level in no way reduces our appreciation of the unique intellectual, moral, and esthetic capacities of our species. Rather, we can only stand in awe that life, evolving from inorganic matter, could develop these qualities.

We should also note the increasing implications of biology for philosophy. A modern approach to the classical problems of epistemology should surely take into account the perception that evolution has provided us with a great deal of information encoded in our genome, and this information, expressed in part in our brain structure (and thus justifying the Kantian a priori categories), interacts with personal experience to give us our knowledge of the external world. Advances in neurobiology will no doubt eventually provide more detailed insights. In another area, the potential impact of sociobiology on ethics has recently aroused much discussion.

Biology is also having an increasing impact on the philosophy of science. The revolution in physics led to the widely accepted view that science makes its main progress not by small steps within a universally accepted conceptual framework or paradigm, but by periodically overturning that paradigm. The revolution in biology, however, has not had this character: instead of destroying paradigms, and overturning previous convictions about mechanisms, it has opened up areas, in an infinitely complex material, where biologists knew that they did not know. In a word, this revolution has overturned only previous limits to our powers of experimental analysis, thereby destroying an almost vitalistic earlier attitude toward complexity.

I would close by briefly commenting on some areas of recent public concern. We have recognized, belatedly, that large-scale technological applications of the physical sciences have costs and dangers as well as benefits. In biology, in contrast, concern has been directed not at present harm but at hypothetical future harm. In particular, recombinant DNA research was seen as a possible source of novel epidemics. The anxiety has now abated considerably: extensive work with recombinants failed to produce any harm, and sober professional analyses displaced unrealistic demands for absolute protection against conjectural risks. A retrospective analysis may help us to create better social mechanisms for utilizing the knowledge and judgment of the scientific community in assessing dangers and benefits, and for involving the general community in ways that serve its interests in reality and not only in appearance.

Genetic engineering has also been a source of concern, on the tacit assumption that if we should learn how to cure monogenic hereditary diseases we could use the same power to modify personalities genetically. On technical grounds, however, the extrapolation seems unwarranted, both because most of the large number of genes contributing to any behavioral trait and because most of them will have made their contribution to individuality before birth. But the most fundamental consideration is that any basic knowledge is double-edged, with both good and bad possible applications—and we cannot foresee these in detail. I would suggest that this principle applies not only to knowledge yielding novel powers to manipulate genes, but also to knowledge about the biological roots of human nature. To be sure, such knowledge often encounters resistance, because its possible contradiction of treasured preconceptions, and even more its possible distortions, can have political consequences. One safeguard is to recognize the limited power of science in this area: it cannot prescribe solutions to moral problems, for these involve value judgments as well as estimates of reality. At the same time, a more accurate perception of reality will surely be helpful. The extent of this help is one of the large uncertainties in the future of biology.

Frontiers in Chemistry

Robert M. Joyce, Editor

Chemistry is a multifaceted science. It provides new substances, ranging from complex organic pharmaceuticals and agricultural chemicals to sophisticated inorganic solids that control the flow of electrons to make computers work. It unravels the intricate atomic combinations that nature has learned over millennia to assemble. It discovers catalysts that make it possible to duplicate and to modify complex natural substances, to control the stereochemistry of reactions at chiral sites, and to convert petroleum and coal into basic chemical compounds. It creates synthetic macromolecules, and is developing a wealth of information about the structures and mechanisms of action of natural biomacromolecules. It probes the intimate details of chemical events that occur in less than 1 nanosecond, and detects atoms and compounds at levels in the picogram range in complex mixtures. It studies reactions of atoms and small molecules in various quantum states. This article describes some of the recent advances in a few of the many areas of chemical science.

Instrumentation and Analytical Chemistry

Analytical instrumentation has progressed markedly in the last few years, spurred on by a variety of technical advances. As often is the case, a few basic inventions have been extended and developed by others to provide a vast array of new and complex analytical systems. For example, semiconductor technology has pervaded nearly all aspects of analytical science, providing the sophisticated electronic instrument controls and readout devices we know today. Digital computers, especially fast and accurate micro- and miniprocessors, and in some cases large number-crunchers or data analyzers, have become essential and integral parts of modern measurement

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Summary. Chemical synthesis is the ultimate source of most of the new materials that serve society. Progress in chemical synthesis depends on comparable advances in other branches of chemistry, such as in analysis, methods for determining the intimate details of chemical structures and of reaction mechanisms, and theories of chemical structure and reactions. Recent progress in some of these areas of chemistry is described.

technology. What was once often an entire thesis project, the generation of a complete organic molecular structure by single-crystal x-ray diffraction, can now be as little as a week's work for an expert crystallographer using modern x-ray equipment and computerized data analysis. Almost no area involving complex analytical measurements has escaped the influence of the semiconductor and computer technologies.

Other developments have also had broad effects. High-vacuum technology has led to the evolution of many new techniques for studying surface properties and the chemistry occurring at surfaces—ESCA, AES, ISS, SIMS, LEEDS, and SEM (*1*)—as well as furthering other disciplines such as mass spectroscopy. The advantages of Fourier-transform (FT) methods have become well recognized and have encouraged invention of physical methods to encode and decode information with great gains in sensitivity, resolution, and speed. Examples include pulsed FT-NMR and FT-ICR (*1*) and the interferometer approach to FT-infrared spectroscopy. Infrared spectra of excellent quality are now obtained routinely with less than 1 microgram of sample, whereas not long ago a fraction of a gram was required. The development of rigid, small (5 to 30 micrometers) porous particles for use as packings in chromatographic columns has led to heretofore unattainable separations of nonvolatile or thermally sensitive materials by liquid chromatography. Development of the laser has revitalized such diverse molecular characterization techniques as Raman, Rayleigh light scattering, and correlation spectroscopies. A recent Raman experiment provided a good spectrum of a pesticide particle inside a single biological cell.

While these and other developments have provided a great deal of information in many areas, several unique contributions have also expanded the horizons of analytical measurement. Some of these are set forth in the following paragraphs.

Superconducting magnets with FT interfaces now permit greatly improved sensitivity and dispersion in NMR. Carbon-13 NMR spectroscopy has become routine, and samples of less than 1 μg can be used for ^{1}H work. Many other nuclei, such as ^{31}P (in natural abundance in single biological cells) and ^{15}N, have become accessible. By addition of magic-angle spinning and specific radio-frequency pulse technology to this technique it is possible to obtain resolved NMR spectra of solids and thus new information on the solid state.

Reverse geometry mass spectroscopy, coupled with the collision activation technique, allows isolation and identification of a single molecular species in a complex mixture without gas chromatography. For example, the plant hormone abscisic acid has been studied with whole plant parts used as the sample. In addition, the field desorption technique now permits mass spectroscopy with such materials as cationic dyes and thermally sensitive organometallic salts, and accurate mass measurement for molecular weight determination can now be made routinely.

Gas chromatography is a modern technique used extensively by the organic chemist. Compared to packed columns 2 meters long and 2 millimeters in inside diameter, which require 2 to 5 microliters of sample, new flexible fused-silica capillary columns measuring 30 m by 0.2 mm need only 0.05 μl of sample and are four times faster and 50 times better in resolution. These capillary columns also permit direct analysis of many materials for which it was formerly necessary to prepare chemical derivatives.

New instrumentation for techniques such as differential pulse, a-c, and fast-sweep polarography has revitalized and expanded the scope of electrochemistry to permit much greater sensitivity, resolution, and accuracy than were obtainable with d-c methods.

In quantitative emission spectroscopy many matrix effects have been eliminated and orders-of-magnitude improvements have been made by use of new stable sources employing inductively coupled plasmas and d-c arc, high-temperature plasmas.

Many promising techniques are yet to come, and the growth in analytical instrumentation will continue. One exciting new technique, not currently commercially available, is field flow fractionation. This one-phase, two-dimensional chromatography-like technique holds great promise for particle separations and size analysis.

Chemical Synthesis

In 1828 the German chemist Wöhler synthesized a natural product, urea, and liberated chemistry from the dogma that synthesis of natural products was the exclusive province of living systems. The sophistication developed in chemistry since then is exemplified by the total synthesis of vitamin B_{12}, a compound with the formula $C_{63}H_{88}CoN_{14}O_{14}P$ that has 14 chiral carbon centers.

One of the keys to such complicated syntheses is a host of novel catalysts and reagents based on combinations of organic groups with inorganic elements (Li, B, Al, Si, P, S, Ti, Cu, Rh, Pd) that can effect reactions with a degree of specificity that was no more than a dream 10 years ago. Thus, use of an organoboron reagent gives a measure of control over the stereoisomers formed in the aldol condensation, which nature employs with complete specificity to construct portions of many natural compounds. An organorhodium complex with a chiral center catalyzes the hydrogenation of α,β-unsaturated amino acids to only a single stereoisomeric α-amino acid. Another rhodium complex is used commercially to catalyze the combination of carbon monoxide with methanol to give acetic acid in 99 percent yield.

The remarkable specificity of nature's catalysts—the enzymes—has stimulated research to imitate them with synthetic materials. Like enzymes, these materials have a spatial cavity to accommodate reactive sites of molecules and functional groups that catalyze specific reactions. In a related area, large ring polyethers of different ring sizes have been shown to form complexes selectively with ions of different sizes. Such polyethers, synthesized with a chiral center, can now be used in an automatic machine to resolve α-amino acid derivatives into their stereoisomers.

Organic molecules so highly strained that they had been thought incapable of existence are now being made in the laboratory. An example is the tetrahedrane structure, in which four mutually bonded carbon atoms form a regular tetrahedron with three of the C–C bond angles distorted from the normal 109°28′ to 60°; the tetra-*t*-butyl derivative of this molecule has been synthesized and shown to be stable up to 130°C. Photochemical techniques have yielded all three of the structurally allowed, highly strained isomers of benzene.

A currently active area in organic synthesis is the application of computer technology in planning routes for synthesizing complex molecules. Using a graphic display, the chemist can "draw" the structure of a target molecule and, by calling on a stored data base, explore various synthesis reactions one step back from the target. Successive iterations of this process enable the chemist to work back to reasonable starting materials and to lay out the most promising routes to the target molecule.

The search for new and more specific pharmaceuticals continues to include synthetic modifications and analogs of biologically active natural products. In addition, the accumulating knowledge of biological mechanisms in providing a basis for the design of compounds that can inhibit certain enzymes or bind to certain receptor sites that are involved in disease. Computer graphics technology is beginning to be a valuable tool in the design and synthesis of such compounds.

Nonmetallic electrical conductors are being found in studies of organic charge-transfer complexes and such polymers as $(SN)_x$ and $(CH)_x$. Intercalation of inorganic ions into materials with sheet structures, such as graphite, has led to complexes that conduct current easily in the sheet plane but poorly perpendicular to it.

Superconductivity, a phenomenon once associated exclusively with liquid helium temperatures, has been demonstrated at temperatures near the boiling point of hydrogen in some new intermetallic compounds. Progress toward higher temperature superconductors is being made through control of synthesis conditions to produce particular, often metastable, structural phases of such compounds.

The magnetic properties of amorphous alloys and compounds of transition metals, prepared by synthesis at a high temperature followed by rapid quenching ($>10^5$ °C per second), are of both theoretical and practical importance because they are not influenced by the grain boundary effects shown by their polycrystalline analogs (*2*).

Optical communications has become a reality through the synthesis of silicon-germanium oxide fibers with a radial composition gradient. These fibers permit low-loss, wide-bandwidth transmission of modulated monochromatic light signals over practical distances.

Synthesis of new chemicals may be undertaken in search of a desired property, to test theories of structure and chemical bonding, or as a result of an original concept of a new kind of structure. The products of this endeavor, in turn, continue to open new lines of thought about chemical structure and to provide novel materials with useful and sometimes unexpected properties.

Agricultural Chemicals

The use of chemicals to reduce crop losses due to the ravages of agricultural pests, weeds, insects, and diseases has been practiced from Roman times. The evolution of pest-control technologies as practiced today is largely a phenomenon of the past century. However, even though great advances have been made, recent estimates (*3*) indicate that such losses, worldwide, still destroy 33 to 45 percent of our food, feed, and natural fiber.

Notable first-generation pest-control agents included such materials as Paris green, copper acetate arsenite, Bordeaux mixture, metallic dialkyl dithiocarbamates, and DDT. Around the time of World War II, new discoveries included the phenoxy herbicides and organophosphate and carbamate insecticides.

The real explosion in numbers of new synthetic pest-control agents began in the 1950's and 1960's as a result of the search for materials that would be more effective, safer, and more selective. Developments included a host of new herbicides (chloroacetamides, triazines, dinitroanilines, quaternaries, and substituted ureas), insecticides (organophosphates, organochlorine compounds, and carbamates), and fungicides (phenolics, imides, and organometallics).

Although the rate of introduction of new pest-control chemicals has decreased in the last decade, the rate of innovation has not. The search continues for new herbicides and pest-control agents that are more effective, more selective, active in low concentrations, and have a minimal potential for adverse environmental effects. Examples of recent innovations include the following.

Herbicides. Diphenyl ether derivatives are proving especially effective on some hard-to-kill perennial and annual weeds, yet are tolerated in some food crops such as soybeans. Phosphonomethyl glycines are very effective, broad-spectrum herbicides that translocate downward in the plant to kill the root. They are not sufficiently selective for use on many food crops. The *unsymm*-triazines and the benzothiadiazinones are new chemical classes that are particularly effective against broadleaf annual weeds. Arylsulfonyl-*symm*-triazinylureas have broad-spectrum activity against weeds and can be used in some food crops. For example, they can control weeds in wheat when applied at 1/40 the concentrations required for 2,4-D.

Fungicides. The benzimidazole carbamates represent a major advance in the control of many kinds of fungi that attack food crops because they are systemic, highly effective at low concentrations, and disappear from the product in a reasonable time. An equally important advance, which evolved from knowledge of biomechanisms, led to the sterol synthesis–inhibiting systemic fungicides, which interfere with an essential mechanism of fungal growth. These compounds are proving very effective by themselves and in combination with the benzimidazole carbamates.

Insecticides. Synthetic pyrethroids, such as the aralkylcyclopropane carboxylates, are finding wide use because they do not present the residue problems of some of the older polychlorinated insecticide compounds.

Plant growth regulators may become major agricultural chemicals of the future. They are materials that, when applied to growing plants, elicit reactions that lead to improved productivity, better quality of produce, or lower production costs. Use of such chemicals, which is now expanding at a modest rate, is presently limited to specialty situations. For example, *N*,*N*′-bis(methylphosphonyl)glycine hastens the ripening of sugarcane. β-Chloroethylphosphonic acid decomposes in the plant to release ethylene, which has such varied effects as ripening tomatoes, promoting pineapple flowering, and stimulating latex flow in rubber trees. An important target for agricultural chemists is the identification of plant growth regulators that are useful on the principal food and feed crops.

Integrated pest management is the name given to systems in which chemical, cultural, genetic, and biological methods are combined to control all kinds of pests. As described recently (*4*), chemical controls include both traditional and new pesticides. Cultural methods consist of cultivation, crop rotation, use of optimum planting regimes, and field sanitation. Inbred plant resistance is achieved by developing and using varieties and hybrids that are resistant to certain pests. Biological control centers on encouraging natural pest predators.

As a corollary to concerns about feeding the rapidly increasing world population has come the realization that land areas suitable for agriculture are finite, and that much of the increase in food required to meet demands over the next century must come from raising the productivity of land already under cultivation. Plant growth regulators, new plant varieties, improved pesticides (*5*), better farm implements, and user education are seen as keys to meeting this global challenge. For the long term, the use of plant growth regulators combined with all the elements of integrated pest management is expected to offer the best approach to this challenge.

Macromolecules

Ordinary "small" molecules consist of 2 to around 200 atoms; macromolecules may consist of thousands to hundreds of thousands of atoms, chemically bonded in a characteristic repetitive array. Synthetic macromolecules, which are the components of most synthetic fibers, films, and plastics, have been discussed recently elsewhere (*6*). Biomacromolecules, such as proteins, nucleic acids, and oligosaccharides, are responsible for the structural integrity and functional competence of living cells. Some of the recent developments in biomacromolecular science, discussed below, are leading to better understanding of biological processes at the molecular level, as well as creating conceptual and practical challenges for chemists.

Synthesis of macromolecules in living organisms is mediated by enzymes—proteins that are among the most effective catalysts known. Many types of natural macromolecules are copolymers that incorporate more than one monomeric species. Proteins are polyamides that are derived from some 20 different α-amino acids linked in a predetermined order. The chemical and functional variety of proteins is manifested not only in the enormous number of permutations of these building blocks, but also in the comparably large number of folding conformations that such polyamides can assume through hydrogen bonding between various amide groups in various environments. The speed and fidelity with which a particular protein molecule is assembled at the ribosomes of a living cell show the gulf between present capability and future goals in synthetic macromolecular chemistry.

The covalent structures of proteins are becoming accessible through sophisticated techniques in which successive degradation reactions are carried out to identify the α-amino acid sequences (*7*). In addition, x-ray studies have led to descriptions of the three-dimensional structures of protein crystals. Combinations of these kinds of information are leading to some comprehension of enzyme action and are providing a glimpse into the mechanism of antibody action. Recent advances in determining the nucleotide sequences in DNA (*8*) have provided some understanding of the structure of genes, have raised new questions about the structural basis of genetic information storage and processing (*9*), and are playing a major role in the development of recombinant DNA technology.

An outstanding question in macromolecular science is how the biomacromolecule assumes three-dimensional structures with such varied and specific functions. As an example of progress in this area, E. Katchalski-Katzir has studied the dynamics of thermal motions in protein chains and has identified "breathing" vibrations that may contribute to the attachment and release of a substrate by an enzyme. Fluctuations in vibrational energy may also be involved in the opening of the DNA double helix for replication. S. Krimm has recently measured and interpreted in fine detail the vibrational spectra of chain macromolecules. The vibrational frequencies turned out to be very sensitive to chain conformation, which can be studied under changing conditions of temperature and stress.

Such spectroscopic studies are providing insight into the dynamic nature of folded biopolymers, such as proteins and nucleic acids, and the molecular transformations they undergo during their functions. Specific topographical arrangements of biological macromolecules in cellular assemblies such as membranes and other organelles are now being elucidated by techniques such as photoaffinity labeling (*10*). Synthesis of oligonucleotides of defined sequence, pioneered by H. G. Khorana, has matured into a practical methodology that is now used extensively in recombinant DNA technology. The newly discovered Z form of DNA (*11*) may provide insight into the effects of variations of the classical double helix structure of DNA and may help us to understand the effects of endogenous and exogenous chemicals on genes.

As our knowledge of the chemical mechanisms of biological processes increases, so should our ability to design molecules—for example, for medicinal or agricultural use—that will be highly functionally selective with minimal biological side effects and minimal perturbation of the biological system.

Feedstocks in Transition

The raw materials base for organic chemical feedstocks includes natural gas, natural gas liquids, petroleum naphthas, and light gas oil. During the next several decades, significant changes will occur in the mix of raw materials that supply chemical feedstocks. Although the transition to new feedstocks will be neither precipitous nor total, the future of the organic chemical industry is dependent on the discovery and development of new feedstock processes. Three areas of research and development related to feedstock are discussed below.

Petroleum and shale oils. As supplies of light, high-quality crude oil become less accessible, both physically and economically, progress is being made in using heavy, less pure fractions as feedstock sources. Heavy oils cannot be successfully cracked in conventional furnaces because of severe coking. They have also been considered undesirable as feedstocks because of their high content of sulfur compounds and heavy metals. Similarly, shale oils are notorious for coking propensity and for high levels of nitrogen compounds and heavy metals. In recent commercial processes these problems are dealt with by deliberately coking such materials in special reactors and collecting the coker distillates for use as a source of liquid hydrocarbons.

A second approach to use of these materials employs hydrogenolysis catalysts that specifically remove sulfur and nitrogen compounds. In addition, processes are being developed to crack heavy fractions of crudes directly to ethylene and other low-molecular-weight hydrocarbons while managing the problem of coke deposition that has plagued such processes in the past. This approach typically involves noncatalytic cracking under very severe conditions—high temperature and short contact time.

Continued research on the chemistry of such processes is expected to extend the utilization of petroleum and shale oil as raw materials for feedstock sources.

Coal. Coal will become a principal raw material for chemical feedstocks, primarily as a source of syngas—a mixture of carbon monoxide and hydrogen. Catalysts are the key to utilization of syngas; the list of basic chemicals that can be made from syngas by catalytic processes is already impressive and is growing.

A well-known process is the conversion of syngas to methanol or dimethyl ether (DME). Commercially, methanol is a source of formaldehyde or formic acid by oxidation, and of acetic acid by carbonylation. Methyl acetate, obtained from methanol and acetic acid, can be carbonylated to acetic anhydride. Alternatively, reaction of methyl acetate with syngas gives ethylidene diacetate, which can be cracked to vinyl acetate and acetic acid.

The Fischer-Tropsch synthesis converts syngas to chemicals and gasoline, but produces complex mixtures. Now, the discovery of shape-selective catalysts, such as certain zeolites, has opened the way to the conversion of methanol or DME selectively to aromatic compounds or olefins, and processes based on this chemistry are being developed.

Looking to the future, a catalyst has been found that converts syngas to ethylene glycol, but as yet only at uneconomically high pressure. A ruthenium catalyst can carbonylate methanol to a mixture of ethanol and methyl acetate, and catalysts are being sought for the conversion of syngas directly to ethanol. Coal liquefaction is being developed primarily as a route to liquid fuels; however, coal naphthas are rich in one- and two-ring aromatics, and as these processes come on stream, their products should become important sources of aromatic chemicals.

Biomass. This potential source of chemical raw materials faces substantial logistical problems, but it should nevertheless become significant in the next century. Since starches and sugars are chemically close to $C(H_2O)_x$, these materials are likely sources of oxychemicals; examples are the former production of furfural and the current production of ethanol for gasohol from such sources.

Some plants, such as euphorbia and guayule, produce hydrocarbon-like products, and their cultivation is being explored. Genetic engineering and the development of low-cost cultivation may make such plants candidates for "energy farms" for the production of certain feedstock materials.

In the long term, feedstock materials may emerge from the discovery of catalysts that can mediate such solar energy-promoted reactions as the production of hydrogen from water.

We have entered an era when efficient use of resources will be essential to effect the necessary transition from complete dependence on petroleum and natural gas. Whether this transition occurs in a well-ordered manner with economic growth depends largely on the quality of the planning and R & D now in progress.

Statistical Mechanics in Chemistry

Developments in the last two decades have transformed our knowledge of the properties of liquids and the nature of phase transitions. These developments have followed from new insights into statistical mechanics and the development of techniques for computer simulation.

It used to be said that the properties of gases are well understood because gases consist of nearly independent molecules, and that crystalline solids are well understood because they may be deemed to consist of nearly independent oscillators, but that there is no adequate theory of the liquid state. That is no longer true, and it has become possible to calculate from first principles the properties of liquids and liquid mixtures consisting of molecules of ever-increasing complexity. Subtle problems of phase transitions and critical points in both fluids and solids have become soluble.

An important premise in modern studies of liquids is that their structure is determined primarily by strong repulsions between molecules at short distances. A liquid can then be treated as a slightly perturbed form of a hypothetical reference fluid in which the molecules interact through repulsive forces alone, the attractive components of the intermolecular forces being the perturbation (*12*). The properties of the reference system as well as the effects of the perturbation can be found from a combination of analytical and numerical techniques. While this theory had its initial successes in describing liquids composed of atoms or spherical molecules, the same ideas are now being successfully applied to liquids of charged or polar molecules or more complex shapes. The theory has reached the point where the properties of liquid mixtures of practical industrial importance can often be predicted.

New developments in the theory of phase transitions and critical points started with persistent observations of discrepancies between the predictions of all the simple theories and the experimental results on the quantitative nature of the singularities in thermodynamic functions in the neighborhood of critical points: liquid-vapor critical points, consolute points of mixtures, ferromagnetic Curie points, and so on. The thermodynamic quantities of significance—compressibility or osmotic compressibility, specific heat, interfacial tension—all vanish or diverge at critical points with characteristic powers, called critical-point exponents, of the distance from the critical point. These powers were agreed on by all the classical equations of state; the experiments likewise agreed among themselves over all the great variety of critical phenomena. However, the theoretical values were in clear contradiction with the experimental values.

It came to be recognized that the defects of the older equations of state rested on their failure to take proper account of the extensive fluctuations that characterize the neighborhood of a critical point. New equations of state with a homogeneity of form, called scaling, were developed as generalizations of the classical equations, but now accommodating nonclassical critical-point exponents (*13*). Relations among these exponents, called scaling laws, were predicted, and then found to be satisfied in nature. The universality of these exponents was explained by the ever-increasing distances over which fluctuations in density or composition are correlated as a critical point is approached. These fluctuations are manifested by critical opalescence, seen by eye in ordinary light and by scattering of x-rays or neutrons in solids. Once the range of composition fluctuations becomes greater than the intermolecular spacings or than the range of intermolecular forces, the microscopic details that distinguish one substance from another become nearly irrelevant, and the phase equilibria assume a universal character—the same for all substances. The development of the scaling ideas has culminated in the renormalization-group theory of phase transitions, a set of ideas of great power and scope in statistical mechanics (*14*).

Important elements in these theoretical advances have been the recognition of the value of exactly soluble, albeit drastically simplified, models and modern digital computing. The properties of the Ising model of a ferromagnet, or of the equivalent lattice-gas model of a fluid, were found exactly by analytical and numerical methods (*15*) and were seen to be very close to those found in experiment, but different from those given by any of the classical theories. It became clear that the inadequacies of the earlier ideas were due to the approximations that had been applied in obtaining the equations of state by statistical mechanics.

Computer simulations of the properties of dense systems now provide almost exactly the properties of model systems with known, prescribed intermolecular interactions. From these has come a large body of "experimental" results on fluids in which there are no uncertainties about the nature or strengths of the intermolecular forces, and on which the adequacy of theories can be tested with greater certainty than by comparison with experiments on real fluids. Acceptance of this intermediate stage between theory and experiment as legitimate has been mainly responsible for subsequent advances. The computer simulations have been largely of two kinds: Monte Carlo and molecular dynamics. The former is a method of sampling the space of molecular configurations to make feasible the evaluation of the partition functions of systems with many degrees of freedom—at first of tens and now even of 1000 or more molecules. In the second technique, one follows the motions of the molecules of a similarly large but finite system as they move subject to the laws of classical mechanics, and then one evaluates the properties of the system just as one might measure them in the laboratory.

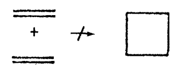
These developments are making a significant contribution to the understanding of the theory of dense matter.

Quantum Mechanics and Chemistry

The equations can be written down, but their explicit, exact solution is unattainable. That has been and is the problem of the quantum mechanics of molecules, the discipline of quantum chemistry. Yet an analogous situation exists in the description of the classical motion of celestial objects, which has hardly prevented a human working with a computer from describing the location of a space module orbiting Mars very, very precisely. While the equations may be solved only approximately, the solutions can be obtained to a high degree of accuracy.

So it is in quantum chemistry. For small molecules, those with less than ten atoms, the development of new computational algorithms has allowed the calculation of essentially any observable property of the molecule, as well as some that are unobservable. For two-, or three-, and four-atom molecules the calculations are so good that they may be used to predict the spectrum of a molecule not found on the earth but detected in interstellar space, such as HNC, or they may lead to the correction of an erroneous experimental finding of a linear geometry for methylene, CH_2.

1



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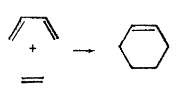

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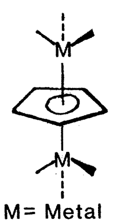
A most promising recent trend in quantum chemistry is the reintegration of theory with experimental organic and inorganic chemistry. For some time it seemed as if the more and more computer-intensive calculations of the electronic structure of small molecules would lead theoreticians away from the mainstream of chemistry—from the making, analysis, and mechanistic exploration of molecules of substantive complexity. But in the late 1960's the Woodward-Hoffmann rules for orbital symmetry control of concerted reactions, such as **1**, **2**, and **3**, proved to be much more than an incisive and unifying application of molecular orbital theory to organic chemistry. They turned out to be a guidepost for the productive interaction of theorist and experimentalist. They renewed experimental confidence in the ability of theory to describe, predict, and build conceptual frameworks.

Since then, approximate symmetry-based analyses have assisted experimentalists in understanding the remarkable wealth of information about molecular energy levels coming from photoelectron spectroscopy, in elucidating selectivities and specificities in cycloadditions, and in understanding organic photochemical reactions. Computerized models of molecules, in which only semiclassical atom-atom and electrostatic potentials are introduced, have reproduced reliably and predicted the geometries of molecules ranging in complexity from hydrocarbons to proteins.



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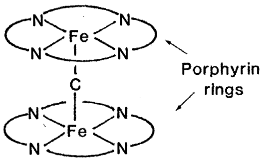

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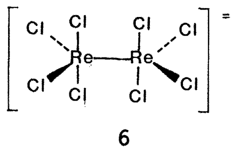

6

Qualitative yet fruitful theories have been provided for bonding in geometrically complex transition metal clusters—metal polyhedra with associated ligands (*16*). A new molecular orbital view of mineral and solid-state structures is developing (*17*). The geometric and electronic features of transition metal complexes are beginning to be understood (*18*), and totally new structural types, such as the inverse sandwiches **4** and **5**, have been predicted and synthesized.

For intrinsic beauty and a demonstration of the intricacy of interaction among synthesis, structure determination, and theory in modern chemistry, it is hard to match the new subfield of inorganic chemistry—metal-metal bonding—exemplified by structure **6**.

These recent developments in chemical theory are beginning to have a significant impact on many areas of chemistry, particularly synthesis and catalysis.

Chemical Kinetics and Lasers

The speed of chemical reactions—less than 1 nsec for the breaking and making of bonds—makes the study of such events very challenging. Until recently, chemists have had to be content with observing overall reaction rates as a function of concentration and temperature. This situation is being changed dramatically by the advent and combination of two powerful techniques, molecular beams and laser spectroscopy.

Molecules from ovens or other high-pressure sources are cross-fired at one another inside a container evacuated to such a low pressure that the molecules travel in straight paths (beams), in effect permitting reactions to be studied one collision at a time. Lasers are used to prepare the molecular reagents in known internal states (to fix the degree of vibration and rotation) and to probe the internal state distributions of the reaction products. In this manner one can learn how the states of the reactants evolve into the states of the products. This new chemistry is providing not only a deeper understanding of the forces operative during that fleeting moment when reactants interlock and products separate, but also the basis for control of chemical processes such as separation of isotopes and gas-phase chemical etching of semiconductor wafers.

One of the simplest of chemical reactions is that between a hydrogen molecule and a hydrogen atom or one of its isotopic analogs, yet there is much about it that is not understood. Because of the problem of preparing known concentrations of H_2 in the first excited vibrational state ($v = 1$) with this infrared-inactive molecule, it has only recently become possible to use this reaction in assessing the effect of vibrational excitation. Wolfrum and co-workers (*19*) overcame this problem, studying the reaction $D + H_2 \rightarrow DH + H$, by exposing a low-pressure flow of $HF + H_2$ in a helium carrier to short pulses (10 microseconds) from an HF laser tuned to the HF ($v = 0$) → HF ($v = 1$) fundamental. Rapid population of H_2 ($v = 1$) occurs by near-resonant vibrational transfer from HF ($v = 1$). Upstream D atoms, generated by dissociation of D_2 in a microwave discharge, are introduced into the flow. Absolute concentrations of vibrationally excited HF molecules are determined from time-resolved infrared emission. Concentrations of H atoms are determined from time-resolved absorption, using Lyman-α resonance radiation. Because H_2 ($v = 0$) reacts relatively slowly with D atoms at room temperature, the concentrations of H_2 and D can be adjusted so that the H atom product gives no strong background absorption of the Lyman-α radiation when the HF laser is off. Moreover, the concentrations of H_2 and HF are chosen so that only a small fraction of H_2 is excited to $v = 1$, ensuring that the concentration of H_2 ($v > 1$) is negligible.

It was found that the $D + H_2$ ($v = 1$) reaction was some 4000 times faster than the $D + H_2$ ($v = 0$) reaction, yet the latest quasi-classical trajectory calculations employing highly accurate H_3 potential energy surfaces yield a rate at the same temperature that is more than 40 times lower than the experimental result for $D + H_2$ ($v = 1$). Fully quantum treatments have not narrowed this gap appreciably, indicating that this simplest of chemical processes is not yet well understood.

A similar technique has been used by Zare and co-workers (*20*) to study the chemistry of vibrationally excited HF in the reaction $Sr + HF$ ($v = 1$) → $SrF + H$. A beam of Sr atoms was fired through a scattering chamber filled with HF gas at a pressure of 10^{-4} to 10^{-5} torr. The reaction $Sr + HF$ ($v = 0$) has an energy threshold of 6.4 ± 1.6 kilocalories per mole. When the HF is irradiated, SrF products appear. The rate of the $Sr + HF$ ($v = 1$) reaction once again was found to be orders of magnitude greater than that of $Sr + HF$ ($v = 0$).

Lasers are used to detect reaction products in such experiments by a technique called laser-induced fluorescence (LIF). Light from a tunable laser is directed into the reaction zone. As the wavelength of the laser is scanned, molecules in the zone are excited when the laser output overlaps an absorption line. Once excited, the molecules reemit the radiation, and some fraction of their fluorescence is imaged onto a photomultiplier. Recording the photomultiplier signal as a function of laser wavelength gives an "excitation spectrum," which is akin to an absorption spectrum but in emission. The observation of bright fluorescence against a dark background makes LIF extremely sensitive; molecular densities in the range 10^4 to 10^5 per cubic centimeter have been measured. The resolution depends on the line width of the laser source. In some studies by J. L. Kinsey and co-workers, single-mode tunable lasers have permitted measurement of the velocity of the molecule along the line of sight of the laser (Doppler effect) as well as the internal state distribution. Not all molecules are suitable for LIF detection, but when the technique can be employed, it brings all the power of molecular spectroscopy to bear on the analysis of reaction products.

In the study of Sr with HF, it was possible not only to determine the internal state distribution of the SrF products but also to investigate how this distribution changes when the HF ($v = 1$) reagents are prepared (i) with different states of rotational excitation and (ii) with different spatial orientations. The former was accomplished by tuning the HF pump laser to different vibrational-rotational transitions, the latter by exploiting the plane polarization of the pump laser output to select a preferred spatial distribution of the vibrationally excited HF molecules. Conversely, the spatial orientation of the SrF products can also be measured by varying the polarization of the tunable probe laser.

In addition, by comparing the $Sr + HF$ ($v = 1$) to the $Sr + HF$ ($v = 0$) reaction when the latter is carried out with excess collisional energy, Zare and co-workers have determined which form of energization is more effective in promoting reaction. It was found that vibrational excitation enhanced the rate up to ten times more than translational excitation at the same total collision energy. This finding is in accord with the generalizations of J. C. Polanyi, based on classical trajectory calculations, that barriers occurring late in the reaction path are more readily surmounted by reagent vibration, but that this mass combination minimizes the requirement of vibrational energy in overcoming the endothermic reaction barrier.

It was recently reported that lasers can provide radiation fields sufficient to influence intermolecular interactions during that brief moment when there are neither reagents nor products but only a transition state, thereby causing laser-assisted chemistry to occur (*21*). A molecular beam of K atoms was crossed with a beam of $HgBr_2$ molecules and the interaction volume irradiated with the pulsed output of a flash lamp-pumped dye laser tuned to 595 nanometers. At this wavelength the laser can excite neither reactants nor products. When the laser was on, luminescence was observed at 500 nm and attributed to emission from electronically excited HgBr. This product was presumed to have been formed by absorption of light ($h\nu$) during the reactive collision $[K\text{-}HgBr_2] + h\nu \rightarrow KBr + HgBr^*$. Such studies may permit chemists to probe the transition state and to obtain direct information about the bond-making–bond-breaking process.

These new experimental techniques are enabling chemists to focus on the role of individual reactive collisions and are providing a hitherto unseen view of chemical reactions.

References and Notes

1. ESCA, electron spectroscopy for chemical analysis; AES, Auger electron spectroscopy; ISS, ion-scattering spectroscopy; SIMS, secondary ion mass spectroscopy; LEEDS, low-energy electron diffraction spectroscopy; SEM, scanning electron microscopy; NMR, nuclear magnetic resonance; ICR, ion cyclotron resonance; and ICP, inductively coupled plasma.
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