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THE
CARBON ATOM

*Inaugural Lecture of the
Professor of Chemistry
delivered at the College on
27 January 1949*

by

PROFESSOR C. W. SHOPPEE
D. PHIL., PH. D., D. SC., F. R. I. C.

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THE CARBON ATOM

AS a preface to this lecture, it will be appropriate to say a few words about the science of chemistry. The science of chemistry deals with the properties of the ninety-two natural elements and their compounds; there has, however, arisen a tradition of dividing the subject into three separate sections: organic chemistry comprising the study of the element carbon and its compounds, inorganic chemistry involving the study of the other ninety-one natural elements and their compounds, and physical chemistry, which may be described as the application of physical methods to the study of chemical problems involving any of the ninety-two elements. The compounds of carbon known now number almost half a million, and the foregoing division has a certain degree of practical convenience; it is, however, without any philosophical basis, and has tended to the creation in some quarters of an exclusive outlook—in brief, to the development of three closed chemical compartments. I would like to take this opportunity to emphasize the essential unity of chemistry; there are not three chemistries, but one, for the principles of chemistry must apply to *all* the elements and their compounds. Thus a student graduates, not in physical chemistry, or in inorganic chemistry, or in organic chemistry, but, simply in chemistry.

I come to this University College as the second Professor of Chemistry in succession to Emeritus Professor J. E. Coates, who occupied the Chair for some twenty-five years, and for whom I have formed a high regard during a very brief acquaintance. The Chemistry Department was created by Professor Coates, and the successful manner in which the Department has met the demands

of recent years is the best possible tribute to the thought, care, and foresight exercised by him when planning the Department some twenty-five years ago.

My teaching and research activities for the past twenty years have been connected with the compounds of carbon, and the application to them of the general principles of chemistry. I shall therefore to-night briefly discuss some properties of the carbon atom, in particular its spatial character. I think that it may be of interest to trace the development of our knowledge of the stereochemistry of carbon, and I propose to review the outstanding developments and briefly to comment upon them, to point out some practical consequences of the geometry of the carbon atom, and to indicate some unsolved problems. We shall see how an advance in one of the physical sciences is nearly always reflected in another field of knowledge. Let us therefore turn back the pages of the Book of Time to the year 1808.

In 1808, the French physicist, Etienne Louis Malus, discovered the phenomenon of the plane polarization of light; he discovered that light transmitted by a crystal of Iceland spar, a transparent variety of the doubly refracting mineral calcite, differs from normal light in being polarized in a single plane determined by the orientation of the crystal. We may picture ordinary monochromatic light as a train of waves vibrating in all planes perpendicular to the direction of propagation along the axis O (Fig. 1). The crystal permits the passage only of those light waves vibrating in a specific plane, say $X'—X$, eliminating completely those vibrating in the plane $Y'Y$ and passing only the resolved components $OK—OK'$ of other waves such as AOE . Actually the crystal transmits two rays, 'ordinary' and 'extraordinary', which are polarized in planes perpendicular to one another; by a simple optical device, termed a Nicol prism,

it is possible to arrange for complete reflection of the 'ordinary' ray, and the 'extraordinary' ray is alone transmitted. A superficial analogy to the action of a Nicol prism is that a closed book will permit insertion of a

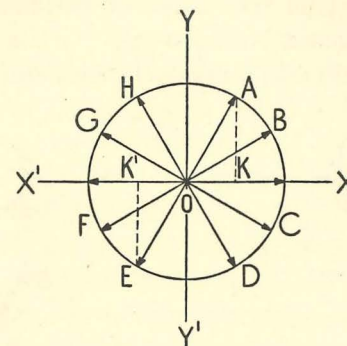


FIG. 1.

paper-knife between the pages only when the knife is held in a specific plane.

Malus died prematurely in 1812 at the age of 37, but the investigation of polarized light was carried on by the French physicist, J. B. Biot, who observed that a crystal of quartz, cut parallel to the optic axis and traversed by polarized light normal to the axis, is able to rotate the plane of polarization, and who found that some quartz crystals rotate the plane to the right whilst others rotate it to the left (*Mémoires de l'Institut de France*, 1812, 1, 1).

In 1815 the mineralogist Haüy observed that some crystals of quartz exist in hemihedral forms, each form being characterized by the presence of a set of faces arranged in either a right-handed or a left-handed manner and numbering exactly one-half of the faces required to give the usual, fully symmetrical crystal.

Sir John Herschel, in 1820, suggested that the crystallographic and optical properties of quartz were related, and, in fact, it was soon established that hemihedral

quartz crystals rotate the plane of polarized light in opposite directions; whilst in 1824 Fresnel postulated a helical arrangement of the atoms in quartz crystals (a concept proved a century later to be correct by X-ray crystallography) as the cause of their optical activity (*Bull. Soc. Philomat.*, 1824, 147).

In the year 1815 Biot made the fundamental discovery

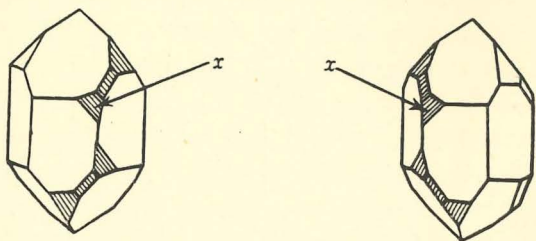


FIG. 2. *x* indicates hemihedral faces.

that a number of naturally occurring organic substances possess the power of rotating the plane of polarization either in the liquid or dissolved state, e.g. turpentine, solutions of camphor, sugar, tartaric acid. Biot immediately perceived the enormous theoretical importance of this discovery, and pointed out that whereas in the previously known phenomena exhibited by crystals such as quartz the rotation is conditioned by the crystalline form, disappearing completely as soon as that form is destroyed, here the rotation must be a property of the molecules themselves (*Bull. Soc. Philomat.*, 1815, 190).

Two years later, in 1817, Biot demonstrated the rotation of the plane of polarization by turpentine vapour, and so confirmed his deduction of the molecular origin of optical activity in organic substances (*Mémoires de l'Académie des Sciences*, 1817, 2, 114).

To-day we know that the plane of polarization can be rotated by various organic compounds in the gaseous phase. We also know that the mechanism by which opti-

cally active substances rotate the plane of polarization involves fission of the plane-polarized beam into two circularly and oppositely polarized beams of light, and the slowing down of one of the two spirals.

We must now pass over some thirty years, remarking, however, in 1844 a note on sodium ammonium racemate by the German chemist and mineralogist Mitscherlich, which Biot communicated to the Academy of Sciences. Racemic acid, a by-product of the crystallization of tartaric acid—the main acidic product of alcoholic fermentation, had been found by Berzelius in 1831 to have the same chemical composition as tartaric acid, but different physical properties. Mitscherlich reported his observations as follows (*Comp. rend.*, 1844, 19, 720):

Sodium ammonium racemate and sodium ammonium tartrate have the same chemical composition, the same crystalline form, with the same angles, the same specific gravity, the same double refraction, and therefore the same angles between their optic axes. Their aqueous solutions have the same refraction. But the solution of the tartrate rotates the plane of polarisation whilst that of the racemate is inactive; yet the nature and the number of the atoms, their arrangement and their distances are the same in the two compounds.

In brief, these two salts differ only in that one is dextro-rotatory and the other optically inactive.

In 1848 Louis Pasteur, on completion of his courses at the École Normale, Paris, sought to perfect his crystallographic technique by a repetition of work on the crystalline form of various salts of tartaric acid which had been published by de la Provostaye in 1841. Pasteur's measurements confirmed those previously reported, but he also observed that all the 19 tartrates which he examined exhibited hemihedral faces, precisely analogous to those discovered by Haiüy in quartz crystals; moreover, the hemihedral faces were all similarly situated, i.e. all the crystals were hemihedral in a right-handed

sense. Since Biot had shown that solutions of these tartrates were all dextro-rotatory, Pasteur inferred that hemihedral form and optical rotatory power were related.

Such a relationship was incompatible with the 1844 statement of Mitscherlich, viz. that optically active sodium ammonium tartrate and optically inactive sodium ammonium racemate have the *same* crystalline form.

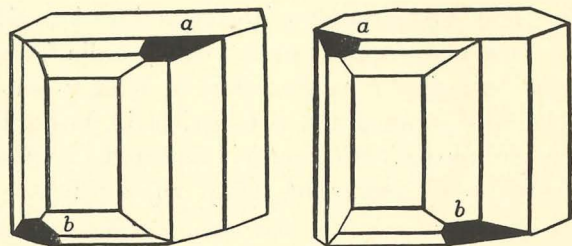


FIG. 3. Hemihedral crystals of sodium ammonium racemate.

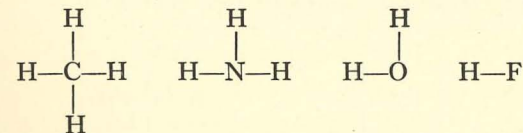
Pasteur therefore re-investigated these two salts; he found sodium ammonium tartrate to furnish hemihedral crystals like all other tartrates studied, but discovered to his intense surprise and apparently contrary to his hypothesis that sodium ammonium racemate was hemihedral also. Further, whilst in the tartrate crystals the hemihedral facets were all turned to the right, in the racemate crystals they were inclined sometimes to the right and sometimes to the left. By hand-picking, Pasteur separated the two types of racemate crystals and examined their respective solutions in water; he found that the solution of the right-handed crystals rotated the plane of polarized light to the right, and the solution of the left-handed crystals to the left. When equal weights of the two kinds were dissolved in water, the solution of the mixture, like the initial racemate, was indifferent to polarized light.

Pasteur summarized the position and anticipated the

future in a lecture to the Chemical Society of Paris delivered on 3 February 1860:

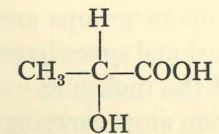
Compounds can be and really are distinct through possessing different arrangements of the atoms within their molecules. We know that the molecular arrangements of the two tartaric acids are asymmetric, and that these arrangements are absolutely identical save that they exhibit asymmetry in opposite directions. Are the atoms of the *dextro*-tartaric acid grouped in the form of a right-handed spiral, or are they placed at the apices of an irregular tetrahedron, or have they some other asymmetric arrangement? We do not know, but it cannot be doubted that there exists an asymmetric arrangement having a non-superposable image. It is not less certain that the atoms of the *laevo*-tartaric acid possess precisely the inverse asymmetric arrangement.

In 1860 Kekulé suggested that the carbon atom has always a combining capacity or valency of four and introduced the convention of attaching to the symbol for an element one short line for each available valency.



If more than one formula could be written for a compound then Kekulé's principle was to determine by experiment which one of all theoretically possible formulae is consistent with the properties and reactions of the compound.

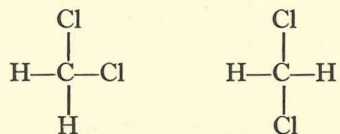
During the decade 1863-73 Wislicenus at Zürich showed that the *dextro*-lactic acid from muscular tissue and the optically inactive lactic acid from sour milk constitute two distinct chemical entities but possess the same composition and have the same structure



since they undergo the same chemical reactions to afford the same products. At the conclusion of these experiments in 1873 Wislicenus wrote:

If molecules can be structurally identical and yet possess dissimilar properties, this can be explained only on the ground that the difference is due to a different arrangement of the atoms in space.

In the following year, 1874, a theory of beautiful simplicity yet accommodating all the experimental facts adduced by Pasteur and Wislicenus during the preceding 25 years was announced simultaneously and independently by van't Hoff in Holland and Le Bel in France; van't Hoff was 22 and Le Bel 27 years of age! van't Hoff reasoned that the four carbon valencies cannot be arranged at right angles in two dimensions as in the Kekulé representations because compounds of the type CH_2R_2 exist only in one and not in two forms:



He therefore passed to a three-dimensional model, when these two-dimensional formulae become identical. The theory as stated by van't Hoff is that the four valencies of a carbon atom are directed to the corners of a tetrahedron; if four different atoms or groups are attached to the four corners, then the molecule Cabcd exists in two different non-superposable forms related as object and mirror image or as left- and right-handed hemihedral crystals. Le Bel saw that molecular asymmetry can exist if four different atoms or groups are united to a carbon atom in three-dimensional space irrespective of the actual geometrical form of the molecule.

A tetrahedral carbon atom carrying four different atoms

or groups must constitute a centre of asymmetry and permit two arrangements of the groups in space; this

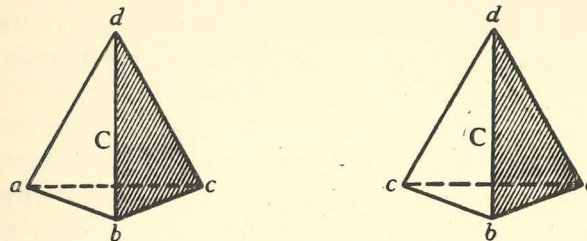


FIG. 4.

calls for the existence of two lactic acids and of two tartaric acids identical in all respects except optical properties.

For convenience, we usually employ regular tetrahedra in pictorial representations, e.g. of the *d*- and *l*-lactic acids (Fig. 5A), or the *d*- and *l*-tartaric acids (Fig. 5B):

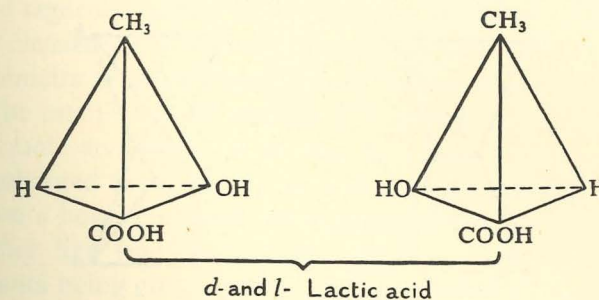


FIG. 5A.

But it should be noted that van't Hoff never specified a *regular* tetrahedron, whilst Le Bel avoided definition of the geometrical form.

In his classical paper of 1874 van't Hoff not only developed the theory of optical isomerism, but predicted the existence of a second form of stereoisomerism, on

the ground that two carbon atoms connected by a double bond, i.e. by union of two tetrahedra at *two* common apices, should be incapable of rotation, and so give rise

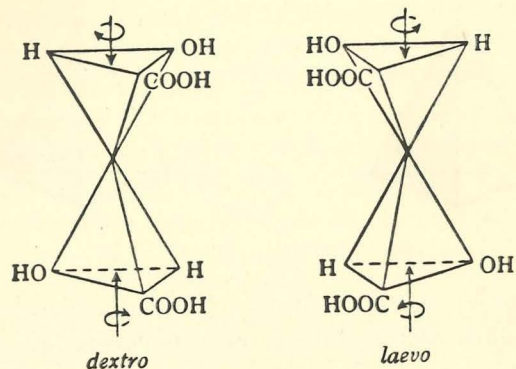


FIG. 5B.

to *cis*- and *trans*-configurations (Fig. 6); these are different but not asymmetric, for each configuration possesses at least one plane of symmetry. The existence of such

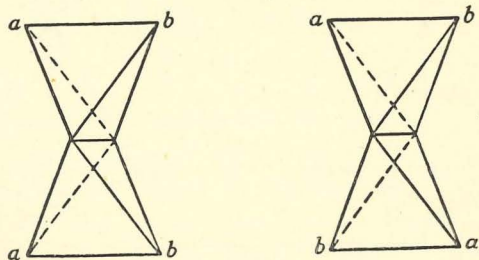


FIG. 6.

geometrical isomers was demonstrated by Wislicenus in 1887.

The theory of van't Hoff gives a complete qualitative description of the stereochemical pattern followed by the tetravalent compounds of carbon; such is its success in this sphere that no single discordant fact has been discovered during the last seventy-five years.

During recent years some advances toward a quantitative description of the stereochemical properties of the carbon atom have been achieved. These advances had their origin in the revolutionary changes which occurred in physics some fifty years ago, and in order to trace their development we must notice certain outstanding discoveries, which had tremendous consequences for both physics and chemistry. Let us therefore pass over twenty-five years from 1874 to 1897.

In 1897 Sir J. J. Thomson discovered the electron—an entity regarded as a particle weighing $1/1,800$ of a hydrogen atom and soon found to be a constituent of all matter and one of the fundamental units of the universe. The atoms of the various elements could no longer be regarded as the ultimate indivisible units of the material world.

In the year 1899 the old quantum theory was introduced by Planck. The classical Newtonian mechanics had regarded matter as consisting of atoms and radiation as consisting of waves; Planck's theory called for an atomicity of radiation analogous to that which appeared to be established for matter. It suggested that radiation, to quote an analogy of the late Sir James Jeans, was not discharged from matter in a steady stream like water from a hose, but came off in separate chunks or quanta rather like lead from a machine-gun, the size of the quanta being governed by the frequency of the radiation according to the relation $E = h\nu$.

In 1911 Lord Rutherford put forward a theory of atomic structure in which the atom was pictured as a submicroscopical solar system with negatively charged electrons revolving round a massive positively charged central nucleus. Such a structure was nevertheless incompatible with the classical mechanics, since the electrons would continually radiate energy as the result of

their orbital motion and would gradually spiral down into the nucleus.

In 1913 Bohr attempted to remedy this defect by incorporating Planck's theory of quanta. He assumed that an electron could revolve about its nucleus in certain orbits, characterized by a quantum number n , in which it contained an integral number of quanta of energy defined by the expression $E_n = Kh/n^2$, and so long as an electron remained in a given orbit there was neither emission nor absorption of radiation. If an electron passed from one permitted orbit of quantum number n_1 to another of quantum number n_2 , it emitted or absorbed energy $\Delta E = Kh(1/n_2^2 - 1/n_1^2)$, and so by Planck's relation $E = h\nu$, the frequency of the radiation involved would be $\nu = \Delta E/h = K(1/n_2^2 - 1/n_1^2)$.

The frequencies calculated in this way agreed exactly and completely with those observed in the spectrum of the hydrogen atom, which contains one solitary electron. For more complex atoms, Bohr placed the increasing numbers of electrons in various energy levels termed *K, L, M, N...* shells with a total quantum number $n = 1, 2, 3, 4...$ for circular orbits, combined with a subsidiary quantum number $l = 1, 2, 3...$ for elliptical orbits. The maximum numbers of electrons in these shells (*K* 2; *L* 8; *M* 18; *N* 32) are precisely the numbers of the elements in the six complete periods of the periodic classification, but the Bohr atomic model, whilst giving a perfect interpretation of the spectrum of the simplest atom hydrogen, failed completely with the spectra of more complex atoms.

In 1916 G. N. Lewis put forward an electronic concept of chemical reactivity: every atom strives to attain the electronic configuration of the nearest inert gas in the periodic table. Using the symbolism devised by Lewis whereby a dot represents a valency electron, it is readily

seen (Fig. 7) that lithium by loss of its one *L*-electron becomes electronically like helium with the permitted maximum of 2*K* electrons, but unlike helium it will bear a single positive charge and will form a univalent positive

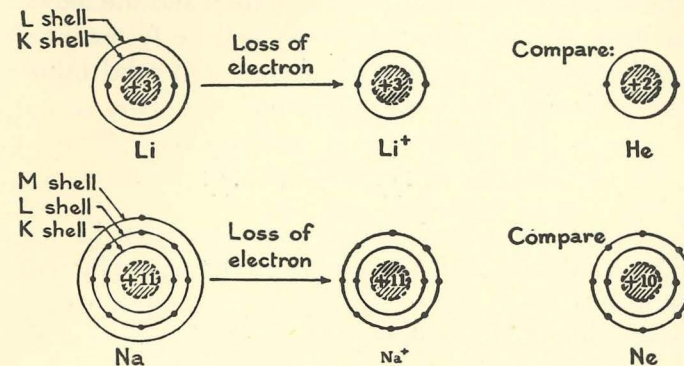


FIG. 7.

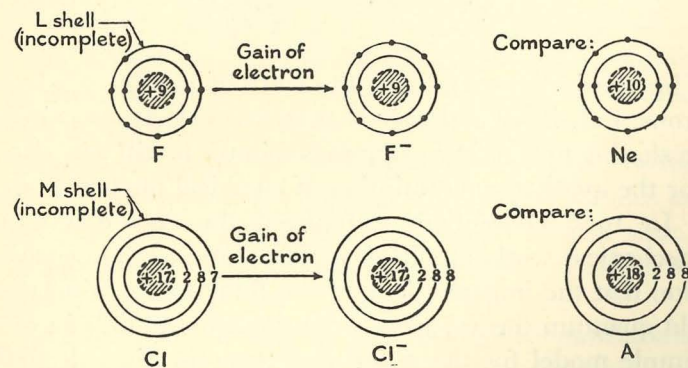
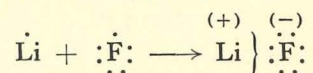


FIG. 8.

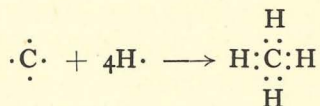
ion. Fluorine (Fig. 8) has seven electrons in its *L* shell, requiring to gain one electron to become electronically like neon with the permitted maximum of 8 *L*-electrons, but unlike neon it will bear a single negative charge and will form a univalent negative ion.

Lewis was also the first to point out that chemical bonds

may be of two types, electrovalent and covalent. If a lithium atom and a fluorine atom collide, the electronic requirements of both can be satisfied by transfer of one electron from the metal to the halogen whereby the lithium attains the helium configuration and the fluorine the neon configuration; two ions will be formed, held together only by electrostatic forces, and solid lithium fluoride is simply an ion aggregate.



A carbon atom needs four electrons to complete its octet, and can combine with four hydrogen atoms, not by transfer of electrons, but by sharing of electrons to give a non-polar structure representing the neutral hydrocarbon methane.



The Lewis theory ignores the state of motion of electrons, but, if we add only that the two electrons paired in sharing must possess opposed spins, it is still adequate for the qualitative description of chemical phenomena.

In 1925 Heisenberg introduced the new quantum mechanics; working with Bohr, he came to the conclusion that the imperfections of the Bohr atom, using the old quantum theory, arose from the assumption of a too simple model for the atom. He therefore discarded all models and pictorial representations and finally arrived at an abstract, purely mathematical theory termed matrix mechanics which, so far as is at present known, invariably gives complete and correct solutions to problems, is able in principle to predict every possible phenomenon of physical science, and includes the classical mechanics as a special case. The new quantum theory

contains no mention of atoms, nuclei, or electrons because these are mental constructs, pictorial representations that we make for ourselves, and exist by inference and not by direct experimental observation.

In 1926 de Broglie and Schrödinger introduced wave mechanics. There is experimental evidence that the entity termed an electron and originally pictured as a material particle possesses some of the properties of waves—thus an electron is associated with a definite wave-length which is inversely proportional to its speed. These waves form the subject-matter of the wave-mechanics, which mathematically is completely equivalent to the abstract matrix mechanics of Heisenberg and forms a pictorial representation of this, in which the pictorial details may or may not correspond with reality. The waves of the wave-mechanics are not physical waves but waves of probability, the intensity of the waves at any point being a measure of the probability of an electron being found at that point. An electron or system of electrons is represented by a wave function ψ , and the electron density is represented by ψ^2 .

We are now in a position to examine what *quantitative* information can be furnished by the wave mechanics in regard to the spatial characteristics of the carbon atom. Such information was first given by Linus Pauling in 1928.

If we look at a table of electronic configurations of atoms in stationary quantum states with maximum stabilities, we see that the element carbon has six electrons. Two of these electrons have a total quantum number $K = 1$ and a subsidiary quantum number $l = 0$, this condition leading to their designation as *1s* electrons; they correspond with the pair of electrons in the helium atom and, because they are inert chemically, we may dismiss them from further consideration. The residual four electrons

Electron Configurations of Atoms in their Normal States

	At.	K	L			M			N			O			P			Q
	No.	1s	2s	2p	3s	3p	3d	4s	4p	4d	4f	5s	5p	5d	6s	6p	6d	7s
H	1	1																
He	2	2																
Li	3	2	1															
Be	4	2	2															
B	5	2	2	1														
C	6	2	2	2														
N	7	2	2	3														
O	8	2	2	4														
F	9	2	2	5														
Ne	10	2	2	6														

all possess a total quantum number $L = 2$, which for two of them is combined with a subsidiary quantum number $l = 0$, so that they are designated $2s$ electrons; for the other two electrons, the total quantum number $L = 2$ is combined with a subsidiary quantum number $l = 1$, this condition leading to their designation as $2p$ electrons.

The wave-function of an s electron has spherical symmetry, i.e. the electron is almost certainly to be found within the sphere (cf. Fig. 9) and can form a bond in any direction, the bond strength being taken as unity.

The wave-function of a p electron differs markedly from that of an s electron in its angular distribution. The electron is almost certainly confined to a region resembling a dumb-bell (Fig. 9), and there are three possible orientations, p_x , p_y , and p_z ; p electrons thus tend to form bonds in directions at right angles to one another, and of strength 1.73.

The whole of experience with saturated carbon compounds indicates that the four valency electrons of the carbon atom are identical in regard to bond formation; in the preparation of a compound $Cabcd$, the order of introduction of the groups a , b , c , d is a matter of indifference.

The quantum theory, however, requires that the four valency electrons of the normal carbon atom are of different types, two of $2s$ type and two of $2p$ type; we can diminish this apparent discrepancy by increasing the energy of the carbon atom to furnish an excited state,

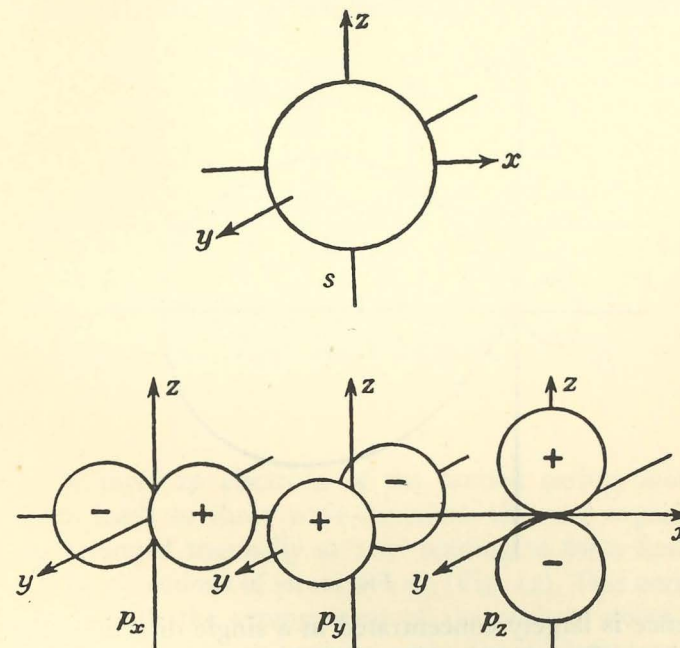


FIG. 9.

whereby one of the $2s$ electrons becomes a $2p$ electron making three $2p$ electrons all told, but we cannot remove it by repeating the process with the residual $2s$ electron because this transition would lead to pairing with one of the three existing $2p$ electrons to give a closed group, e.g. $2p_x^2, 2p_y, 2p_z$ or $2p_x, 2p_y^2, 2p_z$, or $2p_x, 2p_y, 2p_z^2$, on one of the axes x , y , or z . To obtain four equivalent electrons, we must combine or mix the wave function of the single $2s$ electron with those of the three $2p$ electrons.

This hybridization is unpicturable in its ultimate detail, but, as Pauling showed, can readily be achieved mathematically and approximately; a rigorous treatment has not yet been given because the wave equation cannot be rigorously solved. It is found that one particular combination gives a wave-function whose angular depen-

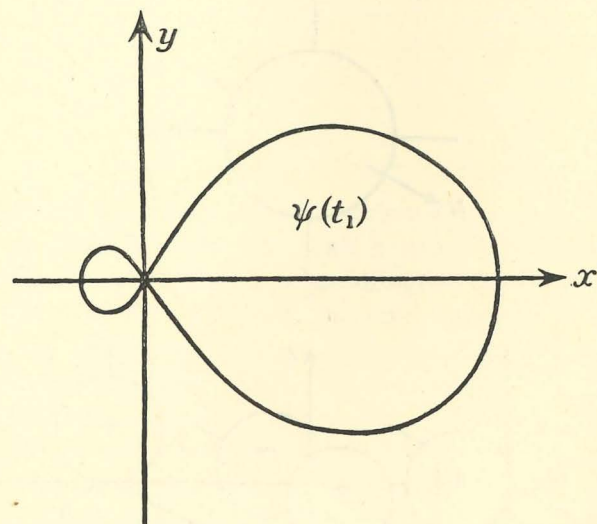


FIG. 10.

dence is largely concentrated in a single direction (Fig. 10), so that a bond will tend to be formed in this direction, and of strength 2. When the production of three other hybrid wave-functions is investigated, it is found that they also have bond strengths of 2, and directions mutually inclined at an angle of $109^{\circ} 28'$, i.e. all are directed to the four corners of a regular tetrahedron. The four valencies of a carbon atom prepared to form a molecule such as methane, CH_4 , are thus directed to the corners of a regular tetrahedron, and this is the true basis of the stereochemistry of the saturated carbon atom. Experimentally, this regular tetrahedral arrange-

ment has been shown to be present in the diamond (Fig. 11) and compounds such as carbon tetrachloride, CCl_4 , by X-ray crystallographic analysis or by electron diffraction.

There is another type of combination, that of the wave-function of the single $2s$ electron and those of two

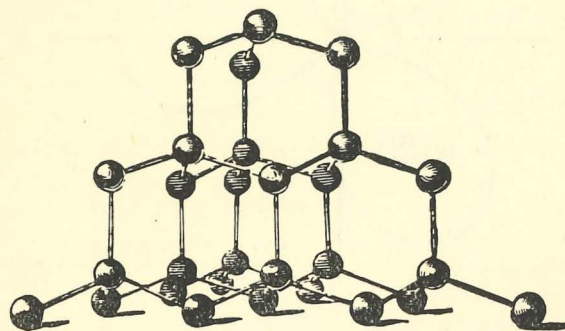


FIG. 11.

of the three $2p$ electrons of the excited carbon atom, which leads to three wave-functions that are coplanar and arranged trigonally at 120° tending to form bonds in these directions of strength 1.99 (Fig. 12). This corresponds with the arrangement of the carbon atoms in graphite (Fig. 13), in benzene, or in dimethylethylene in which the $\text{C}-\text{C}=\text{C}$ angles have been shown experimentally to be near or exactly 120° .

Finally, for completeness, it may be noted that a third type of hybridization, involving the single $2s$ electron and one of the three $2p$ electrons of the excited carbon atom, leads to two wave-functions which are collinear (Fig. 14) tending to form two bonds pointing in opposite directions along a straight line and of strength 1.93. This corresponds with the arrangement present in acetylene and hydrogen cyanide, the molecules of which have

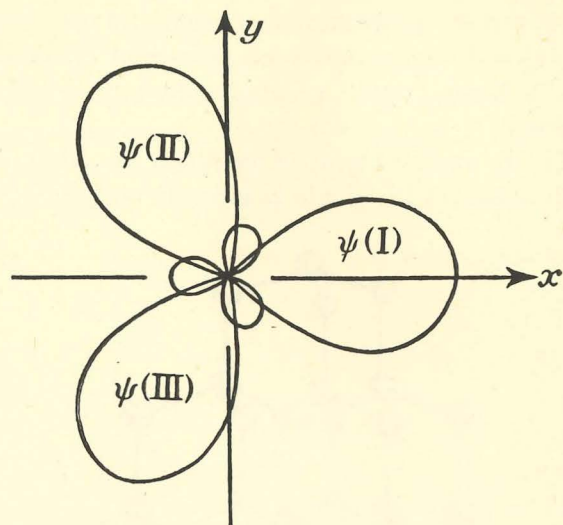


FIG. 12.

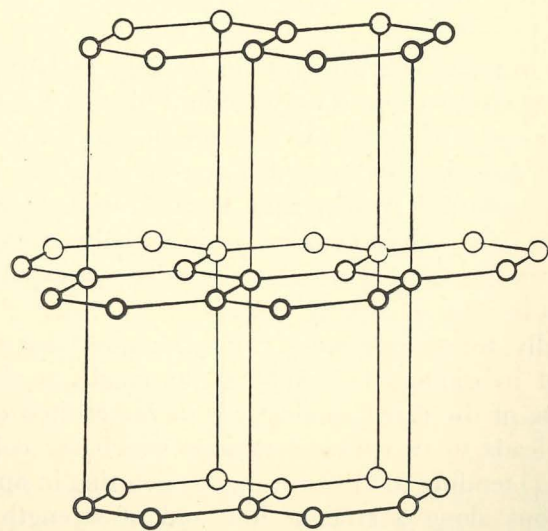


FIG. 13.

been shown to be linear and to possess an axis of symmetry by infra-red spectroscopy.

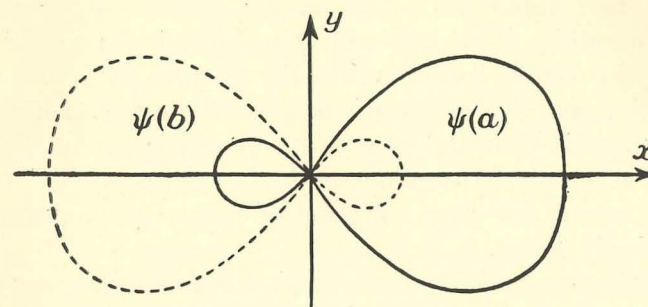


FIG. 14.

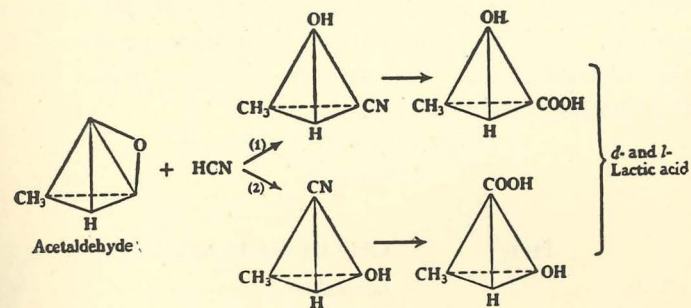


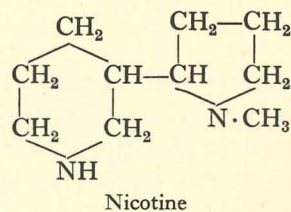
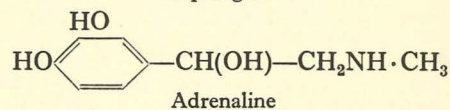
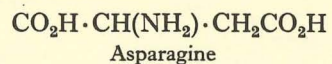
FIG. 15.

Let us now examine some practical consequences of the stereochemistry of carbon. Chemical reactions carried out in the laboratory in glass apparatus are characterized by two features: (i) the occurrence of equilibria, e.g. $A+B \rightleftharpoons C+D$, and (ii) symmetric synthesis, that is the production of equal amounts of the right- and left-handed forms of asymmetric compounds, e.g. acetaldehyde affords equal numbers of molecules of *d*- and *l*-lactic acid.

In the cells of plants and animals, the same chemical reactions take place as in the laboratory, and are subject

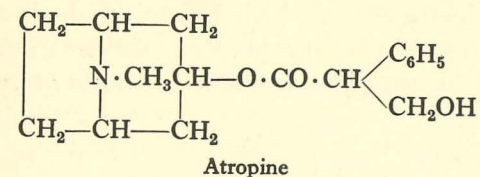
to the same laws, but they occur not in test-tubes of glass but in test-tubes of cellulose or of protein. This has two important consequences: (i) because of the permeability of the cell-wall, the equilibrium point of a reaction can be evaded so that the reaction goes to completion, and (ii) because of the asymmetric carbon atoms involved in the cellulose or protein molecules composing the cell-wall, asymmetric synthesis can occur. This is the reason that large numbers of natural products are optically active.

It is not surprising that in general *d*- and *l*- compounds produce unequal physiological responses. Thus *d*-asparagine has a sweet taste and so differs from *l*-asparagine which occurs in asparagus and other vegetables and is insipid. Similarly, the natural *l*-nicotine produced by the tobacco-plant is two or three times as poisonous as the synthetic *d*-isomeride.

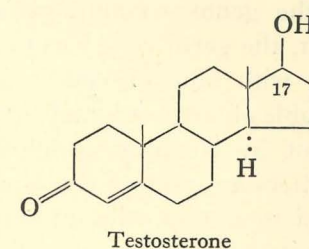
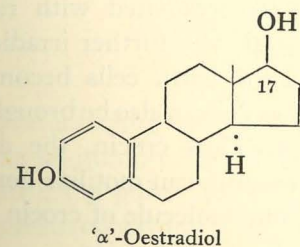
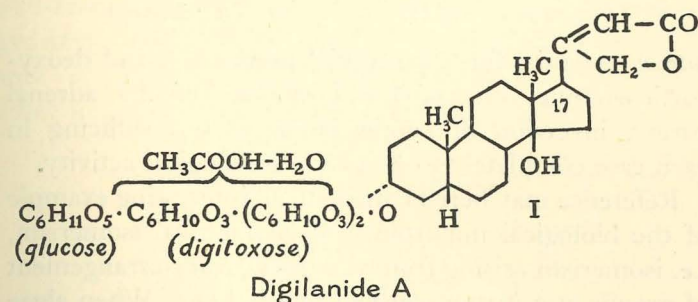


l-Adrenaline, the natural hormone produced by the medulla of the adrenal gland, is twelve times more physiologically active than the artificial *d*-isomeride. Again, the natural alkaloid *l*-hyocyanine has some eighteen times the activity of the *d*-isomeride on the peripheral nerve-endings; the mixture of these *d*- and *l*-forms

in equal proportions, forming the alkaloid atropine, has some nine times the activity of the *d*-isomeride and so constitutes an exact mean.

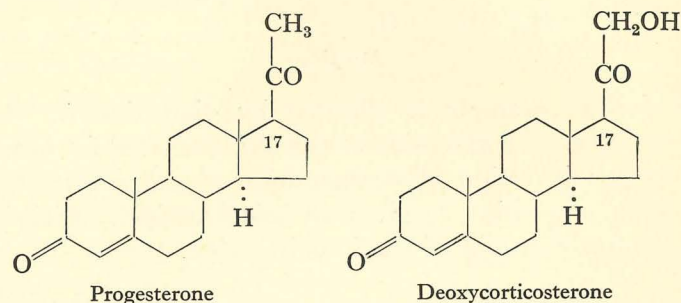


A further example is afforded by digilanide A, the genuine natural glycoside of *Digitalis* and used for heart therapy; inversion of configuration at the asymmetry centre at position 17 gives an 'alloglycoside', which is completely devoid of cardiotoxic action.



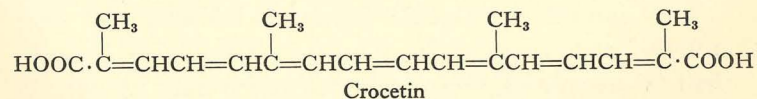
The natural oestrogenic hormone 'α'-oestradiol secreted by the ovaries is about 50 times more potent than 'β'-oestradiol, which differs from it only by inver-

sion of configuration at C₁₇; likewise the natural androgenic hormone testosterone, produced by the testes, is about 25 times more potent than the epimeride, the so-called *cis*-testosterone, which differs only by inversion of configuration at C₁₇, and precisely similar examples are furnished by progesterone, the hormone of the *corpus*



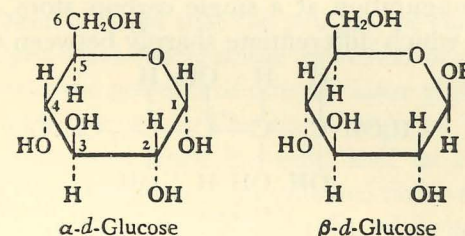
luteum essential for a successful pregnancy, and deoxycorticosterone, one of the hormones of the adrenal cortex, inversion of configuration at C₁₇ sufficing in each case completely to destroy physiological activity.

Reference may here be made to an interesting example of the biological importance of geometrical isomerism, i.e. isomerism arising from the *cis*- or *trans*-arrangement of groups at a carbon-carbon double bond. When algae of the genus *Chlamydomonas* are irradiated with red light, the germ cells become motile; by further irradiation with blue or violet light, the germ cells become capable of fertilization. These changes can also be brought about by chemical compounds. Thus crocin, the digentiobiose ester of the acid crocetin, can motilize non-irradiated germ cells, and only one molecule of crocin is required for each germ cell.



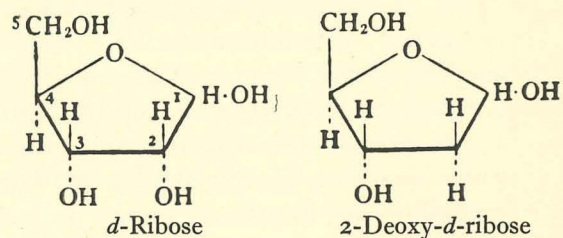
Further, mixtures of the *cis*- and *trans*-forms of the dimethyl ester of crocetin can induce capacity for fertilization, and the proportion of the geometrical isomers is critical. It is known that irradiation with violet light converts *trans*-compounds into their *cis*-isomerides, and clearly an analogous configurational change occurs when the algae are irradiated with violet light. It appears that these specific properties may be associated with the zigzag form of the molecule which results from a succession of *cis*- or *trans*-linkages.

The spatial character of the carbon atom, combined with that of the nitrogen atom, is responsible for the remarkable specificity of the complex protein molecules called enzymes, which led Emil Fischer to suggest his well-known analogy of lock and key. Thus emulsin hydrolyses only 'β'-glycosides, whilst maltase hydrolyses only 'α'-glycosides, and such 'α'- and 'β'- pairs may differ in configuration at a single carbon atom only.



The amazing specificity encountered in the phenomena of immunity rests on a similar basis. An antigen (toxin), the poisonous secretion of a pathogenic micro-organism consisting of a foreign protein, when introduced into an animal stimulates the production in the blood of a specific protein termed an antibody (antitoxin), probably by acting as a template so that the configuration of the antigen molecule is mirrored in the antibody

atom at C₂ and so possessing an extra centre of asymmetry.



Deoxyribose nucleic acid, the so-called chromosome nucleic acid, is the chief reagent in the chemical machinery of heredity. The nucleotides of the acid polymerize in columns of flat plates, not unlike an almost endless pile of pennies, in which the plates are spaced at distances of 3.3 Å apart (cf. Fig. 16). The active groups called genes on the slender protein chromosome fibres, which determine to some extent various morphological, physiological, and mental characters, attach themselves to the flat plates of the nucleic acid columns, and it is these supporting columns which are responsible for the two primary properties of chromosomes, namely, coiling, and reproduction. The distance of 3.3 Å is almost exactly that of the fully extended polypeptide units (cf. Fig. 17) composing the protein of the chromosome fibre, so that the column and the fibre can fit together exactly. It is clear that the stereochemical arrangement (bond lengths and bond angles) associated with carbon and nitrogen atoms plays a fundamental part in the ultimate processes of the activity which we term 'life'.

The foregoing review will, I hope, have given some indication of the way in which a simple but fundamental scientific concept may develop and so ramify that it comes to be regarded as a basic factor in diverse and complicated phenomena.

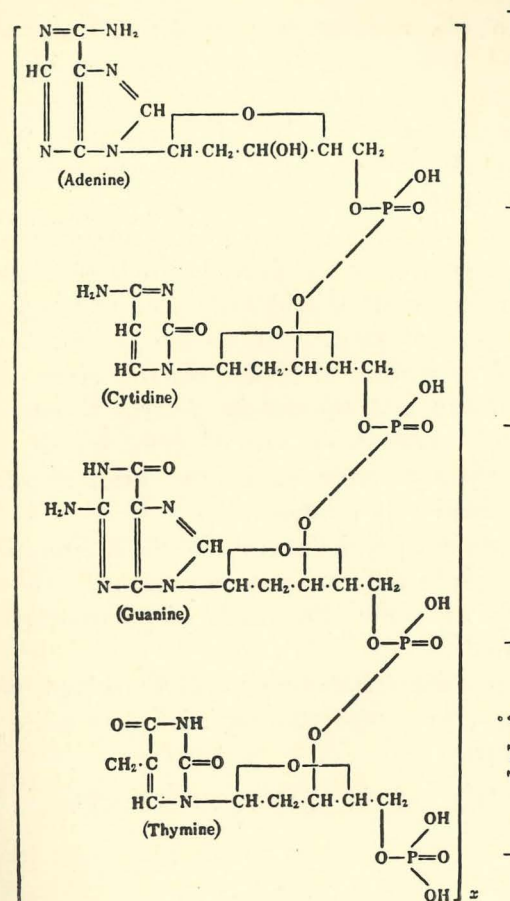


FIG. 16.

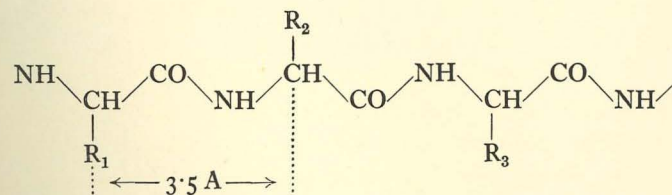


FIG. 17.

Much has been elucidated; much more remains to be discovered. Thus, there are four simple problems connected with the stereochemistry of the carbon atom to which the answers are as yet not precisely known:

- (i) It is not clear how the first asymmetric molecule originated.
- (ii) We do not know which of the two mirror-image arrangements of the formula for lactic acid corresponds to *d*-lactic acid and which to *l*-lactic acid.
- (iii) We do not know how an asymmetric molecule resolves a beam of plane polarized light into two circularly and oppositely polarized beams, and why it slows down one of these spirals so that, on their recombination, the original plane of polarization is rotated.
- (iv) We cannot predict accurately the extent to which four given different groups attached to a carbon atom will cause the plane of polarization to be rotated.

These problems and others will be solved, possibly neither to-morrow nor the day after, but quite surely in the future.

'ET AUGEBITUR SCIENTIA'