

A PROPOSAL OF D_p/L_p NOTATION FOR NUCLEOTIDE ANALOGUES WITH A CHIRAL PHOSPHORUS CENTREMichał SOBKOWSKI^{a,*}, Jacek STAWIŃSKI^{a,b} and Adam KRASZEWSKI^a^a Institute of Bioorganic Chemistry, Polish Academy of Sciences, Noskowskiego 12/14, 61-704 Poznań, Poland; e-mail: msob@ibch.poznan.pl^b Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, S-106 91 Stockholm, Sweden

A proposal of a new notation for *P*-chiral nucleotide analogues is outlined. In contrast to the absolute R_p/S_p convention, the new D_p/L_p system is based on a geometrical relationship between substituents at the phosphorus atom, and thus appears to be particularly convenient for comparative analyses of physical, chemical, and biological properties of nucleotide and oligonucleotide analogues.

INTRODUCTION

The absolute R/S notation system by Cahn, Ingold, and Prelog (CIP) is applicable to a wide range of chiral compounds, including these with heteroatom stereogenic centres. Despite universality of this convention, there are still some classes of compounds for which the traditional D/L notation remains the convention of choice (e.g. amino acids or carbohydrates). The convenience of the latter system is due to the fact that it is based on a structural correlation between compounds, allowing thus an immediate comparison of their relative configurations without invoking rather non-intuitive CIP system analysis.

For *P*-chiral compounds, an R_p/SP variant of the CIP convention seems to be practically the only one in use¹, although for nucleotide analogues a notation that would take into consideration structural relationships of the phosphorus-bounded ligands could be much more convenient than the universal CIP system.

DISCUSSION

The most common way of presenting a dinucleoside monophosphate unit is by placing the nucleosid-3'-yl moiety above the phosphorus centre while the nucleosid-5'-yl one, below. Taking this graphical convention as a starting point and treat it as a Fischer's-like projection (Fig. 1), one can define the configuration at the phosphorus atom as follows:

- compounds having the single bonded ligand Z to the right are denoted as D_p ,
- compounds having the single bonded ligand Z to the left are denoted as L_p .

The phosphoryl group is placed always opposite to the ligand Z.

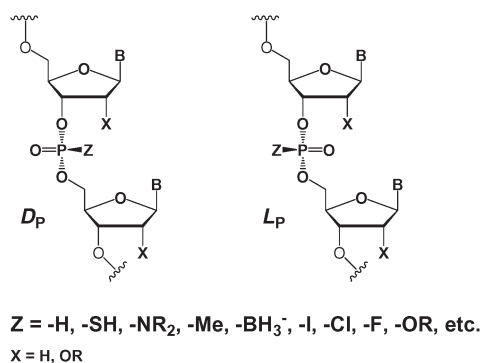


FIG. 1
Perspective view of D_p and L_p configurations

The D_p/L_p system can be conveniently applied to many nucleotide analogues, in which the single-bonded ligand Z stands for -H, -SR, -NR₂, -Me, -BH₃⁻, -I, -Cl, -F, -OR, etc., or the ones in which one of the nucleosidic residues has been replaced by alkyl, aryl or acyl group. In addition, the P=O residue may be substituted by the P=S, P=Se or any other double-bonded atoms system. The main advantage of the proposed notation is that it reflects a spatial relationship of the ligands rather than absolute configuration of the compounds. Several examples for typical nucleotide analogues are given in Table I².

TABLE I
Assignment of R_p/S_p configuration for dinucleotide analogues. Note that despite the changes of character of the Z substituent, all analogues have D_p conformation

Z	-H	-SR'	-NR' ₂	-F	-Cl	-I	-CH ₃	-BH ₃ ⁻
	S_p	R_p	S_p	R_p	R_p	R_p	S_p	S_p

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REFERENCES AND NOTES

1. An application of "pseudo-axial" and "pseudo-equatorial" notation was indicated in: Lebedev A. V., Wickstrom E.: *Perspect. Drug Discov. Design.* **1996**, *4*, 17. However the system was not developed further.
2. For more details see: Sobkowski M., Stawinski J., Kraszewski A.: *Nucleosides Nucleotides Nucleic Acids* **2005**, *25* (accepted), and further papers.