

TOPIC 7: Introduction to Organic Chemistry

Carbon Naming Empirical and molecular formulae Structural formula Isomers Stereoisomerism (chirality) Optical activity Fisher projections Diasteroisomers Intermolecular forces Electronic shifts Organic reactions Intermediates: Radicals, carbocations ans carbanions Substitution reactions Addition reactions Elimination reactions Transposition reactions Condensation reactions





<u>Carbon</u>

•Carbon atoms are present in nature in a number of different compounds

•Those considered Inorganic are:

•Compounds with other non metals:

•**Oxides**: CO_2 , CO, mellitic anyhidride $(C_{12}O_9)$, oxalic anhydride (C_2O_4) •**With halogens**: CCI_4 , CF_4 , ...

•Compounds with metals:

- •Carbonates, CO₃²⁻, and oxalates, ⁻OOC-COO⁻,
- •**Carbonyls** (with CO): Cr(CO)₆, Co₂(CO)₈, Fe(CO)₅, Ni(CO)₄....
- •With the CN group: Cyanide, C=N⁻, Cyanate, [OCN]⁻, Thiocyanate, [SCN⁻] and Isocyanate [-C=N=O]
- •Carbides: Al₄C₃ B₄C, CaC₂, Fe₃C, SiC, TaC, TiC, WC,...
- •Alloys: steel...

•Allotropic forms of carbon:

- Diamond
- •Graphite

•Fullerenes, nanobuds, nanotubes and graphene sheets





http://en.wikipedia.org







*Until 1828 it was thought impossible to make "living" compounds in the lab. *Friedrich Wholer discovers how to make urea, an unquestionable organic, from a typically inorganic compound: ammonium cyanate

 $^{\ominus}O-C\equiv N \iff O=C=N^{\ominus} [O=C\equiv N]^{-}$

*Cyanate is an oxidized form of cyanide, $C \equiv N^-$, (permanganate or hydrogen peroxide as oxidizing agents).

$$NH_4^+OCN \xrightarrow{Heat} NH_2CONH_2$$

•In living organisms urea is formed as the oxidation product of aminoacids or ammonia.

•Organic synthesis was born with this discovery

•Nowadays there are about 10^7 organic compounds with an average increase rate of 10^5 /year









sp³



Naming

Naming begins identifying the largest hydrocarbon chain, its branches and functional groups



http://www.chem.qmul.ac.uk/iupac/ Nomenclature

http://www.iupac.org/

http://www.iubmb.unibe.ch/ International Union of Biochemistry and Molecular Biology 5



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Homologous series is a series of organic compounds with a similar general formula, possessing similar chemical properties due to the presence of the same functional group, and shows a gradation in physical properties as a result of increase in molecular size and mass.

Number of arbon atoms	Alkane	Alkene	Alkyne	Cycloalkane	Alkadiene
1	Methane	-	-	-	-
2	Ethane	Ethene (ethylene)	Ethyne (acetylene)	-	-
3	Propane	Propene (propylene)	Propyne (methylacetylene)	<u>Cycloprop</u> ane	Propadiene (allene)
4	Butane	<u>But</u> ene (butylene)	Butyne	Cyclobutane	Butadiene
5	Pentane	<u>Pent</u> ene	Pentyne	Cyclopentane	Pentadiene (piperylene)
6	<u>Hex</u> ane	<u>He</u> xene	Hexyne	Cyclohexane	Hexadiene
7	<u>Hept</u> ane	<u>Hept</u> ene	Heptyne	Cycloheptane	Heptadiene
8	<u>Oct</u> ane	<u>Oct</u> ene	Octyne	Cyclooctane	Octadiene
9	Nonane	<u>Non</u> ene	Nonyne	Cyclononane	Nonadiene
10	Decane	<u>Dec</u> ene	Decyne	Cyclodecane	Decadiene









Functional group: set of bonded atoms with a characteristic reactivity

Class	alkane	alkene	alkyne	alcohol	ether
Name					
Structure	-CH ₂ -	-C=C-	-C≡C-	-OH	-0-R
Suffix		- ene	- yne	- ol	ether

Class Name	nitrile	sulphide	thiol	carboxylic acid
Structure	-C≡N	-S-R	-S-H	-COOH
Suffix	-nitrile	sulphide	-thiol	- oic acid

Class Name	ketone	aldehyde	carboxylic acid ester	anhydride	amide	amine
Structure	-CO-	-COH	-COOR	-CO-O-CO-	-CONH ₂	-NH ₂
Suffix	-one	- al	- oate	-oic anhydride	-amide	-amine

PRIORITY

acid>anhydride>amide>aldehyde>ketone>alcohol>phenol>amine>halogenide>alkene>alkyne



Straight chain parent molecule. Principal chain

- •Contains the principal functional group named as suffix
- •The longest
- Contains maximum substituent's
- Contains maximum number of multiple bonds
- •Begins by the end nearest to principal functional group

Branching chains

- Named as prefix in alphabetical order
- •Carbon number to which the branch is bonded is put before

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Empirical and molecular formulae

Elemental analysis of a compound yield 40% C, 6.7% H and 53.3% O (w/w). The molecular mass was 60 g/mol. Determine the empirical and molecular formulae

EMPIRICAL FORMULA: Atomic ratio between the elements

С	40,0 %	40/12=3,3	1	
Η	6,7 %	6,7/1=6,7	2	CH ₂ O
0	53,3 %	53,3/16=3,3	1	

MOLECULAR FORMULA: nº of atoms of each element

$$n = \frac{M(CH_2O)_n}{M(CH_2O)} = \frac{60}{30} = 2$$

$$\mathbf{CH}_{2}\mathbf{O} \rightarrow \mathbf{C}_{2}\mathbf{H}_{4}\mathbf{O}_{2}$$

Which compound is it?



Structural formula $C_2H_4O_2$ CH₃-COOH H-COOCH₃ COH-CH₂OH Condensed Ethanoic acid Methyl methanoate hydroxyethanal •Expanded H-C-•Tridimensional (2.5D) •Tridimensional (3D) 11



<u>Isomers</u>





Conformational isomerism

Is a form of stereoisomerism in which the isomers can be interconverted exclusively by rotations about formally single bonds. Such isomers are generally referred to as conformational isomers or conformers and specifically as rotamers.







Trans conformer



Intermediate conformer



As torsion angle decreases from 60° (trans) to 0° (eclipsed) H-H distance decreases from 2.552 to 2.392 Å. Potential energy increases due to repulsions of electron clouds



Is a form of stereoisomerism in which the isomers can be interconverted exclusively by rotations about formally single bonds. Such isomers are generally referred to as conformational isomers or conformers and specifically as rotamers.



Let us consider rotation of the C-C bond in ethane CH₃-CH₃.



Newman projections.

In eclipsed conformer, H atoms are nearer than their radius appearing repulsion: potential energy increases.

Trans or staggered is more stable than eclipsed in about 12.5 kJ/mol.

Trans Eclipsed







Chair conformation





Ring flipping or chair-flipping: the conformation of the ring changes, leading to the axial hydrogens becoming equatorial and the equatorial hydrogens becoming axial



http://chemwiki.ucdavis.edu/Organic_Chemistry/Virtual_Textbook_of_OChem/ Stereoisomers/Stereoisomers%3A_Ring_Conformations



http://en.wikipedia.org/wiki/Cyclohexane_conformation

Other high energy conformers are possible. Twisted chair TC Boat B Twisted boat TB

Only TB can be isolated



Stereoisomerism (Chirality)

Enantiomers are two stereoisomers that are related to each other by a reflection: they are mirror images of each other, which are non-superimposable



http://en.wikipedia.org/wiki/Chirality_ %28chemistry%29 Human hands are perhaps the most universally recognized example of **chirality**: The left hand is a non-superposable mirror image of the right hand.

Quirality appears when the four substituents of a **C** atom are **different**. That C atom is called quiral center

Convention rules for naming: R/S, +/-, D/L conventions

Cahn-Ingold-Prelog priority rules (CIP), based on atomic number (R/S):

Consider a C atom with four substituents. 1 has highest priority and 4 the lowest. Orient the center so that 4 is pointed away from a viewer



If the priority of the remaining three substituents decreases in clockwise direction, it is labeled R (from the Latin Rectus, meaning "right"), if it decreases in counterclockwise direction, it is S (from the Latin Sinestra, meaning "left").



The Sequence Rule for Assignment of Configurations to Chiral Centers

1. The higher the atomic number of the immediate substituent atom, the higher the priority. For example, H- < C- < N- < O- < Cl-. (Different isotopes of the same element are assigned a priority according to their atomic mass.)

2. If two substituents have the same immediate substituent atom, evaluate atoms progressively further away from the chiral center until a difference is found. For example, $CH_3 - < C_2H_5 - < CICH_2 - < BrCH_2 - < CH_3O -$.

3. If double or triple bonded groups are encountered as substituents, they are treated as an equivalent set of single-bonded atoms. For example, $C_2H_5- < CH_2=CH- < HC\equiv C-$

Exercises

3) Consider lactic acid and alanine. Find their structures and their quiral centers and draw structures for their R and S enantiomers.

4) Carvone has two enantiomers. The R smells like spearmint (menta); S smells as caraway (alcaravea o comino). Study the molecule and propose structures for the R and S enantiomers $_{\odot}$





Optical activity

Enantiomers have the property of polarizing light: to change the polarization angle of light when it passes through a solution containing them



http://chemwiki.ucdavis.edu/Organic_Chemistry/Chirality/ Optical_Activity

Specific rotation $[\alpha]$

An enantiomer can be named by the direction in which it rotates the plane of polarized light.

If it rotates the light clockwise (as seen by a viewer towards whom the light is traveling), that enantiomer is labeled (+). Its mirror-image is labeled (-).

An equimolecular mixture of both is called racemic and has no optical acivity

The (+) and (-) isomers have also been termed *d*- and *l*-, respectively (for dextrorotatory and levorotatory). NOT CONFUSE WITH D- AND L- NAMING

 $[\alpha]$ is defined as the observed angle of optical rotation α when plane-polarized light is passed through a sample with a path length of 1 decimeter and a sample concentration of 1 gram per 1 milliliter.

 $[\alpha]_{\lambda}^{T} = \frac{100\alpha}{l \times c}$

L is the path length in decimeters; c, the concentration in g/100 mL; T is the temperature at which polarization has been measured; λ is the wavelength, typically 598 nm, the visible line of the sodium D line

Sucrose +66.47° ; Lactose +52.3° ; Cholesterol -31.5° ; Penicillin V +223° (S)-bromobutane +23.1° ; (R)-bromobutane -23.1°





D/L convention system

Relates the molecule to glyceraldehyde. Glyceraldehyde is chiral itself, and its two isomers are labeled D and L (typically typeset in SMALL CAPS D, L or d, l).

Those molecules derived from D-glyceraldehyde are termed D- enantiomers and those derived from L-glyceraldehyde, L-enantiomers.

For aminoacids there is a rule of thumb to dentify D / L enantiomers (CORN rule).

The quiral center of an aminoacid always has the following four groups -COOH, R, $-NH_2$ and H (R is a variant carbon chain). If these groups are arranged clockwise around the carbon atom, then it is the L-form. If counter-clockwise, it is the D-form





Fisher projections

Is a two-dimensional representation of a three-dimensional organic molecule by projection on a plane.



Two rules:

1)It is only allowed to rotate 180 °, NOT 90° NOR 270° because Y and W are below the plane.

2)You can fix ONE group and rotate the other three in clockwise http://en.wikipedia.org/wiki/Fischer_projection or anticlockwise without changing the configuration.

Fisher projections are useful for determining R/S configurations in enantiomers:

- 1) Set priority of groups
- 2) Make any of the two allowed movements to locate upwards the minimum priority group
- 3) Find the rotation direction for $1 \rightarrow 2 \rightarrow 3$

Exercises

5) Consider lactic acid and alanine. Find the Fisher projections for their R and S enantiomers. 6) Synthetic drugs usually consist of a mixture of enantiomers (racemic mixtures) sometimes with adverse effects on health. The active form of Ibuprofen is the S enantiomer and the presence of R reduces the speed of its analgesic effect. Find the quiral centre in the shown structure of Ibuprofen and draw the R and S isomers





<u>Diasteroisomers</u>

When molecules contain more than one quiral center (n centers), the number of stereoisomers roughly grows as 2ⁿ. Some of these isomers are not enantiomers because they are not mirror images. These isomers are called Diastereoisomers.





Intermolecular forces

COMPOUND	FORMULA	Ть(К)
methane	CH 4	109
ethane	CH ₃ -CH ₃	184
propane	CH ₃ -CH ₂ -CH ₃	231
butane	CH 3-CH 5-CH 5-CH 3	272
pentane	CH ₃ -CH ₂ -CH ₂ -CH ₂ -CH ₃	309
2-methylbutane	(CH ₃) ₂ -CH-CH ₂ -CH ₃	301
2,2-dimethylpropane	(CH ₃) ₃ -C-CH ₃	283
1-chloropropane	CH ₃ -CH ₂ -CH ₂ Cl	320
1-propanol	CH ₃ -CH ₂ -CH ₂ OH	321
1-propanal	CH ₃ -CH ₂ -COH	322
propanoic acid	CH ₃ -CH ₂ -COOH	414

• London Forces: dipole-induced dipole F_{d-di} = f(size)



• Van der Waals forces: dipole -dipole $F_{d-d} = f(\Delta \chi)$



•Hydrogen bonding: dipole -dipole $F_{d-d} = f(\chi_H - \chi_X)$ X has lone pairs





$\frac{Electronic \ shifts}{Electronic \ shifts \ on \ \sigma \ bonds}$

Inductive effect (I): Polarity induced in a covalent bond	X	K _a (10 ⁵)
due to the difference in electronegativities of the bonded	Н	1,8
atoms.	$CO_2C_2H_5$	22
	OCH ₃	34
8- 8t o	CI	160
$\Delta \chi \uparrow \Rightarrow \mathbf{K}_{a} \uparrow$	CN	300
$X \leftarrow CH_2 \leftarrow C$	NO ₂	4800
$\Delta \chi_x > \Delta \chi_c$ $O \leftarrow H$	n	K _a (10 ⁵)
δ- δ+ Ο	1	160
$CI \leftarrow (CH_2)_n \leftarrow C^{\prime\prime}$ $-I n^{\uparrow} \Rightarrow K_{-\downarrow}$	2	8,2
	3	3,0
∪	4	1,9

Electron withdrawing (-I): attract electrons more strongly than hydrogen

-C₆H₅<-OCH₃<-I<-Br<-Cl<-F<-SO₃H<-COOH<-CN<-NO₂<-CCl₃<-NR₃

Electron releasing (+I): attract electrons less strongly than H, electron donating $-O^{-} < -CO_{2}^{-} < -C(CH_{3})_{3} < -CH(CH_{3})_{2} < -CH_{2}CH_{3} < -CH_{3}$



Electronic shifts on п bonds

Resonance effect (R): π electrons delocalization by overlapping molecular orbitals in specific directions





Electronic shifts: Aromaticity



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Electronic shifts: Substitution effects in п systems





Positions 2,4 and 6 are electron rich sites

Donating groups (+R): $-O^- >> -NH_2 > -SH > -OH > -CI$

+R





Positions 2,4 and 6 are electron deficient sites

Withdrawing groups (-R):

-A=B: -N=N>>>-NO₂>-SO₂R>-RCO>-CO₂R>-C=N \approx -COOH



of the polar bond



Intermediates: Radicals

Radical formation: removal of a H atom **Geometry:** *planar* (sp²) How can we prove this geometry?



Naming: the same as the corresponding alkyl group plus "radical"



Addition of chlorine atoms



Important consequence: radical reactions do not keep stereochemical details



Radicals: Stabilization

RESONANCE
$$CH_2 = CH - \dot{C}H_2$$

 \leftrightarrow

 $\dot{C}H_2 - CH = CH_2$

HYPERCONJUGATION





Stability order

$$\bigcirc$$
 \dot{C} $\dot{C$







TRANSPOSITION: spontaneous rearrangement of atoms looking for the highest stability













Substitution (S)

An atom or group of atoms is replaced by other.

Substrate. Molecule at which substitution takes place.

Incoming group or reactant. Atoms or group of atoms that attack substrate,

Product. The newly formed molecule.

Leaving group. Atom or groups of atoms expelled from the substrate.



• HOMOLYTIC: breakdown of low polarity bonds. THREE STEPS





http://chemwiki.ucdavis.edu/Organic_Chemistry/Hydrocarbons/Alkanes/Chlorination_of_Methane_and_the_Radical_Chain_Mechanism



Termination

 $Cl \bullet + \bullet Cl \rightarrow Cl:Cl$

 $Cl \bullet + \bullet CH_3 \rightarrow CH_3:Cl$

 $CH_3 \bullet + \bullet CH_3 \rightarrow CH_3: CH_{339}$



• HETEROLYTIC:

Electrophilic substitution (S_E): electron rich molecules (O.M. π)





Nucleophilic substitution (S_N):

• 2nd order (S_N2): $v=k_2 \cdot [CH_3-CH(Br)-CH_2-CH_3] \cdot [OH^-]$



• 1st order (S_N 1): v=k₁·[CH₃-(CH₂)₂-CH(CH₃)(Br)-CH₂-CH₃]





Addition (A)

$A + B \rightarrow A-B$

• HOMOLYTIC: (anti-Markovnikov)



• HETEROLYTIC:

Electrophilic addition (A_E): (Markovnikov)



Nuleophilic addition (A_N):







$X - A - B - Y \rightarrow A = B + X - Y$

• α -ELIMINATION: from the same carbon atom



• β -ELIMINATION: from adjoining carbon atoms, forms double bonds.

$$H_3C-CH-CH_2 \longrightarrow H_3C-CH=CH_2$$

Br H

• $\alpha_{\mu}\omega$ -ELIMINATION: from distant carbon atoms, creates cyclics.





Transposition

• Stabilization of intermediates. Appears jointly with substitution, addition or elimination reactions



Condensation

• A small molecule is lost. It can be considered as an elimination coupled with an addition.

$$H_3C-CH_2O+H + HO+CH_2CH_3 \longrightarrow H_3C-CH_2O-CH_2-CH_3$$