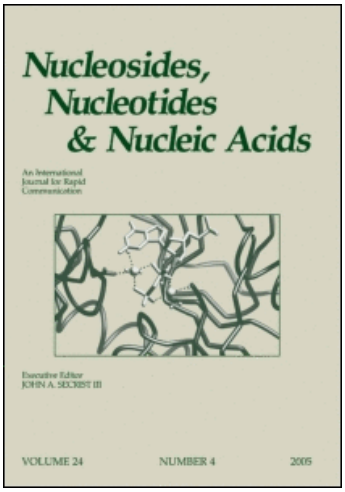

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More Efficient Alkylating Oligonucleotide Derivatives for the Sequence Specific Chemical Modification of dsDNA

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MORE EFFICIENT ALKYLATING OLIGONUCLEOTIDE DERIVATIVES FOR THE SEQUENCE SPECIFIC CHEMICAL MODIFICATION OF dsDNA

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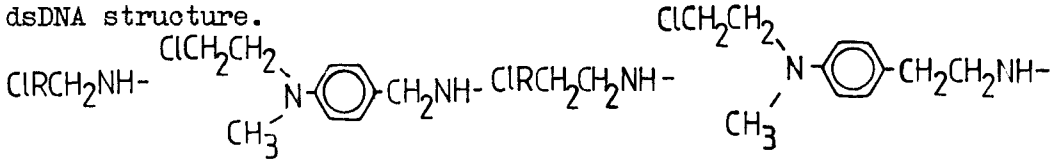
Abstract. Derivatives of (pT)16 bearing alkylating groups coupled to the 5'-terminal phosphate by the flexible linker alkylates the dsDNA efficiently in vicinity of (A18)(T18) sequence.

Alkylating oligonucleotide derivatives represent a perspective type of the compounds for the specific chemical modification of dsDNA(1) since the main reactive center, guanosine atom N7 is readily available for the attack in the dsDNA structure.



We have compared the ability of alkylating oligonucleotide derivatives bearing 2-chloroethylamine groups(2) to modify dsDNA. Alkylating derivatives of $(pT)_{16}$ bearing the two alkylating groups were compared with respect to the ability to react with a dsDNA fragment containing $(A_{18})(T_{18})$ sequence flanked by the reactive guanosine residues

CTGAAAAAAAAAAAAAAAAAAGAA
GACTTTTTTTTTTTTTTTTTTCTT

The fragment was excized from the cloned λ chain gene of mink immunoglobuline with restriction endonuclease EcoRI (3) and terminally ^{32}p labeled at 3'-end. Figure 1 shows the results of the experiments.

From the data it is seen that both the reagents attack exclusively guanosine G in the DNA in accordance with the structure of the expected triple stranded complex. The rea-

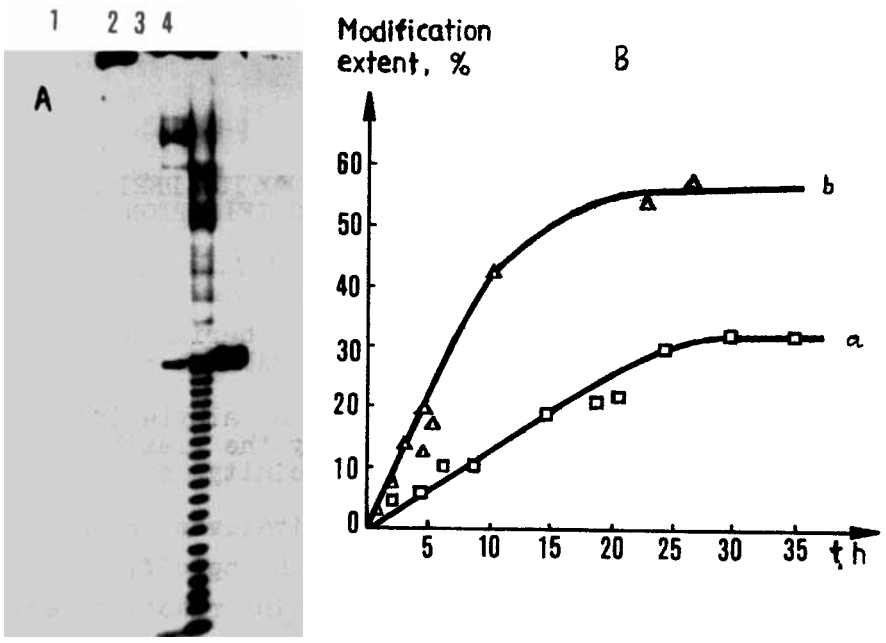


Figure 1. A, reaction of the DNA fragment ^{32}p-labeled at the 3'-end of the A18-containing strand and the oligonucleotide derivative $ClRCH_2NH(pT)16$, 20% denaturing PAAG. Reaction conditions: 10°C, DNA, 0,6 μM, reagent, 60 μM. DNA was cleaved at the modified residues by the piperidine treatment. 1)Starting fragment;2)G-cleavage;3)A+G-cleavage;4)Alkylated fragment after pyperidine treatment. B, Kinetics of the reaction of the DNA fragment with the alkylating oligonucleotide derivatives $ClRCH_2NH(pT)_{16}$ (a) and $ClRCH_2CH_2NH(pT)_{16}$ (b) at 10°C.

gent bearing more flexible alkylating grouping attacks DNA more efficiently apparently due to more conformational freedom of the reactive group. One can hope to develope efficient alkylating oligonucleotide derivatives for sequence specific modification of dsDNA can be elaborated by the appropriate desing of the reactive grouping structure.

REFERENCES

1. Podust L.M.; Gaydamakov S.A.Bioorgan. Khim.15, 363 (1989)
2. Godovikova T.S.; Zaritova V.F.Bioorgan.Khim.12,187 (1986)
3. Chlebodarova T.M.; Karasik G.I.Dokl.Akad.Nauk SSSR.311, 487 (1990)