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DEFINITIVE NOMENCLATURE  
FOR VITAMINS B-6 AND  
RELATED COMPOUNDS

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### CORRIGENDUM

The running headlines appearing on pages 449 and 451 of *Pure and Applied Chemistry*, Vol. 33, Nos. 2-3 (1973) should be corrected to read "IUPAC-IUB DEFINITIVE RULES". The phrase "Tentative Rules" should be replaced by "Definitive Rules" in the list of contents on the outside back cover (item, page 445) and in the list of contents included at the beginning of this same issue. Correspondingly, the phrase "Tentative Rules" should also be replaced by "Definitive Rules" in the last entry on page xxiv of *Pure and Applied Chemistry*, Vol. 33, No. 4 (1973).

IUPAC-IUB COMMISSION ON  
BIOCHEMICAL NOMENCLATURE

**DEFINITIVE NOMENCLATURE FOR VITAMINS B-6  
AND RELATED COMPOUNDS\*†**

**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‡ (I; R = —CH<sub>2</sub>OH). 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<sub>2</sub>NH<sub>2</sub>), 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 phosphorylated 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<sub>2</sub>NH<sub>2</sub>), which has coenzyme activity for the aminotransferases (EC 2.6.1.—), but not for other types of vitamin B-6-dependent enzymes<sup>2, 3</sup>.

In the IUPAC *Definitive Rules for the Nomenclature of Vitamins*, published in 1960<sup>4</sup>, 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<sub>2</sub>OH) previously designated as pyridoxine (Rule V-7). In the IUPAC-IUB *Tentative Rules* of 1966<sup>1</sup> 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

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\* 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 (with minor revision) of Section M-7 of the earlier IUPAC-IUB *Tentative Rules, Trivial Names of Miscellaneous Compounds of Importance in Biochemistry*<sup>1</sup>.

† Those who have served on the IUPAC-IUB Commission on Biochemical Nomenclature for varying periods during 1967-1972 are the following. Present Members are shown by an asterisk \*. O. Hoffmann-Ostenhof\* (Chairman), W. E. Cohn\* (Secretary), A. E. Braunstein\*, J. S. Fruton, B. L. Horecker\*, P. Karlson\*, B. Keil\*, W. Klyne\*, C. Liébecq\*, E. C. Slater, N. Tamiya, S. Veibel, E. C. Webb\*, W. J. Whelan\*. Comments on and suggestions for future revisions of this nomenclature should be sent to: Prof. O. Hoffmann-Ostenhof, Lehrkanzel für Biochemie der Universität Wien, Währinger Strasse 38, A-1090 Wien, Austria.

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

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).

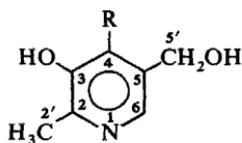
An extensive literature has accumulated on the chemistry and biochemistry of the B-6 vitamins and coenzymes, of their metabolites and of many related synthetic compounds that often exhibit biological activity as substitutes for or as antagonists of the corresponding natural products. A number of trivial 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, PaIP, PALPO are in use for pyridoxal 5'-phosphate, and similar abbreviated forms 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<sup>1</sup>, 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 *Definitive Rules* are based on drafts prepared by A. E. Braunstein and E. E. Snell after consultation with other active workers in the field.

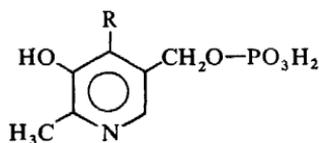
## RULES

[replacing Section M-7 of Ref. 1]

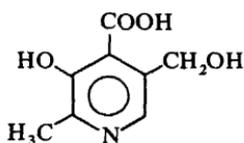
The term vitamin B-6 should be used as the generic descriptor for all 3-hydroxy-2-methylpyridine derivatives exhibiting qualitatively in rats the



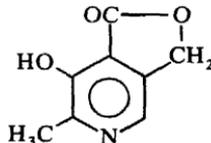
(I)



(II)



(III)



(IV)

biological activity of pyridoxine. This term should be used in derived terms such as vitamin B-6 deficiency, vitamin B-6 activity, vitamin B-6 antagonists<sup>5, 6</sup>.

7.1. Compound I (R = —CH<sub>2</sub>OH), 3-hydroxy-4,5-bis(hydroxymethyl)-2-methylpyridine\*, should be designated *pyridoxine*†. The alkyl residue formed

\* See note ‡ on page 1 of these rules.

† The previous synonym (see Introduction and Ref. 1) is no longer recommended.

by removal of the 4'—OH group is named *pyridoxyl* (e.g. in compounds such as *N*<sup>6</sup>-pyridoxyl-L-lysine and the like).

*Comment*

'Pyridoxine' should not be used as a generic name synonymous with 'vitamin B-6'<sup>5, 6</sup>.

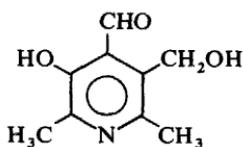
7.2. Compound I (R = —CHO) should be designated *pyridoxal*. The bivalent radical formed by removal of the oxygen atom from the CHO group is named *pyridoxylidene*.

7.3. Compound I (R = —CH<sub>2</sub>NH<sub>2</sub>) should be designated *pyridoxamine*.

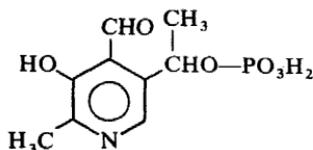
7.4. The commonly occurring oxidized metabolites of pyridoxal, namely 3-hydroxy-5-hydroxymethyl-2-methylpyridine-4-carboxylic acid (III) and the corresponding lactone (IV), should be designated *4-pyridoxic acid* and *4-pyridoxolactone* respectively. (Three less commonly occurring metabolites of pyridoxine, 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<sub>2</sub>OH, —CHO, —CH<sub>2</sub>NH<sub>2</sub>) 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.



(V)



(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*<sup>6</sup>-(5'-P-pyridoxyl)-L-lysine; *P*-pyridoxylideneimines.

### Derivatives and Analogues

7.6. From the trivial names already indicated, semitrivial 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, 2'-ethylpyridoxal (not ω-ethylpyridoxal),
- 6-methylpyridoxal (Compound V),

2'-hydroxypyridoxal (2-hydroymethyl-2-desmethylpyridoxal, 2-hydroxy-methyl-2-norpyridoxal; not  $\omega$ -hydroxypyridoxal),  
 4'-deoxypyridoxine 5'-phosphate,  
 5'-methylpyridoxal-5'-P (Compound VI),  
 pyridoxal *N*-oxide 5'-phosphate.

### 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* 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 these 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.

### 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.

*Table.* Abbreviated designations

Trivial name (abridged)*	Abbreviation†
Pyridoxal	PL
Pyridoxamine	PM
Pyridoxine	PN
Pyridoxal- <i>P</i>	PLP
Pyridoxamine- <i>P</i>	PMP
Pyridoxine- <i>P</i>	PNP

\* Recommended for use in text.

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

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 symbol *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<sup>7-9</sup>.

## Examples

$\begin{array}{c} \text{Pxy} \\ | \\ \text{Pxy}-\overset{\epsilon}{\text{Lys}}-\text{or } \text{Pxy} \text{ Lys- or } \text{Lys- or } \text{Lys(Pxy)-} \end{array}$  for the  $N^6$ -pyridoxyl-L-lysyl residue;\*

$\begin{array}{c} \text{P-Pxy} \\ | \\ \text{P-Pxy}-\overset{\epsilon}{\text{Lys}}-\text{or } \text{P-Pxy} \text{ Lys- or } \text{Lys- or } \text{Lys(P-Pxy)-} \end{array}$  for the corresponding  $N^6$ -(*P*-pyridoxyl)-L-lysyl residue;\*

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

$\text{Pxy}-\overset{\alpha}{\text{Lys}}$ - or  $\text{Pxy}-\text{Val-}$  etc. for  $N^2$ -pyridoxyl-L-lysyl and other  $N^2$ -pyridoxyl-L-aminoacyl residues;†

$\text{P-Pxy}-\overset{\alpha}{\text{Lys}}$ -,  $\text{P-Pxy}-\text{Val-}$  etc. for the corresponding  $N^2$ -(*P*-pyridoxyl)-L-aminoacyl residues;†

$\text{Pxd}=\text{Val-}$ ,  $\text{P-Pxd}=\text{Val-}$  etc. for  $N^2$ -pyridoxylidene-L-aminoacyl residues and the corresponding phosphoric esters;

$\text{P-(3deoxy)Pxd}=\overset{\epsilon}{\text{Lys}}$ - for the  $N^6$ -(3-deoxy-5'-*P*-pyridoxylidene)-L-lysyl residue;

$(3\text{Me-2nor})\text{Pxy-P}$

$\dots -\text{Leu}-\overset{\text{Pxy-P}}{\text{Lys}}-\text{Gly}-\dots$  for an  $N^6$ -(3-*O*-methyl-2-nor-5'-*P*)-pyridoxyl-L-lysyl residue in a peptide sequence;

$(6\text{Me})\text{Pxd}$

$\dots -\text{Leu}-\overset{\text{Pxd}}{\text{Lys}}-\text{Gly}-\dots$  for an  $N^6$ -(6-methylpyridoxylidene)-L-lysyl residue in a peptide sequence;

$\text{Pyridoxal-P}$

$\dots -\text{Gly}-\overset{\text{Pyridoxal-P}}{\text{Ser}}-\text{Val}-\dots$  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:

$[3-^{18}\text{O}]\text{pyridoxal-P}$  for pyridoxal 5'-phosphate labelled with  $^{18}\text{O}$  at O-3;

$6-[^3\text{H}]\text{methylpyridoxamine}-[^{32}\text{P}]\text{P}$  for 6-methylpyridoxamine 5'-phosphate with tritium at C-6' and  $^{32}\text{P}$  in the phosphate group;

$[2'-^{14}\text{C}]\text{Pxd}$

$\dots -\text{Leu}-\overset{\text{Pxd}}{\text{Lys}}-\text{Ser}-\dots$  for a peptide sequence with an  $N^6$ -pyridoxylidene-L-lysyl residue labelled with  $^{14}\text{C}$  at C-2'.

\* The latter two symbols are more suitable for use in sequences (see last three examples).

† In N-terminal position.

## REFERENCES

- <sup>1</sup> *Biochem. J.* **102**, 15 (1967) and elsewhere.
- <sup>2</sup> E. E. Snell, *Vitamins Horm.* **16**, 77 (1958).
- <sup>3</sup> A. E. Braunstein, (1960). In *The Enzymes*, 2nd ed., vol. 2, p. 113. Ed. by P. D. Boyer, H. Lardy and K. Myrbäck. New York : Academic Press Inc.
- <sup>4</sup> *J. Am. Chem. Soc.* **82**, 5581 (1960).
- <sup>5</sup> International Union of Nutritional Sciences. *Tentative Rules for Generic Descriptors and Trivial Names for Vitamins and Related Compounds.* *Nutr. Abstr. Rev.* **40**, 395 (1970).
- <sup>6</sup> American Institute of Nutrition. *J. Nutr.* **101**, 133 (1971).
- <sup>7</sup> *Amino Acid Derivatives and Peptides* (IUPAC-IUB Tentative Rules). *Biochem. J.* **126**, 773 (1972) and elsewhere.
- <sup>8</sup> *Abbreviations and Symbols for Chemical Names of Special Interest in Biological Chemistry.* 1965 Revision (IUPAC-IUB Tentative Rules). *Biochem. J.* **101**, 1 (1966) and elsewhere.
- <sup>9</sup> *Abbreviations and Symbols for Nucleic Acids, Polynucleotides and their Constituents*, Tentative Nomenclature Appendix No. 9 to IUPAC *Information Bulletin*, February 1971.