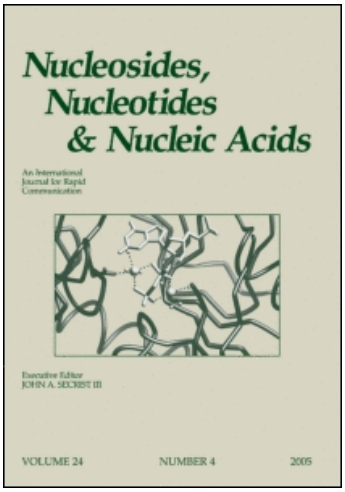

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ELECTROCHEMICALLY DIRECTED COPOLYMERIZATION OF PYRROLE AND OLIGONUCLEOTIDES

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Abstract : DNA matrices are prepared by electrochemically directed copolymerization of pyrrole-modified oligonucleotides and pyrrole.

In order to obtain DNA matrices, only three main strategies have been described. The first one involves a microrobotic spotting of oligonucleotides (ODN) on an activated support.[1] The second one uses a mechanical synthesis mask to perform *in-situ* synthesis[2] and the third one a photochemical process.[3] In the field of biosensors, electroconducting

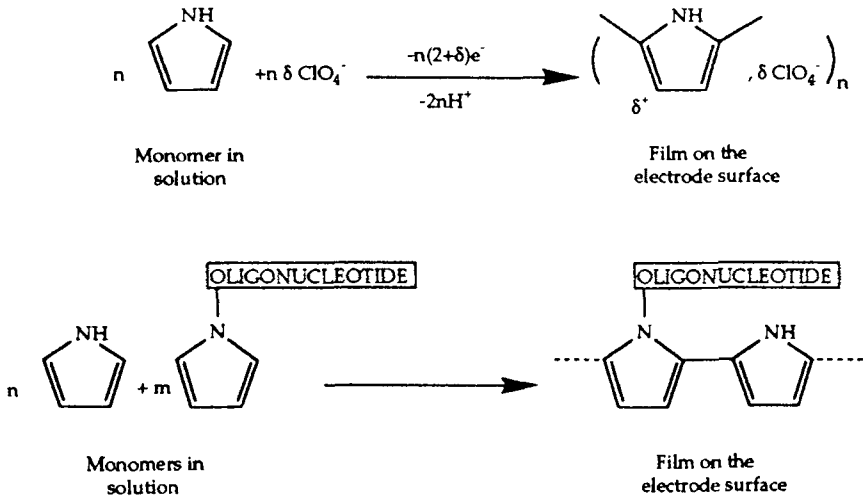

Figure1. Polypyrrole formation by oxydative electrocopolymerization

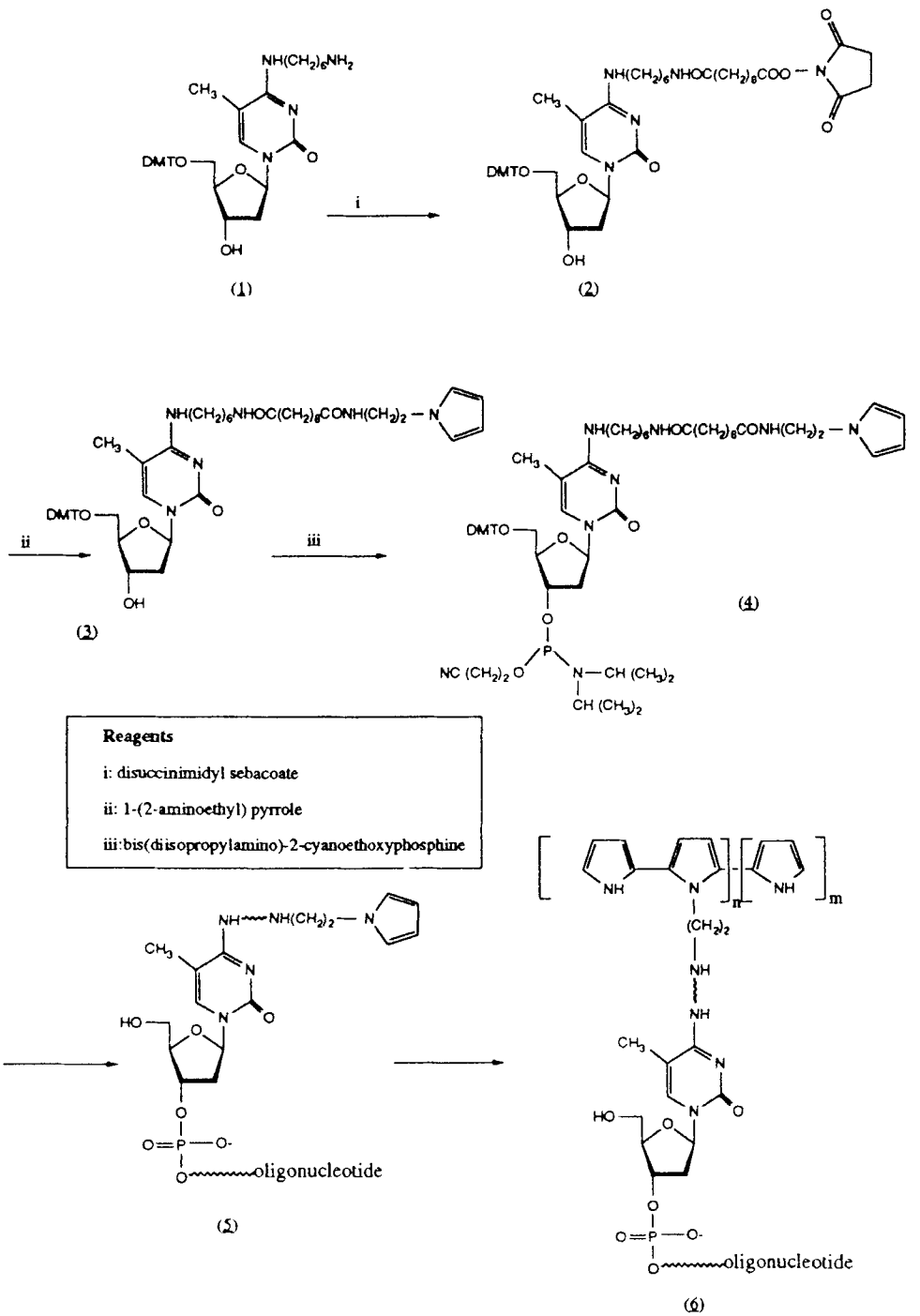

Figure2. Synthesis of ODN pyrrole conjugates and their electrochemical copolymerization with pyrrole

conjugated polymers (ECP) have been used for the immobilization of enzymes or other small molecules.[4] We propose herein a convenient method to prepare addressed DNA matrices by copolymerization of pyrrole and ODN bearing a pyrrole group. Electrochemical oxidation of pyrrole gives, in one step, a solid polypyrrole film deposited on the surface of the electrode. The copolymerization of pyrrole and ODN bearing a pyrrole group allows the formation of a solid copolymer constituted by an ODN grafted on a polypyrrole chain. The synthesis of polypyrrole is limited to the surface of the electrode, so that, the size of the organic support is the same as that of the electrode. The addressing of the successive electropolymerizations is insured by the selective switching of the electrode and by the selection of the modified ODN used for the copolymerization (Fig 1).

The synthesis of modified ODN involves the preparation of a phosphoramidite of a nucleoside derivative bearing a pyrrole with a spacer arm (Fig. 2). This monomer is used as described previously for the synthesis of 5' modified oligonucleotide probes.[5] After deprotection with ammoniaca under standard conditions, the ODN modified with pyrrole are purified by reversed phase HPLC.

Each support is made by oxidation of pyrrole on a gold or platinum electrode dipped in a solution containing 20 mM of pyrrole and 2 μM of pyrrole-ODN in 0.1 M $LiClO_4$. Electrosynthesis is carried out by a potentiodynamic method which allows a coulometric control of the film thickness. Yields and specificity of the ODN incorporation can be checked by copolymerization with a 5'-^{32}P labelled ODN bearing or not a pyrrole group. The amount of ODN linked to the support is estimated to be 2 pmole/cm^2. Preparation of polypyrrole supports on 50 μm wide gold microelectrodes is carried out under the same conditions (Fig. 3) and each electrode can be coated by polypyrrole grafted with different ODN.

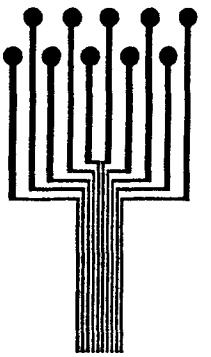

Figure 3

Hybridization with ODN probes complementary to those grafted on the matrix shows that the ODN linked to the support are accessible to hybridization. Two methods of detection can be applied : the first one involves a radioactive labelling with ^{32}P or ^{35}S for a better resolution and the second one a fluorescent tag detected with an epifluorescence microscope.

The easy electrosynthesis of polypyrrole films with covalently linked oligonucleotides and their high chemical stability make these materials very attractive

candidates for DNA sensors. In this way, addressable DNA matrices can be constructed on microelectrodes devices by electrochemically directed synthesis of grafted polypyrrole. These supports allow DNA hybridization and the detection of hybridized nucleic acids can be carried out by classical ways.[6]

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