# *Part I*

# *From Fundamentals to Applications*

# 1

# *Let's Get Physical*

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Marye Anne Fox is a distinguished professor of chemistry and the seventh chancellor at the University of California, San Diego (UCSD). She received her Bachelor of Science in Chemistry at Notre Dame College and her PhD, also in Chemistry, at Dartmouth College. After a National Science Foundation (NSF) postdoctoral appointment at the University of Maryland, she joined the faculty at the University of Texas, where she was appointed ultimately to the Waggoner Regents Chair in Chemistry and was named Vice President for Research. She served as Chancellor and Distinguished University Professor at North Carolina State University before assuming her present position. She has been recognized nationally and internationally for her contributions to chemical research, science education, and innovative service to higher education. She is a member of the U.S. National Academy of Sciences, the American Academy of Arts and Sciences, and the American Philosophical Society, and has served on the National Science Board and the President's Council of Advisors on Science and Technology. She has received 12 honorary degrees.

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*Letters to a Young Chemist*, First Edition. Edited by Abhik Ghosh.

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Dear Angela,

I am delighted to hear that you had a great summer working in a chemistry lab! And combining that experience with study abroad in Norway, which is such a beautiful place, must have been truly wonderful! Quite a change for a Southern California girl.

I assume you had a very positive experience, and I suspect it also means you've been bitten by the research bug. By that, I mean that you've probably had that indescribable feeling that comes when you've synthesized a molecule that never existed before or when you were the first in human history to understand why a particular reaction takes place the way it does. Nothing like it, really. And once you've experienced it, you'll find it hard to live a life that doesn't include the possibility of discovery. The pursuit of new ways of thinking about nature is addictive, and getting to the goal by proving or disproving your original proposal about what might happen will keep you working long hours for months or years at a time. Your friends may think you're crazy to work all night on occasion, but you know something they'll never understand.

I'm also glad to hear that you've chosen to pursue your degree. That shows a lot of good sense, given the proximity of your family at UCSD and your determination to make scientific research a big part of your life. Quite aside from the natural beauty of the campus and the fact that San Diego has the world's best weather all year long, UCSD is a fabulous place to undertake serious scientific studies. *Newsweek* magazine announced a couple of years ago that UCSD is the "hottest place to do science" in the United States. One indicator of the quality of our scientific research programs is that the 2008 Nobel Prize in Chemistry was awarded to one of our long-time faculty members.

As is true in most research universities worldwide, you'll have a chance to get involved in research right from the beginning. Once you demonstrate that you want to do serious research, you'll likely be able to work with faculty who are well funded by federal granting agencies, and some will be able to offer stipends to students who work half-time or so with the research group on their research projects. As a result, working on a project you love can also help you address the costs of attending a premiere college or university.

One of our highest priorities at UCSD has always been to involve undergraduates in research as soon as they can demonstrate that they can contribute to a particular research group's efforts. Having worked in a lab for a summer already, you should be ready as soon as you arrive on campus to connect with one or more professors whose research work interests you.

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## MY LIFE AS A RESEARCH CHEMIST

I think it's a great idea that you want to find out a bit more about opportunities in different areas of chemistry so you can make a more informed choice about the direction you'll ultimately pursue. My area of choice has been physical organic chemistry, with specialization in photochemistry, electrochemistry, and materials chemistry. Virtually all of our work is aimed at understanding how a particular reaction takes place, often in great detail. It includes the scientific question of how changes in structure induce changes in chemical reactivity, in the ground state or the excited state of a molecule or a family of molecules.

Given that reactions take place through a series of bond-making and bond-breaking steps, this work often involves reactive intermediates. A full description of a reaction also defines the rates of reaction (kinetics) and the energy changes encountered as the reaction proceeds (thermodynamics). This is exactly where organic chemistry interfaces with physical chemistry. This description of a chemical reaction, in fact, defines the field of physical organic chemistry. A key step in accomplishing such a description consists of characterizing the electron flow and the reactive intermediates forming along a reaction pathway. In a larger sense, physical organic chemistry defines how a local environment can affect reaction rates by influencing the stability of a key transition state. In many cases, it is also possible to make models of transition states with the help of theoretical calculations and to use theory to predict evolving chemical reactions. It's extremely rewarding intellectually to work with theorists to establish by inference how a series of chemical bonds are broken and formed, and hence to be able to devise new chemical transformations.

Although I spend a great deal of my time as a chancellor at UCSD, I am still a chemistry professor at heart. In that capacity, I've worked with a highly talented group of students to study a variety of physical organic problems. I'm especially proud that we were able to make a major contribution toward defining a new field of organic photoelectrochemistry, which involves a combination of surface chemistry and excited state chemistry. This work involved syntheses of new molecules, in ground and excited states, and observing how their structure affects subsequent chemical reactivity. We also carried out theoretical calculations in order to test our interpretation of experimental observations. We are often interested in being able to predict physical properties for compounds or materials that don't even exist until we make them.

I'm happy to say that over 60 students have completed advanced degrees in my research group, and many of them have themselves established well-regarded research programs of their own. Because of their hard work, I was elected at a relatively young age to membership in the National Academy of Sciences, which is a profound honor for any scientist. I really miss the days when I could spend most of my time with students in the lab.

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## LEARNING TO DO RESEARCH: PHYSICAL ORGANIC PRINCIPLES

Perhaps it would be useful to you to learn how I came to develop an interest in the physical properties of organic molecules. It was basically a series of very positive research experiences that led me to become a research chemist, and thereafter an independent faculty member at a research-focused university.

My first exposure to chemistry research was as a student in a summer program supported by the NSF at the Illinois Institute of Technology in Chicago. As a student in the program called Research Experience for Undergraduates (REU), I was assigned to Professor Jerry Kresge's research group, thereby working side by side with postdoctoral fellows, visiting faculty members, and graduate and undergraduate students. I was very pleased to be accepted so cheerfully into the group, given my status as an inexperienced REU student. Professor Kresge was interested in determining how acids could effect changes in the hydrolysis of vinyl ethers. We wished to determine whether Bronsted or Lewis acidity was involved, as well as to identify key reaction intermediates encountered as the reaction took place. The work would provide important information about how acids can catalyze (i.e., accelerate) certain reactions.

My contribution to the project was to synthesize cyclohexenylethyl ether and to monitor the kinetics of its hydrolysis to cyclohexanone. The rate of hydrolysis could be followed by monitoring the appearance of the ultraviolet absorption of the ketone product. We then established reaction rates for other vinyl ethers, for example, those with smaller rings or appended functional groups, and with enhanced or reduced sensitivity toward various acids. The question was whether a general acid ($H^+$) or a specific acid (HX, where $X^-$ is a counterion that is involved in the key transition state) induces the catalytic acceleration of the observed rates. In turn, this allowed us to find out exactly how this reaction proceeds. Ultimately, the work led to my first paper in the *Journal of the American Chemical Society*.

Having had a very positive experience in a physical organic group, I loved the idea of undertaking simple syntheses to make new compounds in which fundamental changes in reactivity could be brought about by changes in structure. So, when I had the chance to work with Professor Roger Binkley on problems involving photochemical excitation, I jumped at it. Photochemical reactions are those that take place after the absorption of light. Photochemical excitation is perhaps the easiest way of inducing a reactivity change with minimal structural change. Photochemistry is therefore an exceptionally important subarea of physical organic chemistry.

Although Dr. Binkley was interested in carbohydrate photochemistry, I chose to work on a structurally simpler compound, benzalazine. We wanted to measure the relative rates of cleavage of the C–N bond by monitoring the quantum yields for consumption of the starting material and for the appearance of product. The underlying goal of this work was to determine the multiplicity of the excited state leading to each product; that is, we wanted to know whether a singlet or triplet state was involved. The insight afforded by establishing the reaction kinetics has profoundly influenced my research for the rest of my career.

Perhaps even more important, the Binkley research group met each Wednesday night at his home to have a simple dinner in which the dessert consisted of working together to solve a tantalizing mechanistic problem. Sometimes, the problems involved reactive intermediates, often radicals or diradicals produced by photochemical excitation. As a beginner, it was hard to imagine how a molecule could be twisted so much to yield highly strained or rearranged compounds. In general, we practiced arrow pushing to determine the electron flow that defines a reaction mechanism.

Moving to Hanover, New Hampshire, to attend graduate school at Dartmouth College was one of the most important decisions of my life. Not only did I find a brilliant mentor, Professor David Lemal, a person who cared equally about teaching excellence in research and about his students, but because the program was small, I was also able to work frequently with other faculty working on quite different projects. I recall fondly working with Professors Walter Stockmeyer (a polymer chemist), Chuck Braun (a physical spectroscopist), Tom Spencer (a biochemical kineticist), and Gordon Gribble (a synthetic organic chemist). Because of their invaluable insights, I was able to finish my doctoral work quickly, in 3 years, so I could join my husband in Washington where he was assigned after having been drafted into the U.S. Air Force.

The project I began in graduate school was to prepare perfluorotetrahedrane, a highly strained compound in which four carbon atoms were arranged so as to resemble a pyramid with a fluorine atom at each corner. The molecule was bound to be highly strained and to have interesting physical properties. I worked for nearly a year preparing various precursors and applying what I had already learned about photochemistry. I discovered some interesting routes to strained compounds, but the goal remained elusive. This was the first time I had to deal with failure in the lab. But even in this failure I learned an important lesson: when a project is worthwhile, there will be challenges, and sometimes it will be useful to fail quickly and get on to another project. I did have the chance several years later to collaborate with a German friend who had synthesized tetrakis(*t*-butyl)tetrahedrane, so the project continued to be close to my heart.

In my case, my failing to synthesize my target meant shifting to studying the valence isomerization of several families of halogenated arenes. I discovered a new reactive biradical derived from chlorobenzene and several interesting interconversions among halogenated pyrazine, pyridazine, and pyrimidines, along with fully defined mechanisms by which the conversions took place.

Besides learning about broad areas of science, I used my graduate school experience to learn time management and how to balance various competing demands from my personal and professional life. The norms of graduate life in chemistry also reinforced a strong core work ethic that I've had throughout my life. To this day, administration colleagues marvel at my work capacity, which is simply normal by chemists' standards.

I will always be indebted to my research advisor David Lemal for encouraging me to realize that children should not be forgone as part of the life of an academic, whether male or female. He was gracious in letting me work odd hours and still keep my stipend when my first son was born, in order to stay on track to achieve my 3-year completion goal. In doing so, he taught me invaluable life lessons. (These lessons, even now, I have observed, are not consistently understood or practiced by many of my professional colleagues. I've found it remarkable to observe how much more efficient some of my male and female colleagues became once they took on the responsibility of parenting a child.) I hope that as you pursue your interest in science, you will be fortunate to have a research supervisor and/or colleague who will be similarly supportive at crucial junctions in your life. Special advice: choose your mentor (and your spouse!) carefully.

Next I accepted a position in a new NSF postdoctoral program Research Applied to National Needs (RANN) at the University of Maryland. Consistent with the applied nature of the program, I developed a new instrument for using fluorescence spectroscopy to monitor air quality in real time. That work resulted in my first publication in *Science*, a highly prestigious broad-interest journal. The experience also encouraged me to think deeply about directions I wanted to pursue in my independent career.

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## BECOMING A CHEMISTRY PROFESSOR: CONDUCTING INDEPENDENT RESEARCH

The decision to become a professor and to pursue an academic research career is an important one. It requires a commitment to work with students to investigate areas that are (1) original, (2) interesting, and (3) important. Only if all three criteria are met will you attract federal or foundation support for your research. I was fortunate that my research group was well funded from its inception. NSF, Department of Energy (DOE), and the Welch Foundation provided reliable and continuous funding for my projects as soon as I took my first job at the University of Texas at Austin.

From the background I described above, you could probably guess that I would try to incorporate photochemistry or physical organic chemistry as major directions for my independent research program. I was interested in chemical bonding and quickly made arrangements to teach a course on molecular orbital and perturbation theory with the brilliant theorist Michael J. S. Dewar. I joined a literature seminar on Wednesday nights with four other faculty and their graduate students to work on reactive intermediates, isotope effects, molecular strain, aromaticity, pericyclic reactions, and electronic effects. We also worked on noncovalent molecular recognition and supramolecular chemistry, which was then a newly emerging field. We worked on kinetics and thermodynamics, especially on transition state theory, focusing on Hammett plots and the Hammond postulate. I contributed what I knew of acid–base chemistry and photochemical mechanisms, with a strong emphasis on catalysis, both organic and enzymatic. We taught ourselves about organic magnets, organometallic compounds and of materials such as polymers and liquid crystals. Above all, we worried about electron flow in reaction mechanisms. The experience was invaluable, and I strongly urge you, as your time permits, to find a similar group wherever you pursue your graduate degree.

I began my own work as an assistant professor by scouring the literature for important but unanswered scientific questions. I was particularly interested in those in which there had been recent progress but with less than complete success. With this goal in mind, I was fascinated to find a report by Fujishima and Honda of The University of Tokyo that illuminating an electrochemically poised semiconductor surface could split water into oxygen and hydrogen, thus making a combustible fuel from an abundant and safe precursor. The reality, however, was that the applied potential was too high and the quantum efficiency too low for practical applications. It was an ideal challenge for an assistant professor.

We hoped we could contribute to understanding the fundamentals of this important reaction while addressing its practical consequences in parallel. Accordingly, we set out to characterize photoinduced electron transfer (PET), with applications ranging from fundamental theory through very practical applications.

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## PET

We have focused on environmental control of chemical reactions using the absorption of light as a trigger to allow spectroscopic monitoring of a series of bond-making and bond-breaking steps. We have been particularly interested in the excited states of species called reactive intermediates, especially those involving PET. We frequently use laser spectroscopy to follow the reaction progress on the nanosecond or picosecond time frame. When conducted in an appropriately configured multicomponent system, this work also provides practical new vehicles for solar energy utilization and storage.

Figure 1.1 presents a simple schematic of how an electron donor *D* can interact with an electron acceptor *A* and the experimental

One-electron transfer

$$D + A \rightleftharpoons D^{\bullet +} + A^{\bullet -}$$

Distance

Orientation

Solvation

Thermicity

***Figure 1.1.*** *Experimental variables affecting donor–acceptor interactions.*

variables that can affect the course of this simple reaction. First, notice that radical ions are produced from neutral precursors. To understand the reaction, we must know about reactive intermediates and about how the distance between reactants and products can influence the efficiency of PET. By changing the energetics and kinetics for the forward and back electron transfers, many practical applications were uncovered. In addition, the rates of these laser-induced chemical reactions were used to define the influence afforded by the polarity of the solvent or the structure of the solid to which the *A/D* system was adsorbed. It has also led us to think in more detail about the orientation of molecules bound to surfaces.

We then began to construct more complex arrays that have two acceptors for each donor, as shown in Figure 1.2. Upon photoexcitation of either the donor or acceptor, PET takes place. The electron can then hop to the second acceptor, creating an energetic and physical barrier to back electron transfer that would dissipate the initial photonic energy. By inhibiting back electron transfer, three component arrays like this lengthen the lifetime of an oxidized/reduced ion pair. As a result, the chance of observing net photochemical change is much higher. Figure 1.2 uses a straight line to indicate the bonding between the donor and the two acceptors. This is simply intended to indicate that any linking agent could fulfill the role, so long as the $D–A_1–A_2$ sequence is attained.

What kind of intervening materials could be used? We can look to nature for models: for example, photosynthesis itself takes place by light absorption by a special pair of porphyrins rigidly held within a

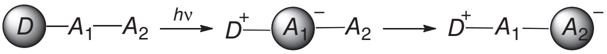

***Figure 1.2.*** *Schematic representation of an electron donor–acceptor array.*

protein matrix. The initial PET then causes an electron to hop (as in Figure 1.2) to another position and then to another. This accomplishes directional electron transfer across a lipid bilayer membrane, with the electron ultimately being trapped as a reduced quinone, and finally by an iron–sulfur complex. It is impossible to understand photosynthesis, possibly the most important process for the sustainability of our planet, without a fundamental understanding of the variables that control the efficiency and directionality of PET.

Suppose that the intervening material (between the donor and acceptor) is more conformationally flexible than what is encountered in the photosynthetic reaction center, as shown in Figure 1.3. Under these circumstances, the distance between the donor and acceptor would be controlled by the movement of the intervening chain. Three situations are illustrated here: (1) a rigid backbone in which separation distance is controlled by the original synthesis, (2) a flexible backbone in which distance changes with time after pulse photoactivation, and (3) a situation in which the polarity of the backbone differs sufficiently from that surrounding the highly solvated radical ion pair that phase separation takes place. These are the same structural criteria that represent major design goals in functional polymer chemistry. As a result, the study of PET, when induced by a laser pulse, provides an excellent probe for an entirely different area of chemistry, that is, polymers and polymer blends.

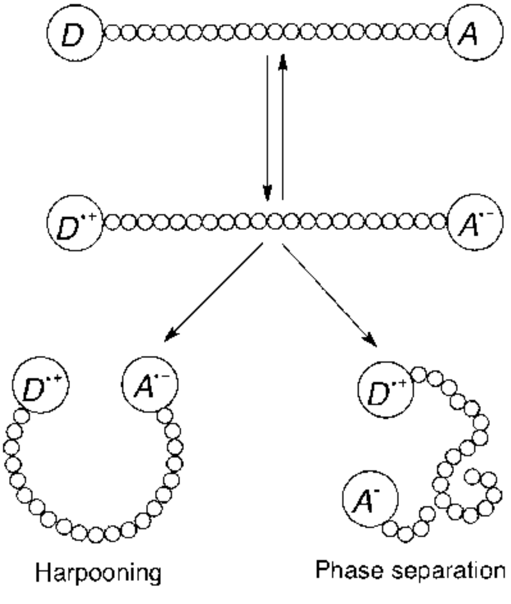

*Figure 1.3.* Dynamics of a donor–acceptor pair linked by a flexible chain.

Furthermore, there is no requirement that the individual components (represented by balls in Figure 1.3) are covalently bound. In fact, we have shown that discotic liquid crystals can similarly act as intervening supports for PET. Liquid crystals display a long-range order induced by noncovalent stacking of individual units. In some cases, hundreds of component molecules are aligned, producing an order over hundreds of nanometers. One might therefore expect differences in PET activity on both sides of the transition temperature between one liquid crystalline phase and another.

Peptides represent yet another family of intervening materials that provide a probe for conformational effects. Because peptides can aggregate as helices or as sheets, they produce a macromolecular order comparable to that of liquid crystals. Dipole effects in helical peptides are additive, so that a macroscopic dipole from the C- to the N-end of the peptide (or vice versa) can enhance or oppose the pulsed PET.

Nor do the donor and acceptor need to be equally soluble in polar or nonpolar solvents. Consider the situation if the donor were a nanoparticle surrounded by an acceptor strongly adsorbed on its surface, as depicted in Figure 1.4. In such a shell–core composite, light absorption would initiate charge separation in a pathway directly

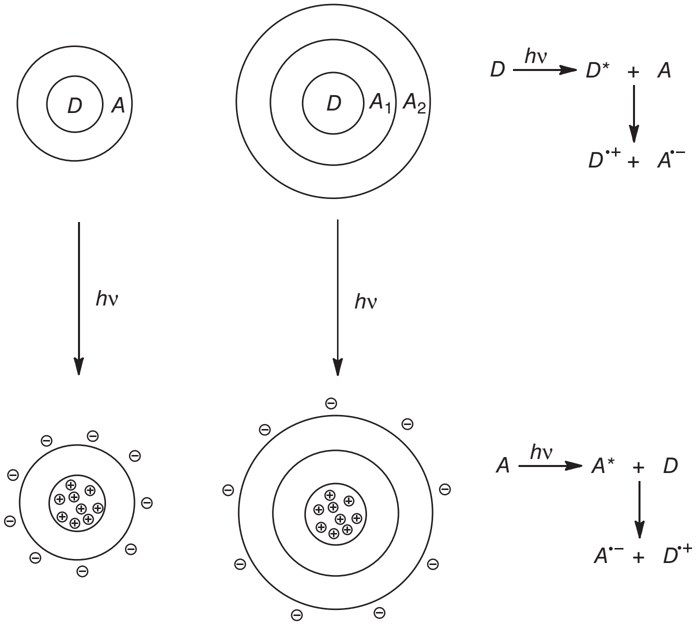

*Figure 1.4.* Photodynamics of acceptors adsorbed on a donor nanoparticle.

comparable to that seen in the linear arrays. Spectroscopic probes for lifetimes of the charge-separated pairs and for direct measurements of the rate of back electron transfer will be critical measurements before these size-differentiated materials can be included as manufactured components of nanodevices. As nanoscience progresses, it is likely that pulsed laser-induced PET will become a major characterization technique for defining physical properties as a function of size and surface composition.

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## PHOTOELECTROCHEMISTRY

The above considerations also apply to situations in which a donor and an acceptor are both reversibly adsorbed on a common surface. For example, it has been known for over a century that molecules adsorb and desorb reversibly on electrodes, producing a complex nonhomogeneous layer near the electrode surface with a substantially different composition relative to the bulk solution with which it is in contact. Electrochemists refer to this space as an electrode surface region, or a double layer, if the contacting solution is an aqueous electrolyte. Chemical reactions take place with ease in this region as the electrode potential is scanned through the oxidation or reduction potential of the reactant. After the redox reaction has taken place, equilibration takes place with the neighboring bulk solution.

The electrochemical cell in which these transformations take place consists of an anode where oxidation reactions take place, a cathode where the counterreduction occurs, and a reference electrode that allows for measurement of applied potential. Within the last several decades, it has been discovered that a potential difference can be attained not only by using a battery or a potentiostat but also by using light to produce an electron–hole pair by the photoexcitation of a doped semiconductor. This kind of cell is called a photoelectrochemical cell, and its catalytic behavior is determined by the oxidation potential of the hole and the reduction potential of the electron.

Substantial work has been done to study the properties of the doped semiconductors employed, as there was general consensus for several decades that such cells might be important for solar energy conversion and storage. Much of our work in photoelectrochemistry was done with my colleague Allen Bard. Together we wrote an article arguing that photoelectrochemical cells could be viewed as the "Holy

Grail" for electrochemists, potentially leading to efficient water splitting to produce fuel for the hydrogen economy.

Every semiconductor, by definition, has a filled valence band, separated by an energy difference (band gap) from the vacant conduction band. In an undoped state, conductivity is observed only by thermal population of the conduction band by electrons sufficiently energetic to jump across the band gap to the conduction band. This is an energetically unfavorable process and occurs only infrequently. An undoped semiconductor therefore has very low conductivity and is generally considered to be insulating.

When doped with electron-rich species, however, electrons are placed into the conduction band, which has the effect of reducing the potential of the band edges, so that the excess electrons move away from the surface of the semiconductor into the bulk. The material thus becomes conductive, and an electrode made out of such a material can function as a normal electrochemical component.

We became fascinated by potential modifications of such cells. In your mind, try a thought experiment: envision a photoelectrochemical cell in which the wire connecting the semiconductor anode (perhaps a metal oxide like $TiO_2$) and the metallic cathode (perhaps platinum, which is a good hydrogen evolution catalyst) is shrunk until the counter electrodes are in direct contact. Now fragment the electrode so it is a powder, which is depicted in Figure 1.5.

Now provide photons rather than dopants to the semiconductor surface. When the $TiO_2$ particle absorbs light of an energy greater than the band gap (wavelengths shorter than about 400 nm), an electron is promoted from the valence band to the conduction band. This absorption thus produces an electron–hole pair. This pair has an

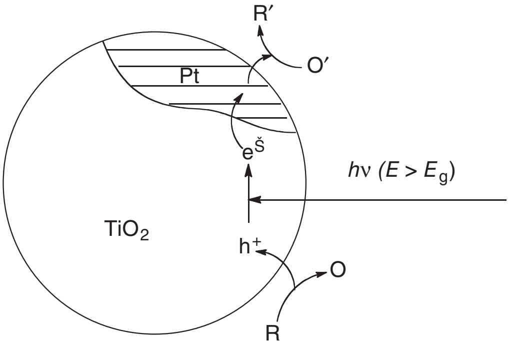

***Figure 1.5.*** *A platinized titania particle as a photoelectrochemical cell. O symbolizes the oxidized form of a generic organic compound, R.*

oxidizing power equivalent to the band gap of the semiconductor and can strip an electron from any compound with an oxidation potential less positive than about +2.0V (relative to the standard hydrogen electrode). This category includes essentially any organic compound containing either a heteroatom or any form of conjugation.

The photoexcitation also places an electron into the conduction band, whose redox potential is virtually identical to that of the reduction potential of adsorbed oxygen. The conduction band electron is thus converted to adsorbed superoxide. Trapping an electron–hole pair thus starts a reaction cascade between the adsorbed organic cation radical and superoxide and its cleavage products. This route, which we called organic photoelectrochemistry, allowed us to discover a wide array of new reactions that emanate from the inherent reactivity of an adsorbed cation radical. An early example of how this takes place can be seen in a 1981 *Journal of the American Chemical Society* article (see Further Reading), our first on organic photocatalysis, where we reported a fairly high-yield aerial oxidation of olefins to carbonyl compounds.

By employing different semiconductor powders suspended in a series of solvents with and without deposited metal islands, we soon developed a whole new subarea of mechanistic/physical organic chemistry. Others also joined in and expanded the repertoire of photocatalytic conversions. In addition to solar splitting of water, as noted above, this general approach has been used for detoxification of pollutants, for cleaning oil spills, as a hospital-based antibacterial, for water purification, for cleaning office windows, and much more. Suspended semiconductor powders have been used in conjunction with dye sensitizers bound or adsorbed to the semiconductor surface, as single molecules, as aggregates, or even as dye-loaded dendrimers. It's been extremely rewarding to see so many useful chemical transformations follow from such simple principles.

## SOME FINAL ADVICE

Angela, I assume you'll be writing to some other chemists as well and I hope they will also take the time to tell you in some detail about their work. I hope you'll take away some of the enthusiasm that is typical of practicing chemists. Yes, chemists work long hours, but that's generally because they love what they do. Because chemistry is a central science, it is easy to apply what you have learned and will learn in a variety of settings. With a chemistry background, you can easily move to the life sciences, to medicine, to law, to public policy, to management, to teaching, to public service, and to so many others. Who knows? You may even end up as a chancellor!

I just wish my schedule still permitted me to take on undergraduate and graduate students instead of only postdoctoral fellows. I'd surely try to make space for someone as committed as you seem to be. Best wishes for a successful stay at UCSD. I'll look forward to giving you your degree a couple of years from now.

Sincerely,

Marye Anne

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## FURTHER READING

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