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# ABBREVIATIONS AND SYMBOLS FOR NUCLEIC ACIDS, POLYNUCLEOTIDES AND THEIR CONSTITUENTS

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# ABBREVIATIONS AND SYMBOLS FOR NUCLEIC ACIDS, POLYNUCLEOTIDES AND THEIR CONSTITUENTS†

IUPAC–IUB COMMISSION ON BIOCHEMICAL NOMENCLATURE‡

Rules Approved 1974

## INTRODUCTION

The 1965 Revision of *Abbreviations and Symbols for Chemical Names of Special Interest in Biological Chemistry* was completed and published (IUPAC–IUB) in 1965 and 1966[1], almost coincidentally with the elucidation of the first complete nucleic acid sequence[2,3] and with the development of methods for the synthesis of specific polynucleotide sequences[4]. The latter developments and others (e.g. modification of sugar components, synthesis of unnatural linkages) require a unified system for representing long sequences containing unusual or modified nucleoside residues. The system should facilitate comparisons between two or more such extended molecules, as in the search for homologies. At the same time, it must retain sufficient flexibility to accommodate the large variety of polymers synthesized by polymerases and be consistent, in this regard, with the rules governing the representation of polymerized amino acids[5].

The workers who first encountered these various needs, invented a number of devices to achieve the representations required in their own papers, basing these for the most part upon the one-letter system presented in Section 5.4 of *Abbreviations and Symbols*[1]. Few of these devices have the capability of

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† This document is a revision of proposals published in provisional form as Tentative Nomenclature Appendix No. 9 (February 1971) to IUPAC *Information Bulletin* and in *Arch. Biochem. Biophys.* **145**, 425 (1971); *Biochem. J.* **120**, 449 (1970); *Biochemistry*, **9**, 4022 (1970); *Biochim. Biophys. Acta*, **247**, 1 (1971); *Europ. J. Biochem.* **15**, 203 (1970); *J. Biol. Chem.* **245**, 5171 (1970); *J. Mol. Biol.* **55**, 299 (1971); *Molek. Biol.* (in Russian), **6**, 167 (1972); *Z. Physiol. Chem.* (in German), **351**, 1055 (1970).

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meeting all the situations that are now apparent. Hence the effort was undertaken to construct a system meeting as many of the latter as possible, preserving the previous, basic system and introducing additional conventions. This effort, as did the previous one, involved consultation with a large number of active workers in many countries over a period of some years. The conventions added here (indicated by ▲ for major additions, △ for minor revisions) were already in use by many of them[3–8].

The present Recommendations are the result; they replace Section 5 of the previous Tentative Rules[1].

## 1. ABBREVIATIONS

### 1.1. Simple nucleotides†

The 5′-mono-, di- and triphosphates of the common ribonucleosides may be represented by the customary abbreviations exemplified by AMP, ADP, ATP in the adenosine series. The corresponding derivatives of other nucleo-
△ sides are abbreviated similarly, using the symbols in Section 3, i.e. A, C, G, I, T, U, Ψ, X for the known nucleosides; R and Y for unspecified purine and pyrimidine nucleosides, respectively; N for unspecified nucleoside (not X or Y); B, S and D are reserved for 5-bromouridine, thiouridine, and 5,6-dihydro-
△ uridine, respectively. Orotidine may be designated by O to give OMP for orotidine 5′-phosphate†.

△ The di- and triphosphates may on occasion be better expressed in the alternative form ppN or pppN, as in the polymerization equation $n$ ppN → $(pN)_n$ + $n$ $P_i$, or when the outcome of specific labelling is to be indicated, e.g. $ppp^{*}N \rightarrow (p^{*}N)_n + nPP$.

Uridine diphosphate glucose may be represented as UDPG or UDP-Glc; the latter form is preferred if there is the possibility of confusing G for glucose with G for guanosine.

In the context of the chemistry of the nucleosides or nucleotides, the more systematic three-letter symbols (Section 2) should be used, e.g. Ado-5′*PPP* or Urd-5′*PP*-Glc (paragraph 2.4.3).

### 1.2. Nucleotide coenzymes and related substances

| | |
|---|---|
| Riboflavin 5′-phosphate (flavin mononucleotide) | FMN |
| Flavin-adenine dinucleotide (oxidized and reduced) | FAD, $FADH_2$ |
| Nicotinamide mononucleotide | NMN |

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▲ † When abbreviations for single bases or nucleosides are required and permitted, the three-letter symbols listed in subsections 2.2 and 2.3 should be used (see *Comment* in these sections), not single letters and not, e.g. UR, TdR, etc. Examples:

| | *Proscribed* | *Proposed* |
|---|---|---|
| fluorouracil | FU | FUra |
| fluorouridine | FUR | FUrd |
| fluorodeoxyuridine | FUdR | FdUrd |
| thymidine | TdR | dThd |
| bromouracil | BU | BrUra |
| bromodeoxyuridine | BUdR | BrdUrd |

| | |
|---|---|
| Nicotinamide-adenine dinucleotide‡ (oxidized and reduced) | $NAD^+$, NADH |
| Nicotinamide-adenine dinucleotide phosphate§ | $NADP^+$, NADPH |

△ Analogues of NAD or NADP (the generic terms require neither the plus sign nor the H) may be named by substituting an appropriate defined symbol for the N or the A, e.g. AcPd (for acetyl-pyridine) in place of N; H (for hypoxanthine) in place of A, etc.

Semi-systematic names (see Section 2) may often be used to advantage in discussing the chemistry of these dinucleotides, e.g. NADP can be written Nir-5′*PP*5′-Ado-2′*P*.

### 1.3. Nucleic acids

1.3.1. The two main types of nucleic acids are designated by their customary abbreviations. RNA (ribonucleic acid or ribonucleate) and DNA (deoxyribonucleic acid or deoxyribonucleate). Ribonucleoprotein and deoxyribonucleoprotein should not be abbreviated.

1.3.2. *RNA fractions*

Fractions of RNA or DNA or functions exercised by preparations of RNA may be designated as follows:

| | | | | |
|---|---|---|---|---|
| messenger RNA | mRNA | transfer RNA† | tRNA | |
| ribosomal RNA | rRNA | complementary RNA | cRNA | △ |
| nuclear RNA | nRNA | mitochondrial DNA | mtDNA | △ |

These are generic terms and apply to preparations as well as to specific molecules.

1.3.3. *Transfer RNAs*†

Those that accept a specific amino acid are designated as follows (using alanine tRNA as an example): (a) non-acylated: alanine tRNA or $tRNA^{Ala}$; (b) aminoacylated: alanyl-tRNA or Ala-tRNA or Ala-$tRNA^{Ala}$.

*Comment*: (i) The hyphen in (b) represents the aminoacyl bond and should not be used to connect a noun-adjective; (ii) the attached aminoacyl residue [in (b)] has the -yl ending, whereas the adjective describing the non-acylated form (a) does not; (iii) the superscript designator utilizes the conventional symbols for amino acid residues[1,9] exactly—one capital, two small letters.

*Isoacceptors*, i.e. two or more tRNAs accepting the same amino acid, are designated by subscripts, e.g. $tRNA_1^{Ala}$, $tRNA_2^{Ala}$, etc.

Specification of source may be made in parentheses before or after the abbreviation, e.g. (*E. coli*) $tRNA_1^{Ala}$, alanyl-$tRNA_2^{Ala}$ (*E. coli*).

The special problem of the particular methionine tRNA ($tRNA^{Met}$) that, once aminoacylated to give Met-tRNA, can be formylated to fMet-tRNA may be solved by the use of a subscript f (in the isoacceptor position) or by the use of $tRNA^{fMet}$. Thus $tRNA_f^{Met}$ (or $tRNA^{fMet}$) can be converted enzymically to Met-$tRNA_f^{Met}$ (or Met-$tRNA^{fMet}$) and then to fMet-$tRNA_f^{Met}$ (or fMet-$tRNA^{fMet}$); Met-$tRNA^{Met}$ cannot be formylated enzymically.

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‡ Formerly diphosphopyridine nucleotide (DPN, $DPN^+$, DPNH) and coenzyme I.

§ Formerly triphosphopyridine nucleotide (TPN, $TPN^+$, TPNH) and coenzyme II.

† Replaces 'soluble' RNA (sRNA), which should no longer be used for this purpose. RNA soluble in molar salt, or non-sedimentable at 100000 *g*, or exhibiting a sedimentation coefficient of 4 S, should not be termed sRNA.

# SYMBOLS

## General concepts and conventions

Two systems are recognized, designated the 'three-letter' and the 'one-letter' system, respectively. The first (Section 2), patterned after the systems in use for amino acid and saccharide residues in polymers[1], is designed largely for descriptions of chemical work involving bases, nucleosides, nucleotides and very small oligonucleotides, or for abbreviating these in minimum space (as on chromatograms or Figures or Table headings). The 'one-letter' system (Sections 3 and 4) is designed for the representation of oligonucleotides or polynucleotides, or parts thereof, and for their noncovalent associations, not for mononucleotides or nucleosides. Neither system is intended to replace the names of the latter substances in the text of papers.

In both systems, it is assumed, in the absence of appropriate symbols, that (a) all nucleosides (except pseudouridine) are 1-(pyrimidine) or 9-(purine) glycosyls, (b) all nucleoside linkages are β, (c) all sugar configurations are D, (d) all sugar residues are ribosyls unless otherwise specified, (e) all deoxyribosyls are 2′-deoxyribosyls, and (f) only 3′ → 5′ linkages, read from left to right, are involved.

## 2. THREE-LETTER SYMBOLS†

### 2.1. Phosphoric acid radical

The phosphoric acid radical, whether monoesterified or diesterified, is designated by an italic capital *P*.

### ▲ 2.2. Purines and pyrimidines

These are designated by the first three letters of their trivial names:

| | | | |
|---|---|---|---|
| Ade | adenine | Thy | thymine |
| Gua | guanine | Cyt | cytosine |
| Xan | xanthine | Ura | uracil |
| Hyp | hypoxanthine | Oro | orotate |
| Pur | unknown purine | Pyr | unknown pyrimidine |
| | Base unknown base | | |

Sur and Shy may be considered for thiouracil and thiohypoxanthine (6-mercaptopurine), respectively.

When abbreviations for single purines or pyrimidines are required and and permitted, the above symbols should be used rather than A, C, G, T, U,‡ etc.

### 2.3. Nucleosides

2.3.1. The ribonucleosides are designated by the following symbols, chosen to avoid confusion with the corresponding bases:

† The IUPAC Commission on Nomenclature in Organic Chemistry prefers these symbols to the one-letter ones (Section 3), designed for polymer representation. The three-letter symbols should be used whenever chemical changes involving nucleosides or nucleotides are being discussed.

‡ See footnote † on p. 280.

| | | | | | |
|---|---|---|---|---|---|
| | Ado | adenosine | Thd | ribosylthymine (not thymidine) | |
| | Guo | guanosine | | | |
| | Ino | inosine | Cyd | cytidine | |
| △ | Sno | thioinosine (mercaptopurine ribonucleoside) | Urd | uridine | |
| | | | Srd | thiouridine | △ |
| | Xao | xanthosine | Ψrd | pseudouridine | |
| △ | Puo | 'a purine nucleoside' | Ord | orotidine | △ |
| △ | Nuc | 'a nucleoside' | Pyd | 'a pyrimidine nucleoside' | △ |

Ribosylnicotinamide may be designated by Nir.

*Comment.* The prefix r (for ribo) may be used for emphasis or clarity. It may precede a single residue or, if applicable, a connected series.

2.3.2. The 2′-deoxyribonucleosides are designated by the above symbols (Subsection 2.3.1) prefixed by d, e.g. dAdo for 2′-deoxyribosyladenine (deoxyadenosine), dThd for 2′-deoxyribosylthymine (thymidine). The d may be used as a prefix to a connected series if all members of that series are 2′-deoxyribosyl derivatives. In mixed series, r and d should both be used before the appropriate residues, e.g. *P*-dAdo-*P*-rThd-*P*.

Other sugar residues may be indicated by similar prefixes, e.g. a for arabinose, x for xylose, l for lyxose.

*Comment.* For special purposes, the base and the sugar may be designated separately, using the base abbreviations of Subsection 2.2 and the standard sugar abbreviations[1], i.e. Rib, Ara, Glc, etc. Thus, adenosine ≡ Ado ≡ Ade-Rib; thymidine ≡ dThd ≡ Thy-dRib. (The 'de' used in Section 3.5. of *Abbreviations and Symbols*[1] for deoxy may be shortened to 'd' in this context.)

When abbreviations for single nucleosides are required and permitted, the above symbols should be used, e.g. Urd (not UR, Ur or U) and dThd (not TdR, Tdr, TDR, T or dT), for uridine and thymidine, respectively†.

## 2.4. Nucleotides

2.4.1. *Mononucleotides*

In the three-letter symbols, mononucleotides are normally expressed as phosphoric esters, such as Ado-3′-*P* or *P*-3′-Ado for adenosine 3′-phosphate, *P*-2′-Guo or Guo-2′-*P* for guanosine 2′-phosphate, Cyd-5′-*P* or *P*-5′-Cyd for cytidine 5′-phosphate (see 2.4.4 below).

2.4.2. Cyclic phosphodiesters are designated by two primed numerals, one for each point of attachment, as in Cyd-2′:3′-*P* (or *P*-2′:3′-Cyd) or in Ado-3′:5′-*P* (or *P*-3′:5′-Ado). (The corresponding bisphosphates would be Cyd-2′,3′-$P_2$ and Ado-3′,5′-$P_2$.)

△ 2.4.3. Nucleoside diphosphate sugars, which centre about a pyrophosphate group, are represented by, e.g. Urd-5′*PP*-Glc for uridine diphosphate glucose, i.e. uridine 5′-α-D-glucopyranosyl diphosphate), often termed UDPG or UDP-Glc (see paragraphs 2.4.4 and 1.1).

△ 2.4.4. Points of attachment in oligo- or polynucleotides are designated by primed numerals, e.g. 2′*P*5′, 5′*P*5′, etc., as in Ado-2′*P*5′-rThd-2′*P* or Ado-5′*PP*5′-Nir (for NAD: see paragraphs 2.4.3 and 1.2). The positional numerals

† See footnote † on p. 280.

may precede a series, as in (2′-5′)Ado-*P*-Guo-*P*-Urd-*P* to specify Ado-2′*P*5′-Guo-2′*P*5′-Urd-2′*P*. They may be omitted when the series in the left to right direction is 3′*P*5′.

*Comment.* Phosphoric groups at the ends of chains may appear without numerals. In this case it is understood that *P*- at the left end means a 5′-phosphate, -*P* at the right means a free 3′-phosphate. Thus AMP can be represented by Ado-5′-*P*, *P*-5′-Ado, or *P*-Ado, but not by Ado-*P* (which would represent the 3′-phosphate).

## 3. ONE-LETTER SYMBOLS

### 3.1. Phosphoric acid residues

A monosubstituted (terminal) phosphoric residue is represented by a small p. A phosphoric diester (internal) in 3′-5′ linkage is represented by a *hyphen* when the sequence is *known*, or by a *comma* when the sequence is *unknown*. Unknown sequences adjacent to known sequences are placed in parentheses; these replace, at the points where they occur, the need for other punctuation. All these symbols thus replace the classical 3′-5′ or 3′p5′ symbols (cf. paragraphs 3.3.1 and 3.3.2). A 2′:3′-cyclic phosphate residue may be indicated by > or >p.

*Comments.* (i) The terminal ps should be specified unless their presence is unknown, in doubt, or of no significance to the argument. (ii) 'Polarity' (direction other than 3′ → 5′) is dealt with in subsection 3.3.2. (iii) Linkages other than 3′ and 5′ are specified by other means (see 3.3.1.). (iv) A codon triplet, in which definite left-to-right order and 3′-5′ linkages are assumed and in which the termini are not of importance, may be written without punctuation as, e.g. AGC.

### 3.2. Nucleosides

3.2.1. *Ribonucleosides*†

The *common ribonucleoside residues* (radicals) are designated by single capital letters, as follows:

| | | | |
|---|---|---|---|
| A | adenosine | T | ribosylthymine (not thymidine) |
| G | guanosine | C | cytidine |
| I | inosine | U | uridine |
| X | xanthosine | Ψ | pseudouridine‡ |
| △ R | unspecified purine nucleoside | Y | unspecified pyrimidine nucleoside |

N unspecified or unknown nucleoside (do not use X, P, or any of the above).

*Rare nucleosides*—It is often advantageous, e.g. in comparing long sequences, to represent every nucleoside residue by a single letter rather than by a group of letters and numbers. In such cases, those capital letters not assigned to common nucleosides (above) may be arbitrarily defined and used. It is recommended that the following be reserved for the substances listed (cf. Subsection 4.4):

| | | | |
|---|---|---|---|
| △ D | 5,6-dihydrouridine | B | 5-bromouridine |
| △ S | thiouridine (for locants, see Subsection 4.4) | O | orotidine (see Subsection 1.1) |

† See footnote † on p. 280.

‡ Q may replace Ψ for computer work.

Other symbols for these and for other modifications are listed in Section 4.

*Comments.* (i) The prefix r for ribo should be used when there is need for the additional specification. (ii) Other sugars or modified sugars are considered in paragraphs 3.2.2, 3.2.3 and 4.2.

3.2.2. *Deoxyribonucleosides*

The common 2′-deoxyribonucleosides are designated by the above symbols, modified in one of the following ways:

(a) When space is available and no other prefixes are required, the *prefix* d is used; thus (i) dA-dG-dC . . . or d(A-G-C . . .); (ii) poly[d(G-C)] or poly-(dG-dC) (these are identical substances); d may precede each residue or a whole chain, as applicable.

▲ (b) When space is available but other, possibly confusing, prefixes are involved, a *subscript* d is used; thus, $mmtT_d$-$bzA_d$-$T_d$-$anC_d$ for a protected tetradeoxynucleotide[4] (The prefixes are defined in subsection 4.1.)

▲ 3.2.3. *Unusual sugar residues*

Sugar moieties other than ribosyl or 2′-deoxyribosyl may be indicated as described in paragraphs 3.2.2 above, depending on requirements for base-modifying prefixes (subsection 4.1) and space available, using a, x and 1 (see paragraphs 2.3.2) for the other pentosyls, *ad hoc* letters for others, each defined; thus -aC- or -$C_a$- for an arabinosylcytosine residue. Symbols for substituents on sugars are given in subsection 4.2 (see also subsection 4.4).

**3.3. Oligo- and polynucleotides**

3.3.1 *Points of attachment*

The diesterified phosphate residue, represented by hyphen or comma or parenthesis (cf. subsection 3.1) is considered to be attached to the oxygen atom of the 3′ carbon on its left and to that of the 5′ carbon on its right. For other types of linkage, the simple hyphen must be replaced by its numerical form, as in 2′-5′ (or 2′p5′), 5′-5′, etc.[6], e.g. G3′p5′A2′p5′A or G3′-5′A2′-5′A. These locants may precede a chain or a polymer if the internucleotide linkage is identical throughout, e.g. (2′-5′)A-U-G-C for the corresponding tetranucleotide.

▲ 3.3.2. *Direction of the phosphodiester link*

The hyphen used in known sequences is a contraction of the arrow( → ) that is understood to point to the 5′ terminus of the phosphodiester bond (unless other numerals are used, as in paragraph 3.3.1). When left-to-right direction is *not* the case, this must be indicated by an appropriate locant preceding the chain, or by an arrow to indicate the 3′ → 5′ direction, as in the peptide rules[9]. Thus, associated hydrogen-bonded segments (see paragraphs 3.4.2) may be represented by, e.g.

(3′-5′)A-C-A-C-A-C, etc.

(5′-3′)U-G-U-G-U-G, etc.

or by

A→C→A→C→A→C, etc.

U←G←U←G←U←G, etc.

Another device used to represent 'reverse polarity' is rotation of the symbols[10, 11]. Thus the above associated polymers may be shown as

A-C-A-C-A-C, etc.

etc. U-G-U-G-U-G

In such representation, the left-to-right 3′-5′ convention is assumed to hold when the letters appear right side up.

*Examples of oligonucleotides*—A-G-Up (for ApGpUp): 3′ → 5′ trinucleotide, terminal 3′ phosphate; A-G-U > p: the same, with terminal 2′:3′-cyclic phosphate; pA-G-U: the same, commencing with a 5′ phosphate, terminating in a uridine with unsubstituted 2′ and 3′ hydroxyls.

△ pppG-G . . . . Ap: this nucleotide (of unspecified length and sequence) has a 5′-triphosphate residue on the G at one (the 5′) end and a 3′-phosphate on the A at the other (the 3′) end.

pG-A-Ψ($C_2$,U)T-C-C-A; a decanucleotide, commencing (5′ end) with a 5′ phosphate, including a trinucleotide of unknown sequence between the Ψ and the T, and terminating (3′ end) in an adenosine residue with unsubstituted 2′ and 3′ hydroxyl groups.

d(pG-A-C-T); tetranucleotide (all deoxy), with 5′ terminal phosphate on G.

d(T←C←A←Gp); the same (arrow indicates 5′←3′ direction).

p$G_d$-$A_d$-C-T; the same, with two deoxy, two ribo residues [see paragraphs 3.2.2(b)].

(2′-5′)pG-A-C-T; the same, all ribo, all in 2′-5′ linkage.

pG2′-5′A-C-T; the same, with a single 2′-5′ linkage (between G and A).

AGC; a codon (note: the symbols for phosphoric residues may be omitted in describing codons. This is an exception to Subsection 3.1).

### 3.4. Polymerized nucleotides

#### 3.4.1. *Single chains*

Polynucleotides composed of repeating sequences or of unknown sequences may be represented by either of two systems essentially identical with those devised and recommended by the IUPAC Commission on Nomenclature of Macromolecules and by the American Chemical Society's Polymer Nomenclature Commission (see also *Synthetic Polypeptides*[5]).

(a) The repeating unit is preceded by 'poly', meaning 'polymer of'. Thus, polynucleotide or poly(N); polyadenylate or poly(A); poly(adenylate-cytidylate) or poly(A-C) (alternating); poly(adenylate, cytidylate) or poly(A,C) (random).

(b) The repeating unit, enclosed in parentheses if complex, is followed by a subscript denoting length, e.g. a number $(A\text{-}C)_{50}$, an average number $(A\text{-}C)_{\overline{50}}$ or a range $(A\text{-}C)_{40\text{–}60}$, if desired. Where the number of residues has not been determined and this form is required by the context, the subscript 'n' may be used (as in ref. 5). However, two ns should not appear in the same formula unless equal length is implied. When equal length is not the case, additional letters should be used, such as m, k, j, etc.

In either case, the symbols may carry prefixes or subscripts as required for proper specification. Note that 'poly' is not used in the second system.

*Examples*: poly(A-U), alternating copolymer of A and U[12]; poly(A,U), random copolymer of A and U; *not* poly AU or poly A + U; poly($A_2$, U), as above but 2:1 in average composition; $(A_2, U)_{\overline{50}}$, as above, average length of chain, 150 residues; poly[d(A-T)] or poly(dA-dT), for alternating dA and dT† (see subsection 3.1 and ref. 12).

*Comment*. Multiple parentheses or brackets may be used for blocks within polymers, and vertical lines for side chains, etc.[5, 9]. 'Oligo' may replace 'poly' where applicable. Terminal phosphate residues need not be specified unless they are essential to the argument.

### 3.4.2. *Association between chains*

Association (noncovalent) between two or more polynucleotide chains, such as that ascribed to hydrogen-bonding, is indicated by the *centre dot* (not the hyphen, which indicates covalent linkage), e.g. refs. 12, 14.

(a) Poly(A) · poly(U) not poly(A · U), nor poly AU, nor poly A + U‡; poly(A · U) may be used when it is implied that each A is paired with a U, regardless of chain lengths.

(b) Poly(A)·2 poly(U) not poly(A·2U), nor poly(A·$U_2$); (polyA·2U) indicates the same triple-stranded complex and that each A is matched by two Us, regardless of individual chain lengths.

(c) Poly[d(A-T)] · poly[d(A-T)] or poly[d(A-T) · d(A-T)].

(d) A · poly(U) or A · $(U)_n$ for single adenosine residues associated with polyuridylate or poly(uridylic acid).

*Absence of association* between chains is indicated by the *plus* sign (traditional in chemistry for coexisting but nonassociated species), e.g.: (a) poly(dC) + poly(dT), not poly(dC + dT); (b) poly(dA.r$T_2$) + poly(dG); (c) 2[poly(A)·poly(U)] $\leftrightharpoons$ poly(A)·2 poly(U) + poly(A)[12].

The *absence of definite information on association* is indicated by the comma (as before, indicating 'unknown'), e.g.: (a) poly(A),poly(A,U); (b) poly[d(G-C)],poly[d(A,T)].

*Comments*. (i) Hyphens are *not* used for association (noncovalent); poly(A-U) specifies a single chain, not two chains. (ii) The *centre dot* should always be used to indicate base-pairs involved in noncovalent associations (see subsection 3.3.2), e.g. A·T base pair, or G·C hydrogen bonds (not A-T, or G-C, which indicate covalent linkages). The centre dot is located as shown, *above* the line. (iii) In describing *base ratios*, the form (A + T)/(G + C) should be used, not AT/GC, nor A + T/G + C. Two capital letters should not be juxtaposed [except as in subsection 3.1, comment (iv)], to distinguish sequence G-C, from content G + C, from ratio G:C or G/C, from base pair G·C.

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† Poly[d(A-T)] or poly(dA-dT) was originally[13] termed poly dAT. While this has the advantage of brevity, it has proved ambiguous (see footnote ‡ below) in other situations and is inconsistent with the general principles of polymer symbolism (e.g. ref. 5). Hence, its use is not recommended.

‡ Poly AU and poly(A + U), etc., have been used for poly(A)·poly(U)[15]. The similarity of this system for associated homopolymers to that originally proposed for alternating copolymers (see footnote † above) can lead to confusion, in that it indicates one covalent chain rather than two. Its use is not recommended. Similar potential confusion attends the use of the other incorrect terms given in subsection 3.4.2.

# 4. MODIFIED BASES, SUGARS OR PHOSPHATES IN POLYNUCLEOTIDES

## 4.1. Designation of substituents on bases

In long sequences, as in transfer RNAs, where it is preferable to have not more than one capital letter per nucleoside residue, the standard symbols for nucleosides (i.e. A, U, G, C, etc.) may be modified by a symbol of lower case letter(s) placed immediately before the single capital letter (see subsection 3.2.1). Those symbols recommended for more common modifications are listed below (for locants and multipliers, see below; for unusual sugar residues, see subsections 3.2.2 and 3.2.3):

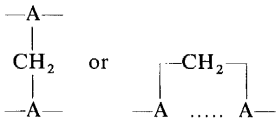
| | |
|---|---|
| m, e, ac | methyl, ethyl, acetyl |
| n, o | amino (N replaces H), deamino (O replaces N) |
| z, c | aza (N replaces C), deaza (C replaces N) |
| h | dihydro (hU ≡ dihydrouridine; see also subsections 3.2.1. and 4.4) |
| hm, ho (or oh) | hydroxymethyl, hydroxy |
| aa | aminoacyl |
| f | formyl (as in the conventional fMet for formylmethionyl) |
| fa | formylaminoacyl |
| i | isopentenyl (≡ $\gamma$, $\gamma$-dimethylallyl) |
| s | thio or mercapto (sU ≡ thiouridine; see also subsections 3.2.1 and 4.4) |
| fl, cl, br, io | fluoro, chloro, bromo, iodo (not encountered in natural polynucleotides; see also subsections 3.2.1 and 4.4). |

Symbols for some N-protecting radicals used in synthetic work[4, 9] are:

| | |
|---|---|
| bz, bzl, tos | benzoyl, benzyl, tosyl |
| tr, an, bh | trityl, anisoyl, benzhydryl (diphenylmethyl) |
| mmt | monomethoxytrityl (*p*-anisyldiphenylmethyl) |
| dmt | dimethoxytrityl (di-*p*-anisylphenylmethyl) |
| thp, dns | tetrahydropyranyl, dansyl (but see ref. 9, revision) |
| cmc | *N*-cyclohexyl-*N'*-[$\beta$-(4-methylmorpholino)amidino] (reaction product from the corresponding carbodiimide)[16]. |

In simpler situations where the avoidance of multiple capital letters in a single residue symbol seems not to be necessary, the standard chemical symbols (Me, Br, etc.) may be used. In such cases, no punctuation should appear between modifier and nucleoside symbol, e.g. $6Me_2A$, 5BrU. The prefix 'di' should not be used; subscript numerals suffice (cf. subsection 4.4).

*Comments.* (i) Symbols for other protecting groups may be constructed according to the principles indicated here and in Section 6 of *Amino Acids and Peptides*[9]. (ii) When space is severely restricted, these symbols may appear above the nucleoside symbol (see subsection 4.4)[3, 4, 7, 8], e.g. $\overset{ac}{C}$ for acC. (iii) Symbols for bifunctional adducts must lie above or below the chain (or chains) (see conventions for branched peptides in refs. 5 and 9) and hence may utilize any appropriate symbols. Thus a methylene bridge between two adenosines[17] could be represented as




for inter- or intra-chain linkages, respectively.

## ▲ 4.2. Designations of substituents on sugars

4.2.1 *Internal modifications*

The symbols are *lower case* when the modified sugar is internal; they are placed immediately *to the right* of the nucleoside symbols and indicate substitution at the (internal) 2′ position unless otherwise specified. Thus -Am- indicates a 2′-*O*-methyladenosine residue[7,8].

4.2.2. *Terminal radicals*

The common, natural termini, phosphate and hydroxyl, are represented, if necessary. by p (3.1) and oh or ho (subsection 4.1); the latter is only required for emphasis as it is implied in the nucleoside symbol itself.

Other terminal radicals (hydroxyl-substituents) may utilize standard chemical symbols or abbreviations. These are placed in parentheses (following the appropriate nucleoside symbol, as noted above). Recommended abbreviations (aside from normal chemical symbols) are[4,9]:

| | |
|---|---|
| (EtOEt), (EtOMe) | 1-ethoxyethyl, ethoxymethyl |
| ($Ph_2CH$), (Bzl), (Tr) | benzhydryl, benzyl, trityl |
| (MeOTr), [$(MeO)_2Tr$] | monomethoxytrityl, dimethoxytrityl |
| (Me), (Et), (Ac), (Tos) | methyl, ethyl, acetyl, tosyl |
| (Thp), $F_3CCO$- | tetrahydropyranyl, trifluoracetyl |
| (AA), (Gly), (Leu), etc. | aminoacyl, glycyl, leucyl, etc. |

Terminal glycol-protecting (bifunctional) radicals, bridging the 2′ and 3′ hydroxyls unless otherwise indicated, may require the following:

| | |
|---|---|
| ($>CMe_2$) | isopropylidene: e.g. -C-C-A($>CMe_2$) |
| ($>BOH$), ($>CO$) | borate, carbonyl |
| >p or > | 2′:3′-phosphate (cyclic) (cf. subsection 3.1) |

## ▲ 4.3. Phosphoric acid protecting groups

Since these must be located at termini, standard chemical symbols should be used. These adjoin the appropriate hyphen (for phosphate; cf. subsection 3.1). Examples, in addition to any above[4]:

| | |
|---|---|
| (CNEt)-; -(CNEt) | 5′-cyanoethyl; 3′(or 2′)-cyanoethyl |
| (MeOPh), (Bzl), (Ph) | anisyl, benzyl, phenyl, with appropriate hyphen. |

## ▲ 4.4. Locants and multipliers

Multipliers, when necessary, are indicated by the usual *sub*scripts[3,8,11]; thus -$m_2$A signifies a dimethyladenosine residue, neither methyl being at the 2′-*O* position (see subsection 4.2.1). Locants are indicated by *super*scripts; thus -$m^6_2$A- indicates an $N^6$-dimethyladenosine residue [ribosyl-6-(dimethylamino)purine], -$ac^4$C indicates an $N^4$-acetylcytidine, -$m^{1,6}_2$A- or $m^1m^6$A a

1,$N^6$-dimethyladenosine, etc.[3, 8, 11]. Utilizing the convention of paragraph 4.2.1, we can write -$m_2^6$Am- for the 2′-*O*-methyl-$N^6$-dimethyladenosine residue. Other examples are $s^2$U for 2-thiouridine and $h_2^{5,6}$U for 5,6-dihydrouridine, (but see the alternatives available in subsections 3.2.1 and 4.1, namely $^2$S, and hU or D respectively; the locants and/or multipliers may be included in the definition). The prefix 'di', which has no place in chemical symbolism, should not be used; subscript numerals suffice. The prefix 2′-*O*-Me is best replaced by the suffix m (see subsections 4.2.1 and 4.4), especially when other substituents must be placed before the nucleoside symbol. Thus 2′*O*Me6$Me_2$A is better symbolized as $m_2^6$Am; similarly, 2MeS6iPeA becomes $ms^2i^6$A.

In presenting several homologous sequences, it is often desired to keep the capital letters representing nucleotides one below another. The presence of modifying symbols may interfere with such a presentation. One way of meeting this situation is to place the *prefixes* (including locants and multipliers) directly *over* the capital letter they modify, and to place the *suffix* (usually m for 2′-*O*-methyl) as a right-hand superscript [see also comment (ii) in 4.1], e.g., $\overset{m_2^6}{A}$ ; $C^m$.

Examples of this usage exist[3, 7, 8]. When so placed, smaller letters and/or numbers may be used to advantage[4, 8]. Such positioning is consistent with the rules regarding designation of functional groups and their substituents in peptides[5, 9].

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