



Viewpoints: Chemists on Chemistry

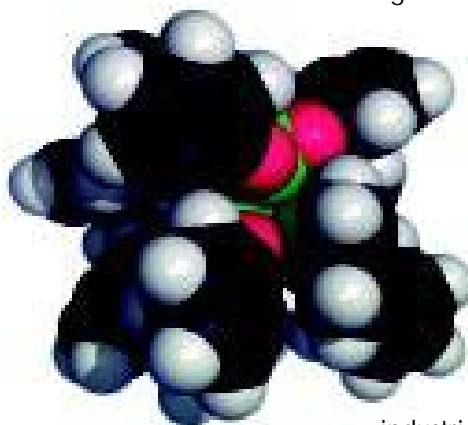
Fifty-Year Trends in the Chemical Industry: What Do They Mean for Chemical Education?

Chadwick A. Tolman and George W. Parshall

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The chemical industry and the way people work in it have changed dramatically during the past fifty years. This article describes some of these changes from the perspectives of the authors, whose careers span most of the preceding half-century. We describe five illustrative technological developments in the industry and changes we have seen in the industrial research laboratory, and offer viewpoints on how these changes affect the educational needs of students going into industrial careers. Finally, we make some predictions of future trends.

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Fifty-Year Trends in the Chemical Industry: What Do They Mean for Chemical Education?

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Enormous changes have occurred in the chemical industry in the half century since the end of World War II. It has grown in value to the U.S. economy to \$375 billion annually (1), or almost \$1500 for every man, woman, and child in the country. Products that did not exist in the mid-1940s—such as polyester and high-density polyethylene (HDPE)—have become commodities produced on a scale of millions of tons per year. Inventions such as photoimageable polymers have led to whole new industries. At the same time, the production of fine chemicals has increased in sophistication to the point where specific optical isomers are produced using catalysts with enzyme-like selectivity. Technological progress as well as changes in economic and environmental aspects of producing chemicals have greatly altered the way that industrial chemists and technicians work. The same factors have also changed what they need to know and to do in order to be effective in their jobs.

In this article, we review some technological changes as seen from our perspectives as industrial chemists whose careers span much of the past 50 years. One of us began his industrial research career in 1954; the other, in 1965. Our viewpoints and choices of illustrative examples reflect our experiences in DuPont. After the discussion of technological change, we examine the accompanying changes in the industrial laboratory environment and the implications of these changes for chemical education. We conclude with glimpses of the future for both the industry and the people who work in it.

50 Years of Technological Change

New Products and Processes

The new products mentioned fall into two categories: (i) large-volume, low-priced materials that we use every day, such as high octane gasoline, nylon tire cord and fabrics, Spandex fibers, polyethylene packaging, and cups made from polystyrene foam; (ii) low-volume, high-value products like pharmaceuticals, selective herbicides, photopolymers, chemicals for microelectronics, and high-performance composites. In many examples of the first category, new processes or catalysts have given improved ways to make a known product. In the second type, the need for products with special properties has led to development of brand new, sophisticated process technologies. In both categories, there has been a need to develop processes that are economical as well as environmentally friendly. We illustrate some of these technology developments, often using DuPont examples.

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Petroleum Refining

The largest chemistry-based industry is petroleum refining, the process of converting petroleum to gasoline, diesel and jet fuels, and other products. It is a technology-intensive process in which crude oil is distilled to separate its hundreds of components into fractions based on their boiling points. The distillates are treated with catalysts to make hydrocarbon products suitable for applications ranging from high-test gasoline to coloring crayons. The improvements in this technology during the past 50–60 years were a significant factor in winning World War II, as well as in the development of our automobile-based society. They have also kept the cost of gasoline relatively constant (in inflation-adjusted dollars) throughout this time period, despite depletion of the most accessible U.S. petroleum reserves. Further, the development of new technology to improve the performance of gasoline made possible the elimination of the highly toxic tetraethyllead (TEL) as a component of motor fuel. Many innovations have contributed to these achievements, but arguably the greatest was the development of catalytic cracking processes, especially those based on zeolites (2).

Only a small fraction of crude petroleum is directly usable as a motor fuel. The major fractions consist of high-molecular-weight compounds, which lack the volatility needed for use in internal combustion engines. In addition, a large fraction is made up of linear alkanes having undesirable combustion characteristics such as low “octane number”, an empirical measure of the tendency of fuel to preignite or “knock” in a gasoline engine. (TEL was an “octane enhancer”). The heart of a petroleum refinery (Fig. 1) is the “cracking” unit, which breaks high-molecular-weight hydrocarbons into volatile compounds, convertible to gasoline by processes such as catalytic alkylation and reforming (3).

Until 1940, the cracking of the high-molecular-weight fractions was carried out by simply heating the materials to temperatures at which they decompose to more volatile compounds. Roughly half of the product derived from thermal cracking of long-chain hydrocarbons was C_2 and C_3 gases, useful for their ethylene and propylene content, but not for the gasoline technology of the 1930s. Even worse, the products with vapor pressures corresponding to gasoline were largely linear hydrocarbons with poor octane numbers. The introduction of acidic aluminosilicates as cracking catalysts in the 1940s led to higher yields of branched hydrocarbons with improved octane numbers. However, the yield of gasoline was still low relative to the amount of petroleum processed, and the quality, as measured by octane number, was inadequate for high-performance engines.

A major breakthrough in refinery technology was the development of zeolite-based cracking catalysts that increased



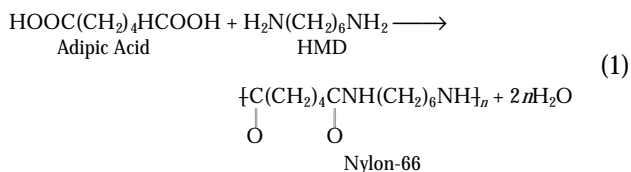
Figure 1. Photograph of a modern oil refinery.

both the yield and the quality of gasoline. Zeolites are crystalline aluminosilicates that have channels a few angstroms in diameter threaded through the crystal lattice, as illustrated in Figure 2. The size and shape uniformity of these channels enables them to serve as "molecular sieves", which will admit small molecules up to certain critical diameters. In addition, based on the Si:Al ratio and the mode of preparation, the channels in zeolites can have either Brönsted or Lewis acid sites, which can catalyze the isomerization of hydrocarbons that find their way in. The ability of certain zeolites to exclude branched alkanes while admitting straight chains (with molecular diameters $< 5 \text{ \AA}$) permits selective isomerization of linear alkanes to their branched isomers. This property is used to increase the percentage of branched compounds in the product mixture and thus increase the octane number of the gasoline.

Production of Nylon

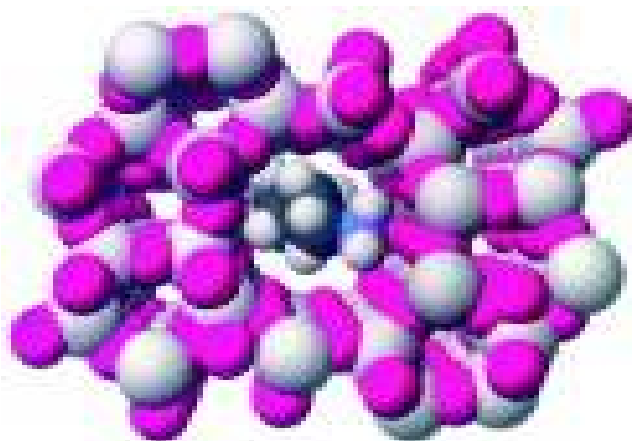
Perhaps the most important development in terms of changing the chemical industry was the synthesis and production of totally synthetic polymers. Rayon, a semisynthetic polymer produced by chemical modification of cellulose, had made a major impact on the textile industry by 1930, but totally manmade polymers were still a gleam in the eyes of a few visionaries.

One of the visionaries was a Harvard professor, Wallace Carothers. DuPont hired him in 1928 to start a basic research program that might lay the foundation for new businesses. He chose to study the properties of long-chain organic compounds (polymers) formed by joining together simple repeating units. His research group made hundreds of totally synthetic polymers, of which the most important was nylon-66. This polyamide was made from adipic acid and hexamethylenediamine (HMD) as shown in eq 1:



It could be spun into tough, durable, silklike fibers by techniques developed in Carothers' group. Nylon fiber was commercialized in 1938 and succeeded brilliantly with women's stockings. During World War II, its production was diverted to making parachutes. Civilian production resumed after the war and the technologies for making the polymer and its two starting materials have evolved continuously since.

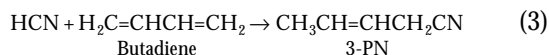
Figure 2. Schematic representation showing the snug fit of a dimethylamine molecule within a channel of a ZSM-5 zeolite. The zeolite crystal is made up of Si and Al ions (both shown in silver) linked together by oxygens (red). The nitrogen atom (blue) of the organic molecule is ionically bound to an acidic site in the channel wall.



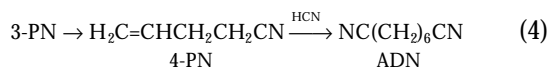
A major breakthrough in producing HMD was the discovery of a catalytic process to add two molecules of HCN selectively to butadiene to give adiponitrile (ADN), which can be hydrogenated to HMD in high yield as shown in eq 2:



This selective terminal addition of an HX molecule to a C=C double bond had no precedent outside free radical chemistry, but the economic and environmental incentives to produce ADN and HMD by this route were considerable.¹ Several DuPont scientists attempted to find catalysts for the selective HCN addition. In the 1950s, their exploratory research showed that Cu⁺ salts can catalyze a single HCN addition (eq 3), but the remaining C=C bond in the 3-pentenitrile (3-PN) product was located in the middle of the molecule. It seemed to be a dead end in terms of the desired double addition (eq 2) to the ends of the butadiene molecule:



In 1963, William C. Drinkard of DuPont resumed the search for the desired reaction sequence. After about a year of testing, he found that a newly discovered class of nickel compounds produced 3-PN as well as did the Cu⁺ salts. More importantly, the nickel catalysts also brought about the desired second addition (eq 4), by a combination of C=C migration to the end of the chain and HCN addition to the terminal double bond:



The selectivity for terminal addition to the intermediate 4-PN olefin left much to be desired, but another discovery provided the key to a practical catalytic system. Drinkard found that adding Lewis acids like ZnCl₂ greatly improved both the rate and the selectivity of the second HCN addition (4). One of the remarkable features of the Drinkard process is that all the steps are carried out by the same nickel catalyst (shown in Fig. 3), a nickel atom surrounded by four triaryl phosphite molecules.

The significance of Drinkard's discoveries was immediately apparent. Within a short time a team of chemists and engineers was assembled to optimize the chemistry and evaluate possible designs for a manufacturing facility. The critical reactions were carried out on a continuous basis, first in laboratory glassware, then in an integrated pilot plant. After about five years of development and engineering research, the new ADN synthesis was commercialized in a production-scale plant at Orange, Texas. This chemistry is now practiced at two sites in Texas and one in France. Every year, more than a billion pounds of ADN are manufactured in this way at a very favorable price.

Because of the economic and environmental importance of the ADN process, research on the catalysts has continued for more than 30 years. Improved fundamental understanding of the chemistry has yielded two major benefits: nylon-66 has remained economically competitive with other polymers in a variety of applications that call for strength and temperature resistance, and studies of the catalytic mechanism have deepened our understanding of the fundamental principles of homogeneous catalysis. Research in this area by one of us (see sidebar and Fig. 4) helped elucidate the concept of the catalytic cycle (5, 6), the role of 16- and 18-electron metal complexes (7), and the importance of size (steric) effects in determining the chemistry of transition metal complexes (8).

Replacing Chlorofluorocarbons

A recent challenge for the chemical industry has been the replacement of chlorofluorocarbons (CFCs). CFCs were introduced in the 1930s as a new, apparently benign class of refrigerants for air conditioners and home refrigerators. Their properties seemed nearly perfect: good cooling efficiency, high stability, low toxicity, and nonflammability.

The problem that doomed the commercial future of CFCs was unexpected. They are too stable. When released into the atmosphere, they survive for decades and migrate to the stratosphere, where they finally dissociate under the action of ultraviolet radiation. The chlorine atoms thus formed catalyze the decomposition of the stratospheric ozone that shields us from harmful UV radiation from the sun. Rowland and Molina postulated this effect in 1974 (9). In response to this prediction, the United States began to phase out the use of CFCs

Figure 3. A space-filling model of an NiL₄ molecule (L = triphenyl phosphite). The nickel atom is almost invisible amongst the four green phosphorus atoms. Oxygen atoms are shown in red.





as propellants in aerosol containers, a step that was relatively easy and effective in stabilizing U.S. emissions of the CFCs.

Rowland and Molina's prediction was confirmed in the 1980s with the discovery of the Antarctic ozone hole. The firm evidence for the deleterious effect of the CFCs called for strong action to reduce and eventually end CFC emissions. In 1987, many nations agreed to the so-called Montreal Protocol, which mandated the phase-out of CFC production and sales. Rowland and Molina shared a Nobel Prize with Paul Crutzen in 1995.

The chemical industry faced a difficult challenge in developing alternative materials having most of the desirable properties of the CFCs without endangering the ozone layer. At DuPont, computer modeling of the structures and properties of dozens of potential CFC alternatives was carried out to help narrow the field for process development; many of

the alternatives had not previously been made. The technical strategy adopted was to replace the CFCs with HFCs (hydrofluorocarbons), chlorine-free compounds that are destroyed in the lower atmosphere by hydroxyl radical ($\text{HO}\cdot$) attack. To give the physical properties required, the HFCs must have more complex molecular structures than the corresponding CFCs (10). This effect can be seen in Figure 5 by comparing the structure of CFC-12, a common refrigerant used in automotive air conditioners, with that of HFC-134a, the generally accepted replacement.

The structural complexity of the HFCs requires more complex production technology. For example, CFC-12 is made by a single step catalytic fluorination of carbon tetrachloride, as shown in eq 5:

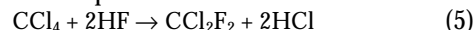


Figure 4. The catalytic cycle for the addition of one mole of HCN to butadiene catalyzed by NiL_4

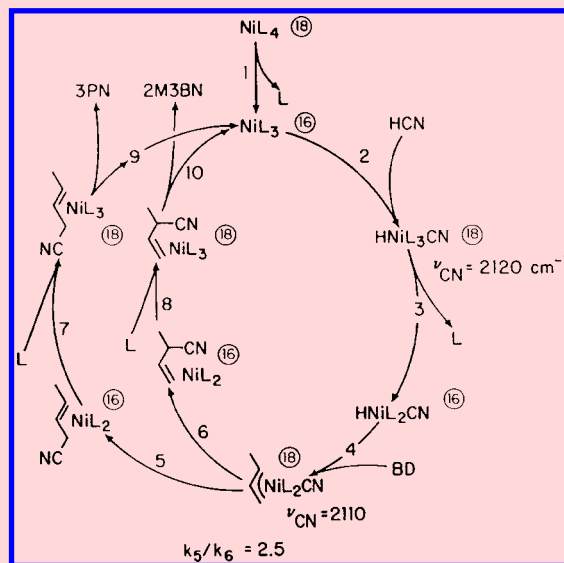


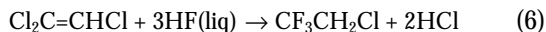
Figure 4 shows a simplified catalytic cycle (5) for the formation of 3-PN (3-pentenitrile) and 2M3BN (2-methyl-3-butenitrile), which occurs in step I of butadiene (BD) hydrocyanation. The cycle has two branches because two products can form from the common $\eta^3\text{-C}_4\text{H}_7\text{NiL}_2\text{CN}$ intermediate shown at the bottom of the cycle. Because all the steps shown are reversible, the scheme also accounts for how the same NiL_4 catalyst can isomerize the branched 2M3BN to the desired linear 3-PN, before the second HCN is added in Step II. (Since many intermediates are involved in a catalytic cycle, we use the term "catalyst" to refer to the compound added to the reaction mixture to cause the desired reaction. The ability of the system to avoid adding a second mole of HCN while unreacted butadiene is present [step I conditions] depends on the greater stability of the η^3 [π -allyl] intermediate shown compared to the η^1 (σ -alkyl) intermediates involved in step II.)

The numbered circles show the numbers of valence electrons on the central nickel atom at each stage of the reaction. The commonality of 16- and 18-electron complexes in this chemistry—for all the organometallic complexes that can be isolated or observed spectroscopically, or for which there is kinetic evidence—led to the 16- and 18-electron rule (7). The individual numbered reaction steps, which occur in reversible pairs (ligand dissociation/association in reaction 1, oxidative addition/reductive elimination in 2) have rates and equilibria that depend on the steric and electronic characteristics of the phosphorus

ligands, shown as L. For example, the K_1 at 25° for dissociation of L from NiL_4 increases by 8 orders of magnitude on changing L from $\text{P}(\text{O}-p\text{-tolyl})_3$ to $\text{P}(\text{O}-o\text{-tolyl})_3$ (*J. Am. Chem. Soc.* **1974**, *96*, 53). This increase is caused by a change in the ligand cone angle (8) from 128° to 141°. Oxidative addition of HCN to NiL_4 to form HNiL_3CN and L (a combination of reactions 1 and 2) shows declining equilibrium constants (K_1K_2) of 0.03, 0.005, and 0.0001 as the electron withdrawing ability of the ligand increases in the series $\text{L} = \text{PPh}(\text{OEt})_2$, $\text{P}(\text{OEt})_3$, $\text{P}(\text{OCH}_2\text{CH}_2\text{Cl})_3$ (5).

That the decrease (a factor of 300 across the series) has an electronic rather than a steric origin is indicated by two facts. First, ligand competition equilibria for $\text{Ni}(\text{O})$ (*J. Am. Chem. Soc.* **1970**, *92*, 2956), where steric effects dominate, show that the three ligands are sterically equivalent (K_1 for $\text{Ni}[\text{P}(\text{OEt})_3]_4$ is too small to measure directly [no dissociation is spectroscopically detectable up to 70°]; the ligand cone angle of $\text{P}(\text{OEt})_3$ is 109°). Second, the CN stretching frequencies in the HNiL_3CN complexes increase in the series in the same order: 2113, 2120, and 2130 cm^{-1} . Carbonyl stretching frequencies of the $\text{Ni}(\text{CO})_3\text{L}$ complexes show the same trend. These easily measurable frequencies provide a way to characterize the electronic character of phosphorus ligands (*J. Am. Chem. Soc.* **1970**, *92*, 2953) even in cases where HNiL_3CN complexes do not form to a measurable extent, for example with $\text{L} = \text{P}(\text{OCH}_2\text{CCl}_3)_3$.

The HFC replacement requires a difficult multistep process. The researchers developing a new process faced another challenge: the new process had to have few if any external emissions. Although the companies competing to replace CFC-12 agreed on HFC-134a as the material that came closest to providing the required properties, they developed different processes for its manufacture. The British firm ICI, for example, chose the two-step sequence shown in eqs 6 and 7.



The ICI process, like those developed by DuPont and others (11) required extensive catalyst development research. The result of several years of concentrated R&D was the timely commercialization of HFC products as refrigerants and foaming agents for polymeric foams.

The overall effect of this intensive R&D and commercialization effort has been to slow the accumulation of CFCs in the atmosphere and to reduce the rate of ozone depletion. Models indicate that further ozone depletion should cease in about ten years, but healing the stratospheric ozone layer will require several decades (12).

Selective Crop-Protection Chemicals

The past half-century has seen dramatic changes in the way that farmers control insect, weed, and fungus pests. There were once great expectations for the potential benefits of new synthetic pesticides, especially the chlorinated hydrocarbon insecticides such as DDT, the structure of which is shown in Figure 6. These chemicals failed to live up to their promise because of two unanticipated problems: the rapid development of resistance to such chemicals by common insect pests, and long-lasting ecological effects of these stable, fat-soluble compounds. The dangers were first effectively called to public consciousness by Rachel Carson's book *Silent Spring* (13). More recently, another warning flag has been raised by *Our Stolen Future* (14), which describes developmental abnormalities in fish, birds, reptiles, and mammals, including humans, possibly attributable to prenatal endocrine disruption caused by trace quantities of persistent chlorinated organic chemicals in the environment. The phase-out of 12 of these compounds has been agreed to in an international protocol (15).

In the past two decades, the persistent, broad-spectrum pesticides have been replaced in many applications by highly selective compounds such as the sulfonylurea herbicides (16) and the synthetic pyrethroid insecticides (17, 18). These new crop-protection chemicals target specific enzyme systems in plants or insects and have low mammalian toxicity. They also minimize environmental effects by their very low application rates (grams rather than pounds per acre) and by their not persisting. They are designed to hydrolyze or photodegrade in a few days or weeks instead of lingering in the soil for long periods. Examples of this new generation of crop-protection chemicals are Glean, a sulfonylurea herbicide, and esfenvalerate (Asana), a synthetic analog of the natural insecticide pyrethrum (Fig. 7).

In many respects, development of these new agrochemicals resembles the drug discovery process in the pharmaceutical industry, involving the synthesis of thousands of new compounds to be tested for a specific biological activity. The search for selective herbicides required synthesis of tens of thousands of



Figure 5. Molecular structures of compounds used as refrigerants in automotive air conditioners. The previously used CFC-12 is simple compared to the current standard refrigerant, HFC-134a.

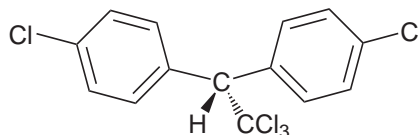


Figure 6. The molecular structure of DDT. The acronym is derived from the trivial name for the compound, DichloroDiphenylTrichloroethane. Some insects acquire resistance to the compound by enzymatic dehydrochlorination of the CHCl_3 function.

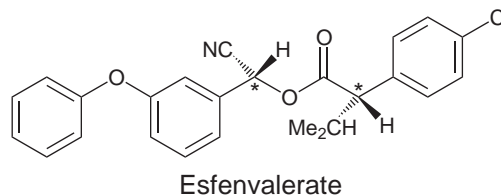
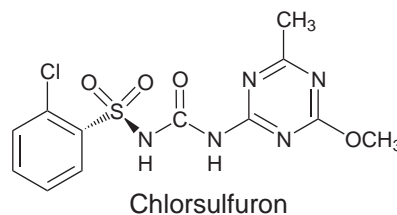


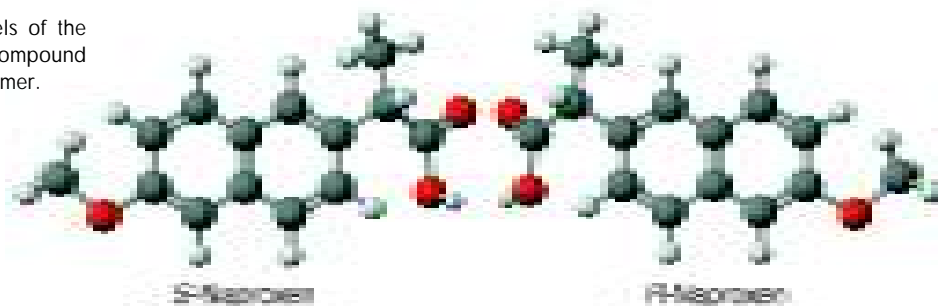
Figure 7. Molecular structures of two highly active agrochemicals with low mammalian toxicity. Chlorsulfuron is a selective herbicide. Esfenvalerate is a specific optical isomer (chiral centers marked with asterisks) of a synthetic compound related to the natural insecticide pyrethrum.

new sulfonylureas in order to identify compounds that would kill weeds, but be safe for people and important crops (wheat, in the example of Glean). Because the amount of effort required is so great, future R&D in this area is likely to utilize combinatorial approaches (19), which we discuss later.

Another feature of the new crop-protection chemicals reminiscent of pharmaceuticals is the complexity of their chemical structures. The structure of esfenvalerate in Figure 7 contains two chiral centers. As a consequence, the compound has four stereoisomers, only one of which maximizes the desired biological selectivity and activity. The manufacturing process for this isomer utilizes enantioselective catalysis to form one of the centers. Separation of mixed isomers of an intermediate compound is used to obtain the other. These technologies closely resemble those now used in the production of chiral pharmaceuticals.



Figure 8. Ball-and-stick models of the anti-inflammatory analgesic compound S-naproxen and the toxic R isomer.



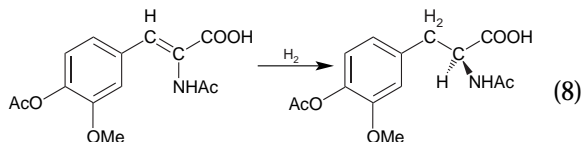
Chiral Pharmaceuticals

Most therapeutic chemicals act by interaction with specific biological receptor sites in the human body or on the surface of invading microorganisms. These receptors are commonly proteins or polysaccharides, which have inherent chirality or handedness. As a consequence, the therapeutic effectiveness of a compound containing chiral centers may depend on whether it is the left- or right-handed stereoisomer. A typical example is the antiinflammatory drug naproxen, which is sold over the counter as Aleve. The S isomer has the desired medicinal properties, but the R isomer is a liver toxin (Fig. 8).

The difference in physiological properties exemplified by the naproxen isomers is typical of chiral pharmaceuticals. Sometimes the therapeutically inactive isomer is innocuous and the drug can be sold as the racemic mixture. However, there are several examples of unexpected and undesirable side effects of "inactive" isomers. Thalidomide is a case in which the desired sedative effect resides in one isomer, but the other isomer is responsible for teratogenic side effects that lead to birth defects in children. Such examples have induced caution in approving racemates for sale. There is an increasing trend to sell drugs as single enantiomers (20).

The manufacture of enantiomerically pure drugs is a major challenge for pharmaceutical companies. Some, such as S-naproxen, are produced by separation (resolution) of racemic mixtures. Others, like the penicillins, are made by biosynthesis in which an enzyme or a microorganism is used to produce the desired enantiomer directly. A third alternative, which has emerged in the past 30 years, is to use an enantioselective synthesis catalyst with very high selectivity.

The pioneering example of enantioselective catalysis in drug manufacture is Monsanto's commercialization of synthetic L-DOPA, which is used in the treatment of Parkinson's disease. The key step in this process is the selective hydrogenation (eq 8) of a prochiral enamine to give specifically the levo isomer of DOPA, bearing protective groups to be removed in a later step. This selectivity for making a single enantiomer was achieved (21) using a soluble rhodium catalyst bearing the chiral diphosphine ligand DIPAMP shown in Figure 9.



In recent years, the demand for chiral pharmaceuticals and agrochemicals has stimulated intensive research on new enantioselective synthetic methods. Some of the most prom-

ising processes are the selective epoxidation (22) and vicinal dihydroxylation of olefins (23) and enantioselective hydrogenations of olefins. The enzyme-like catalysts for these reactions are transition metal complexes of chiral organic ligands. Research in this area appears to have great promise for both fundamental and practical advances.

Changes in Manufacturing

Along with new chemical products, there have been major changes, both quantitative and qualitative, in the ways that chemicals are manufactured. The sheer volume of production has increased both because markets are larger and because wholly new chemistry-based industries have arisen—for example, synthetic fibers and rubberlike materials, structural plastics, and packaging films. Manufacturing has also become more sophisticated. The changes are partly technology-driven by the availability of automated control systems and online analytical instrumentation. Change is also driven by the need to meet higher standards of safety, health, and environmental responsibility.

World-Scale Production Facilities

The scale of production has risen dramatically for commodity chemicals, such as methanol and ammonia, which are sold on the basis of price rather than unique physical properties. Modern plants for making ammonia and methanol are typically scaled to produce over 1000 tons per day (Fig. 10).

The driving force for constructing larger plants is economy of scale. The capital investment for a continuous production facility generally does not increase linearly with capacity, but scales with about the 0.7 power. The cost savings are not so much in the chemical reactors as in the auxiliary facilities such as piping, control systems, waste disposal, and



Figure 9. Structure of the chiral ligand DIPAMP used to make the catalyst for L-DOPA production.



Figure 10. Photograph of a world-scale methanol production facility.

utilities (steam, cooling water, electricity, and the like). There are also significant savings in operating costs for a larger facility, especially for labor.

The cost savings associated with bigger plants often provide economic incentives to build and operate facilities large enough to supply the product demands of several countries. Particularly with highly sophisticated processes such as the hydrocyanation discussed above, it can be desirable to concentrate the production of a chemical intermediate at one site. The intermediate may then be exported to several countries for conversion to a final product. As the markets in these other countries grow, the demand for the intermediate may become large enough to justify local production facilities. In this way, supply networks expand to involve several countries and even multiple companies.

Automated Control

Most modern chemical plants operate with a high degree of computer control (Fig. 11). This serves to keep the process close to optimum chemical efficiency and to insure safe operations.

The efficacy of automated controls depends on rapid feedback from the process reactors to the computers that control process inputs such as reactants, diluents, heating, or cooling. Physical parameters such as temperature, pressure, and flow rates can be related to the input controls in a relatively straightforward fashion. Other parameters relating to process chemistry and product quality are more subtle and have required development of new monitoring technologies such as online spectroscopy or chromatography. Online optical scanners and automated imaging systems have been developed to monitor the size and color of particulate solids or the crystallinity and clarity of fibers and films. Inclusion of such devices in integrated control systems both improves product quality and reduces environmental impacts by reducing the amount of off-specification product that must be reprocessed or discarded.

The rapid growth in computer capabilities has played a major role in the effective use of monitored inputs to control chemical processes. Dramatic changes have also occurred in the sophistication of the process models that provide the basis for control strategies. In addition to "getting that last half percent performance", the control systems must also be "robust" (24). The systems must control effectively under both normal operation and conditions of process upset caused by uncontrolled factors such as variations in feedstock, utility interruptions, or changes in weather conditions. The robustness built into the better control systems pays dividends in terms of protecting safety, health and the environment by reducing the danger of runaway reactions and toxic emissions.

Enhanced Safety, Health, and Environmental Protection

The safety and environmental responsibility of the chemical industry have improved dramatically over the past half-century. Many of the waste disposal practices of earlier decades would be unthinkable today: for example, the dumping of raw chemical wastes into the Love Canal (25). Old practices such as ocean dumping and injection of wastes into deep wells have been discontinued or are being phased out. Today's hazardous waste incineration is a far cry from old practices of uncontrolled waste burning. Modern incinerators operate at high temperatures for complete combustion, have sophisticated pollution-control systems to remove harmful vapors and particulates, and are monitored to meet strict regulatory standards. For many aqueous organic wastes, incineration and direct discharge have been replaced by biological oxidation processes that may discharge cleaner water than that taken in by the plant.

In preference to improved disposal operations, much effort is being devoted to the elimination of process wastes. This approach not only leads to a cleaner environment, but tends to reduce consumption of energy and feedstocks. The reduced use of fossil fuels in turn reduces the discharge of carbon dioxide, nitrogen oxides, and other gases that contribute to air pollution and global warming.

Another positive change in the operations of the chemical industry is more comprehensive and stringent testing of new products. This change has come about through a combination of public pressure, government regulation, and a greater self-awareness on the part of industry. In this last respect, it is enlightening to consider the changes in attitudes among chemists and their managements.

From the late 1940s, there was an attitude of "get the job done" without much consideration of possible consequences. This attitude led to the release of new chemicals into the environment without adequate testing for potential biological effects. The attitude was partially a holdover from World War II, but it also reflected inadequate knowledge. Prime examples are the chlorinated hydrocarbons such as DDT insecticide, PCB transformer fluids, and 2,4-D and 2,4,5-T herbicides, which often contained polychlorinated dioxins. Each new material offered potential economic and societal benefits. DDT, for example, provided a cheap and effective way to control houseflies, mosquitoes, and other disease-carrying insects (26). DDT has saved hundreds of thousands of people from death by malaria. The collateral damage to the bird, animal, and human populations (13, 14) was totally unexpected.

In the 1990s, it is hard to imagine the widespread release of a new chemical without intensive scrutiny of its potential



effects on people, wildlife, and domestic animals. The pressures of government regulation and potential legal liability, as well as a greater sense of social responsibility, have led to routine testing for a broad range of possible biological effects. The tests measure not only acute toxicity but also subtle effects from long-term, low-level exposure in a wide variety of living creatures. The Environmental Protection Agency recently announced an extensive new screening and testing plan to identify potentially endocrine-disrupting chemicals (27).

Despite the progress in the past half-century, many challenges remain for the chemical industry in both the technical and societal arenas. Chemical manufacturers must cope daily with the dangers of handling highly toxic chemical intermediates in the manufacture of many consumer products. Failure of process safeguards can have disastrous consequences, such as the death and injury of thousands of people from a release of methyl isocyanate vapor in Bhopal, India. In the particular case of toxic gases such as MeNCO, HCN, and phosgene, the hazards can be greatly reduced by making the intermediate on site as needed, without maintaining significant inventories. Rail transport of toxic materials such as chlorine remains a challenge.

Changes in Business—Globalization

Science has always had an international flavor, but the corporations comprising the chemical industry have had historical affiliations with individual countries. Fifty years ago, it was simple to say that DuPont and Dow were American, ICI was British, and Hoechst, BASF, and Bayer were German. Now all six companies (and many others) operate globally. Their headquarters and research facilities may be located in their home country, but their production and sales operations span four or more continents. For example, 40–45% of DuPont's 1997 sales and fully 50% of its income were generated outside the United States (28). Networks of business alliances have enhanced the international character of the industry. An example is the DuPont–BASF joint venture to build and operate a world-scale nylon intermediates facility in China (29).

At the R&D level, international collaboration is at an all-time high. While national boundaries have seldom stopped the flow of scientific ideas, many developments of the past 50 years have combined to accelerate the movement of ideas, data, and people between countries. In the 1950s, the advent of rapid and affordable air travel opened the way for thousands of scientists to attend international meetings and conferences. The personal links formed through face-to-face interactions led to many research collaborations. These international research programs were assisted by new funding mechanisms such as NATO grants, Fulbright fellowships, and international programs supported by the National Science Foundation (30). For global companies, the ease of international travel has facilitated cooperation between personnel in different countries as well as collaborations between companies. The tacit acceptance of English as the international language of science has also facilitated such collaborations. The latest boost to international programs has been digital electronic communications that permit nearly instantaneous transmittal of data between corporate laboratories on different continents.

Changes in the Research Laboratory

When we began our industrial research careers in 1954 and 1965, it was common to have a male chemist and his assisting technician (also male) working in the laboratory on the chemist's own project (Fig. 12). There were few team projects, and even fewer women in the lab. The chemist worked at the bench, doing most of the experimental work. The technician set up equipment, washed glassware, and ran errands; few had more than a high school education. Data collection was slow and laborious; recorders were strip-chart. Most instrumentation (IR or UV–vis spectrophotometers or GCs) was not in the chemist's lab, but in a shared instrument area, often operated as a service by a dedicated technician reporting to an analytical chemist. Graphs were plotted on coordinate paper by hand. Draftsmen drew ink plots for publication. Reports were hand written and typed by secretaries. In those days cc meant carbon copy.

Figure 11. Photograph of a modern control room.



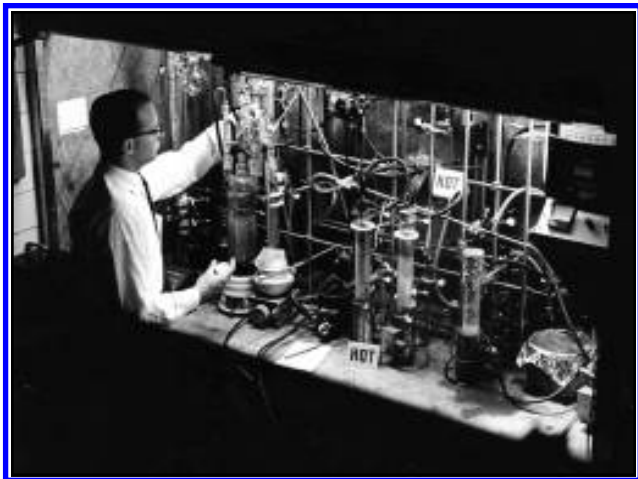


Figure 12. Photograph of an industrial research laboratory, ca. 1960.

Today's research enterprise is much different (Fig. 13). Many chemists and technicians, as well as managers, are women. Most of the work is done in teams, often involving scientists and engineers with different areas of specialization and expertise. Except for the most expensive instrumentation, like high-field NMR spectrometers or the automated equipment for high-throughput testing of catalysts or biologicals, the instruments are now in the chemist's laboratory and are rapid, sophisticated, and computer-controlled. The technician prepares samples, collects data, and often provides a written description of what was observed, along with any deviations from the agreed procedure. The chemist spends much of the day at a desktop computer or in meetings—planning the experiments, analyzing the data, and communicating the results to other team members and management. Drafting, plotting, and writing are now done by the scientist and technician on the desktop computer. The shifting of experimentation to the technician means that he or she must be much more highly skilled and better educated than formerly. Technicians hired today in



Figure 13. Photograph of a contemporary industrial laboratory. The scientists in the picture are wearing safety glasses, which are considered the minimum level of eye protection in an industrial laboratory. Current DuPont safety standards require attachment of side shields to the safety glasses worn for routine operations. In addition, most laboratory synthesis procedures are carried out behind fixed or movable shields.

most companies have at least a two-year Associate degree; many have a B.S. or M.S. degree, especially in the life sciences. Technicians need to understand basic chemistry, physics, biology, mathematics, and computer operations. Communication skills, both oral and written, are now important for technicians as well as chemists.

Everyone now devotes considerable time and effort to the safety and health aspects of laboratory work—reviewing or drawing up MSDSs (Material Safety Data Sheets), complying with waste disposal regulations and prudent practices, and doing preexperiment reviews of operating procedures.

Teams working on a project may include individuals at different sites and in different countries. Video-conferencing, email, and electronic data transmission facilitate communications between sites. Statistical design of experiments and both empirical and fundamental mathematical modeling are becoming common, facilitated by computer networks that include high-speed computers and by easy-to-use commercial software.

Implications for Chemical Education

The qualities that chemical companies seek in chemists and technicians include the abilities to:

- Work creatively on complex and unfamiliar problems;
- Communicate effectively in both speaking and writing;
- Work in teams; and
- Assess one's own knowledge and learn what one needs to know over the course of one's entire career.

The last item in the list is growing in importance because of the rapid growth in scientific knowledge and because of continual changes in technology. No one can learn everything he or she needs to know in school. Learning how (and what) to learn is becoming more important than any fixed body of knowledge, although a solid understanding of the fundamentals is still essential. An increasing amount of the learning will be self-paced and Internet-based, although there will always be a place for classrooms, labs and workshops where learners can interact face to face with teachers and peers.

Becoming adept at using the Internet and finding information in databases and other electronic sources will be necessary for success. As an example, databases of patents, which are a key source of information for the industrial chemist, are provided by information service firms. Two free databases provide access to the abstracts of most US patents published in the past 25 years (31, 32).

It should be noted that the fraction of Ph.D.'s in chemistry going into industry is increasing while the fraction going into academia declines (33). Colleges and universities need to pay attention to the kind of education their students at all levels require. Many already do. Major efforts to revise chemistry courses and curricula are going on, several of which are supported by the Division of Undergraduate Education at the National Science Foundation (34). We have participated in one of these at the University of Wisconsin–Madison.

The modern industrial laboratory has a very cosmopolitan aspect, with scientists and engineers from many nations and ethnic backgrounds coming together to work toward common objectives. It is important for both chemists and technicians to appreciate the cultures and languages of others and to be able to work in a highly diverse environment.



Glimpses of the Future

Predicting 25 years into the future is risky, but some historic trends have been discernible that far in advance. For example, the potential impact of transition metal organometallic chemistry on homogeneous catalysis seemed obvious in the 1950s. In fact, one of us wagered his career on it (see George Parshall's biographical sketch at the end of this article). The chemical industry's early investment in exploring soluble catalysts paid off in the early 1970s with a wave of innovative new technology, which is still being exploited. Examples include the DuPont hydrocyanation technology discussed earlier, Monsanto's process for making L-DOPA by enantioselective hydrogenation, the Rh-catalyzed manufacture of acetic acid and oxo alcohols, and the production of propylene oxide by catalytic epoxidation. While the histories of these developments differ considerably, what they have in common is that the scientific advances of the 1950s set the stage for applied research in the 1960s that led fairly directly to commercial development (35).

In seeking trends that will shape the chemical industry in the next quarter-century, we can begin by looking at the "hot" research topics of today that seem to have the potential for major commercial impact. Two that come immediately to mind are at the interfaces of chemistry with biology and with materials science. New medical therapies based on a chemical understanding of the mammalian immune system and of the human genome rank high on the list of topics at the chemistry-biology interface. Developments in this area seem to offer the best leads yet in dealing with difficult diseases such as cancer and AIDS. Closely allied to these biological approaches are the new chemical technologies needed to discover and produce the actual therapeutic agents.

Combinatorial chemistry, which generally combines elements of automated synthesis with high-throughput testing, appears to have great potential for the discovery process in both pharmaceuticals and agrochemicals (36). Simultaneously, enantioselective catalysis can be the tool for making the biologically active, usually chiral, chemicals used for therapy. The catalysts used may be either synthetic or enzymatic. It seems likely that there will be keen competition between catalyst chemists and biochemists to devise the most cost-effective and environmentally acceptable technology for any given application. The work of the biochemists will be facilitated by new ways to genetically engineer organisms to produce enzymes with the desired capabilities. Both types of chemists will benefit from new fundamental understanding of reaction mechanisms and from new computer modeling techniques for catalyst design.

Development of ecologically acceptable production technologies will remain a major challenge for the chemical industry. We anticipate that new chemical processes will be designed to generate minimal wastes through efficient use of feedstocks. This approach is in contrast to "end of pipe" treatment of unwanted by-products, which has commonly been used to make existing processes con-

form with environmental standards. The development of inherently low-emission processes will challenge both the catalyst chemist and the process engineer. Ever-closer collaboration between these two disciplines will be required to maximize selectivity and minimize emissions. Success in process development will pay off both in reduced environmental impact and in reduced costs for feedstocks, waste disposal, and energy. Reducing energy requirements will reduce the burning of fossil fuels and the resulting emission of carbon dioxide. The demand for petroleum and natural gas may also be reduced by increased use of biomass as a feedstock for industry. A prototype of this trend is DuPont's announcement of a switch from a hydrocarbon-based starting material to a carbohydrate-based feedstock for the production of 1,3-propanediol, a component of a new polyester engineering resin (37).

The second cluster of emerging technologies is at the interface of chemistry and materials science, especially as applied to electronics. The ongoing trend in the electronics industry toward smaller, faster, and cheaper devices requires innovative new materials, providing rich opportunities for the synthesis chemist. One example is the drive to integrated circuitry with circuit line widths of 0.25 μm or less. Because conventional imaging technology begins to fail at these dimensions, new chemistry-based imaging technologies are being studied. These are part of the emerging field of nanotechnology, the controlled fabrication of devices with features whose dimensions are in the range of 1–100 nanometers. For most chemists, this length scale is awkward. We are accustomed to thinking of angstrom-scale molecules and of micrometer-sized fibers and films. However, nanoscale molecular aggregations present fascinating opportunities for both new science and new technology.

One of the most promising approaches to nanotechnology lies with self-assembled films, whether they are prepared on metallic surfaces or on surfaces of liquids (Langmuir-Blodgett films). The former approach has been used to pattern submicron devices on surfaces by remarkably simple techniques derived from lithography (38). The Langmuir-Blodgett films have been used to fabricate simple devices for optical applications. Polymer films containing nonlinear optical functionality may be developed into practical media for optical switching devices (39). These various ways of arranging molecules in orderly arrays will receive increasing attention as ways to overcome the inherent scale limits on current electronic and optical devices.

The methods of combinatorial chemistry are also likely to play a significant role in the search for materials with particular electronic properties. Two recent examples illustrate this trend: combinatorial solid state syntheses and screening have been used to identify new blue photoluminescent materials (40) and new insulator (41) compositions. The power of the new methods will make them valuable tools for the industrial materials chemist in the next quarter century.

Note

1. The older process involved converting sodium chloride to sodium hydroxide and chlorine by electrolysis, chlorinating butadiene to mixed dichlorobutenes, reacting the NaOH with HCN to produce NaCN, displacing chloride from the dichlorobutenes with cyanide to give sodium chloride and 1,4-dicyano-2-butene, and then hydrogenating the dicyanobutene to HMD. More than a pound of NaCl was processed for each pound of HMD produced.

Literature Cited

1. *U.S. Chemical Industry Statistical Handbook*, Chemical Manufacturers Association: Arlington, VA, 1996.
2. National Research Council. *Catalysis Looks to the Future*, National Academy Press: Washington, DC, 1992.
3. Occelli, M. L. *Fluid Catalytic Cracking: Role in Modern Refining*, ACS Symposium Series 375; American Chemical Society: Washington, DC, 1988.
4. McKinney, R. J. In *Homogeneous Catalysis*, Parshall, G. W.; Ittel, S. D., Eds.; Wiley: New York, 1992; pp 42–47.
5. Tolman, C. A. *J. Chem. Educ.* **1986**, *63*, 199–201.
6. Tolman, C. A. *J. Am. Chem. Soc.* **1972**, *94*, 2994–2999.
7. Tolman, C. A. *Chem. Soc. Rev.* **1972**, *1*, 337–353.
8. Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313–348.
9. Rowland, F. S.; Molina, M. J. *Nature* **1974**, *249*, 810.
10. Manzer, L. E. *Science* **1990**, *249*, 31–35.
11. Parshall, G. W.; Ittel, S. D. *Homogeneous Catalysis*, Wiley: New York, 1992; pp 305–308.
12. *Chem. Eng. News*, **1998**, *76*(26), 22.
13. Carlson, R. *Silent Spring*, Houghton Mifflin: Boston, 1962.
14. Colburn, T.; Dumanoski, D.; Myers, J. K. *Our Stolen Future*, Penguin: New York, 1996.
15. *Chem. Eng. News* **1998**, *76*(12), 4–5.
16. Sauers, R. F.; Levitt, G. In *Pesticide Synthesis through Rational Approaches*, Magee, P. S.; Kohn, G. K., Eds.; ACS Symposium Series 255; American Chemical Society: Washington, DC, 1984; pp 21–28.
17. Ohno, N. In *Organic Synthesis in Japan*, Noyori, R., Ed.; Tokyo Kagaku Dozin: Tokyo, 1992; pp 317–326.
18. Naumann, K. *Synthetic Pyrethroid Insecticides: Structures and Properties*, Springer: New York, 1990.

Viewpoints: Chemists on Chemistry



George W. Parshall

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George W. Parshall joined DuPont's Chemical Department in 1954 and was assigned to develop new processes for nylon intermediates. It was an exciting time when university scientists were opening up the organometallic chemistry of the transition metals and industrial researchers were exploring these new compounds as catalysts. After six years on the fringes of these areas, he persuaded an enlightened manager to send him to Imperial College (London) in 1960 to learn more about this new chemistry. At that time, Geoffrey Wilkinson was pioneering new transition metal chemistry and, in an unusual role for an academic, studying possible catalytic applications.

After a year in Wilkinson's laboratory, Parshall returned to full-time research on organometallic chemistry at DuPont. In 1965, he assembled a group to work on both industrial applications and the fundamental chemistry of soluble catalysts. In 1979, he was appointed Director of Chemical Science to oversee a broad range of activities from computer science to nonlinear optical materials, in addition to his earlier interests. Since retirement at the end of 1992, he has participated in many National Research Council studies on disposal of nuclear wastes and chemical warfare agents. He is a member of the National Academy of Sciences.

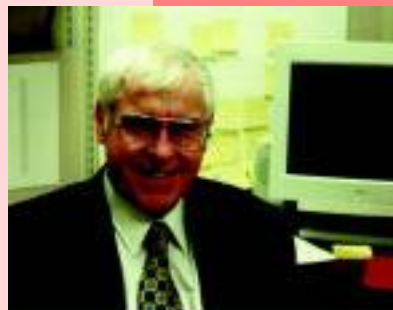


19. Hunt, D. A.; Baker, D. R.; Fenyves, J. G.; Basarab, G. S. In *Synthesis and Chemistry of Agrochemicals*; Hunt, D. A.; Baker, D. R.; Fenyves, J. G.; Basarab, G. S., Eds.; ACS Symposium Series 686; American Chemical Society: Washington, DC, 1998; pp 1–5.
20. Stinson, S. C. *Chem. Eng. News* **1998**, 74(39), 83–104.
21. Knowles, W. S. *J. Chem. Educ.* **1986**, 63, 222–225.
22. Sharpless, K. B. *Chemtech* **1985**, 15, 692–700.
23. McKee, B. H.; Gilheany, D. G.; Sharpless, K. B. *Org. Syn.* **1991**, 70, 47–50.
24. National Research Council. *Frontiers in Chemical Engineering*; National Academy Press: Washington, DC, 1988; pp 146–152.
25. Ethics Center for Engineering and Science. URL: <http://ethics.cwru.edu/CONTEST/canal/errors/html> (accessed Nov 1998).
26. Hileman, B. *Chem. Eng. News* **1998**, 76(27), 4–5.
27. Wu, C. *Science News* **1998**, 154(10), 154.
28. *1997 Annual Report*; DuPont Co.: Wilmington, DE, 1998.
29. *Chem. Eng. News* **1998**, 76(14), 17–18.
30. National Science Foundation. *Social, Behavioral, and Economic Sciences International Programs*, URL: <http://www.nsf.gov/sbe/int> (accessed Nov 1998).
31. US Patent and Trademark Office. *USPTO Patent Databases*, URL: <http://patents.uspto.gov> (accessed Nov 1998).
32. *IBM Intellectual Property Network*. URL: <http://www.patents.ibm.com> (accessed Nov 1998).
33. Raber, L. R. *Chem. Eng. News* **1998**, 76(2), 117.
34. *Web Sites of DUE-Supported Projects: Course and Curriculum Development (CCD)*. URL: <http://www.ehr.nsf.gov/EHR/DUE/web/ccd/ccdlist.htm#chem> (accessed Nov 1998).
35. Parshall, G. W.; Putscher, R. E. *J. Chem. Educ.* **1986**, 63, 189–191.
36. Nicolaou, K. C.; Sorensen, E. J.; Winssinger, N. *J. Chem. Educ.* **1998**, 75, 1225–1258.
37. McCoy, M. *Chem. Eng. News* **1998**, 76(25), 13–18.
38. Xia, Y.; Whitesides, G. M. *J. Am. Chem. Soc.* **1995**, 117, 3274–3275.
39. Marder, S. R.; Sohn, J. E.; Stucky, G. D. *Materials for Nonlinear Optics*; ACS Symposium Series 455; American Chemical Society: Washington, DC, 1991.
40. Wang, J.; Yoo, Y.; Gao, C.; Takeuchi, I.; Sun, X.; Chang, H.; Xiang, X.-D.; Schultz, P. G. *Science* **1998**, 279, 1712–1714.
41. van Dover, R. B.; Schneemeyer, L. F.; Fleming, R. M. *Nature* **1998**, 392, 162.

Fifty-Year Trends in the Chemical Industry: What Do They Mean for Chemical Education?

Chadwick A. Tolman joined DuPont's Central Research Department in 1965 and began work on the kinetics and mechanisms of rapid organometallic reactions by stop-flow methods. The discovery of Ni(0) homogeneous catalysts for butadiene hydrocyanation had recently been made, and he quickly got involved in trying to understand the chemistry involved. This work led to the concepts of the catalytic cycle, the 16- and 18-electron rule, and the ligand cone angle, perhaps his best known contribution to chemistry.

After a period of time in organometallic chemistry, Tolman worked on the mechanism of the air oxidation of cyclohexane to give intermediates in the manufacture of adipic acid, the other major ingredient in nylon-66. He was also involved in areas such as metal atom vapor synthesis, reactions in zeolites (including inorganic mimics of cytochrome P₄₅₀), destruction of toxic organic compounds in wastewater, synthesis of BaTiO₃ ferroelectrics, and the biocorrosion of steel. He also helped to found the Science Alliance, a nonprofit collaboration to improve K–12 science, math, and technology education. Since "retirement" at the end of 1996, he has consulted, taught graduate courses in organometallic chemistry and environmental chemistry, and become a Program Officer in the Chemistry Division of the NSF.



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