Method for quantitative, light-controlled synthesis of oligonucleotides on microarrays (P-346)

Facts

- Pivotal method for producing high-quality DNA or RNA oligonucleotides on planar solid support media by use of a base additive during the irradiation step of light-controlled synthesis

Abstract
Oligonucleotides are nowadays prepared almost exclusively by phosphoramidite chemistry. DNA synthesizers automatically produce the desired DNA oligomer, usually using controlled pore glass (CPG) as a matrix. Stepwise, one nucleoside reagent after the other is pumped through the synthesis column; the order determines the sequence of the product. Alternatively, many different oligonucleotides can be produced in parallel by light-controlled synthesis on a planar solid support. This array is either used directly or the oligonucleotides are released and used subsequently in pools or separately.
The presented invention provides a method to synthesize oligonucleotides at nearly quantitative yield per synthesis step, thus resulting in high-quality, and thus long, DNA or RNA oligomers.

The Technology
The presented invention is achieved by means of a light-controlled microarray synthesis with nucleosides that have a photolabile protecting group of the 2-(2-nitrophenyl)ethyl type. The irradiation step – a common feature of light-controlled on-chip synthesis – is carried out in the presence of a base (Fig.1) and increases the yield of each synthesis step significantly.

Development Stage
The method was tested successfully. The results demonstrate that satisfactory DNA synthesis of this type is only possible in the presence of a base additive.

Applications and Commercial Opportunity
The process is essential for all DNA, RNA, LNA, and PNA light-controlled biochip syntheses using protecting groups of the 2-(2-nitrophenyl)ethyl type.

Inventors
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Intellectual Property
The patent is granted in Europe (EP1 149 110) and the United States (US 6,673,544).

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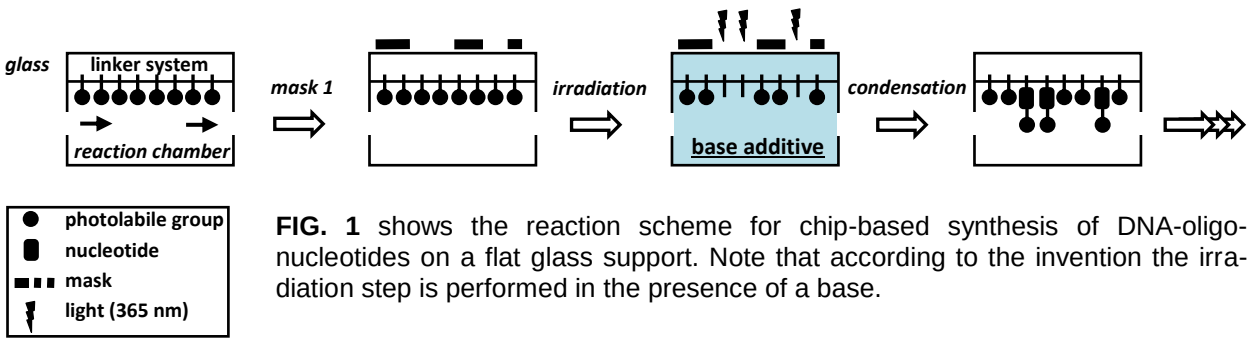

FIG. 1 shows the reaction scheme for chip-based synthesis of DNA-oligonucleotides on a flat glass support. Note that according to the invention the irradiation step is performed in the presence of a base.