Molecular Literacy for All

making sense of the “monstrous and boundless thicket” of everyday chemistry

The covalency model will help us understand
“Why Nature Chose…”

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Today's Outline

- Covalent bonding descriptions
- Oxidation state
- Connectedness and the functional groups
- Implied hydrogen atoms
- Bonding in phosphorus and sulfur
- The universe of organic molecules

Concepts to describe bonding in molecules

Table 1. Simple Definitions of Common Terms

Term	Definition
Valence	Number of electrons that an atom uses in bonding.
Oxidation number	The charge remaining on an atom when all ligands are removed heterolytically in their closed form, with the electrons being transferred to the more electronegative partner; homonuclear bonds do not contribute to the oxidation number.
Formal charge	The charge remaining on an atom when all ligands are removed homolytically.
Coordination number	The number of atoms bonded to the atom of interest.

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Assigning oxidation number

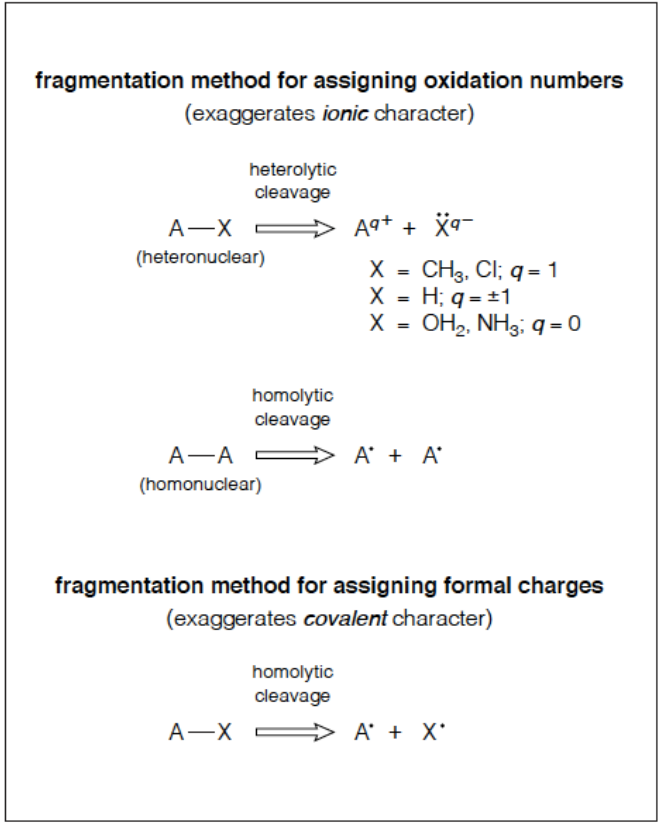

Figure 2. Fragmentation methods for assigning oxidation number and formal charge.

Bonding descriptions in practice

Table 2. Comparison of the Valence, Oxidation Number, Number of Bonds, and Coordination Number for Some Simple Molecules

Molecule	No. of Electrons in Valence Shell of Free Atom (*N*)	No. of Nonbonding Electrons on Atom in Molecule	Valence	Oxidation Number	No. of Bonds	Coordination Number
AH_n: Examples Where Valence = |Oxidation Number| = No. of Bonds = Coordination Number						
BH_3	3	0	3	+3	3	3
CH_4	4	0	4	–4	4	4
NH_3	5	2	3	–3	3	3
OH_2	6	4	2	–2	2	2
FH	7	6	1	–1	1	1
Examples Where Valence ≠ |Oxidation Number|						
$H_3C{-}CH_3$	4	0	4	–3	4	4
CMe_4	4	0	4	0	4	4
CH_2Cl_2	4	0	4	0	4	4
$[NH_4]^+$	5	0	5	–3	4	4
$[OH_3]^+$	6	2	4	–2	3	3
Examples Where Valence ≠ Number of 2-Center, 2-Electron Bonds						
$[BH_4]^-$	3	0	3	+3	4	4
$[NH_4]^+$	5	0	5	–3	4	4
Examples Where Valence ≠ Coordination Number						
$H_2C{=}CH_2$	4	0	4	–2	4	3
$HC{\equiv}CH$	4	0	4	–1	4	2
$H_3N\underline{B}H_3$	3	0	3	+3	4	4

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Tracking Oxidation State

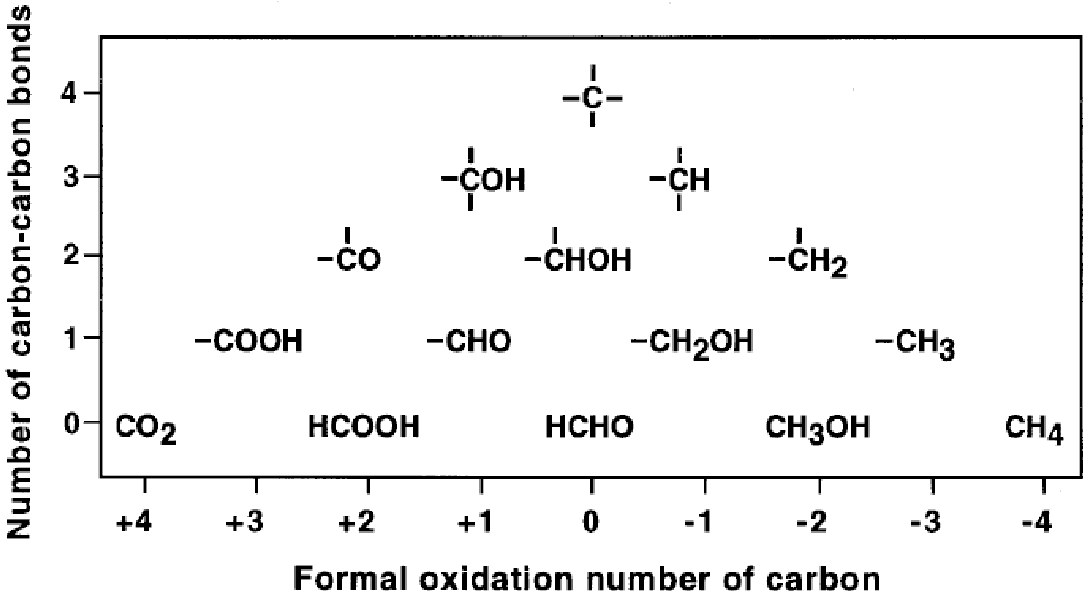


Figure 1. Carbon groups and one-carbon molecules positioned according to their formal carbon oxidation number on the abscissa, and their number of carbon-carbon bonds on the ordinate. The dash representing bonds to other carbon atoms can be saturated, unsaturated, or aromatic. The oxygen (O) in carbon groups can be replaced by heteroatoms, like nitrogen (N) or sulfur (S).

From: “Sugars as the Optimal Biosynthetic Carbon Substrate of Aqueous Life Throughout the Universe”
Origins of Life and Evolution of the Biosphere 30: 33–43, 2000

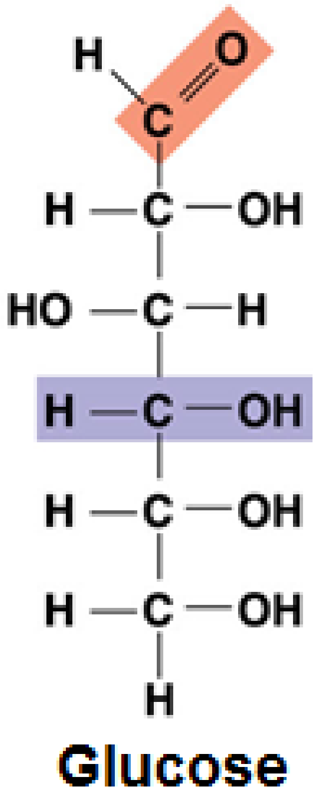
Why nature chose carbohydrates

to facilitate biochemical transformations

the carbonyl group (>C=O) strongly facilitates the reversible making and breaking of carbon-carbon bonds necessary for the synthesis of intermediates of varying size

the number of high energy electrons per carbon

alcohols – both internal alcohol groups (>CHOH and >COH–) and terminal alcohol groups (-CH2OH) – are the best biosynthetic substrates, because they have the largest number of biosynthetically useful high energy electron pairs/carbon

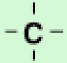
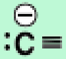


EPDs vs. Connectedness

EPDs are useful for predicting geometry
Connectivity map is experimentally determined by X-ray diffraction
Connectedness is useful to efficiently draw molecular structures, assign charges and lone pairs

Show amine – 4 EPDs but 3-connected

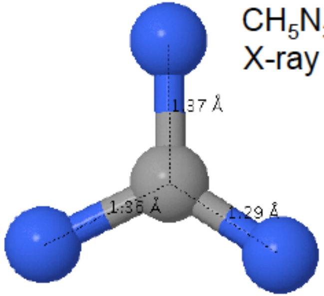
Building blocks by connectedness (i.e., coordination number)

charge	connectedness			
	1	2	3	4
hydrogen				
neutral	−H			
carbon				
neutral		−C≡ =C=		
+1				
-1				

charge	connectedness			
	1	2	3	4
nitrogen				
neutral	:N≡	–N̈=	–N̈(–)–	
+1		–N⊕≡ =N⊕=	–N⊕(–)=	–N⊕(–)(–)–
-1	=N̈⊖	–N̈⊖–		
oxygen				
neutral	=Ö:	–Ö–		
+1	:O⊕≡	–Ö⊕=	–Ö⊕(–)–	
-1	–Ö:⊖			
fluorine				
neutral	–F̈:			
+1	=F̈⊕	–F̈⊕–		

Connectivity maps are experimentally determined by X-ray crystallography

Experimental structural data, such as that obtained from X-ray crystallography, provides chemists with a molecule's "connectivity map" for all atoms that are heavier than hydrogen. This powerful technique even provides the Cartesian coordinates for each non-hydrogen, so bond distances and angles can be determined. However, it is up to the chemist to determine the electron configuration of each atom and the location of the hydrogen atoms. The connectivity map for CH_5N_3 is shown below. You are told that the structure is neutral, i.e., it has a net charge of zero. Your task is to draw a satisfactory structure.

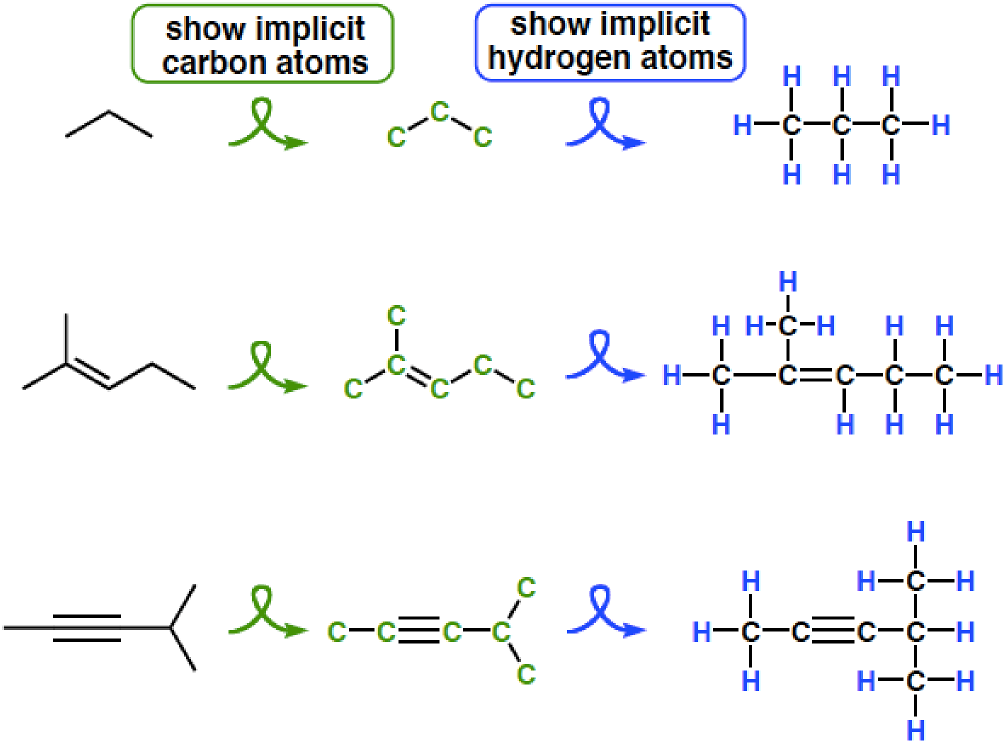


CH_5N_3 determined by X-ray crystallography

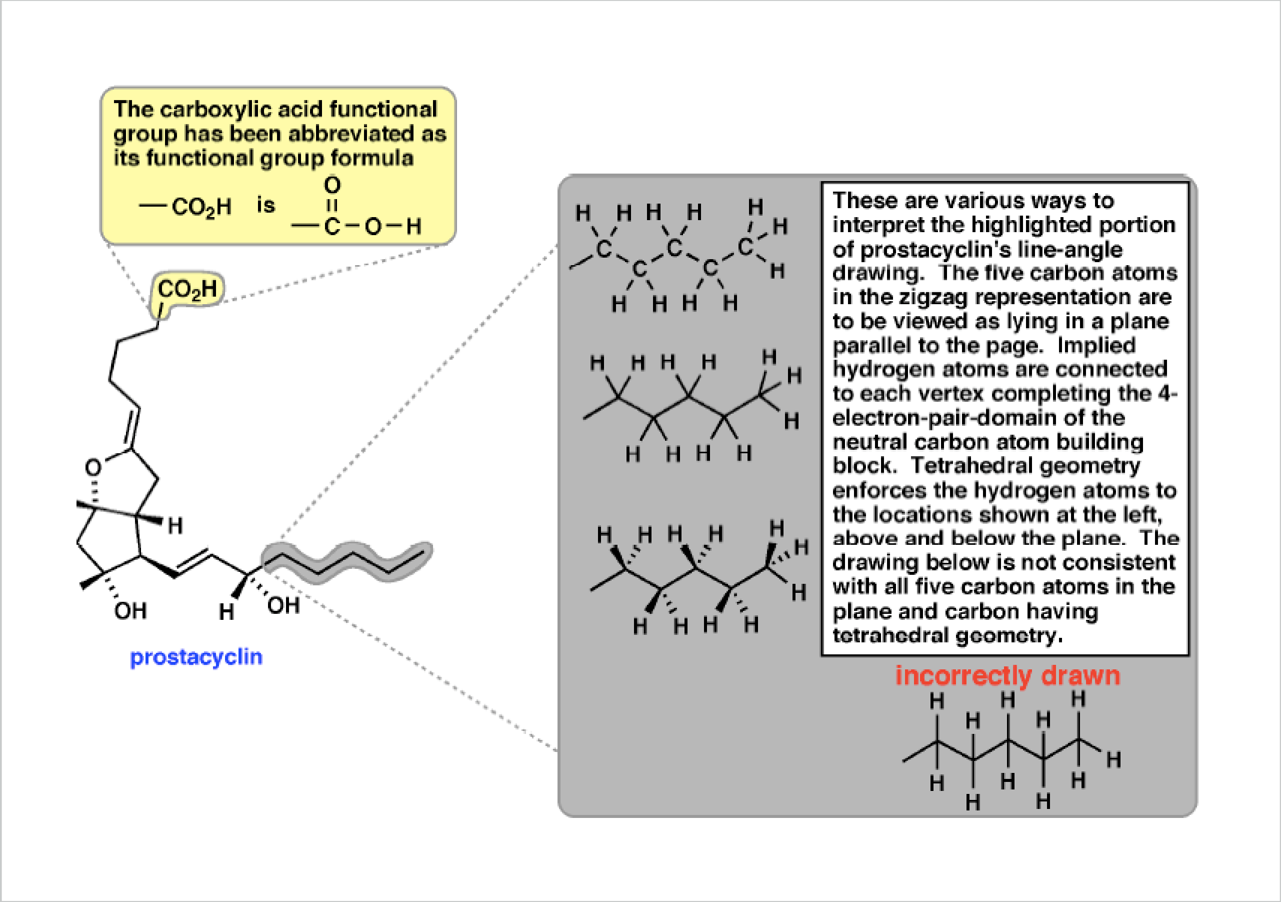
Draw the structure

REFERENCE: *Chem. Commun.*, **2007**, 3180-3182, **DOI**: 10.1039/b705100j

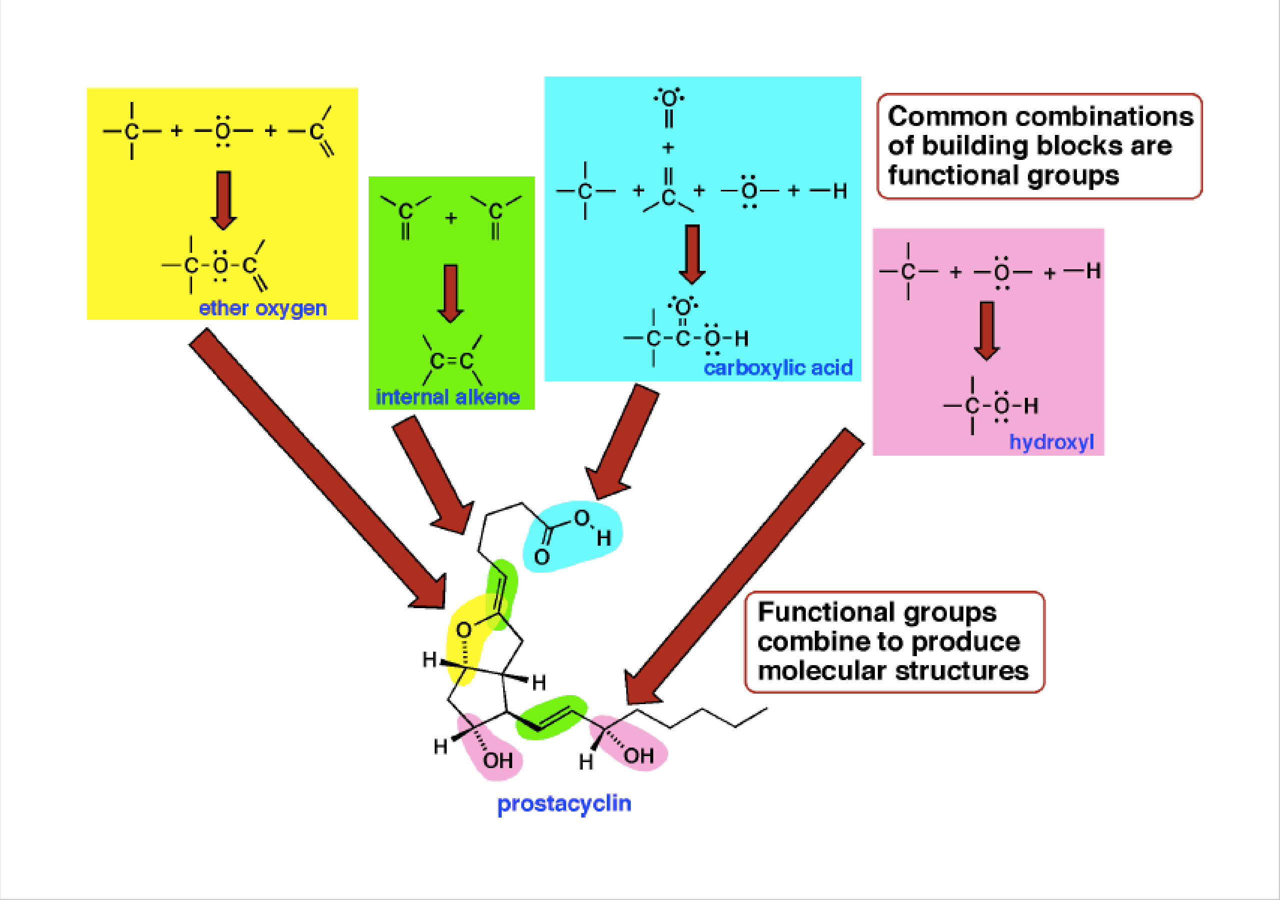
Implied atoms in molecular structure drawings

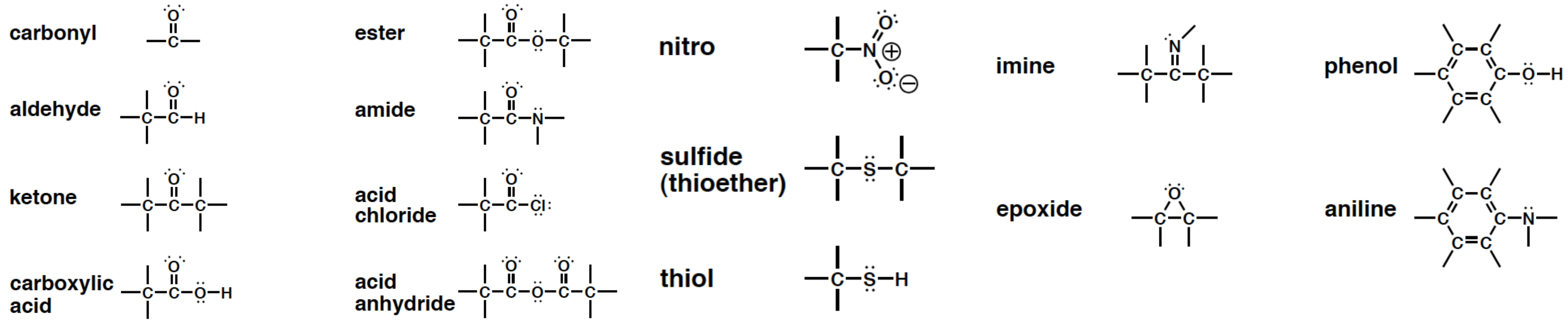


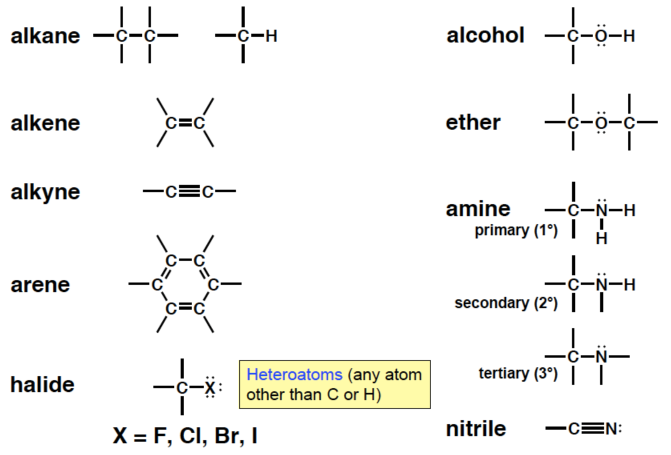
Interpreting molecular structures



Functional groups are the common combinations of the building blocks





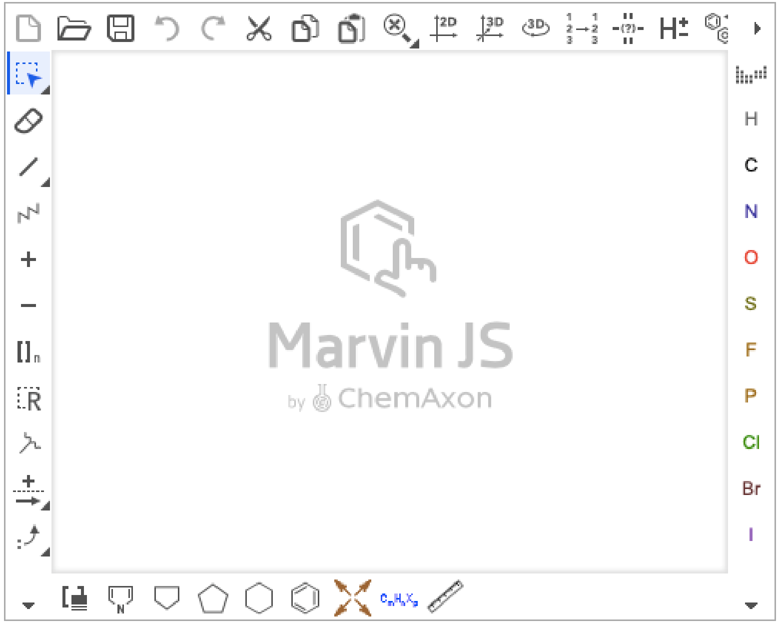


Common functional groups

Functional Group Finder

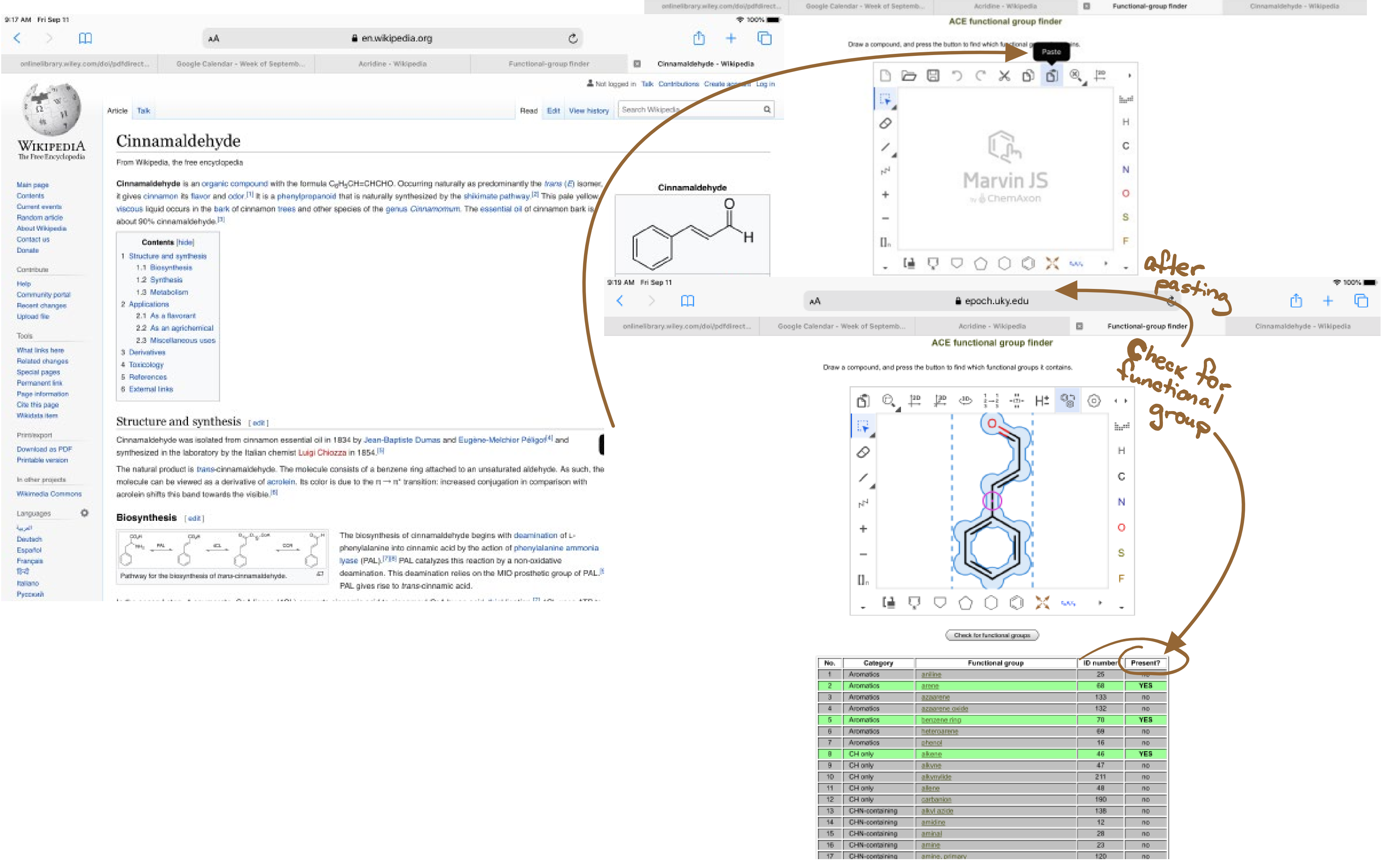
ACE functional group finder

Draw a compound, and press the button to find which functional groups it contains.

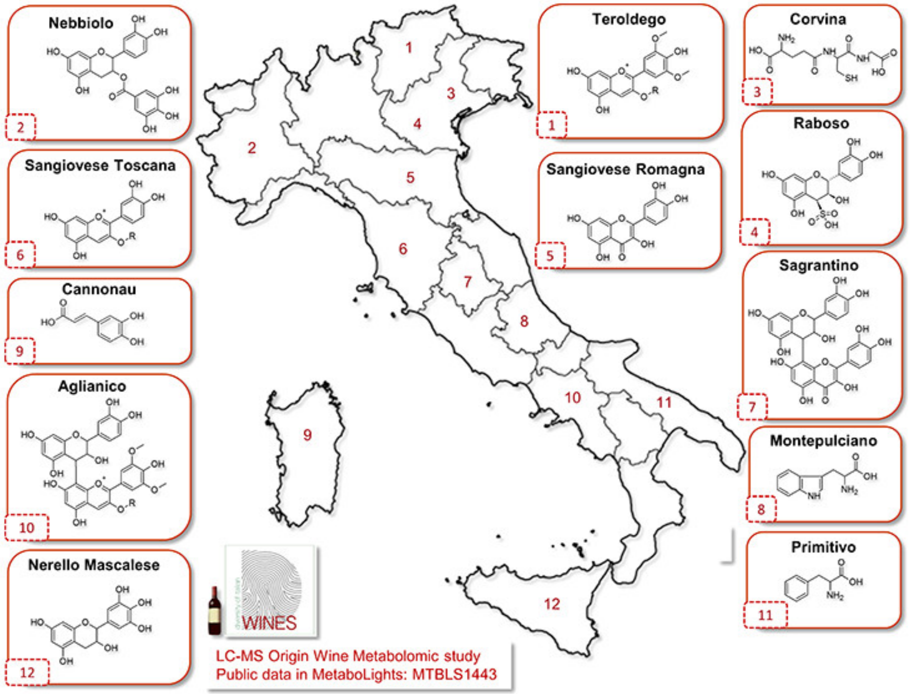


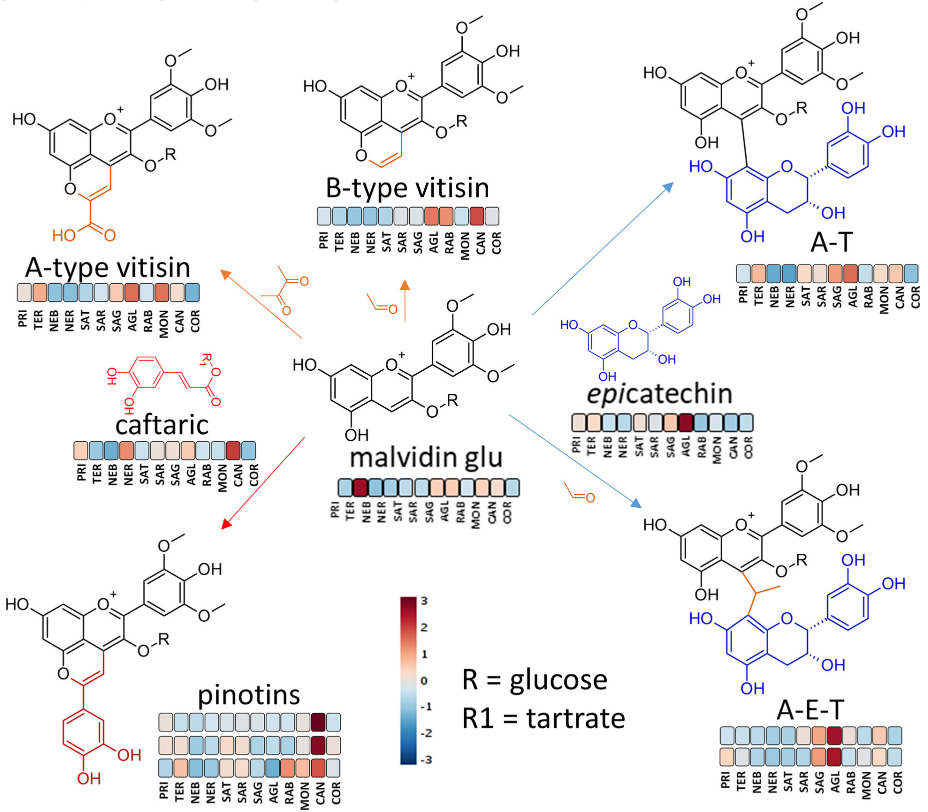
https://epoch.uky.edu/ace/public/fnalGroups.jsp

Check for functional groups


Cinnamaldehyde
ACE functional group finder
Draw a compound, and press the button to find which functional groups it contains.
Paste
after pasting
check for functional group
Check for functional groups
No.
Category
Functional group
ID number
Present?

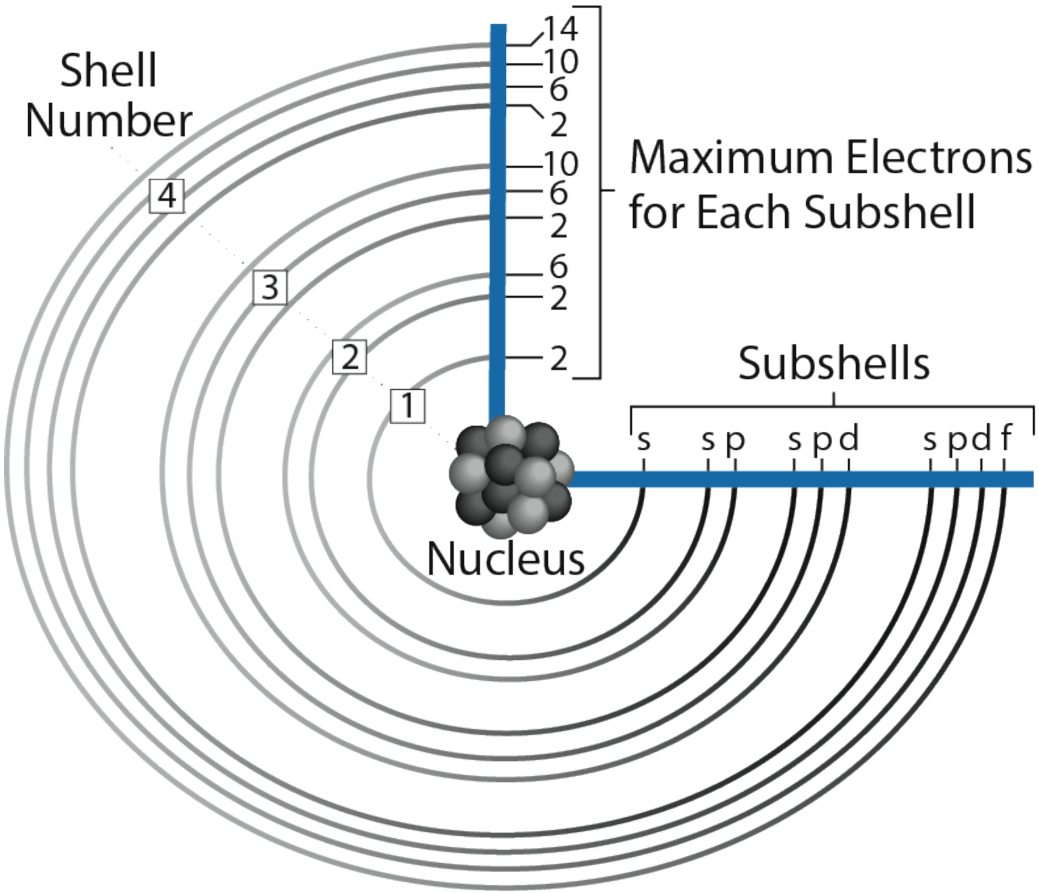
Discriminating Italian Monovarietal Red Wines from Different Terroirs



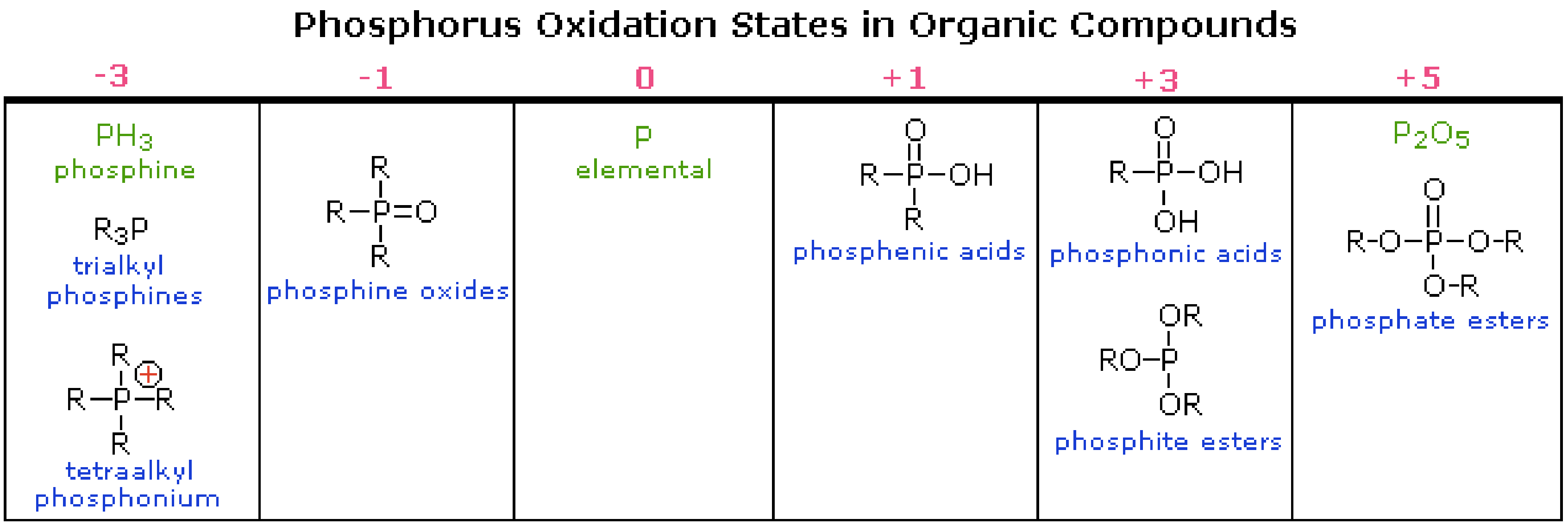


https://doi.org/10.1021/acs.jafc.0c00879

Bonding in Phosphorus and Sulfur



Bonding in Phosphorus



Why nature chose phosphates

Phosphate esters and anhydrides dominate the living world but are seldom used as intermediates by organic chemists. Phosphoric acid is specially adapted for its role in nucleic acids because it can link two nucleotides and still ionize; the resulting negative charge serves both to stabilize the diesters against hydrolysis and to retain the molecules within a lipid membrane. A similar explanation for stability and retention also holds for phosphates that are intermediary metabolites and for phosphates that serve as energy sources. Phosphates with multiple negative charges can react by way of the monomeric metaphosphate ion PO_3^- as an intermediate. No other residue appears to fulfill the multiple roles of phosphate in biochemistry. Stable, negatively charged phosphates react under catalysis by enzymes; organic chemists, who can only rarely use enzymatic catalysis for their reactions, need more highly reactive intermediates than phosphates.

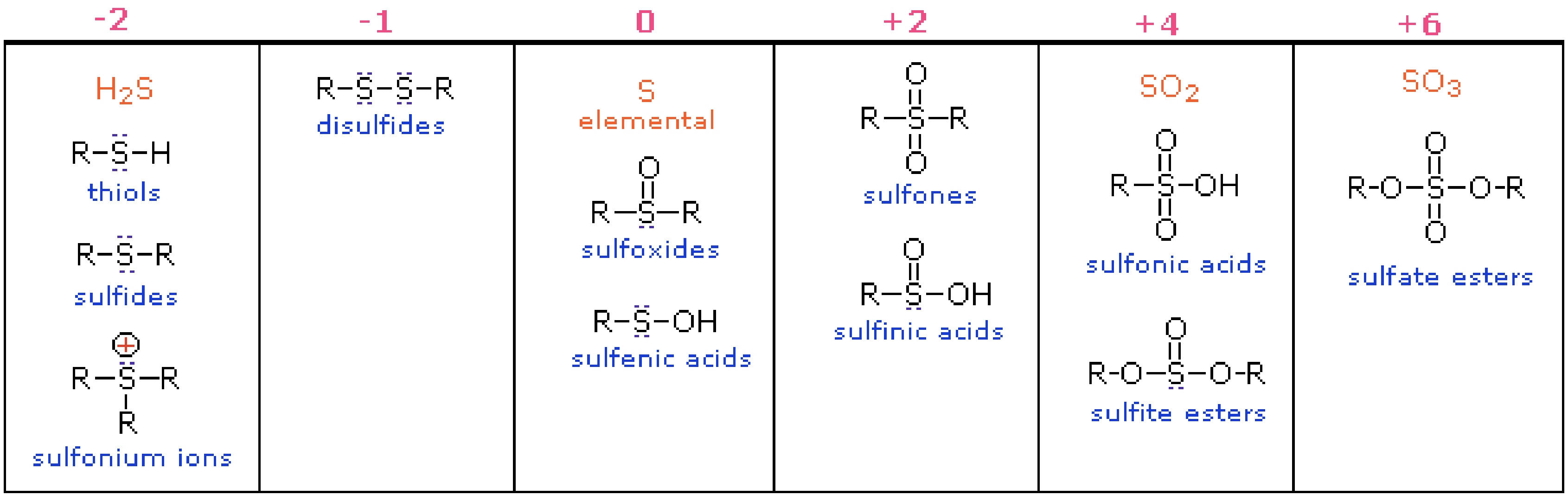
Science 06 Mar 1987: Vol. 235, pp. 1173-1178
DOI: 10.1126/science.2434996

Table 1. Examples of phosphates in biochemistry.

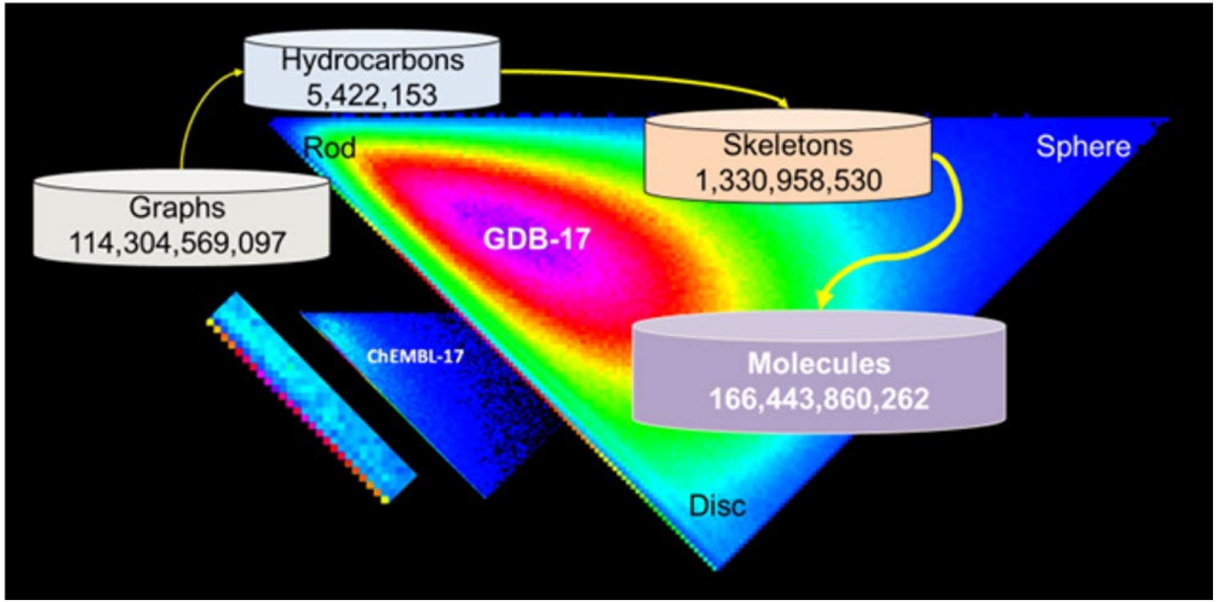
Phosphate	Acid derivative
DNA	Diester of phosphoric acid
RNA	Diester of phosphoric acid
ATP	Anhydride of phosphoric acid
Creatine phosphate	Amide of phosphoric acid
Phosphoenolpyruvate	Enol ester of phosphoric acid
Pyridoxal phosphate	Phenol ester of phosphoric acid
Nicotine adenine dinucleotide	Ester and anhydride of phosphoric acid
Fructose 1,6-diphosphate	Ester of phosphoric acid
Glucose-6-phosphate	Ester of phosphoric acid
Isopentenyl pyrophosphate	Ester of pyrophosphoric acid
Ribose-6-phosphate-1-pyrophosphate	Ester of phosphoric and pyrophosphoric acids

Bonding in Sulfur

Sulfur Oxidation States in Organic Compounds



The universe of organic molecules



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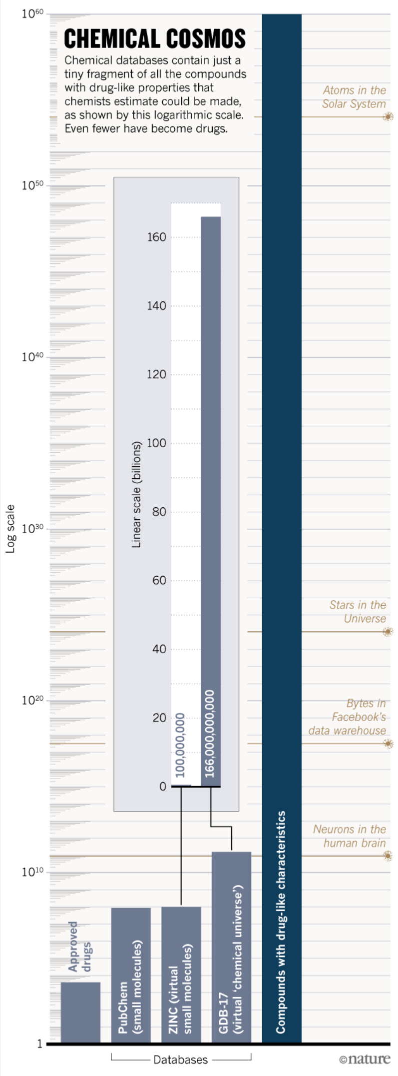
Modular is a good word to describe the structure of organic molecules. The parts are interchangeable and come together in many different ways. The building blocks are combined to construct functional groups. The functional groups, in turn, are combined to construct molecules. Given the large number of building blocks and functional groups and their various combinations, it is no wonder that the "Universe of Organic Molecules" – the subset of molecules containing up to 30 C, N, O and S atoms – is estimated† to be something like $1x10^{60}$. That's a really big number! It should be obvious that if we are to make sense of this complexity, we need to develop good skills in recognizing the functional groups in organic molecules. With just a little practice you will be able to instantly look at a new molecule and see it for the functional groups that it contains.

Acc. Chem. Res. 2015, 48, 3, 722–730



How machine learning and big data are helping chemists search the vast chemical universe for better medicines