

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>

The Derivatives of Phosphorothioate Oligonucleotides

N. V. Amirkhanov^a; V. F. Zarytova^a

^a Siberian Division of Russian Academy of Sciences, Novosibirsk Institute of Bioorganic Chemistry, Novosibirsk, Russia

To cite this Article Amirkhanov, N. V. and Zarytova, V. F.(1997) 'The Derivatives of Phosphorothioate Oligonucleotides', *Nucleosides, Nucleotides and Nucleic Acids*, 16: 7, 1563 — 1564

To link to this Article: DOI: 10.1080/07328319708006230

URL: <http://dx.doi.org/10.1080/07328319708006230>

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.

THE DERIVATIVES OF PHOSPHOROTHIOATE OLIGONUCLEOTIDES

N.V. Amirkhanov and V.F. Zarytova*

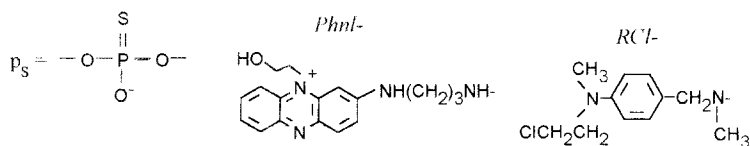
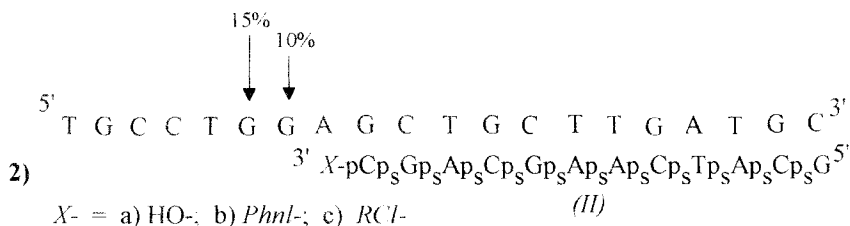
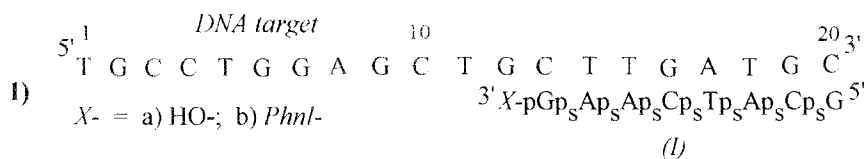
Novosibirsk Institute of Bioorganic Chemistry, Siberian Division
of Russian Academy of Sciences, Novosibirsk 630090, Russia

ABSTRACT Derivatives of phosphorothioate oligonucleotide analogues bearing alkylating N-methyl-4-(N-2-chloroethyl)-N-methylamino)benzylamine or stabilizing complementary complexes N-(2-hydroxyethyl)phenazinium residues at the 3'-terminal phosphate group were synthesized and investigated.

Phosphorothioate (PS) oligonucleotide analogues are extensively studied as promising therapeutic agents in the antisense approach^{1,2}. Various chemical groups such as reactive, complementary complex stabilizing and other ones may be attached to PS oligonucleotides to enhance their antisense effect. The well-known methods of preparation of the PS oligonucleotide derivatives on polymer supports^{1,2} do not allow to attach active chemical groups to PS oligonucleotides. In this case the reactive residues may be deactivated by the removing of blocked PS oligonucleotides from the support.

Previously we have described the simple and effective method of the synthesis of PS oligonucleotide derivatives^{3,4} bearing alkylating N-methyl-4-(N-2-chloroethyl-N-methylamino)benzylamine (*RCl*) or N-(2-hydroxyethyl)phenazinium (*Phn*) residues at the 3'-end.

In the present work the synthesis of these PS oligonucleotide derivatives is fulfilled and the some properties of these compounds are examined with the use of the model complexes **1** and **2**:



It was shown that PS oligonucleotide derivatives *Ib* and *IIf* bearing *Phnl*-residues formed complexes **1** and **2** more stable than parental PS oligonucleotides *Ia* and *IIf* did (melting points were 11°C and 6°C higher, respectively). Thus, *Phnl*-residue linked to 3'-terminal phosphate group of PS oligonucleotide stabilizes its complementary complexes.

Reactive derivative of PS oligonucleotide *IIf* was found to modify the DNA-target site-specifically. The extent of target modification was 25% at 20°C (G6 and G7).

This research was supported by grant of the Russian State Program: "The newest methods of bioengineering".

REFERENCES

1. Letsinger, R.L.; Zhang, G.; Sun, D.K.; Ikeuchi, T.; Sarin, P.S. *Proc. Natl. Acad. Sci USA* **1989**, *86*, 6553-6556.
2. Stein, C.A.; Mori, K.; Loke, S.L.; Subasinghe, C.; Shinozuka, K.; Cohen, J.S.; Neckers, L.M. *Gene*, **1988**, *72*, 333-341.
3. Amirkhanov, N.V. and Zarytova, V.F. *Nucleosides and Nucleotides* **1995**, *14* (3-5), 9935-937.
4. Amirkhanov, N.V. and Zarytova, V.F. *Russian J. Bioorgan. Chemistry* **1995**, *21*, 365-375.