The Shapes of Organic Molecules

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Organic Molecules

MODERN CHEMISTRY BACKGROUND READERS

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Head of Chemistry, Glasgow Academy

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Preface

You can't depend on your eyes when your imagination is out of focus.

MARK TWAIN

The purpose of this small book is to persuade the student of organic chemistry to think in three dimensions about even the simplest molecule or reaction. So often in introductory treatments the spatial aspects are reserved as a separate 'topic' discussed late in the course. This is why the title has avoided the term 'stereochemistry' which, for many, implies such narrow concepts as lactic and maleic acids, asymmetric carbon atoms and optical activity.

The text falls roughly into three portions. The first deals with the molecular architecture of simple compounds and is mainly three-dimensional geometry. The chemical and biochemical implications of this geometry are discussed and illustrated in the second section, while the third affords a brief glimpse at the fascinating architecture of some complex molecules of biological importance. Some small topics requiring amplification, which would otherwise interrupt the flow of the main text, have been collected together as an Appendix.

I am most grateful to Messrs Griffin and George for the loan of molecular models, to the Department of Employment and Productivity for financial assistance, and to my wife for her tolerance and an inexhaustible supply of coffee.

Wye College (University of London)   N. G. Clark
near Ashford, Kent

Nomenclature

Throughout the text, I.U.P.A.C. organic nomenclature has been used. However, in many cases of historical or traditional usage, it is not systematic; nevertheless, it employs the *preferred* I.U.P.A.C. names. Where the latter are first encountered, they are accompanied in brackets by their systematic equivalents (if considered helpful); throughout the text, occasional reminders are inserted as appropriate. Systematic names are cross-referred to preferred names in the Index.

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William Hyde Wollaston was a brilliant but eccentric English chemist and philosopher who was predicting, as early as 1808, that chemists would one day have to imagine molecular architecture in three dimensions. The advantages of doing this are now so obvious (and so fascinating) that it is shameful to realise it has become general practice only within the last few years. The fact that printed pages, blackboards and projection screens are two-dimensional might provide an explanation, but not an excuse.

Take, for example, the simplest organic compound, methane CH_4, which undergoes mono-chlorination to give *only one* compound of formula CH_3Cl. This and similar evidence points to the equivalence of the four hydrogen atoms in the methane molecule—otherwise CH_3Cl would represent two or more chloromethanes. How, then, may the structure of methane be pictured so that all four hydrogen atoms are equivalent? This is illustrated by the structures in Fig. 1:

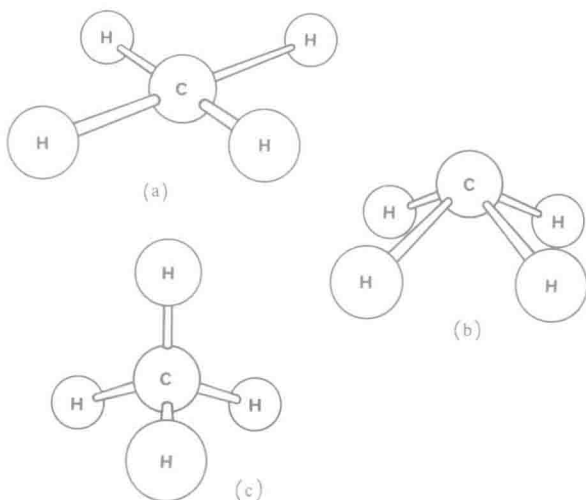(a) *planar*, with the hydrogen atoms at the corners of a square (or rectangle) and the carbon atom at the centre;

Figure 1

1

(b) *pyramidal*, with the hydrogen atoms at the corners of a square base and the carbon atom at the apex;
(c) *tetrahedral*, with the hydrogen atoms at the corners of a regular tetrahedron and the carbon atom at the centre.

By replacing any one of the hydrogen atoms in structure (a) by a chlorine atom, a structure for CH_3Cl is obtained; by repeating this operation with any other hydrogen atom in structure (a), a second structure for CH_3Cl is (apparently) produced. It is easy to visualise, or demonstrate with models, that the two resulting structures for CH_3Cl are identical in every respect and are *superimposable*; in other words they represent two identical molecules. The same argument may be seen to apply (with perhaps a little more imagination) to structures (b) and (c). Had the alternative structures not been superimposable, they would have represented different compounds, that is, *isomers*. Which, then, of the three feasible structures for methane is correct?

It has been found that further chlorination of chloromethane again leads to *only one* compound of formula CH_2Cl_2. On replacing two hydrogen atoms by chlorine atoms in each of the methane structures (a), (b) and (c), it is found that only the latter gives a unique solution. By
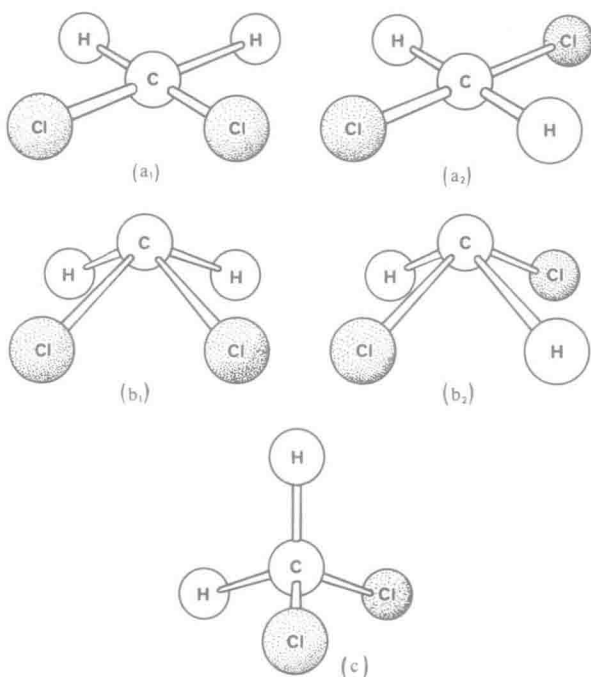

Figure 2

contrast, structure (a) leads to two alternatives (a_1) and (a_2) (three in the case of a rectangle), while structure (b) leads to two alternatives (b_1) and (b_2) (Fig. 2). Consequently methane can be represented correctly only by the molecular structure (c) (Fig. 1). This argument, based on the possible number of isomeric structures, was used in 1874 by van't Hoff when, as a 22-year-old Dutch student, he published (at his own expense) his famous pamphlet on stereochemistry.

It is salutary to note that Gaudin, a pupil of Ampère, had already postulated the regular tetrahedral structure for methane in 1865.

Bond lengths and bond angles

It is unfortunately not possible to 'see' molecular structures in three dimensions, but the reality of the situation was accepted with increasing confidence during the later part of the nineteenth century as the classical hypotheses of Wislicenus, Pasteur, van't Hoff and others were seen to explain and correctly predict many cases of isomerism. The advent of sophisticated physico-chemical techniques involving dipole moments and spectral properties, especially infra-red (i.r.) and nuclear magnetic resonance (n.m.r.) spectra, has provided quantitative and indisputable confirmation. Electron and X-ray diffraction studies have allowed a close approach to actually 'seeing' molecules.

These modern studies have provided accurate measurements of inter-nuclear distances (bond lengths) for a wide variety of organic (and inorganic) molecules. As a consequence it has become clear that many of these values are relatively constant and are characteristic of the individual atoms and their valency state. Thus, in the case of organic compounds, it is possible to deduce from a set of values for

Table 1 Some covalent and van der Waals radii

Element	Covalent radius/nm*			van der Waals radius/nm
	Single	Double	Triple	
C	0.077	0.067	0.060	
N	0.070	0.060	0.055	0.15
O	0.066	0.055		0.14
S	0.104	0.094		0.19
P	0.110	0.100		0.19
Si	0.117			0.20
F	0.064			0.14
Cl	0.099			0.18
Br	0.114			0.20
I	0.133			0.22
H	0.030			0.12

*1 nm (nanometre) = 10 Å (angström).

covalent inter-nuclear distances what portion of those distances is attributable to individual atoms. By the adoption of the somewhat naive picture of a molecule as a cluster of spherical atoms in contact, each atom can be ascribed a value for its *covalent radius*; some of these are given in Table 1.

Similarly the directions in which other atoms disport themselves around a polyvalent central atom has led to the concept of *bond angle*, many bond angles being sufficiently constant to be regarded as normal for a particular atom and valency state. Some important examples are illustrated in Fig. 3.
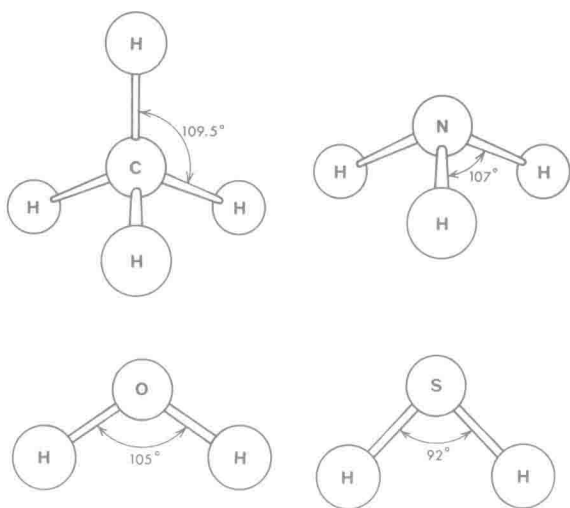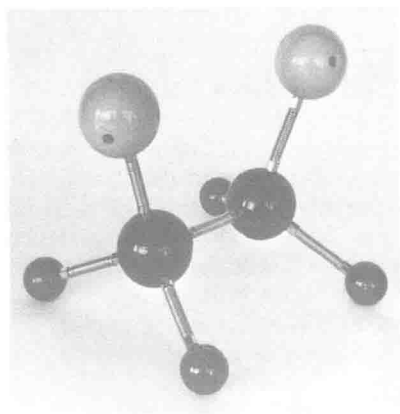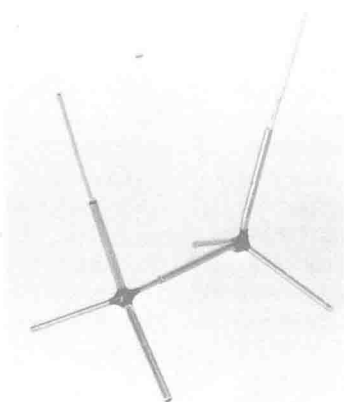

Figure 3

When atoms are not held together as molecules through covalent bonding, they may nevertheless attract one another at relatively short distances by weak van der Waals forces. There comes a point, however, as the atoms approach one another more closely, when the weak attractive force is replaced by a rapidly increasing repulsive force. Consequently there is an equilibrium position (the distance of closest approach) where the two opposing forces balance each other; in the picture of a spherical atom this corresponds to the two spheres 'touching'. The distance of closest approach has been calculated for many atoms from X-ray crystallographic measurements, and allows the allocation of a *van der Waals radius* to individual atoms—a quantitative expression of their effective 'size'. Some of these are also given in Table 1. It will be seen (as is to be expected) that these are all larger than the corresponding covalent radii.

Molecular models

It will be clear from the previous section that the dimensions of individual atoms are sufficiently well known and constant to enable scale models to be constructed, from which the structures of molecules can be assembled. They are valuable aids to the imagination with even simple compounds, and are indispensable in the case of proteins, nucleic acids and so on. The many makes of molecular models may be classified into three groups.

(a)

(b)

(c)

Figure 4

(a) 'Ball-and-spring' models are the oldest and are best suited for considering the geometry and symmetry of relatively simple molecules. They concentrate solely on bond angles and ignore atomic radii; the coloured balls used to distinguish different atoms take no account of van der Waals radii.

(b) Dreiding models dispense with atomic balls as such, retaining only sufficient material to ensure that the union of several valency bonds is structurally sound. The bonds themselves consist of hollow or solid metal rods, proportional in length to atomic radii, which are joined together at the appropriate bond angles; covalent bonds are formed by slotting a solid rod into a hollow rod. Bond lengths and angles are thus correctly represented, but the 'bulk' of the atoms is missing.

(c) Stuart models comprise solid spheres whose faces are cut away at appropriate angles to enable union with other spheres. This is achieved by inserting short plastic tubes into holes in the cut faces of the spheres, thus allowing a degree of flexibility in the 'bond'. The spheres are of a size proportional to the atoms' van der Waals radii, but the faces are cut so that the spheres may be joined together at distances proportional to the (smaller) atomic radii. These space-filling models give an excellent representation to scale of the 'bulk' of a molecule; as a consequence there is a certain loss of clarity with bond angles.

Models representing 1,2-dibromoethane $Br \cdot CH_2 \cdot CH_2 \cdot Br$ are shown in Fig. 4.

Abnormalities

The feasibility of using standard models is based on the experimental finding that certain values of bond lengths and bond angles are 'normal' for specific atoms and valency states. Deviation from the expected values indicates some abnormality in the molecule, and such abnormalities are generally attributable to either steric or electronic factors (although it is arguable whether these two factors can be entirely separated).
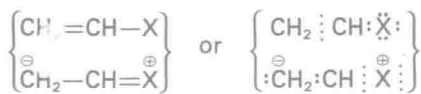
A simple example of the former is provided by the dihalogenomethanes, CH_2X_2. When the halogen atom X is the small fluorine atom, there is plenty of room to attach two of them to the same carbon atom without distorting the normal tetrahedral angle, 109.5°. As the size of the halogen atom increases through chlorine to bromine, the natural tetrahedral angle becomes slightly enlarged (112°), until the effect is at its maximum with two massive iodine atoms (115°) (this 'bulk' effect is admirably demonstrated using Stuart models, although the widening of the bond angle is not clear).

An electronic effect is nicely demonstrated by the vinyl halides (halogenoethenes), $CH_2=CH \cdot X$. It will be seen from Table 2 that the

Table 2 Some inter-nuclear distances d

'Pure' bonds: d/nm				Abnormal: d/nm
C—C	0.154	C—F	0.138	C=C—F 0.134
C=C	0.134			
C≡C	0.120			
		C—Cl	0.178	C=C—Cl 0.172
C—N	0.147			
C=N	0.132			
C≡N	0.116	C—Br	0.194	C=C—Br 0.189
C—O	0.143			
C=O	0.123	C—I	0.214	C=C—I 0.209
C—S	0.182			
C=S	0.162			

inter-nuclear distance decreases as the type of bonding between two atoms changes from single to double and finally to triple. Further inspection shows that the carbon–halogen bond in all the vinyl halides is significantly *shorter* than the normal single bond distance, thus implying a proportion of multiple-bond character in all of them. This is regarded as evidence for the delocalisation of electrons within the molecule of a vinyl halide, represented by the two contributing structures in Fig. 5. Similar arguments have been used widely to support electronic interpretations.

$$\begin{Bmatrix} CH_2 {=} CH{-}X \\ \overset{\ominus}{CH_2}{-}CH{=}\overset{\oplus}{X} \end{Bmatrix} \quad or \quad \begin{Bmatrix} CH_2 \vdots CH \colon \ddot{\ddot{X}} \colon \\ \colon \overset{\ominus}{CH_2} \colon CH \vdots \overset{\oplus}{X} \colon \end{Bmatrix}$$

Figure 5 Electronic structures of the vinyl halides (halogenoethenes)

One asymmetric carbon atom

Turning once again to the methane molecule, and the distribution of the hydrogen atoms at the corners of a regular tetrahedron round the carbon atom, van't Hoff demonstrated that replacement of three of the hydrogen atoms by three different atoms (or groups) could be achieved in two ways. This is illustrated in Fig. 6 by bromochlorofluoromethane, the simplest organic compound of this type, the two forms of which have only very recently been prepared. It is not possible to superimpose the two models, and consequently they represent two isomeric compounds. Further, it is important to notice that each structure is the mirror-image of the other; this can be appreciated quite easily by
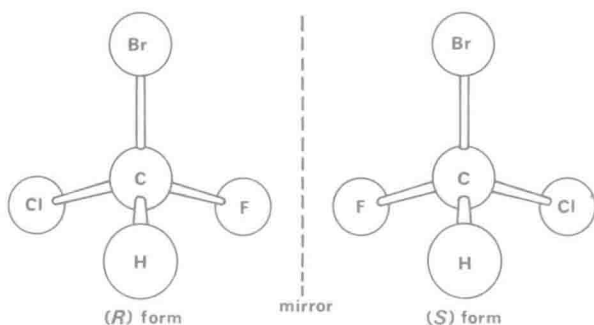
Figure 6 The two enantiomers of bromochlorofluoromethane

imagining a plane mirror placed in the position shown. Mirror-image isomers are known as *enantiomers*. A molecular structure that is not superimposable on its mirror image is *dissymmetric* (or *chiral*), and this is the only condition necessary for the existence of enantiomers.

Bromochlorofluoromethane contains the structural feature most commonly responsible for the occurrence of enantiomers in simple organic compounds, viz. an *asymmetric carbon atom*; this is one covalently linked to *four different* atoms (or groups). It is generally quite easy to detect in the structural formula of a compound and will give rise to a pair of enantiomers.

The above concept of van't Hoff is pure three-dimensional geometry and, so far, need not have involved chemistry at all. What he was able to show, however, was that many simple organic compounds, already known to be structural isomers, contained an asymmetric carbon atom and were related as pairs of enantiomers. In addition, if either of the pair of enantiomers underwent a reaction in which the asymmetric nature of the carbon atom was destroyed, the same (symmetrical) product was obtained.

To add a little more reality to this topic let us try to predict the sort of physical and chemical properties to be expected from a pair of enantiomers. On examining again the two structures in Fig. 6, it becomes clear that, in each of them, the fluorine atom is the same distance from the carbon atom, the chlorine atom is the same distance from the carbon atom, the fluorine–carbon–chlorine angles are identical, and so on. In other words the dimensions and geometry of the two enantiomers are identical, except for the spatial arrangement of the atoms which characterises each enantiomer; this is known as its *configuration*. (Fig. 6 illustrates the two possible configurations of bromochlorofluoromethane designated (*R*) and (*S*).*) It must surely

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*See the Appendix for a discussion of these symbols.

be expected, therefore, that enantiomers exhibit identical physical and chemical properties. This has been found to be true in all cases, with the following two general exceptions:

(*a*) in a chemical reaction, if the reagent is itself one of a pair of possible enantiomers, the *rate* of reaction will be different for the two enantiomeric starting materials (this is the basis of some remarkable specificity in biochemistry and physiology; see pp. 92 et seq.);

(*b*) the two enantiomers exhibit differing optical behaviour towards plane-polarised light.

Optical activity

A ray of ordinary light consists of electromagnetic vibrations in all directions at right-angles to the direction XY in which the light is
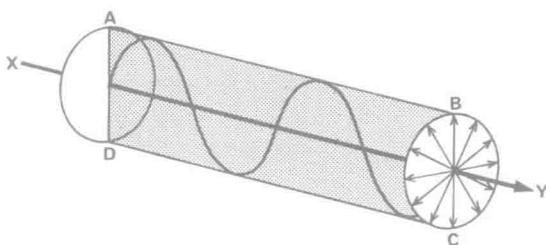

Figure 7

travelling (Fig. 7). One of these vibrations, represented by the wave-shape lying in the plane ABCD, corresponds to the diameter BC, but all the other infinite number of diameters (some of which are indicated) have their own wave-shape, and the light ray consists of a complete 'cylinder' of these transverse vibrations. Plane-polarised light, how-ever, comprises transverse vibrations in one plane only (the plane of polarisation, e.g. ABCD).

In 1815 the French physicist Jean-Baptiste Biot discovered that certain crystals, for instance quartz, were capable of rotating the plane of polarisation when a beam of plane-polarised light was passed through the specimen. While performing some routine crystallo-graphic work (for experience) Louis Pasteur, in 1848, discovered that the crystals of many salts were capable of rotating the plane of polarisation *even when dissolved*. This led him to the conclusion that the observed optical activity of these compounds was due to their *molecular* structure and not that of the crystals. He further suggested that molecular dissymmetry (chirality) was the cause of the plane of polarisation being rotated and, as any dissymmetric (chiral) structure had a mirror-image partner, each partner would rotate the plane of