QFL1221 – Estrutura e Propriedades de Compostos Orgânicos

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Monitor: Guilherme Bumerad (guilherme.bumerad@usp.br)

Local: Bloco 7, Sala 767; Horários: 2ª 19:00 às 20:40h; 6ª 21:00 às 22:40 h.

Material: STOA-USP

QFL0137 – Química geral

Programa Resumido

Substâncias puras e misturas. Solubilidade. Estudo de soluções. Estequiometria e unidades de concentração. Tipos de reações químicas: ácidos-base, oxido-redução, complexação e precipitação.

Estrutura atômica. Configuração eletrônica dos elementos.

Propriedades periódicas.

Ligação química: iônica, covalente. Interações intermoleculares.

QFL1221 Programa Resumido

1. Contextualização acerca da importância histórica e atual da Química Orgânica.
2. Grupos Funcionais, Nomenclatura e representação de moléculas orgânicas.
3. Geometria de moléculas orgânicas.
4. Ligações Químicas Localizadas em moléculas orgânicas.
5. Ácidos e Bases em Química Orgânica.
6. Ligações Químicas Deslocalizadas em Moléculas Orgânicas (Ressonância, Tautomerismo, Aromaticidade e Anti-Aromaticidade).
7. Propriedades Físico-Químicas.
8. Espectroscopia e espectrometria de compostos orgânicos (UV, IV, RMN, EM).
9. Análise conformacional e estereoquímica.

Programa Resumido (QFL0342) Reatividades de compostos orgânicos

1. Considerações Gerais sobre Reações Orgânicas (Cinética vs. Termodinâmica, Intermediários Reativos em Química Orgânica, Reações Estereosseletivas e Estereospecíficas, Postulado de Hammond).

2. Reações de Adição Eletrofílica: adição eletrofílica de halogênios, HX e água em alcenos e alcinos, hidrogenação, hidroboração/oxidação, oximercuriação/desmercuriação, epoxidação, ozonôlise e di-hidroxilação.

3. Reações de Adição Nucleofílica: reatividade relativa de aldeídos e cetonas, adição de água, HCN, hidretos e carbânions a compostos carbonílicos.

4. Reações de Adição-Eliminação: reatividade relativa de ácidos carboxílicos e derivados, reação de compostos carbonílicos e carboxílicos com água, álcoois e aminas.

5. Reações de Substituição e de Eliminação: substituição nucleofílica alifática (SN1, SN2), eliminação 1,2 (E1, E2, E1CB) para formação de alcenos e alcinos.

6. Reações de Substituição Eletrofílica Aromática: mecanismo e aplicações da substituição eletrofílica aromática (SEAR); nitração, sulfonação, halogênio, alquilação e acilação, métodos sintéticos.

7. Reações Radicalares; reações de halogenação radicalar de alcanos; reações de adição radicalar a insaturações (adição radicalar de HBr a C=C, polimerização radicalar).

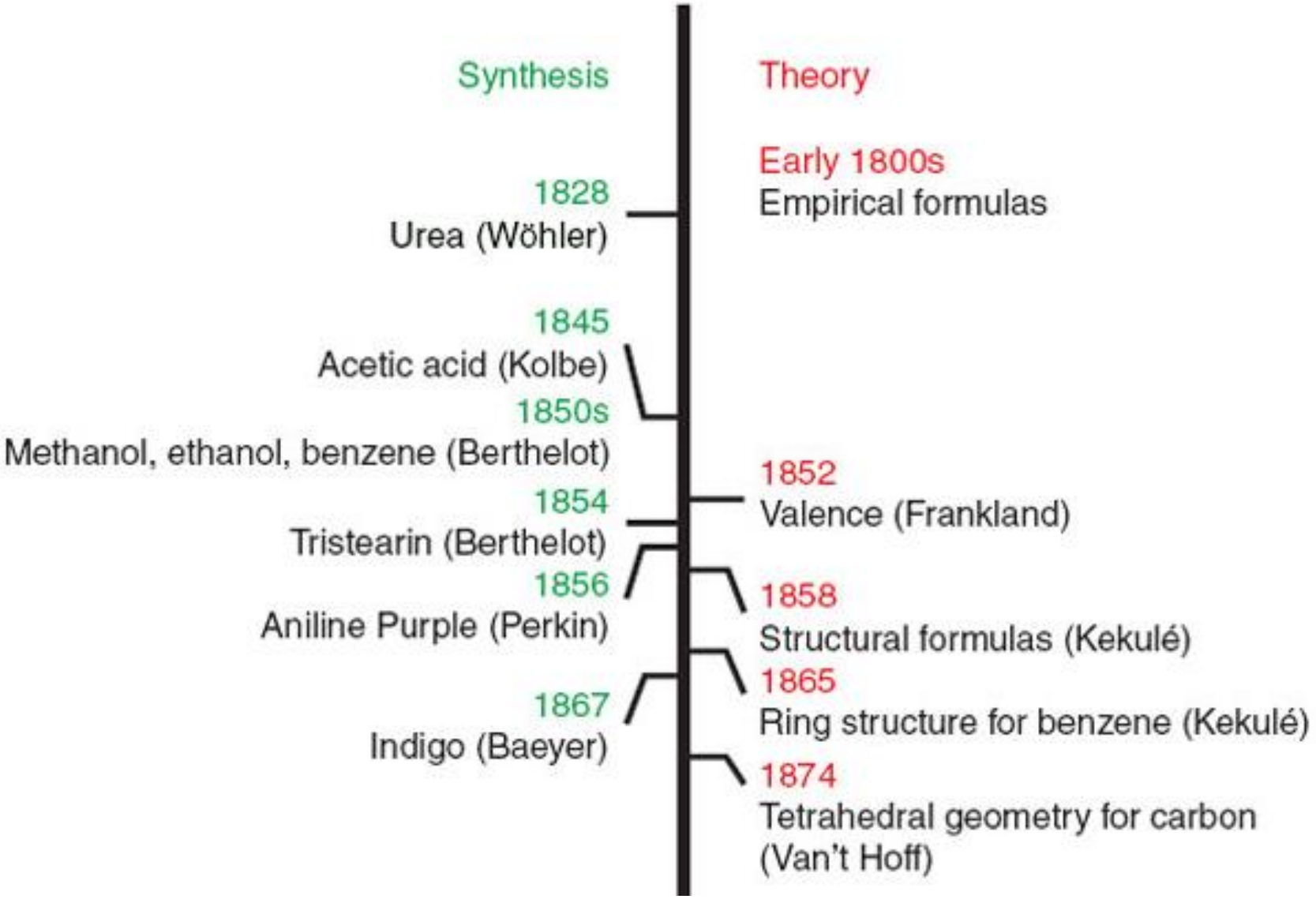
QFL1221 - Literatura

1) A. BURROWS, J. HOLMAN, A. PARSONS, G. PILLING, G. PRICE – Chemistry^3 - Introducing inorganic, organic and physical chemistry, 3rd ed Oxford, 2017.
2) P. Y. BRUICE - Organic Chemistry, Prentice Hall, 4ª ed., 2004.
3) J. McMURRY - Química Orgânica, Thomson, 6ª ed., 2005.
4) T. W. G. SOLOMONS, C. B. FRYHLE - Organic Chemistry, John Wiley & Sons, 8ª Ed., 2004.
5) K. PETER C. VOLLHARDT, NEIL E. SCHORE, W. H. FREEMAN, Organic Chemistry: Structure and Function, 5th edition, 2005.
6) J. CLAYDEN, S. WARREN, N. GREEVES, P. WOTHERS - Organic Chemistry, Oxford University Press, 2001.
7) Espectroscopia e espectrometria: Livros de química orgânica
8) R. M. SILVERSTEIN, G. C. BASSLER, T. C. MORRIL; “Spectrometric Identification of Organic Compounds”, 5a Ed., John Willey & Sons, 1991.
9) D. H. WILLIAMS, I. FLEMING, “Spectroscopic Methods in Organic Chemistry”, 4a Ed., McGraw-Hill, 1989.

Aula 01 (02/03/2020)

Apresentação da disciplina. Contextualização histórica e atual da Química Orgânica.
Ligações químicas e grupos funcionais. Nomenclatura e representação de moléculas orgânicas. Hidrocarbonetos (alcanos, alcenos e acetilenos) 1ª Lista de exercícios.

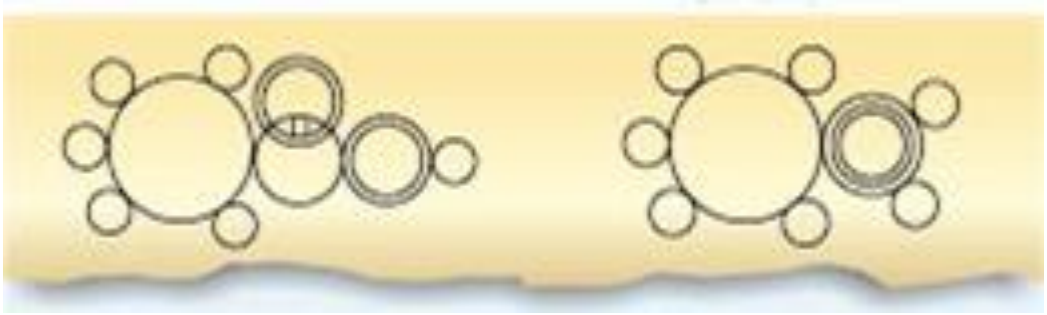
Desenvolvimento da química orgânica



As representações de compostos orgânicos não eram como conhecemos atualmente!

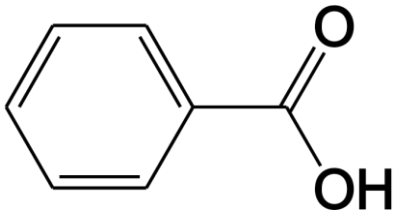
1824 - 1825 Isolated from burnt whale oil by Michael Faraday
1834 Eilhardt Mitscherlich finds benzene has formula of C_6H_6

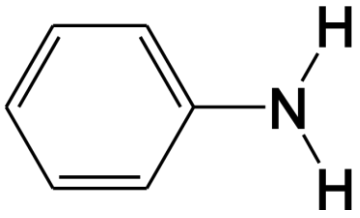
1861 Loschmidt proposes structure for benzoic acid and aniline



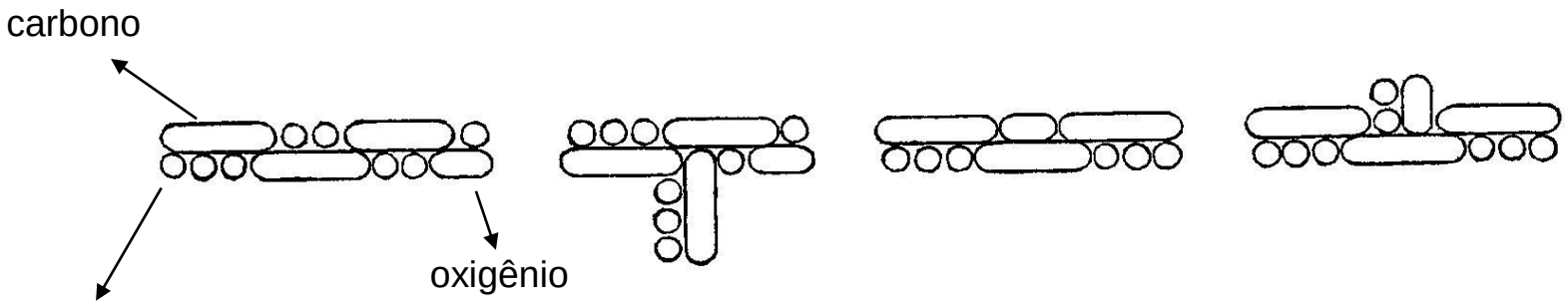
benzoic acid

aniline



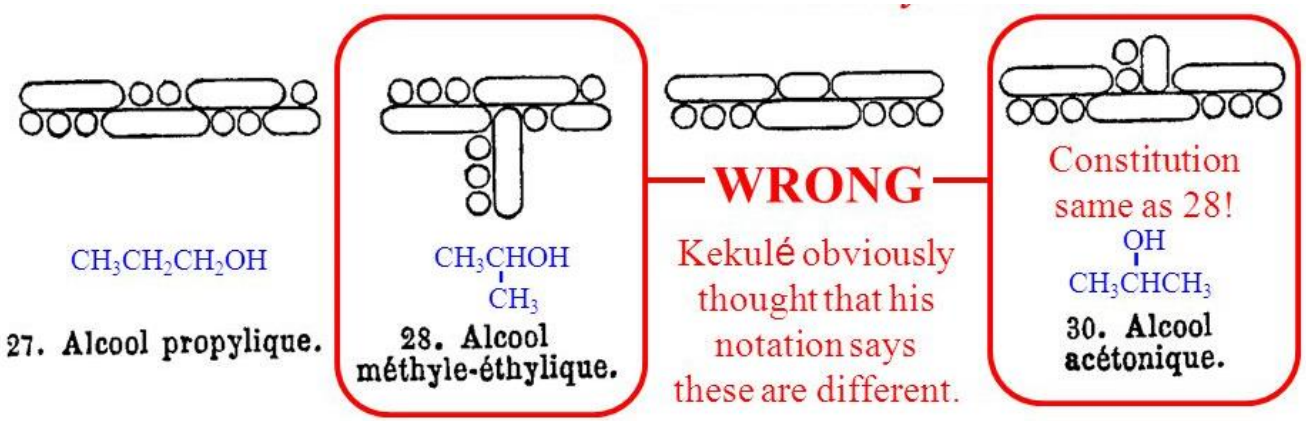


1865 Kekule invokes sausage (*salsichas*) diagrams

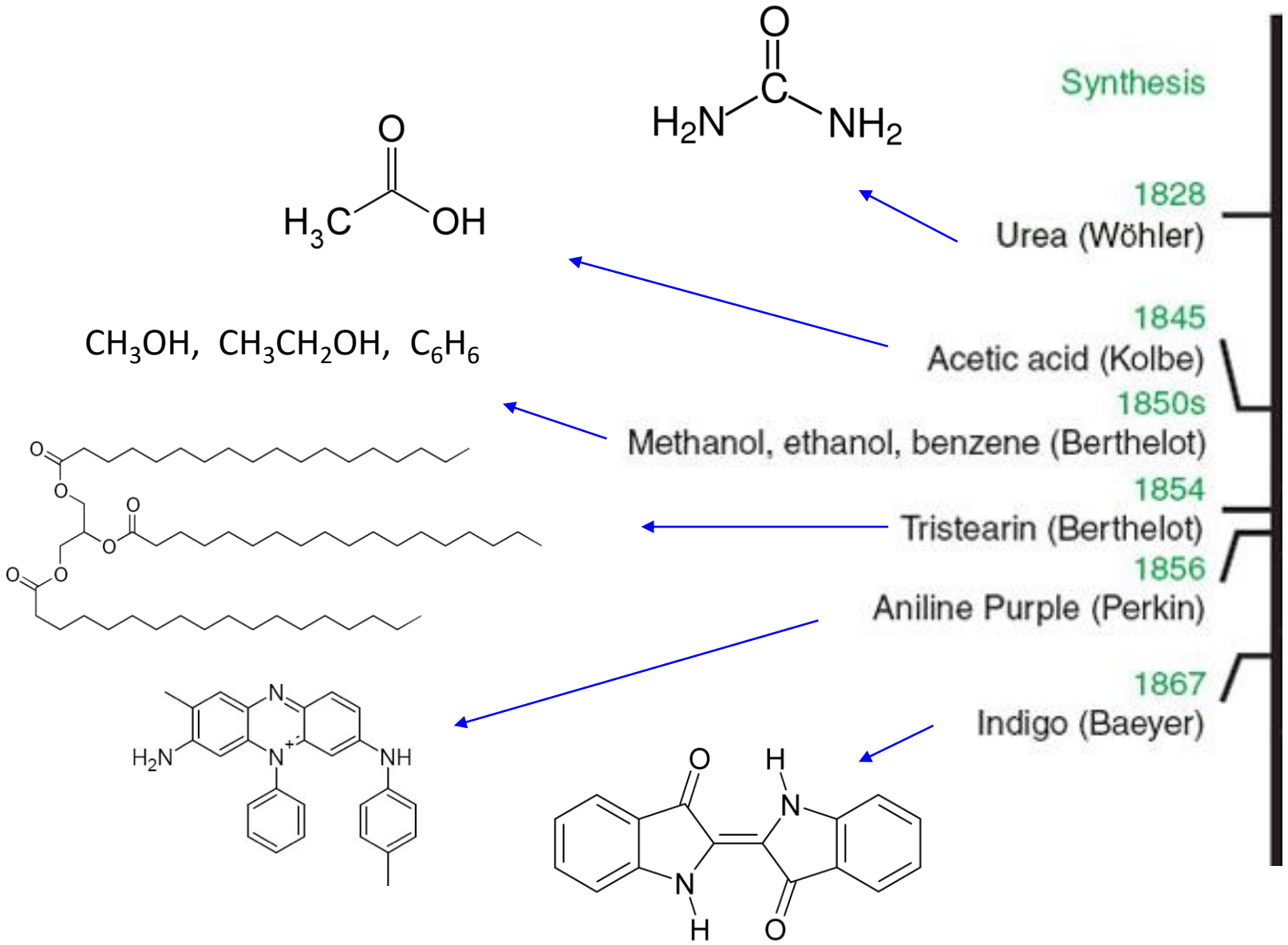


Quais substâncias são essas?

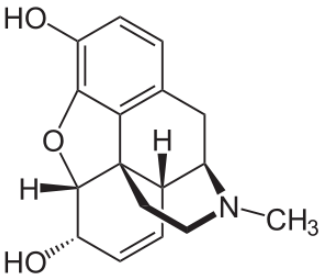
Alcool propylique. | 28. Alcool méthyle-éthylique. | Acétone. | 30. Alcool acétonique.



Desenvolvimento da química orgânica

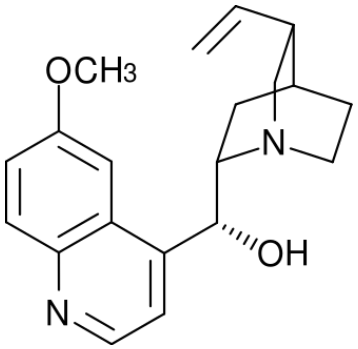


Early discovery of organic compounds was primarily motivated by bioactivity and their structural determination was mostly based on degradative reactions

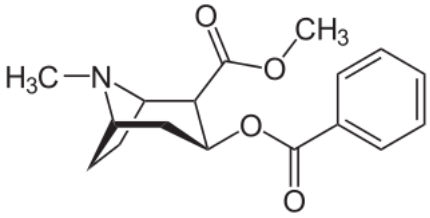


Morfina: Sertürner, 1805

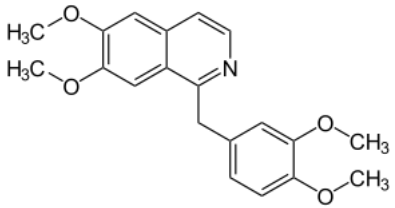
Papaver somniferum



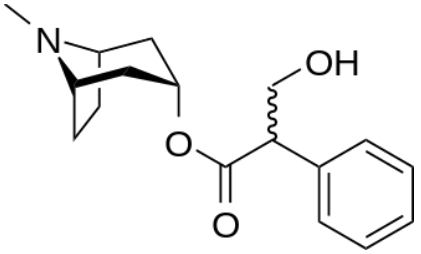
Quinina: Pelletier e Magendie, 1820



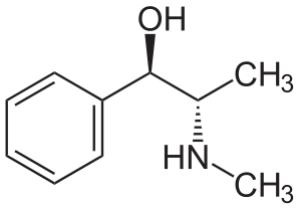
Cocaína: Wöhler, 1859.



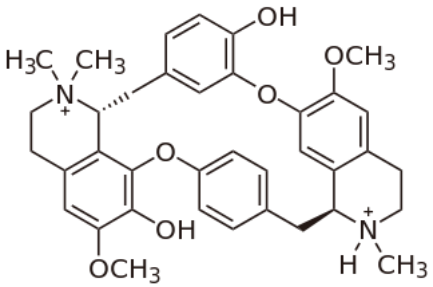
Papaverina: Merck, 1848.



Atropina: Mein, 1831.

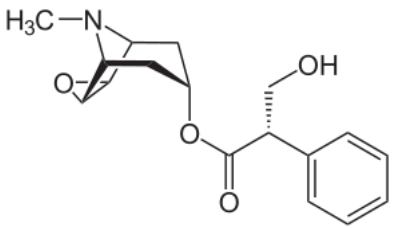


Efedrina: Nagai, 1885.



Tubocurarina: Boehm, 1895.

Chondrodendron tomentosum,



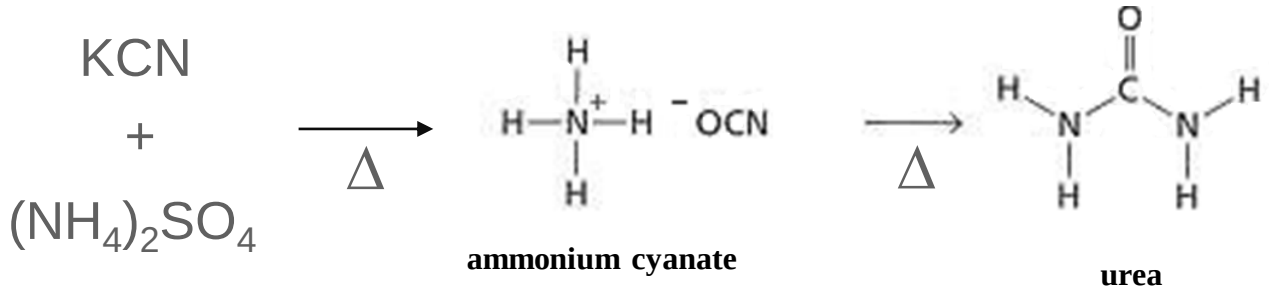
Escopolamina: Landenburg, 1881.

The death of vitalism and the birth of organic chemistry

1828: Friedrich Wohler

1823 Wöhler finished his study of medicine in Heidelberg and went to Sweden to study chemistry with **Berzelius** in Stockholm.

Friedrich Wöhler
(31 July 1800 – 23 September 1882)
Lithographie von Rudolf Hoffmann, 1856



First report of isomerism!

Wohler (at 27 years old) tried to obtain ammonium cyanate from potassium cyanide and ammonium sulfate

Berzelius and Wohler placed more emphasis upon the aspect of isomerism than upon the impact it might have on the vitalism theory.

Roberts, R.M. 1989 Serendipity – accidental discoveries in Science. John Wiley & Sons, Inc.

Milestones

Terpenes: Otto Wallach (Nobel Prize 1910) and later by Leopold Ružička (Nobel Prize 1939)

Dyes based on porphirins (including chlorophyll and heme), by Richard Willstätter (Nobel Prize 1915) and Hans Fischer (Nobel Prize 1930)

Steroids: Heinrich Otto Wieland (Nobel Prize 1927) and Adolf Windaus (Nobel Prize 1928)

Carotenoids: Paul Karrer (Nobel Prize 1937)

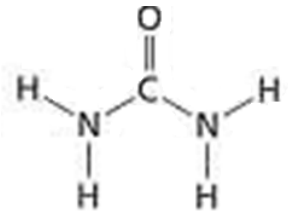
Vitamins: Paul Karrer, Adolf Windaus, Robert R. Williams, Norman Haworth (Nobel Prize 1937), Richard Kuhn and Albert Szent-Györgyi (Nobel Prize 1938)

Hormones: Adolf Butenandt (Nobel Prize 1939) and Edward Calvin Kendall (Nobel Prize 1950); introduction of oral contraceptive (1960)

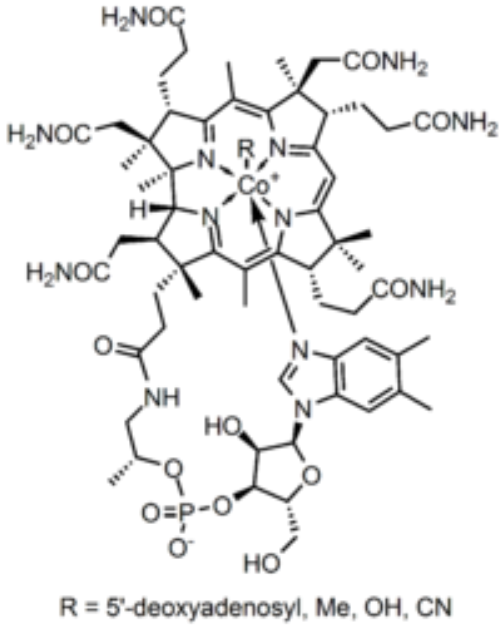
Alkaloids and anthocyanins: Robert Robinson (Nobel Prize 1947)

Artemisinin and avermectin: **Youyou Tu** and William Campbell - Satoshi Ōmura (Nobel Prize 2015)

Química Orgânica: química dos compostos de carbono...



ureia

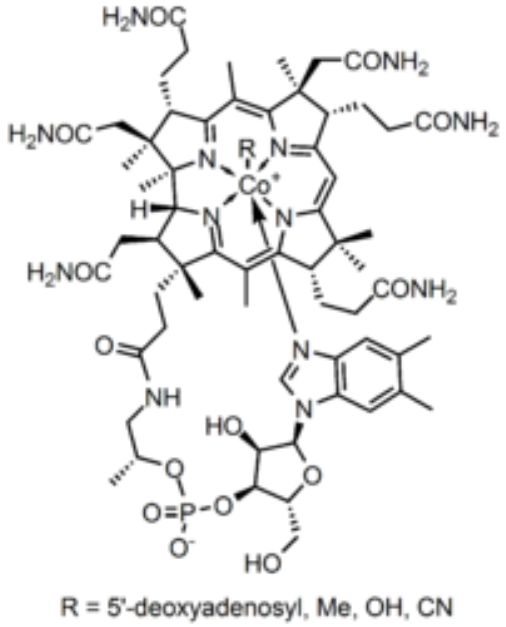


R = 5'-deoxyadenosyl, Me, OH, CN

Vitamina B12

Roberts, R.M. Serendipity – accidental discoveries in Science. John Wiley & Sons, Inc. 1989.

Synthesis of vitamin B-12



R = 5'-deoxyadenosyl, Me, OH, CN

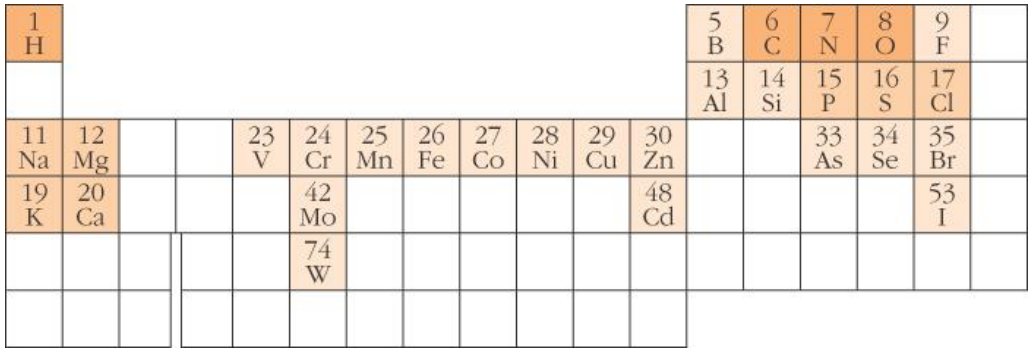
1972: Robert B. Woodward and Albert Eschenmoser

Synthesis of vit B12, a collaborative work at Harvard and Zurich by 100 chemists from 19 countries for 11 years!!!

Roberts, R.M. Serendipity – accidental discoveries in Science.
John Wiley & Sons, Inc. 1989.

Martin, W. (2006) Finding the final pieces of the vitamin B12 biosynthetic jigsaw
Proc Natl Acad Sci U S A.; 103(13): 4799–4800. doi: 10.1073/pnas.0601030103

Organic chemistry: Elements of Life and their Availability



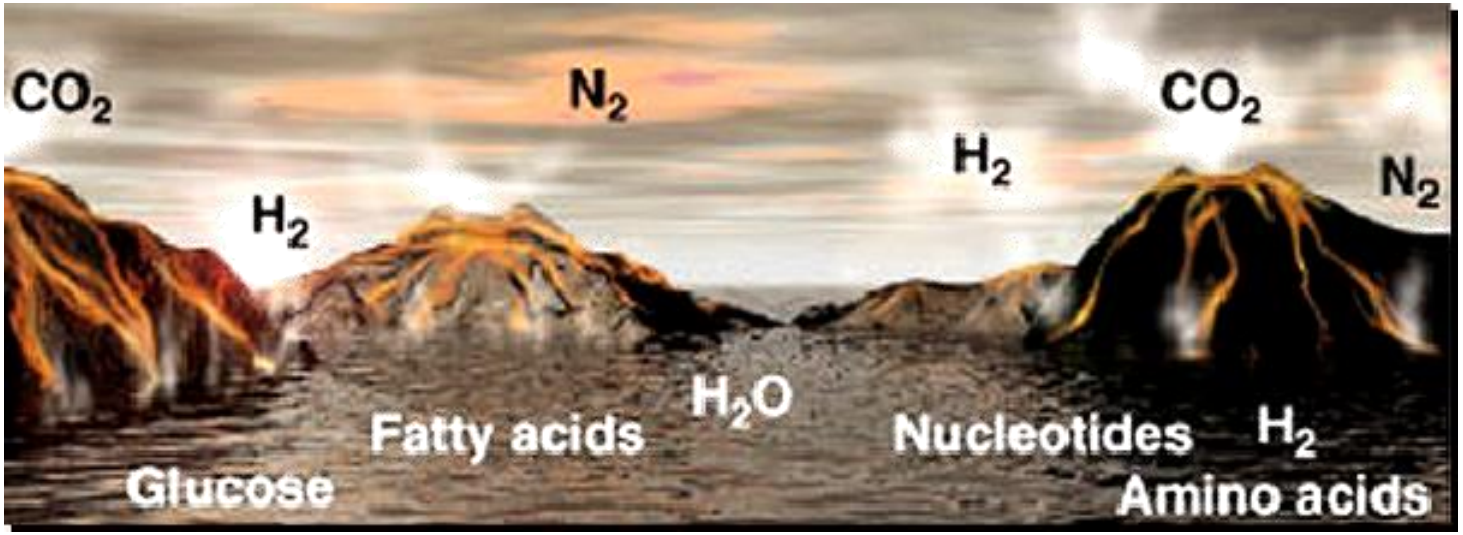
Element	Composition in Human beings (%)	Seawater (%)	Earth's crust (%)
Hydrogen	63	66	0.22
Oxygen	25.5	33	47
Carbon	9.5	0.0014	0.19
Nitrogen	1.4	<0.1	<0.1
Calcium	0.31	0.006	3.5
Phosphorus	0.22	<0.1	<0.1
Chloride	0.03	0.33	<0.1
Potassium	0.06	0.006	2.5
Sulfur	0.05	0.017	<0.1
Sodium	0.03	0.28	2.5
Magnesium	0.01	0.003	2.2
Silicon	<0.1	<0.1	28
Aluminum	<0.1	<0.1	7.9
Iron	<0.1	<0.1	4.5
Titanium	<0.1	<0.1	0.46
All others	<0.1	<0.1	<0.1

Origin of early organic molecules

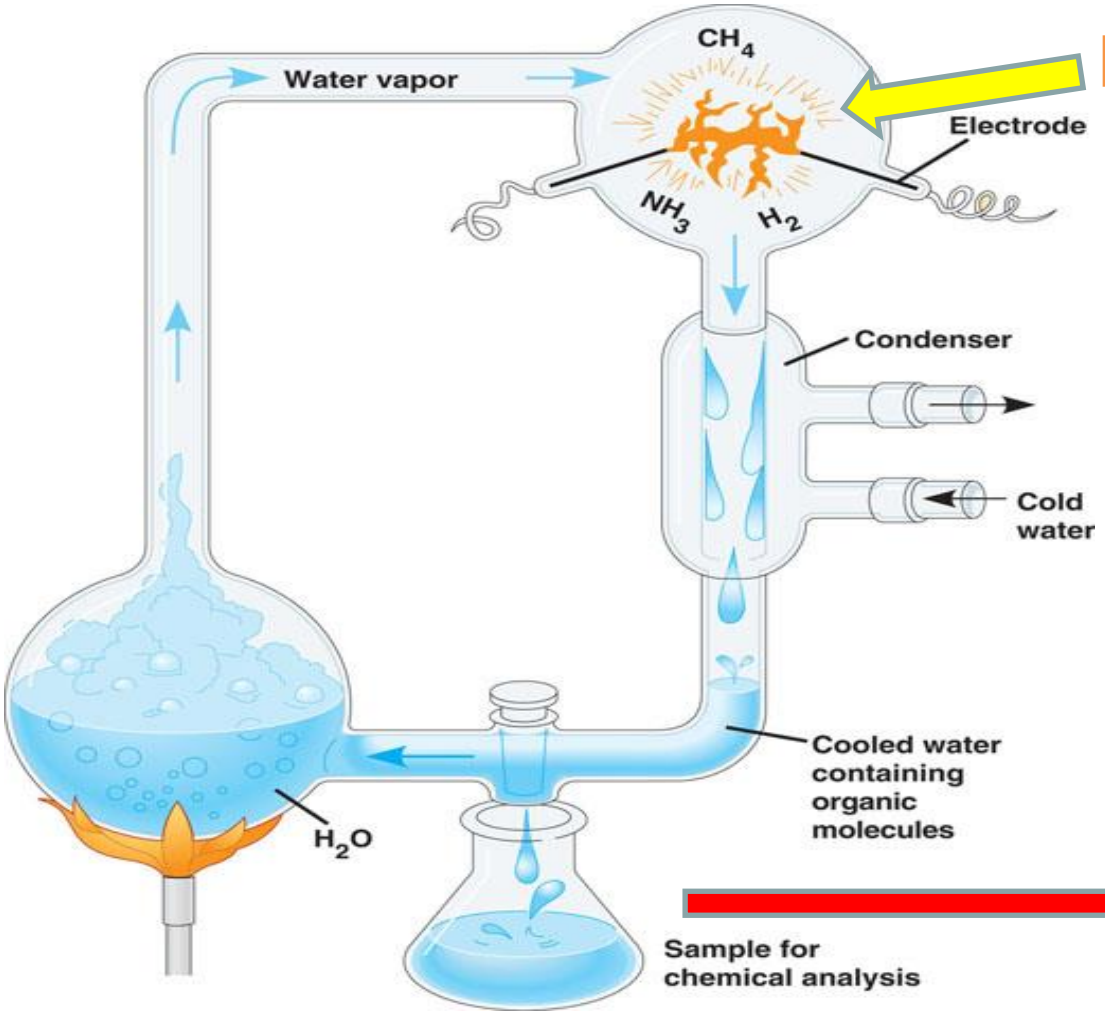
Life began~ 3.5 bya

Simple Organic molecules (C H O N P S) swimming in shallow seas

Stage 1: Abiotic synthesis of organic molecules such as proteins, amino acids and nucleotides



Miller and Urey's Experiment (1952)



ELECTRICITY!!!

Organic molecules like amino acids

Miller-Urey experiment - Work by the C3BC consortium, licensed under CC-BY-3.0.webm; Author: Courtney Harrington

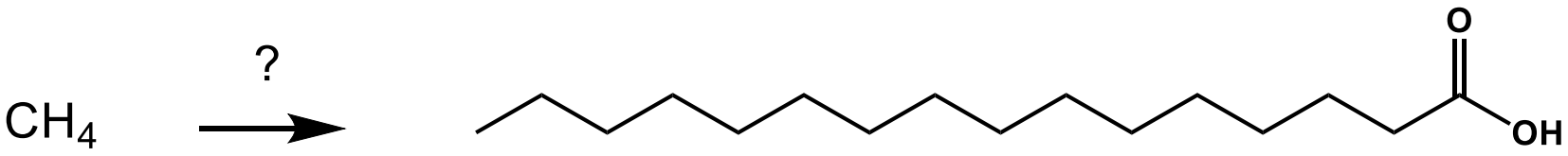
Miller, Stanley L. (1953). "Production of Amino Acids Under Possible Primitive Earth conditions". *Science* **117** (3046): 528–9

Miller and Urey's Experiment

Products:

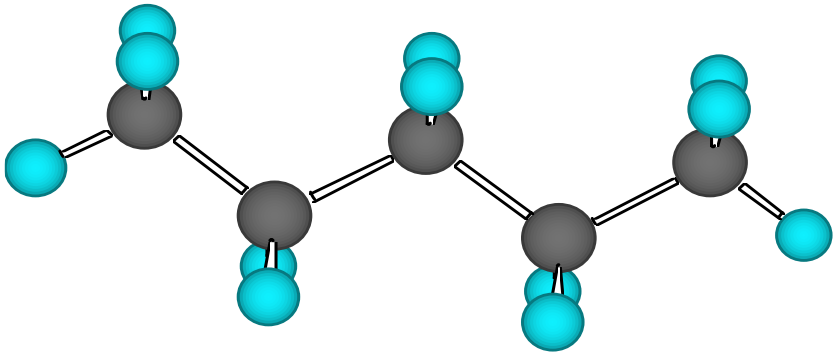
- Lipids
- 20 amino acids
- Several sugars
- Purine and pyrimidine bases (found in DNA, RNA & ATP)

Como tais moleculas orgânicas mais complexas poderiam ser formadas sob condições pré-bióticas?

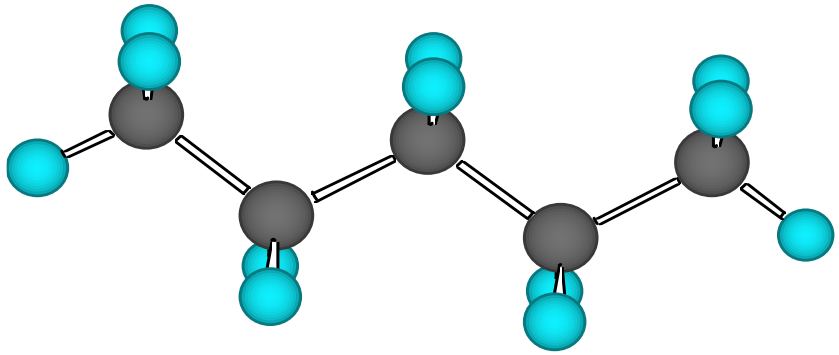


ácido láurico (C-16)
(Comum em lipídeos)

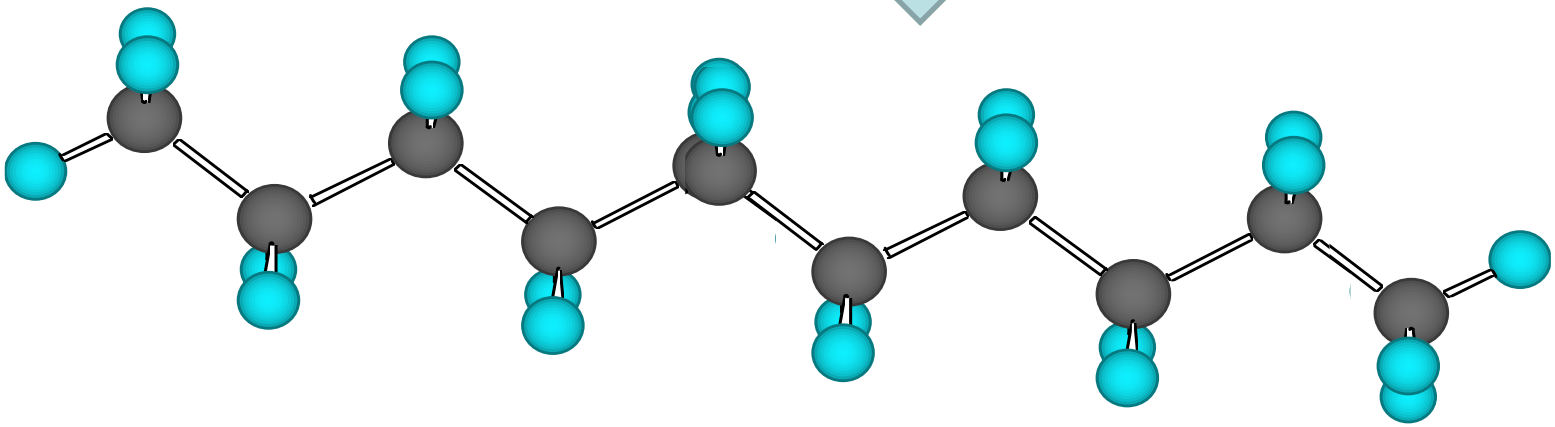
Como fazer a reação?



n-pentano



n-pentano

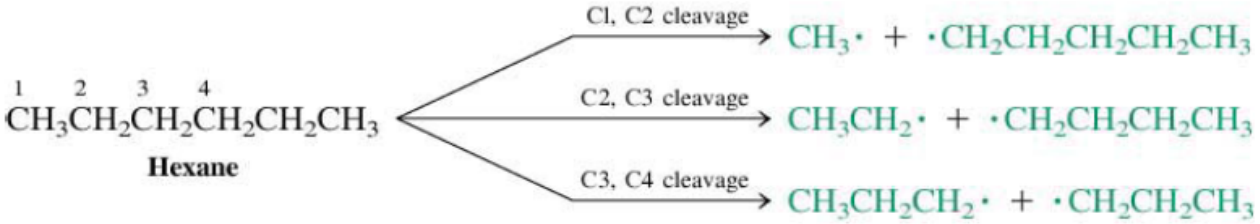


n-decano

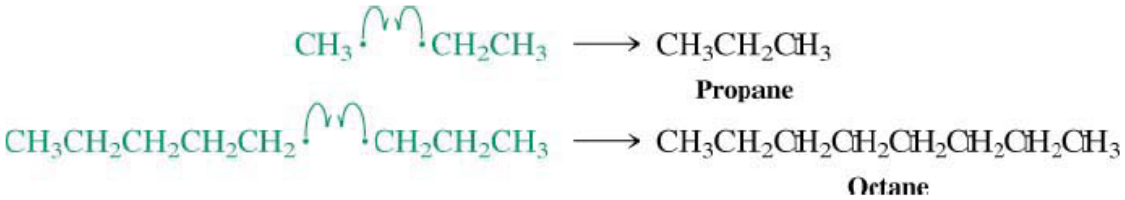
Conversion of Petroleum: Pyrolysis

High temperatures cause bond homolyis.

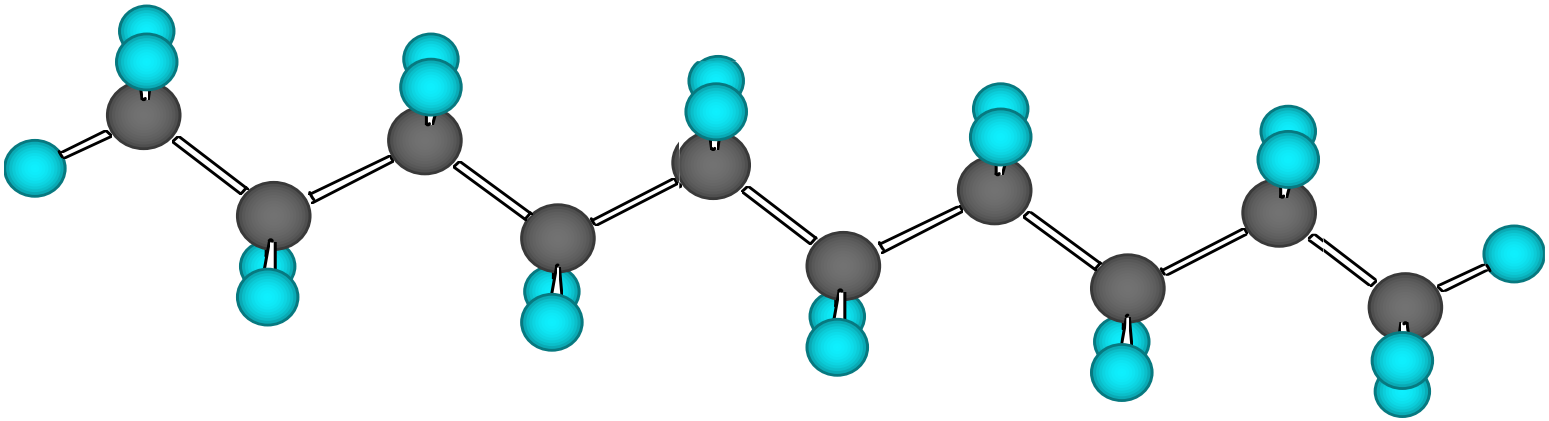
Both C-H and C-C bonds are ruptured at high temperature in a process called pyrolysis.



The resulting radicals can combine to form higher or lower molecular weight compounds, or form alkenes by further hydrogen extraction:



Craking de hidrocarbonetos



n-decano

zeolita
482 °C
2 min

17%

propano

+

31%

n-butano

+

23%

n-pentano

+

18%

n-hexano

+ **outros**

11%

Química orgânica e sua importância

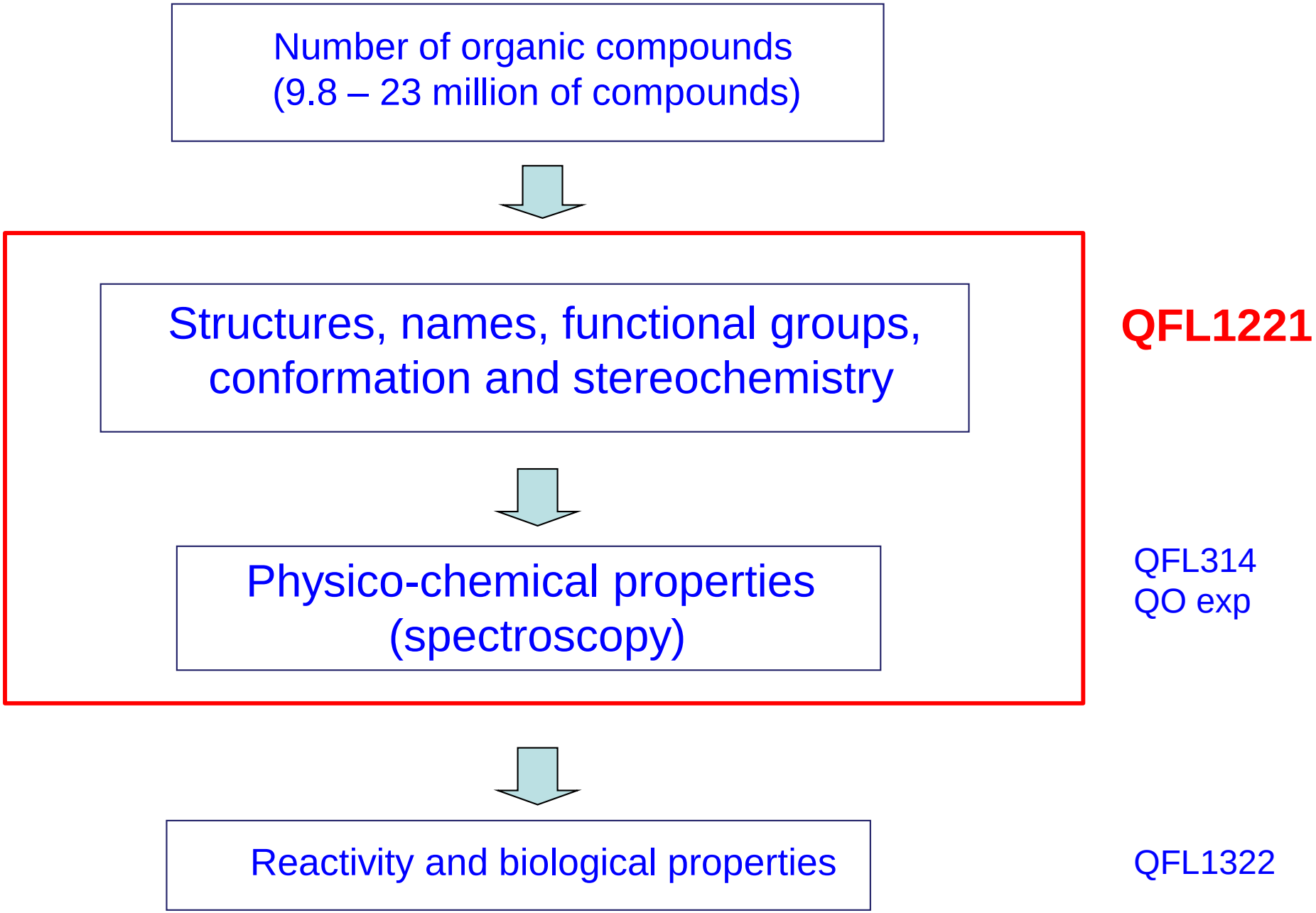
Número de compostos orgânicos (naturais: 10%; sintetizados: 90%)

Databases of compounds:

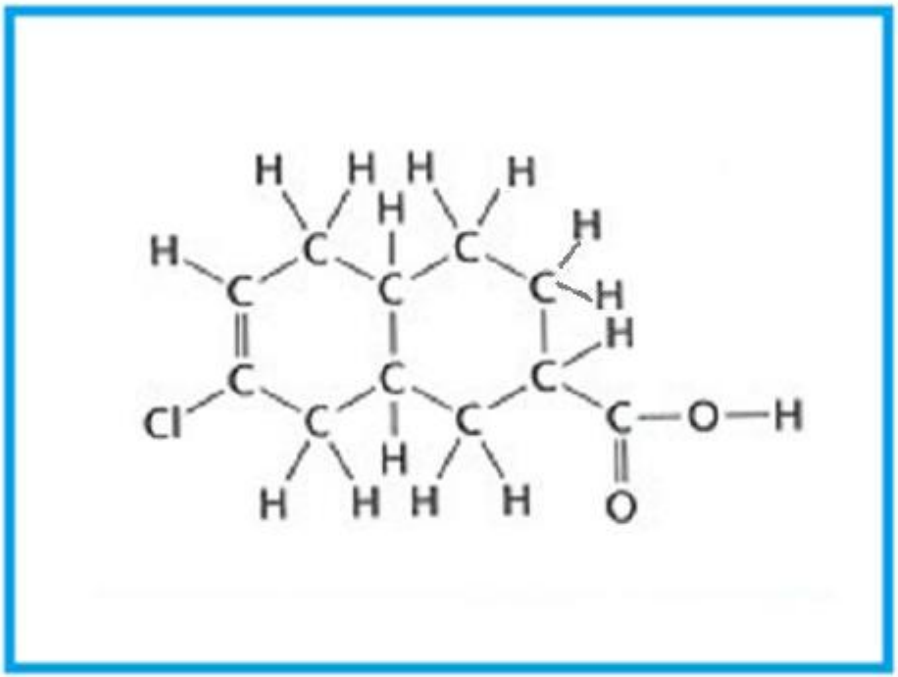
The CAS (Chemical Abstracts Service) database is the most comprehensive repository for data on organic compounds.
The search tool SciFinder: **23 million chemicals**.

The Beilstein database contains information on **9.8 million** substances, covers the scientific literature from 1771 to the present, and is today accessible via Reaxys.

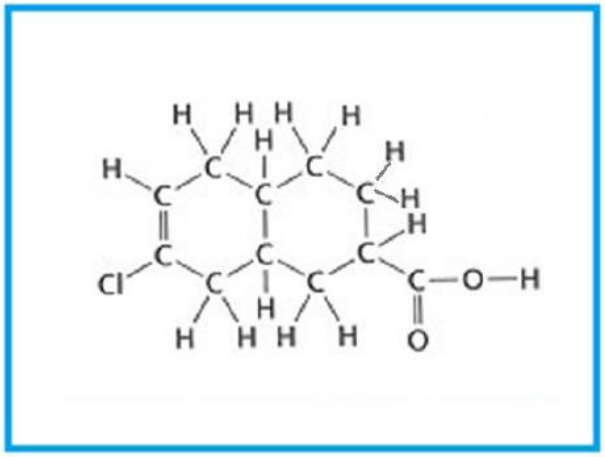
PubChem contains **18.4 million** entries on compounds and especially covers the field of medicinal chemistry.

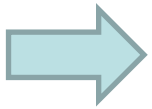

Number of organic compounds
(9.8 – 23 million of compounds)
Structures, names, functional groups, conformation and stereochemistry
QFL1221
Physico-chemical properties (spectroscopy)
QFL314
QO exp
Reactivity and biological properties
QFL1322

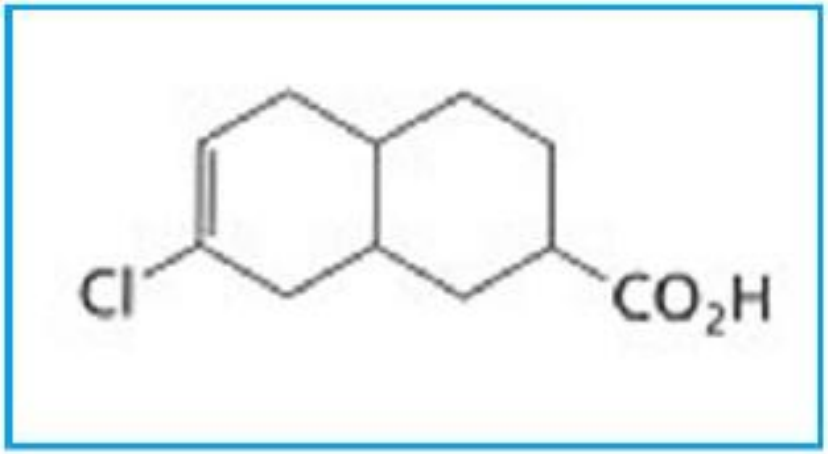
Linguagem química requer nomes e representação de compostos orgânicos



Representação de compostos orgânicos







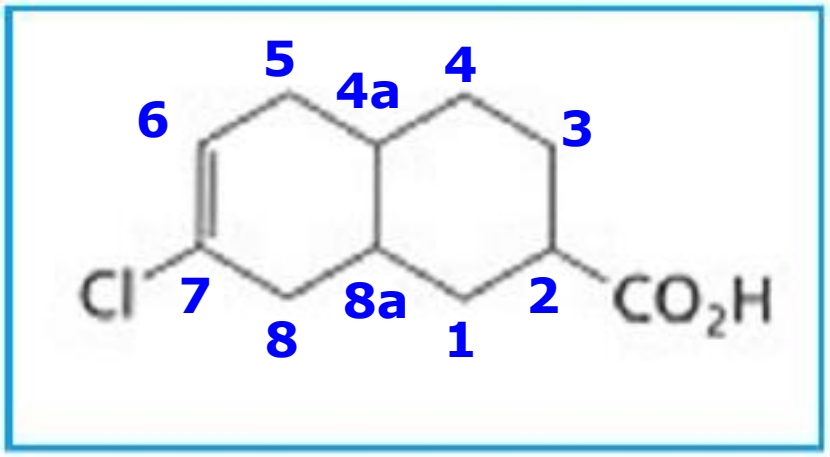
Mas ainda não está bem representada:

O que falta?

Quantos carbonos assimétricos temos aqui?

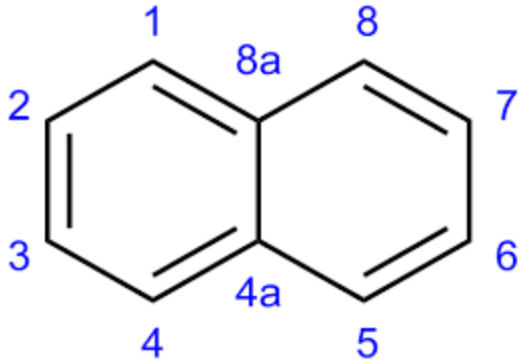
Quantos isômeros são possíveis?

Qual o nome desse composto?



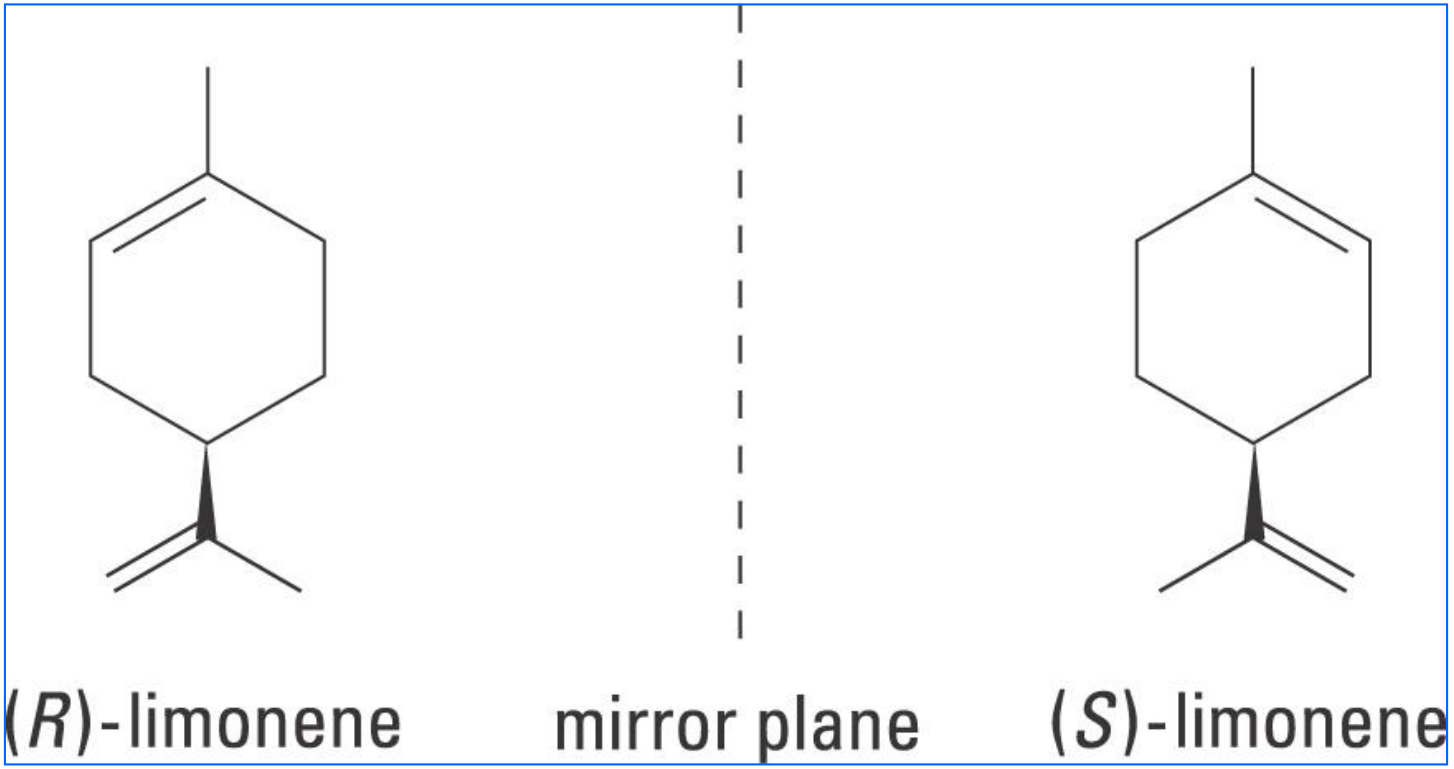
Ácido 7-cloro-1,2,3,4,4a,5,8,8a-octaidronaftaleno-2-carboxilico

Numeração de naftaleno:



Quatro ligações duplas hidrogenadas: octaidronaftaleno

Qual a importância da quiralidade?
diferentes propriedades biológicas



Odor de laranja

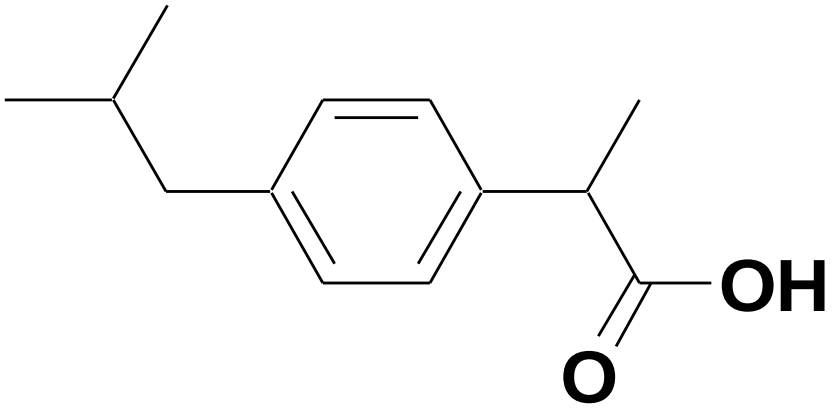
Odor de limão

Mistura de Enantiômeros como Fármacos

Ibuprofen (Advil, Motrin, Nuprin): vendido na forma racêmica

Isômero (*S*): anti-inflamatório, analgésico.

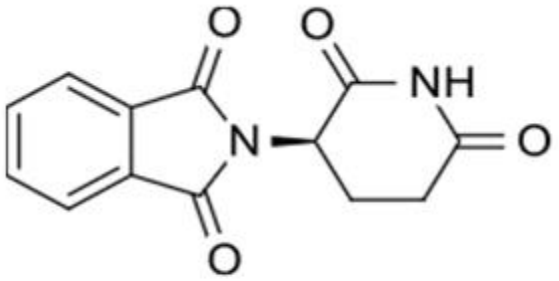
Isômero (*R*): não tem ação.



Ibuprofen

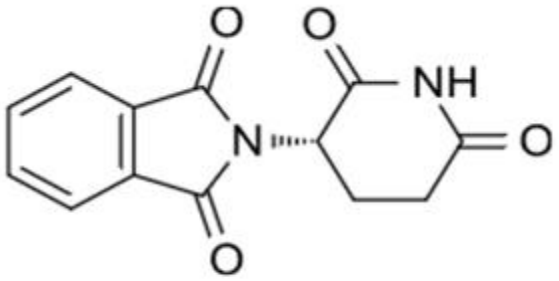
Mistura de Enantiômeros como Fármacos: desastres da humanidade

- ✓ Talidomida: A partir do final da década de 1950 foi usada na forma racêmica para aliviar a náusea matinal e insônia em mulheres grávidas.
- ✓ Resultado: cerca de 12.000 crianças com deformações congênitas!



(R)-thalidomide

anti-nausea and sedative drug

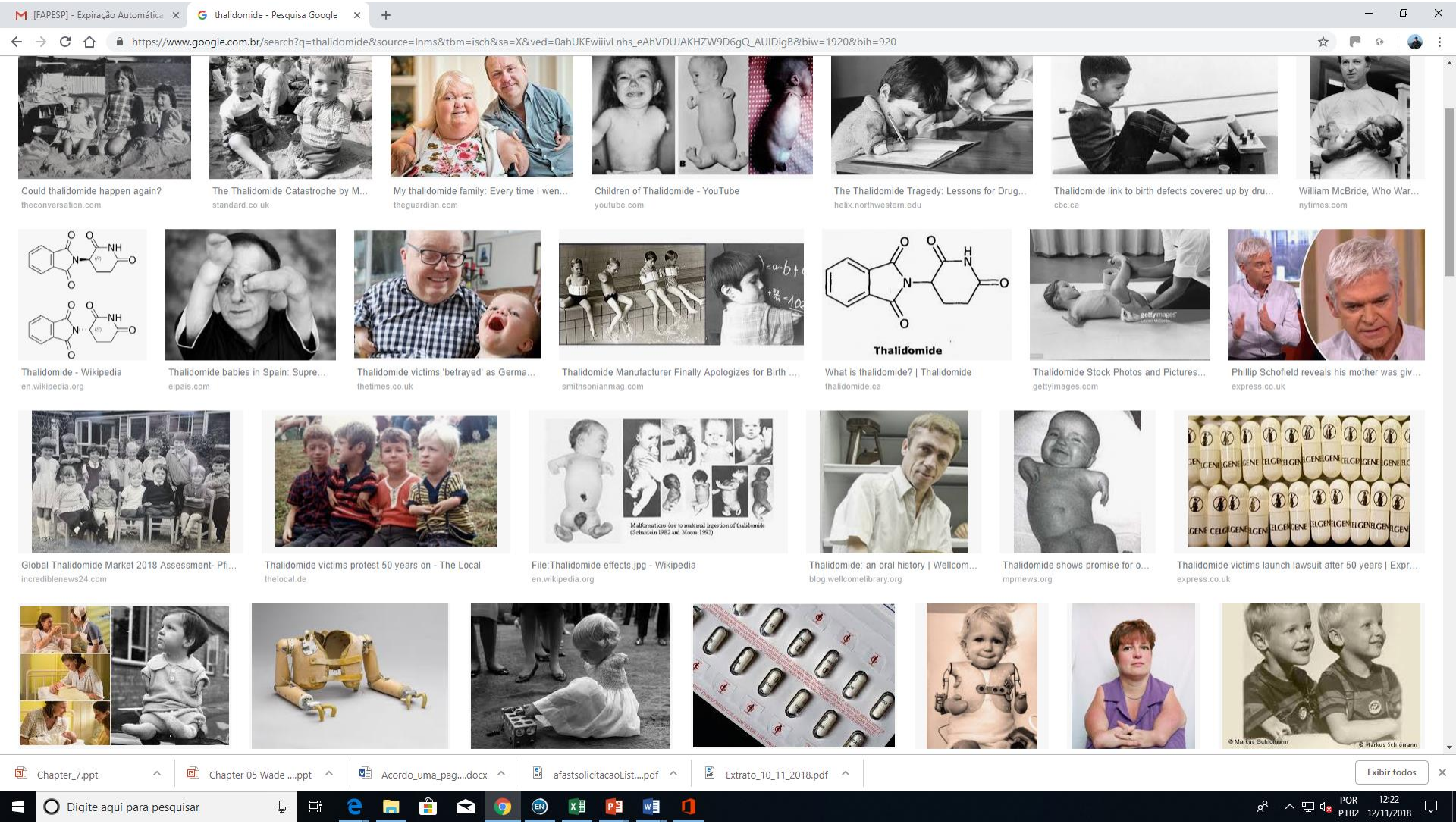


(S)-thalidomide

Teratogenic

- ✓ *Agente teratogênico* tudo aquilo capaz de produzir dano ao embrião ou feto durante a gravidez

Effect of (*S*)-thalidomide

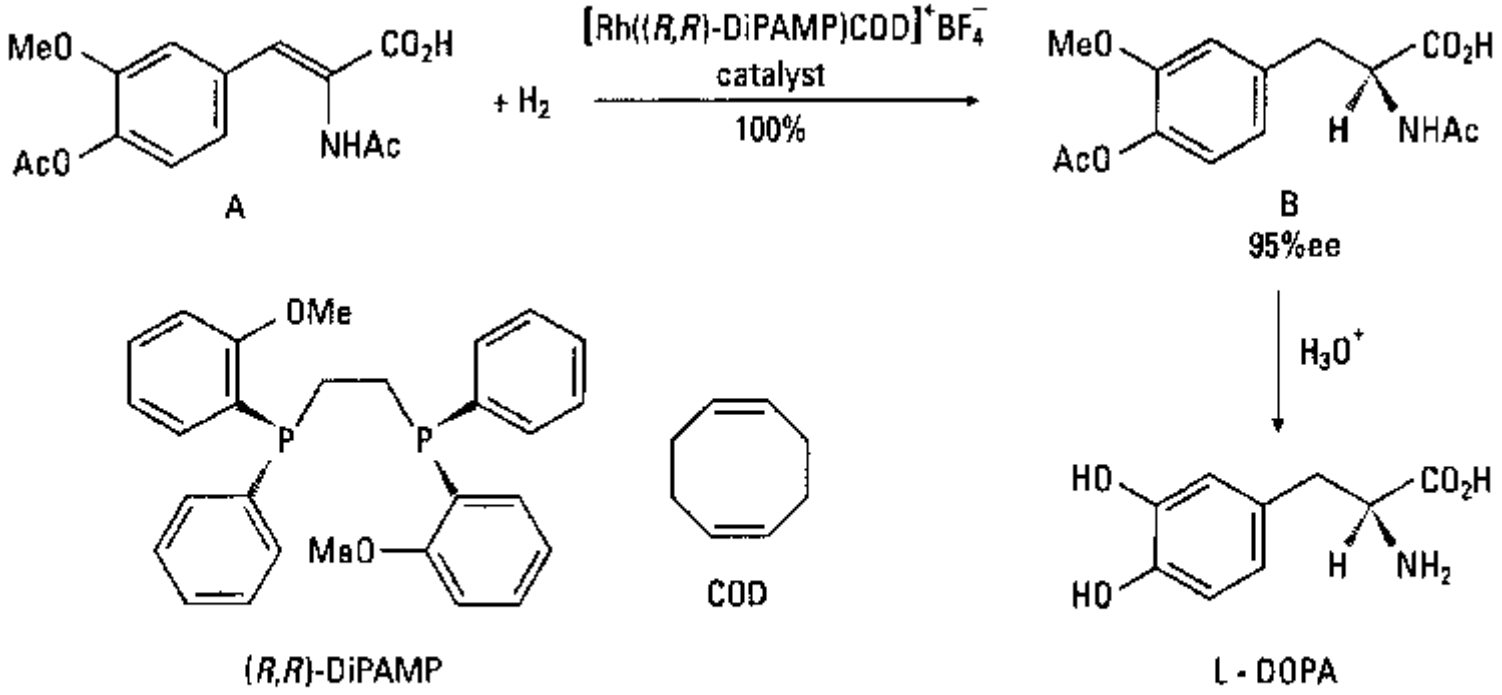


Prêmio Nobel de 2001:

William S. Knowles, Ryoji Noyori e K. Barry Sharpless

"Desenvolvimento de catalisadores quirais que permitiram a síntese de moléculas oticamente ativas."

Knowles (Monsanto): produção de L-DOPA via hidrogenação:



Usada no tratamento de Parkinson

http://nobelprize.org/

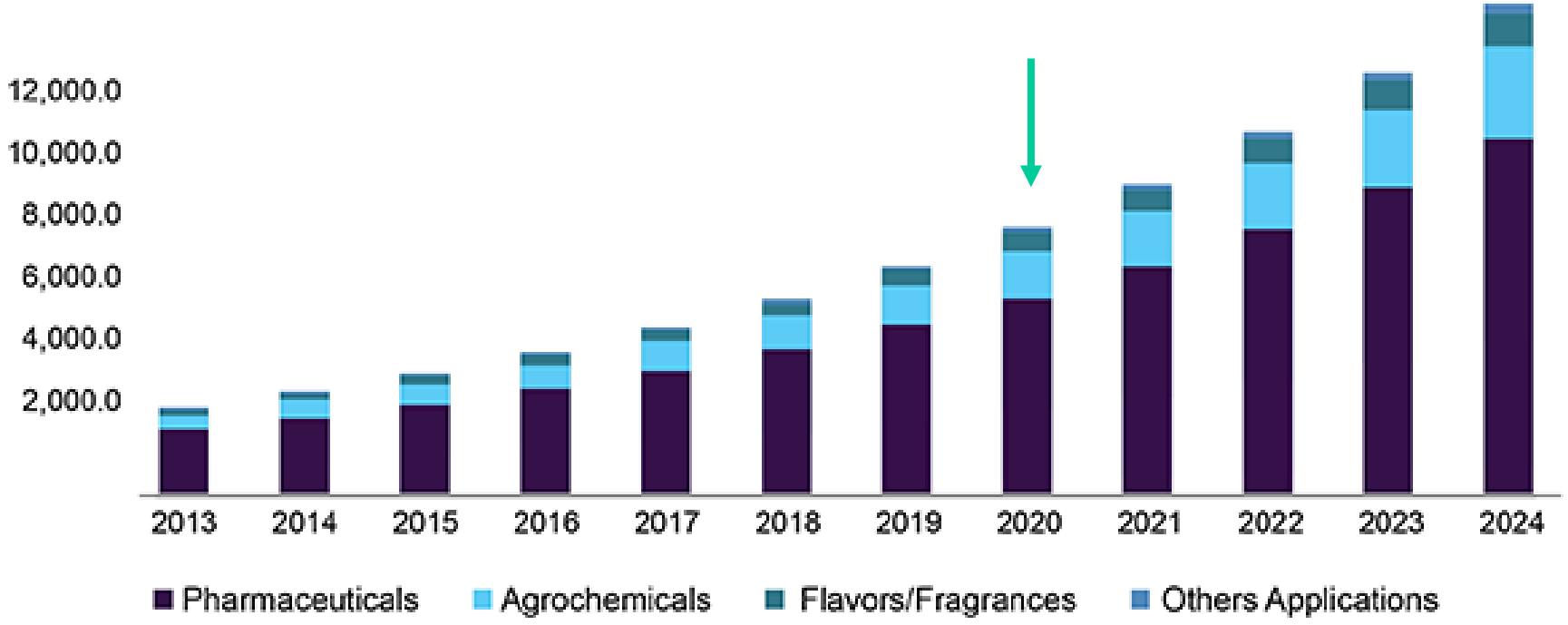
Mercado Global de Drogas
US$ Bilhões

Todas as drogas	
1999	2000
360	390

Drogas enantiomericamente puras		
1999	2000	2005
117	**132**	**171**

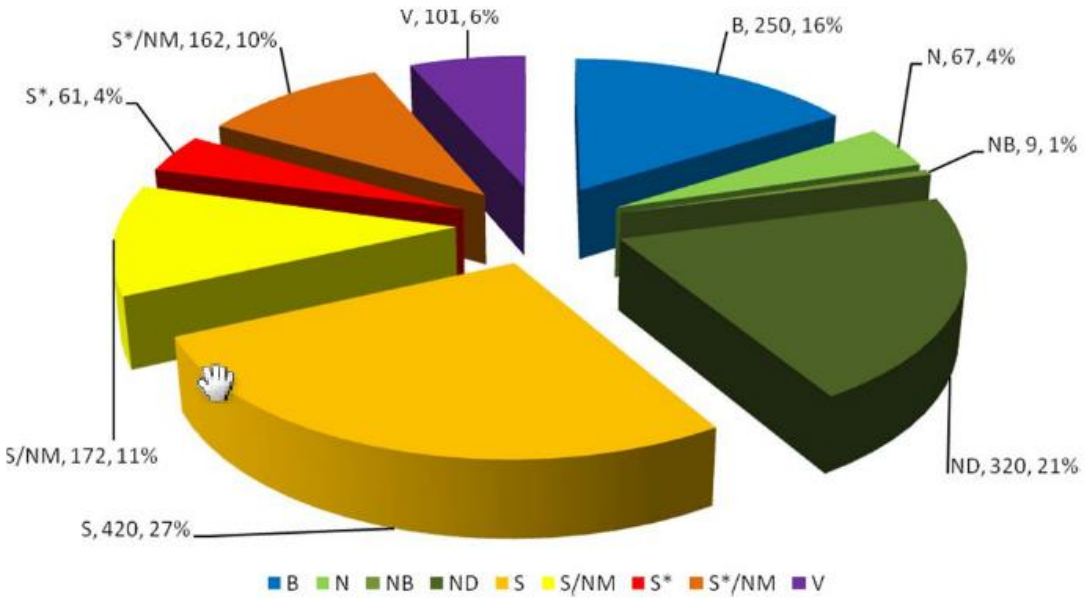
C & EN, 79, 40 (2001)

U.K. chiral chemicals market size, by application, 2013 - 2024 (USD Million)



Source: www.grandviewresearch.com

All new approved drugs 1981-2014, by source (*N* = 1562)



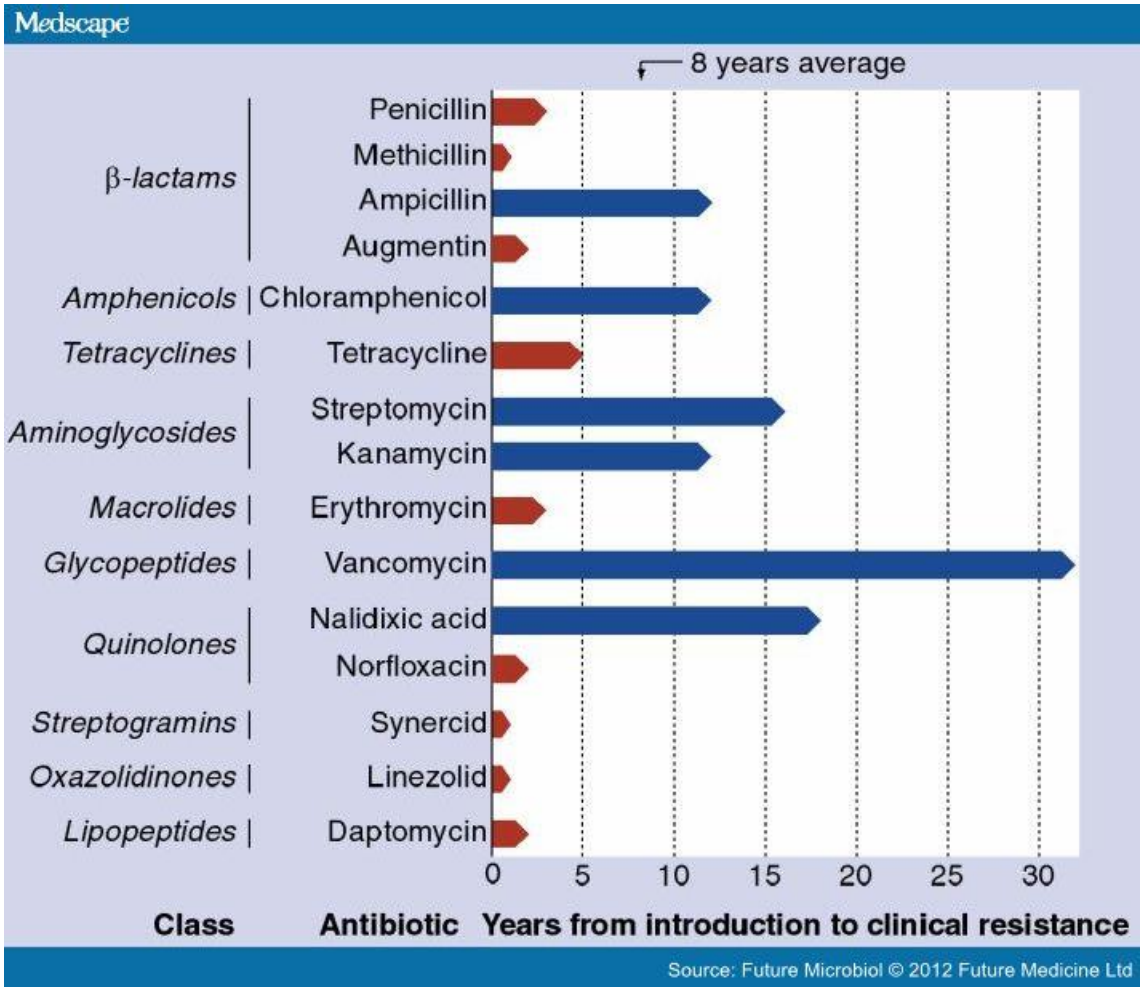
Totally synthetic drug

Derived from natural products

"B": Biological; usually a large (> 45 residues) peptide or protein either isolated from an organism/cell line or produced by biotechnological means in a surrogate host.
"N": Natural product.
"ND": Derived from a natural product and is usually a semisynthetic modification.
"S": Totally synthetic drug, often found by random screening/modification of an existing agent.
"S*": Made by total synthesis, but the pharmacophore is/was from a natural product.
"V": Vaccine.
"NM": Natural Product Mimic.

Newman and Cragg (2016) Natural Products as Sources of New Drugs from 1981 to 2014. J. Nat. Prod., 79 (3), pp 629–661.

Antibiotic resistance evolution showing the rapid development of resistance for several classes of antibiotics



Nosocomial (hospital-linked) infections result in approximately 100,000 deaths and cost more than US$25 billion per year in the USA alone.

Worldwide, it is estimated that 5–10% of patients entering hospitals develop an infection as a result of their stay.

Schmieder and Edwards (2012) Future Microbiol. 7(1):73-89.

Cenário mundial

- Explosão populacional (6.78 bi, 10.0 bi em 2035; um aumento de 45%);
- Devastação florestal e perda da biodiversidade;
- Aumento do consumo de combustíveis fósseis e aquecimento global;
- Novas moléstias ainda sem cura (SARS, gripe aviária, **coronavirus**, etc);
- Aumento da resistencia de microorganismos (MRSA, VRSA);
- Drogas do Norte vs. Sul (o novo Muro)

  [*entre os 1556 novos medicamentos aprovados nos últimos 30 anos pelo FDA, somente 1,3% (20) foram para doenças do terceiro mundo*]

Uses of natural products

perfumes

insecticides

aromas

drugs

toiletries

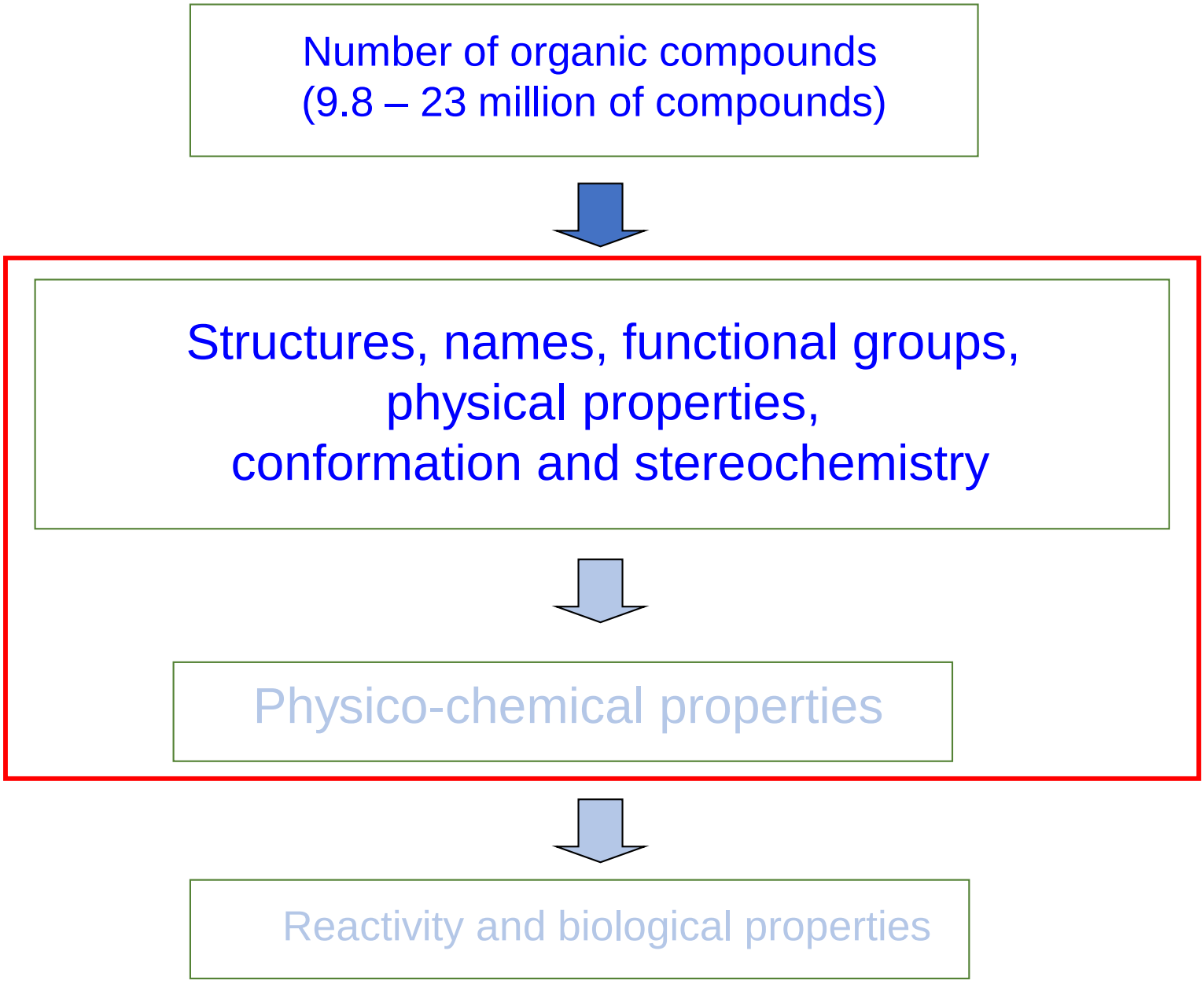
etc

Dewick, P. M. (2009) Medicinal Natural Products – A biosynthetic approach. John Wiley & Sons Ltd.

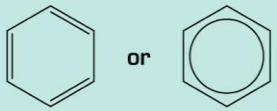
https://en.wikipedia.org/wiki/Natural_product

Dias DA et al. (2012) A Historical Overview of Natural Products in Drug Discovery. *Metabolites*. 2(2):303-336. doi:10.3390/metabo2020303.

Ser humano moderno e sua dependência por remédios


Number of organic compounds
(9.8 – 23 million of compounds)
Structures, names, functional groups,
physical properties,
conformation and stereochemistry
Physico-chemical properties
Reactivity and biological properties

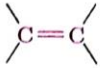
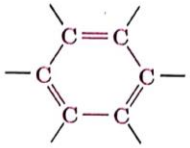
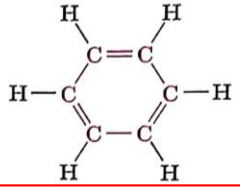
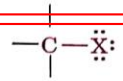
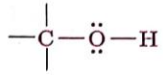
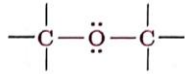
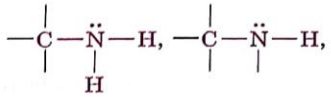
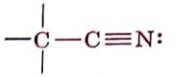
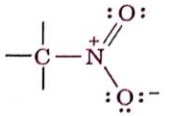
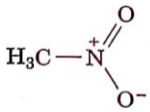
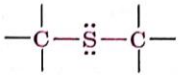
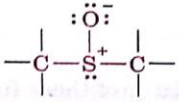
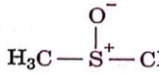
Hydrocarbons

Family	Key Feature	Class	Example	Name
Alkanes	Atoms joined by single bonds only	Saturated	$CH_3CH_2CH_3$	Propane
Alkenes	At least one carbon–carbon double bond	Unsaturated	$CH_2{=}CHCH_3$	Propene
Alkynes	At least one carbon–carbon triple bond	Unsaturated	$HC{\equiv}CCH_3$	Propyne
Aromatic compounds	Contains a ring of alternating single and double bonds	Unsaturated		Benzene

Localized bonds

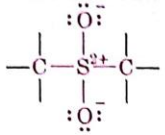
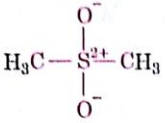
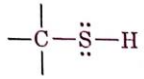
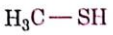
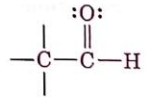
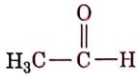
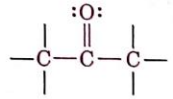
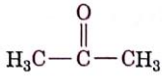
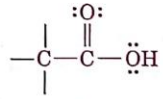
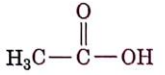
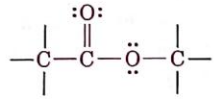
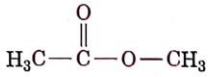
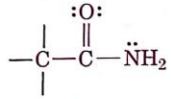
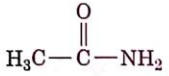
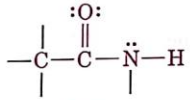
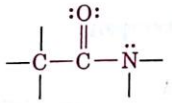
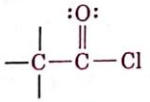
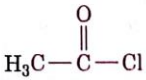
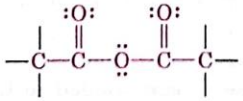
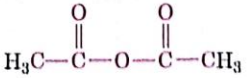
delocalized bonds

Functional groups

Family name	Functional group structure[a]	Simple example	Name ending
Alkane	(Contains only C—H and C—C single bonds)	CH_3CH_3	*-ane* Ethane
Alkene		$H_2C{=}CH_2$	*-ene* Ethene (Ethylene)
Alkyne		$H{-}C{\equiv}C{-}H$	*-yne* Ethyne (Acetylene)
Arene			None Benzene
Halide	 (X = F, Cl, Br, I)	$H_3C{-}Cl$	None Chloromethane
Alcohol		$H_3C{-}O{-}H$	*-ol* Methanol
Ether		$H_3C{-}O{-}CH_3$	*ether* Dimethyl ether
Amine		$H_3C{-}NH_2$	*-amine* Methylamine
Nitrile		$H_3C{-}C{\equiv}N$	*-nitrile* Ethanenitrile (Acetonitrile)
Nitro			None Nitromethane
Sulfide		$H_3C{-}S{-}CH_3$	*sulfide* Dimethyl sulfide
Sulfoxide			*sulfoxide* Dimethyl sulfoxide

Functional groups

Carbonyl derivatives

Family name	Functional group structure[a]	Simple example	Name ending
Sulfone			*sulfone* Dimethyl sulfone
Thiol			*-thiol* Methanethiol
Carbonyl, 			
Aldehyde			*-al* Ethanal (Acetaldehyde)
Ketone			*-one* Propanone (Acetone)
Carboxylic acid			*-oic acid* Ethanoic acid (Acetic acid)
Ester			*-oate* Methyl ethanoate (Methyl acetate)
Amide			*-amide* Ethanamide (Acetamide)
			
			
Carboxylic acid chloride			*-oyl chloride* Ethanoyl chloride (Acetyl chloride)
Carboxylic acid anhydride			*-oic anhydride* Ethanoic anhydride (Acetic anhydride)