

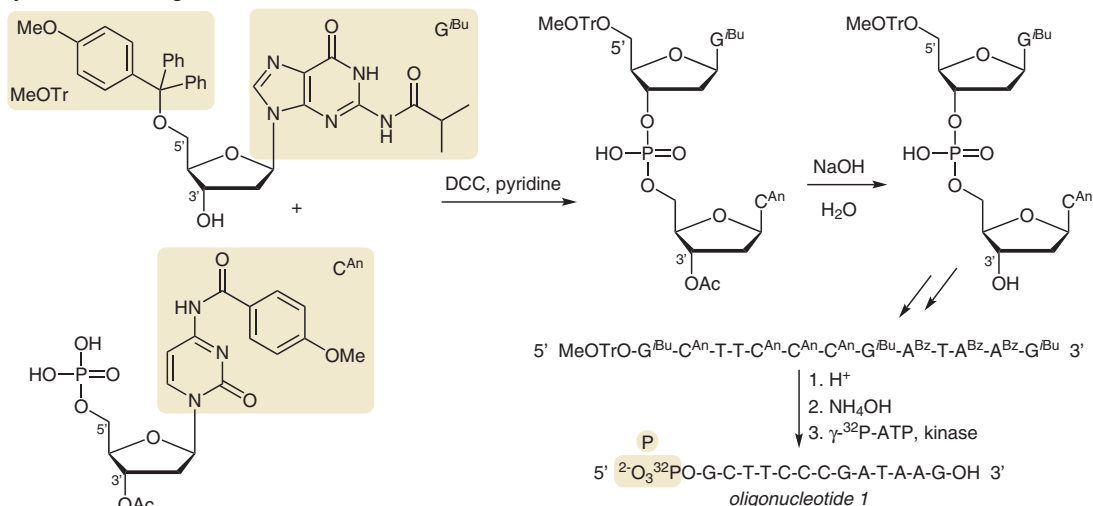
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Total Synthesis of a Gene

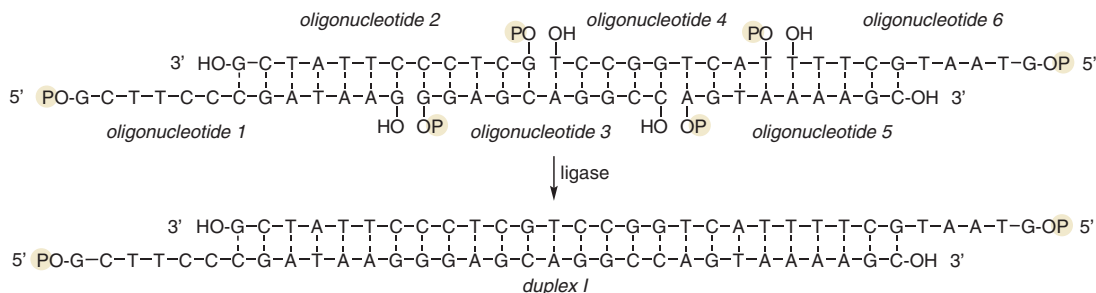
Science 1979, 203, 614–625.

Total Synthesis of a Gene

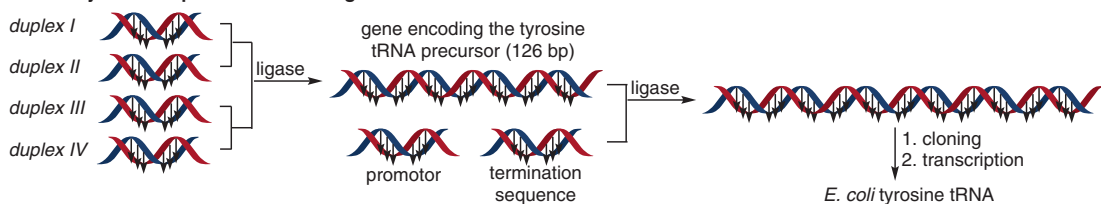
Synthesis of the oligonucleotides:



Ligase-mediated synthesis of DNA duplexes:



Assembly of the duplexes to the final gene:



Significance: The entire gene encoding the precursor of the *E. coli* tyrosine tRNA was synthesized from protected mononucleotides. The final DNA fragment consists of 207 base-pairs and also includes a promoter region as well as a termination-inducing element. After successful cloning of this duplex, transcription was demonstrated in *E. coli*.

Comment: First, 26 distinct oligonucleotides were synthesized using cycles of DCC-mediated coupling and basic hydrolysis to release the free 3'-OH. Remaining protecting groups of the 9- to 13-mers were cleaved and a radioactive phosphate was installed enzymatically at the 5'-OH. Ligase-mediated couplings of four to six oligonucleotides afforded six different double-stranded duplexes, which were further ligated to yield the final gene.