

This article was downloaded by:

On: 26 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597286>

From Pro-nucleotides to Pro-oligonucleotides

Jean-Louis Imbach^a, Gilles Gosselin^a, Bernard Rayner^a

^a Laboratoire de Chimie Bio-Organique, URA 488 CNRS, Université de Montpellier II, Montpellier Cedex, France

To cite this Article Imbach, Jean-Louis , Gosselin, Gilles and Rayner, Bernard(1995) 'From Pro-nucleotides to Pro-oligonucleotides', *Nucleosides, Nucleotides and Nucleic Acids*, 14: 3, 459

To link to this Article: DOI: 10.1080/15257779508012406

URL: <http://dx.doi.org/10.1080/15257779508012406>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

FROM PRO-NUCLEOTIDES TO PRO-OLIGONUCLEOTIDES

Jean-Louis Imbach,* Gilles Gosselin and Bernard Rayner

*Laboratoire de Chimie Bio-Organique, URA 488 CNRS, Université de Montpellier II, 34095
Montpellier Cedex 5, France*

Abstract. Consequences of masking the phosphate functions of nucleic acid derivatives by enzyme labile bioreversible protecting groups are discussed.

One of the main problems which arise with potential bioactive phosphorylated or phosphonylated compounds concerns their poor uptake by cells. One way to overcome this drawback is to transitorily neutralize their negative charge(s) with enzyme labile bioreversible protective groups, which could be selectively removed inside the cells.

Taking the 5'-mononucleotide structure as a first example, it has been shown that the corresponding SATE (S-acylthioethanol) or DTE (dithiodiethanol) phosphotriester may intracellularly deliver the expected nucleotide, thus by-passing the first activating step of the parent nucleoside.¹⁻³ When applied to anti-HIV dideoxynucleosides, such a concept leads to numerous biological consequences going from the activation of an inactive nucleoside (i.e., ddU)^{1,2} to an increase of the anti-HIV effect, as shown for ddA (due to metabolism modification)⁴ or for PMEA (due to an uptake increase).³

Extension of this concept to oligonucleotides has also been considered and some interesting preliminary data have been obtained.

The proposed approach for "*in vitro*" intracellular delivery of phosphorylated bioactive nucleoside analogues may be of great interest in the design of new antiviral and antitumor agents.

REFERENCES

1. Gosselin, G.; Imbach, J.-L. *Int. Antiviral News*, **1993**, *1*, 100.
2. Périgaud, C.; Gosselin, G.; Fefebvre, I.; Girardet, J.-L.; Benzaria, S.; Barber, I.; Imbach, J.-L. *Bioorg. Med. Chem. Lett.*, **1993**, *3*, 2521.
3. Puech, F.; Gosselin, G.; Lefebvre, I.; Pompon, A.; Aubertin, A.-M.; Kirn, A.; Imbach, J.-L. *Antiviral Res.*, **1993**, *22*, 155.
4. Périgaud, C.; Aubertin, A.-M.; Benzaria, S.; Pelicano, H.; Girarde, J.-L.; Maury, G.; Kirn, A.; Imbach, J.-L. *Biochem. Pharmacol.*, **1994**, *48*, 11.