Biomolecules

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Terms to be understand
functional group
Stereoisomers
cis-trans isomer or geometric isomers
chiral center
enantiomers
diastereomers
racemic mixtures
configuration
conformation
stereospecificity
dehydrogenations
nucleophiles
electrophiles
SN_1 & SN_2 substitution reaction

heterodimer: <*biochemistry*> A **dimer** in which the two subunits are different.

Dalton: Unit of mass equal to the unified atomic mass (atomic mass constant). [IUPAC Compendium] After John Dalton (1766-1844) British chemist and physicist.

dimer: A molecule which consists of two similar (but not necessarily identical) subunits. The term could also be used as a verb referring to the act of the two subunits coming together (to dimerize).

isomer: Molecules with identical molecular formulas but different structural formulas

macromolecular systems: Complexes or cellular systems composed of macromolecules (**proteins, DNA**, **RNA**, polysaccharides, etc.) such as RIBONUCLEOPROTEINS, CHROMATIN, MULTIENZYME COMPLEXES and other **multimeric proteins**.

macromolecule (polymer molecule): A molecule of high relative molecular mass, the structure of which essentially comprises the multiple repetition of units derived, actually or conceptually, from molecules of low relative molecular mass. Notes: 1. In many cases, especially for synthetic **polymers**, a molecule can be regarded as having a high relative molecular mass if the addition or removal of one or a few of the units has a negligible effect on the molecular properties. This statement fails in the case of certain macromolecules for which the properties may be critically dependent on fine details of the molecular structure. 2. If a part or the whole of the molecule has a high relative molecular mass and essentially comprises the multiple repetition of units derived, actually or conceptually, from molecules of low relative molecular mass, it may be described as either macromolecular or polymeric, or by polymer used adjectivally. [IUPAC Compendium]

A general term to describe a "huge molecule." Although there is no set criteria for macromolecules, they are generally considered to be structures with over 1000 atoms. **DNA** and **proteins** are common examples of macromolecules.

-mer This suffix is often used to indicate the number of **nucleotides** in an oligonucleotide, e.g. 30-mer, 19-mer. Related terms **dimer**, monomer, trimer, up to 10 nucleotides decamer. Eleven and above are the number plus -mer.

nucleic acid: A macromolecule composed of linear sequences of **nucleotides** that perform several functions in living cells, e.g., the storage of genetic information and its transfer from one generation to the next **DNA** (deoxyribonucleic acid), the expression of this information in **protein synthesis** (**mRNA, tRNA**) and may act as functional components of subcellular units such as **ribosomes** (**rRNA**). [IUPAC Medicinal Chemistry]

Either of two kinds of molecules (**DNA** and **RNA**) formed by chains of nucleotides, that carry genetic information. [NIGMS]

nucleotide, nucleotides: Nucleosides with one or more phosphate groups esterified mainly to the 3'- or the 5'- position of the sugar moiety. Nucleotides found in cells are adenylic acid, guanylic acid, uridylic acid, cytidylic acid, deoxyadenylic acid, deoxyguanylic acid, deoxycytidylic acid and thymidylic acid. [IUPAC Bioinorganic]

The building block of DNA or RNA. Each nucleotide consists of a sugar component, a phosphate group, and an organic base. Four organic bases exist in **DNA** **(adenine, cytosine, guanine,** and **thymine**) and in **RNA** (adenine, cytosine, guanine, and **uracil**). [NHLBI] Half a "rung" on the DNA ladder. [CHI SNPs]

oligo: A prefix meaning "a few" and used for compounds with a number of repeating units…The limits are not precisely defined, and in practice vary with the type of structure being considered, but are generally from 3 to 10. [IUPAC Compendium]

A shortened form of **oligonucleotide.**

Chemical composition & bonding

About 30 elements with lower atomic number are essential to living organisms, among them only 5 have atomic number above Selenium (Z 34).

Most abundant elements are H, O, N, C, and constitute more than 99% of cell weight. They can form one, two, three and four bonds. In general, the lightest element forms strongest bonds.

Some elements exist in cell in trace amount, but they are very important and essential to cell. Such as Fe, Mg, Cu, Se, etc.

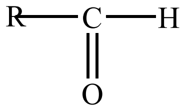
Carbon, the smallest element which can form four bonds, is the key element in living systems, this is based on that carbon can form four stable single bonds with other carbon, proton atoms, and carbon can also form stable double bond, triple bond with other carbon atoms, or other elements, such as O, N, etc. This capability provides the complexity and versatility of the world. No other element can be an alternative.

On the other hand, element silicon has similar bonding possibility, becomes the basic element in inorganic world. It is improbable that silicon could serve as the central organizing element for life on Earth, for several reasons. Long chains of silicon atoms are not readily synthesized, and thus the polymeric macromolecules necessary for more complex functions would not readily form. Also, oxygen disrupts bonds between two silicon atoms, which would cause problems for silicon-base life forms in an oxygen-containing atmosphere. Once formed, the bonds between silicon and oxygen are extremely stable and difficult to break, which would prevent the breaking and making (degradation and synthesis) of biomolecules that is essential to the processes of living organisms.

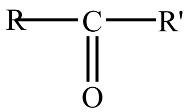
Functional groups determine chemical properties

The hydrocarbon provides the versatile biomolecules when other atom, or a group of atoms (called functional group) replaces hydrogen atom on hydrocarbon. These functional groups commonly found in biomolecules are:

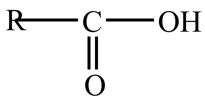
R-OH hydroxyl in alcohol and sugar



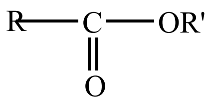
carbonyl in aldehyde and sugar



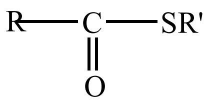
carbonyl in ketone and sugar



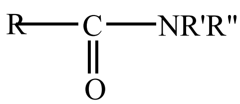
carboxyl in acid and amino acid



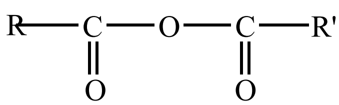
ester



thioester



amido



anhydride (can be mixed)

R—NH_2 amino

R—SH suflhydryl

R—O—R' ether

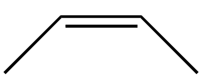
R—S—R' thioether

R—CH_3 methyl

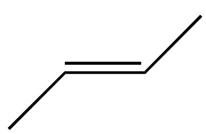
Configuration & Conformation

Configuration denotes the fixed spatial arrangement of atoms in organic molecules that is conferred by the presence of either double bonds or chiral centers.

Geometric or cis-trans isomer

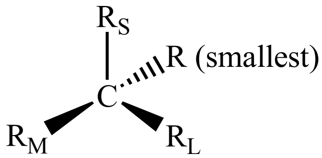


cis-isomer
or *Z* isomer

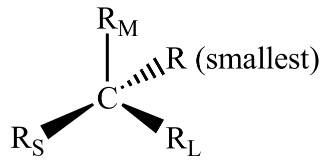


trans-isomer
or *E* isomer

<u>Cannot rotate along the double bond without breaking the double bond</u>!!!



R



S

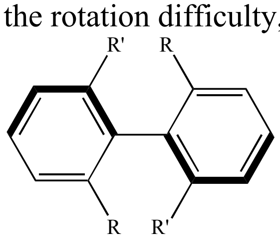
Cannot change the specific spatial sequence of substituents without breaking the bonds.

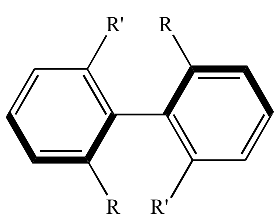
Priority rule:

1. the smallest atom or substituent group is always set in back. The other three substituents are put in the sequence from large, middle, small, in clockwise, with chirality R, counter-clockwise, with chirality S.
2. The atom connects to carbon with largest atomic number has the highest priority, e.g., Br has the priority over Cl.
3. If the two substituents with same atomic number, but different atomic weight, then the substituent with higher atomic weight has the priority over another, for example, deuterium with atomic number 1 but atomic weight 2, has priority over proton with atomic number 1 but atomic weight 1.
4. Two substituents of which the atoms connect to carbon with same atomic number, and then the substituted groups on these substituents will be compared to set the priority sequence, the larger one has the priority over the smaller one. The comparison will be continued until the sequence has been determined

Conformation is changed by rotation along single bond

Staggered conformer is the most stable conformation within a molecule, and eclipsed conformer on the other hand, is most unstable conformation within molecules with highest energy. Every molecule has the thermodynamic distribution of all possible conformations, the lower the energy, the higher percentage of that conformation. At room temperatures, normally the conformation cannot be differentiated, except for extremely condition, where two large substituents exist on two neighboring carbon atoms, and make the rotation difficulty, a sample is shown as follows.

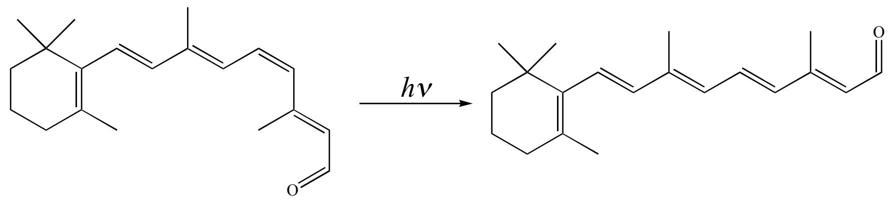




Some conformation can be studied when temperature is lowered, and the molecule is fixed or at least the rotation is reduced to a minimum level such as at -78°C.

The configuration & conformation determines the interaction between biomolecules

1) Configuration & conformation can be studied by X-ray, NMR and other techniques
Some molecules with geometric difference in configuration as cis & trans isomers, might have different chemical properties, and could be separated.



Molecules with R & S difference have identical chemical properties, and cannot be separated, but might have different physical and biological properties.

For example, if ligand with R chirality can fit into the binding cavity of a protein, then the ligand with S chirality normally cannot fit into. For the synthesized drugs with both R & S configuration, only half of them has certain medicinal functionality, and the rest half is waste or even inhibitor of the drug. Penicillin, for example.

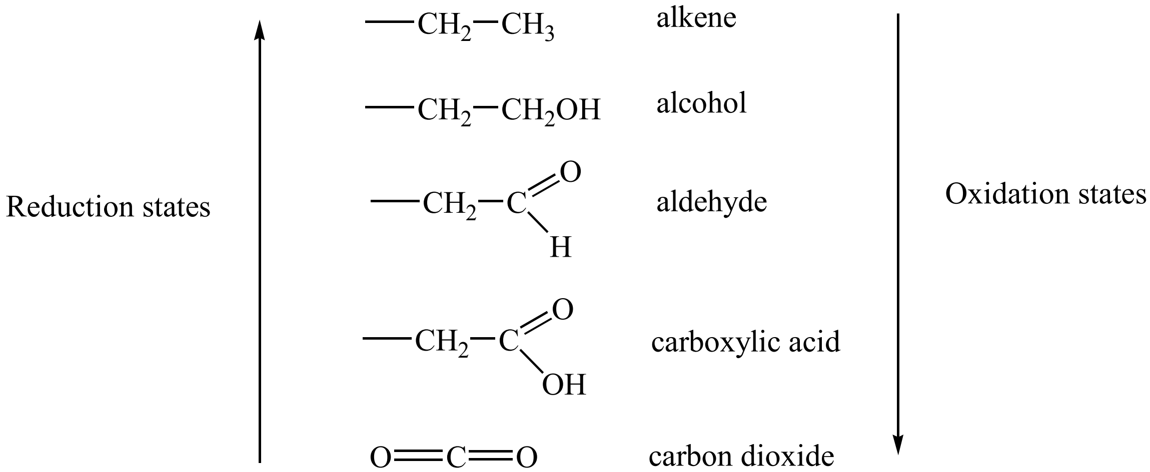
Chemical Reactivity
Normal hydrocarbons are very stable, and inert in terms of chemical reactivity, because strong single bonds exist between hydrogen and carbon, and between carbon and carbon. In addition, the electron is well distributed around the whole molecules. However, when hydrogen is replaced by other functional groups, the electron distribution and geometry of hydrocarbon will change, and the reactivity of the molecules is increased.

There are five different major reaction types in cells

chemical reaction type —
- oxidation-reduction
- cleavage and formation of carbon-carbon bonds
- internal rearrangement
- group transfers
- condensation reaction

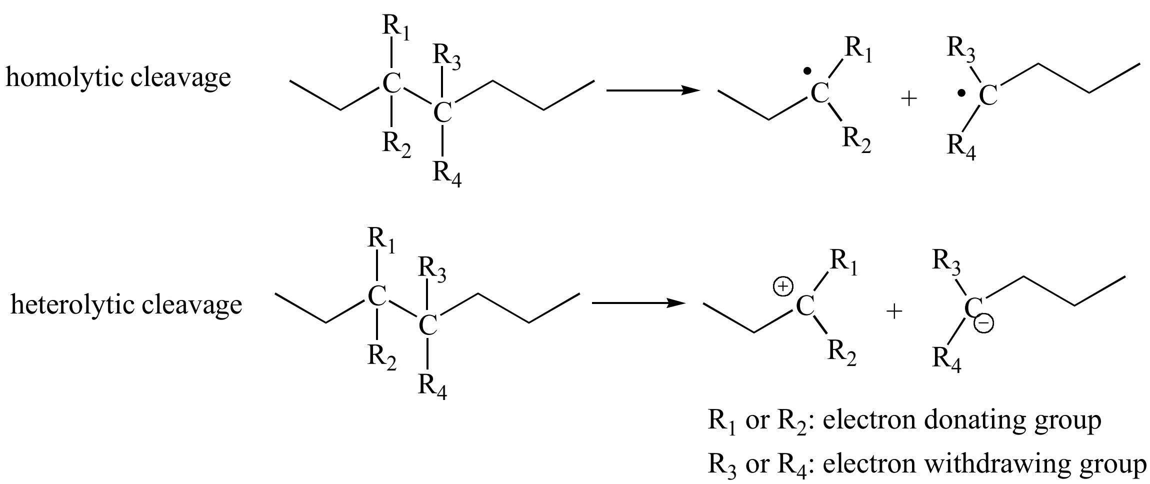
1) Oxidation-reduction
Oxidation reaction involves the giving out of electrons, and after the reaction, the oxidation states of reactant is increased; on the other hand, oxidation is always in pair with reduction, where oxidant reagent obtain electrons from reductant, and the oxidation states of oxidant is reduced. In other words, in oxidation-reduction pair, reductant is

oxidized by oxidant, and its oxidation state is increased; the oxidant is reduced by reductant, and the oxidation state is lowered.
Oxidation-reduction is very common and important in cell, from which the cell can obtain energy to do the work by oxidizing the energy-rich chemicals, such as carbohydrates and fats.



Typical case is dehydrogenation, where a molecule loses two electrons and two hydrogen ions; the enzymes that catalyze this reaction are called dehydrogenases. If the molecule is oxidized, where carbon is covalently bonded to oxygen, the enzymes involved in this reaction are called oxidases, and if the oxygen is derived directly from O_2, the enzymes are called oxygenases.

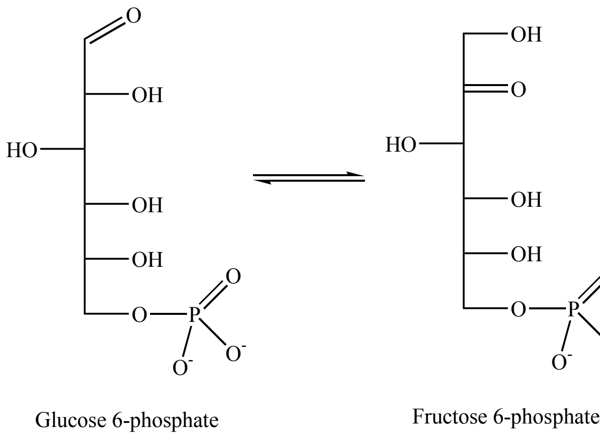
2) Cleavage and formation of carbon-carbon bond



Nucleophilic substitution is a reaction where another electron-rich group replaces a part of molecule. In this reaction, the electron-rich group that is willing to give electron is called nucleophile, and functional group, which is deficient in electron and intended to obtain electron is called electrophile. When nucleophile attacks the electrophile before the cleavage of carbon-carbon bond, the nucleophilic substitution is called SN_2 reaction, which means two molecules involved in the reaction. In contrast, when the carbon-carbon bond breaks before the adding of nucleophiles, the reaction is called SN_1 reaction, which means only one molecule is involved in the beginning of the reaction. Because of this difference, SN_2 reaction always results in the inversion of original configuration, from R to S or S to R in terms of their chirality, and SN_1 reaction will lead to either the retention of configuration or racemization.

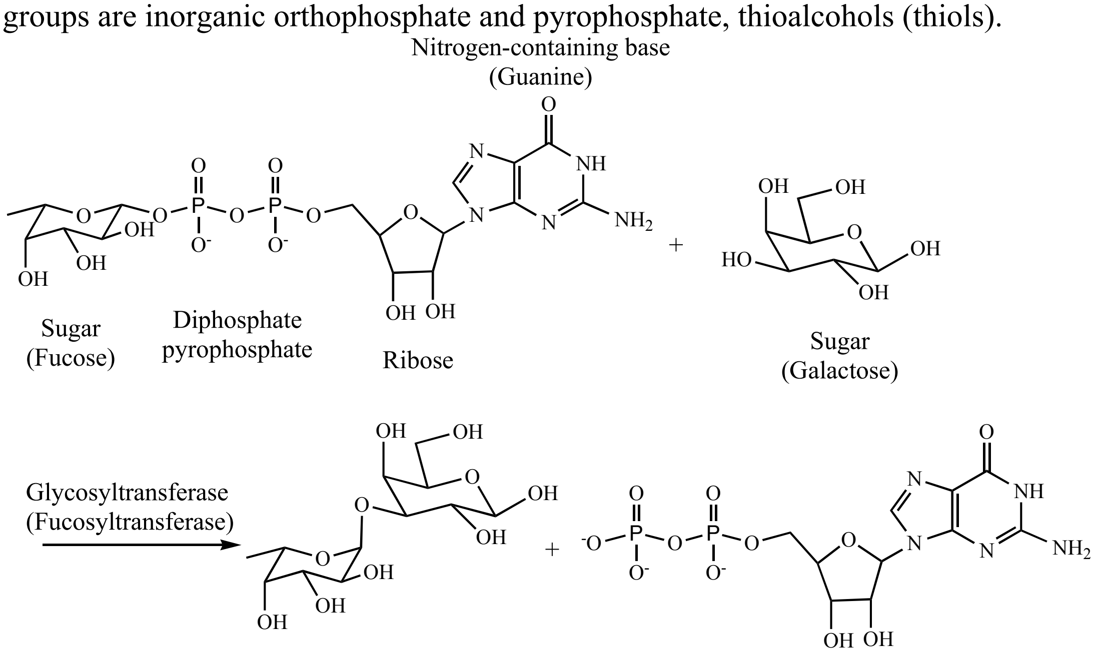
3) Internal rearrangement

Internal rearrangement is a kind of reaction, in which the electron redistribution results in isomerization, transposition of double bonds, and cis-trans rearrangements of double bonds.

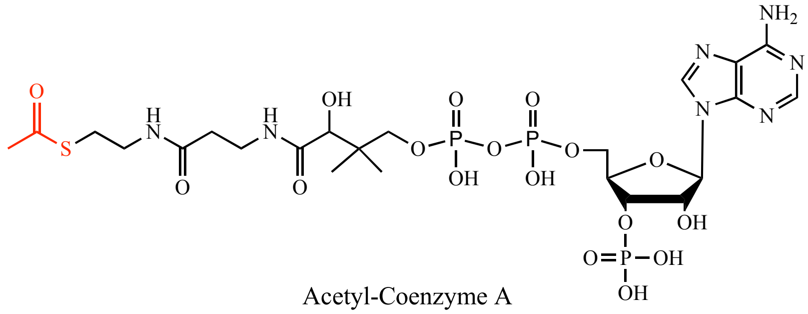


4) Group transfers

A general theme in metabolism is the attachment of a good leaving group to a metabolic intermediate to “activate” the intermediate for subsequent reaction, and the good leaving groups are inorganic orthophosphate and pyrophosphate, thioalcohols (thiols).



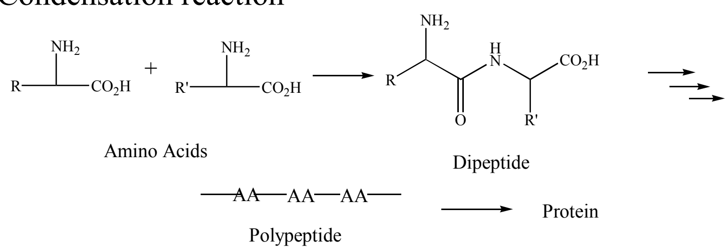
Transfer of sugar happened

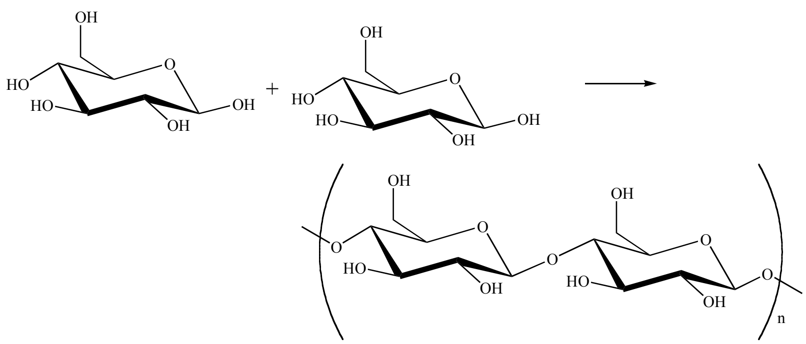


Acetyl-Coenzyme A
(Acetyl-CoA)

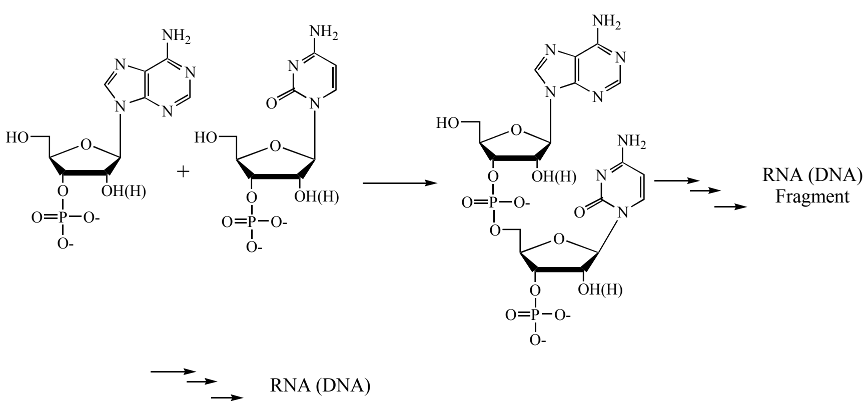
Agent used to transfer of acetyl group

5) Condensation reaction





Polysaccharide
(Starch or Cellulose)



Biomolecules first arose from chemical evolution

Simple inorganic molecules, such as CO, CO_2, H_2O, N_2, NH_3 can form organic compounds, under extremely condition, for example high temperature when volcano happens, or high energy from sunlight or lightning, alpha, beta particles). The simple organic molecules such as HCN, methane, formaldehyde, acetaldehyde, acetic acid, formic acid, can further react and give a variety of other relative complex molecules, such as amino acids, nucleotides, monosaccharides. This monomeric unit of biomolecules can react further to give biomolecules such as proteins, nucleic acids and polysaccharides.

Instruments can be used to detect some simple molecules or fragment of organic molecules in the universe, such as H_2O, CH, HCN and so on. Especially important is the presence of water in other planet, because life may be possible in that planet, not just on earth!