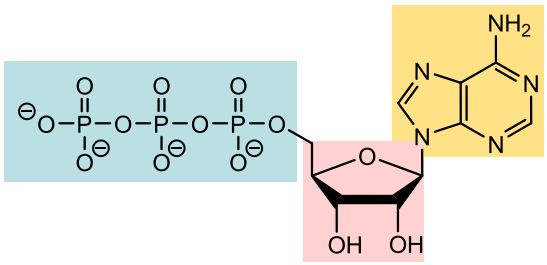
Nucleic Acids

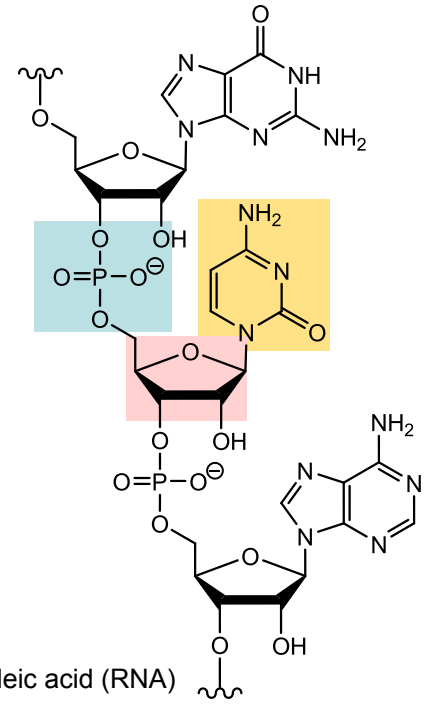


adenosine triphosphate (ATP)

a mononucleotide

Nucleic acids consist of:

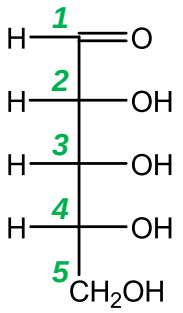
- a ribose (aldopentose) sugar;
- a heteroaromatic, glycosidic base;
- a phosphoester.



ribonucleic acid (RNA)

a polynucleotide

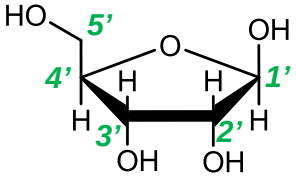
The Ribose Sugar



D-ribose

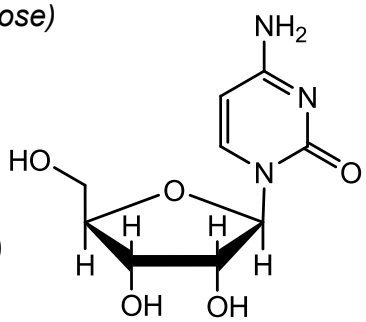
(an aldopentose)

cyclizes to



β-D-ribofuranose

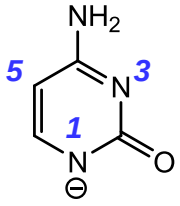
Numbering of rings:
1-n for base;
1'-5' for sugar.



cytidine

(a nucleoside)

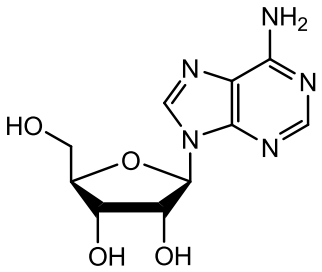
glycoside formation



cytosine

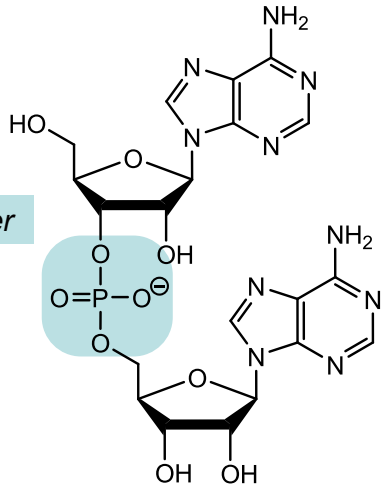
(a base)

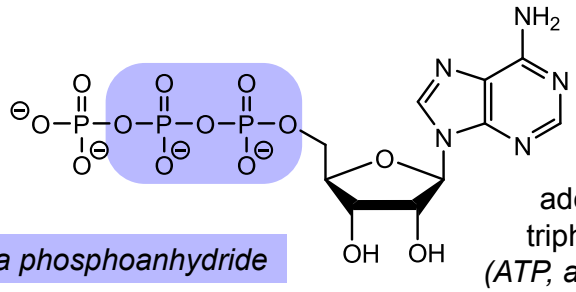
Phosphates and Phosphoesters of Ribonucleosides



adenosine
(a nucleoside)

a phosphodiester



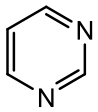


a phosphoanhydride

adenosine triphosphate
(ATP, a nucleotide)

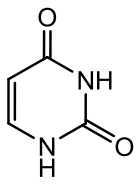
Bases Found in Nucleic Acids

pyrimidines

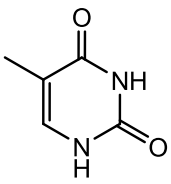


pyrimidine

cytosine

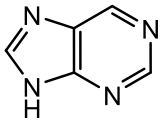


uracil

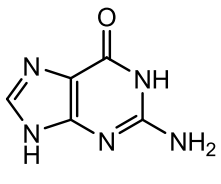


thymine

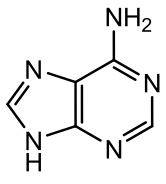
purines



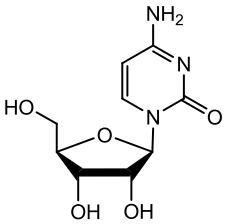
purine



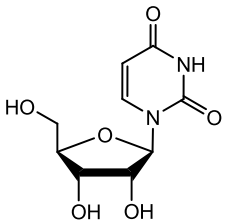
guanine



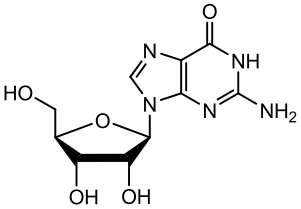
adenine



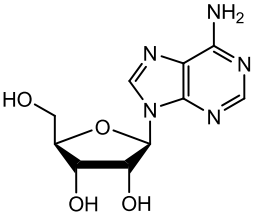
cytidine (**C**)



uridine (**U**)

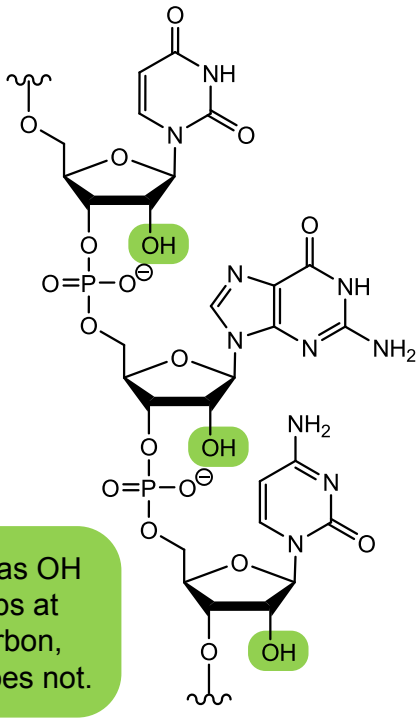


guanosine (**G**)



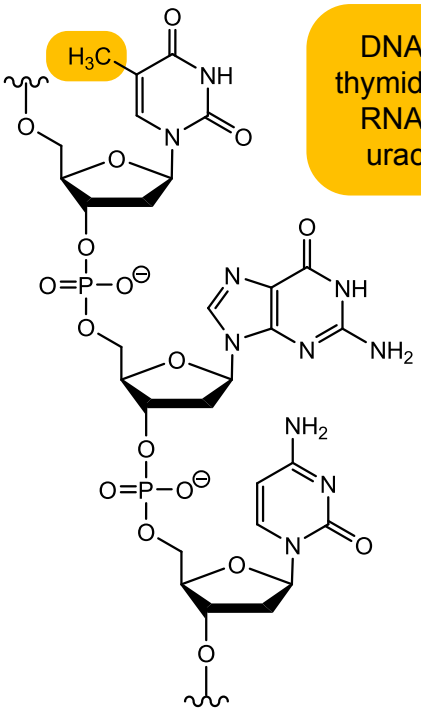
adenosine (**A**)

Polynucleotides: RNA and DNA



RNA has OH groups at 2'-carbon, DNA does not.

ribonucleic acid (**RNA**)



DNA uses thymidine (**T**), RNA uses uracil (**U**)

deoxyribonucleic acid (**DNA**)

Polynucleotides

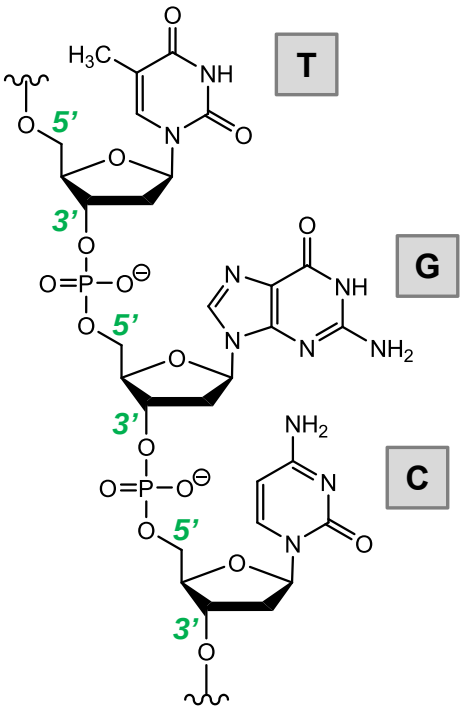
- Nucleotide units in DNA and RNA are linked by 5' and 3' oxygens.
- Backbone is negatively charged.
- Information is stored in sequence of bases.

So, this DNA sequence would read:

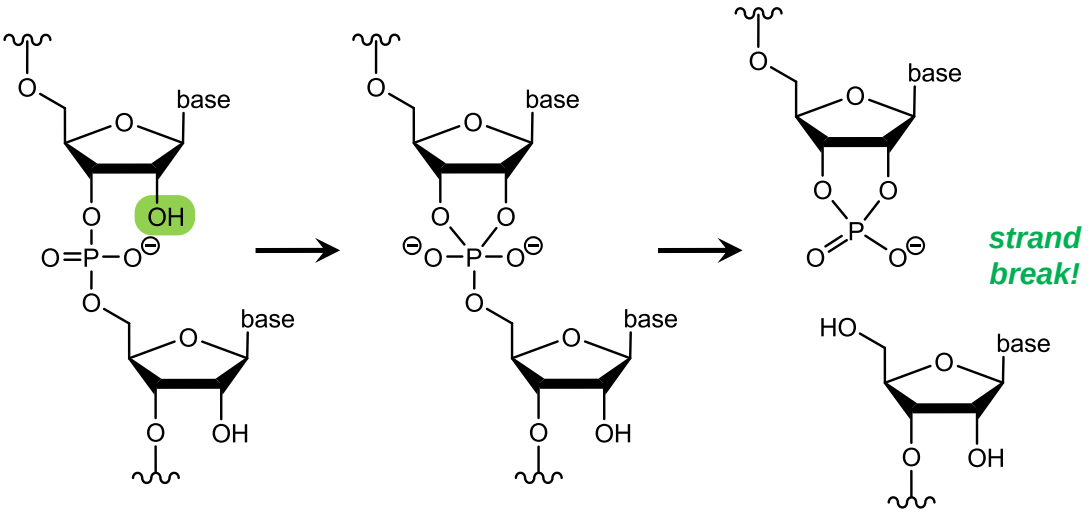
TGC

5′-end 3′-end

(typically read 5′ → 3′)



RNA Is Less Stable Than DNA



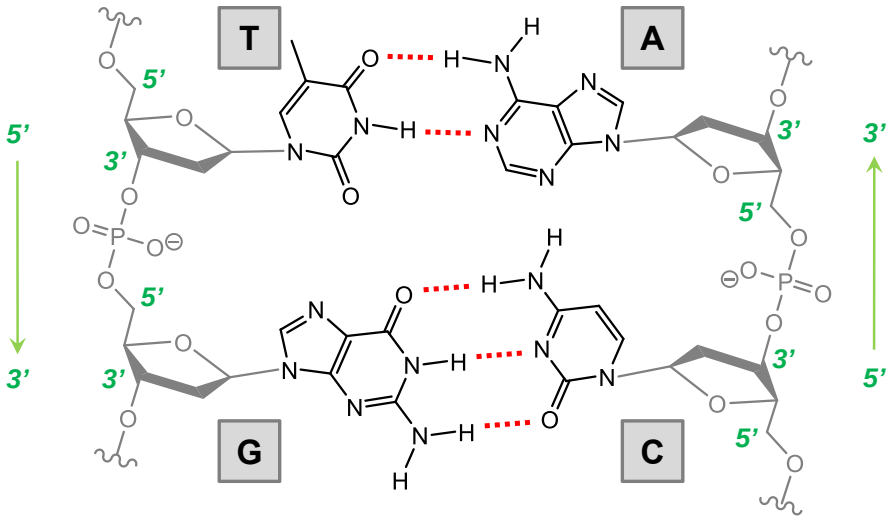
2'-OH can serve as intramolecular nucleophile to cleave RNA strand

DNA lacks a 2'-OH, so it does not self-cleave in this way. So,

$t_{½}$(RNA) = minutes – hours

$t_{½}$(DNA) = centuries

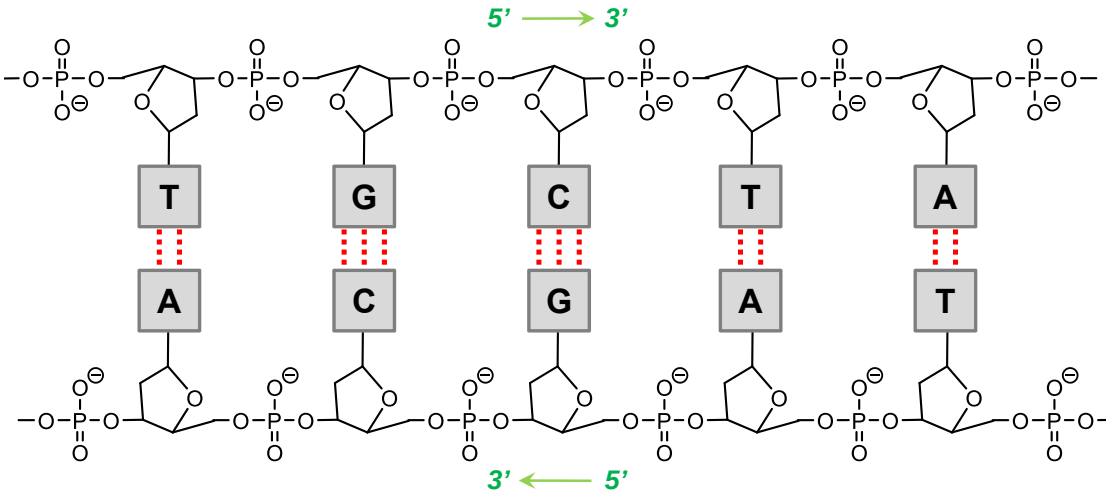
Nucleotide Bases Pair with One Another Via Hydrogen Bonding



Each pair matches one purine with one pyrimidine.

Optimal organization for DNA strands is "antiparallel".

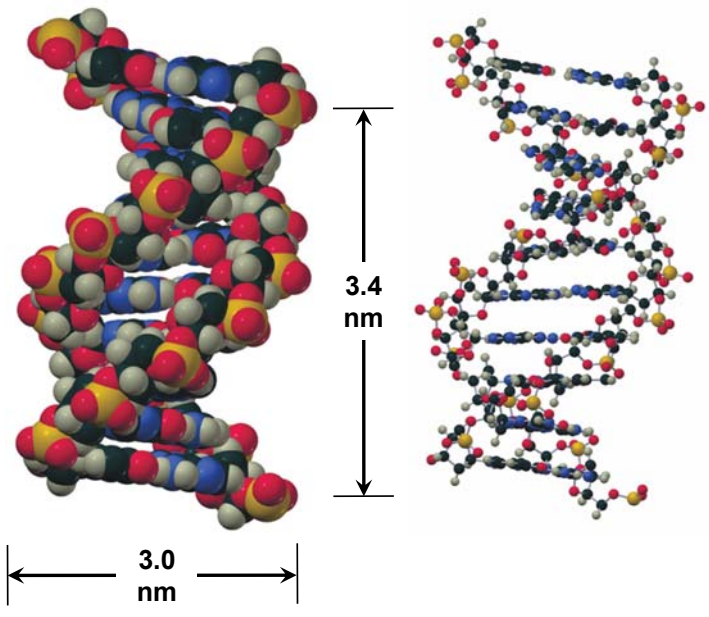
Every DNA Sequence Has A Unique, "Complementary" Sequence



So, the DNA sequence complementary to *5'*-**TGCTA**-*3'*
would be *5'*-**TAGCA**-*3'*

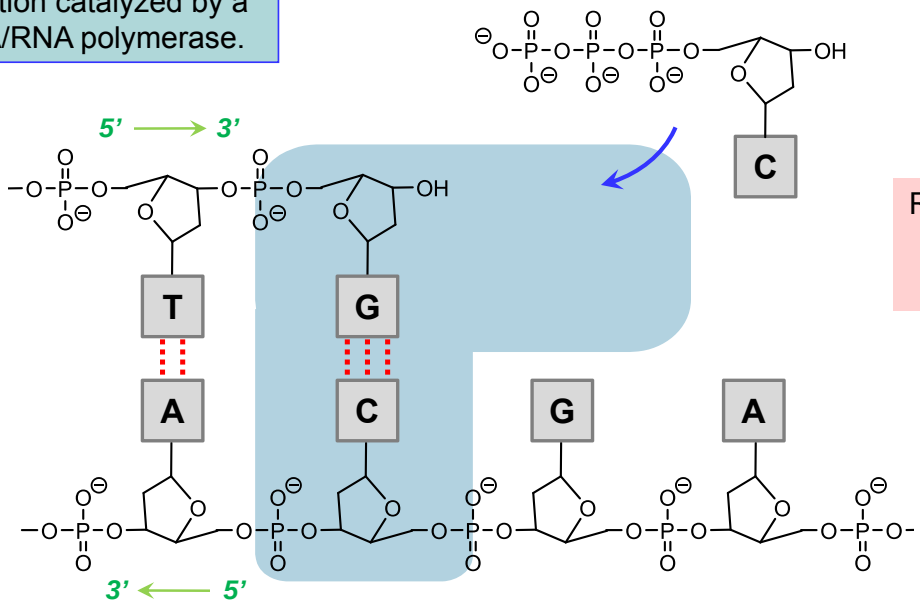
Strands of DNA Form a Right-Handed Double Helix

- DNA base pairs lie flat, stretch across center of helix.
- Each turn of the helix is 10 base pairs, 3.4 nm long.



In Nature, DNA and RNA Are Synthesized by Copying a Single-Strand Template

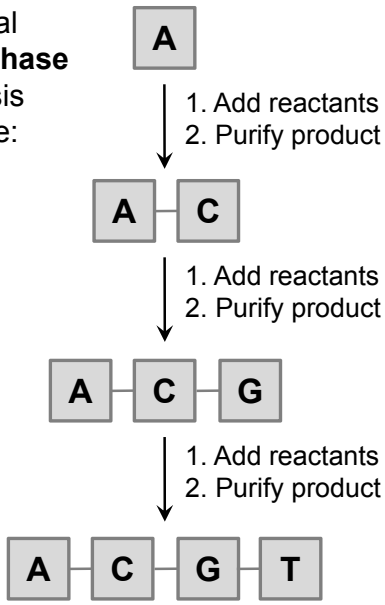
Addition catalyzed by a DNA/RNA polymerase.



Reaction fidelity: > 99%

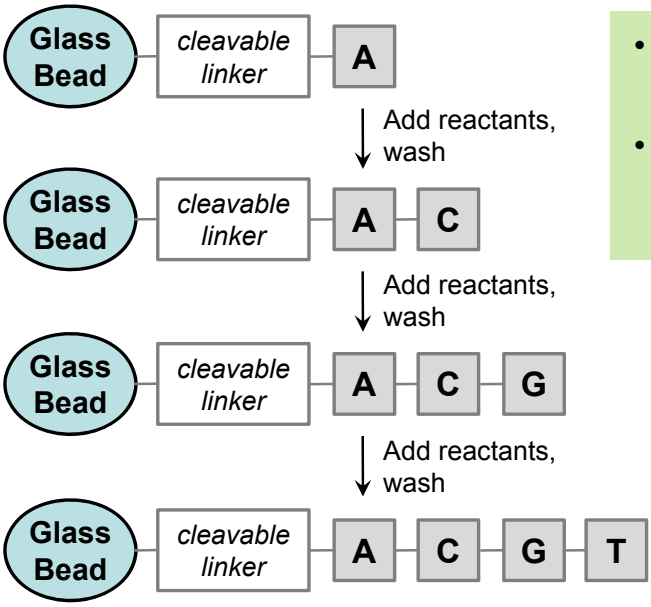
Synthesizing DNA in the Laboratory: Limits of Solution-Phase Synthesis

A typical **solution-phase** synthesis scheme:

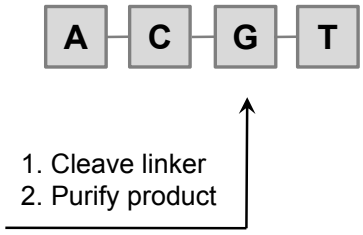


- After each synthetic step, products must be purified away from reagents, unreacted starting material, side products
- *Weakness:* Material often lost in purification steps. For long synthesis, these losses multiply.
- So, DNA cannot be synthesized chemically by solution-phase methods.

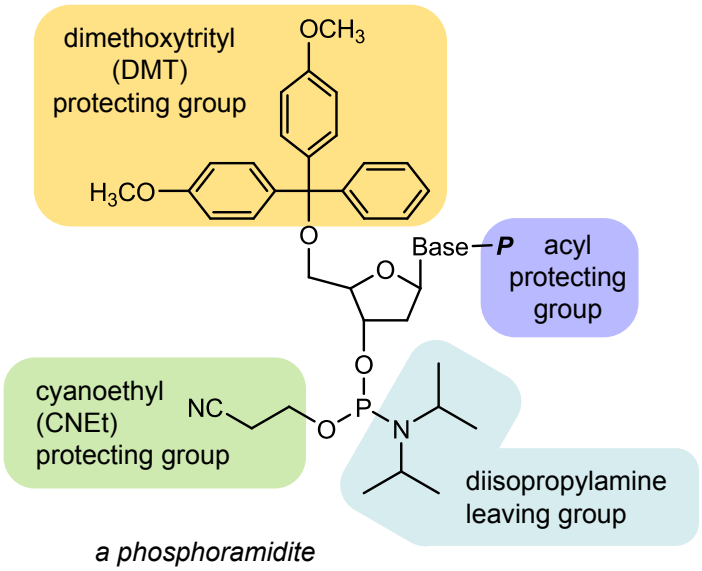
Synthesizing DNA in the Laboratory: Solid-Phase Synthesis



- *Advantage:* Eliminates most purification steps.
- *Weakness:* Reactions must be extremely high-yield, because losses multiply.

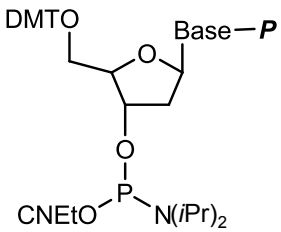


Solid-Phase Synthesis of DNA with Phosphoramidites

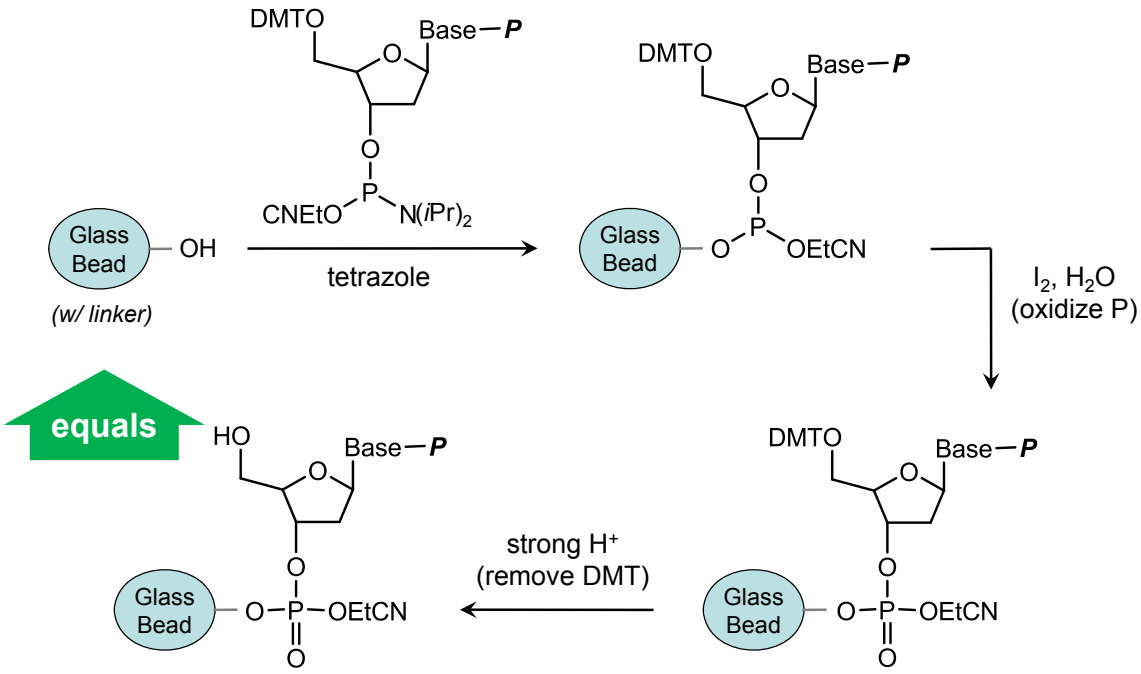


a phosphoramidite

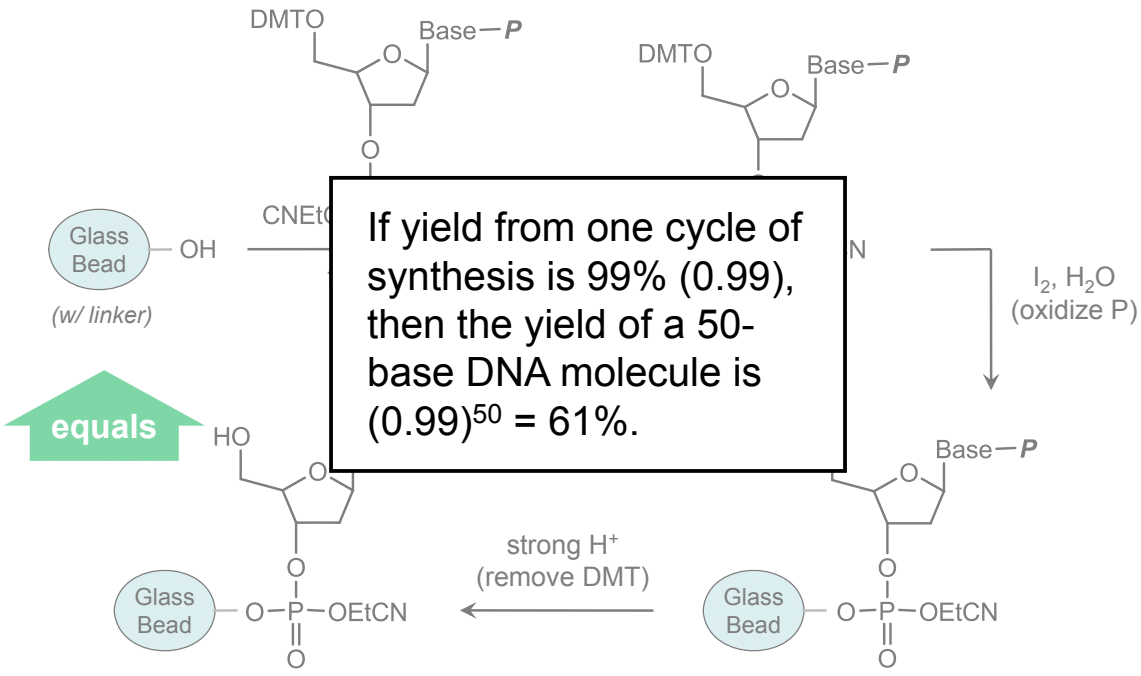
≡



Solid-Phase Synthesis of DNA with Phosphoramidites

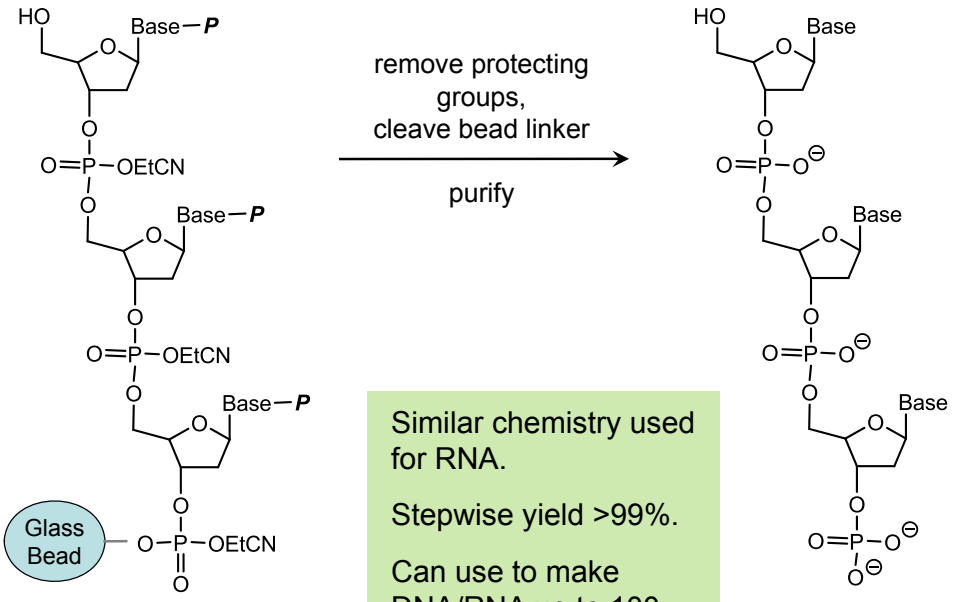


Solid-Phase Synthesis of DNA with Phosphoramidites



If yield from one cycle of synthesis is 99% (0.99), then the yield of a 50-base DNA molecule is $(0.99)^{50}$ = 61%.

Solid-Phase Synthesis of DNA with Phosphoramidites



Similar chemistry used for RNA.

Stepwise yield >99%.

Can use to make DNA/RNA up to 100 bases long.