Université Concordia University

Organic IV
Structure & Stereochemistry

CHEM 325 – Summer 2010

"EXCUSE ME SIR, COULD YOU DIRECT ME TO CULPEPPER ROAD?"

1

Optical Activity

"No other chemical characteristic is as distinctive of living organisms as is optical activity."

George Wald (1957)

This is in reference to Jean Baptiste Biot's discovery in 1812 that some substances of biological origin cause polarized light rays passing through them to be rotated clockwise or counterclockwise.

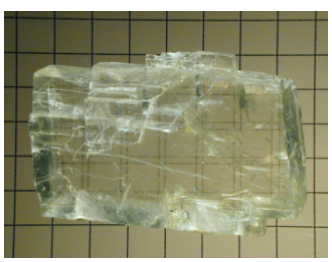
This phenomenon is known as optical rotation, and substances which exhibit this are said to be optically active.

The rotation of polarized light by optically active substances has provided insight into the physics of light, the structure of molecules, and the nature of life.

2

Seminal Discoveries in the History of Stereochemistry

1669 ➔ The Danish professor of mathematics and medicine, Erasmus Bartholinus, observed that Iceland spar (calcite, calcium carbonate) exhibits double refraction - images viewed through crystals are doubled.



Birefringence ➔ double refraction of light in a transparent, molecularly ordered material (orientation-dependent differences in refractive index).

3

Seminal Discoveries in the History of Stereochemistry

Many transparent solids are optically **isotropic** ➔ the index of refraction is equal in all directions throughout the crystalline lattice.

All isotropic crystals have equivalent axes that interact with light in a similar manner ➔ light entering an isotropic crystal is refracted at a constant angle and passes through the crystal at a single velocity without being polarized by interaction with the electronic components of the crystalline lattice.

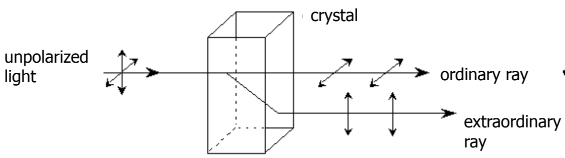
Crystals can be either isotropic or anisotropic depending upon their optical behavior and whether or not their crystallographic axes are equivalent.

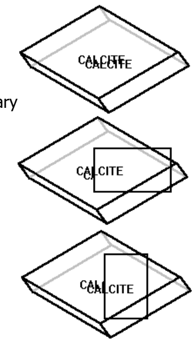
Anisotropy refers to a non-uniform spatial distribution of properties, resulting in different values being obtained when samples are probed from different directions within the same material.

4

Seminal Discoveries in the History of Stereochemistry

1677 ➔ The Dutch mathematician/astronomer/physicist, Huggens, noted that each ray emerging from Iceland spar was polarized.





The refractive indices of the clacite crystal are 1.6584 (ordinary ray) and 1.4864 (extraordinary ray).

Seminal Discoveries in the History of Stereochemistry

Material	n_o	n_e	Δn
calcite $CaCO_3$	1.658	1.486	-0.172
calomel Hg_2Cl_2	1.973	2.656	+0.683
ice H_2O	1.309	1.313	+0.014
lithium niobate $LiNbO_3$	2.272	2.187	-0.085
magnesium fluoride MgF_2	1.380	1.385	+0.006
quartz SiO_2	1.544	1.553	+0.009
ruby Al_2O_3	1.770	1.762	-0.008
rutile TiO_2	2.616	2.903	+0.287
peridot $(Mg, Fe)_2SiO_4$	1.690	1.654	-0.036
sapphire Al_2O_3	1.768	1.760	-0.008
sodium nitrate $NaNO_3$	1.587	1.336	-0.251

6

Seminal Discoveries in the History of Stereochemistry

Biaxial birefringence (**trirefringence**) ➔ anisotropic materials that have more than one axis of anisotropy.

Material	n_α	n_β	n_γ
borax	1.447	1.469	1.472
epsom salt $MgSO_4 \cdot 7(H_2O)$	1.433	1.455	1.461
mica, biotite	1.595	1.640	1.640
mica, muscovite	1.563	1.596	1.601
olivine $(Mg, Fe)_2SiO_4$	1.640	1.660	1.680
perovskite $CaTiO_3$	2.300	2.340	2.380
topaz	1.618	1.620	1.627

7

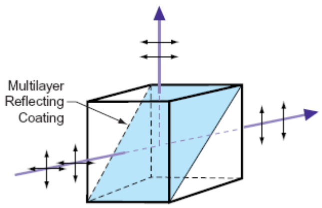
Seminal Discoveries in the History of Stereochemistry

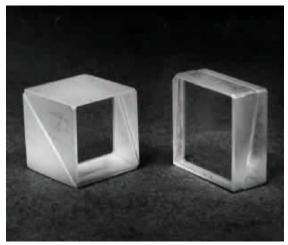
1828 ➔ William Nicol devised a polarizing prism by cutting a rhombohedral section of calcite diagonally and cementing them back together.

The result is a transparent birefringent crystal, known as a **Nicol** prism which separates polarized light at the interface between the two crystal halves.

The extraordinary ray passes through the interface and emerges from the prism.

The resulting plane-polarized light can be used in microscopes or any other device that needs polarized light.



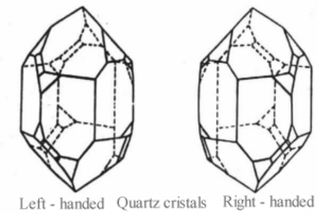


Seminal Discoveries in the History of Stereochemistry

1769 ➔ Scheele isolates tartaric acid from the sludge in wine casks (D-tartaric acid).

1801 ➔ Haüy, a French mineralogist observed that some quartz crystals rotate polarized light clockwise, while other crystals rotate polarized light to the left.

Haüy also noticed that quartz crystals exhibit the phenomenon of hemihedrism (externally, some crystals are non-identical mirror images of other crystals ➔ different truncation pattern (left or right) of the crystal).



Seminal Discoveries in the History of Stereochemistry

1808 ➔ Etienne Louis Malus observed that light reflected from flat reflective surfaces became polarized. (Light reflected from puddles on the roof of a building was not completely reflected from vertical windows.)

1811 ➔ Arago, a student of Malus, observed that a quartz plate, cut at right angles to its crystal axis, rotates the plane of polarized light through an angle proportional to the thickness of the plate. This phenomenon was called **optical rotation**.

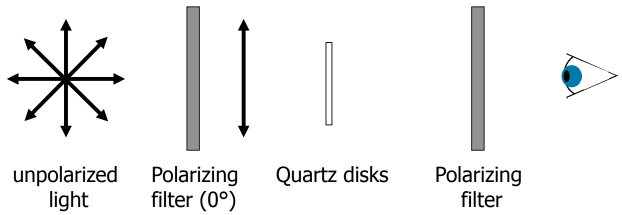
Seminal Discoveries in the History of Stereochemistry

In 1811 François Arago performed a **colorful** experiment that Biot (another student of Malus) repeated in 1812.

- Ordinary light consists of electric and magnetic waves at right angles to one another, emanating in all possible planes relative to the source. The polarization at this point is considered random and has no preferred direction.
- If a piece of polarizing material is used, the planes in which the electromagnetic waves travel can be controlled such that only a single plane exists.
- This is evident when two polarizers are used in conjunction with one another. If the transmission axes (polarized planes) are parallel, the light will be transmitted. If they are perpendicular, no light will pass.

Seminal Discoveries in the History of Stereochemistry

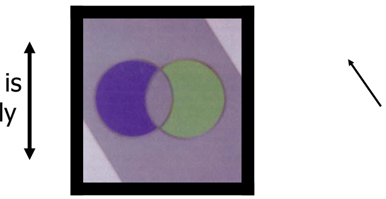
- Quartz exists in two crystal forms which rotate light in opposite directions.
- In the following slides, the optical rotation of two colorless quartz disks is displayed by viewing polarized white light transmitted by the disks through a polarizing filter.
- The polarizing filter is the rectangular strip across each frame.



13

Seminal Discoveries in the History of Stereochemistry

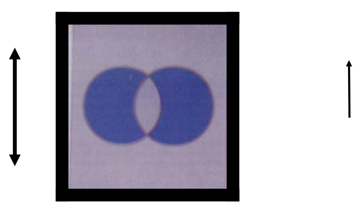
background light is polarized vertically



- As the light passes through the quartz, the direction of polarization is rotated counterclockwise by the left disk, and clockwise by the right disk.
- The polarizing filter (rotated clockwise during the experiment) only transmits light polarized parallel to the length of the strip.

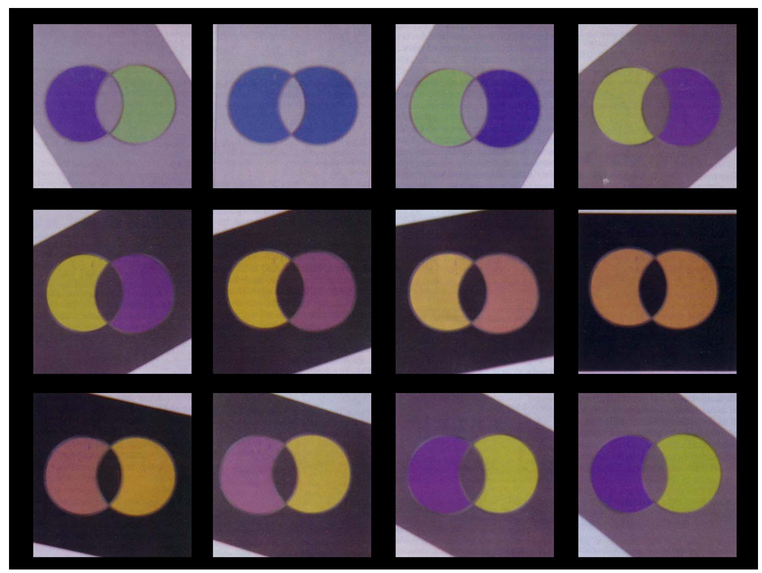
14

Seminal Discoveries in the History of Stereochemistry

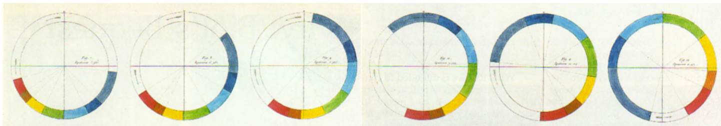


- The appearance of colors in the disks is due to different angles of rotation for each wavelength of light.
- Where the disks overlap, there is no color because the rotation of light by one disk is cancelled by the other disk.

15

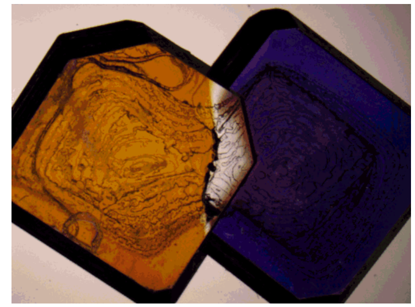


Seminal Discoveries in the History of Stereochemistry



- The appearance of colors in the disks is due to different angles of rotation for each wavelength of light.
- Biot showed the rotation angles for different colors transmitted through quartz plates of different thicknesses.
- These measurements allowed Biot to conclude that the angle of optical rotation is proportional to the thickness of the quartz plate (and inversely proportional to the wavelength of light).

Ethylenediammonium sulfate



Seminal Discoveries in the History of Stereochemistry

- A remarkable fact discovered during these experiments was that quartz crystals occur in two forms which are similar in almost all properties, except that they rotate polarized light in opposite directions.
- While observing quartz crystals immersed in organic liquids, Biot made his biggest discovery ➔ certain organic liquids were optically active!
- Solutions that Biot studied included: distilled oils of terpentine and lemon and solutions of sugar and camphor.
- Unlike quartz, the organic substances were optically active as liquids and were never found in two forms of opposite handedness.

Optical Activity – an early experiment

1815 ➔ Jean Baptiste Biot observed that organic substances, both liquids (such as turpentine) and solids in solution (such as sucrose, camphor and tartaric acid) were also capable of optical rotation.

In the 1800's, it was thought that organic compounds could only be produced through the action of a vital force in living organisms.

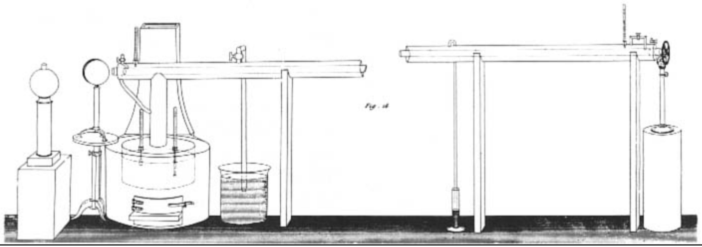
The discovery of optical rotation is in agreement with vitalism because organic materials behaved differently from inorganic materials.

For Biot, optical activity of organic compounds was special because it reflected an inherent property of the molecules – not their state of aggregation.

To test this idea Biot wanted to measure the optical rotation of a gas – where there is no chance of aggregation.

Optical Activity – a powerful experiment

- Biot set out to measure the optical rotation of turpentine gas.
- Because of the low density of gases, it was necessary to allow the light to travel a long distance through the sample.
- Biot set up a tube 30 meters long in an old church.
- At one end there was a polarized light source and a furnace to boil the turpentine and fill the tube with vapor.



Optical Activity – a powerful experiment

- At the other end Biot looked through the calcite analyzer for the appearance of colors ➔ optical rotation.
- Just as Biot was about to rotate the analyzer to measure the optical rotation angle, the boiler exploded!
- Luckily nobody was hurt and Biot was convinced that the optical activity of turpentine was a molecular property.
- In his scientific paper he encouraged others to repeat his experiment to determine the direction and magnitude of optical rotation:

"The explosion of the vapor could cause persons located at some distance to perish miserably, and in the most inevitable and cruel manner."

Seminal Discoveries in the History of Stereochemistry

"The explosion of the vapor could cause persons located at some distance to perish miserably, and in the most inevitable and cruel manner."

Seminal Discoveries in the History of Stereochemistry

Jean-Baptiste Biot (1774-1862)

- The history of stereochemistry begins in 1815 when Biot performed experiments using polarized light.
- Biot passed polarized light through various solutions and noted that certain solutions such as sugar can rotate polarized light.
- He also found the degree of rotation is a direct measure of the concentration of the solution.
- Substances capable of rotating a plane of polarized light were designated "optically active."

Seminal Discoveries in the History of Stereochemistry

ca. 1815 ➔ Kestner, the owner of a chemical plant, had obtained, as a by-product of tartaric acid preparation, a substance he believed to be oxalic acid (HOOC-COOH).

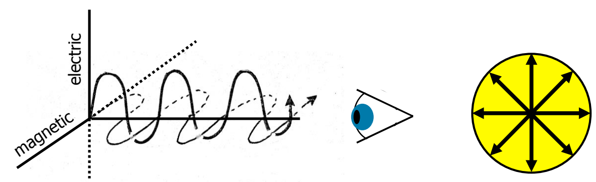
It was pointed out in a handbook in 1819 that the substance was not oxalic acid or tartaric acid. Gay-Lussac pointed out that the analytical values were identical to tartaric acid. He named the new substance racemic acid ('racemes' in Latin means a bunch of grapes).

1819 ➔ Eilhardt Mitscherlich observed that compounds known to have similar composition tend to crystallize together. He observed that racemic acid and tartaric acid both formed hemihedral crystals.

25

Seminal Discoveries in the History of Stereochemistry

- 1821-1822 ➔ Augustin Fresnel introduced a wave theory that agreed with all propterties of light at that time.
- Light behaves as a wave with a direction of oscillation perpendicular to the direction of travel.

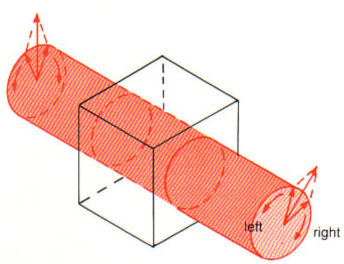


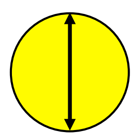
In unpolarized light, there are many waves randomly oriented to each other.

26

Seminal Discoveries in the History of Stereochemistry

- When linearly polarized light enters an optically active material, the oscillating vector is resolved into two opposite rotating vectors of equal magnitude (circularly polarized components).
- The change in direction of polarization is because the left circular light travels slower (or faster) than the right circular light.



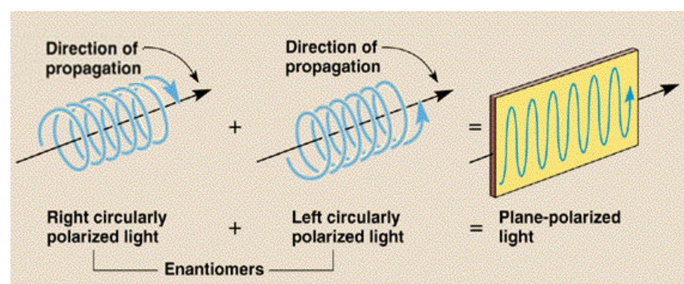


In linearly polarized light, light waves oscillate in a single direction.

27

Seminal Discoveries in the History of Stereochemistry

- Plane polarized light is comprised of right circularly polarized light and left circularly polarized light.
- Optical rotation is due to different rates of travel of circularly polarized light through an optically active material.



28

Seminal Discoveries in the History of Stereochemistry

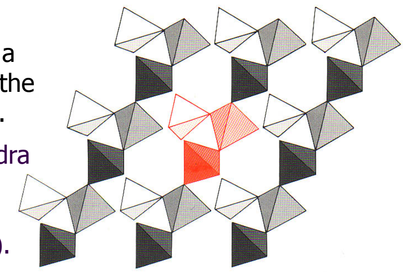
How did Fresnel explain that the refractive index of certain materials is different for the two circularly polarized rays?

"This may result from a particular constitution of the refracting medium or of its integral molecules which establishes a difference between the sense of right to left and that of left to right; such would be, for example, a helical arrangement of the molecules of the medium which would present opposite properties according as these helices were right-handed or left-handed."

29

Seminal Discoveries in the History of Stereochemistry

- In 1822 Fresnel suggested that the refractive index is different for the two circularly polarized rays because the molecules of quartz are arranged in helices.
- This was confirmed with x-ray crystallography in 1958 (De Vries).

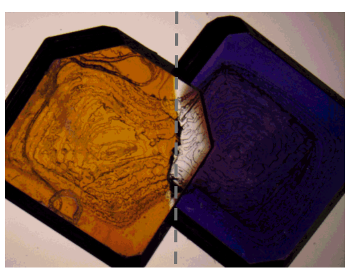


- Each tetrahedron represents a SiO_4 group (four O atoms at the corners and Si at the center).
- In the crystal lattice, tetrahedra are arranged in long helices along the optic axis (perpendicular to the screen).
- The red tetrahedra show one turn of the helix.

30

Optical rotatory dispersion

EDS crystals

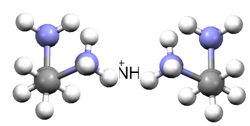


levorotatory crystal | *dextrorotatory* crystal

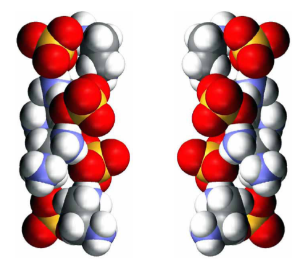
31

Ethylenediammonium sulfate (EDS)

- Groth (1910)
- Chiral space group: $P4_1$
- Ethylenediammonium: chiral gauche conformation



molecular structure of EDS



left-handed and right-handed unit cell of EDS

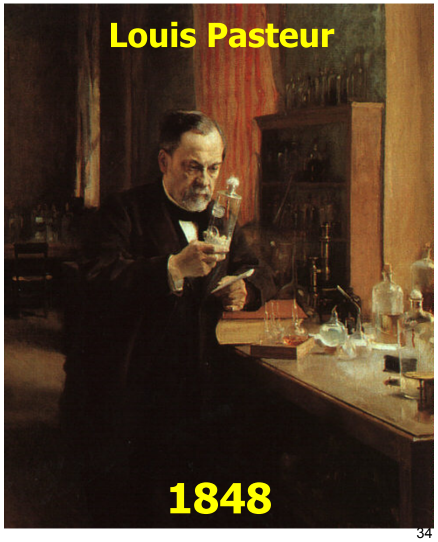
Jayaraman, K.; Choudhury, A.; Rao, C. N. R. *Solid State Sciences* **2002**, *4*, 413-422.

32

Seminal Discoveries in the History of Stereochemistry

1830 ➔ Jons Jakob Beraelius found that the two organic compounds, racemic acid and tartaric acid, had the same empirical formula. He coined the term isomerism to describe the phenomenon.

The discovery of molecular dissymmetry



Seminal Discoveries in the History of Stereochemistry

1848 ➔ Louis Pasteur studied 20 different salts of tartaric acid and noted that all were hemihedral.

He postulated that there was a relationship between crystal symmetry and optical activity.

What property of optically active molecules enables them to rotate polarized light?

Pasteur made the important finding that for a number of substances, the presence of dissymmetric crystals was correlated with the existence of optical activity in solution.

Having formulated this rule, he was disturbed to find an exception to the rule ➔ An optically inactive form of sodium ammonium tartrate that crystallized in a dissymmetric form.

➔ Mitscherlich had reported that crystals of salts of tartaric and racemic acid were identical in all respects except that all salts of tartaric acid gave dextrorotatory solutions whereas solutions of racemic acid were optically inactive.

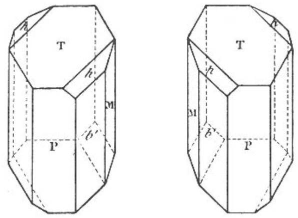
Seminal Discoveries in the History of Stereochemistry

Pasteur repeated Mitscherlich's work and was disappointed to find that crystals of racemic acid were hemihedral. ➔ But on close inspection he saw that some of the tartrate crystals were mirror images of others in this same batch.

He reported that *"the hemihedral faces which in the tartrate are all turned one way are, in the racemate, inclined sometimes to the right and sometimes to the left".*

The normal tartrate formed only one crystalline structure but the racemic salt formed crystals with some faces turned one way and some the other.

Seminal Discoveries in the History of Stereochemistry



This image shows Pasteur's drawing of the two crystal forms from his original report (1850).

The one on the left is identical to the crystals of naturally occurring optically active tartrate – a product of fermentation.

The isolated form on the right had never been seen before.

37

Seminal Discoveries in the History of Stereochemistry

Using tweezers, Pasteur carefully separated the left-handed crystals from the right-handed crystals.

When he dissolved each in water, and measured their optical rotations he discovered that one solution was dextrorotatory, identical with the known tartaric acid, while the other solution was levorotatory.

38

Seminal Discoveries in the History of Stereochemistry

"I carefully separated the crystals hemihedral to the right and the crystals hemihedral to the left; I observed separately their solutions in the polarizing apparatus. I then saw with no less surprise than pleasure that the crystals hemihedral to the right deviated the plane of polarisation to the right, and that those hemihedral to the left deviated it to the left; and when I took an equal weight of each of the two crystals, the mixed solution was indifferent towards the light in consequence of the neutralization of the two equal and opposite individual deviations."

39

"Une dissymetrie dans les molecules"

Louis Pasteur

Pasteur at 26 years old

"I have just made a great discovery - I am so happy I am shaking all over and I am unable to set my eyes again to the polarimeter."

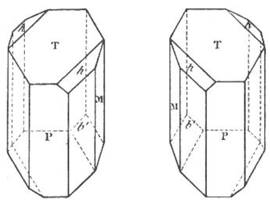
40

Pasteur & crystal shape

Crystals derived from optically active samples may be holohedral or hemihedral.

Holohedral crystals have the highest symmetry within their crystal class; each face is accompanied by a corresponding parallel face on the other side of the crystal.

In Hemihedral crystals parallel faces are absent.



Hemihedral faces are in a chiral environment ➔ Hemihedral faces turned in the opposite way identify enantiomorphic crystals.

41

Seminal Discoveries in the History of Stereochemistryc

Pasteur reasoned that the similarity of the two crystal forms implied a similarity of the molecules in most respects.

But the opposite rotations in solution told him that the molecules were not identical but were mirror images of each other.

Pasteur called this ***'molecular dissymmetry'***.

Biot was skeptical of Pasteur's results and asked Pasteur to repeat his experiments in his lab.

42

Seminal Discoveries in the History of Stereochemistry

"When [the solution] had furnished about 30 to 40 grams of crystals, he asked me to call at the Collège de France in order to collect them and isolate before him, by recognition of their crystallographic character, the right and left crystals, requesting me to state once more whether I really affirmed that the crystals which I should place at his right would deviate [polarized light] to the right, and the others to the left. This done, he told me that he would undertake the rest....

43

Seminal Discoveries in the History of Stereochemistry

He prepared the solutions with carefully measured quantities, and when ready to examine them in the polarizing apparatus, he once more invited me to come into his room.

He first placed in the apparatus the more interesting solution, that which ought to deviate to the left.

Without even making a measurement, he saw by the appearance of the tints of the two images, ordinary and extraordinary, in the analyzer, that there was a strong deviation to the left.

Then, very visibly affected, the illustrious old man took me by the arm and said, "My dear child, I have loved science so much throughout my life that this makes my heart throb".

– Pasteur 1897

44

Seminal Discoveries in the History of Stereochemistry

Louis Pasteur (1822-1895)

- In 1848 Pasteur resolved (separated) an optically inactive substance (sodium ammonium tartrate) into two optically active components.
- Each of the optically active components had properties identical to tartaric acid (density, melting point, solubility, etc.) except that one of the components rotated the polarized light clockwise (+) while the other component rotated the polarized light by the same amount counterclockwise (-).

Seminal Discoveries in the History of Stereochemistry

Louis Pasteur (1822-1895)

- Pasteur made a proposal that still stands as the foundation of stereochemistry: *The twin molecules of tartaric acid were mirror images of each other!*

Additional research by Pasteur revealed that one component of tartaric acid could be utilized for nutrition by micro-organisms but the other could not.

Pasteur concluded that biological properties of chemical substances depend not only on the nature of the atoms comprising the molecules but also on the manner in which these atoms are arranged in space.

Seminal Discoveries in the History of Stereochemistry

Louis Pasteur (1822-1895)

The fact that some molecules can be left or right-handed helps set the complex rules of chemical structure.

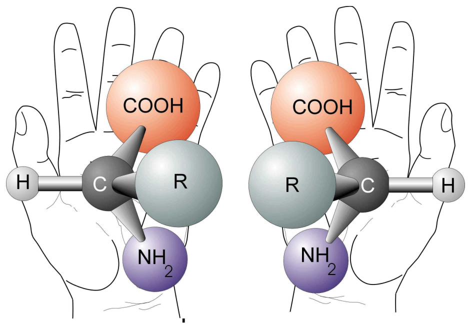
Chance played its part in Pasteur's discovery. He prepared his racemic acid on a cool window sill. Above 23 ºC he would have obtained mixed crystals.

He was also fortunate that sodium ammonium tartrate forms an equimolar mechanical mixture of enantiomeric crystals (conglomerate).

"Chance favours only the prepared mind." – Louis Pasteur

Seminal Discoveries in the History of Stereochemistry

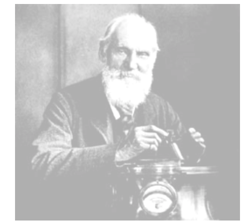
Seminal Discoveries in the History of Stereochemistry



van't Hoff recognized that a carbon atom with four different substituents arranged in a tetrahedron would account for the two isomers observed experimentally.

Seminal Discoveries in the History of Stereochemistry

Definition of Chirality



W.H. Thompson (Lord Kelvin)

➔ 1884 Baltimore Lectures:

"I call any geometrical figure, or any group of points **chiral** (χειρ, greek for hand), and say it has chirality, if its image in a plane mirror, ideally realized, cannot be brought to coincidence with itself".

Seminal Discoveries in the History of Stereochemistry

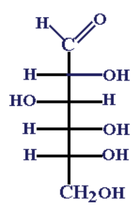
Emil Fisher (1852-1919)

In 1894 Fisher performed one of the most remarkable feats in the history of chemistry:

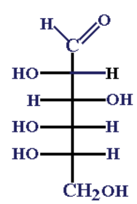
He identified the 16 stereoisomers for the aldohexoses ($C_6H_{12}O_6$), the most prominent member being D-glucose.

Fisher used cross representations (now called Fisher projections) to distinguish three dimensional shapes.

2nd Nobel Prize 1902

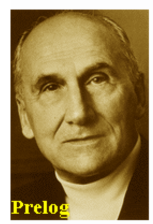


D-Glucose



L-Glucose

Seminal Discoveries in the History of Stereochemistry



Vladmir Prelog (1906-1998)

Prelog was awarded Nobel Prize in chemistry (1975) for research into the stereochemistry of alkaloids, antibiotics, enzymes, and other natural compounds.

He designed the stereochemical descriptors used today: **R/S** designations for enantiomers and **Z/E** for diastereomers.