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The Nomenclature of Tetrapyrroles¹⁾

A Report

compiled from Nomenclature of Tetrapyrroles,
Recommendations 1978 of the IUPAC-IUB Joint Commission on Biochemical Nomenclature

By *P. Karlson*

Chairman of the Nomenclature Committee of IUB (NC-IUB) and IUB-IUPAC Joint Commission of Biochemical Nomenclature (JCBN)

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A number of biologically very important substances – the chlorophylls, the prosthetic groups of the cytochromes and hemoglobins and their breakdown products, the bile pigments – belong to the class of tetrapyrroles. The nomenclature generally used hitherto in this field was developed by *Hans Fischer* in his extensive work on the chemistry of porphyrins and related substances, culminating in 1929 in the synthesis of heme.

The *Fischer* nomenclature is based on a very large number of trivial names that are not easy to memorize. New interest in the field made a revision of the nomenclature desirable. Therefore, the International Union of Pure and Applied Chemistry (IUPAC) and the International Union of Biochemistry (IUB), through their Nomenclature Committees, have issued recommendations on the nomenclature of tetrapyrroles, based on the proposals of a subcommittee of which Prof. *R. Bonnett* (Queen Mary College, London) was convener.

The full document (1), over 50 pages long, contains many special rules of interest mainly to the chemist working in this field. However, the new proposals have some implications on porphyrins of biochemical, clinical-chemical and clinical interest. The following report selects the recommendations important in the field of heme pigments, its precursors and metabolites which are of primary interest in mammalian (and human) biochemistry; chlorophyll derivatives are only partly considered here. It is hoped that this report will help to make the new proposals generally known and accepted.

In the following, the specific recommendations are quoted by their section number in the tetrapyrrole document. Not all sections are reviewed. For details, the reader is referred to the full publication (1).

TP-1. The fundamental macrocyclic tetrapyrrolic system shown in figure 1 is named porphyrin. The older term porphine is abandoned. The system of double bonds is represented in a formal way; also, the two hydrogen atoms at the nitrogen atoms not involved in the conjugated system are drawn conventionally at N-21 and N-23.

As seen from figure 1, porphyrin is numbered from 1–24. The former system of numbering is shown to the left for easy comparison. The 1–24 numbering system is adopted from the corrinoid nomenclature (2). The numbering system is one of the most important changes in the nomenclature of porphyrins. Note that the carbon atoms at the methylene bridges formerly designated by greek letters are now numbered 5, 10, 15 and 20.

Systematic names of substituted porphyrins are formed by application of the rules of systematic organic nomen-

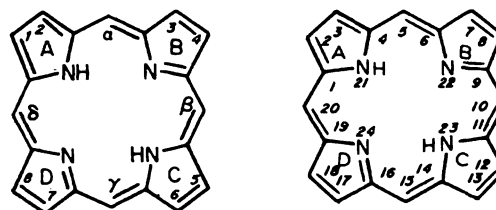


Fig. 1. *Fischer* numeration and porphyrin 1–24 numbering scheme.

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clature (3). These rules result often in a numbering scheme that differs from the numbering in trivial names. Examples are given below (see also fig. 4).

TP-2 *Trivial names*. Eleven well-established trivial names of porphyrins are retained, and a twelfth one (phytoporphyrin, fig. 2, for the compound formerly called phylloerythrin) has been coined; they are listed in table 1. The numbering system used with these trivial names is shown in figure 3 with mesoporphyrin as example. Moreover, the designation of the positional isomers in the coproporphyrin, uroporphyrin and etioporphyrin series (tab. 2) introduced by *H. Fischer* is retained. Thus, no change is necessary in the designation of the common porphyrins excreted in cases of porphyria.

TP-3 *Semisystematic names*. The trivial names listed in table 1 may also be used to derive semisystematic names by applying the general rules of organic nomenclature. The porphyrin with the highest rank (tab. 1, column 2)

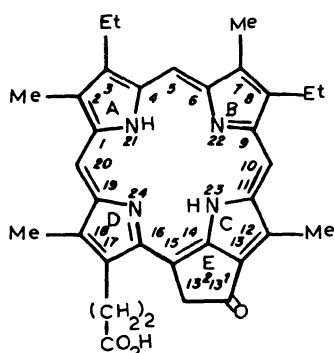


Fig. 2. Phytolporphyrin.

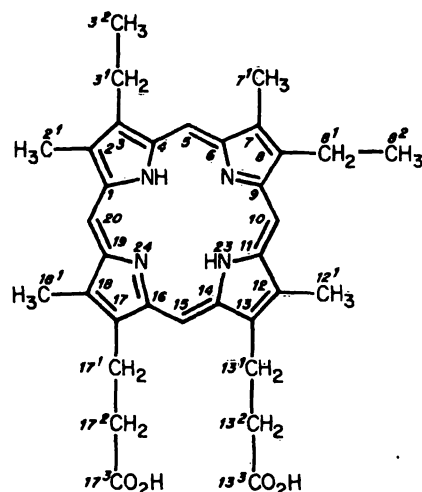


Fig. 3. Numbering of mesoporphyrin.

should be used as stem name. This is illustrated in the following examples (fig. 4).

TP-4. This section is dealing with reduced porphyrins. In this report, it may suffice to say that the term porphyrinogen is retained for the cyclic tetrapyrrole system with methylene bridges (fig. 5).

TP-5 gives recommendations for ring-expanded and ring-contracted systems.

TP-6 *Linear tetrapyrroles*. Though many of the well-known names for the bile pigments are retained as trivial names, the numbering system and designation of rings is different. The fundamental system is termed bilin; two derived systems are termed bilinogen and

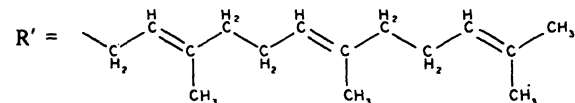
Tab. 1. Trivial names for substituted porphyrins^a.

| Trivial name ^b | Rank | Substituents ^c and locants | | | | | | | | | |
|---------------------------------|------|---------------------------------------|---------------------------|----|------------------------|----|-------------------------|-----|-----|------|--|
| | | 2 | 3 | 7 | 8 | 12 | 13 | 15 | 17 | 18 | |
| Coproporphyrin I | 9 | Me | Cet | Me | Cet | Me | Cet | H | Me | Cet | |
| Cytoporphyrin ^c | 11 | Me | -CH(OH)CH ₂ R' | Me | Vn | Me | Cet | H | Cet | -CHO | |
| Deuteroporphyrin ^{d,e} | 1 | Me | H | Me | H | Me | Cet | H | Cet | Me | |
| Etioporphyrin I | 3 | Me | Et | Me | Et | Me | Et | H | Me | Et | |
| Hematoporphyrin ^e | 8 | Me | -CH(OH)CH ₃ | Me | -CH(OH)CH ₃ | Me | Cet | H | Cet | Me | |
| Mesoporphyrin ^e | 7 | Me | Et | Me | Et | Me | Cet | H | Cet | Me | |
| Phylloporphyrin ^f | 4 | Me | Et | Me | Et | Me | H | Me | Cet | Me | |
| Protoporphyrin ^e | 6 | Me | Vn | Me | Vn | Me | Cet | H | Cet | Me | |
| Pyroporphyrin ^f | 2 | Me | Et | Me | Et | Me | H | H | Cet | Me | |
| Rhodoporphyrin ^f | 5 | Me | Et | Me | Et | Me | -CO ₂ H | H | Cet | Me | |
| Uroporphyrin I | 10 | Cm | Cet | Cm | Cet | Cm | Cet | H | Cm | Cet | |
| Phytolporphyrin | 12 | Me | Et | Me | Et | Me | -C(O)-CH ₂ - | Cet | Me | | |

^a) The porphyrins are arranged alphabetically. They are ranked according to (i) number of component rings, (ii) number of carbon atoms, (iii) molecular weight. A porphyrin of higher rank number is preferred to one of lower rank for selection as parent for semisystematic names according to TP-3.1 and TP-3.3..

^b) For explanation of Roman numerals associated with some of the trivial names see TP-2.2, and table 2 of this report.

^c) The following abbreviations are used; Cm for -CH₂CO₂H; Cet for -CH₂CH₂CO₂H; Me for -CH₃; Et for -CH₂CH₃; Vn for -CH=CH₂; see *Eur. J. Biochem.* 74, 1-6 (1977). The use of the symbols A and P, which is a parochial practice in the field of porphyrin chemistry for -CH₂CO₂H and -CH₂CH₂CO₂H, respectively, is not recommended.



trans, trans-farnesyl which is (2*E*,6*E*)-3,7,11-trimethyl-2,6,10-dodecatrienyl. See *J. Chem. Soc. Chem. Commun.* 278 (1977).

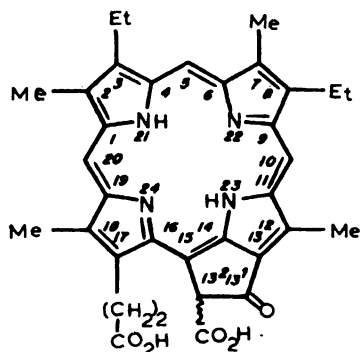
^d) Not to be confused with deuterioporphyrin, a possible name for an isotopically labeled compound.

^e) Formerly type IX.

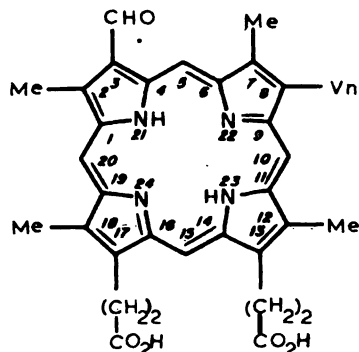
^f) Formerly type XV.

Tab. 2. Positional isomers. Abbreviations used are Me for 'methyl', Cet for 'carboxyethyl', Et for 'ethyl', and CM for 'carboxymethyl': see Eur. J. Biochem. 74, 1-6 (1977).

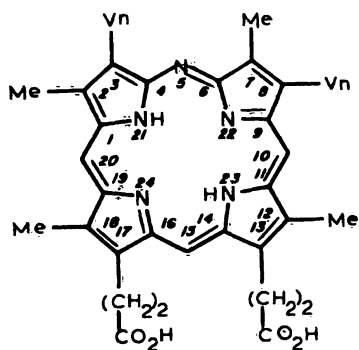
| Name | Substituents and locants | | | | | | | | |
|--------------------|--------------------------|-----|-----|-----|-----|-----|----|-----|-----|
| | 2 | 3 | 7 | 8 | 12 | 13 | 15 | 17 | 18 |
| Coproporphyrin I | Me | Cet | Me | Cet | Me | Cet | H | Me | Cet |
| Coproporphyrin II | Me | Cet | Cet | Me | Me | Cet | H | Cet | Me |
| Coproporphyrin III | Me | Cet | Me | Cet | Me | Cet | H | Cet | Me |
| Coproporphyrin IV | Me | Cet | Me | Cet | Cet | Me | H | Cet | Me |
| Etioporphyrin I | Me | Et | Me | Et | Me | Et | H | Me | Et |
| Etioporphyrin II | Me | Et | Et | Me | Me | Et | H | Et | Me |
| Etioporphyrin III | Me | Et | Me | Et | Me | Et | H | Et | Me |
| Etioporphyrin IV | Me | Et | Me | Et | Et | Me | H | Et | Me |
| Uroporphyrin I | Cm | Cet | Cm | Cet | Cm | Cet | H | Cm | Cet |
| Uroporphyrin II | Cm | Cet | Cet | Cm | Cm | Cet | H | Cet | Cm |
| Uroporphyrin III | Cm | Cet | Cm | Cet | Cm | Cet | H | Cet | Cm |
| Uroporphyrin IV | Cm | Cet | Cm | Cet | Cet | Cm | H | Cet | Cm |



Semisystematic: Phytoporphyrin-13²-carboxylic acid
 Systematic: 2²-Carboxy-7,12-diethyl-2,2-dihydro-3,8,13,17-tetramethyl-2-oxocyclopenta[*a*]porphyrin-18-propionic acid
 Fischer: Pheoporphyrin *a*₅



Semisystematic: 3-Formyl-8-vinyldeuteroporphyrin
 Systematic: 8-Formyl-3,7,12,17-tetramethyl-13-vinylporphyrin-2,18-dipropionic acid
 Fischer: Chlorocruoroporphyrin or Spirographisporphyrin



Semisystematic: 5-Azaporphyrin
 Systematic: 2,7,12,18-Tetramethyl-3,8-divinyl-5-azaporphyrin-13,17-dipropionic acid

1,19-secocorrin; they differ in the number of hydrogen atoms. Their structures are given in figure 6.

The trivial names biliverdin, bilirubin, mesobilirubin, urobilin and stercobilin are retained, but they are now confined to the positional isomers IXa according to the Fischer system (fig. 7). The isomers derived from elimina-

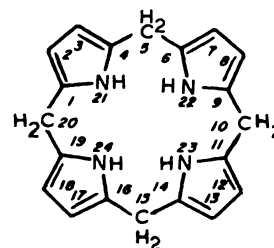
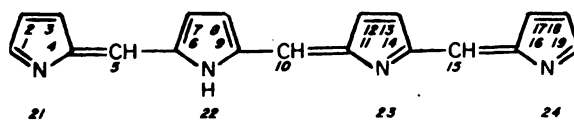
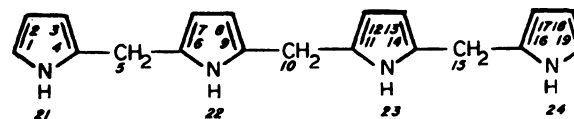


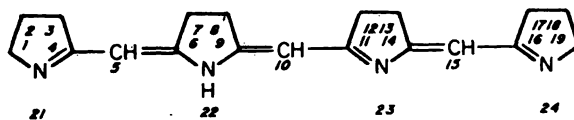
Fig. 5. Porphyrinogen. 5,10,15,20,22,24-Hexahydro porphyrin.



Bilin. 22*H*-form drawn conventionally



Bilinogen or 5,10,15,21,23,24-hexahydrobilin



1,19-Secocorrin or 1,2,3,7,8,12,13,17,18,19-decahydrobilin

Fig. 6. Numbering scheme for linear tetrapyrroles.

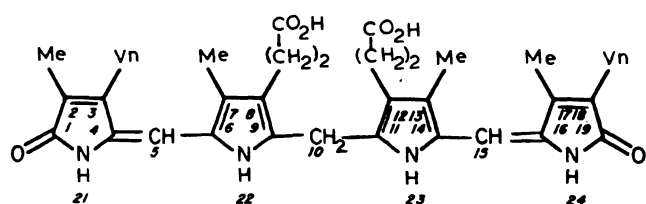
Fig. 4. Semisystematic and systematic names for some substituted porphyrins. Note the change in numbering system in the systematic names, due to application of the rules of systematic organic nomenclature.

tion of the bridge atoms 10, 15 and 20 should be named according to the systematic names; no semi-trivial or semi-systematic names are recommended. The following figure 8 gives some structures together with the numbering. It will be seen that all structures are drawn in the lactam form, not in the tautomeric form of 1,19-dihydroxybilin; the keto form is believed to be predominant in the natural compounds.

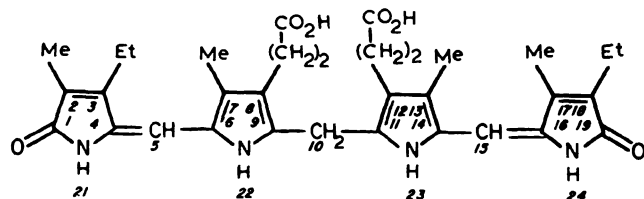
TP-7 is dealing with tripyrroles; the fundamental structure is called tripyrrin.

TP-8 *Metal coordination complexes*. They are named according to the IUPAC Rules for Coordination Compounds (4). The stereochemistry of the ligands may be designated by the greek letters α and β as defined in figure 9. The tetrapyrrole system is oriented in such a way that the numbering appears clockwise when viewed from above.

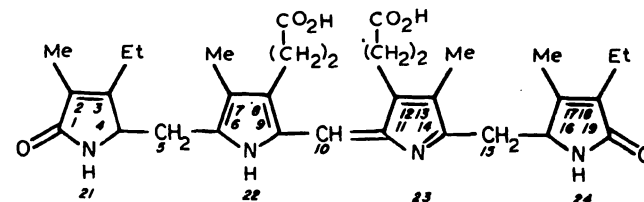
Most of the biochemically important metal complexes retain trivial names. The document lists nine chlorophylls with trivial names. The term "heme" is now used as generic term for iron porphyrin complexes; it may be used as suffix in trivial names like protoheme or



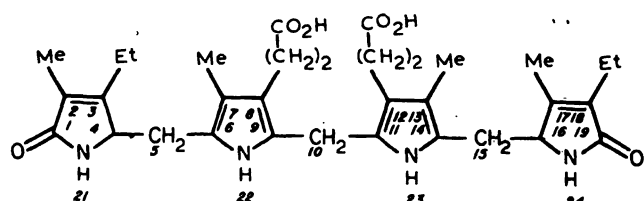
Bilirubin. Formerly bilirubin IX α



Mesobilirubin. Formerly mesobilirubin IX α

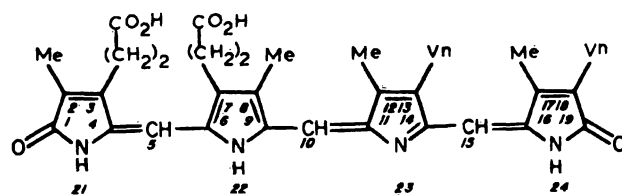


Urobilin. Formerly urobilin IX α



Urobilinogen. Formerly mesobilirubinogen IX α ; urobilinogen IX α

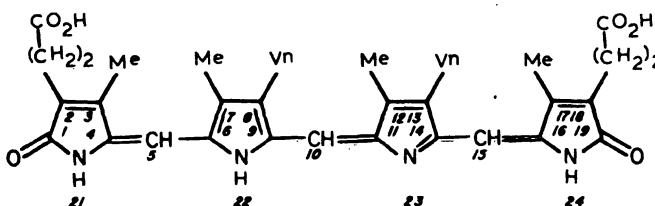
Fig. 7. Numbering scheme for some common bile pigments



1,19,21,24-Tetrahydro-2,8,12,17-tetramethyl-1,19-dioxo-13,18-divinylbilin-3,7-dipropionic acid (formerly biliverdin IX β)

or

3,7-Bis(2-carboxyethyl)-21,24-dihydro-2,8,12,17-tetramethyl-13,18-divinylbilin-1,19-dione



1,19,21,24-Tetrahydro-3,7,12,17-tetramethyl-1,19-dioxo-8,13-divinylbilin-2,18-dipropionic acid (formerly biliverdin IX γ)

or

2,18-Bis(2-carboxyethyl)-21,24-dihydro-3,7,12,17-tetramethyl-8,13-divinylbilin-1,19-dione

Fig. 8. Systematic names of some less common bile pigments

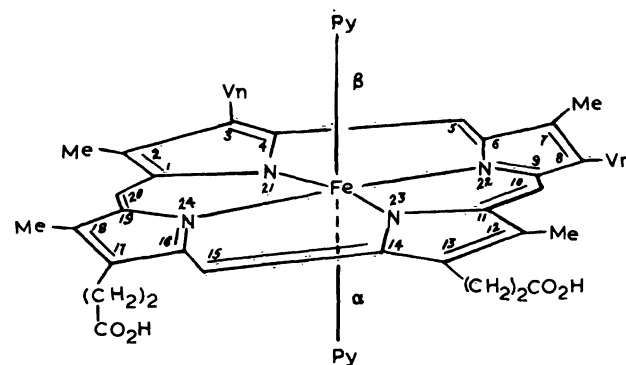


Fig. 9. A protoheme as an example of a tetrapyrrole coordination complex containing a tetrapyrrole tetradentate dianionic ligand and two pyridine molecules as axial ligands.

Tab. 3. Iron coordination complexes.

| | |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| Heme: | an iron porphyrin coordination complex |
| Ferroheme: | an iron(II) porphyrin coordination complex |
| Ferriheme: | an iron(III) porphyrin coordination complex |
| Hemochrome: | a low-spin iron porphyrin coordination complex with one or more strong field axial ligands (e.g. pyridine) |
| Ferrohemochrome: | an iron(II) hemochrome |
| Ferrihemochrome: | an iron(III) hemochrome |
| Hemin: | a chloro(porphyrinato)iron(III)coordination complex. For example protohemin = chloro(protochlorophyrinato)iron(III) or chloroiron(III) protoporphyrinate |
| Hematin: | a hydroxo(porphyrinato)iron(III)coordination complex |

cytochrome (the hemes derived from protoporphyrin and cytoporphyrin, respectively; cf. tab. 1). The term heme does not specify the valence state of the iron atom. If this is desirable, "ferro-" or "ferri-" may be used as

prefix. Thus, ferroprothemo would be the full trivial name for the prosthetic group of hemoglobin. The following table 3 summarizes the recommendations for iron coordination complexes.

References

1. IUPAC-IUB Joint Commission on Biochemical Nomenclature. Nomenclature of Tetrapyrroles. *Pure & Appl. Chem.* 51, 2251-2304 (1979); *Eur. J. Biochem.* 108, 1-30 (1980).
2. IUPAC-IUB Commission on Biochemical Nomenclature, "Nomenclature of Corrinoids, Rules Approved 1975." *Pure & Appl. Chem.* 48, 495-502 (1976) which supersedes IUPAC Commission on the Nomenclature of Biological Chemistry, "Definitive Rules for the Nomenclature of Vitamins". *J. Am. Chem. Soc.* 82, 5582 (1960) Rule V-15.
3. IUPAC, "Nomenclature of Organic Chemistry (1969)" Sections ABCDEF. Pergamon Press Oxford, 1979, Rule C-15. 1. See also TP-1.7.
4. Section D in l. c. (3).

Prof. Dr. Dr. h. c. Peter Karlson
Institut für Physiologische Chemie I
Lahnberge
D-3550 Marburg (Lahn)