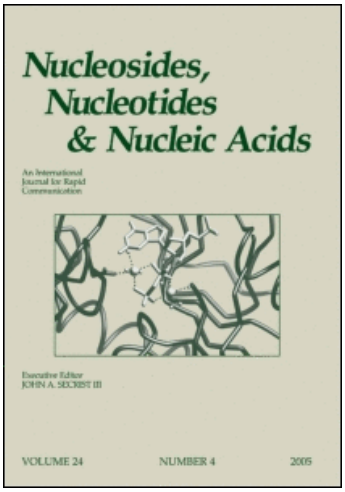

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Synthesis of New Oligonucleotide Derivatives with Porphyrins and Phthalocyanins

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SYNTHESIS OF NEW OLIGONUCLEOTIDE DERIVATIVES WITH PORPHYRINS AND PHTHALOCYANINS†

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ABSTRACT: The derivatives of oligonucleotides with carboxysubstituted porphyrins and phthalocyanins, Fe(III)hematoporphyrin, Pd(II)coproporphyrin I and Co(II)tetracarboxyphthalocyanin, were synthesized using the common approach.

The design of chemically modified oligonucleotides as a reagents for the inhibition of gene expression is currently a possible approach in the chemotherapy of cancers and viral diseases. Among the chemical groups the porphyrins and related molecules are the very promising for photodynamic and dark therapy. Previously the porphyrin derivatives of oligonucleotides were prepared using various synthetic approaches (see [1] and references in this book). One of them is based on the activation of the carboxylic groups of attaching molecules to N-hydroxysuccinimide esters and the subsequent condensation with aliphatic aminogroups of the spacer on the 5'-phosphate of oligonucleotides [2]. But the conjugation reaction was done in organic solvent. The more convenient method, based on the same coupling reaction but in water/organic solvent, was applied earlier for the attachment of some another labelling molecules to oligonucleotides [3]. In present work we develope this method for synthesis of oligonucleotide derivatives with Fe(III)hematoporphyrin (I), Pd(II)coproporphyrin I (II) and Co(II)tetracarboxyphthalocyanin (III) in DMF/H_2O solution (Fig. 1). Antisense deoxyribooligonucleotides against mRNA of genes c-myc and bcr/abl and containing cholesterol residues at 3'-phosphate and trifluoroacetylaminopropanol residue at 5'- phosphate were synthesized

†Abbreviations: TPS, triisopropylbenzoylsulfochloride; N-MeIm, N-methylimidazole; tfa,-trifluoroacetyl protecting group; Chol, cholesterol residue; R, porphyrin or phthalocyanin residue; *p*, protected phosphate group; p, unprotected phosphate group; n=2 for I and n=4 for II and III.

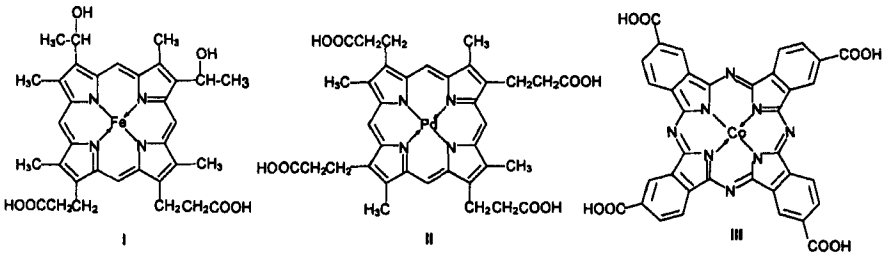
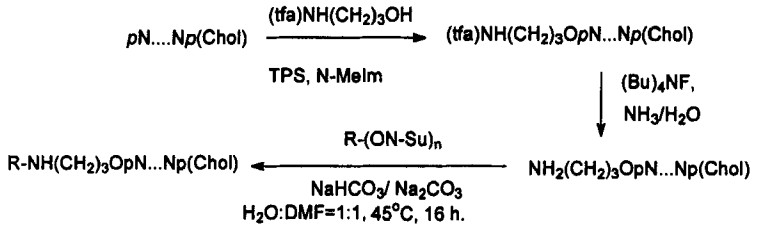


FIG. 1. The structures of compounds I, II and III.

according to [4, 5]. The carboxylic groups of I, II and III were converted to their N-hydroxysuccinimide ester forms. For the coupling reaction the solutions of esters in DMF were mixed with the equal volume of the aqueous solutions of appropriate oligonucleotide derivatives in 0.2 M $NaHCO_3$: 0.2 M Na_2CO_3 (1:1 v/v) (Scheme 1).

SCHEME 1.



The oligonucleotide conjugates with I and III caused the cleavage of complementary chains in the presence of hydrogen peroxide and oxygen, respectively. The appropriate derivative with II revealed the photochemical activity.

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