Lecture 17: Molecular Shapes
  • Valence Shell Electron-Pair Repulsion (VSEPR) Theory

Lecture 18: Effects of Molecular Shape
  • Chemical Communication
    • Smell, Receptors, The Lock and Key
  • Liquid Crystals

Lecture 19: Water
Molecular Shape and Function

We have seen that shape is one of the defining characteristics of molecules. Molecular shape can be determined by considering the number of bonding and non-bonding electron pairs surrounding an atom, using VSEPR theory.

In large molecules such as organic compounds, many atoms may play a role in determining the overall shape and flexibility.

The second characteristic of organic molecules is the number, type, and arrangement of functional groups. These are also important in defining molecular shape as well as reactivity and function.
Smell: Benzaldehyde & Vanillin

Benzaldehyde, which we have seen before, has a strong smell of bitter almonds.

Phenylethanal, which differs by only one -CH₂- group, smells of the flower hyacinth (and is known as hyacinthin).

Vanillin, one of the main ingredients of the vanilla bean, is a derivative of benzaldehyde that includes an -OH group as well as an -OCH₃ group attached to the benzene ring.

The R-O-R’ functional group is called an ether.

Why do these similar molecules smell so different?
Chemical Communication: The Lock & Key

Smell is one of the very few ways that we can **directly** sense chemicals in the world around us. Our sense of smell is directly connected to one of the oldest and most primitive parts of our brain. For this reason it is believed to be one of the first senses to have developed. (This is also conjectured to be why smells are often strongly connected to emotional responses and memories.)

When we smell something, a molecule directly stimulates a **receptor** in our *olfactory epithelium*, a bare nerve ending. Unlike pain, smell is discriminating. **Vanillin** does not smell like **benzaldehyde** or **phenylethanal**.

There are over 30 different kinds of **anosmia**, or partial odour “blindness.” This suggests at least 30 different kinds of receptors that can discriminate between molecules.

The process by which we smell is not completely understood. However the mechanism of recognition of a receptor for a smelly molecule is based on **molecular shape**. We can regard the receptor as a lock and the stimulant molecule as a key that somehow matches it.
Shapes of Smell Receptors

There are many open questions about how molecules actually stimulate such receptors, but the idea of shape recognition is a well-established one in the biological arms of chemistry such as biochemistry and pharmacology. It also applies to taste, as well as to many intermolecular interactions including enzyme catalysis, drug action, nerve action, pheremones,...

The shapes of a few smell receptors are shown schematically at right.

E.g.

“Sweet-aromatic” receptors respond to benzene-like molecules.

“Fatty” refers to long alkane or alkene chains.
Perfumes: Musk and Civet

The most expensive animal product in the world is musk, which is extracted from the anal glands of the Ethiopian civet cat, or rutting Himalayan musk deer. At about $44,000 per kg, it is around three times as expensive as gold, and is an ingredient in perfumes and fragrances.

Musk is a mixture, but the key active compounds are fifteen- and seventeen-membered rings with a ketone functional group. Such large ring structures are uncommon in nature.

Unlike benzene and other small rings, these larger rings are quite flexible.

This is a general feature of long alkane chains. Groups can rotate around single C-C bonds, giving them a lot of flexibility.

Current practice involves chemical synthesis that has largely replaced these animal products.
Other Types of Receptors: Opiates

Opiates are one of many drugs that operate through receptors.

Shown at right is the shape of an idealised receptor for this class of compounds, together with the structure of two typical opiates, morphine and heroin.

The receptor has a flat surface that accommodates the planar rings, a cavity for the protruding groups, and an anionic charge centre. This attracts the nitrogen which is positively charged by the addition of a proton (H\(^+\)) in solution.

![molecule structures]
Agonists and Antagonists

Drugs like morphine and heroin interact with a receptor site and produce a physiological effect. These are known in pharmacology as agonists.

Molecules that act at a receptor but do not produce a physiological effect are known as antagonists. That is, they compete with the drug for uptake at the receptor site, and can effectively block uptake and hence the physiological effect. Antagonists generally have similar structures and shapes (some similar components) as the agonists they block.

The existence of antagonists for opiates is a strong piece of evidence that they work by interacting with receptors.
Representing Receptors and Substrates

The lock and key concept is so widespread that the role of molecular shape is often presented reduced to its most basic idea. E.g. The interaction between an enzyme, E, and a substrate, S, is represented without any molecular detail except for the idea of shape recognition.

In other cases the level of detail known is much greater.

E.g. the structure of hexokinase and the details of its interaction with glucose as shown at right. The hexokinase closes about the glucose molecule.
Condensed Phases

Condensed Phases is the general description given to states of matter in which the molecules are close to each other. That is, everything except gases and supercritical fluids (dense, high-temperature gases).

Condensed phases form because of attractions between the atoms, ions, or molecules that make them up. We have already looked at some classes of crystalline solids:

- **Ionic Solids (salts).** These form because of attractive electrostatic interactions between cations and anions. As an attraction, this lowers potential energy.

- **Covalent (Network) solids.** These form due to electron delocalisation into covalent bonds between atoms. Bond formation lowers the total energy.

- **Metals.** These form due to electron delocalisation throughout the material.
Molecular Solids

These crystalline solids overlook a huge and important class of condensed phases whose properties depend on other kinds of intermolecular attractions.

Atomic and molecular solids are made up of discrete molecules held in their positions on the crystal lattice by a variety of other attractive forces. We have seen how bonds, functional groups, and entire molecules may have dipoles. These lead to weaker interactions than those between ions, but are still electrostatic in origin.

Two other important classes of intermolecular attractions will be discussed later. These are Hydrogen Bonds and Dispersion Forces.

The structure of these solids depends on both the shape and the nature and strength of the intermolecular attractions between the molecules.
Solids, Liquids and Gases

The normal sequence of phases we expect to see on warming is

Solid $\rightarrow$ Liquid $\rightarrow$ Gas

The melting transition from solid to liquid is not a good way of measuring intermolecular forces, as the molecules are held together by attractive forces in both phases. In order to get an idea of the strength of the interaction, we need to separate the molecules. This requires a transition to a gas, i.e.

\[
\text{Liquid} \rightarrow \text{Gas (vaporisation or boiling)} \\
\text{Solid} \rightarrow \text{Gas (sublimation)}
\]

Low boiling or sublimation points indicate weak intermolecular interactions, and high boiling points strong ones.

Melting points (Solid $\rightarrow$ Liquid) can only be used as a rough guide, as the melting point must be below the boiling point.
Intermolecular Forces

1. Non-polar atoms and molecules
   Low boiling points E.g. Ar $T_b = 87K$; $N_2$ $T_b = 77K$

2. Polar molecules
   Broad range of boiling points depending on attractions. (More details later)
   E.g. Propane $T_b = 231K$; chloromethane $T_b = 249K$; acetonitrile $T_b = 392K$.
   Boiling point increases with increasing dipole moment of molecule.

3. Metals
   High $\rightarrow$ very high boiling points. (Only Hg and Ga liquid near room temp.)

4. Salts
   Very high boiling points. Extremely difficult to put an ion into the gas phase.

5. Network Solids
   Very high boiling points. You have to break covalent bonds to make a vapour.
Liquids

Most molecules form liquids when they melt. That is, a disordered *isotropic* structure. A simple view of melting is that enough thermal energy is provided to shake the molecules off their lattice points.

This raises an important point about materials that we often overlook. The atoms and molecules are constantly moving.

*In solids, atoms and molecules *vibrate* around their equilibrium position on the crystal lattice. Packing is determined by molecular shape.*

*In gases they move ballistically (translation) and tumble (rotation), as well as vibrating internally. The mean free path between collisions in a gas is long. Shape doesn’t matter much.*

*In liquids they collide with their neighbours, so their motion is not ballistic but diffusive. (Molecules wobble their way through the crowd.) They also *vibrate* and *rotate* as they move.*

In liquids, rotations, vibrations, and flexibility smear out the effects of shape, so that most molecules “act like spheres.”
Liquids versus Liquid Crystals

Benzene melts from the crystal into a liquid. Although its aspherical shape allows it to interact with a receptor, in the liquid it adopts an isotropic structure by rotational motions.

However more anisotropic molecules can form liquid crystals due to anisotropic interactions with their neighbours. The molecule p-azoxyanisole (PAA, below) does not melt directly into a liquid state, but instead

\[ \text{Solid} \rightarrow \text{Nematic Phase} \rightarrow \text{Liquid} \]

Its shape is not so easily averaged out by tumbling about its long axis.
The nematic phase of PAA is an example of a thermotropic liquid crystal, a liquid crystal formed by heating. (The other kind is a lyotropic liquid crystal, formed by mixing with a solvent.)

In a nematic phase, the molecules exhibit preferential orientation in a particular direction - orientational order.

The long axes all point in roughly the same direction. This requires the molecule to be both elongated and rigid. E.g. PAA and other nematic phase formers have highly delocalised MO’s

Further heating increases the tumbling and induces a conventional (isotropic) liquid.
Smectic or Layered Phases

Rigid rod-like molecules also form liquid crystals with positional as well as orientational order. These are called smectic phases, and form at lower temperatures than nematic phases.

In a smectic phase, the molecules are aligned but also organised in layers. This is due to packing of the rigid groups and also due to some entanglement and intercalation of the flexible alkyl chains.

In the smectic A phase the molecules are layered and oriented on average normal to the layers.

In the smectic C phase the molecules are layered and more highly oriented at an angle to the layer normal.

The normal sequence (if all phases are present) is

Solid $\rightarrow$ Smectic C $\rightarrow$ Smectic A $\rightarrow$ Nematic $\rightarrow$ Liquid
Properties of Liquid Crystals

The molecular alignment in liquid crystals gives rise to a number of properties intermediate between liquids and crystals that are technologically important.

1. Flow behaviour
   Liquid crystals are often quite viscous, but do flow. They can be poured into moulds and take on the shape of the container, or spread into thin films.

2. Optical Characteristics
   Liquid crystals interact differently with light of different polarisations. Because the molecules are all aligned, the electrons are not distributed isotropically as they are in the liquid state. This has two consequences

   Polarised electronic spectroscopy. The UV absorbance spectrum depends on the orientation of the electric field (polarisation) of light with respect to the molecular axis.

   Birefringence. The refractive index of light transmitted through a liquid crystal also depends on its polarisation. This also occurs in anisotropic crystals.
Optical Textures in Liquid Crystals

The large scale structure of liquid crystals is similar to that of a powdered solid. They consist of domains of similar orientation. However because of the less highly-developed order, the domains and molecular orientations are flexible.

This can lead to a combination of effects including structural defects. In stiff, highly-ordered smectic phases these look like tears under a polarising optical microscope.

In the more fluid nematic phases the optical texture is more “gentle.”
Liquid Crystal Displays

The birefringence and phase transitions of liquid crystals can be used to create displays in several ways.

Nematic phases are quite fluid, so the molecules can re-orient and align themselves quickly in a magnetic or electric field. In the unoriented state, as we have just seen, they contain a large number of defects and this makes them poor transmitters of light. However in the aligned state they will transmit light, or allow it to be reflected from a surface. This allows them to be used to create a light-dark contrast and hence as a display.

In the simple display shapes shown, each element can be turned on or off by applying an electric field and switching it from dark to light.

The 7-element unit can be used for digits as in a calculator, or the 14-element display can be used for letters & numbers.
Smectic phases are in general too stiff to re-orient quickly enough for use as a display. Instead some smectic LCDs use local heating to induce phase transitions.

A region is heated with an applied voltage to cause a transition to a lower viscosity phase. Individual pixels are then allowed to cool with or without a lower applied voltage. Those with no voltage cool into a polycrystalline, scattering (opaque) state, whereas those with a voltage cool into an aligned, clear state. This achieves contrast, but more slowly than the nematic LCDs.

Colour displays can achieved in both of these implementations simply by including dye molecules into either of the liquid crystals in various pixel elements.

Colour displays are also constructed using optical interference effects, but these are outside the scope of this course.
Lyotropic Liquid Crystals

Lyotropic liquid crystals are formed from aggregates of smaller molecules in a solvent, usually water. They are also a direct consequence of molecular shape and intermolecular forces, but in this case molecular shape determines the aggregates formed, and the aggregate shape defines the liquid crystal.

Lyotropic liquid crystals are formed by *amphiphilic* molecules. These are molecules that contain water-soluble (hydrophilic) and water-insoluble (hydrophobic) groups. This class of molecules includes soaps, detergents, and biological lipids.

The oleate anion (a soap) \[
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3\text{COO}^-\]

The dodecylsulfate anion (a detergent) \[
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3\text{SO}_3^-\]
Lyotropic Liquid Crystals

Amphiphilic molecules aggregate into spherical, cylindrical, or planar (bilayer) structures according to the shape of the molecule. Molecules with large hydrophilic (‘head’) groups form spheres, and those with small heads form bilayers.

These aggregates then organise themselves into structures known as:

- **cubic phases** (spheres)
- **hexagonal phases** (cylinders)
- **smectic or lamellar phases** (bilayers)
Summary

You should now be able to

- Explain the lock-and-key hypothesis for molecular recognition as it relates to smell and other chemical communication processes.
- Define agonists and antagonists
- Describe nematic and smectic A & C thermotropic liquid crystals
- Describe cubic, hexagonal and lamellar lyotropic liquid crystals
- Explain the general features of the liquid crystal state, and distinguish between lyotropic and thermotropic lc’s, and a simple liquid.
- Describe how lc’s can be used to generate displays
- Relate intermolecular forces to boiling points.

Next Lecture

Water