# Structure Identification of Organic Compounds

Zsuzsanna Sánta

Gedeon Richter Plc
Spectroscopic Research Department

E-mail: zsuzsanna.santa@gmail.com

# 2019 autumn

| Date | Topic |
|---|---|
| 09. 09. | Introduction |
| 09. 16. | IR, VCD, XRay |
| 09. 23 | - |
| 09. 30. | MS |
| 10. 07. | MS+NMR |
| 10. 14. | NMR |
| 10. 21. | NMR |
| 10. 28. | 1st exam |
| 11. 04. | Combined problems |
| 11. 11. | Combined problems |
| 11. 18. | Combined problems |
| 11. 25. | Combined problems + 1st corr. exam |
| 12. 02. | 2nd exam + History |
| 12. 09. | 2nd corr. exam |

# Structure Identification of Organic Compounds

Verification
Elucidation

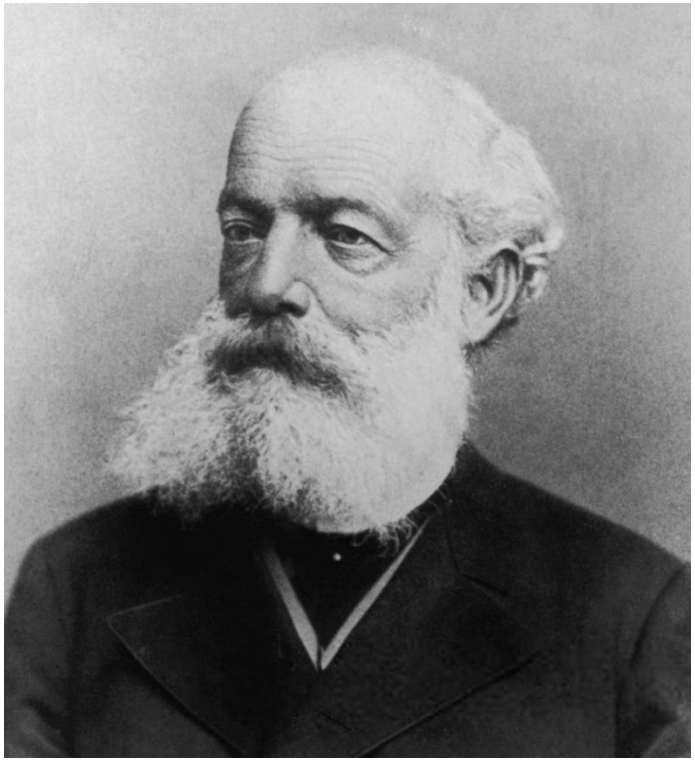
Small molecules:
M<1000Da
No polymers,
biomolecules,
mineral oil…
**Medicinal chemistry**

C,H,N,O,S,F,X,P
No metal complexes

Verification: we know properties of the compound, need Y/N answer
Elucidation: we do not know the structure at all (maybe assumptions)

# STRUCTURE

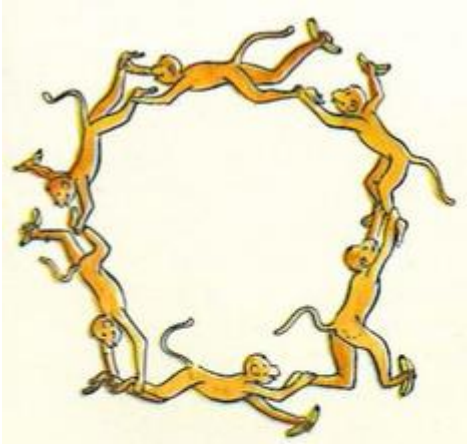
Speciality of organic compounds?



**Friedrich August Kekule**
7 September 1829 – 13 July 1896

**1858**: tetravalence of carbon, atoms connected in definite order, existence of C-C bonds

**1865**: structure of benzene

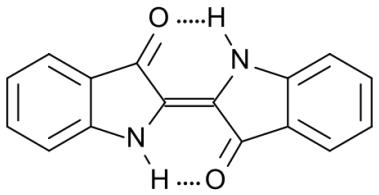


YOU CAN THINK OF THE BENZENE RING AS SIX MONKEYS HANGING ON TO EACH OTHER WITH ONE OR TWO HANDS, HOLDING BANANAS IN THEIR FREE HANDS.

Number of organic compounds (CAS): ~ 100 million

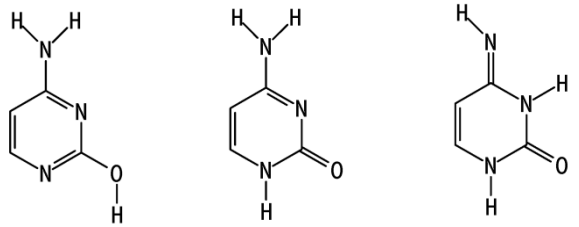
# STRUCTURE

Intermolecular associations

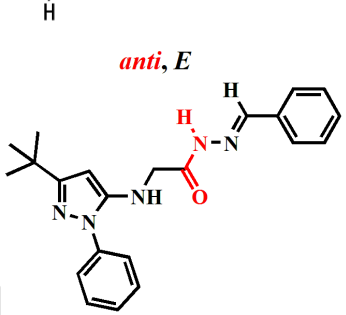


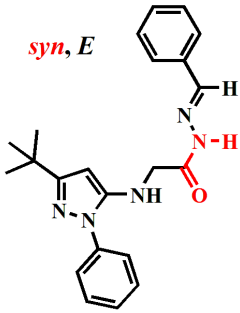
Intramolecular bonds

Tautomerism

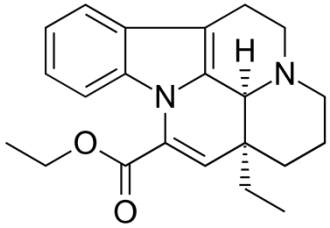


Conformational variability

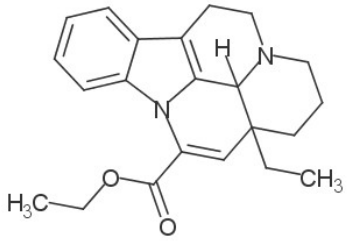



Configuration
relative, absolute



Constitution



Molecular formulae $C_{22}H_{26}N_2O_2$

# STRUCTURE

Intermolecular associations

Intramolecular bonds

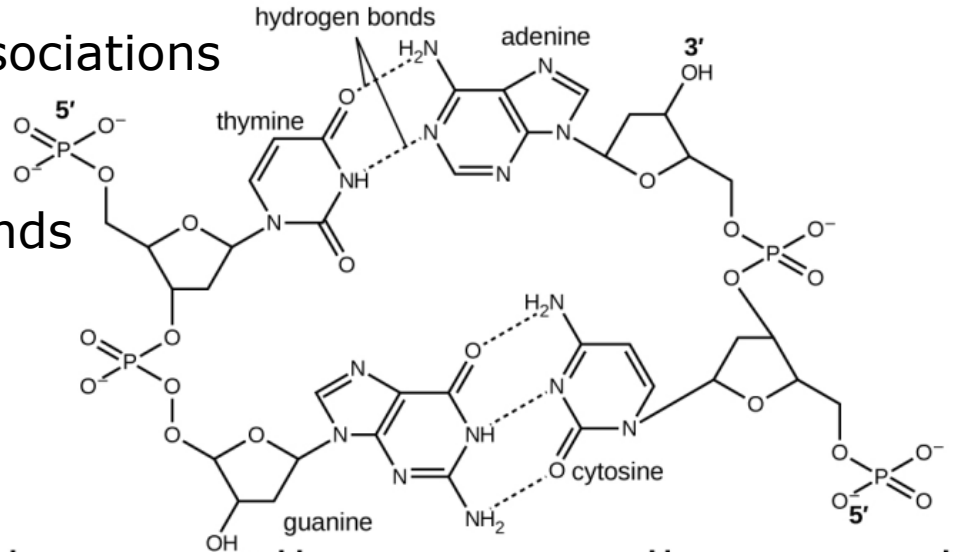
Tautomerism

Conformational variability

Configuration

Constitution

Molecular formulae



## Aspects to consider

**Solid**
**Liquid**
(Gas)

**SAMPLE**

# Main component(s)

Organic impurities
Inorganic impurities
Moisture
Residual solvent

Invasive/Noninvasive??

# Amount!

# STRUCTURE

Intermolecular associations

Intramolecular bonds

Tautomerism

Conformational variability

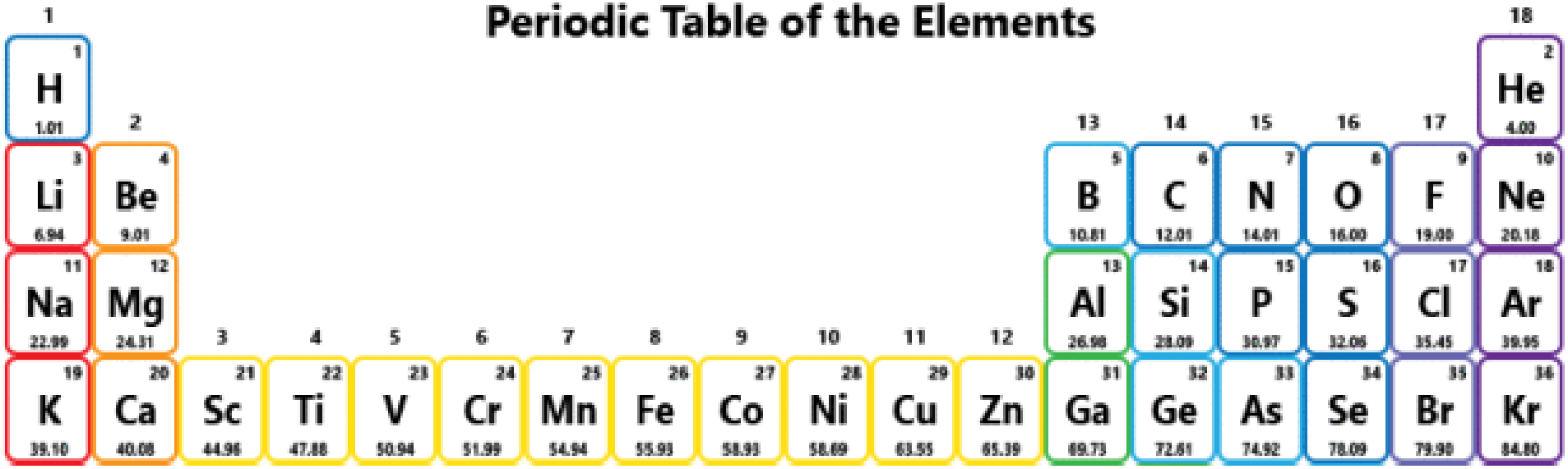
Configuration
relative, absolute

Constitution

Molecular formulae $C_{22}H_{26}N_2O_2$

Molecular formulae $C_{22}H_{26}N_2O_2$

M, Elemental composition M=350.4; C(75.40%) H(7.48%) N(7.99%) O(9.13%)




M=334.4 C(57.47%) H(5.43%) N(8.38%) O(19.14%) S(9.59%)

$C_{16}H_{18}N_2O_4S$

M=334 C(57.6%) H(5.3%) N(8.2%) O(19.1%) S(9.8%)

# STRUCTURE

Intermolecular associations

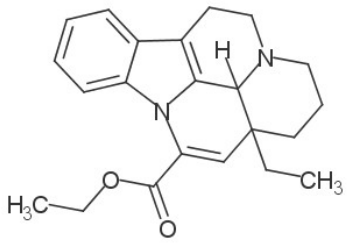
Intramolecular bonds

Tautomerism

Conformational variability

Configuration
relative, absolute

**Constitution**




Molecular formulae $C_{22}H_{26}N_2O_2$

# STRUCTURE

Intermolecular associations

Intramolecular bonds

Tautomerism

Conformational variability

Configuration
relative, absolute

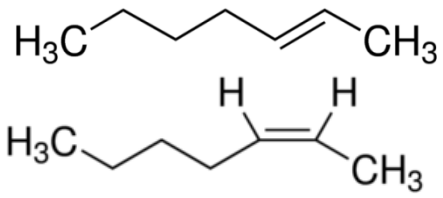
Constitution

Molecular formulae $C_{22}H_{26}N_2O_2$

## Configuration

Geometric isomers

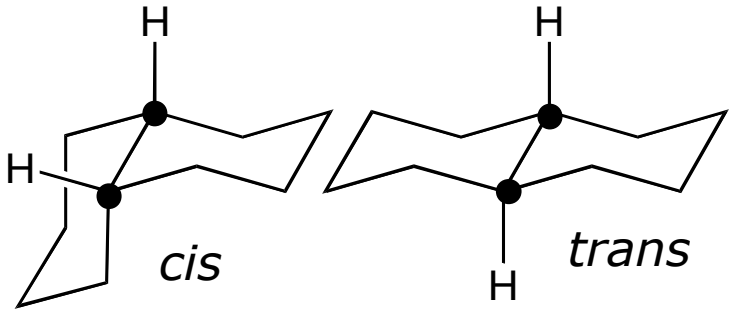
Double bond

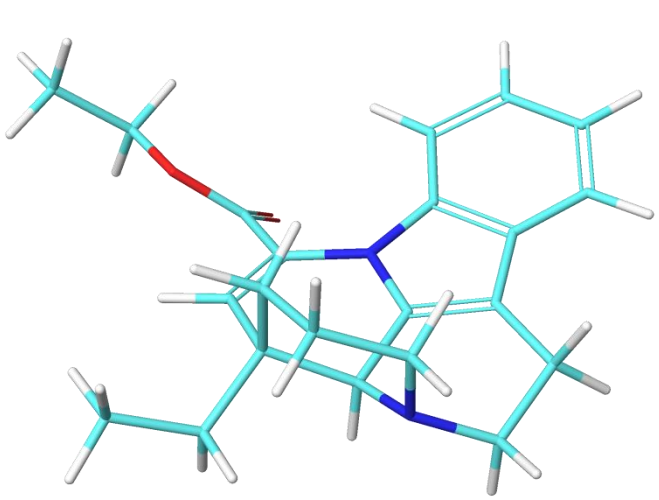


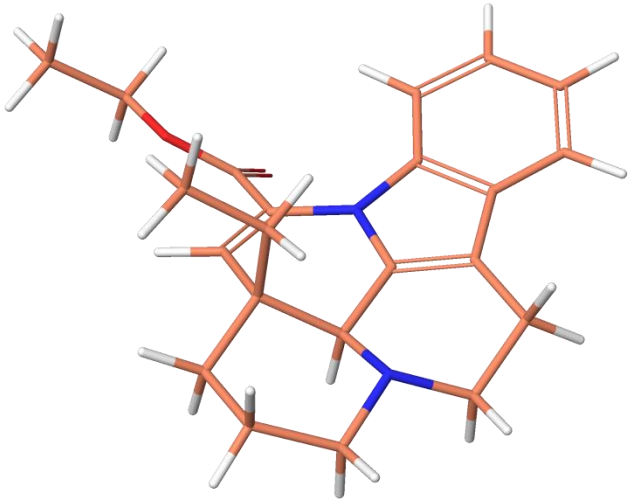

*E*

*Z*

Rings

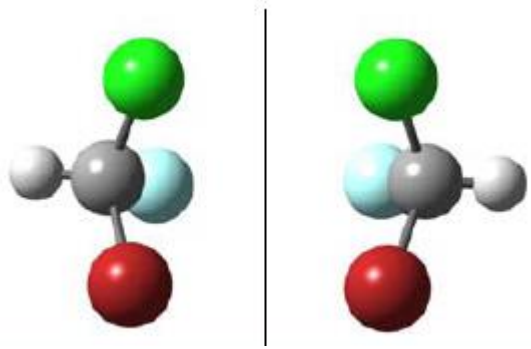




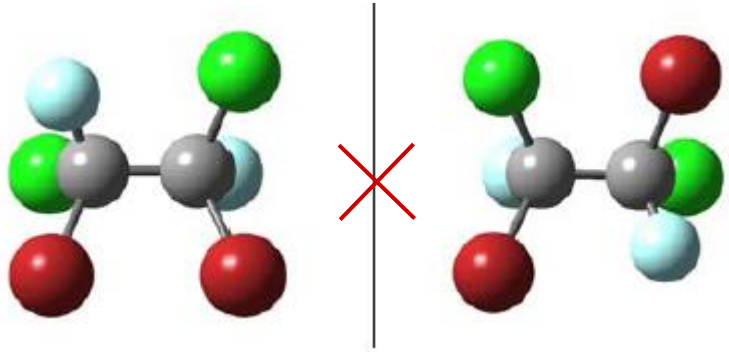
Stereoisomers

Enantiomers

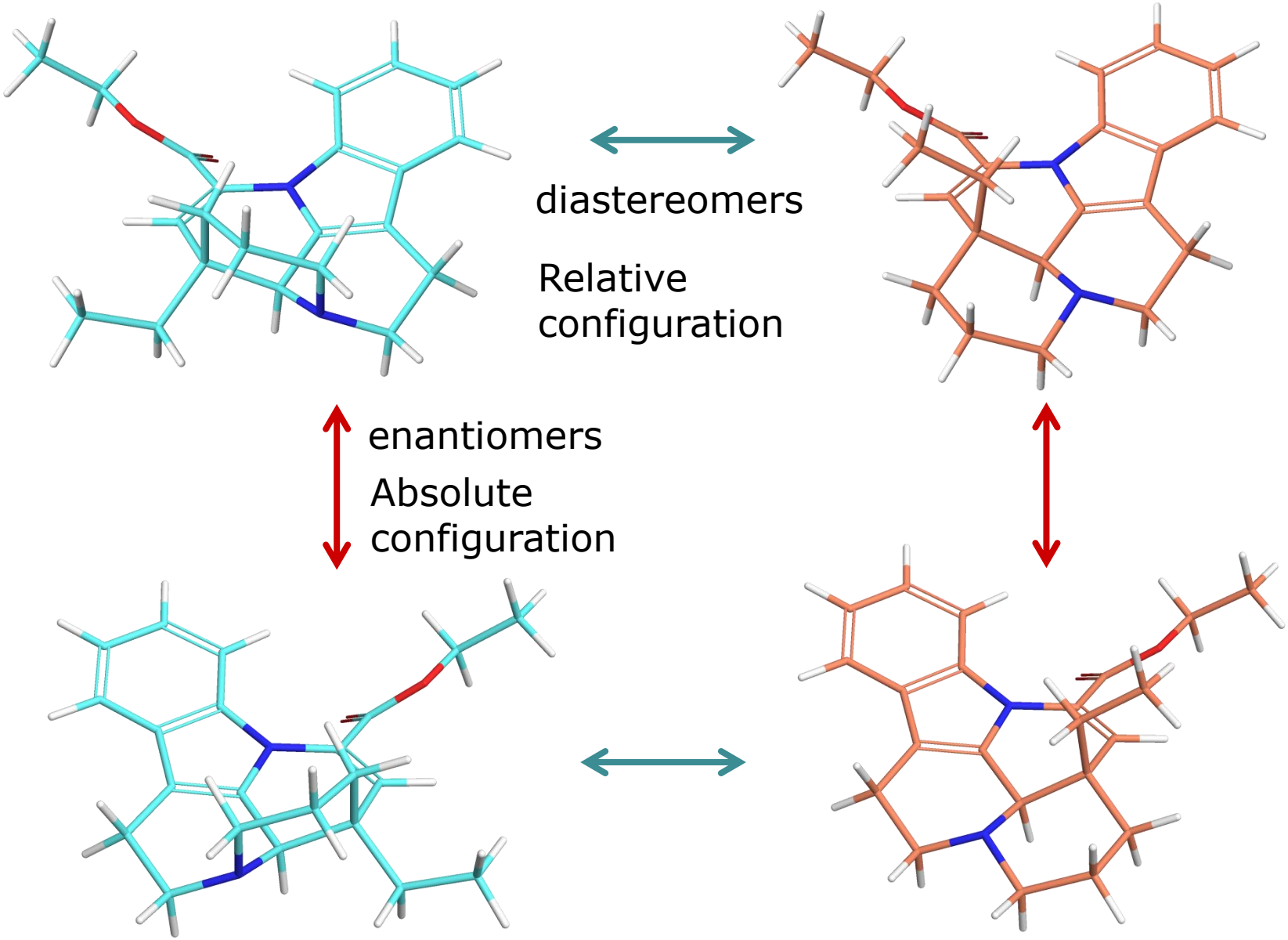


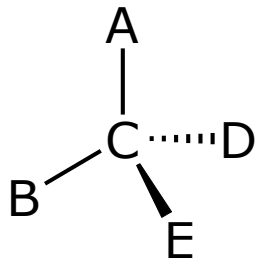
**Identical** melting and boiling point, chemical properties. Difference only if chiral interaction is involved

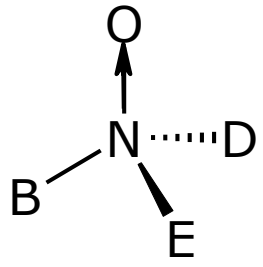
Diastereomers

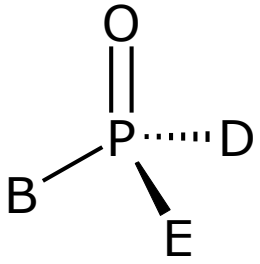


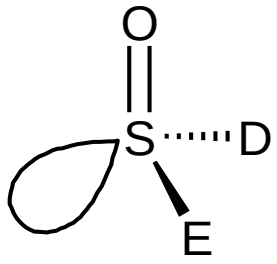
**Different molecules** (eg. melting and boiling point, chemical properties, etc.)

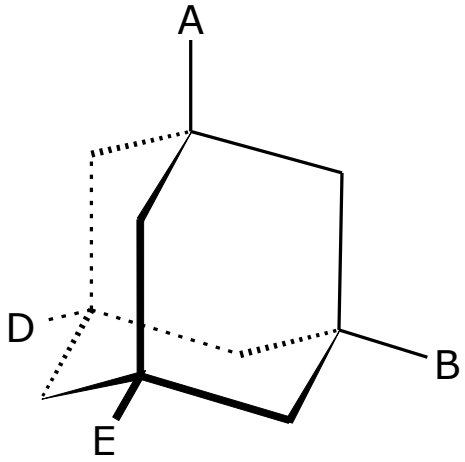

diastereomers
Relative
configuration
enantiomers
Absolute
configuration




Other special cases

# STRUCTURE

Intermolecular associations

Intramolecular bonds

Tautomerism

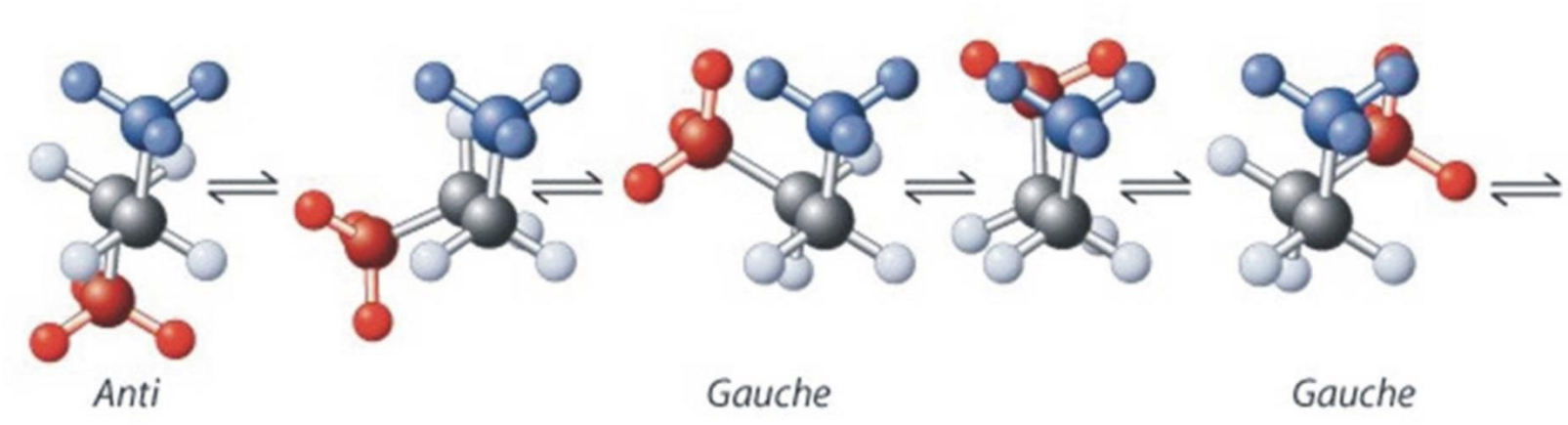
Conformational variability

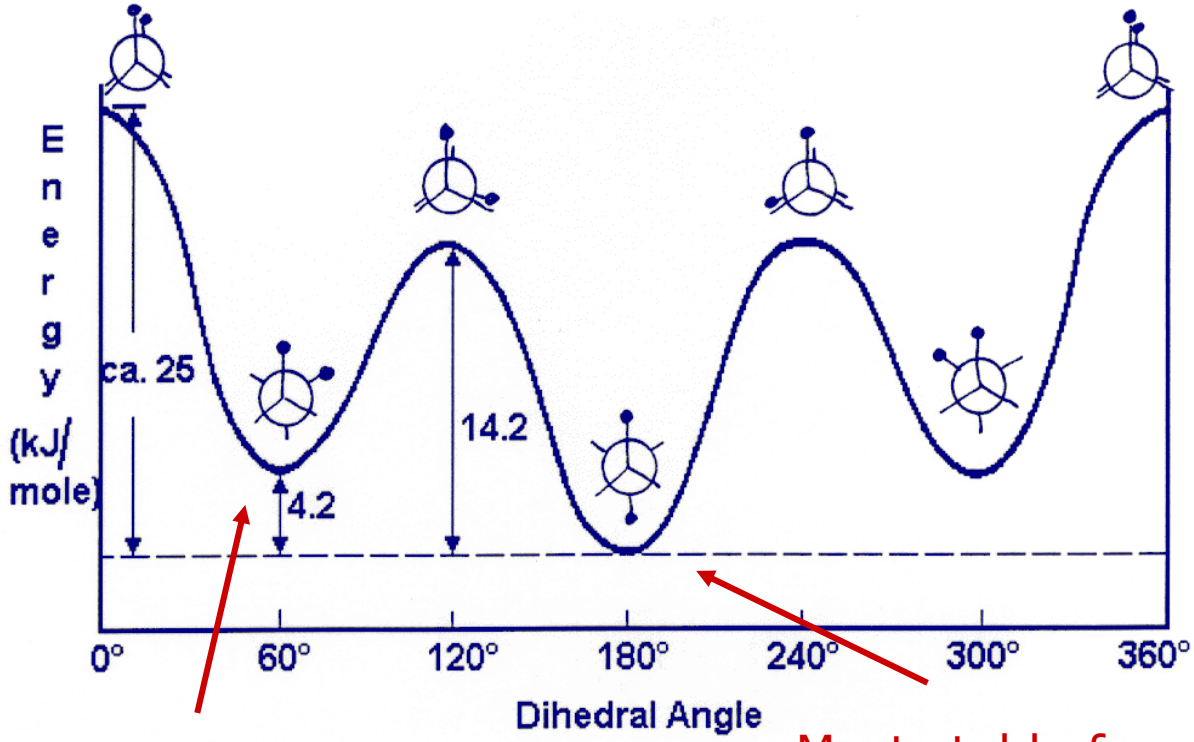
Configuration
relative, absolute

Constitution

Molecular formulae $C_{22}H_{26}N_2O_2$

# Butane conformational variability

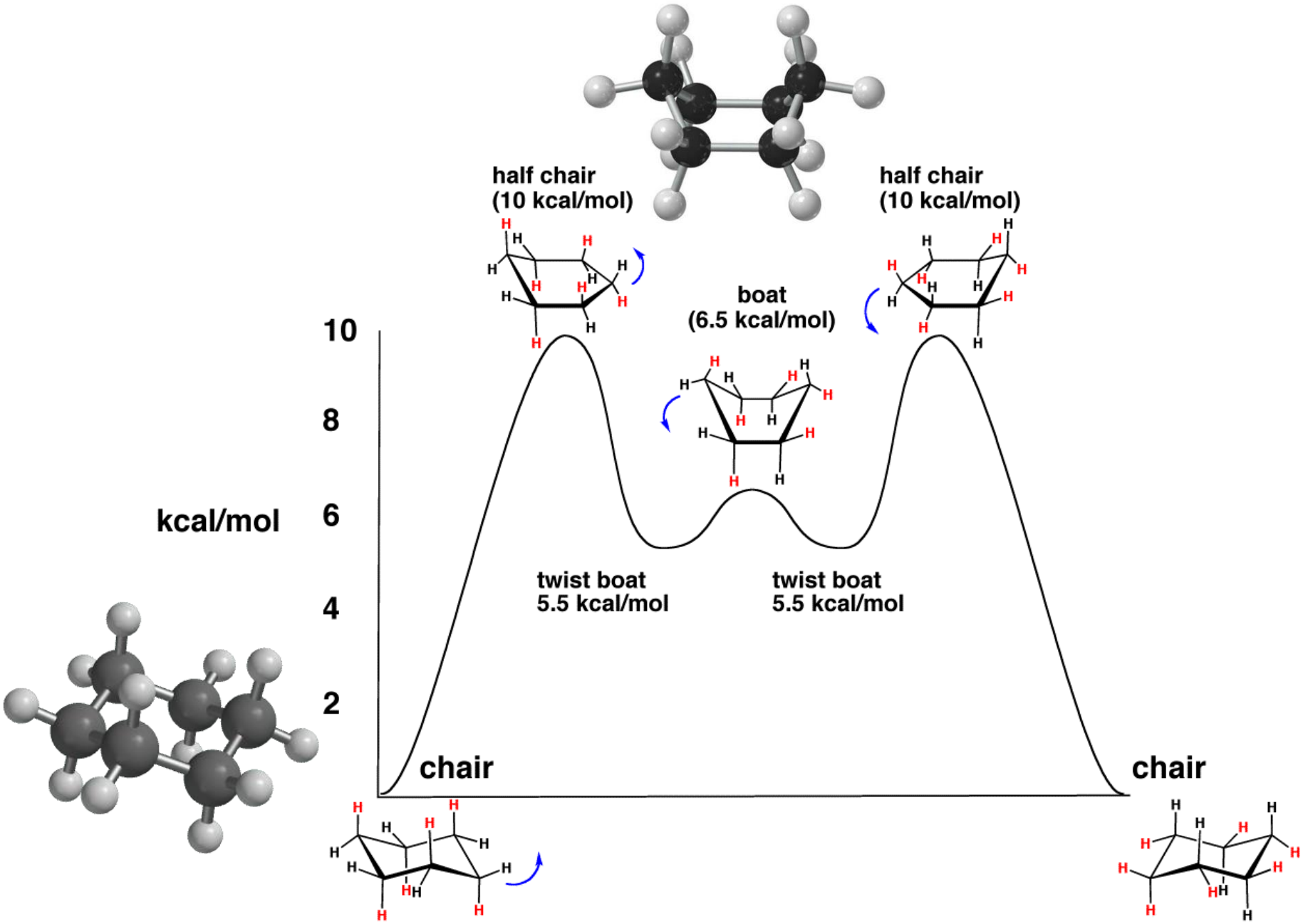


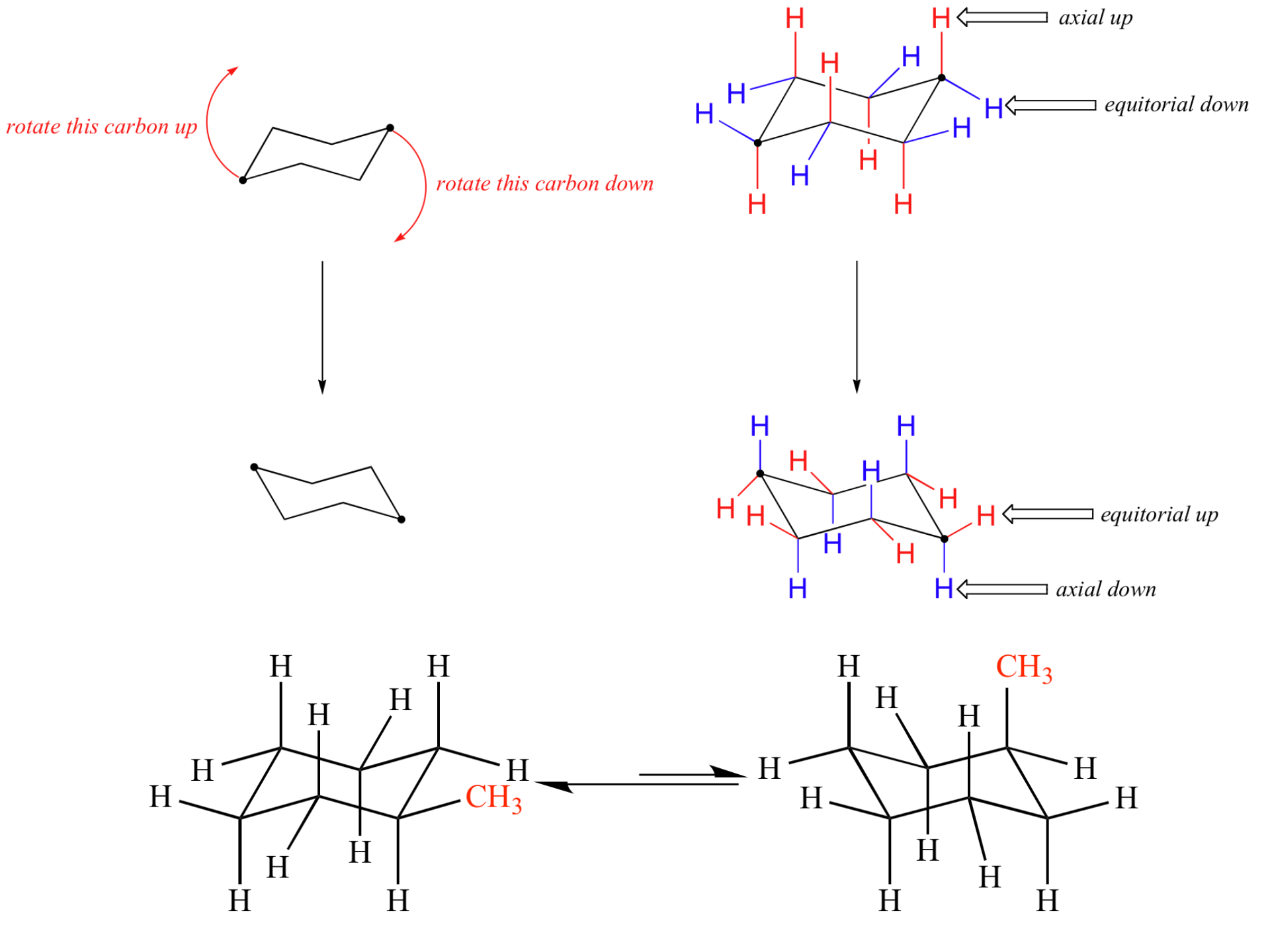




local minimum

Most stable form

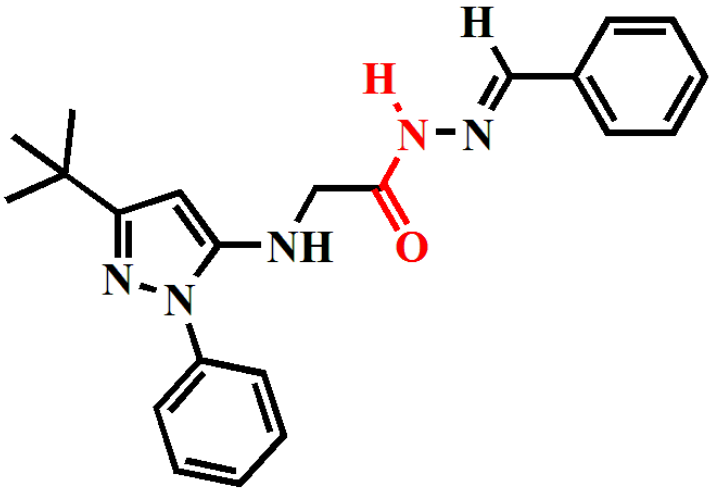
# Cyclohexane conformation



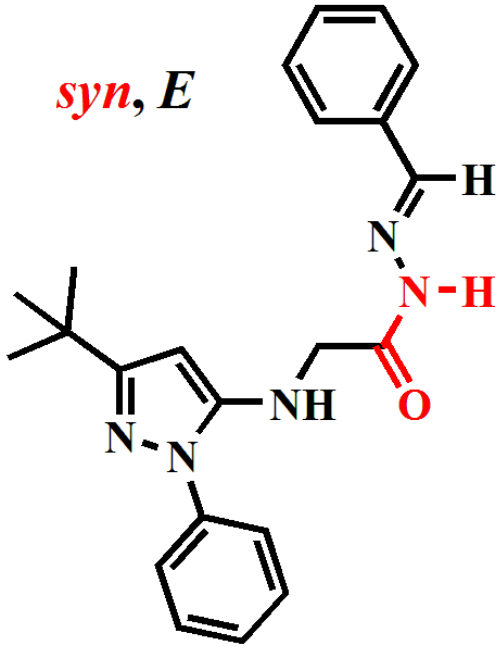

rotate this carbon up
rotate this carbon down
axial up
equitorial down
equitorial up
axial down
CH3
CH3

## Conformation around amide bonds

*anti*, *E*




*syn*, *E*



# STRUCTURE

Intermolecular associations

Intramolecular bonds

Tautomerism

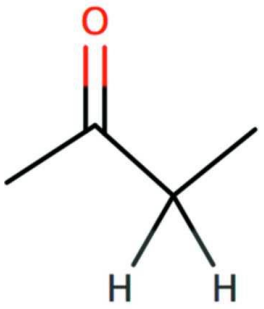
Conformational variability

Configuration
relative, absolute

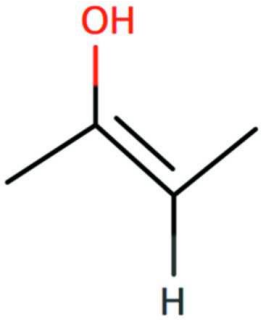
Constitution

Molecular formulae $C_{22}H_{26}N_2O_2$

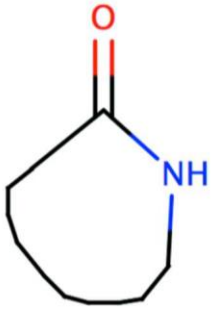
Keto



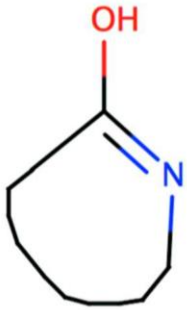

Enol



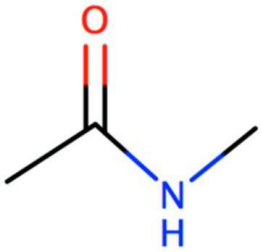

Lactam



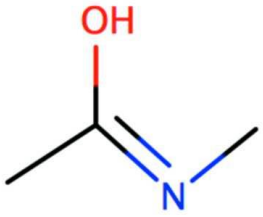

Lactim



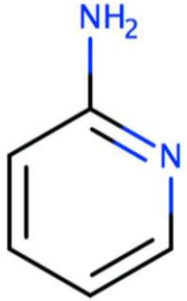

Amide



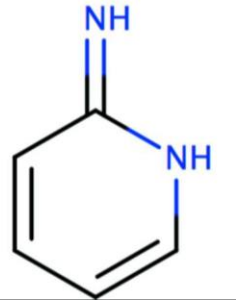

Imidic acid

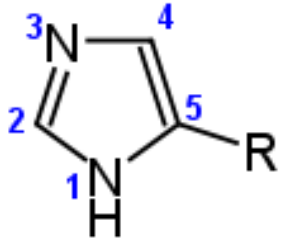



Amine

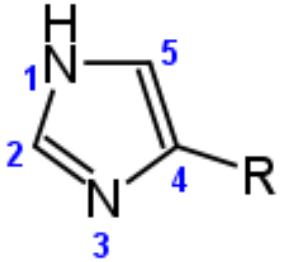



Imine

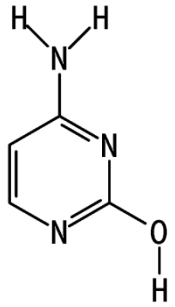


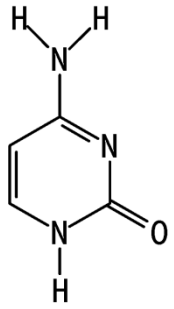



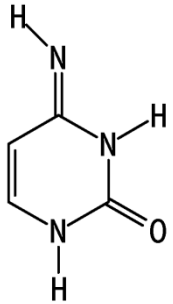

1H 5-metil imidazole



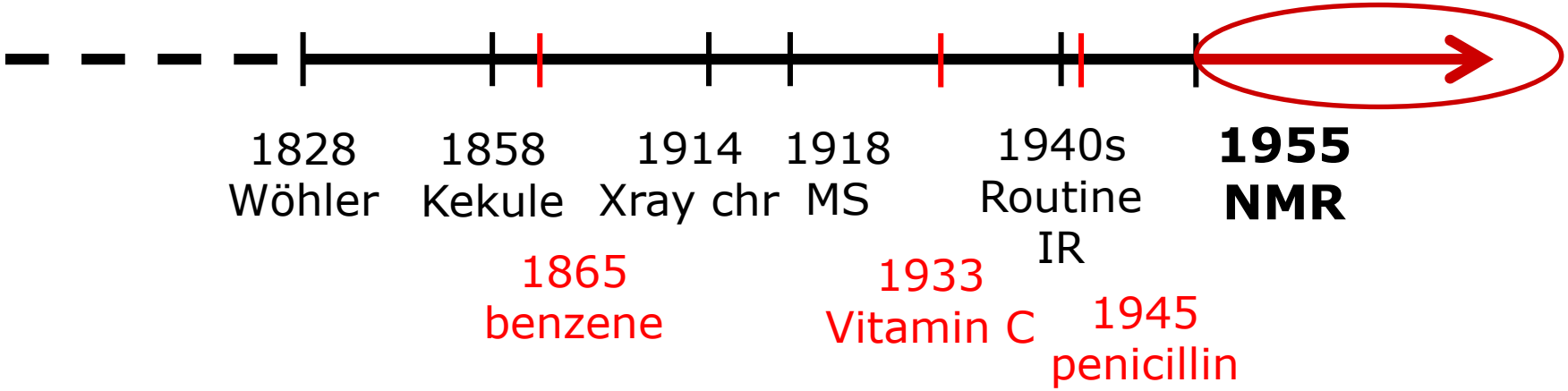

1H 4-metil imidazole



# Evolution of methods



# STRUCTURE

Intermolecular associations

Intramolecular bonds

Tautomerism

Conformational variability

} **NMR**, XRay

Configuration **NMR**, X-Ray Chrystallography, VCD

Constitution IR, MS, **NMR**

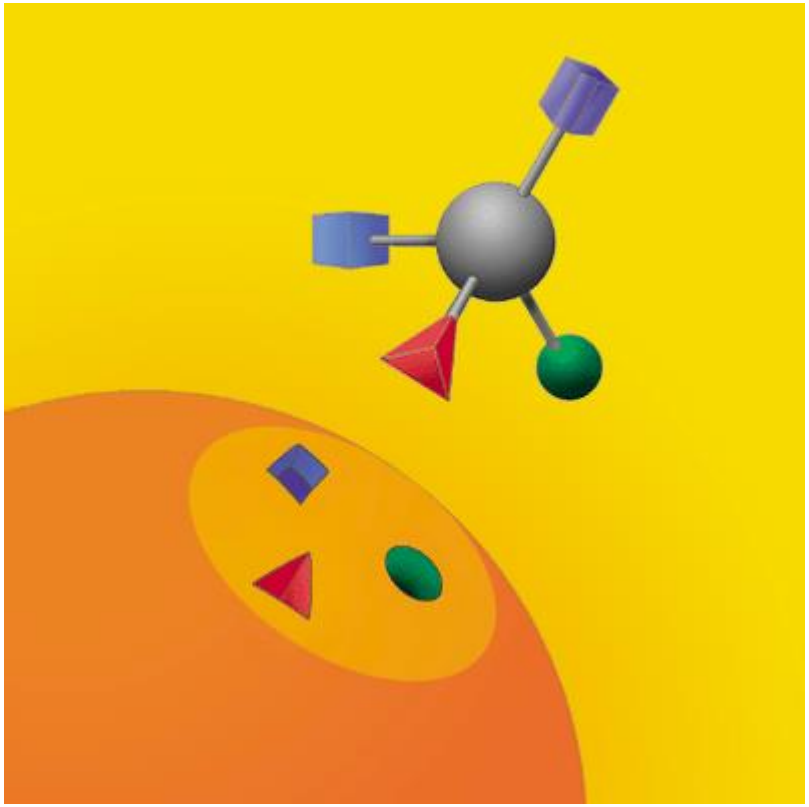
Molecular formulae ← M, Elemental composition

← **HRMS**

# WHY?

**To be able to understand their properties (physical, chemical, biological).**

**Structure / activity relationship**



# Elemental composition

We need the percentages of the different elements

Amount of gases measured

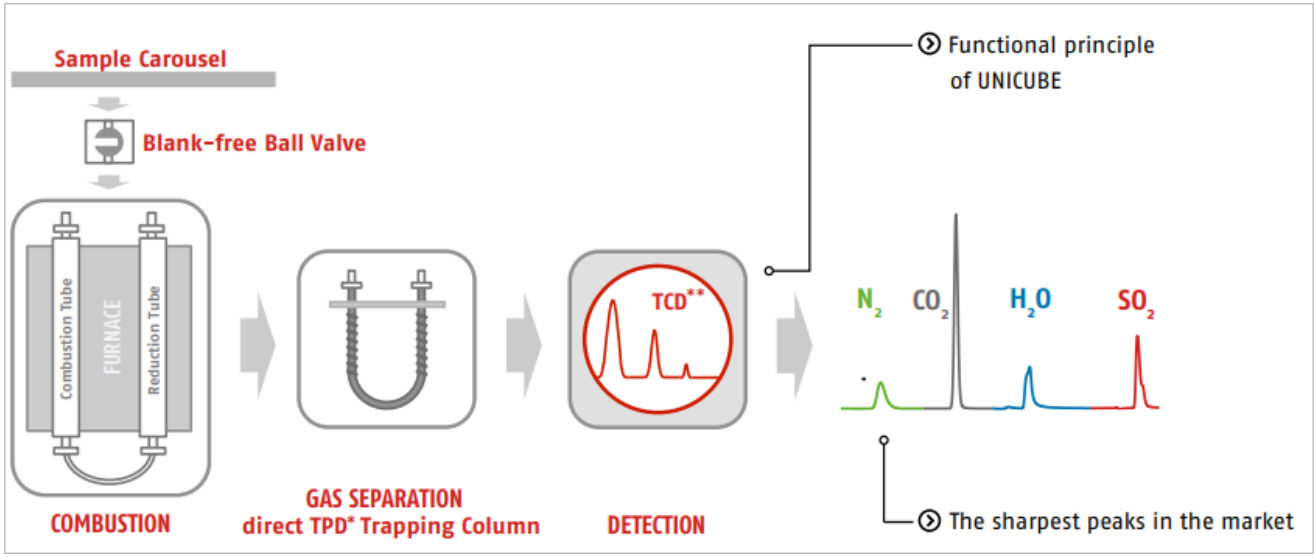

Weighting with high precision!!!

# Elemental composition

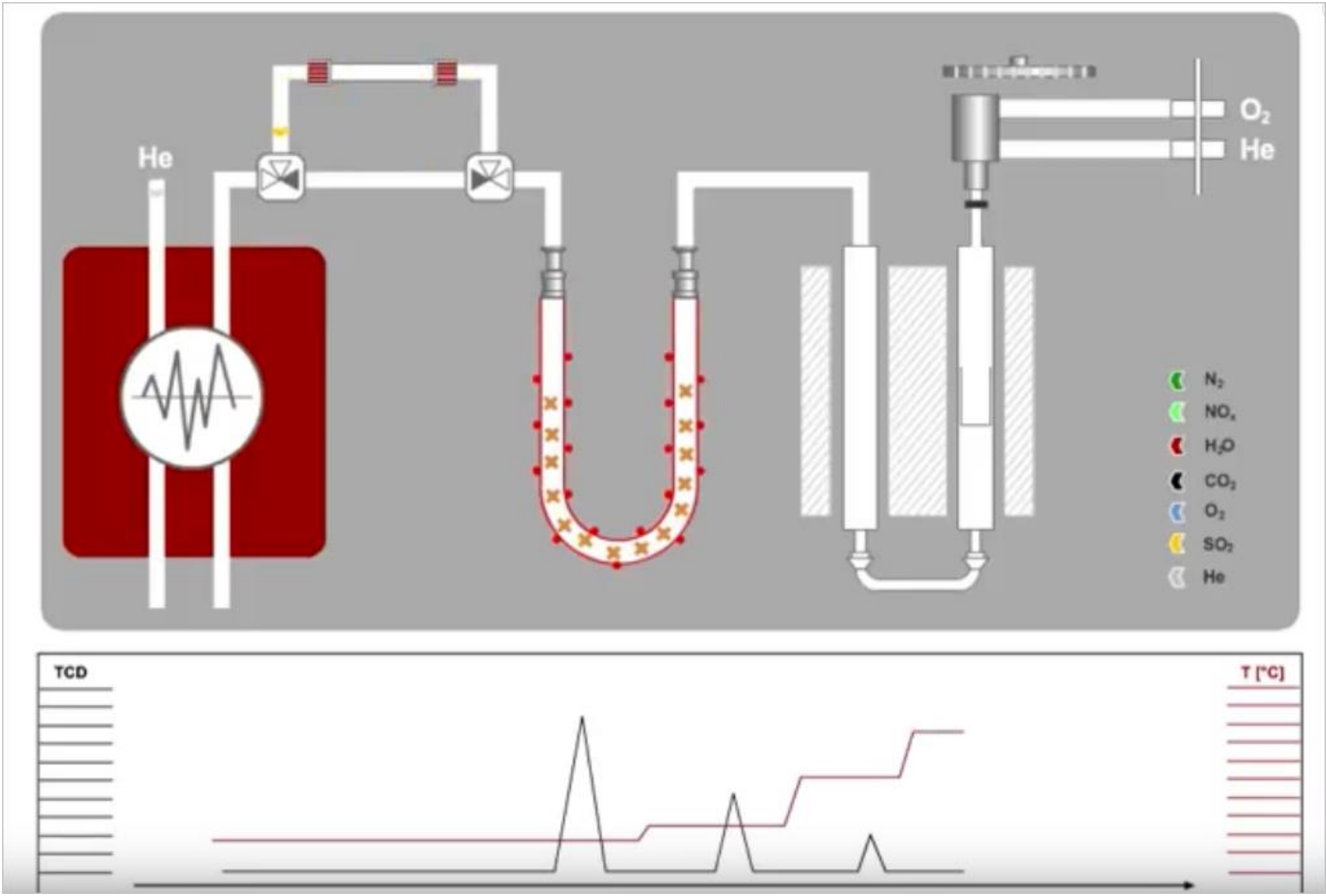
NO Universal technique!!!

**CHNS(O)**

Automated systems, designed specially for purpose


Simultaneous C, H, N, S determination is based on high-temperature (up to 1200°C) combustion of the sample in the oxygen stream. Gaseous products of combustion ($N_2$, $CO_2$, $H_2O$ a $SO_2$) are purified, separated and finally determined by TCD. Typical samples are organic chemicals but lot of inorganic matters can be  analyzed as well.




https://www.youtube.com/watch?v=jTSh5k4yQvo

## ***Oxygen:***

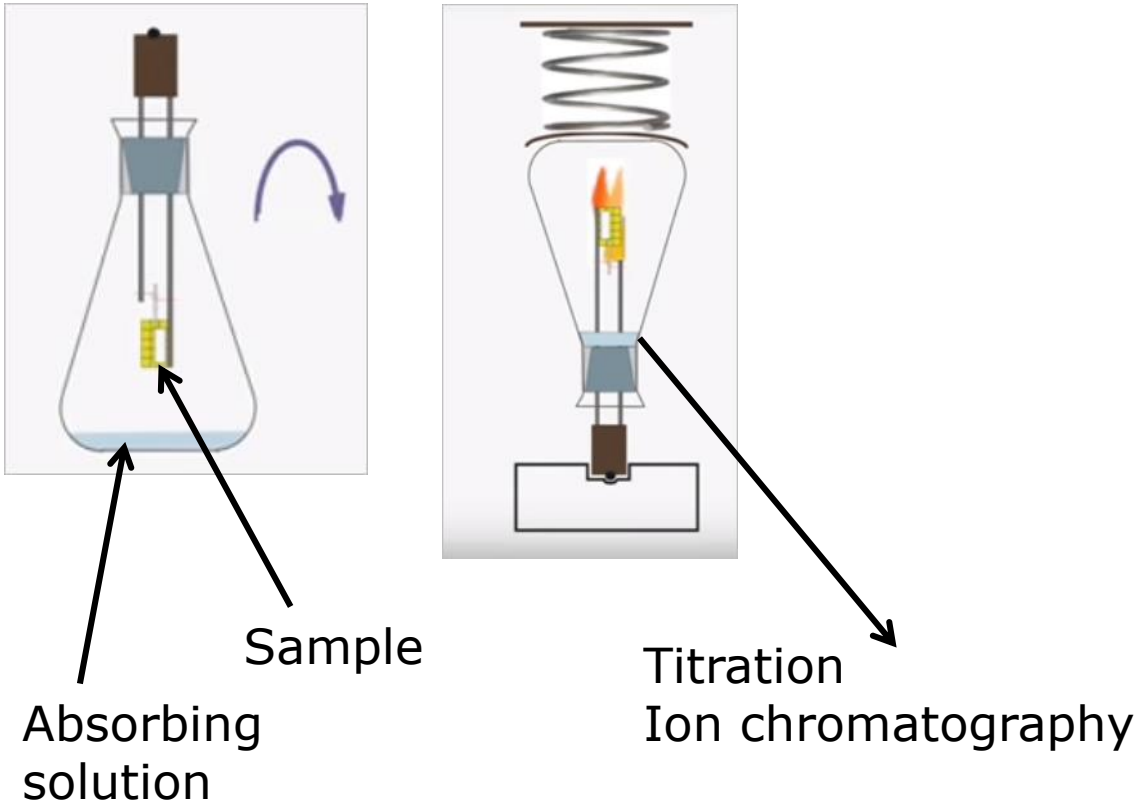
In most cases calculated: 100% – ∑other% = O%

The sample is pyrolysed in a pyrolysis tube operating at 1060°C. The resulting pyrolysed gases are carried over a catalyst (nickelised carbon granules) in the lower half of the combustion tube. This material ensures complete conversion of any oxygen gases into **CO**. A gas chromatography (GC) column separates and elutes the CO (Oxygen) which is quantified by a thermal conductivity detector (TCD).

# Elemental composition

## *Halogenes*

*Schoniger method:* The sample is combusted in a sealed oxygen flask or a hydropyrolysis combustion furnace. The combustion gases (HX) are absorbed in a known volume of absorption reagent.




# Elemental composition

What are the main drawbacks of the method?

Have to know the what elements are in the sample

Several measurements

Precision (0.3wt%)

The sample in whole!!!

**HRMS**

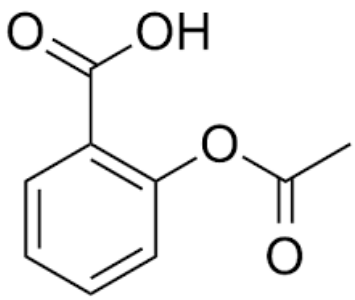
# DBE, **D**ouble **B**ond **E**quivalents

How many double bonds or rings are in the molecule?

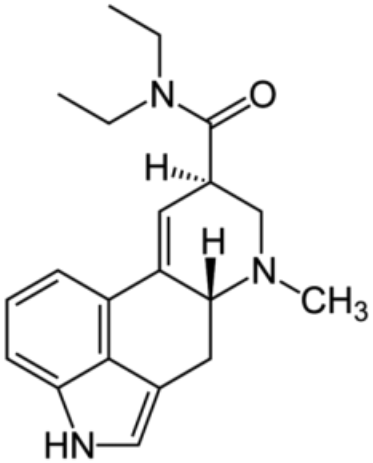
$C_aH(X)_bO(S)_cN(P)_d$

$$DBE = \frac{(2a + 2) - b + d}{2}$$

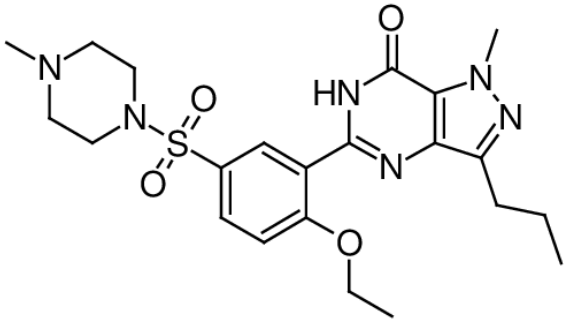
Cyclohexane 1
Benzene 4
Acetylsalicylic acid 6

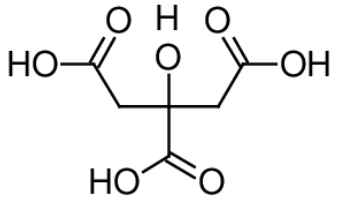



10



# Homework





Calculate sildenafil's (Viagra) M, elemental composition, DBE!
What kind of isomers can it have other than constitutional, draw one example!

M=1 449; C 54,7 %, H 5,22 %, Cl 4,89 %, N 8,7 %, O 26,5 %
Calculate the compound's molecular formula and DBE!