals and found out that their aqueous solutions were dextrorotary and levorotary, respectively. Dextro-tartaric acid had been discovered by Scheele (1770) in the sediment deposited in the vats during the grape juice fermentation (28,29). Stereochemical theory of tetrahedral and asymmetric (chiral) carbon atom (30,31) led van't Hoff to molecular models based on tetrahedrons which unequivocally represented every chiral carbon atom. By constructing and using these models, van't Hoff expanded the idea of enantiomorphism from crystals to molecules, a process initiated by Pasteur. (Dots and wedges representations of today come from van't Hoff's models). However, at that time no scientist could rationally associate structural models with the two enantiomers (32). In fact, the discovery of Pasteur increased the dilemma of representation, i. e., the relationship between a sample of an optically active compound and the unique, characteristic, structural model possibly assigned to it. This dilemma was solved by X-ray diffraction, i. e., of zirconium $K\alpha$ rays, by sodium rubidium tartrate of the dextrorotary species, and the obtained model was assigned to (+)-tartaric acid (33). Configuration of chiral centers of (-)-tartaric acid became also known, by the virtue of the law of enantiomorphism. By an impressive coincidence, this configuration of (+)-tartaric acid had been hypothetically attributed by E. Fischer (1896) (34). Configuration of the two enantiomers has been connected with other chiral compounds, beginning with (-)- and (+)-glyceraldehyde (35). A chemical relationship has been found between E. Fischer and his son, H. O. L. Fischer (36,37), due to a derivative of D- and L-mannitol prepared by the latter, i.e. 1,2-5,6-di-O-isopropylidene mannitol (CTS). By integration of finding of H. O. L. Fischer in the strategy of E. Fischer, structure elucidation of linear aldohexoses becomes more direct (38).

A remarkable and unique feature of CTS compounds is that chemical modification of one of the two component chiral halves produces the same result.

(C) **Irrechi**. The third subgroup of isomers of *meso* compounds are also chiral and they are characterized by a molecular skeleton identical to *meso* and *CTS*, i.e. a phenomenon of isoskeletomeric relationship (39). Still, chiral carbons are irregularly distributed in their molecule (3,4). E. g. glucitol (40), bicubebin (41), bismurrangain (42), hybocarpone (43), asarolignans (44), larreatricin (45), numerous carotenoids (3,46). *Meso* isomers are characterized by a 1:1 ratio of numbers of R and S carbons while in *CTS* ones this ratio is n:0, 0:n or 1:1. In *irrechi* combinations the ratio R/S has other values.

(D) **Constitutional** (positional) (*constit.*) isomers form the fourth group. They are isomer with the preceding ones but their skeleton is different. They are either optactive or optinactive. With relatively few exceptions, compounds currently met in living things, especially in vertebrate tissues, are constitutional isomers. They are probably the most abundant in living things.

An interesting group of *constit.* isomers is formed by a non-uniform linkage of monomers: quadrigemine B (47), aspergilazine A (48), penicillixanthone A, phomoxanthone B, dideacetylphomoxanthone B, rugulotrosin B (49), taondiol dimer (50,51), numerous carotenoids (3,46).

Concerning limits and possibilities of reciprocal changing of types mentioned above, both *CTS* and *irrechi* can be transformed into *meso*. Some interesting facts should be mentioned: the molecule of iditols and idaric acids possesses an equal number of R and S carbons, similarly with galactitol, allitol, galactaric and allaric acids. However they are not *meso* but optactive (25). The difference can be explained probably by the fact that the molecule of the former is formed of two identical chiral halves and the latter of two chiral enantiomeric halves.

The two hydrogen atoms of central methylene of a *meso* derivative, i.e. 3-deoxyxylitol, 3-deoxyribitol, *meso*-diaminopimelic acid, etc., are not equivalent. If they are alternatively replaced by a hydroxy function, the products are different. The two central hydrogen atoms of *CTS* compounds, i.e. 3-deoxyarabinitol, 3-deoxylyxitol, L,L- and D,D-diaminopimelic acid, etc., are equivalent: if they are alternatively replaced by a hydroxy function, exclusively one product is obtained.

The molecular diversity is connected with the following factors: (i) Structures as diamond (52), graphite and fullerenes (53,54) illustrate the best the ability of C atoms to bind with each other. However, all these forms present a very limited structural variety. (ii) What really confer molecular diversity to C combinations is the association of this element with hydrogen and this is evidenced by the remarkable molecular variety of aliphatic hydrocarbons (26,55,56). Isomeric diversity is a physical-chemical magnitude concerning the ability of a compound to present a large number of isomers. (iii) Chemical functional groups, in relative low proportion, also favor molecular diversity. (iv) Aromatic hydrocarbons present the lowest molecular diversity of all organic combinations. They contain an exceeding number of chemical functions, and they are in a state of advanced oxidation. In fact, they fill an intermediate place between elementary carbon and aliphatic hydrocarbons. Another remarkable feature of aromatic hydrocarbons is the fact that they do not present *meso* isomers. (v) Molecular diversity increases exponentially with molecular weight (56-58). (vi) Carbon dioxide is a terminal facet of metabolism and combustion of organic compounds. It is characterized by a high chemical inertia. Carbon dioxide has to be attached to a preexisting structure, as a piece of metal in a lathe, and stepwise reduced, the energy of sun playing an essential role in this process called photosynthesis (59).

Our aim have been especially monomeric units (59), but we prove that compounds called by Metzler in this way can also have *meso* isomers, hence an authentic dimeric character.

2. THE LIMIT OF SYMMETRY OF THE MAJOR METABOLITES. REAL AND POSSIBLE MESO ISOMERS

Major metabolites with symmetric molecule, and especially *meso* ones, are almost exclusively produced by plants and microorganisms (1-6). There are few, if any, symmetric compounds produced by vertebrates. Of the common metabolites, only monosaccharides

(aldoses and ketoses) possess *meso* isomers as natural compounds. However, the potential of natural metabolites to produce *meso* isomers is really huge.

The major metabolites containing a significant alkane moiety possess at least one real or envisaged *meso* isomer. A guiding line of this paper is to find out at least one *meso* isomer for every molecular formula. A serious obstructor to this is an advanced degree of unsaturation. E.g. is impossible to find out a *meso* isomer for $C_4H_4O_4$ (fumaric/maleic acids). However, $C_6H_8O_4$ (2,3-dimethyl derivative, etc) has a *meso* form (Fig. 1). Similarly, every tentative to construct a

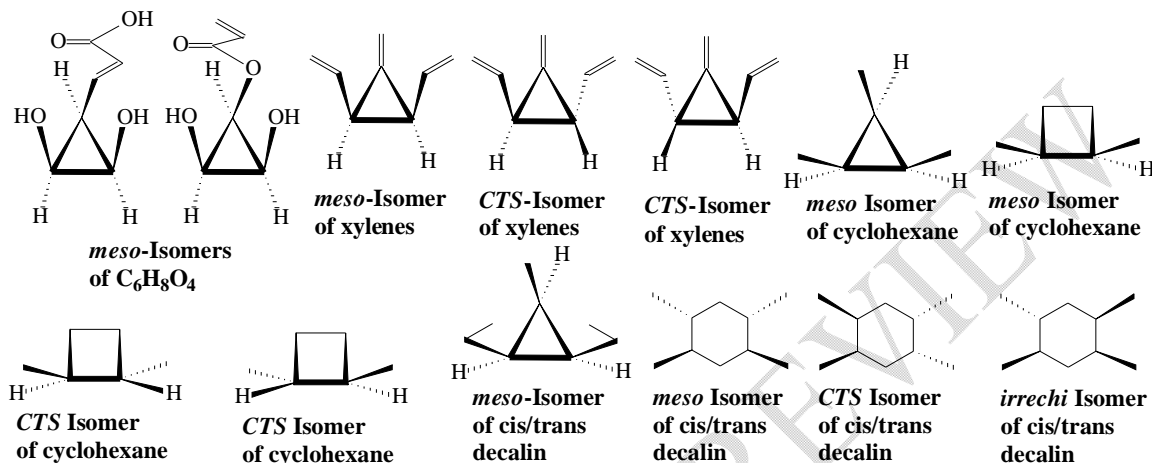


Figure 1. *Meso* isomers of unsaturated (fumaric/maleic acid), aromatic, and the latter's saturated derivatives.

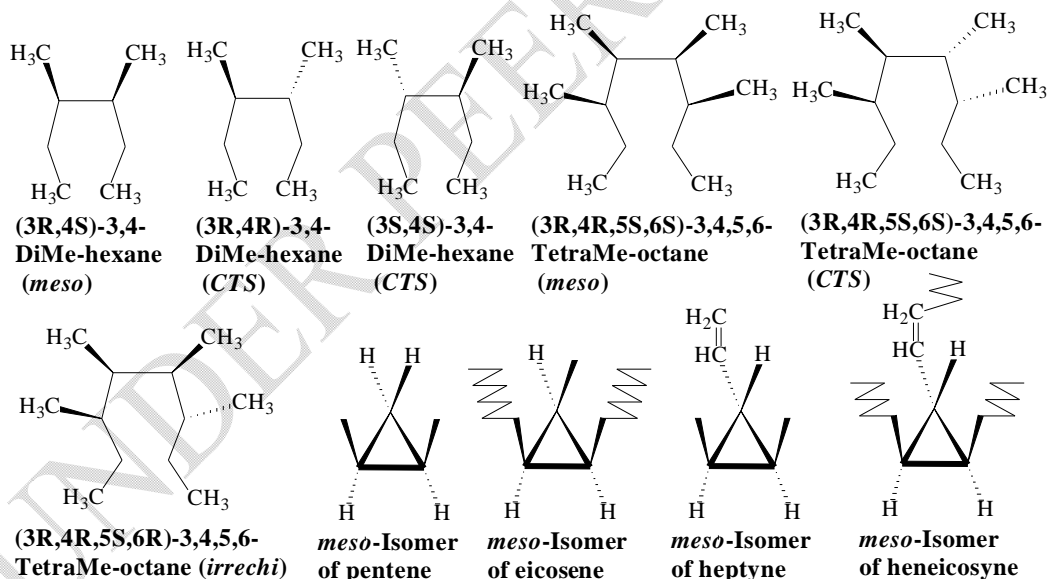


Figure 2. *Meso* isomers of saturated and unsaturated hydrocarbons.

meso isomer of benzene, fails. However, the thing is possible for xylenes, ethylbenzene, propylbenzene, etc. Also, reduction product of benzene, cyclohexane, presents *meso* isomers.

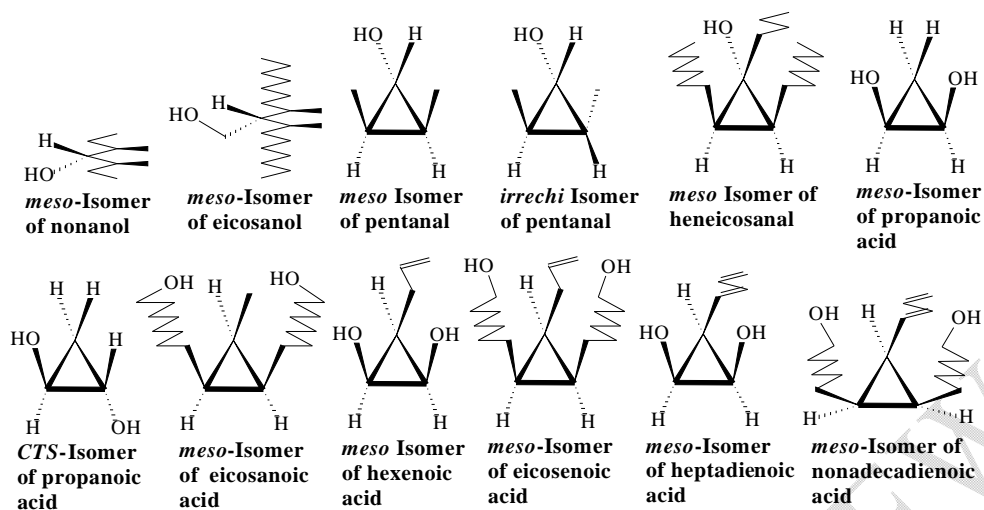


Figure 3. *Meso* isomers of some serial compounds with functional groups.

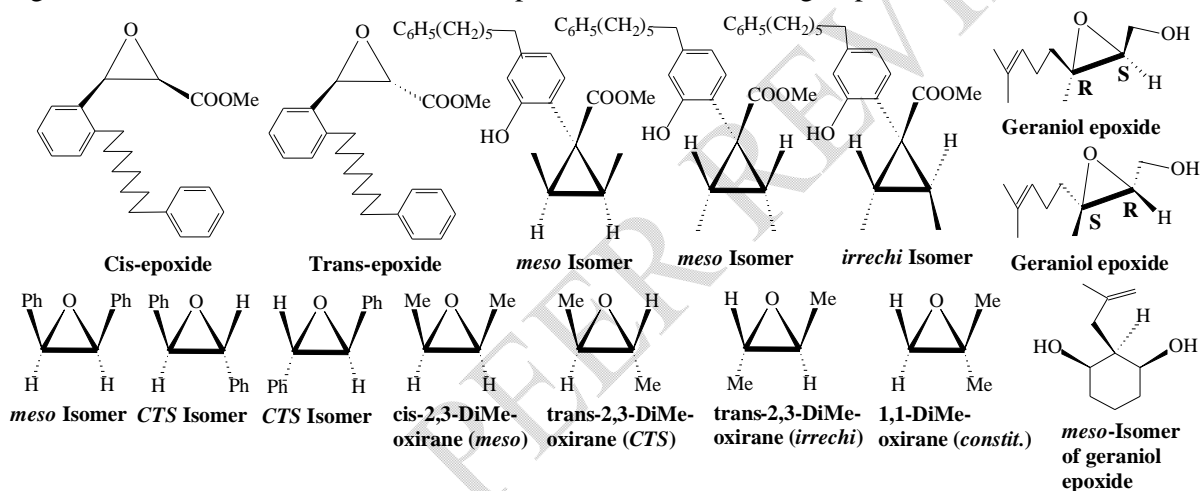


Figure 4. *Meso* isomers of some epoxides.

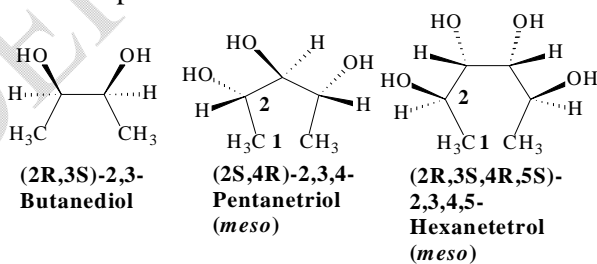


Figure 5. *Meso* isomers of diols, triols, tetrols.

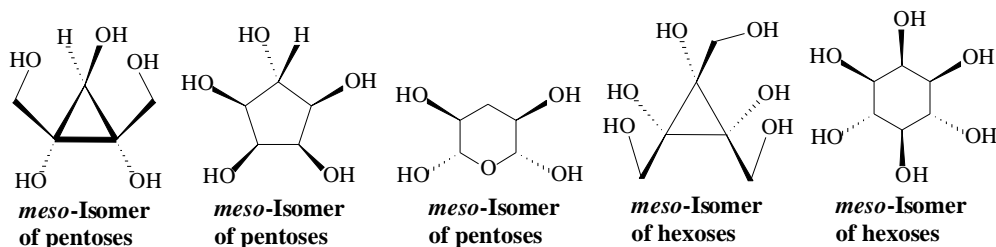


Figure 6. *Meso* isomers of aldoses and ketoses.

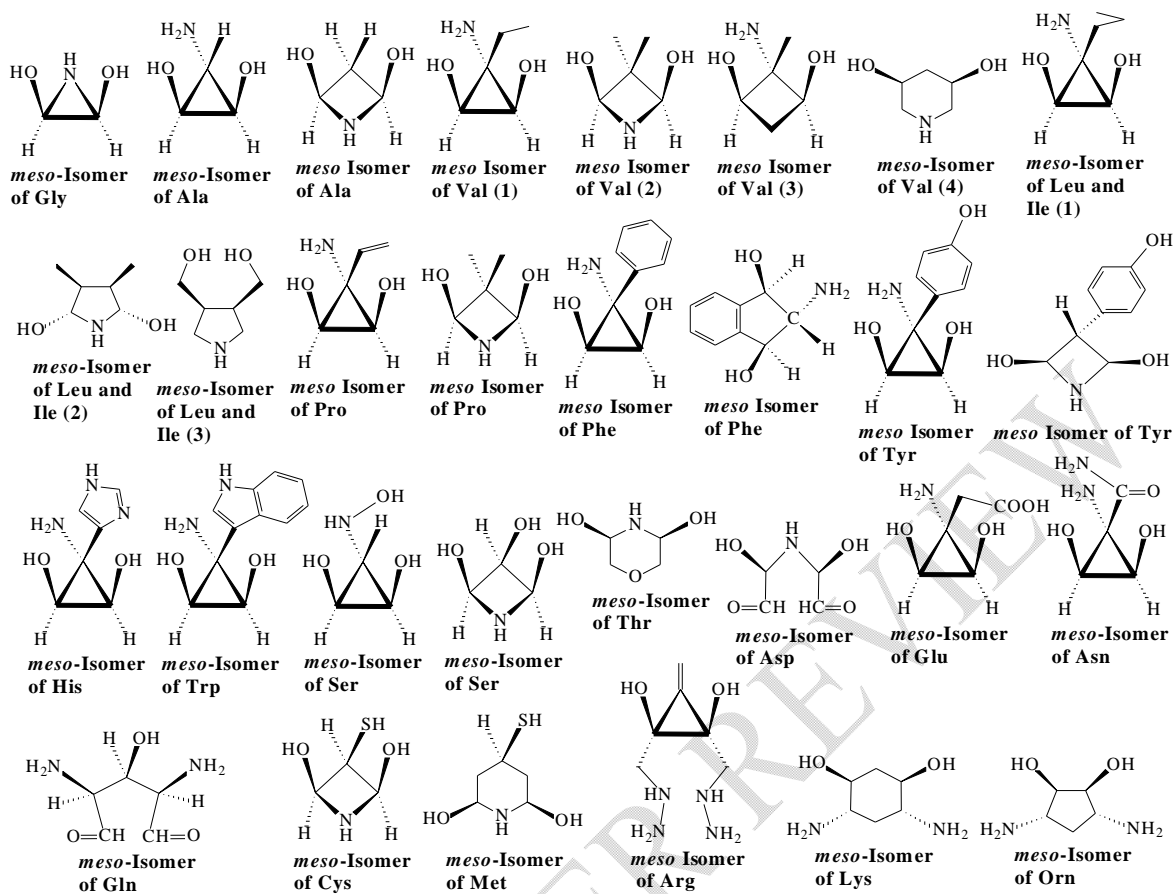


Figure 7. *Meso* isomers of the twenty fundamental amino acids. (see also text).

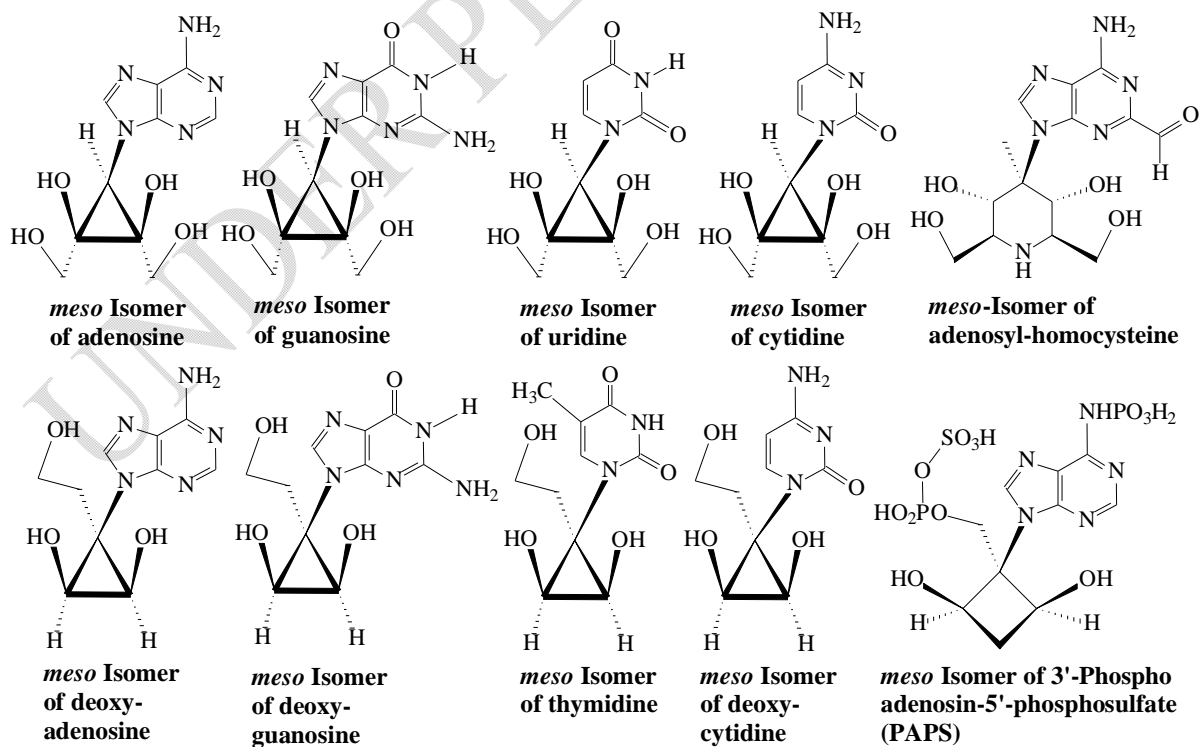


Figure 8. *Meso* isomers of nucleotides, deoxynucleotides, adenosyl-homocysteine and PAPS.

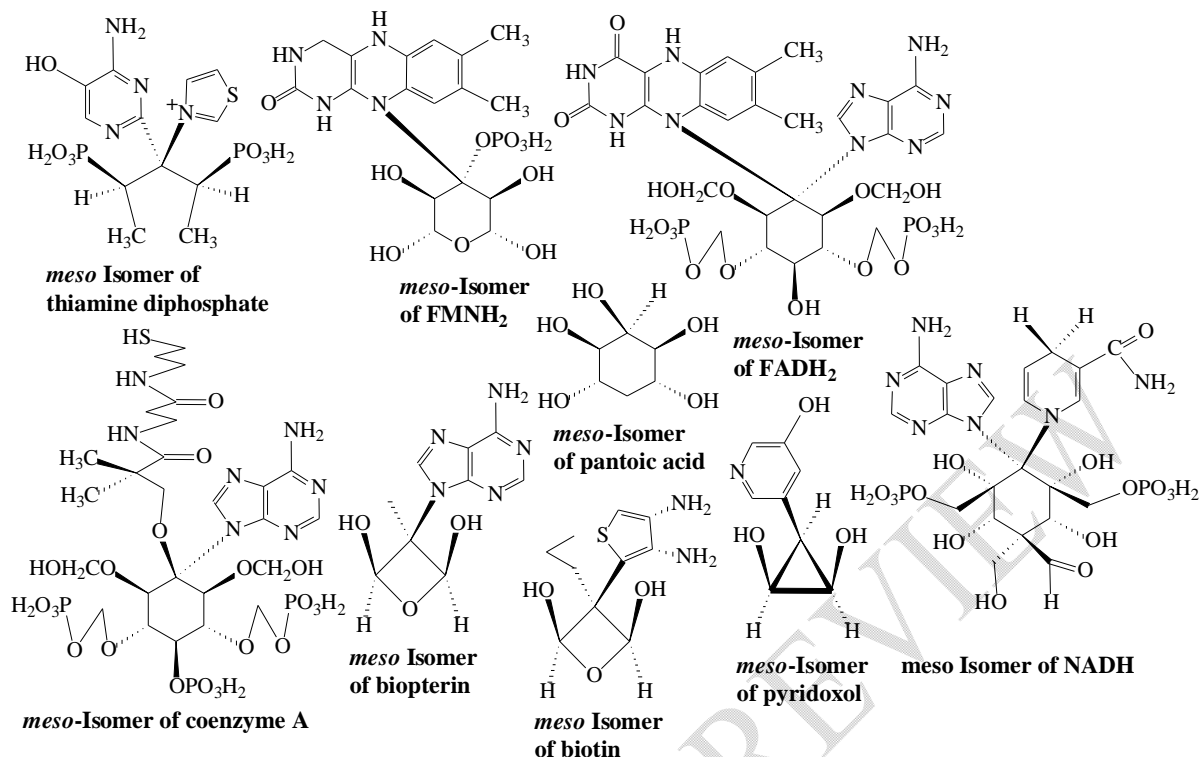


Figure 9. Hydrosoluble vitamins and their natural reagents (FADH₂, FMN, NADH, coenzyme A).

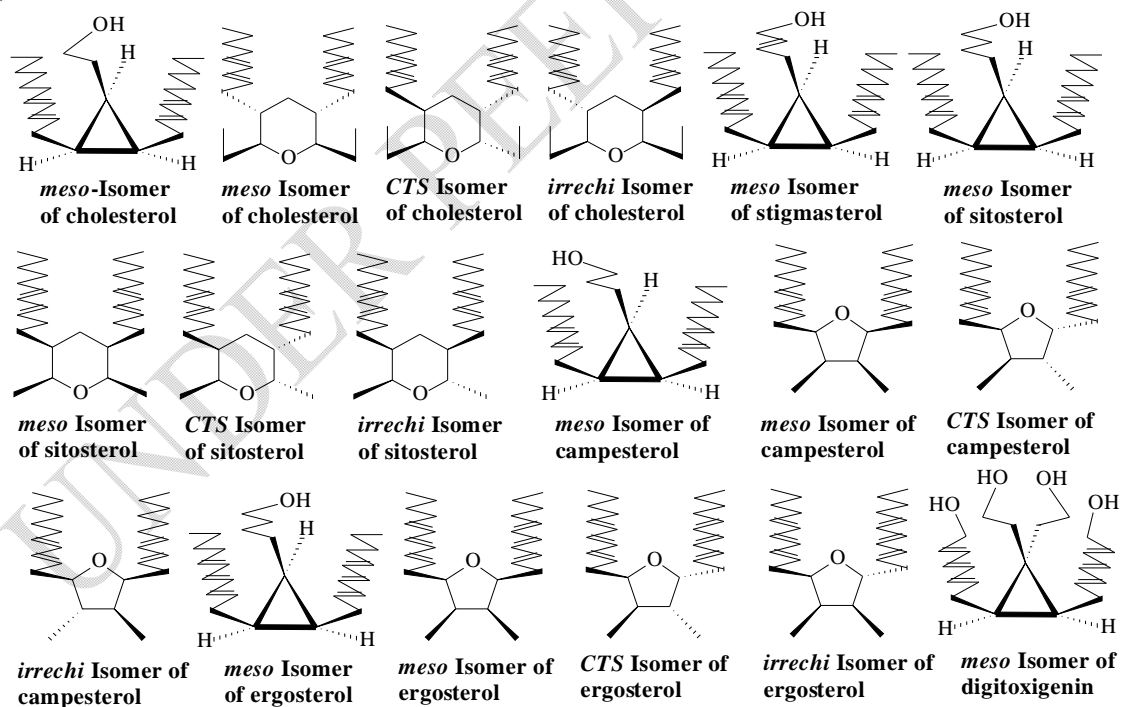


Figure 10. *Meso* isomers of some natural sterols.

Naphthalene, similarly to benzene, fails to give *meso* isomers, decalines instead presents such isomers (Fig. 1). Compounds unable to produce symmetric isomers have been called by us *archaic*. Chemical transformations intermediate between the two groups.

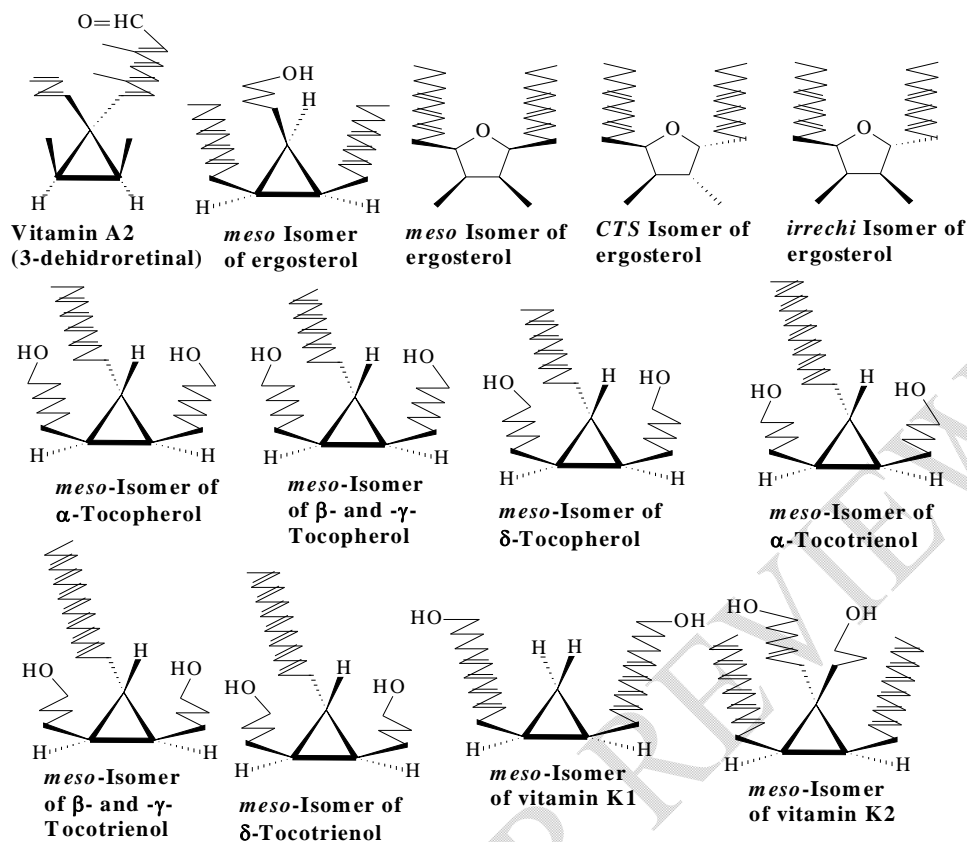


Figure 11. *Meso* isomers of lipophilic vitamins.

At least two dozens of isomers with molecular formula $C_3H_7NO_2$ can be written, just by utilising the consecrated valence of every component element. However, of the envisaged isomers only some present elements of symmetry: two are *meso* (cis-1,2-dihydroxy-3-amino cyclopropane and cis-2,4-dihydroxy-azetidine), and two are *CTS* (trans-2,4-dihydroxy-azetidine, two enantiomers), and all the others, including (R)- and (S)-alanine, are *constit*.

In the following (Figs. 2-14), the envisaged isomers are presented for a large variety of natural and synthetic compounds.

2.1. Compounds with serial structure

Compounds with serial structure present a large variety of molecular formulas (Figs. 2-4), in agreement with their molecular weight.

2.1.1. Aliphatic hydrocarbons: alkanes, alkenes (cycloalkanes), alkynes (alkadienes)

Of aliphatic hydrocarbons, only alkanes fail to present a triangular *meso* isomer (Fig. 2). A tentative to evaluate molecular diversity of C_8H_{18} indicated 18 (58) or 19 (56) isomers, and for C_9H_{20} 38 or 39. If one take into account optical activity (60), the total number of isomers for C_8H_{18} and C_9H_{20} is 24 and 55, respectively. Of these, one is *meso*, two are *CTS* (61) (Fig. 2) and the others are *constit*. An unequivocal conclusion can be drawn: all alkanes beginning with C_8H_{18} present at least one *meso* isomer, and all alkanes below this limit are *archaic*.

As a representative of C_nH_{2n} , alkenes or cycloalkanes, eicosene can be seen (Fig. 2). The first term according to our reasoning is the *meso* isomer, cis-1,2-dimethyl cyclopropane (62). For C_nH_{2n-2} (alkynes and alkadienes) *meso* isomer of heneicosyne is indicated (as cis-1,2-dihexyl-3-hexenyl-cyclopropane), the first term being C_7 , cis-1,2-dimethyl-3-vinyl cyclopropane or cis-3,5-dimethyl-1-cyclopentene; compounds below C_7 are *archaic*.

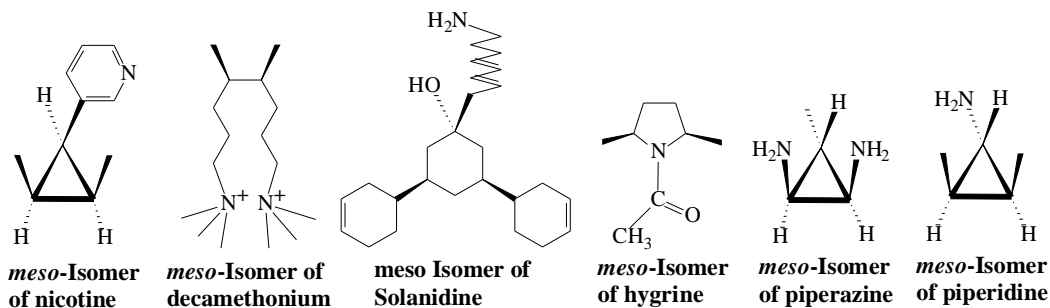


Figure 12. Meso isomers of alkaloids.

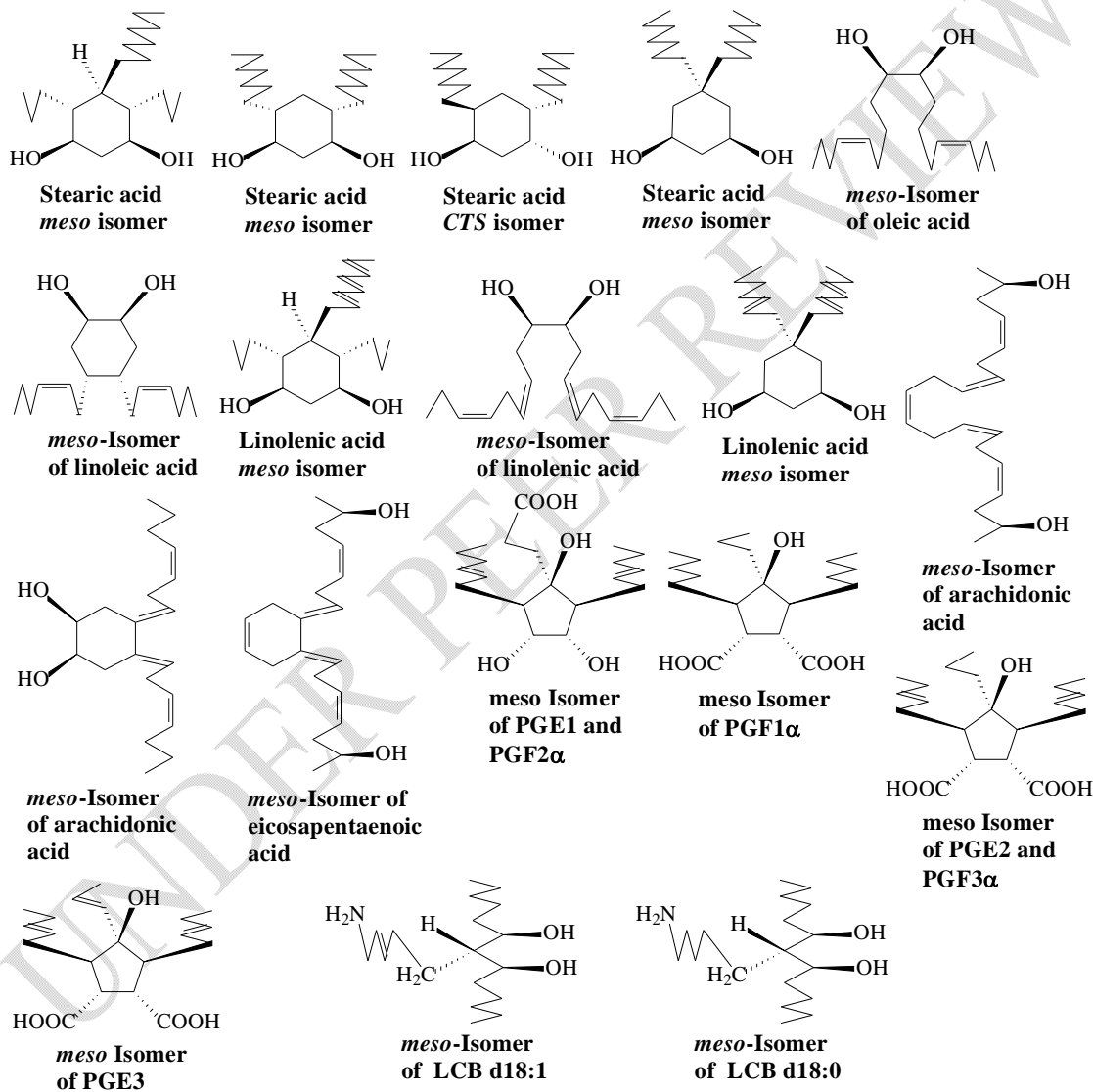


Figure 13. Meso isomers of fatty acids, prostaglandins and sphingosines (long chain bases, LCB).

2.1.2. Serial compounds with functional groups

For monohydroxylic alcohols there is a meso isomer of eicosanol (9-hydroxymethyl-8,10-dimethyl heptadecane), the first term is C₉ (3,5-dimethyl-4-hydroxy heptane) (Fig. 3). For

aldehydes and ketones we introduce *meso* isomer of heneicosanal (cis-1,2-diheptyl-3-hydroxy-3-butyl), the first term is C₅ (cis-1,2-dimethyl-3-hydroxy-cyclopropane), and similar combinations below C₅ are *archaic*.

Meso isomer of eicosanoic acid (cis-1,2-bis(octanol)-3-methyl-cyclopropane) represents organic acids, and the first term is C₃ (cis-1,2-dihydroxy-cyclopropane). C₃ still, as well as C₄ and C₅ have three types of isomers only (*meso*, *CTS*, *constit.*), while C₆ and higher terms possess four (*meso* of C₆ is 1 α ,2 α ,3 β ,4 β -1,2-dihydroxy-3,4-dimethyl cyclobutane); saturated organic acids below C₃ are *archaic*. Monoenoic acids are symbolized by a *meso* isomer of eicosenoic acid (cis-1,2-bis(heptanol)-3-allyl-cyclopropane) and the first term is C₅ (cis-1,2-dihydroxy-3-allyl cyclopropane). The following isomers are considered *constit.* isomers of valproic acid (2-propyl pentanoic acid; C₈H₁₆O₂): 2-ethyl-3-methyl pentanoic acid, di-isopropyl acetic acid, (R)-2-isopropyl pentanoic acid, (S)-2-isopropyl pentanoic acid, octanoic acid (63). According to our systematics, we have to begin with the finding of a C₈H₁₆O₂ *meso* isomer. This can be cis-1,2-dihydroxy-1,2-diethyl-3-methyl cyclopropane, cis-1,3-dihydroxy-2,2-diethyl-cyclobutane, 1 β ,2 β ,3 α ,4 α -1,2-diethyl-3,4-dihydroxy cyclobutane, or 1 β ,3 β ,4 α ,6 α -1,3-dihydroxy-4,6-dimethyl-cyclohexane, or others. As can be seen from their structure, the latter three isomers present also *CTS* and *irrechi* forms. And the C₈H₁₆O₂ isomers mentioned earlier, valproic acid inclusively, are all *constit.* (see below). Dienoic acids are made up by the *meso* isomer of nonadecenoic acid (cis-1,2-bis(6,6'-hydroxy-hexane)-3-butadienyl-cyclopropane) and the first term is C₇ (cis-1,2-dihydroxy-3-(1-butadienyl) cyclopropane).

Epoxides. We have placed epoxides (Fig. 4) distinctively of alcohols and ethers since they are in a higher state of oxidation. The two epoxides (cis and trans) have been prepared and separated by chemists in Pennsylvania aiming at drugs intended to alleviate the symptoms of asthma (64). We have imagined two *meso* and one *irrechi* isomers for the two afore mentioned epoxides. Hence the latter are *constit.* isomers as related to *meso* ones. The same authors describe three isomers of 1,2-diphenyloxirane (stilbene oxide), one *meso* and two *CTS*. Dimethyloxirane is illustrated equivocally (65), although it has four types of isomers: *meso*, *CTS*, *irrechi*, *constit.* Two enantiomeric geraniol epoxides have been prepared (66), and we have imagined a *meso* isomer for them (Fig. 4), hence the two enantiomers are *constit.* isomers.

2.2. Natural compounds of biochemical interest

A general formula can represent diols (6), well exemplified by butane diols. As all the other compounds having two asymmetric carbons only, 2,3-butanediol has but a *meso* isomer and two *CTS*; 1,3-butanediol is a *constit.* isomer. Diols can present *irrechi* isomers only by contribution of alkane chain (see 3,4,5,6-tetra-Me-octane). Triols, similarly to trimethyl alkanes (see 3,4,5-triMe-heptane) cannot have *CTS* isomers, but *meso*, *irrechi* and *constit.*; the first term is 2,3,4-pentanetriol. Tetrols presents all four types of isomers, the first term is (2R,3S,4R,5S)-2,3,4,5-hexanetetrol (Fig. 5).

A spectacular example of coexistence in living things of *constit.* and *meso* isomers can be found in carbohydrate chemistry. *Meso*-isomers of aldo- and keto-pentoses (C₅H₁₀O₅) are 1,2,3,4,5-pentahydroxy cyclopentanes (67-69). Aldo- and keto-hexoses (C₆H₁₂O₆) are represented by six symmetric inositols (25,26) (Fig. 6).

Biochemical compounds also present *meso* isomers (Figs. 5-14). Compounds with a ubiquitous distribution in living matter, the twenty fundamental amino acids are characterized by an unequalled structural variety. However, without any exception, they present *meso* isomers (Fig. 7). These amino acids are met especially integrated in proteins and in this state they manifest themselves by their tails (59). *Meso*, *CTS* and *constit.* isomers present the following amino acids: Gly, Ala, Val, Thr, Asp, Pro, Phe, Arg, Trp. *Meso*, *irrechi* and *constit.* isomers present the following amino acids: Tyr, His, Ser, Glu, Asn, Gln, Cys, Met. Leu, Ile, Lys and Orn present all four types. Amino acids containing an aromatic fragment and/or a relative high level of chemical functions are more limited in structural variety. However, we have had again the opportunity to exploit the planar character of benzenoid structures.

Nucleosides, nucleotides and their deoxy counterparts are represented by their *meso* isomers (Fig. 8); adenosin is cis-3,4-dihydroxy-cis-2,5-dihydroxy-1-adenin cyclopentane. The planar structure of benzenoid compounds has been successfully used in *meso* isomers of hydrosoluble vitamins (Fig. 9): biopterin (cis-2,4-dihydroxy-3-methyl-3-adenin oxetane), biotin (cis-2,4-dihydroxy-3-propyl-3-(3,4-diamino-thiophene-2)oxetane), thiamine (vitamin B1), vitamin B2 (as FADH₂ and FMNH₂), and even coenzyme A and NADH. In order to write *meso* isomer of FMNH₂ we extracted an O atom from a keto bond, however leaving redox system intact. An excellent alternative to this is to link the isoalloxazine system and a phosphonic residue on C-3 of ribitol. Practically, all hydrosoluble vitamins present *meso* isomers. A component of coenzyme A, pantoic acid, has pentahydroxy cyclohexane as a *meso* pair (Fig. 9). Squalene presents at least one *meso* compound (6). Sterols have been exemplified by cholesterol, stigmaterol, sitosterol, campesterol, ergosterol and digitoxigenin. Digitoxigenin also presents the four types of isomers. A similar solution has been found for estrone, C₁₉ (5 α -androstanolone), C₂₁ (prednisolone, 11 β -Hydroxy-progesterone, pregnenolone, progesterone, corticosterone, cortisol, aldosterone), C₂₄ (biliary acids: cholic, chenodeoxycholic, deoxycholic, lithocholic) (Fig. 10). All lipophilic vitamins – A, D, E, K – present *meso* isomers (Fig. 11). Vitamin E is represented by α -tocopherol and α -tocotrienol, but all members of this vitamin have *meso* isomers, and the same are vitamins K1 and K2. Both *meso* isomers of vitamin K1 and K2 are indicated.

All natural and synthetic alkaloids have *meso* isomers (Fig. 12), providing they include a significant alkane moiety e.g. piperidine, piperazine, etc. Camphor, as a *constit.* molecule is also present among the *meso* producing isomers (6).

Saturated, mono- and polyenoic fatty acids are represented by the isomers of stearic acid, oleic and eicosapentaenoic acid (the famous omega-3) (Fig. 13). As is obvious, an isomer of C₁₈H₃₆O₂ (cis-1,3-dihydroxy-cis-4,6-diheptyl-cyclohexane) present all four type of isomers: *meso* (cis-1,3-dihydroxy-cis-4,6-diheptyl-cyclohexane), *CTS* (as pairs of enantiomers) (trans-1,3-dihydroxy-trans-4,6-diheptyl- cyclohexane, etc.), *irrechi* (cis-1,3-dihydroxy-trans-4,6-diheptyl-cyclohexane, etc.) *constit.*, (stearic acid, etc.). A general formula has been elaborated for mono- and polyunsaturated fatty acids (6). For long chain bases (LCB) (sphingosines), LCB d18:1 and LCB d18:0 have been selected. *Meso* isomers have been also found for LCB t16:0, LCB d16:0, LCB d16:1, LCB t18:0, LCB t18:1, LCB t20:0, LCB t20:1. *Meso* isomers of saturated LCB should use *meso* isomer of nonanol as a model. All prostaglandins have matching *meso* isomers, as indicated by PGE1, PGF2 α , PGE2, PGF3 α (Fig. 13).

3. Triangular representation and mathematical equation

A mathematical equation (1) and a triangular representation (Fig. 14) have been imagined to illustrate *meso* isomers. In equation (1), n is the number of chain forming atoms, x, y, z, w are suitably selected numbers. x, y, z, w are connected with R1, R2, R3, R4, respectively, in triangular representation.

$$n-3=2x+2y+z+w \quad (1)$$

The rings of three or four atoms, as cycles or heterocycles, synthetic (70-73) or found in natural materials, are well known. Cis- and trans-1,2-dimethyl cyclopropane are indistinguishable of thermodynamic point of view (74). 1,2,3-Trihydroxycyclopropane is known as an unstable combination (75,76), however no attempt was made to stabilize it. 1,2-Dihydroxycyclopropane has been prepared by a reduction reaction of a diketone derivative (77). Cis-1,2-dihydroxycyclopropane has been discovered in natural material as a glycoside of α -D-galactopyranose (78) as well as in the constitution of mycolic acids (79) and lactobacillic acid (59). Oxirane ring has been identified as (3*S*)-2,3-oxidosqualene in sterols biosynthesis. Two syntheses of cis-1,2,3,4-tetrahydroxy cyclobutane have been reported (80). Lactobacillic acid can be considered as a model for this paper (Fig. 14).

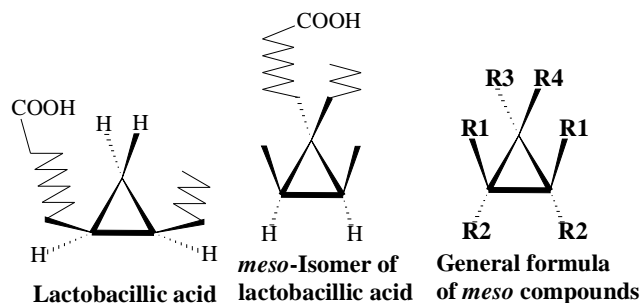


Figure 14. Source of inspiration and the sense of mathematical equation.

4. AN EXERCISE OF COMPARATIVE CHEMISTRY GIVES AN ANSWER TO AN UNANSWERED QUESTION – WHY WERE CONSTITUTIONAL ISOMERS FAVORED ?

A question should be raised concerning the hierarchy (39) of the four types of isomers, in other words which of them fills the top place. An intrinsic property of *meso* combinations is their character of dimerism, hence their molecule is formed of two entities that are contrary in a spatial and optical sense. Of this reason, nine philosophers of ten, probably, should declare *meso* group as being on the top. We ourselves have selected them as structural reference since we thought they have a higher rank than *CTS* and *irrechi*. Nonetheless, that some people could be fascinated by *CTS* molecules, since they are produced by doubling of the same entity. If we compare the four types, it's quite obvious that *meso*, *CTS* and even *irrechi* are characterized by some structural restrictions. *Constit.*, molecules are characterized by fewer such structural restrictions. Of this reason, probably, natural chemistry opted for them.

When physical chemistry appeared and grew stronger, biologists and other scholars connected with biochemistry, optimistically entertained the hope that physical chemists would discover a marker for natural compounds, as density is for gold. Till now such hope never met, according to our knowledge. Nonetheless, natural combinations possess some unique characteristics, and one of them, in our opinion, is the fact that they are less restricted, in structural sense, than *meso*, *CTS* and *irrechi*. A proof for this assertion is the fact that as soon as a living thing dies, nature sends a thousand messengers to recover its component materials. We reckon that at least one of these characteristics is that *constit.* compounds have a higher number of freedom degrees, in comparison with the other types. Somehow, this phenomenon is a chemical expression of freedom.

In different classes of compounds which constitute series, a limit has been noticed, and above this limit at least *meso* isomers are possible, or even all four types. Compounds under this limit have to be considered as *archaic*. They can reach to the group of combinations able of producing *meso* isomers only by chemical transformations. E. g. propane belongs to archaic group, however, by oxidation it becomes propanoic acid, an advanced form able to present *meso* form; however, propenoic acid is again *archaic*. Fischer (40,81,82) illustrated this by preparing a variety of C₆ monosaccharides from formaldehyde or C₃ derivatives.

CONCLUSIONS

1. At most four types (groups) of isomers have been found, in natural things or as envisaged structures: *meso*, *C₂ symmetrical*, *irrechi*, *constitutional*.
2. Practically all fundamental natural combinations, found as *constitutional* isomers in vertebrates, are able to form symmetric isomers. Hence, they keep symmetry as a possibility and not as a reality.

3. An exercise of comparative chemistry is presented between the real *constitutional* isomers and the envisaged *meso* ones.
4. At chemical level symmetry phenomenon is much better represented in plants and microorganisms than in vertebrates.
5. The mirror plane of symmetry has been defined as an area capable to hide (mask) atoms or planar structures of polarized light, and to transform a heterodimer in a homodimer.

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