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(54) Title: OSCILLATING FLUIDIZED BED OLIGONUCLEOTIDE SYNTHESIZER

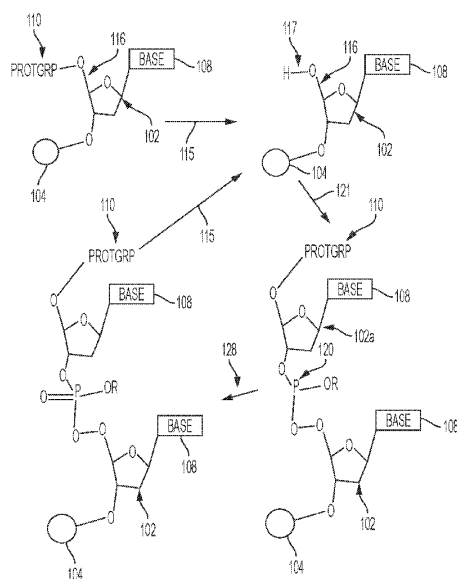


FIG. 1

(57) Abstract: A method and device for building an oligonucleotide on a solid phase resin within a filter reactor, wherein the method and device as used as a solid phase synthesis system. As part of the solid phase synthesis process, a protecting group will be removed from the 5' position of an oligonucleotide that is attached to the solid phase resin and then an activated amidite (phosphoramidite) solution is added. The activated amidite solution flows up and down, or fluidizes and mixes with the resin beads within the bed reactor and reacts at the 5' position of the oligonucleotide, wherein the phosphorous linkage found within the amidite comprises a P atom that is in an oxidation state of III. Once the activated amidite solution has been reacted, the P atom is converted from an oxidation state of III to an oxidation state of V. Any of the reactions including deblocking, coupling, oxidation, sulfuration, or capping can be fluidized or mixed to get complete contacting between the reagents and the resin. Reagents drain from the reactor out the filter bottom before washing. The resin bed is flat and channel free because of the fluidization or mixing prior to the washes and can be re-fluidized during any of the washes. A spray cone or other distributor evenly spreads reagents or wash solvents onto the top of the resin bed without disrupting the flat even spread of resin in the radial direction. Washing after any given reaction can be divided into several individual segments. The cleaner portion of washes after a particular reaction in one cycle, can be collected in a holding vessel and used as the first washes after reaction in the next cycle. In-process integrated multi-pass washing can be used to enable more efficient use of the wash solvent. Excess reagent solution used for deblocking reaction is recycled and reused from one phosphoramidite cycle to the next, making the use of deblocking more efficient.

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