

Chemical Synthesis of DNA:-

Automated DNA synthesis is conceptually similar to the solid state syn. of polypeptide.

The oligopeptide is built upon solid support (silica) one nucleotide at a time in repeated series of chemical reaction, with suitably protected nucleotide precursors.

① The 1st nucleoside (which will be the 3' end) is attached to the silica support at the 3'-OH (through a linking group R) and is protected at the 5' OH with an acid labile dimethoxytrityl group (DMT).

The reactive groups on all bases are also chemically protected.

② The protecting DMT gr. is removed by washing the column with acid (DMT is colored, so this reactⁿ is followed spectrophotometrically).

③ The next nucleotide is activated with a Diphosphoryl amino group & reacted with the bound nucleotide to form a 5'-3' linkage, which in step ④ is oxidised with iodine to produce a phosphodiester linkage (1 of the P-oxygen carries a (methoxy) protected group).

④ Reaction ② through ④ are repeated until all nucleotides are added. At each step, excess nucleotide is removed before addⁿ of next nucleotide.

- ⑥ In step ⑤ & ⑥ the remaining protecting groups on the bases & phosphate are removed.
- ⑦ In 7 the oligonucleotide is separated from the solid support & purified.

Chemical synthesis of RNA is more complicated bcoz of the need to protect 2' OH group of ribose without adversely affecting reactivity of the 3' OH.