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An Integrative Action based on Molecular Formula and an Exercise of Comparative Chemistry Indicate a Relationship of Hierarchy and a Phenomenon of Duality in Chemistry

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Abstract All-natural compounds containing a significant amount of an alkane moiety in their molecule present four types of isomers: (A) *meso*, (B) *C_2 symmetrical* (*CTS*), (C) *dia*stereomeric *chi*ral (*diachi*), (D) *constitutional* (*constit*.). When the alkane fragment is relatively smaller, molecular variety is diminished and only two types of isomers are possible, *meso* and *constit*. The definitions of the four types have been improved and updated according to nowadays data. Moreover, *meso* isomers have been selected as structural references. In molecules with a minimum degree of unsaturation, the skeleton of the first four cycloalkanes have been used in order to present the structure of the envisaged *meso* isomers. However, only cyclobutane, cyclopentane and cyclohexane derivatives are able to present the first three types of isomers. A very wide basis of compounds, and a large variety of classes, has been approached. We have paid the due attention to plausible, envisaged isomers as an instrument of interpretation and development.

Keywords isomers, meso, C_2 symmetrical (CTS), diastereomeric chiral (diachi), constitutional, comparative chemistry, integrative, duality

Introduction

Different classes of compounds develop at varying pace, and when they reach a certain extent, they should become independent. According to a previous definition, diastereomers are all isomers that are not enantiomers [1-3]. Since this group became too heterogenous we have fragmented it in four parts, by keeping the old nomenclature: (A) *meso*; (B) C_2 symmetrical (*CTS*); (C) *dia*stereomeric *chi*ral (*diachi*); (D) *constitutional* (*constit*.). In the *diachi* group, we have kept only chiral members. It's obvious that all these groups [4,5], except *meso* [6], appreciably increased, hence they deserve an independent place. For this reason, an updating of terms and systematization is periodically needed [7,8]. We have undertaken an integrative approach based on molecular formula, and an exercise of comparative chemistry, by using *meso* compounds as structural references. Every molecular formula concerning natural or synthetic compounds, with a significant moiety of an alkane skeleton, and a given level of complexity, might produce the above mentioned four types (groups) of isomers. In fact, the significance given by us to the four types will become quite obvious from their use and application.

(A) *Meso* isomers. There are three types of *meso* compounds: (**A1**) the molecule of the first type is formed of two enantiomeric chiral halves uniformly linked with each other [9-11]; (**A2**) the two enantiomeric chiral halves of the second type are uniformly linked on an atom or on a matrix devoid of handedness, or a matrix characterized by a mirror plane of symmetry [12]; (**A3**) The third type of *meso* compounds is devoid of elements of symmetry (dissymetric compounds) and they have to be analyzed by Cahn-Ingold-Prelog rules [13,14]. Their molecule

contains two sets of asymmetric carbons with opposed handedness. (In the latter case one can assert that molecules are formed of two imaginary enantiomeric halves separated by an imaginary mirror plane of symmetry).

(**A1**) and (**A2**) are characterized by a mirror plane of symmetry. *Meso* isomers are optically inactive (optinactive) due to an internal compensation. The existence of two enantiomeric sides in *meso* compounds was proved by Fischer and Hertz [15] in an elegant experiment on galactaric acid. They kinetically reduced this acid and the product was a racemic mixture of galacturonic acids. The two enantiomeric acids were separated as strychnine salts and characterized. In this way the internal enantiomorphy of *meso* derivative become externalized. Subsequently, chemists would try to overturn this feature of *meso* compounds and to predominantly, if not exclusively, prepare one product only [6, 16-18].

Meso heterodimers polyols discovered (or invented) by Fischer – xylitol [19], ribitol (adonitol) [20], xylaric (trihydroxiglutaric) acid, ribaric acid [21] – have been a trailblazing achievement and they turned out to be models for other combinations of the same category. 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. Mirror plane of symmetry cuts either a bond (bonds) or atoms. Relative to polarized light, mirror plane of symmetry transforms a heterodimer into a homodimer. 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. *Meso* heterodimers constitute a chemical duality, the two opposed sides of duality are their heterodimeric character, on one hand, and their expression as homodimers. According to Kelvin and Prelog theory [22-24] *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.

(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 [25-27], and all *CTS* compounds are chiral and optically active (optactive). Their molecule is either formed of two identical chiral halves uniformly linked with each other [28,29] or of two identical chiral halves uniformly linked on an atom [29] or on an achiral [29] or *CTS* matrix [30]. According to Kelvin and Prelog theory [22-24], *CTS* formed exclusively of two identical chiral halves are homochiral with each other and internally homochiral [2,27]. Of this reason, they could be named also *twin* molecules [31]. The exceptional properties of *twin* (*CTS*) compounds were also noticed by Vickery [32]. Homodimeric *CTS* compounds constitute a chemical duality, the two opposed sides of duality are optical activity, on one hand, and their symmetry. There is one universal rule concerning *CTS* compounds: every member of this group possesses a real or imaginary *meso* isomer. Two cases should be mentioned. Compounds based on 1,2-diamino-cyclohexane [17,26,33,34] 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 [1,35], five are characterized by 1,4 mirror plane of symmetry, while allo-inositol is devoid of such a plane. Its *meso* nature ca 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) [36-38]. 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 [39,40]. Another isomer, devoid of optical activity and not cleavable by any chemical or biological method, was discovered also by Pasteur (1853) and called *meso*-tartaric acid [36,37]. Stereochemical theory of tetrahedral and asymmetric (chiral) carbon atom [41,42] 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. (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 [43]. 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 Kα rays, by sodium rubidium tartrate of the dextrorotary species, and the obtained model was assigned to (+)-tartaric acid [44]. By an impressive coincidence, this configuration of (+)-tartaric acid had been hypothetically attributed by E. Fischer (1896) [45]. Configuration of chiral centers of (–)-tartaric acid became also known, by the virtue of the law of enantiomorphism. Configuration of the two enantiomers has been connected with other chiral compounds, beginning with (–)- and (+)-glyceraldehyde [46]. A chemical relationship has been found between E. Fischer and his son, H. O. L. Fischer [47,48], 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 [49].

(C) ***Diachi***. The third group is formed of chiral diastereomers which possess a carbon skeleton identical to *meso* and *CTS*, i.e. a phenomenon of isoskeletomeric relationship [8]. E. g. glucitol [21], , bicubebin [50], bismurrangain [51], hybocarpone [30], asarolignans [52], larreatricin [53], numerous carotenoids [4,54]. However, their asymmetric carbons are distributed in an irregular manner in comparison with *meso* or *CTS* [55]. We have called them *diachi*. *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 *diachi* 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 are constitutional isomers. *Constit*. isomers present probably the highest molecular diversity.

An interesting group of *constit*. isomers is formed by a non-uniform linkage of monomers: quadrigemine C [56], aspergilazine A [57], penicillixanthone A, phomoxanthone B, dideacetylphomoxanthone B, rugulotrosin B [58], quadrigemine B [56], taondiol dimer [59,60], numerous carotenoids [4,54].

The application of our systematization to monosaccharides, discovered/invented by Fischer and others, produces the following results. (**A**) *meso* monosaccharides: galactitol [(2S,3R,4S,5R)-hexitol] [15,61], allitol [(2S,3S,4R,5R)-hexitol] [62-65], galactooctitol [(2S,3S,4R,5S,6R,7R) octitol] [66-68], galactaric acid (2R,3S,4R,5S) [15], allaric acid (2R,3R,4S,5S) [69]. (**B**) *CTS* monosaccharides: D-mannitol [(2R,3R,4R,5R)-hexitol], L-mannitol [(2S,3S,4S,5S)-hexitol] D-mannaric acid [(2S,3S,4S,5S)], L-mannaric acid [(2R,3R,4R,5R)] [70], D-iditol [(2R,3S,4S,5R)-hexitol], L-iditol [(2S,3R,4R,5S)-hexitol], D-idaric acid [(2R,3S,4S,5R)], L-idaric acid [(2S,3R,4R,5S)] [71-73]. (**C**) *diachi* monosaccharides: D-glucitol [L-gulitol (2S,3R,4R,5R)-hexitol] [74], L-glucitol [D-gulitol (2R,3S,4S,5S)-hexitol], D-glucaric acid [L-gularic (2R,3S,4S,5S)], L-glucaric acid [D-gularic (2S,3R,4R,5R)], D-altitol [D-talitol (2R,3S,4R,5R)-hexitol], L-altitol [L-talitol (2S,3R,4S,5S)-hexitol], D-altraric acid [D-talaric (2S,3R,4S,5S)], L-altraric acid [L-talaric (2R,3S,4R,5R)] [19,21,71,72,75] and 1,1,1,2,2,3-hexanehexol [76]. (**D**) *constitutional*: D-hamamelitol [77-79]. 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 [35]. 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 [80], graphite and fullerenes [81,82] 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

[1,83,84]. Molecular 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 [2,84,85]. (**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 [86].

Our aim has been especially monomeric units [86], but we prove that compounds called by Metzler in this way can also have *meso* isomers, hence an authentic dimeric character.

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 *meso* isomer of benzene, fails. However, the thing is possible for xylenes (Fig. 1), ethylbenzene, propylbenzene, etc.

At least two dozens of isomers with molecular formula $C_3H_7NO_2$ can be written (Fig. 2), just by utilising the concecrated 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.*

A spectacular example of coexistence in natural materials of *constit.* and *meso* isomers in nature can be found in carbohydrate chemistry. *Meso*-isomers of aldo- and keto-pentoses ($C_5H_{10}O_5$) are 1,2,3,4,5-pentahydroxy cyclopentanes [87-89]. Aldo- and keto-hexoses ($C_6H_{12}O_6$) are represented by six *meso* inositols [1,35].

A tentative to evaluate molecular diversity of C_8H_{18} indicated 18 [85] or 19 (84) isomers. If one take into account optical activity [90], the total number of isomers is 24 and 55, respectively. Of these, one is *meso*, two are *CTS* [91] (Fig. 1) and the others are *constit.* An unequivocal conclusion can be drawn: all alkanes beginning with C_8H_{18} present at least one *meso* isomer.

As a representative of C_nH_{2n}, eicosene can be seen (Fig. 1). The first term according to our reasoning is the *meso* isomer, cis-1,2-dimethyl cyclopropane [92].

For C_nH_{2n-2} (alkynes and alkadienes) *meso* isomer of heneicosyne (as cis-1,2-dihexyl-3-hexenyl-cyclopropane) is indicated, the first term being C_7, cis-1,2-dimethyl-3-vinyl cyclopropane or cis-3,5-dimethyl-1-cyclopentene.

For monohydroxylic alcohols there is a meso isomer of eicosanol (9-hydroxymethyl-8,10-dimethyl heptadecane), the first term is C_9 (3,5-dimethyl-4-hydroxy heptane). A general formula represents diols, 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 *diachi* isomers only by contribution of alkane chain (see 3,4,5,6-tetra-Me-octane above). Triols, similarly to trimethyl alkanes (see 3,4,5-triMe-heptane) cannot have *CTS* isomers, but *meso*, *diachi* and *constit.*; the first term is 2,3,4-pentanetriol.

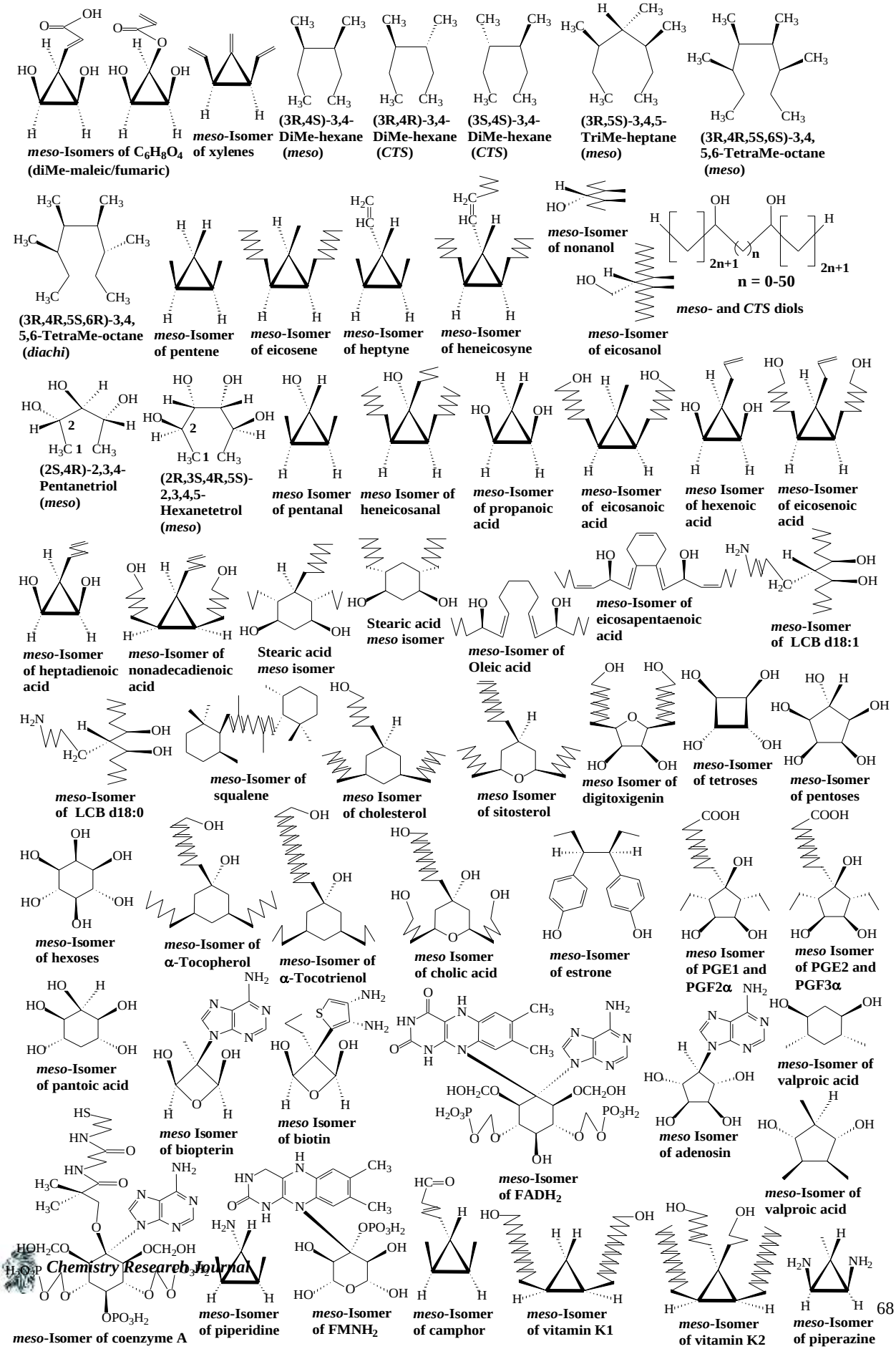
meso-Isomers of C6H8O4 (diMe-maleic/fumaric)
meso-Isomer of xylenes
(3R,4S)-3,4-DiMe-hexane (meso)
(3R,4R)-3,4-DiMe-hexane (CTS)
(3S,4S)-3,4-DiMe-hexane (CTS)
(3R,5S)-3,4,5-TriMe-heptane (meso)
(3R,4R,5S,6S)-3,4,5,6-TetraMe-octane (meso)
(3R,4R,5S,6R)-3,4,5,6-TetraMe-octane (diachi)
meso-Isomer of pentene
meso-Isomer of eicosene
meso-Isomer of heptyne
meso-Isomer of heneicosyne
meso-Isomer of nonanol
meso-Isomer of eicosanol
n = 0-50
meso- and CTS diols
(2S,4R)-2,3,4-Pentanetriol (meso)
(2R,3S,4R,5S)-2,3,4,5-Hexanetetrol (meso)
meso Isomer of pentanal
meso Isomer of heneicosanal
meso-Isomer of propanoic acid
meso-Isomer of eicosanoic acid
meso Isomer of hexenoic acid
meso-Isomer of eicosenoic acid
meso-Isomer of heptadienoic acid
meso-Isomer of nonadecadienoic acid
Stearic acid meso isomer
Stearic acid meso isomer
meso-Isomer of Oleic acid
meso-Isomer of eicosapentaenoic acid
meso-Isomer of LCB d18:1
meso-Isomer of LCB d18:0
meso-Isomer of squalene
meso Isomer of cholesterol
meso Isomer of sitosterol
meso Isomer of digitoxigenin
meso-Isomer of tetroses
meso-Isomer of pentoses
meso-Isomer of hexoses
meso-Isomer of α-Tocopherol
meso-Isomer of α-Tocotrienol
meso Isomer of cholic acid
meso-Isomer of estrone
meso Isomer of PGE1 and PGF2α
meso Isomer of PGE2 and PGF3α
meso-Isomer of pantoic acid
meso Isomer of biopterin
meso Isomer of biotin
meso-Isomer of FADH2
meso-Isomer of valproic acid
meso Isomer of adenosin
meso-Isomer of valproic acid
meso-Isomer of coenzyme A
meso-Isomer of piperidine
meso-Isomer of FMNH2
meso-Isomer of camphor
meso-Isomer of vitamin K1
meso-Isomer of vitamin K2
meso-Isomer of piperazine

Figure 1. *Meso* isomers of natural compounds, save amino acids. (see also text).

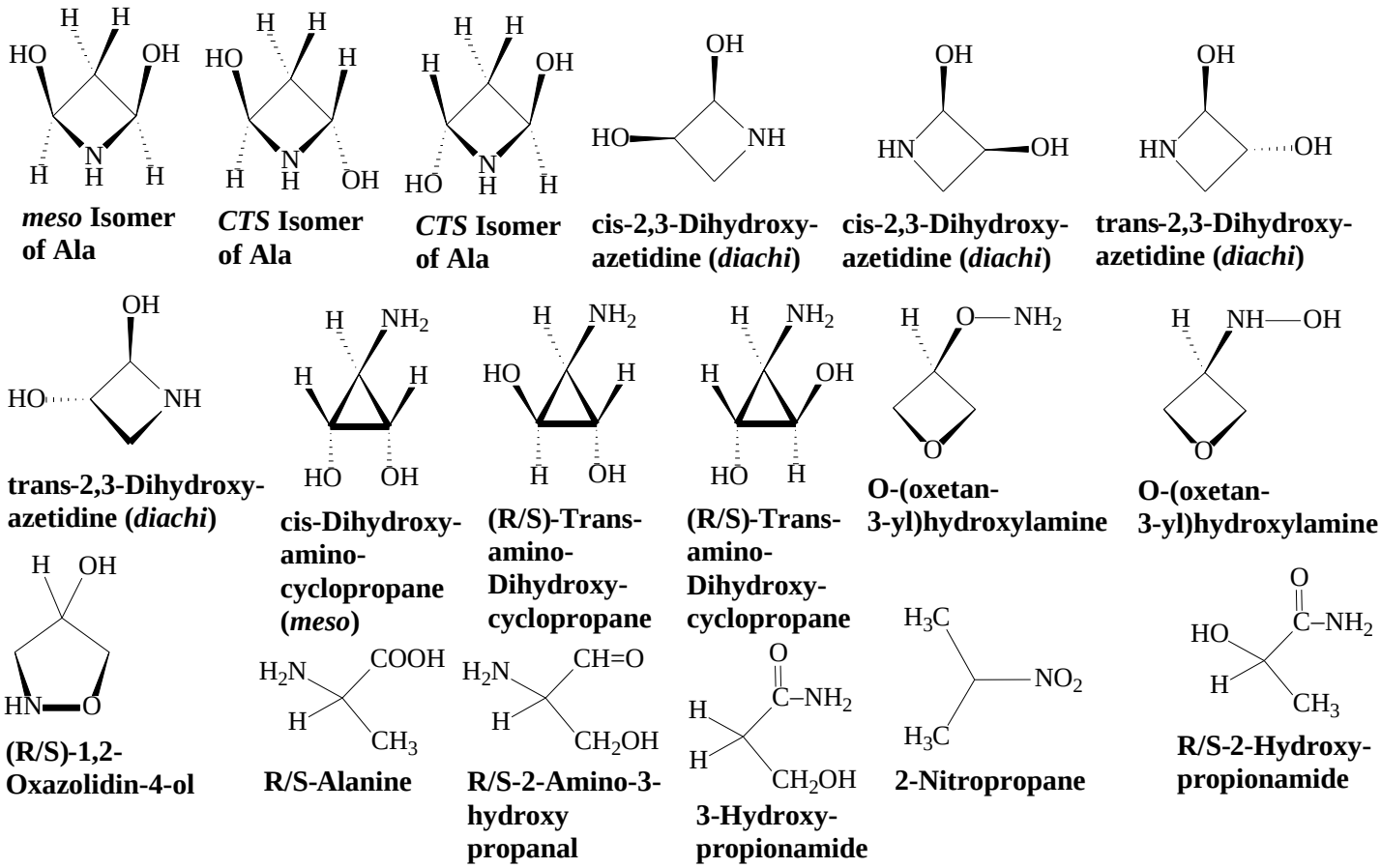

Figure 2: Isomers with the molecular formula $C_3H_7NO_2$ (the list is not exhaustive)

Tetrols presents all four types of isomers, the first term is (2R,3S,4R,5S)-2,3,4,5-hexanetetrol.

For aldehydes and ketones we introduce *meso* isomer of heneicosanal (cis-1,2-diheptyl-3-hydroxy-3-butyl), the first term is C_5 (cis-1,2-dimethyl-3-hydroxy-cyclopropane).

Meso isomer of eicosanoic acid [cis-1,2-bis(octanol)-3-methyl-cyclopropane] represents organic acids, and the first term is C_3 (cis-1,2-dihydroxy-cyclopropane). C_3 still, as well as C_4 and C_5 have three types of isomers only (*meso*, *CTS*, *constit*.), while C_6 and higher terms possess four (*meso* of C_6 is 1α,2α,3β,4β-1,2-dihydroxy-3,4-dimethyl cyclobutane). Monoenoic acids are symbolized by a *meso* isomer of eicosenoic acid [cis-1,2-bis(heptanol)-3-allyl-cyclopropane] and the first term is C_5 (cis-1,2-dihydroxy-3-allyl cyclopropane). The following isomers are considered *constit*., isomers of valproic acid (2-propyl pentanoic acid; $C_8H_{16}O_2$): 2-ethyl-3-methyl pentanoic acid, di-isopropyl acetic acid, (R)-2-isopropyl pentanoic acid, (S)-2-isopropyl pentanoic acid, octanoic acid [93]. According to our systematics, we have to begin with the finding of a $C_8H_{16}O_2$ *meso* isomer. This can be cis-1,2-dihydroxy-1,2-diethyl-3-methyl cyclopropane, cis-1,3-dihydroxy-2,2-diethyl- cyclobutane, 1β,2β,3α,4α-1,2-diethyl-3,4-dihydroxy cyclobutane, or 1β,3β,4α,6α-1,3-dihydroxy-4,6-dimethyl-cyclohexane, or others. As can be seen from their structure, the latter three isomers present also *CTS* and *diachi* forms. And the $C_8H_{16}O_2$ isomers mentioned earlier, valproic acid inclusively, are all *constit*. 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 C_7 [cis-1,2-dihydroxy-3-(1-butadienyl) cyclopropane].

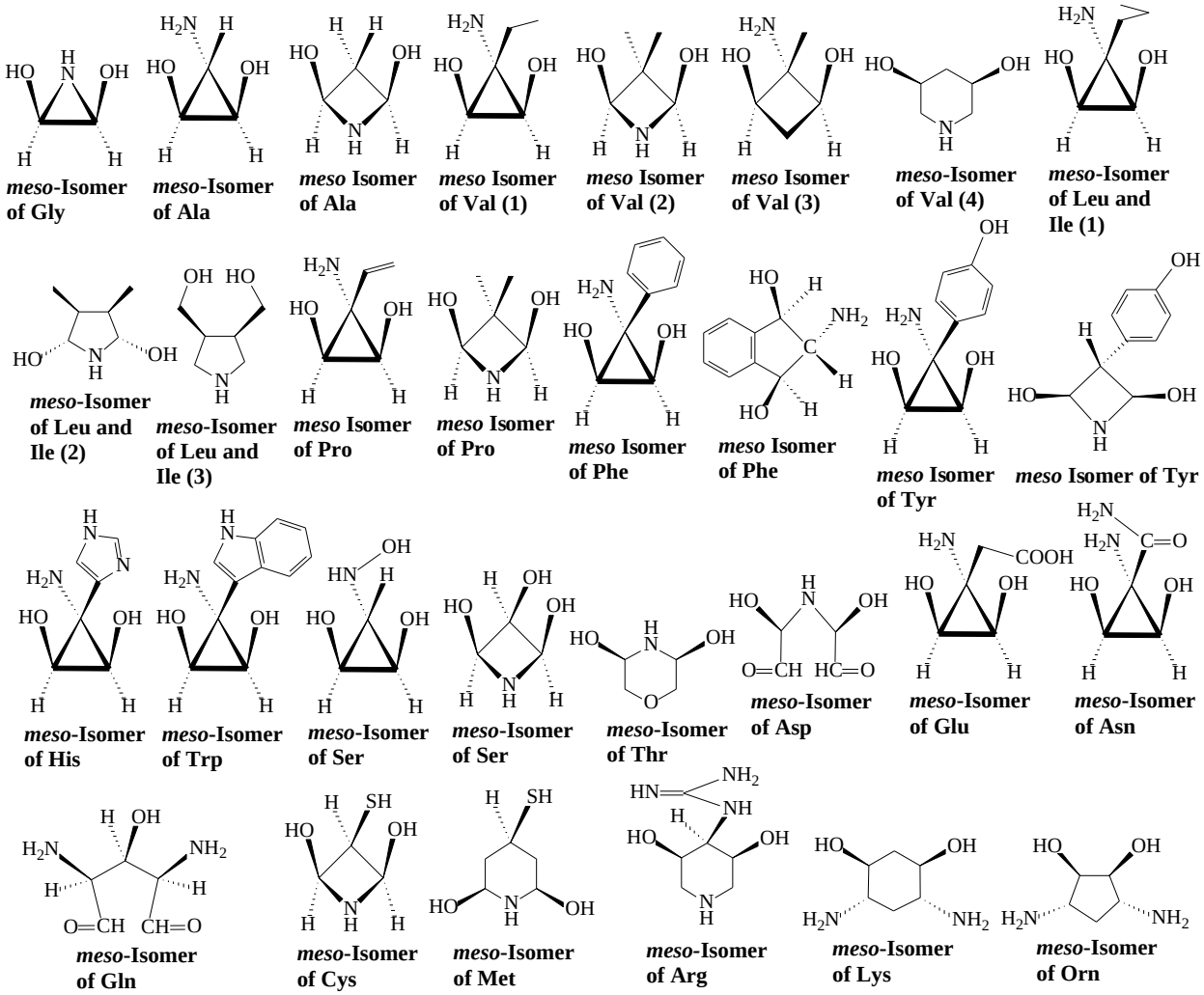

Figure 3: Meso isomers of the twenty fundamental amino acids. (see also text).

Biochemical compounds also present *meso* isomers (Figs. 1-3). Saturated, mono- and polyenoic fatty acids are represented by the isomers of stearic acid, oleic and eicosapentaenoic acid (the famous omega-3). As is obvious, an isomer of $C_{18}H_{36}O_2$ (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.), *diachi* (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 (see *meso* isomers of oleic and pentaenoic acid) (Fig. 1).

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.

Squalene presents at least one *meso* compound. Sterols have been exemplified by cholesterol, sitosterol and digitoxygenin. A similar solution has been found for estrone, stigmasterol, campesterol, ergosterol, C_{19} (5α-androstanolone), C_{21} (prednisolone, 11β-Hydroxy-progesterone, pregnenolone, progesterone, corticosterone, cortisol, aldosterone), C_{24} (biliary acids: cholic, chenodeoxycholic, deoxycholic, lithocholic).

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 prostaglandins have matching *meso* isomers, as indicated by PGE1, PGF2α, PGE2, PGF3α. A component of coenzyme A, pantoic acid, has pentahydroxy cyclohexane as a *meso* pair.

The planar structure of benzenoid compounds has been succesfully used in *meso* isomers of the following: biopterin (cis-2,4-dihydroxy-3-methyl-3-adenin oxetane), biotin [cis-2,4-dihydroxy-3-propyl-3-(3,4-diamino-thiophene-2)oxetane], adenosin (cis-3,4-dihydroxy-cis-2,5-dihydroxy-1-adenin cyclopentane), $FADH_2$, $FMNH_2$, and even coenzyme A. In order to write *meso* isomer of $FMNH_2$ 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 (not phosphoric!) on C-3 of ribitol. The fact that adenosin possesses a *meso* isomer indicates that all nucleosides and nucleotides do the same. *Meso* deoxy-nucleosides and -nucleotides are represented e.g. as cis-1,3-dihydroxy-2-hydroxymethyl-2-adenin cyclobutane or cis-1,3- dihydroxy-2-hydroxy-2-adenin cyclopentane. Camphor is also present. All alkaloids have *meso* isomers, providing they include a significant alkane moiety e.g. piperidine and piperazine.

Compounds with a ubiquitous distribution in living matter, the twenty fundamental amino acids are characterized by an unequaled structural variety. However, without any exception, they present *meso* isomers (Fig. 3). These amino acids are met especially integrated in proteins and in this state they manifest themselves by their tails [86]. *Meso*, *CTS* and *constit*. isomers present the following amino acids: Gly, Ala, Val, Thr, Asp, Pro, Phe, Arg, Trp. *Meso* 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.

An Exercise of Comparative Chemistry Gives an Answer to an Unanswered Question – Why is Natural Chemistry as it is?

A question should be raised concerning the hierarchy [8] 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 *diachi*. 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*, *CT*S and even *diachi* 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 filled, 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 *diachi*. 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 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. Fischer [21,74] illustrated this by preparing a variety C_6 monosaccharides from formaldehyde or C_3 derivatives.

Conclusions

1. Atoms or fragmens cut by the mirror plane of symmetry are masked (hidden) of polarized light, and what remains, as evidenced by this physical instrument, is a homodimer.

2. All major natural metabolites possessing a significant alkane moiety have a *meso* isomer, hence a dimeric matching.
3. Of the four types of isomers – *meso*, *C_2 symmetrical*, *diastereomeric chiral*, *constitutional* – nature selected *constitutional* ones, since they are characterized by the highest number of freedom degrees.

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