IUPAC-IUB Commission on Biochemical Nomenclature (CBN)

Nomenclature for Vitamins B-6 and Related Compounds

Recommendations 1973[1,2]

INTRODUCTION

The first naturally occurring form of vitamin B-6 was isolated in 1938. It has the structure, confirmed by chemical synthesis (1939), of 3-hydroxy-4,5-bis(hydroxymethyl)-2-methylpyridine[3] (I; R = $-CH_2OH$). The trivial name "pyridoxine", proposed for this compound by P. György, came into general use as a synonym for "vitamin B-6". Two other natural compounds possessing vitamin B-6 activity, detected in 1944 and recognized as the aldehyde, or 4-formyl analogue (I; R = $-CHO$) of pyridoxine, and the corresponding amine, or 4-aminomethyl analogue (I; R = $-CH_2NH_2$), were designated "pyridoxal" and "pyridoxamine" respectively.

Within the next few years, I. C. Gunsalus, E. E. Snell, A. E. Braunstein and others demonstrated that a phosphoryic derivative of pyridoxal, later identified as pyridoxal 5′-phosphate (II; R = $-CHO$), is the coenzyme of a large group of specific enzymes catalysing reactions of amino-group transfer, decarboxylation and other metabolic transformations of individual amino acids. In the course of enzymic transamination, pyridoxal 5′-phosphate undergoes reversible conversion into pyridoxamine 5′-phosphate (II; R = $-CH_2NH_2$), which has coenzyme activity for the aminotransferases (EC 2.6.1.–), but not for other types of vitamin B-6-dependent enzymes [2,3].

In the IUPAC Definitive Rules for the Nomenclature of Vitamins, published in 1960 [4], the term "pyridoxine" was recommended as a generic designation of the B-6 vitamins, and "pyridoxol" as the trivial name for the alcohol form (I; R = $-CH_2OH$) previously designated as pyridoxine (Rule V-7). In the IUPAC-IUB Tentative Rules of 1966 [1] for the nomenclature of vitamins and related compounds (Rule M-7.1), it was suggested that the latter compound should be designated "pyridoxine" or "pyridoxol" (see 7.1 below).

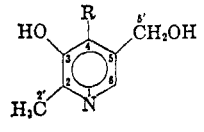
One regrettable consequence of these conflicting recommendations, giving rise to justified criticism, is the continuing use of the word "pyridoxine" in two different meanings—as a generic term for substances with vitamin B-6 activity, and as the trivial name of a definite chemical compound (which, incidentally, is one of the less abundant among the naturally occurring forms of vitamin B-6).

An extensive literature has accumulated on the chemistry and biochemistry of the B-6 vitamins and coenzymes, of their metabolites and of many related synthetic compounds that often exhibit biological activity as substitutes for or as antagonists of the corresponding natural products. A number of trivial and semitrivial names, sometimes incorrect or ambiguous, have been coined for vitamin B-6 derivatives and analogues, and several forms of abbreviated designations for these compounds have been introduced. For example, the abbreviations pyridoxal-*P*, *P*-pyridoxal, PLP (the symbol used most frequently), PALP, PalP, PALPO are in use for pyridoxal 5′-phosphate, and similar abbreviated froms have been used for other members of the group and their derivatives.

The IUPAC-IUB Commission on Biochemical Nomenclature (CBN), at its meeting in June 1968, decided to publish a special document, extending Section M-7 of the 1966 Rules [1], to put in order the nomenclature of the vitamin B-6 field and to unify relevant abbreviations for use in situations where this is essential. The present Recommendations are based on drafts prepared by A. E. Braunstein and E. E. Snell after consultation with other workers active in the field.

RULES (replacing Section M-7 of [1])

The term vitamin B-6 should be used as the generic descriptor for all 3-hydroxy-2-methylpyridine derivatives ▲ exhibiting qualitatively in rats the



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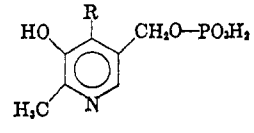

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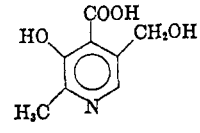

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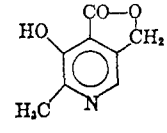


IV

biological activity of pyridoxine. This term should be used in derived terms such as vitamin B-6 deficieny, vitamin B-6 activity, vitamin B-6 antagonists [5,6].

7.1. Compound I (R = $-CH_2OH$), 3-hydroxy-4,5-bis(hydroxymethyl)-2-methylpyridine[4], should be designated ▲

[1] This document is a revision of proposals published as Tentative Nomenclature Appendix No. 6 to *IUPAC Information Bulletin*, September, 1970 which were, in turn, an extension and revision of Section M-7 of the earlier *IUPAC-IUB Tentative Rules, Trivial Names of Miscellaneous Compounds of Importance in Biochemistry* [1].

[2] Comments on, and suggestions for future revisions of these recommendations may be sent to any member of the IUPAC-IUB Commission on Biochemical Nomenclature: O. Hoffmann-Ostenhof (Chairman), W. E. Cohn (Secretary), A. E. Braunstein, B. L. Horecker, P. Karlson, B. Keil, W. Klyne, C. Liébecq, E. C. Webb, W. J. Whelan. Reprints may be obtained from W. E. Cohn (Director), NRC Office of Biochemical Nomenclature, Biology Division, Oak Ridge National Laboratory, Box Y, Oak Ridge, Tennessee, U.S.A. 37830.

[3] The systematic name, by IUPAC Organic Rule C-204.1, is 4,5-bis(hydroxymethyl)-2-methyl-3-pyridinol.

▲ Indicates revision.

[4] See foot-note [3].

pyridoxine[5]. The alkyl residue formed by removal of the 4′-OH group is named *pyridoxyl* (*e.g.* in compounds such as N^6-pyridoxyl-L-lysine and the like).

Comment. "Pyridoxine" should not be used as a generic name synonymous with "vitamin B-6" [5,6].

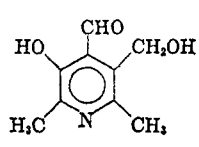
7.2. Compound I (R = —CHO) should be designated *pyridoxal*. The bivalent radical formed by removal of the oxygen atom from the CHO group is named *pyridoxylidene*.

7.3. Compound I (R = $-CH_2NH_2$) should be designated *pyridoxamine*.

7.4. The commonly occurring oxidized metabolites of pyridoxal, namely 3-hydroxy-5-hydroxymethyl-2-methylpyridine-4-carboxylic acid (III) and the corresponding lactone (IV), should be designated *4-pyridoxic acid* and *4-pyridoxolactone* respectively. (Three less commonly occurring metabolites of pyridoxine, formed by oxidation at position 5′, have also been detected, namely the aldehyde, the carboxylic acid and its lactone; they have been designated by the trivial names "isopyridoxal", "5-pyridoxic acid" and "5-pyridoxolactone" respectively.)

Vitamin B-6 Phosphates

7.5. The 5′-phosphoric esters of pyridoxine, pyridoxal and pyridoxamine (II; R = $-CH_2OH$, —CHO, $-CH_2NH_2$) should be designated *pyridoxine 5′-phosphate* (or pyridoxine-5′-*P*), *pyridoxal 5′-phosphate* (or pyridoxal-5′-*P*) and *pyridoxamine 5′-phosphate* (or pyridoxamine-5′-*P*) respectively. The positional numeral, 5′-, may be omitted where no ambiguity arises (in biochemical papers, *etc.*); *e.g.* pyridoxal 5′-phosphate may be abbreviated pyridoxal-*P*.



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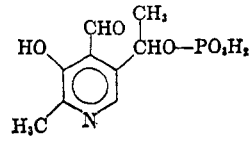

VI

For convenience (for example in names of derived compounds), it is admissible to use the symbol *P* (for "phosphoric ester") as a prefix, for example: N^6-(5′-*P*-pyridoxyl)-L-lysine; *P*-pyridoxylideneimines.

Derivatives and Analogues

7.6. From the trivial names already indicated, semi-trivial names for various derivatives and analogues of the B-6 vitamins and their phosphoric esters (coenzyme analogues) can be constructed according to the conventional rules of organic nomenclature (see also 7.9).

Examples

5′-deoxypyridoxal,
2-demethylpyridoxal, or 2-norpyridoxal,
2-propyl-2-norpyridoxal, or 2′-ethylpyridoxal (not ω-ethylpyridoxal),
6-methylpyridoxal (Compound V),
2′-hydroxypyridoxal (2-hydroxymethyl-2-demethylpyridoxal, 2-hydroxymethyl-2-norpyridoxal; not ω-hydroxypyridoxal),
4′-deoxypyridoxine 5′-phosphate,
5′-methylpyridoxal-5′-*P* (Compound VI),
pyridoxal *N*-oxide 5′-phosphate.

▲ [5] The previous synonym, pyridoxol, (see Introduction and [1]) is no longer recommended.

Abbreviated Designations

7.7. As noted in the Introduction, many abbreviations have been used in the past to represent the three principal forms of vitamin B-6, their phosphoric esters and analogues in the text of papers. Those listed in column 2 of the Table 1 have achieved prominence as the favoured forms. Their use in text in place of the approved trivial names (column 1), which are sufficiently short, is not recommended. It is admissible to use the abbreviations, with *ad hoc* definition in each paper (and with the consent of the editors concerned), when necessary in cases of space restriction, *e.g.* in tables, in figures and in extensive lists of derivatives and their reactions.

Table 1. *Abbreviated designations*

Trivial name (abridged)[a]	Abbreviation[b]
Pyridoxal	PL
Pyridoxamine	PM
Pyridoxine	PN
Pyridoxal-*P*	PLP
Pyridoxamine-*P*	PMP
Pyridoxine-*P*	PNP

[a] Recommended for use in text.

[b] Previous major abbreviations; not recommended for use in text. Admissible (with *ad hoc* definition) in special cases, *e.g.* when required by space limitations (see 7.7); they may also be combined with approved symbols (7) for commonly occurring substituents, *e.g.* 6MePL (Compound V). Compounds involving the pyridoxyl or pyridoxylidene radical should generally be symbolized as indicated in Paragraph 7.8 (see [7]). For isotopic replacement, see Paragraph 7.9.

Use of Symbols in the Designation of Derivatives and Analogues

7.8. Pyridoxyl (7.1) and pyridoxylidene (7.2) groups and similar residues of vitamin B-6 phosphates and analogues (7.5, 7.6) frequently occur in natural substances (B-6-dependent enzymes), and in modified or synthetic products (*e.g.* enzymes reconstituted with coenzyme analogues or reduced with borohydride or both) in combination with aminoacyl or peptidyl residues.

To represent such derivatives in condensed forms similar to those recommended for substituted polypeptides, it is suggested to use the following symbols:

Pxy — (having a single bond) for the pyridoxyl group.

Pxd = (having a double bond) for the pyridoxylidene group.

The corresponding 5′-phosphorylated residues may be designated by adding the symbols *P* as a hyphenated prefix or suffix, and common alkyl or acyl substituents by prefixes in parentheses, composed from the recommended symbols and their locants [7—9].

Examples

Pxy
|
Pxy—$^{\varepsilon}$Lys- or Pxy Lys- or -Lys- or -Lys(Pxy)- for the N^6-pyridoxyl-L-lysyl residue[6]

P-Pxy
|
P-Pxy—$^{\varepsilon}$Lys- or *P*-Pxy Lys- or -Lys- or -Lys(*P*-Pxy)- for the corresponding N^6-(*P*-pyridoxyl)-L-lysyl residue[6]

[6] The latter two symbols are more suitable for use in sequences (see last three examples).

Pxd $\overset{\varepsilon}{=}$ Lys-, etc., *P*-Pxd $\overset{\varepsilon}{=}$ Lys-, *etc.*, for the N^6-pyridoxylidene-L-lysyl residue and its phosphoric ester

Pxy$\overset{\alpha}{-}$Lys-, or Pxy—Val-, *etc.*, for N^2-pyridoxyl-L-lysyl and other N^2-pyridoxyl-L-aminoacyl residues[7]

P-Pxy$\overset{\alpha}{-}$Lys-, *P*-Pxy—Val-, *etc.*, for the corresponding N^2-(*P*-pyridoxyl)-L-aminoacyl residues[4]

Pxd = Val-, *P*-Pxd = Val-, *etc.*, for N^2-pyridoxylidene-L-aminoacyl residues and the corresponding phosphoric esters

P-(3deoxy)Pxd $\overset{\varepsilon}{=}$ Lys-, for the N^6-(3-deoxy-5′-*P*-pyridoxylidene)-L-lysyl residue

(3Me-2nor)Pxy—*P*
|
···-Leu-Lys-Gly-···, for an N^6-(3-*O*-methyl-2-nor-5′-*P*) pyridoxyl-L-lysyl residue in a peptide sequence

(6Me)Pxd
||
···-Leu-Lys-Gly-···, for an N^6-(6-methylpyridoxylidene)-L-lysyl residue in a peptide sequence

Pyridoxal-*P*
|
···-Gly-Ser-Val-···, for a hypothetical pyridoxal-5′-*P*-3-*O*-L-seryl (phosphodiester) residue in a peptide sequence.

Isotopic Replacement

7.9. Isotopic replacement in B-6 vitamins, coenzymes, and derivatives can be designated by the conventional notations.

Examples

[3-^{18}O]pyridoxal-*P*, for pyridoxal 5′-phosphate labeled with ^{18}O at O-3

6-[^{3}H]methylpyridoxamine-[^{32}P]*P*, for 6-methylpyridoxamine 5′-phosphate with tritium at C-6′ and ^{32}P in the phosphate group

[2′-^{14}C]Pxd
||
···-Leu-Lys-Ser-···, for a peptide sequence with an N^6-pyridoxylidene-L-lysyl residue labeled with ^{14}C at C-2′.

[7] In NH_2-terminal position.

REFERENCES

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8. IUPAC-IUB Commission on Biochemical Nomenclature (1967) *Eur. J. Biochem. 1*, 259—266; and elsewhere.
9. IUPAC-IUB Commission on Biochemical Nomenclature (1970) *Eur. J. Biochem. 15*, 203—208; and elsewhere.

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