

The Nomenclature of Lipids^a

(Recommendations 1976)^{b,c}

IUPAC-IUB Commission on Biochemical Nomenclature^d

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^a Document^c of the IUPAC-IUB Commission on Biochemical Nomenclature (CBN) approved by IUPAC and IUB in 1976, and published with the cooperation of the IUB Commission of Editors of Biochemical Journals^d. Comments on these Recommendations and suggestions for future revisions may be sent to any member of CBN^d.

^b These Recommendations are a revision and extension of "The Nomenclature of Lipids", which appeared in 1967, as amended in 1970¹¹.

^c Reprints of this document, supplied by the publishing journals, may be obtained from W. E. Cohn (Director of the NAS-NRC Office of Biochemical Nomenclature), Biology Division, Oak Ridge National Laboratory, P. O. Box Y, Oak Ridge, Tenn., U.S.A., 37830.

^d Members of CBN are: O. Hoffmann-Ostenhof (Chairman), W. E. Cohn (Secretary), A. E. Braunstein, H. B. F. Dixon, B. L. Horecker, W. B. Jakoby, P. Karlson, W. Klyne, C. Liébecq, E. C. Webb.

In 1967, a "Document for Discussion" on lipid nomenclature^[1] was issued by CBN. It included a special system for the designation of configuration in glycerol derivatives that deviated considerably from standard stereochemical nomenclature. This system is based upon a fixed numbering ("stereo-specific numbering") for glycerol, regardless of substituents. It was hoped^[1] that "discussion will lead shortly to the formulation" of recommendations acceptable to chemists in the field of lipids.

In subsequent years, there has been little discussion about this principle of stereospecific numbering; it has been well accepted within the field of glycerol derivatives, for which it has been especially useful^e, and is widely used. However, during this same period, many new and complex lipids and glycolipids have been isolated. Moreover,

the Commissions on the Nomenclature of Organic Chemistry (CNOC) and Inorganic Chemistry (CNIC) issued, in 1973, "Nomenclature of Organic Chemistry, Section D"^[2], which includes a section on the nomenclature of phosphorus-containing organic compounds and necessitates a reconsideration of the earlier nomenclature^[1] in this area.

The present "Recommendations 1976" are based on reports of working groups on lipids^f and glycolipids^g. The main features are:

1. the system of stereospecific numbering is retained;
2. semisystematic nomenclature is extended to the plasmalogens;
3. a semisystematic nomenclature for higher glycosphingolipids, based on trivial names for specific tri- and tetrasaccharides, is proposed.

RECOMMENDATIONS

I. FATTY ACIDS, NEUTRAL FATS, LONG-CHAIN ALCOHOLS AND LONG-CHAIN BASES

A. Generic terms

Lip-1.1. The term **fatty acid** designates any one of the aliphatic monocarboxylic acids that can be liberated by hydrolysis from naturally occurring fats and oils. In the terms "free fatty acids" or "nonesterified fatty acids", now widely in use, "free" and "nonesterified" are actually redundant and should be omitted (See Lip-1.14). [The designation "aliphatic carboxylate (C₁₀-C₂₆, nonesterified)" used by the Commission on Quantities and Units in Clinical Chemistry is correct, but rather cumbersome.] Whenever the *sum* of fatty acids and their esters is determined by an analytical method, this should be explicitly stated. (See also Lip-1.6).

^e CBN does not wish to imply that the idea of stereospecific numbering should be applied to other groups of compounds. It is the symmetry of glycerol itself, but the asymmetry of its derivatives carrying different substituents at O-1 and O-3, as well as the unique place of these compounds in lipid metabolism, that makes this special treatment desirable.

Lip-1.2. **Neutral fats** are mono-, di- or triesters of glycerol with fatty acids, and are therefore termed monoacylglycerol, diacylglycerol or triacylglycerol, as appropriate. "Acylglycerols" includes mixtures of any or all of these.

Comments

ij The term "acyl" is used in Organic Nomenclature^[3] to denote the radical formed by loss of the OH group from the acid function of any acid (cf. Lip-1.6). We are concerned here with acyl radicals of aliphatic carboxylic acids with four or more carbon atoms, the larger members of which (> C₁₀) are also known as "higher fatty acids."

^f Members of the Working Group on Lipid Nomenclature: H. Hirschmann (U.S.A.), P. Karlson (Germany; convenor), W. Stoffel (Germany), F. Snyder (U.S.A.), S. Veibel (Denmark), F. Vögtle (Germany).

^g Members of the Working Group on Glycolipid Nomenclature: S. Basu (U.S.A.), R. O. Brady (U.S.A.), R. M. Burton (U.S.A.), R. Caputto (Argentina), S. Gatt (Israel), S. I. Hakomori (U.S.A.), M. Philippart (U.S.A.), L. Svennerholm (Sweden), D. Shapiro (Israel), C. C. Sweeley (U.S.A.), H. Wiegandt (Germany; convenor).

ii) The old terms monoglyceride, diglyceride and triglyceride are discouraged and should progressively be abandoned, not only for consistency, but mainly because strict interpretation does not convey the intended meaning. "Triglyceride", taken literally, indicates three *glycerol* residues (e.g., cardiolipin), diglyceride two (e.g., phosphatidylglycerol), and a monoglyceride is a mono-acylglycerol.

Lip-1.3. The generic term "long-chain alcohol" or "fatty alcohol" refers to an aliphatic compound with a chain-length greater than C₁₀ that possesses a terminal CH₂OH group. Such alcohols should be named according to systematic nomenclature^[3]. (See Lip-1.7).

Lip-1.4. The term **sphingoid** or **sphingoid base** refers to sphinganine (cf. Lip-1.8), [*D-erythro-2-amino-1,3-octadecanediol* (I)], its homologs and stereoisomers (II, III), and to the hydroxy and unsaturated derivatives of these compounds (IV - VI). The term "long-chain base" may be used in a wider sense to indicate any base containing a long-chain aliphatic radical.

Lip-1.5. The following generic terms are used for the following groups of compounds:

- sphingolipid**, for any lipid containing a sphingoid;
- ceramide**, for an *N*-acylated sphingoid;
- sphingomyelin**, for a ceramide-1-phosphocholine (see ref.^[2] for this use of "phospho"; also Lip-2.11);
- glycosphingolipid**, for any lipid containing a sphingoid and one or more sugars. (See sections I, B, 2 and II, A for other generic terms).

B. Individual compounds

1. Fatty acids and alcohols

Lip-1.6. Fatty acids (cf. Lip-1.1) and their acyl radicals (cf. Lip-1.2, comment i) are named according to the IUPAC Rules for the Nomenclature of Organic Chemistry (ref.^[3], Rule C-4). (A list of trivial names is given in Appendix A.) Fatty acids are numbered with the carbon atom of the carboxyl group as C-1. By standard biochemical convention, the ending -ate in, e.g., palmitate denotes any mixture of the free acid and its ionized form in which the cations are not specified. The ending -ate is also used to designate esters,

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e.g., cholesteryl palmitate, ethylidene dilaurate, etc. (cf. Lip-1.12). Structural isomers of polyunsaturated acids, hitherto distinguished by Greek letters (e.g., α - and γ -linolenic acids), are better distinguished by the locants of the unsaturated linkages (e.g., (9,12,15)- and (6,9,12)-linolenic acids, respectively). (See Lip-1.15). However, the Greek letter prefixes may be useful in (defined) abbreviations (see Appendix A).

Lip-1.7. Long-chain alcohols (fatty alcohols) and the radicals derived from them should be designated by their systematic names (ref.^[3], Rules C-201 and A-1 *et seq.*), but not by trivial names that are derived from those of fatty acids.

Examples: 1-hexadecanol and hexadecyl-, not palmityl alcohol and palmityl-; 1-dodecanol and dodecyl-, not lauryl alcohol and lauryl-.

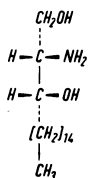
2. Sphinganine and derivatives

Lip-1.8. The compound previously known as dihydrosphingosine [*2D-amino-1,3D-octadecanediol* or *D-erythro-2-amino-1,3-octadecanediol* or (*2S,3R*)-*2-amino-1,3-octadecanediol*] is called **sphinganine** (I).

Lip-1.9. Trivial names of higher or lower homologs of sphinganine may be derived by adding a prefix (ref.^[3], Rule A-1) denoting the total number of carbon atoms in the main chain of the homolog, e.g., icosasphinganine* for the C₂₀ compound (III), hexadecasphinganine for the C₁₆ compound.

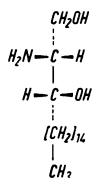
Lip-1.10. Affixes denoting substitution of sphinganine (hydroxy, oxo, methyl, etc.) are used as usual, according to existing rules^[3]. The configurations of additional substituents should be specified by the prefixes "*D*" or "*L*" (italic capitals, cf. ref.^[4]) following the locant of substitution. These prefixes refer to the orientation of the functional groups to the right or left, respectively, of the carbon chain when written vertically in a Fischer projection with C-1 at the top (cf. Formulae I - VI). If the configuration is unknown, the prefix "*X*" may be used. In the case of a racemic mixture, *rac* should be used as a prefix to the name.

* Formerly eicosasphinganine (see footnote *d* in Appendix A).



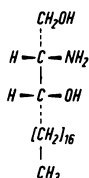
I

Sphinganine
[D-erythro or 2S,3R
configuration implied]



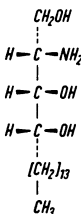
II

(2R,3R)- (or D-threo-)
2-Amino-1,3-octa-
decenediol



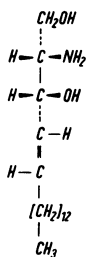
III

Icosasphinganine*



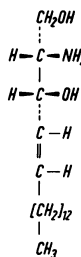
IV

4D-Hydroxysphinganine;
(2S,3S,4R)-2-amino-
1,3,4-octadecanetriol;
(phytosphingosine).



V

Sphingosine;
trans-4-sphinganine;
(4E)-sphinganine;
(2S,3R,4E)-2-amino-4-
octadecene-1,3-diol.



VI

cis-4-Sphinganine;
(4Z)-sphinganine.

* Formerly eicosasphinganine (see footnote *d* in Appendix A).

Sphingoids differing from sphinganine in their configurations at C-2 and/or C-3 should *not* be named as derivatives of sphinganine, but with fully systematic names^[3], using the prefixes D-*threo*-, L-*erythro*-, as appropriate, e.g., D-*threo*-2-amino-1,3-octadecenediol, or (2R, 3R)-2-amino-1,3-octadecenediol, for II (cf. Rule Carb-8 in ref.^[5]). (cf. Lip-1.11, ex. 4).

Comment. The semisystematic names for the sphingoids are significantly shorter than the fully systematic names only if the terms chosen imply not only substituents but also configurations. Therefore, the name "sphinganine" specifies the D-*erythro* configuration, and it is logical that the names of stereoisomers of sphinganine differing in configuration at C-2 and/or C-3 should not include "sphinganine" as a root. (This recommendation differs from that in the previous document^[1].)

The configurations usually encountered have identical configurational prefixes only if a *D/L* but not if the *R/S* system^[6] is used; e.g., C-3 is *D* and *R* in icosasphinganine (III) and *D* and *S* in 4D-hydroxysphinganine (IV). Whenever it is desirable to use the *R/S* system, the fully systematic name should be used with the specification of configuration at every center (and, when applicable, of the configuration at the double bond).

Examples:

(2R,3R)-2-amino-1,3-octadecenediol, for II;
(2S,3S,4R)-2-amino-1,3,4-octadecanetriol for IV;
(2S,3R,4E)-2-amino-4-octadecene-1,3-diol for sphingosine (V). (See also Lip-1.11.)

Lip-1.11. Names for unsaturated compounds are derived from the names of the corresponding saturated compounds by the appropriate infixes, namely ene, diene, yne, etc.^[3]. If the geometry of the double bond is known, it should be indicated by the more modern *E/Z* system (cf.^[6], Rule E-2.2), e.g., (4E)-sphinganine for sphingosine (V).

The trivial name **sphingosine** (V) is retained. If trivial names other than sphingosine are used, they should be defined in each paper in terms of this nomenclature, or of the general nomenclature of organic chemistry^[3].

Other names for the substances described in Lip-1.10 and Lip-1.11:

4D-hydroxysphinganine for IV, formerly known as phytosphingosine;
(4E)-sphinganine for sphingosine (V);
(4Z)-sphinganine for the geometric isomer of sphingosine (VI);

D-*threo*-2-amino-1,3-octadecenediol for the C-2 epimer of sphinganine (II); cf. Lip-1.10, Ex. 1.

3. Glycerol derivatives

Lip-1.12. Esters, ethers and other *O*-derivatives of glycerol are designated according to Rule Carb-15 of the Rules of Carbohydrate Nomenclature^[5] i.e. by a prefix, denoting the substituent, preceded by a locant. If the substitution is on a carbon atom, the compound is designated by its systematic name and not as a derivative of glycerol (e.g., 1,2,3-nonadecanetriol for C₁₆H₃₃CHOH-CHOH-CH₂OH, which could be considered as 1-*C*-hexadecylglycerol). It is permissible to omit the locant "*O*" if the substitution is on the oxygen atoms of glycerol.

Examples: tristearoylglycerol or tri-*O*-stearoylglycerol or glycerol tristearate, or glyceryl tristearate; 1,3-benzylideneglycerol or 1,3-*O*-benzylideneglycerol; glycerol 2-phosphate (a permissible alternative to this term is 2-phosphoglycerol).

Comment. The alternative system set forth in Rule Carb-16 of the Rules on Carbohydrate Nomenclature^[5], i.e. the use of the suffix *-ate*, is less suitable for glycerol esters, with the exception of the phosphates (see Examples). However, this system may be used to designate esters of monofunctional alcohols, e.g. cholesteryl palmitate (cf. Lip-1.6).

Lip-1.13. Stereospecific numbering. In order to designate the configuration of glycerol derivatives, the carbon atoms of glycerol are numbered stereospecifically. The carbon atom that appears on top in that Fischer projection that shows a vertical carbon chain with the hydroxyl group at carbon-2 to the left is designated as C-1. To differentiate such numbering from conventional numbering conveying no steric information, the prefix "*sn*" (for *stereospecifically numbered*) is used. This term is printed in lower-case italics, even at the beginning of a sentence, immediately preceding the glycerol term, from which it is separated by a hyphen. The prefix "*rac*-" (for *racemo*) precedes the full name if the product is an equal mixture of both antipodes; the prefix "*X*-" may be used when the configuration of the compound is either unknown or unspecified (cf. Lip-1.10).

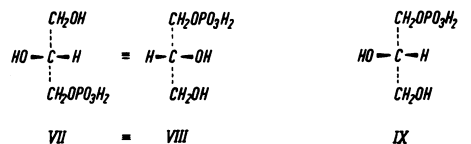
Examples:
sn-glycerol 3-phosphate for the stereoisomer (VII ≡ VIII), previously known as either L-α-glycero-phosphoric acid or as D-glycerol 1-phosphate;
rac-1-hexadecylglycerol;
 1,2-dipalmitoyl-3-stearoyl-*X*-glycerol.

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Comments

i) The problem of distinguishing between stereoisomers was discussed *in extenso* in the 1967 document^[1]. In brief, difficulties arise because glycerol is a prochiral compound. The parent substance of many phospholipids, natural glycerol phosphate, has been named both as L-α-glycerol phosphate^[7] (VII) and, according to standard rules of nomenclature, D-glycerol 1-phosphate^[8] (VIII). When the *R/S* system (sequence rule) is applied, substitution of one of the primary hydroxyl groups often leads to changes in the configurational prefix, thus obscuring chemical and biogenetical relationships; it is generally inapplicable to the steric description of such mixtures as occur in triacylglycerols isolated from natural sources: The stereospecific numbering of glycerol and its derivatives as proposed by Hirschmann^[9], described above (and in ref.^[1]), avoids these difficulties; it has proved useful and is widely accepted.

ii) The enantiomer of *sn*-glycerol 3-phosphate (VII) is *sn*-glycerol 1-phosphate (IX), as is evident from the structures.



sn-Glycerol 3-phosphate *sn*-Glycerol 1-phosphate
 [L-(glycerol 3-phosphate) [L-(glycerol 1-phosphate)
 ≡ D-(glycerol 1-phosphate)] ≡ D-(glycerol 3-phosphate)]

C. Symbols and abbreviations

Lip-1.14. The term "fatty acids" (cf. Lip-1.1) should not be abbreviated. The use of abbreviations like "FFA" for "free fatty acids" or "NEFA" for "non-esterified fatty acids" is strongly discouraged.

Comment. The words "acids" and "esters" serve to distinguish the "free" (nonesterified) and "bound" (esterified) fatty acids, and are as short as or shorter than the abbreviations themselves.

Lip-1.15. In tables and discussions where various fatty acids are involved, the notation giving the number of carbon atoms and of double bonds (separated by a colon) is acceptable, e.g. 16:0 for palmitic acid, 18:1 for oleic acid. Also, terms such as "(18:0)acyl" may be used to symbolize radicals of fatty acids. (See Appendix A).

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