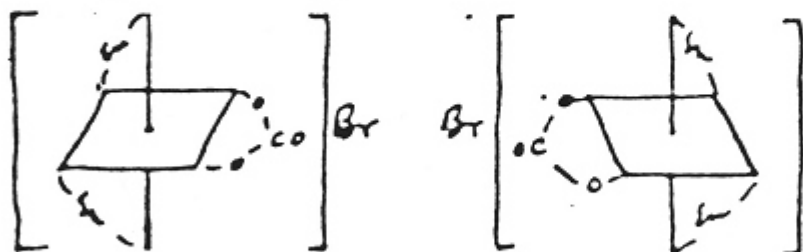
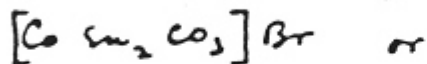


STEREOCHEMISTRY

January 1910

The salt dicythylenediamine carbonate cobaltibromide is usually represented as follows.

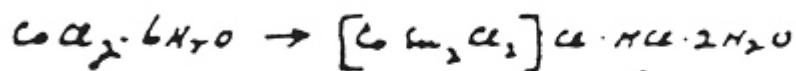


\therefore The above salt molecule is not "decolor" with its "Spiegelbild" & should consist of an equivalent mixture of oppositely optically active isomers.

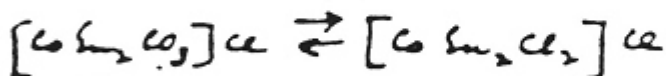
The object is to demonstrate the truth of fallacy of this and if possible separate the optically active isomers. $\text{en} = \text{NH}_2\text{CH}_2\text{-CH}_2\text{NH}_2$

Versuch I

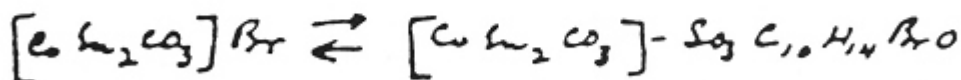
Brau



↓



↓



. Bromcampher sulfonate.

Try to separate optically active isomers by fractionally crystallizing this salt.

Early Ideas

- until early 19th century generally believed that the properties of a substance depended only on the types and proportions of the constituent elements

- discovery of different substances with the same molecular formula forced new thinking

- in 1820s Liebig demonstrated that
 silver fulminate = silver cyanate = AgCNO
 $[(\text{AgCNO})_2]$ $[\text{AgOCN}]$

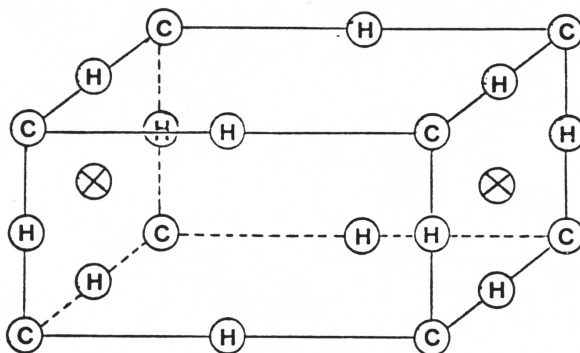
- and in 1828 Friedrich Wöhler made the remarkable discovery that an attempted synthesis of ammonium cyanate yielded urea instead; he determined that both compounds had the same formula, [see Vitalism] ie,



- in 1832 Berzelius gave the name *isomerism* to “substances of the same compositions but of different properties”

- in mid 19th century radical theory accepted stable, polyatomic radicals with unknown internal structure, and type theory emphasized the importance of internal structure, but again with no knowledge of what that structure could be

- in 1830s, for example Dumas' student August Laurent proposed a hypothetical structure for “etherin”, C_8H_{12} , [our ethane, C_2H_6]



- in Laurent's model, positions marked with X could be occupied by other elements, eg, another two H atoms would convert etherin to two units of marsh gas [methane]

- Laurent's contemporaries found his proposals purely speculative; Liebig called them "bizarre" [see text S22-23 for a published satire on the extremes of type theory]



Auguste Laurent

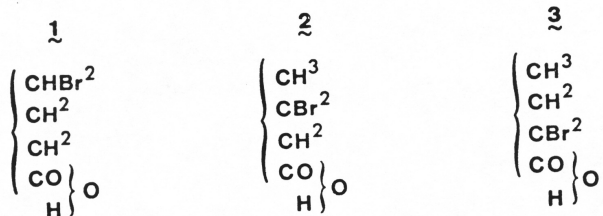
- after 1860, when molecular formulas became generally accepted, people began to speculate about possible structural arrangements that corresponded with expected valences

- the Russian **Alexandr Butlerov** was the first to state unambiguously that every compound must have one unique structure

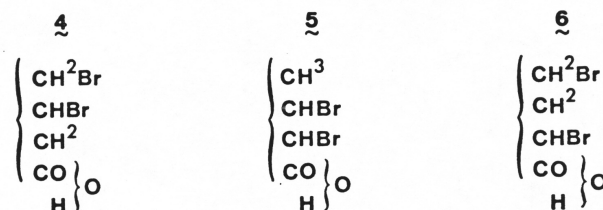
- assuming the tetravalency of carbon (proposed by Kekulé), Butlerov in 1861 suggested six unique formulations for the six isomers of dibromobutyric acid, ie



Alexandr Butlerov



- note how type theory combined with carbon tetravalency can make sense of isomers



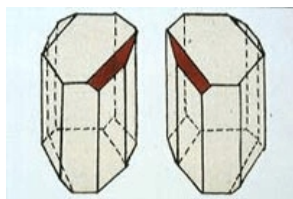
- Butlerov's work is among the first to bring clarity to what we know as **constitutional isomers** (structural isomers), but there is no hint of 3D structure in his work

Spatial (3D) Considerations

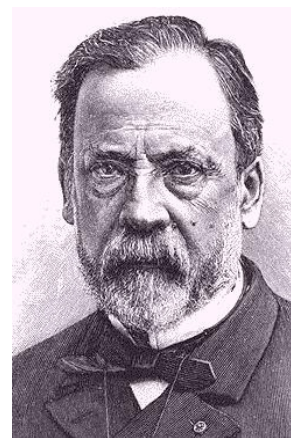
- in 1815, Jean Baptiste Biot (1774-1862), discovered that solutions of some purified natural organic compounds, eg, camphor, could rotate the plane of plane-polarized light, a phenomenon that had been previously noted only in transparent crystals such as quartz; he suggested that the ability to interact with polarized light must be a property of the substance itself, not on crystal packing

- Mitscherlich had reported in 1844 that the solid ammonium salts of tartaric and racemic acids (found in wine residues) had the same formulas but one rotated light and one did not

- Louis Pasteur in 1848 looked at the crystals of sodium ammonium tartrate under a microscope and carefully identified and isolated two mirror-image forms; one rotated light in a clockwise direction and the second in a counter-clockwise direction



Tartrate enantiomers



Louis Pasteur
1822-1895

sodium ammonium tartrate =

(One of only a handful of substances whose enantiomers crystallise out of a racemic solution as separate enantiomers, and only below 28°C)

- in 1869 Wislicenus showed inactive lactic acid (from sour milk) and active acid (from muscle tissue) had the same molecular structure, $\text{CH}_3\text{CH}(\text{OH})\text{COOH}$, and thus that positional isomerism alone was not enough to explain all possible isomers and that the isomers must have “different positions of their atoms in space” [text p.S7]

Tetrahedral Carbon

- in 1874 J.A.LeBel suggested “optical isomerism” could be explained by 3D differences in molecular structure, but he gave no specific examples

- also in 1874, the Dutch chemist **Jacobus van't Hoff** (1852-1911) built on the tetravalent carbon proposal of Kekulé to propose that the four valences of carbon were “directed toward the four corners of a tetrahedron”



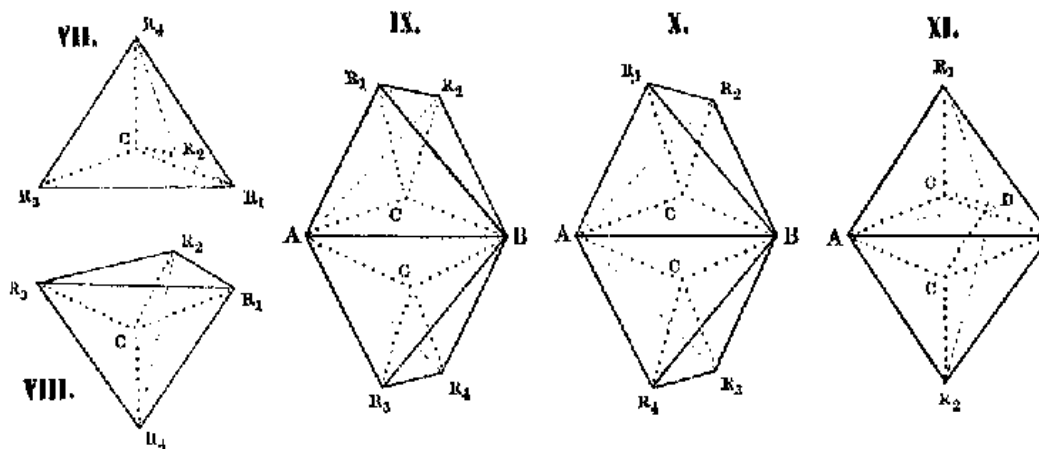
Jacobus van't Hoff

- with this specific geometric model for carbon bonding in mind van't Hoff was able to explain:

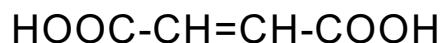
- i) that enantiomers arose only when a C was connected to 4 different groups
- ii) that a single C–C connection was formed when two C atoms were connected corner-to-corner; rotation around the connection meant no isomers resulted
- iii) double C=C connections resulted from edgewise connection of two tetrahedra, and two isomers would result

iii) triple C≡C connections resulted from face-to-face connection, with no isomers being possible

-Van't Hoff drew the possibilities as shown:



- van' Hoff's proposal was the first good explanation of optical isomerism (due to asymmetrical C connections) and double bond isomerism, as in maleic and fumaric acids,



- van't Hoff's proposal (a classic example of 'naive realism') was provisionally accepted by most chemists because it provided the only compelling explanation for all types of isomerism in organic compounds. Nonetheless, it was ridiculed by some chemists who viewed speculation on the metaphysical shape of carbon atoms and compounds as unsound science

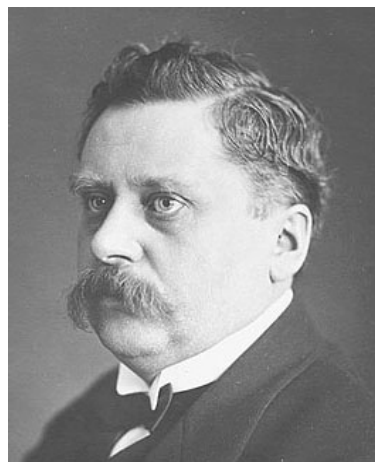
- see the judgement of Kolbe [text S8-9] who concluded van't Hoff's ideas were "trivial and stupid natural philosophy...and absolutely unintelligible to the sober scientist"

- it was not until 1951 that the absolute stereochemistry of the two enantiomers of sodium rubidium tartrate was confirmed by x-ray analysis

Inorganic Stereochemistry

- the greatest contributions to inorganic stereochemistry were made by the Swiss chemist **Alfred Werner** (1866-1919)

- he at first tried to extend van't Hoff's ideas to the N atom, proposing that N was also tetrahedral, but with an N atom at one vertex, ie,



Alfred Werner

- this model did not give a good explanation for the absence of N isomers for N compounds with 3 different substituents, so Werner abandoned it completely in inorganic compounds; he instead developed a model in which a central inorganic atom was surrounded by a primary (1°) and a secondary (2°) coordination sphere, ie,

- groups were strongly bound by affinity forces to the central atom in the 1° coord sphere (this defined the "coordination number" of the central atom, usually a transition metal) and by weaker ionic forces in the 2° ionic sphere,

eg, for divalent Pt, successive addition of neutral NH_3 could displace Cl atoms from the coordination sphere to the ionic sphere:



– groups shown inside the [] are in the 1° coord sphere, and those outside are in the 2° ionic sphere

- Werner proposed a square planar coordination geometry for Pt(II) complexes, such as for $[\text{PtCl}_2(\text{NH}_3)_2]$, since a tetrahedral geometry would not give rise to the two known isomers, ie,

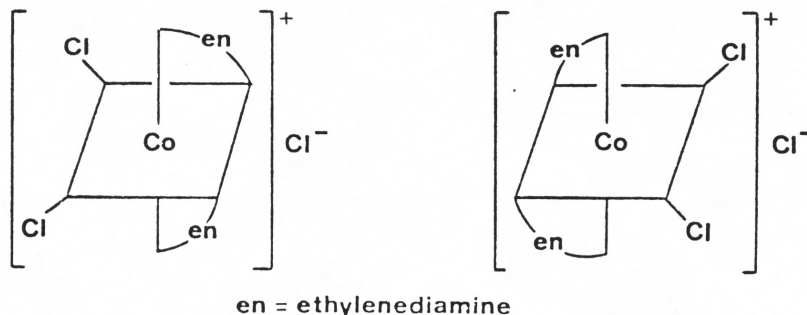
- for six-coordinate transition metals, such as Co complexes, Werner proposed a square bipyramid (octahedral) bonding coordination sphere, eg, for the two isomers ('luteo' and 'purpureo') of $[\text{Co}(\text{NH}_3)_6]\text{Cl}_3$ and $[\text{Co}(\text{NH}_3)_5\text{Cl}]\text{Cl}_2$

- in Werner's scheme for metal complexes, the coordination number (frequently = 6) for most atoms was not equal to the atom's valence; for Co (3+) in above examples the Co valence = 3, but the coordination number = 6

- Werner believed that C compounds were simpler because for C the coordination number and the valence were both constant = 4

- in 1907 Werner prepared and isolated the two possible isomers of $[\text{CoCl}_4(\text{NH}_3)_2]$, ie,

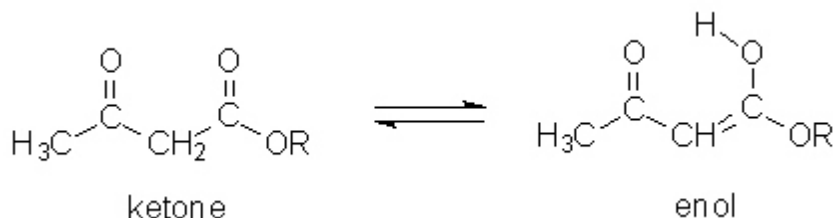
- and in 1910 he synthesized and isolated the two possible enantiomers of $[\text{CoCl}_2(\text{en})_2]^+\text{Cl}^-$ (see p.S1 for notebook entry), ie,



- Werner is the founder of modern coordination chemistry, and his success derived from his decision to distinguish coordination number from valence in coordination complexes
 - we learn modern chemistry with fixed molecular structure as the norm (following Butlerov), but...

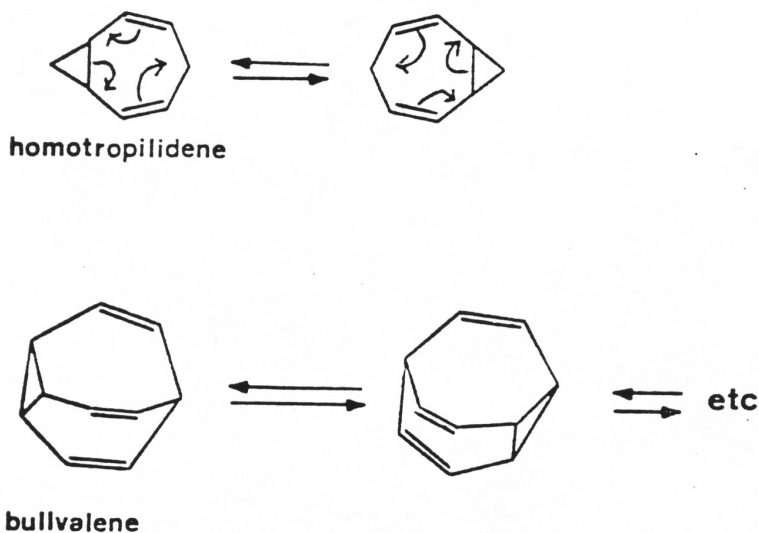
Interchanging Molecular Structures

- Geuther in 1863 prepared the ethyl ester of acetoacetic acid and found it, after repeated purification, showed properties of both a carbonyl group and an alcohol group; he believed that the two compounds responsible could not be separated
 - in 1885, Laar concluded that there were not two compounds present, instead the compound existed as an equilibrium mixture of two interconverting forms, a phenomenon he termed **tautomerism**, ie



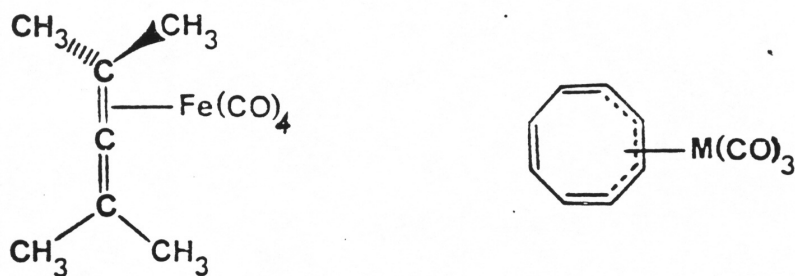
- thus, contrary to Butlerov, ethylacetoacetate is a structure that cannot be correctly represented by a single structure

- in the 20th century homotropilidene was synthesized; it has two equal energy tautomeric forms that equilibrate with each other with a half-life of 1 sec at 50°C
- in 1963 William “Bull” Doering synthesized a tricyclic analogue of homotropilidene that has 1,209,000 equivalent tautomeric forms (and shows a single ¹³C peak at 50°C); his students suggested the name bullvalene

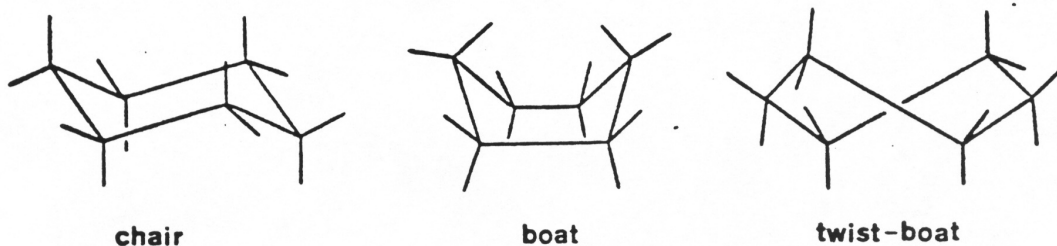


- such structures are now termed “fluxional”, and force chemists to recognise that not all compounds can be properly depicted by a single structure (don’t confuse fluxional cmpds with resonance structures, which have no real existence as they differ only in electron distribution)

- there are also fluxional inorganic cmpds, eg,

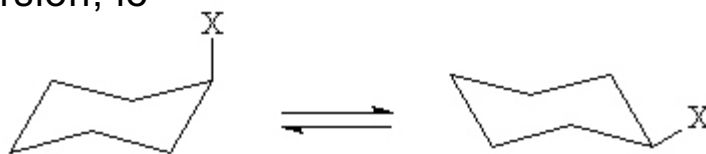


- rotation of groups around a single bond can also lead to different interconverting geometries
- until late in the 19th century cyclohexane was shown as, and believed to be, a planar ring
- only in 1890 did Sachse conclude that tetrahedral carbon would force cyclohexane rings into “chair” and “boat” forms; later 20th century chemists have added “twist boat” to the possibilities, ie,



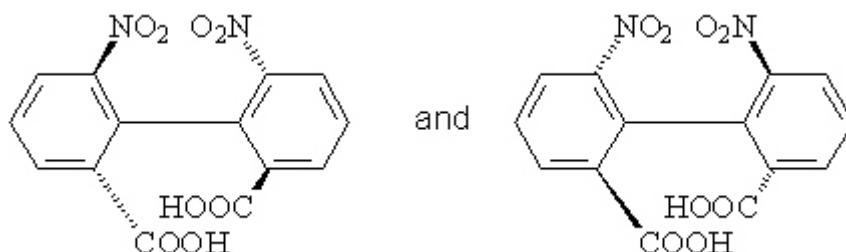
- in 1918, Mohr showed that the two cyclohexane forms could interconvert by rotation around carbon-carbon bonds, and in 1929 Howarth proposed the name **conformations** for interconverting structures caused by rotation around single bonds

- once the two cyclohexane conformers were accepted, chemists recognized that substituents changed positions during interconversion, ie



- but it was only in 1951 that Derek Barton demonstrated that the chemical reactivities of “polar” (now axial) and “equatorial” substituents differed
- Barton’s grad student at the time was Paul deMayo, who moved to UWO in 1959 and was the research supervisor of Mel Usselman, PhD 1973 (which brings history close to home)

- conformations are generally thought to interconvert rapidly at room temp, but already in 1920, the two “enantiomers” of ortho-substituted diphenyls were prepared and resolved, ie,



- thus, conformations can be viewed as a subset of isomers and are treated as such in many modern textbooks

- thus, modern chemistry has a theory of structure that accepts:

i) most compounds have a single, unique structure

ii) some compounds exist in a few interconverting tautomeric forms, or many fluxional ones

iii) momentary spatial arrangements exist for most molecules by rotation of groups around single bonds

iv) conformational “isomers” due to restricted interconversion of conformers can exist

- altho we understand much of the structural variability of molecules, it is likely that more novelty will appear in the future