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Nucleosides, Nucleotides and Nucleic Acids

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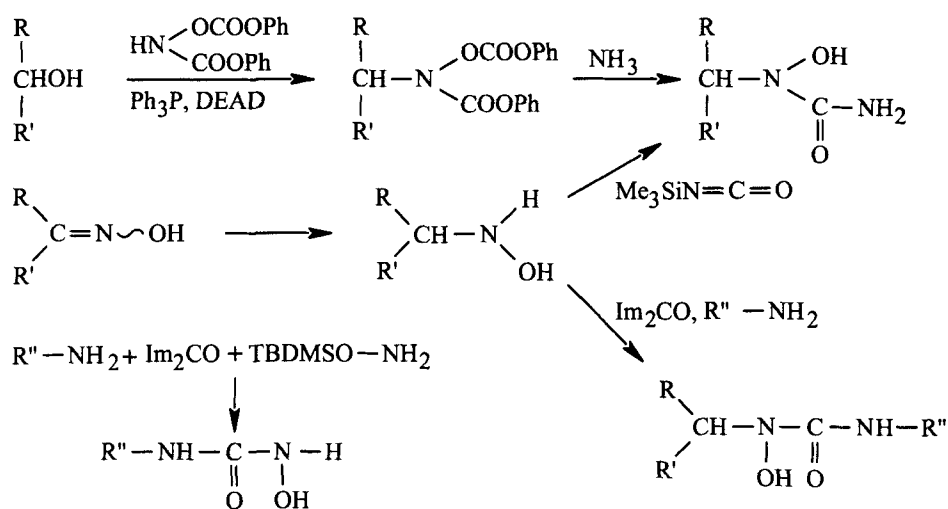
NOVEL TYPES OF SPIN LABELLED NUCLEOSIDE ANALOGUES

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Abstract: A variety of modified nucleosides or dinucleosides bearing one of the following functions have been prepared: *N*-hydroxyureas, *N*-hydroxyamines, *N*-hydroxycarbamates, α -(*N*-hydroxyamino)phosphonates. Upon oxidation, these compounds afford the corresponding aminoxyl free radicals which have been studied by EPR spectroscopy. Some of these compounds exhibited antiviral properties.

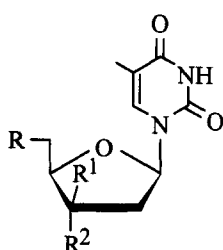
Both positional isomers of *N*-hydroxyureas have been prepared using one of the following procedures (Scheme 1), leading to a number of nucleosides, some examples from the thymidine series being collected in TABLE 1. These reactions have also been applied to acyclonucleosides of the 1-(4-hydroxy-2-oxabut-1-yl)thymine family.



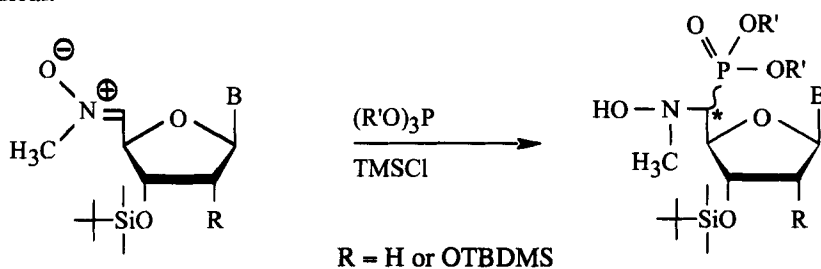
Scheme 1

Dinucleosides in which the internucleosidic bridge has been replaced with either a *N*-hydroxy-2-azatetramethylene or a *N*-hydroxy-1,3-diaza-2-oxotetramethylene group have been recently described.¹

TABLE 1. Some examples of modified thymidine nucleosides.

	Cmpd	R	R ¹	R ²
	1	NHOH	H	OH
	2	N(OH)CONH ₂	H	OH
	3	OH	H	NHOH
	4	OH	N(OH)Me	H
	5	OH	NHOH	H
	6	OH	H	NHCONHOH
	7	OH	H	NHCON(OH)Me
	8	OH	H	N(OH)CONH ₂
	9	OH	N(OH)CONH ₂	H

Nucleotide analogues have been prepared by stereoselective nucleophile addition of phosphates onto a nucleoside nitron (Scheme 2) leading predominantly to the (5'*R*) isomer as established by ¹H, ³¹P, and ¹³C NMR and EPR of the corresponding aminoxyl free radical.



Scheme 2

The best antiviral activities (IC₅₀/μM) were found for **4** (HIV-1 **0.85**, HIV-2 **0.80**), **5** (HIV-1 **0.20**, HIV-2 **0.14**), and **8** (VZV **6.0**).

REFERENCE

1. Tronchet, J. M. J.; Grand, E.; Zsély, M.; Giovannini, R.; Geoffroy, M. *Carbohydr. Lett.*, **1998**, 3(3) in the press.