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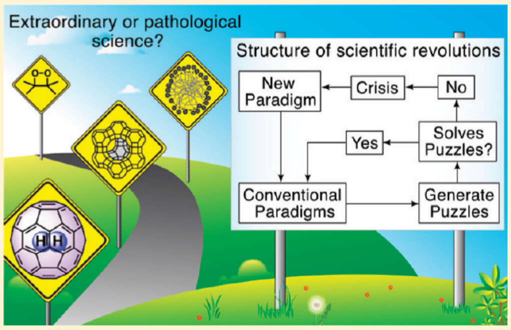
Fun with Photons, Reactive Intermediates, and Friends. Skating on the Edge of the Paradigms of Physical Organic Chemistry, Organic Supramolecular Photochemistry, and Spin Chemistry

Nicholas J. Turro

Chemistry Department, Columbia University, New York, New York 10027, United States

ABSTRACT: This Perspective presents a review and survey of the science and philosophy of my research career over the past five decades at Columbia as a physical organic chemist and photochemist. I explore the role of paradigms, structure, and geometric thinking in my own cognitive and intellectual development. The Perspective describes my investigations of high energy content molecules in electronically excited states and the development of electronic spin and supramolecular photochemistry chemistry. Current research dealing with the nuclear spin chemistry of H_2 incarcerated in buckyballs is illustrated. In the second part of this Perspective, I recount a personal role of the philosophy and history of science and the scientific communities' use of paradigms in their every day research and intellectual activities. Examples are given of the crucial role of geometry and structure in the rapid development of organic chemistry and physical organic chemistry over the past century.



1. PHYSICAL ORGANIC CHEMISTRY AND PHOTOCHEMISTRY: REACTIVE INTERMEDIATES, ELECTRONICALLY EXCITED STATES, AND DEVELOPING AND EXPLOITING PARADIGMS IN CHEMISTRY

Chemistry is the science that explores an ever expanding "universe" existing at the invisible nanoscopic level of inquiry. No one has ever "*seen* or will ever *see*" a molecule. Yet, chemists are continuously challenged to master the structure and dynamics of the invisible world of molecules (we're sure they are there!) at ever increasing levels of diversity and complexity. We only see images that are created by theories and programs that assume that our basic views of molecular structures are correct.

Within chemistry there is a field that has developed over the past 80 years or so that is loosely termed "physical organic chemistry." This field deals with correlations between organic molecular structure and dynamics and measurable physical and chemical and theoretical properties of substances, transient and persistent. The field also accepts the essential need to synthesize molecules, as required, to test hypotheses and the limits of theory.

The intellectual foundations, strategies, and methods of physical organic chemistry have impacted, penetrated, and been absorbed by all areas of organic chemistry and provide profound and authoritative *paradigms* for organic chemistry and all of chemistry. Most recently, the strategies and methods of physical organic chemistry have been successfully adapted and applied to extremely complex and diverse supramolecular systems such as materials science and biological sciences. When I initiated my career in the early 1960s as a physical organic chemist and molecular photochemist, the intellectual structures of structure–property relationships of physical organic chemistry were still in the formative, so-called, *preparadigm* stage. Before a paradigm gains authority over a community of chemists, the chemists in that community usually argue over issues that today we take as fundamentally accepted lore. For example, robust broadly accepted paradigms, such as frontier molecular orbital theory, orbital symmetry rules and fantastic arrays of techniques such as NMR spectroscopy, laser spectroscopy, and powerful computational methods have been developed and are part of the everyday arsenal of tools to explore physical organic systems.

During the early 1960s, when I began my PhD thesis research under George Hammond at Caltech, the nature and possible existence of reactive intermediates such as high energy content ground state molecules and electronically excited states was intensely debated. This is usual and expected for fields that are in the preparadigm stage of development. Also, at this time, it was widely accepted that strained molecules such as bicyclobutanes (now available commercially!) could not exist and certainly could not be isolated and studied. Indeed, the very idea that conventional molecular structures, analogous to Lewis structures, could be used to describe high energy content ground state molecules or electronically excited states was widely questioned as dubious or even reckless. One of the reasons for the suspicion that the familiar Lewis molecular structures were not going to be appropriate or useful to describe high energy intermediates and electronically excited states was *their high energy content.* Looking at the structure of highly strained systems (e.g., Chart 1) certainly gave the viewer

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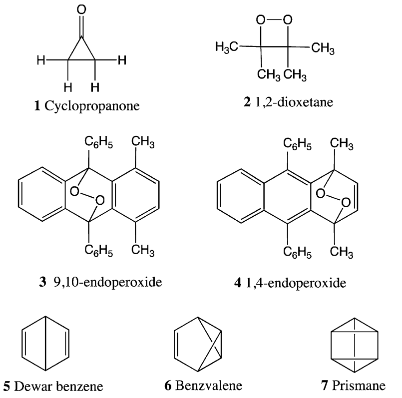
Chart 1. Some High Energy Content Ground State Molecules Studied at Columbia



the impression these structures are ready to break highly strained bonds as fast as they are formed!

In terms of high energy content, let us consider the energy of an electronically excited state. Benzene's electronically excited singlet state (S_1) possesses ~110 kcal^{-1} mol more energy than benzene's ground state, and benzene's excited triplet state (T_1) possesses ~85 kcal^{-1} mol more energy than benzene's ground state. According to the available paradigms of the early 1960s, there was no compelling reason why such electronically excited "reactive intermediates" should behave similarly to molecules with much lower energy since the activation energy for most common chemical reactions in the laboratory are ~50 kcal^{-1} or less. Simply put, the basic assumption was if a ground state molecule possesses a lot of energy, they cannot be studied like normal molecules since they are just too reactive.

Similar arguments can be made against the possible existence of *ground state* molecules possessing high energy content of the order of ~50 kcal mol^{-1} or greater. In thinking about this challenge, I wondered if high energy species could be isolated, put in a bottle, and treated as ordinary, reactive molecules, in spite of their energy content? Or would they just "explode" when you tried to make them? There was no basis from the governing paradigms of chemistry at the time as to why high energy content molecules should be sufficiently stable to isolate, but on the other hand, there did not seem to be a basis that would exclude, definitely, their isolation. After all, existing paradigms would allow their isolation if sufficiently high barriers for their decomposition existed for some reason. Although at the time there was no paradigm that would predict unexpected high energy barriers for reaction of high energy intermediates, we know now that orbital symmetry requirements for pericyclic reactions provide some reasons.

In thinking about designing a research program for my academic career, I thought that in spite of the challenges, the range of possibilities for study from electronically excited states to high energy ground state reactive intermediates was so rich with tremendous promise, scope, and excitement that it was worth the risk to explore the synthesis and characterization of high energy intermediates and electronically excited states. However, the challenges of the field were great because there were not yet guiding, authoritative paradigms to direct a research program that had the backing of guiding paradigms. As a result, dealing with molecules possessing high energy content was considered by many as working with systems for which "extraordinary claims" (findings that appeared to be outside of the authoritative paradigm) were commonly being made. After all, it is a sacred obligation of the scientific community to challenge extraordinary claims, i.e., claims that are not currently within the expectations of the ruling paradigms that already exist in a field. So I had to be ready for some confrontations and arguments with my colleagues.

When I started my research program, I did not fully appreciate the important role of paradigms in determining the way a scientific community operates (I discuss the essential nature of paradigms in some detail in section 11 of this Perspective). But during the first decade of my research at Columbia, I began to appreciate more and more the nature of scientific paradigms and the community's implicit acceptance, respect, and adherence to them. I also noted that some chemists in the community did not consciously appear to recognize the role that paradigms played in determining the way they conducted their own research programs and the way that they viewed research in general. One of my most important discoveries was that the unconscious, unquestioning acceptance of authoritative paradigms could serve as "intellectual blinders" to the possibility of extraordinary science that was fully within the accepted paradigms. By accepting that paradigms determine the way chemists think, I could understand better what to expect when I made an extraordinary claim, since any claim that appeared to be "outside" the currently accepted paradigm would be considered to be "extraordinary" to those completely wed to current paradigms.

This Perspective will be divided into two parts: the first ten sections describe a selection of the basic science and research on which the 2011 Cope Award is based, and the second section (section 11) describes the author's (somewhat foggy) recollection of his intellectual development of effective working paradigms over the past five decades that led to my philosophy of science, teaching, learning, and mentoring research, as well as how my intellectual development involved a consideration of the important role of serendipity, collaboration, scholarship and an understanding of the role of paradigms in science.

The author points out, in the interest of providing students with some context for the dramatic changes in presentation of chemical structures in journal articles, to notice the difference between Figures 30 and beyond with the figures before Figure 30. The latter were produced with ChemDraw, the early chemical structure program, and are typically in ordinary black and white. The figures after Figure 30 were produced by today's powerful graphical software.

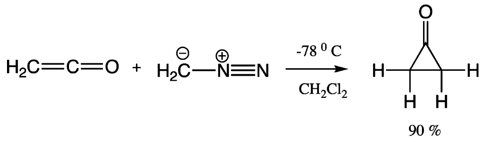
2. REACTIVE INTERMEDIATES: HIGH ENERGY CONTENT GROUND STATE MOLECULES AND MOLECULES IN ELECTRONICALLY EXCITED STATES

We shall use the term "reactive intermediate" to describe in general any species possessing a high energy content, (where high energy can be arbitrarily set as an enthalpy of ~50 kcal mol^{-1} or greater above that of products). By this definition, all reactive intermediates will have a strong thermodynamic driving force to react and release energy to form low energy product(s). In the preparadigm state of the early 1960s, organic molecules possessing a very high energy content were generally associated with kinetic instability and a fleeting and transient existence, i.e., a very short lifetime, much less than a second. At that time, it was not clear at all how to draw acceptable structures of electronically excited states produced by the absorption of a photon. Electronically excited states, the key structures in organic photochemistry, are indeed transient and never last more that a few milliseconds under normal laboratory conditions (solution at room temperature). Indeed, some electronically excited states last only picoseconds (10^{-12} s) or less! Thus, electronically excited molecules are intrinsically transient species. However, it was not at all clear what determined the ultimate lifetime and stability of high energy content ground state reactive intermediates.

3. SELECTED HIGH ENERGY CONTENT GROUND STATE ORGANIC MOLECULES STUDIED AT COLUMBIA: CYCLOPROPANONES, 1,2-DIOXETANES, 1,4-ENDOPEROXIDES, BENZENE VALENCE ISOMERS, AND FRIENDS

I continue to be amazed that over the past five decades structures with remarkably high energy content have been synthesized and have been found to be kinetically stable, and many are even isolable and treatable as ordinary chemicals at room temperature! A selection of some of the high energy intermediates that we have studied at Columbia, and that will be discussed in this Perspective, are listed in Chart 1: cyclopropanones,[1] 1,2-dioxetanes,[2] 1,4-endoperoxides,[3] and benzene valence isomers.[4−6] In addition to these structures, all of which are isolable and can be handled as reactive molecules, singlet molecular oxygen, $^1O_2$, and electronically excited states of carbonyl compounds have commanded our attention.

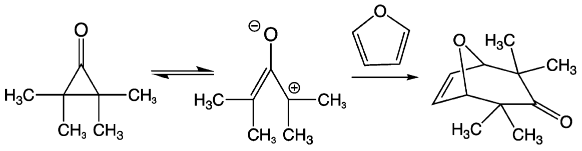
3A. Cyclopropanones. Our first success with high energy intermediates was the preparation, isolation, and characterization of cyclopropanone and some of its derivatives.[1] Addition of a cold (−78°) solution of excess $H_2C{=}C{=}O$ in CH_2Cl_2 to a CH_2Cl_2 solution of CH_2N_2 yields cyclopropanone in 90% yield based on CH_2N_2 (eq 1). The reaction is readily characterized by the appearance of a signature IR carbonyl stretch at 1813 cm^{-1} of the cyclopropanone. Interestingly, cyclopropanone shows a long wavelength UV absorption maximum at 310 nm (compared to acetone which has a maximum at 280 nm). 1,1-Dimethylcyclopropanone[7] and other alkylcyclopropanones[8] can be prepared in a similar manner.



(1)

At the time of the cyclopropanone synthesis in the early 1960s, there were debates as to whether cyclopropanones could be isolated, since the reigning paradigm suggested that such high energy content molecules should be kinetically unstable and therefore only be a transient reactive intermediate. Some chemists even claimed that the cyclopropanone structure was simply a "weakly bound complex" of ethylene and carbon monoxide that could not possibly be kinetically stable! These concerns were widespread before organic chemists embraced *the paradigm of frontier molecular orbital theory*[9] *and orbital symmetry rules*[10] *which provided a new and powerful paradigm of wide scope as to why high energy compounds could be kinetically stable.* Stability was provided to molecules whose "obvious" *pericyclic* reactions were a violation of the orbital system rules.[10] The latter paradigm explained elegantly why exceedingly strained, high energy content molecules could be kinetically stable and put into bottles, especially systems that involved transition states with four electron cyclic arrays in order to react. The basic idea of this new paradigm was that kinetic stability could be available to very high energy content molecules, if in order to break bonds and decompose, an orbital symmetry forbidden pathway was required. Our research showed that you could "put cyclopropanones in a bottle" and treat them as ordinary, if highly reactive, species. To fly apart into CO and ethylene, cyclopropanone would have to decompose through an orbitally forbidden four-electron transition state.

A very interesting reaction, not expected from the classical cyclopropanone structure, is a Diels−Alder reaction with electron rich 1,3-dienes.[1−3] The cyclopropanone structure has the very interesting feature that it is in equilibrium with an open form, termed the oxyallyl structure (eq 2) that can be viewed as a zwitterion, with a two electron allyl system. The latter is a good nucleophile and indeed reacts with electron rich 1,3-dienes in a [4 + 3] concerted cycloaddition reaction. Equation 2 shows an example of the [4 + 3] concerted "Diels−Alder" cycloaddition of tetramethylcyclopropanone and furan.



(2)

3B. Benzene Valence Isomers: Dewar Benzene, Benzvalene, and Prismane. Among the most outstanding examples of the ability of orbital symmetry to preserve massive amounts of energy stored in a small molecule are[4−6] the benzene "valence isomers" **5**−**7** (Chart 1). Benzene itself is a flat planar structure that maximizes the π electron overlap and aromaticity. Structures **5**−**7**, if planar, would represent ***resonance forms*** of benzene. However, the nonplanar structures **5** (Dewar benzene), **6** (benzvalene), and **7** (prismane) represent real, isolable molecules. These molecules are therefore *not resonance forms of benzene, but are* ***valence isomers*** *of benzene; they are nonplanar ground state molecules and possess exceedingly strained structures.* Each of these structures **5**−**7** possesses an enormous massive energy content compared to benzene and simply need to do some bond shifting to flatten out and rearrange to benzene. Yet they are all kinetically stable at room temperature! Each of the valence isomers is produced by the photolysis of the polycyclic azo-compound[5] shown in Figure 1. Indeed, Figure 1 shows that all of the valence isomers

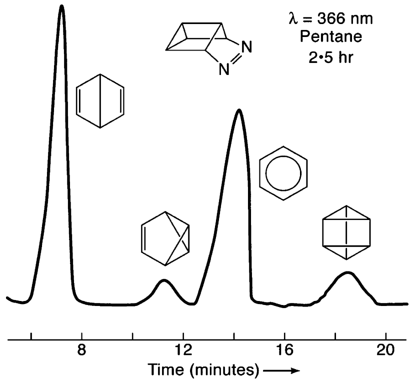


Figure 1. Analytical vpc of the reaction mixture produced by photolysis of the azo compound shown in the top of the figure. Only the C_6H_6 isomers are shown.

of benzene are sufficiently stable to survive passage thorough a gas chromatography column!

The energy stored in the benzene valence isomer structures is enormous (Figure 2). For example,[6] Dewar benzene, **5**, possesses about 60 kcal mol^{-1} more energy than benzene, but it still requires an activation energy of about 30 kcal mol^{-1} to isomerize to benzene! This means that at the transition state for ring-opening, the reactive intermediate possesses 6O kcal mol^{-1} + 30 kcal mol^{-1} = *90 kcal* mol^{-1}*of excess enthalpy above the ground state benzene molecule.* Benzvalene, **6**, stores ~ *67 kcal* mol^{-1} *above benzene and prismane, 7, stores ~90 kcal* mol^{-1} *above benzene.*

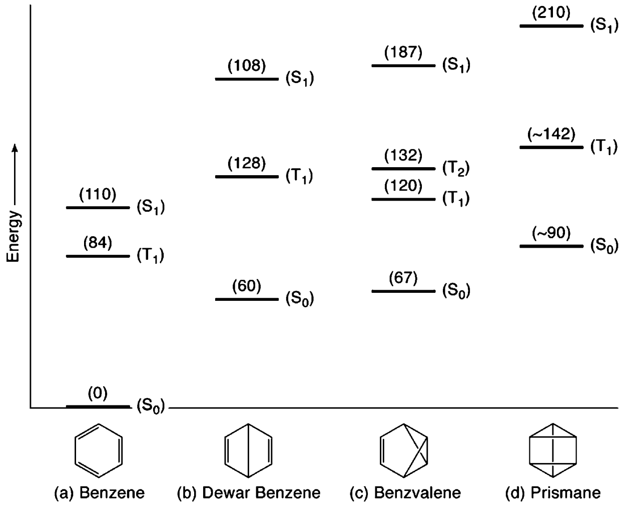


Figure 2. Energy diagram for the ground and excited states of benzene and its valence isomers in kcal mol^{-1}.

3C. 1,2-Dioxetanes. As another example of a high energy structure possessing a four-membered ring, consider[2] the tetramethyl-1,2-dioxetane structure (**2**) shown in Chart 1. As was the case for cyclopropanone and the benzene valence isomers, during the early 1960s such structures were thought to be kinetically unstable, impossible to synthesize and essentially a "complex" of two molecules of acetone. The orbital symmetry paradigm[10] provides an understanding why such molecules do not "instantaneously" fly apart into two acetone molecules. Still, the occurrence of the very weak O−O bond in a four membered ring certainly would make an organic chemist very skeptical about the ability to synthesize and isolate 1,2-dioxetanes. However, 1,2-dioxetanes can be synthesized[2] by a number of methods. **2** is in fact quite stable at room temperature as a crystalline material. Remarkably, **2** *contains ~63 kcal* mol^{-1} *more energy than two acetone molecules* (Figure 3).

A remarkable property of **2** is that when it does decompose thermally, it produces an excited electronic state of acetone (in good yield!) and a molecule of ground state acetone. Even more fascinating, the excited state of acetone produced is the triplet state (T_1), not the excited singlet state (S_1) of acetone. So in review, **2**, as an exemplar of 1,2-dioxetanes, shows the following remarkable properties (Figure 3):

(1) In spite of a an exothermic enthalpy of ~63 kcal mol^{-1}, the TMD molecule requires ~27 kcal mol^{-1} of activation energy before it can decompose.

(2) Upon decomposition, instead of releasing all of its excess enthalpic energy as heat, an acetone triplet possessing ~78 kcal mol^{-1} of energy is produced in good yield, meaning that of the 90 kcal mol^{-1} available to the decomposing molecule at the transition state, ~85% of the excess energy is shuttled into the triplet acetone.

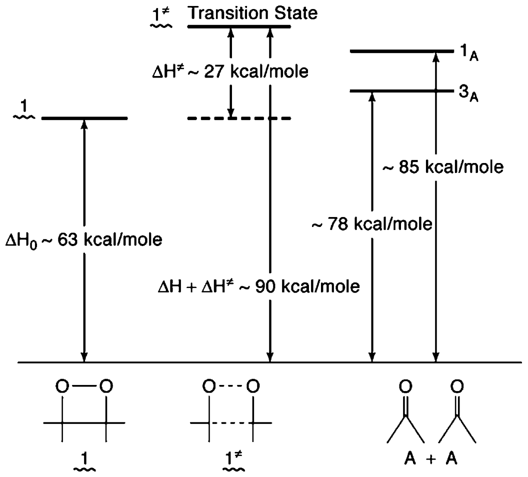


Figure 3. Energy diagram for acetone, acetone's electronically excited states, and 1,2-dimethyldioxetane.

This observation of production of an electronically excited triplet molecule is general for the decompositions of dioxetanes and by no means unique to **2**. However, at the time there was no paradigm to explain the basis for the high yield of triplets upon thermolysis of **2**. As a result, as expected, the community believed that the extraordinary claim was incorrect and the experiments were in error. We had to work hard to prove that they were correct. An important step was to show convincingly that the production of electronically excited states from the decomposition of **2** is theoretically plausible.

Photochemists have an advantage over the general organic community when dealing with situations that involve electron spin in that they are familiar with the paradigm of intersystem crossing (ISC) of singlet and triplet spin states.[11] This familiarity allows photochemists to propose a perfectly plausible explanation for the production of a triplet state of acetone based on the governing ISC paradigm. The spin selection paradigm provides an explanation in the same way that the orbital symmetry paradigm allowed (a community accepted understanding) of the stability of high energy content molecules, such as cyclopropanones, benzene valence isomers and 1,2-dioxetanes. According to the ISC paradigm, spin transitions between singlets and triplets become spin allowed if the system possesses certain features such as "spin-orbital" coupling. The latter is a powerful mechanism for allowing ISC when the electronic system involves the rotation of an atomic p_x to p_y orbital on a single atom.[11] Such an orbital situation is precisely what happens when the O−O bond breaks. Thus, the strong spin−orbit coupling causes the triplet biradical to be formed as the O−O bond breaks, leading to triplet acetone when the C−C bond breaks.

3D. Singlet Molecular Oxygen. Singlet molecular oxygen,[12] $^1O_2$ (termed spectroscopically, $^1\Delta$, Figure 4), is an electronically excited state of ground state triplet molecular oxygen, $^3O_2$ (termed spectroscopically, $^3\Sigma$, Figure 4). The excitation energy of $^1O_2$ is ~22 kcal mol^{-1} higher than the ground state $^3O_2$. There is a second excited state (termed $^1\Sigma$, Figure 4) that is very short-lived (nanoseconds) and is not generally involved in reactions. So when we say $^1O_2$ we are only

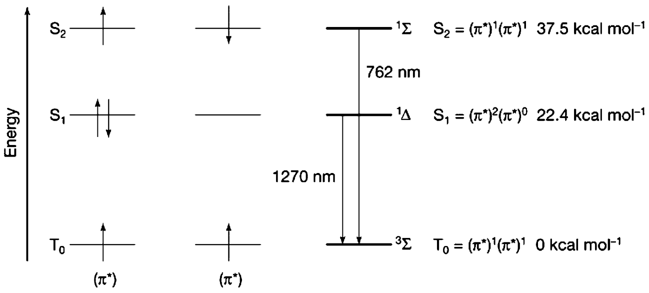


Figure 4. Electronic configurations, energy levels and spectroscopic symbols for the three lowest excited states of O_2.Figure 6. Stereoselectivity of the reaction of $^1O_2$ with the enecarbamates shown. Greater than >95% overall enantioselectivity is achieved.

referring to the $^1\Delta$ excited state. The latter has a readily detectable emission, a $^1\Delta \rightarrow {}^3\Sigma + h\nu$ *phosphorescence* at 1270 nm (Figure 5). The lifetime of the $^1\Delta \rightarrow {}^3\Sigma + h\nu$ *phosphorescence* at 1270 nm depends remarkably on solvent. For example in water the lifetime of $^1\Delta$ is of the order of microseconds, but in solvents without X−H bonds (e.g., CCl_4 Figure 5), the lifetime of $^1O_2$ increases to milliseconds.[13]

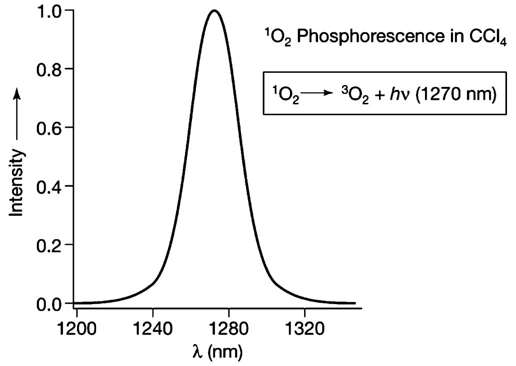
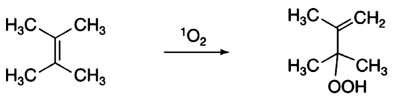


Figure 5. The $^1\Delta \rightarrow {}^3\Sigma + h\nu$ phosphorescence of O_2 in CCl_4.

There are three common reactions[14] of $^1O_2$, an ene reaction with ethylenes to form hydroperoxides (eq 3 A), a [2 + 4] cycloaddition with 1,3-dienes (eq 3 B) and a [2 + 2] cycloaddition to form 1,2-dioxetanes (eq 3 C). In addition to the retro [2 + 2] reactions of 1,2-dioxetane into two carbonyl fragments described above, we shall be interested in the forward and retro [2 + 4] reactions of (eq 3 B) involving 1,4-anthracene endoperoxides and 9,10-anthracene endoperoxides.



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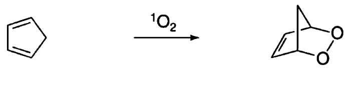

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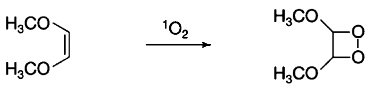


(3c)

We have studied the reaction of $^1O_2$ with encarbamates to form dioxetanes.[15] We discovered a remarkable stereoselectivity for both the facial selective and enantioselectivity of certain enecarbamates. As shown in Figure 6 an enantioselelectivity >90% is achieved. The overall reaction involves an isolable 1,2-dioxetane intermediate! It is remarkable for such a small symmetrical molecule such as $^1O_2$ can show such a high degree of stereoselectivity. We have suggested that the unexpected overall remarkable stereoselectivity is due to the stereoselectivity of deactivation of $^1O_2$ by C−H bonds as the $^1O_2$ approaches the C=C bond of the enecarbamate.[15]

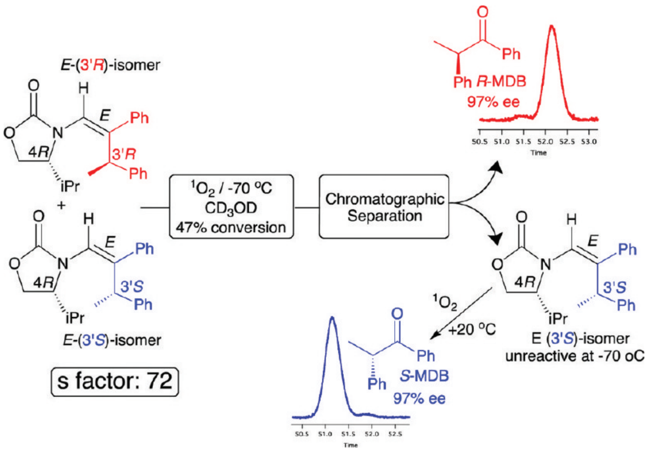
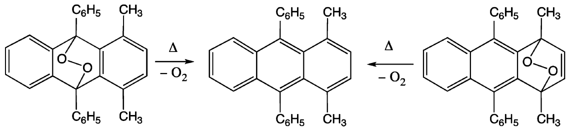


Figure 6. Stereoselectivity of the reaction of $^1O_2$ with the enecarbamates shown. Greater than >95% overall enantioselectivity is achieved.

3E. 1,4-Endoperoxides and 9,10-Endoperoxides of Anthracenes.

Thermolysis (eq 4) of 9,10-anthracene endoperoxides (**3**) and 1,4-anthraceneendoperoxides (**4**) yield the parent hydrocarbon and triplet molecular oxygen, O_2, in nearly quantitative yield in a retro [4 + 2] cycloaddition.[3]



(4)

3 9,10-endoperoxide

4 1,4-endoperoxide

Anthracene endoperoxides do not possess a particularly high energy relative to the products of the allowed thermal [4 + 2] retro cycloaddition. The overall reaction is actually *endothermic* by ∼5 kcal mol^{-1} and *requires ∼33 kcal mol*$^{-1}$ *of activation enthalpy*. So the transition state is located ∼38 kcal mol^{-1} above the energy of the final ground state products. However, the transition state for the [4 + 2] retrocycloaddition therefore possesses enough energy to produce either ground state triplet oxygen, $^3O_2$, or the first excited singlet state of oxygen, $^1O_2$ (see Figure 4). *So it is thermodynamically allowed for either* $^3O_2$ *or* $^1O_2$ *to be formed as products of the [4 + 2] reverse thermal cycloaddition!*

To determine the relative yields of both $^1O_2$ and $^3O_2$ produced in eq 4, a method needed to be invented that could quantitatively determine how much singlet molecular oxygen, $^1O_2$, is produced as the initial product (and then eventually decays to $^3O_2$). We designed trapping experiments[3] which would quantitatively intercept any $^1O_2$ produced before it decays to $^3O_2$. Table 1 shows the results for a 9,10-anthracene endoperoxide, **3**, and a 1,4-anthracene endoperoxide, **4** (Chart 1). The results are that the yield of $^1O_2$ is ca. 50% in the case of thermolysis of anthracene 9,10-endoperoxide, **3** but *nearly 100% in the case of the thermolysis of anthracene 1,4-endoperoxide,* **4**. From Table 1 a correlation can be found between the a near

Table 1. Activation Parameters and Yields of $^1O_2$ in the Thermolysis of 3 and 4[3]

structure	ΔH (kcal mol^{-1})	$\Delta H^{\ddagger}$ (kcal mol^{-1})	ΔS (eu)	$^1O_2$ yield (%)
3 (9,10)	+3	+32	10	50
4 (1,4)	+8	+30	−2	95

zero or low negative value of $\Delta S^{\ddagger}$ and a high yield of $^1O_2$ (1,4-endoperoxides) and a high positive value of $\Delta S^{\ddagger}$ and a low yield of $^1O_2$ (9,10- endoperoxides). *Remarkably, the bulk of the energy for formation of $^1O_2$ comes from the reaction activation energy and not the reaction exothermicity!*

The results are even more intriguing for the thermolysis of 1,4-anthracene endoperoxide, **4**. In this case the yield of $^1O_2$ was 100% (Table 1)!

Our explanation for these contrasting results for the yields of $^1O_2$ from **3** and **4** is that the 1,4-endoperoxide, **4**, undergoes a concerted reaction along its reaction coordinate, but the 9,10-endoperoxide, **3**, breaks one bond completely along the reaction coordinate[4] to form a biradical (Figure 7). The initial intermediate is a singlet biradical, ^{1}BR (step a), that may undergo ISC to a triplet biradical, ^{3}BR (step b), that is competitive with elimination of $^1O_2$ (step c).

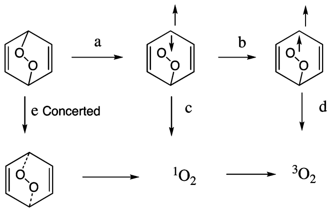


Figure 7. Schematic of the mechanism for the biradical (BR) mechanism of $^3O_2$ (path a → b → d) and the concerted mechanism for the formation of $^1O_2$ (path e).

Both BRs in Figure 7 possess an odd electron on the oxygen atom (C−O−O$^{\bullet}$) which allows for a spin flip from the initially formed singlet biradical to a triplet biradical. When the second C−O bond breaks, the singlet biradical ^{1}BR (↑↓) will yield $^1O_2$ and the triplet biradical will yield $^3O_2$ when the second C−O bond breaks. This is essentially the same mechanism that was proposed for the formation of triplet acetone in the decomposition of 1,2-dioxetanes (Figure 3). Further support for the concerted versus biradical mechanisms comes from magnetic effects discussed in section 6E.

4. ELECTRONICALLY EXCITED STATES OF ORGANIC MOLECULES

Electronically excited singlet spin (S_1 ↑↓) and triplet (T_1 ↑↑) states are the stuff of molecular organic photochemistry.[16] These high energy intermediates differ in a number of profound and important ways from the *ground state* high energy reactive intermediates discussed above. A brief discussion will be given here of the structural, energetic and dynamic parameters that are the basis for the current paradigm for modern molecular organic photochemistry. In particular, we shall discuss the paradigm for the photochemistry of ketones, which served as the bedrock exemplars for developing the current paradigm of molecular organic photochemistry. Although we can only give a brief introduction, fortunately, several excellent texts on molecular organic photochemistry are available for the interested reader.[16]

4A. Developing a Paradigm for Electronically Excited States of Organic Molecules. The most important structural difference between a ground state organic molecule and one of its electronically excited states is that the electronically excited state is a *higher energy electronic isomer of the ground state!* The excited state has the same composition (numbers and kinds of atoms) and constitution (connectivity of the atoms) as the ground state but differs in that *the two highest energy electrons are not orbitally coupled: one electron is in the highest occupied orbital (HO) and the other is in the lowest unoccupied orbital (LU).*[17] This orbital configuration possesses a high energy content (the energy difference between the HO and LU). Through state mixing both radiative and nonradiative pathways back to the ground state or to products occur on very fast time scales. Since the energy difference between the HO and LU can be stored in products, organic photochemical reactions commonly produced strained, high energy structures (such as the benzene valence isomers shown in Figure 2).

A signature pathway for deactivation for an electronically excited state is emission of a photon ($h\nu$) and formation of the ground state.[18] This pathway is not possible for any high energy ground state species, since there is no lower energy state to emit the photon to, and therefore conserve energy, i.e., if a photon is emitted, energy is released and a lower energy state must be produced.

Schematically, the lowest electronically excited states of organic molecules (Figure 8) consist of a spin paired HO-LU configuration termed a singlet state, S_1 (↑↓) and a spin unpaired HO-LU electronic configuration termed a singlet state, T_1 (↑↑). Of these two states, the triplet is the most commonly involved in reactions of ketones, which were the exemplar structures that we studied in detail during the late 1960s and early 1970s.

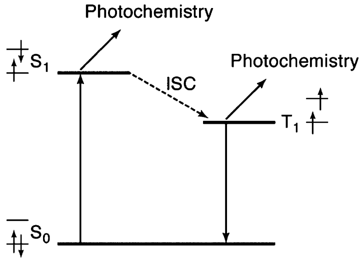


Figure 8. Simplified state energy diagram for the S_1 and T_1 electronically excited states of organic molecules.

With the above general HO-LU paradigm for *all organic photoreactions* in mind, a working, every day paradigm for the molecular organic photochemistry of *ketones* is remarkably, perhaps spectacularly simple (eq 5a):[16c]

$$\begin{aligned} S_0 + h\nu &\rightarrow S_1(\uparrow\downarrow) \\ &\rightarrow T_1(\uparrow\uparrow) \\ &\rightarrow {}^3I(D, \uparrow\uparrow) \\ &\rightarrow {}^1I(D, \uparrow\downarrow) \\ &\rightarrow P(\uparrow\downarrow) \end{aligned} \tag{5a}$$

S_0 (↑↓) represents the initial ground state singlet (orbitally and spin paired) ketone and any associated reagents. S_1 (↑↓) represents an electronically singlet excited state (see energy diagram Figure 8) and T_1, (↑↑) represents the lowest energy triplet state. The elementary step, T_1 (↑↑) → ^{3}I(D, ↑↑) is the primary photochemical step in a photoreaction. For ketones there are only four or so common primary photochemical steps[19] from T_1 and all of them produce a diradical (D)-like intermediate. D is either a radical pair (RP) or a biradical (BR). A critical step, ^{3}I(D, ↑↑) → ^{1}I(D, ↑↓), is the intersystem crossing (ISC) of the initially produced triplet ^{3}D (↑↑) into the singlet, product forming ^{1}D(↑↓). We shall see that this step is responsible for many unexpected supramolecular and magnetic effects on organic photoreactions in section 7A.

4B. Exemplars of Electronically Excited States: The Photochemistry of the n,π* States of Ketones. Since physical organic chemistry deals with the correlation of structure with measurable properties, an important challenge in the early days of organic photochemistry was to determine to what extent, if any, the ideas of ground state molecular organic chemistry could be applied to molecular organic photochemistry. We decided to make use of two well established paradigms, *frontier molecular orbital theory*[9] *and orbital symmetry,*[10] as the basis for developing an everyday working paradigm. The frontier MO theory allowed the use of the ground state HO and LU as the starting point for discussing interactions of the electronically excited state, and orbital symmetry provided a multiple electronic surface view of photochemistry that is absent in ground state chemistry, which takes place on a single ground state potential energy surface.

Let us consider one exemplar of the application of the developing paradigm: the photoreactions of the simplest ketone, acetone.[19] The HO of acetone is an n orbital and LU is a π^* orbital. Thus, the relevant S_1 and T_1 states are both HO = n, LU = π^*, each state is classified in terms of the occupancy of these two orbitals as n, π^*, i.e., S_1 (n, π^*) and T_1 (n, π^*). The working paradigm tells us from experience that we need only consider the T_1 (n, π^*) state, and it condenses to consideration of the following steps shown in eq 5b:

$$\begin{aligned} T_1(\uparrow\uparrow) &\rightarrow {}^3\mathrm{I}(\mathrm{D}, \uparrow\uparrow) \\ &\rightarrow {}^1\mathrm{I}(\mathrm{D}, \uparrow\downarrow) \\ &\rightarrow \mathrm{P}(\uparrow\downarrow) \end{aligned} \tag{5b}$$

We shall see how effective this condensed paradigm is in producing a deep understanding of the photochemistry of all ketones, and also on the spin chemistry of ^{3}I(D, ↑↑) which can display remarkable magnetic field effects and magnetic isotope effects. At the early stages on paradigm development one needs to be confident that the paradigm has a chance of working, but preserve a certain degree of skepticism that it may be completely incorrect or need modification.

Returning to the acetone T_1 (n, π^*) exemplar, we tested[20] the assumption that the photoreactions of this electronically excited state can be understood on the basis of a combination of frontier molecular orbital theory (FMO) and molecular orbital symmetry theory (MOS).[21] In Figure 9, the frontier HO and LU of the n,π^* states of a ketone are shown. FMO theory[9] informs us that there are two "hot spots" in the T_1 (n, π^*) state, the electrophilic, electron poor half filled n orbital and the nucleophilic π^*orbital. We note that the reactivity of these hot spots, assuming a planar structure, is in plane for the n orbital and above and below the plane for the π^* orbital.[22,23] On the left in Figure 9 the possible interactions of the "n-orbital hot spot" with electrons in the HOa of other molecules or groups within the molecules are shown: σ_{CH} bonds, $\pi_{c=c}$ bonds and nonbonding n-electron. The other option for an initial FMO interaction would be for the electron in the π^* LU to overlap with and donate electric charge to some empty π^* LU (right of Figure 9).

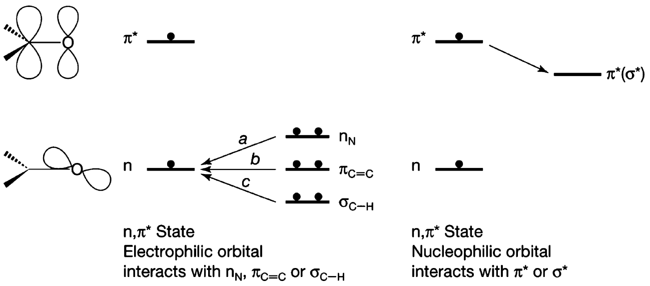


Figure 9. Frontier molecular orbital interactions of the n and π^* orbitals of an n, π^* state.

At this point MOS theory kicks in and symmetry arguments allow us to use state correlations to predict the symmetry allowed and forbidden paths.[17] The general idea of the symmetry basis state correlations diagrams is shown in Figure 10. From the FMO analysis, there are two symmetry distinct approaches to the hot spots of the n,π^* state: (1) a perpendicular approach to the faces of the half-filled, electron rich π^* orbital and (2) an in-plane approach to the half-filled electron deficient n orbital. From an orbital symmetry analysis,[21] the in plane approach is allowed and the perpendicular approach is forbidden. This prediction has been verified in many experimental cases.[20,22]

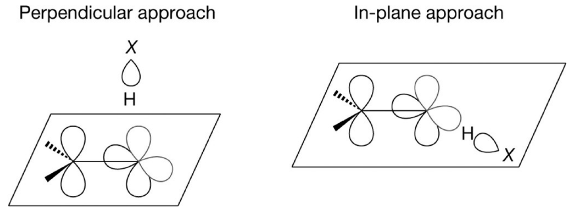


Figure 10. Two possible limiting geometries for the approach of an X–H bond to the n orbital of the n, π^* state of acetone. Left: an approach that is perpendicular to the plane of the carbonyl group. Right: an approach that is in-plane to the plane of the carbonyl group.

5. TRACKING TRANSIENT REACTIVE INTERMEDIATES IN REAL TIME

One of the delights of studying reactive intermediates is actually "seeing" transient species through time-resolved spectroscopy. Techniques have been developed over the past 50 years that allow the spectroscopic determination of species lasting only a few femtoseconds! Our studies have been confined to the nanosecond domain where the equipment is convenient, reliable and easily operated by students. For example, in addition to electronic absorption spectroscopy, we have used ESR spectroscopy[23] and IR spectroscopy[24] as methods for detection of transients produced by photochemical excitation. Here we show two exemplars from the photolysis of ketones, "looking at" the α-cleavage reaction of the C=O–C bond of the n,π^* state of ketones to produce radical pairs.

5A. Exemplar Using Time-Resolved ESR. Figure 11 shows the time-resolved ESR (TR ESR) analysis of the

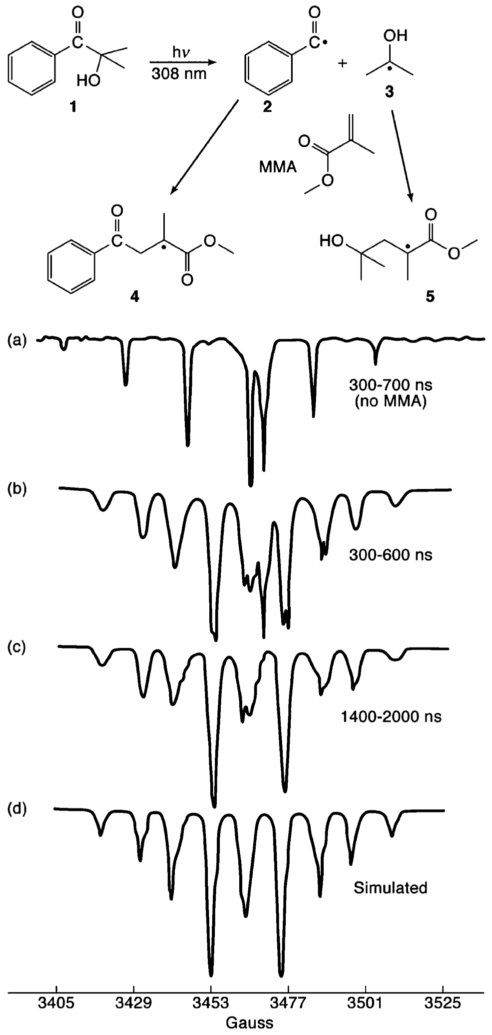


Figure 11. Time-resolved ESR spectrum observed following the laser excitation of 1 (a) 300−700 ns after laser excitation in the absence of methyl methacrylate; (b) 300−700 ns after laser excitation in the presence of methyl methacrylate; (c) 1400−2000 ns after laser excitation in the presence of methyl methacrylate; (d) simulated spectrum for the addition of the radicals to methyl methyl methacrylate.

photolysis of ketone **1**.[23] Two radicals are produced, a benzoyl radical **2** and a ketyl radical **3**. Both radicals are readily detected in the time domain ~500 ns and longer. In the presence of methyl methacrylate, both of these radicals add to the ethylene to form the new radicals **4** and **5** as shown clearly by the change in the TR ESR spectrum in the >600 ns domain. Indeed, a simple inspection of the spectrum shows that the ketyl radical, **3**, reacts faster than the benzoyl radical **2**. So this is a nice example of "taking a movie" of a photochemical primary process and secondary reactions of reactive intermediates in real time.

5B. Exemplar Using Time-Resolved IR. As a second example,[24] the carbonyl group produced by the photolysis of **1** can be detected by TR IR (Figure 12). Note that the carbonyl stretching vibration occurs at ~1820 cm^{-1}. The kinetics of the reaction for the carbonyl with ethylenes and other species can be readily measured by following IR signal ~1820 cm^{-1}.

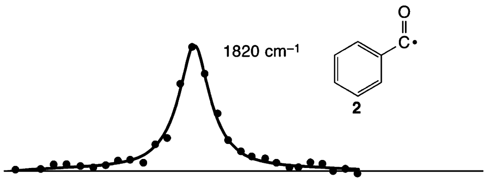


Figure 12. Time resolved IR spectrum taken 500 ns after laser excitation of **1** in Figure 11. The band at ~1820 cm^{-1} corresponds to the carbonyl stretching frequency of the benzoyl group (see Figure 11 for the corresponding ESR of the benzoyl group).

6. THE "CAGE EFFECT" OF GEMINATE TRIPLE RADICAL PAIRS: A POWERFUL TOOL FOR STUDYING SPIN CHEMISTRY

In many organic photochemical reactions a geminate triplet radical pair (eq 5a) is produced in the primary photochemical reaction from T_1. This triplet geminate pair has two general options: (1) undergo ISC to form a singlet geminate pair that undergoes combination (or disproportionation) within the solvent cage in which the pair was born or (2) diffusion from the solvent cage to form free radicals in the bulk solvent. This simple, but very general competition serves as the basis for the observation of many supramolecular and magnetic effects in photochemical reactions.

The "cage effect" is defined as the fraction, **P**, of geminate radical pairs produced by a primary photochemical process that undergoes reaction within a solvent cage. If all of the radical pairs undergo reaction (e.g., combination or disproportionation), the cage effect is 1.0; if all of the radical pairs escape from the primary solvent cage and become free radicals, the cage effect is 0.0. In the latter case all of the escaping radicals can be scavenged and, for example, initiate radical polymerization. In the former case where the cage effect is 1.0, polymerization is not initiated since none of the geminate radicals escape into the bulk solvent. The experimental value of the cage effect is thus a measure of the competition between the escape of the radical pair from the primary solvent cage and reaction in the solvent cage.

Insights of supramolecular chemistry[25] are available from a comparison of the similarities of radical pairs in a homogeneous solvent and in a supercage such as a micelle and a biradical (Figure 13). The supercage serves the same structural feature that a flexible chain connecting two radical centers: it preserves the geminate character of the radical centers. It is therefore expected that some of the features of radical pairs in supercages will be intellectually transferable to biradicals. An Example of a biradical mimicking the behavior of a radical pair will be given in section 3E.

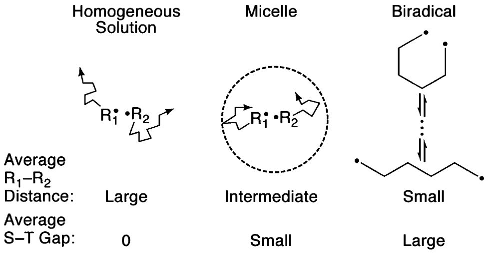


Figure 13. Schematic comparison of a radical pair in homogeneous solution (left) in a supramolecular supercage (middle) and a flexible biradical (right).

6A. Micelles as Supercages. Most organic photoreactions proceed through geminate triplet radical pairs produced in the primary solvent cage, eq 5a. Since triplet radical pairs must undergo ISC to singlet radical pairs before they can undergo cage reactions, in nonviscous solvents (<10 cP, pentane, acetonitrile, benzene) cage escape competes favorably with the cage reaction and the typical value in nonviscous solvents is 0.0.

In 1972, we had begun investigations of micelles,[26] fascinating supramolecular species that appeared to have the potential of serving as "supercages" whose structures could be systematically modified and explored with the intellectual, experimental and attitudinal tools of physical organic chemistry. We conjectured that we could control the cage effect through supramolecular effects. Such control might lead to new phenomena that could be explored with the tools of the physical organic chemist. It was generally unappreciated by organic chemists, as we initiated this research, that micelles composed a small fraction of the remarkable structures of the field of colloid and interface chemistry, fields that we now recognize as belonging to the wider field of supramolecular chemistry. Only later did we recognize that we had opened the door to the incredible richness of what was to become the field of "supramolecular organic chemistry and supramolecular organic photochemistry".

We started with the exemplar of a micelle in aqueous solution as a simple model for a "supercage". The fundamental idea of the latter was *a supramolecular host that could control the cage reaction.* We soon discovered that not only could we completely control the value of the cage effect from any value between 1.0 to 0.0, but serendipitously, and more importantly, that micelles serve as outstanding hosts for the observation of magnetic isotope effects and magnetic field effects on the competition between cage reaction and cage escape of radical pairs (section 7C).

We shall first discuss the structure of micelles as supercages and how micelles can control the values of the cage effect. We will then show how the size and characteristics of the hydrophobic core of a micelle are well suited for the observation of massive magnetic isotope and magnetic field effects on the reactions of geminate triple radical pairs generated in a micelle host.

6B. Micelles as Primitive Models of All Supramolecular Hosts: Analogy to Enzymes and Guest@Host Complexes. A *supramolecular complex* is an aggregate of two or more molecules held together by noncovalent bonds. Enzyme chemistry and *"guest@host"* chemistry provide an intellectual context for designing experiments that explore the foundation of supramolecular chemistry.[25] We decided that micelles possess some of the important topological features (Figure 14, an inside core for binding, an outside shell for defining the host structure, solubility in aqueous environment, etc.) of enzymes and guest@host complexes in general.

Figure 14 shows schematically the basic ideas of topology that connect guest@host supramolecular structures to the familiar Lewis molecular structures that we are used to in everyday organic chemistry. From this topological approach, we can use the familiarity of Lewis structure to ask questions about the composition and constitution of supramolecular structures. In this topological description the host has an inside (**I**), a boundary (**B**) and an outside (**O**). Thus the guest (**G**) can be bound to **I** or **B** of the host or unbound to **O**. In case c of Figure 14, we can see that there is a nice mapping of the Lewis ideas of molecule isomers to the supramolecular concept of supramolecular isomers.

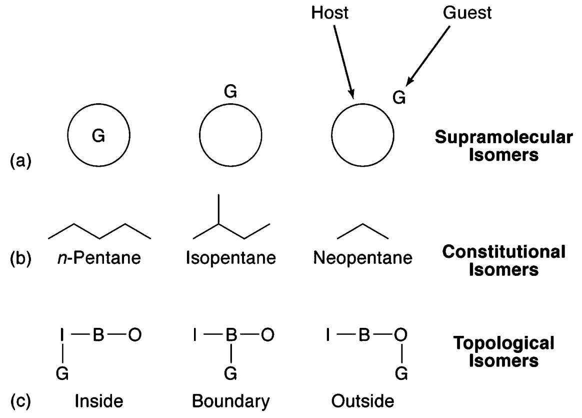


Figure 14. Topological description of a guest@host supramolecular complex. The circle represents a supercage that can bind the guest on its internal or external surface. The guest may also be unbound and dissolved in the solvent of the system. Shown schematically is a comparison of the conventional constitutional formulas (Lewis structures) for pentane and an analogous topological constitution.

6C. Generalization of the Paradigm of Micelles as Supramolecular Hosts: The Enzyme Guest@Host Paradigm. Our mechanistic development of supramolecular organic chemistry[25] focused on the well established paradigm of the mechanism of enzymes: guest@host complexes for which the host structure controls the chemistry of the guest. Figure 15 shows a very simplistic schematic paradigm comparing (a) molecular organic photochemistry to (b) supramolecular organic photochemistry: the latter has a "circle" surrounding the guest photochemical substrate, R. The circle represents the supramolecular environment that will control the photochemistry of R. So we consider the topological circle of Figure 14, a purely intellectual construct, that we shall use in the same way that chemists have successfully used molecular structure for over 100 years.

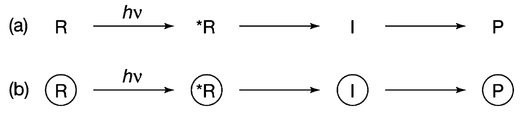


Figure 15. Comparison of the simplified paradigm for molecular photochemistry (a) to the simplified paradigm for supramolecular (guest@host) photochemistry (b). See Figure 17 for the topological meaning of the circle.

From the simple paradigm of Figure 15, it can be seen that the influence of the host can occur at four structural points: the starting material, R, the electronically excited state *R, the reactive intermediate produced in the primary photochemical process, I, and finally in the eventual product(s) produced from I.

These ideas of the topological interpretation of supramolecular chemistry provided us with the tools to design spectacular magnetic field and magnetic isotope effects on photochemical reactions (section 7B). So now let us make an intellectual leap that is provided by the topological paradigm of Figure 14 and as chemists put structure into the circles. We now tell a story about how this may have happened, viewed through the fog of decades and incredible changes in chemistry.

6D. Micelles as Supercages. Control of the Cage Effect of Radical Pairs. A surfactant, the monomer that makes up a micelle (Figure 16), is a "schizophrenic" molecular species that is at once both hydrophobic (possessing a long hydrocarbon chain) and hydrophilic (possessing a polar headgroup). Aqueous solutions of micelles are noncovalently bound aggregates of surfactant molecules that are bound together by hydrophobic forces in aqueous solutions.[26] There is a critical concentration (critical micelle concentration, cmc) of surfactant at which the system is transformed from a molecular solution of surfactant monomers to micellar aggregates. The micelle is a supramolecular structure possessing a hydrophobic core that can absorb organic molecules which are essentially insoluble in water. The size and hydrophobicity of this core can be controlled by a number of experimentally controllable features such as the length of the surfactant chain.

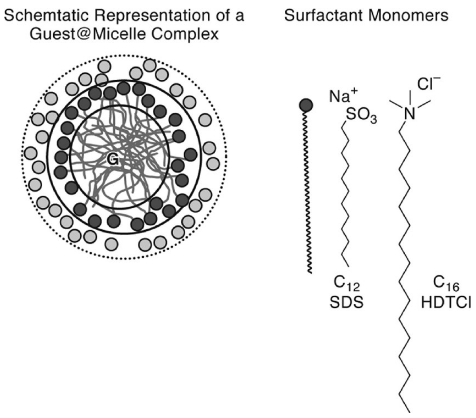


Figure 16. Schematic description of a micelle (left). The structures of two common surfactants, sodium dodecyl sulfate (SDS) and hexadecyl tetramethylammonium chloride (HDTCl), are shown on the right.

A micelle of Figure 16 can be considered as a possible host represented by the topological circle in Figures 14 and 15. *As chemists, we can readily transform the circle into more concrete chemical structures.* Some examples are shown in Figure 17. We shall discuss the photochemistry of some of these hosts.

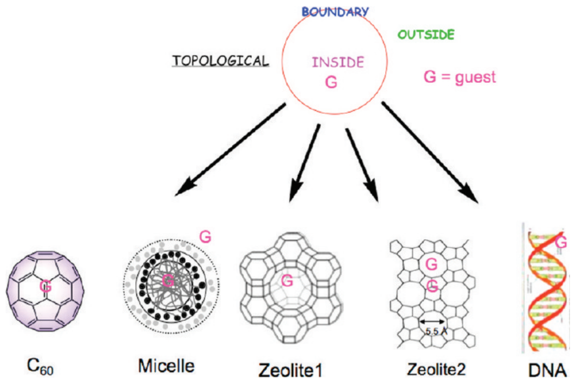


Figure 17. Conversion of the "topological circle" representing a host into chemical structures such as C_{60}, a micelle, a zeolite supercage and DNA.

6E. Exemplars of the Control of Geminate Pair Recombination by Micelle Hosts: Dibenzyl Ketone (DBK) and Friends: The Perfect Guest for Observing Supramolecular Effects. The initial goals of our investigations of micelles were to obtain knowledge concerning the variation of the cage effect in micellar solutions as a function of the systematic variation of micellar structure and to compare the results to those of radical-pair theory for the cage effect in homogeneous solutions and eventually to compare the behavior of supercages to that of flexible biradicals (Figure 13).

Consider a precursor molecule ACOB that undergoes photochemically induced α-cleavage and decarbonylation to produce the products AA + AB + BB (eq 6) in some relative amounts. If the cage effect is 1.0 then only AB is produced as the product; if the cage effect is 0.0, then the products are produced in statistical amounts, i.e., 25% AA + 50% AB + 25% BB.

$$\mathrm{ACOB} + h\nu \rightarrow \mathrm{A} + \mathrm{B} + \mathrm{CO} \rightarrow \mathrm{AA} + \mathrm{AB} + \mathrm{BB} \tag{6}$$

From the measured ratio of products, AA, AB, and BB by simple vpc analysis, cage effects from 0.0 to 1.0 may be readily measured.[27] Figure 18 shows an experimental example: the variation of the cage effects for p-Me-DBK (Chart 2) as a function on increase in the concentration of an aqueous solution of the surfactant hexadecyltrimethylammonium chloride, HDTCl (Figure 16). The value of the % cage effect is ~0.0 in water as expected for a nonviscous solvent, but as the [HDTCl] increases, the % cage effect increases to 50% and then reaches a plateau. The shape of the curve is that expected for the formation of micelles with a critical micelle concentration (cmc) of ~2 × 10^{-3} M, compared to the literature value for formation of micelles of HDTCl. At ~ 4 × 10^{-3} M, all of the surfactant exists as micelles, and all of the ACOB molecules are guests within a micelle.

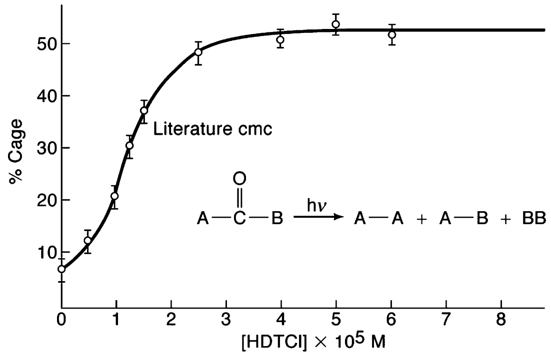
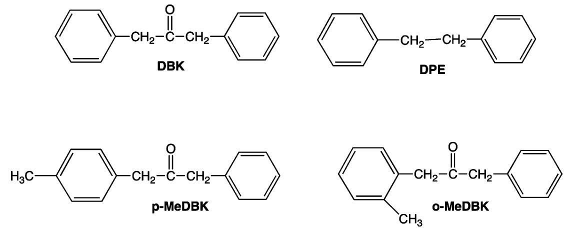


Figure 18. Percent cage effect for the photolysis of 4-Me-DBK in aqueous solutions of HDTCl surfactant as a function of [HDTCl].

Chart 2. Structures of DBK, DPE, *p*-MeDBK, and *o*-MeDBK



Recall that the "cage effect" is defined as the fraction of geminate benzyl radical pairs (A and B in eq 6) that combine within a micelle supercage. As a benchmark for the supercage, the cage effect for photolysis of DBK (Chart 2) in nonviscous homogeneous solution is found to be ~0. However, the cage effect for the photolysis of DBK in micelles depends on the concentration of the micelles and the size of the micelles. For example,[27] Figure 19 shows that for a series of straight chain sulfate surfactants (above their cmc) containing from 6 to 14 carbons in the chain, the cage effect increases monotonically with the size of the surfactant chain. As the chain length increases, the size of the micelle increases. This result is consistent with the hypothesis that the rate of radical escape from a micelle is proportional to the "hydrophobicity" of the micelle complex. Thus, the size of the micelle and its hydrophobicity increase as the size (chain length) of the surfactant of which the micelle is composed is increased.

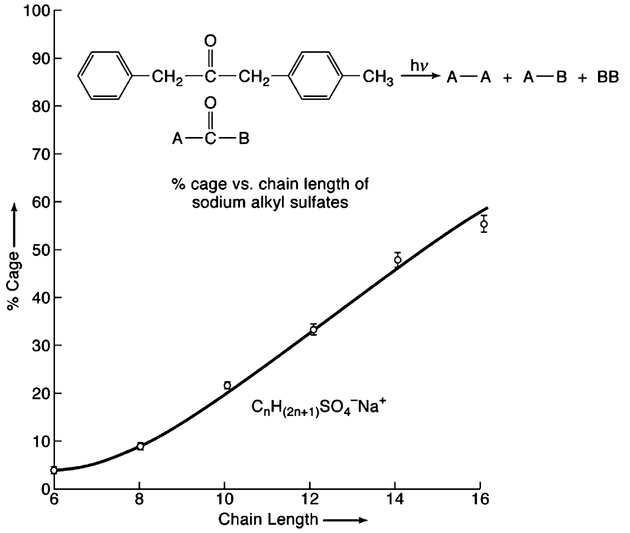


Figure 19. Percent cage effect for the photolysis of aqueous solutions of 4-MeDBK as a function of detergent chain length for series of sodium alkyl sulfonates (see Figure 16 for the structure of the 12 carbon chain sodium alkyl sulfonate, sodium dodecyl sulfonate, SDS. The point with the open circle is a 16 carbon chain cationic surfactant (HDTCl, Figure 16). The 16-carbon chain sulfonate was too insoluble to form micelles under the reaction conditions.

In conclusion, the "supercage" environment of a micelle host for a triplet geminate radical pair results in a much higher cage effect than that found in homogeneous solution. The size of the cage effect depends on both the size of the host micelle, reflecting the overall hydrophobic host core available to the guest. In addition, the special restricted space of a micellar aggregate provides an excellent environment for the observation of significant magnetic field and magnetic isotope effects. We shall see in section 7B how the properties of a micelle are superb for the observation of *magnetic field effects (MFE) and magnetic isotope effects (MIE)* on the extent of cage reaction in supercages. In addition, we shall see how the MIE can be used to separate magnetic isotopes such as ^{13}C ($I = 1/2$) from nonmagnetic isotopes such as ^{12}C ($I = 0$).

A schematic review of the above paradigm for the photolysis of ACOB ketones in HDTCl micelles with pMeDBK as an exemplar is given in Figure 20. We point out the switch from "*molecular*" behavior of the system (premicelle) to "*supramolecular*" behavior (micellar) around the cmc, where the value of the cage effect suddenly rises rapidly with the formation of micelles.

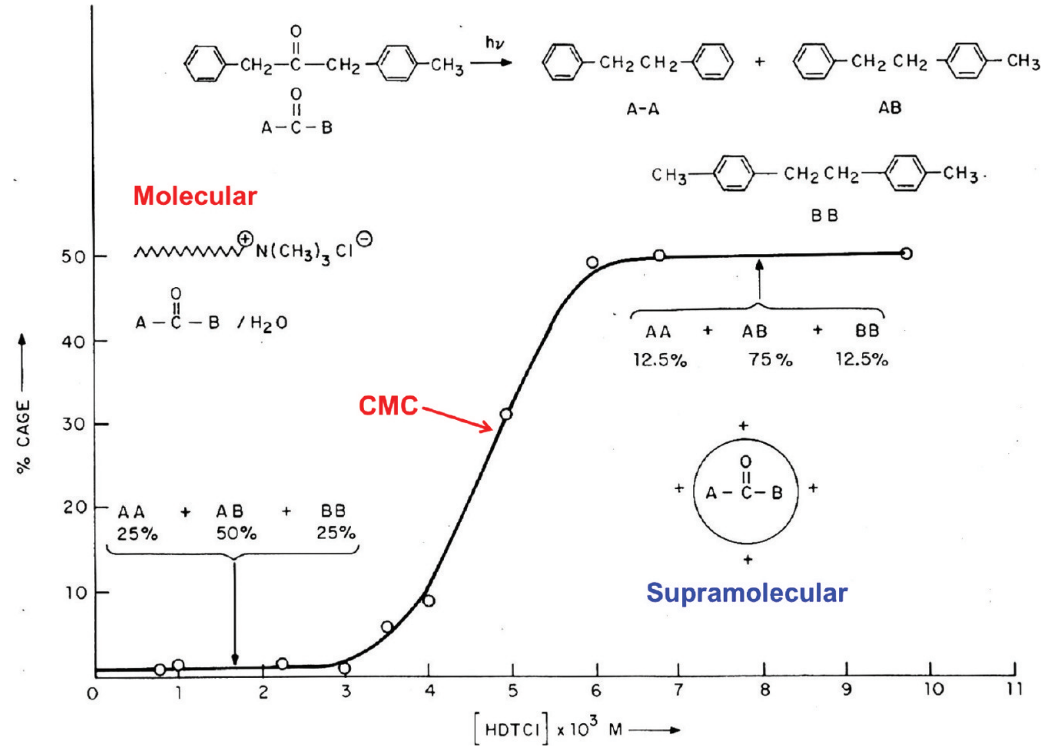


Figure 20. Variation of the cage effect for pMe-DBK as a function of [HDTCl] in aqueous solution. There is a structural switch from "*molecular*" (ACOB shown in H_2O) behavior of the system (premicelle) to "*supramolecular*" behavior (micellar, ACOB shown in circle) around the cmc, where the value of the cage effect suddenly rises rapidly with the formation of micelles.

7. BEYOND SUPRAMOLECULAR PHYSICAL ORGANIC CHEMISTRY AND SUPRAMOLECULAR ORGANIC PHOTOCHEMISTRY: SUPERDUPER ORGANIC PHOTOCHEMISTRY

In the 1970s, we asked, since physical organic chemistry is constantly evolving, what will come after supramolecular physical organic chemistry and supramolecular organic photochemistry? What will the next generation, "superduper" molecular organic photochemistry look like? We decided to explore the possibility that weak magnetic fields provided from nuclear spins and the use of electron spins to control chemical reactivity might be a possibility. This would open a new field of "spin chemistry".

In the late 1960s, the paradigm of the electron spins (S_1 and T_1) that were involved in photochemical reactions was well established.[16] However, *the idea that nuclear spins could have a significant effect on the steps in chemical reactions was considered an extraordinary, perhaps absurd, claim!* Here's where understanding the most fundamental paradigms of chemistry was critical. The claim that nuclear spins, having energies of the order of $\sim 10^{-5}$ kcal mol^{-1}, could influence chemical processes typically having activation energies of the order of >10 kcal mol^{-1} is not reasonable...if thermodynamics and equilibrium dominate the processes under study. However, this argument is only one possibility. If one considers the fundamental paradigm for reaction dynamics, one sees that in addition to activation energy ($\Delta H^{\ddagger}$) there is another critical parameter that determines the *rate* of a chemical process: the reaction entropy $\Delta S^{\ddagger}$. So the challenge is to find situations where the nuclear spin can control reactivity through $\Delta S^{\ddagger}$. While these considerations do not guarantee that the effects of nuclear spins on chemical processes will be significant enough to be measurable, *the claim that this might be the case is completely within the conventional paradigm of molecular kinetics.* However, such a possibility will not be apparent or acceptable to a chemist who is locked into the idea that thermodynamics always dominates nuclear spin effects. We realized that for whatever reason such prejudices might exist, when arguing with chemists who held such beliefs, we could make what seemed like extraordinary claims, but indeed these claims were within the accepted paradigms of chemistry.

Indeed, we were lucky to find, serendipitously, that our micellar systems were superb for observing *extraordinary* nuclear spin effects on the cage reactions. Associated with these effects were massive effects of magnetic fields on photoreactions. The cases that produced these effects involved either triplet geminate radical pairs in a supramolecular host, or biradicals (BR) for which the radical centers were covalently connected by a flexible chain (Figure 13).

7A. Spin Chemistry and Spin Catalysis. Spin chemistry is a field concerned with the nuclear spin and electron spin control of the rates of elementary thermal and photochemical elementary steps.[28] Equations 7 and 8 hold the key to many known exemplars in spin chemistry. Most of spin chemistry deals with systems involving the competition of two steps along a reaction pathway, one whose rate depends on electron or nuclear spin (e.g., eq 7) and a second that does not (e.g., eq 8). An important and common exemplar is given in eq 7 for which an electronically excited triplet state (T_1) undergoes reaction to produce a diradical (geminate triplet radical pair, RP or triplet biradical, BR). *Both ^{3}RP or ^{3}BR must undergo electronic intersystem crossing (ISC) to a singlet ^{1}RP or ^{1}BR before undergoing reaction to form the singlet product ^{1}P.* The rate of eq 7 is determined by magnetic effects available to ^{3}I(D, ↑↑) that can "catalyze" the rate of the ISC step. The rate of eq 8 is assumed not to depend on magnetic effects. For example, this step may be simple diffusional separation of the geminate radical out of the cage to form two free radicals. Therefore, the rate of eq 8 will be the same, whatever the magnetic interactions available for eq 7. The basic idea is that if spin catalysts can accelerate (spin catalyze) the rate of eq 7 to the point that the rate of ISC is competitive with that of eq 8, the formation of product P will depend on the spin catalyst. Both orbitally unpaired electrons and nuclear spins (^{1}H, ^{13}C, ^{17}O) can serve as spin catalysts.

$$\begin{aligned} T_1(\uparrow\uparrow) &\rightarrow {}^3\mathrm{I}(\mathrm{D}, \uparrow\uparrow) \\ &\rightarrow {}^1\mathrm{I}(\mathrm{D}, \uparrow\downarrow) \\ &\rightarrow \mathrm{P}(\uparrow\downarrow) \end{aligned} \tag{7}$$

$$T_1(\uparrow\uparrow) \rightarrow \text{free radicals (or other irreversible non magnetic processes)} \tag{8}$$

We shall describe two exemplars of spin chemistry that show how eqs 7 and 8 operate cooperatively to produce two important spin chemistry effects: (1) the magnetic isotope effect (MIE) in which a nuclear spin is the spin catalyst that influences the rate of eq 7, and 2 the magnetic isotope effect (MIE) in which an external applied magnetic field influences the rate of eq 7.

7B. Magnetic Field Effect (MFE) and the Magnetic Isotope Effect (MIE) on Geminate Radical Pair and Biradical Reactions. We start with two examples of the use of spin chemistry to separate magnetic isotopes from nonmagnetic isotopes.[29] A MIE example involves the photolysis of dibenzylketone (DBK, Chart 2) in micelles in which the magnetic isotope ^{13}C is separated from the nonmagnetic isotope ^{12}C through the competition of rates between eq 7 and eq 8. In this case the spin chemistry of geminate radical pairs produced by photolysis of DBK in micelles is controlled by the micelle supercage. Also, we describe the basis for a MFE example in the photolysis of DBK for which external laboratory magnetic fields can influence the rate of eq 7, and therefore the yield of product P.

A second example of a MIE involves a biradical, rather than a radical pair.[3] The thermolysis of 1,4-endoperoxides, can proceed through either a biradical or concerted retro [2 + 4] cycloaddition mechanism to produce O_2. In this case, we shall see that only in the biradical pathway is there an opportunity for the magnetic isotope, ^{17}O to influence the rate of eq 7 but not of eq 8.

7C. Magnetic Field and Magnetic Isotope Effects on the Photochemistry of DBK@micelles. A detailed overall scheme for the photolysis of DBK in a micelle is shown in Figure 21 where the ovals indicate species that are in the micelle. From Figure 21 we see that there are two distinct ISC steps corresponding to eq 7: (1) the ISC of the triplet geminate phenacyl–benzyl radical pair, which after ISC can reform DBK and (2) the ISC of the triplet geminate benzyl–benzyl radical pair (formed after decarbonylation of the phenacyl radical) after which ISC diphenylethane (DPE) can be formed. Thus, MIE and MFE effects can occur at two different stages during the photolysis of DBK in micelles.

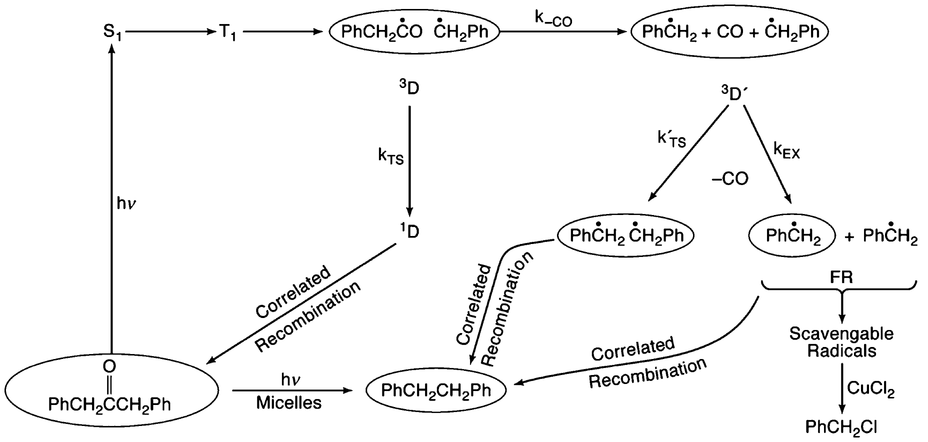


Figure 21. Detailed schematic description of the photolysis of DBK. There are two geminate pairs produced at the first bond cleavage of the triplet $PhCH_2C{=}O\text{--}CH_2Ph$ bond in the primary photochemical process in a micelle and at the cleavage of the phenacyl radical $PhCH_2\text{--}C{=}O$ in a secondary thermal step.

We first consider a qualitative and general framework for understanding how both MIE and MFE operate on reactions of triplet geminate radical pairs in a micelle (Figure 22).

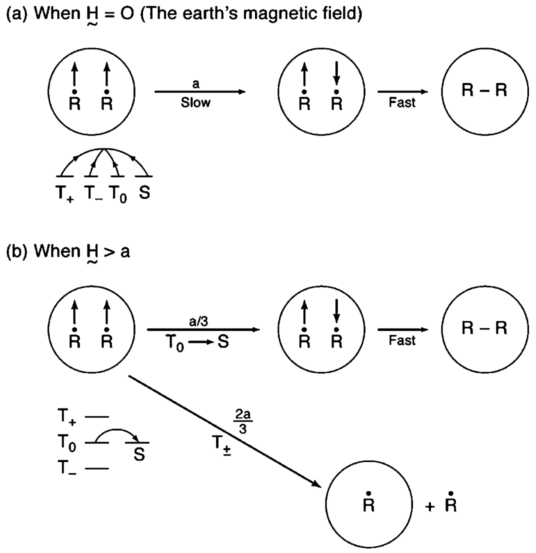


Figure 22. Schematic description of the influence of an applied external magnetic field on the cage effect on a geminate triplet radical in a supercage such as a micelle. Limiting situations are shown. At low field, hyperfine spin catalyzes ISC to the singlet geminate radical pair. At high field, two of the three hyperfine levels are decoupled from the singlet state and no longer can undergo efficient ISC. As a result the decoupled radical pairs escape the host and enter the bulk solvent, reducing the cage effect.

The rate of ISC (k_{ISC}) will be a function of the magnetic interactions that can cause the spin catalysis (or spin inhibition) of the $T_0 \rightarrow S$ ISC step of eq 7 to occur.[28,30] In the absence of a magnetic field at certain separations of the radical pair the exchange interaction J is ~0. When this is the situation the energies of the three triplet levels (T_+, T_0, and T_-) are identical to each other and also have the same energy as the singlet radical pair, S. Under these conditions, the value of k_{ISC} will be maximal since all the sublevels are degenerate. Furthermore, for these conditions the hyperfine coupling, ***a***, between the odd electron of the radical pair and a magnetic nucleus such as ^{13}C will determine the value of k_{ISC} (at $H_z = 0$). This leads to a *magnetic isotope effect (MIE)*. However, when a magnetic field, H_z, is applied that is stronger than ***a***, two of the three triplet levels (T_+ and T_-) will be split in energy from T_0 and S (T_+ will increase and T_- will decrease relative to T_0: thus, T_+ and T_- are no longer degenerate with S. As a result, *T_+ and T_- will be inhibited from undergoing ISC to S and instead will undergo some other process* (eq 8) such as escape of the radical pair from the micelle. If eq 8 competes favorably with eq 7, under these conditions, this reduces the cage effect as a function of the strength of H_z.

The basis of the spin chemistry situations described in the previous paragraph are shown schematically in Figure 22. In Figure 22a, the triplet geminate radical pair in a micelle is considered when the electron exchange, $J = 0$, conditions such that the energy of the triplet radical pair and the singlet radical pair is zero. Under such conditions we can assume that hyperfine couplings, **a**, of the magnetic nuclei that are coupled to the orbitally unpaired electrons of the radical pair determine the rate of ISC in eq 7. In this case, all three triplet levels are degenerate with the singlet so that the rate induced by the magnetic isotope is at a maximum.

In Figure 22b, the triplet geminate radical pair is considered when there is a strong magnetic field that causes T_+ and T_- to be separated in energy from T_0, which remains degenerate with the singlet state, S. *As a result only the $T_0 \rightarrow S$ ISC is feasible and in the limit, 2/3 of the radical pairs cannot undergo ISC. This means that only 1/3 of the radical pairs can undergo reaction to form P.* This is the basis of the MFI on the reactions of radical pairs in micelles. Let ***P*** represent the cage product, the fraction of P formed from the initial geminate radical pair represents the cage effect. We see from Figure 22a the basis for the MIE on the cage effect; and from Figure 22b, the basis for the MFE on the cage effect.

Figure 23 shows experimental examples[27] of both the MFE and MIE on the cage effect of the photolysis of DBK in micelles. The cage effect for DBK is largest (~34%) at low magnetic fields (situation a in Figure 22) and then decreases to a plateau value (~17%) for magnetic fields about 1000 G (situation b in Figure 22). The leveling occurs because T_- and T_+ have been split so far from S that they no longer undergo ISC (eq 7) in competition with eq 8, escape from the micelle. These magnetic effects are completely absent when the reaction is run in ordinary nonviscous organic solvents. The reason, to

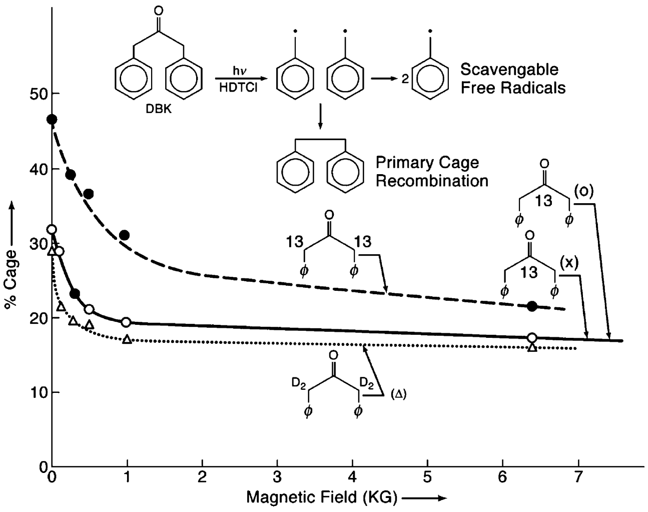


Figure 23. Cage effect for the formation of diphenylethane (DPE) as a function of magnetic field for DBK and several isotopically substituted DBKs shown in this figure.

be explained below, is due to the special nature of the size and diffusional dynamics of a micelle supercage.

Also shown in Figure 23 is the MIE on DBK that has been enriched in ^{13}C in the CH_2 carbon atoms. *The cage effect is much higher, ~ 46%, than that found for DBK with ^{12}C in the CH_2 positions (situation a in Figure 22)*. However, the change in the cage effect is nearly the same for DBK with ^{13}C in the C=O position. This is because the ^{13}C=O is not involved in the combination of the benzyl radicals. These magnetic effects are completely absent when the reaction is run in ordinary organic solvents.

Clearly, the micelle host is having a major effect on the sensitivity of the geminate radical pair guests to undergo recombination. Although the situation is complicated, Figure 24 schematically describes the basis of this remarkable effect in terms of a "supramolecular spin ball machine" that explains the MIE. Let $\boldsymbol{P}_r$ be the probability of the cage effect of any geminate radical pair produced in the micelle host and $1 - \boldsymbol{P}_r$ be the probability of escape of the radical pair from the host. On the lower left of the figure is schematically shown the spin orientation of the initially formed geminate triplet (↑↑) radical pair, with α (up spin) and β (down spin) representing the orientations of the electron spins. The two partners of the radical pair separate and begin a diffusional random walk in the hydrophobic space of the micellar host. During a portion of the walk the pair are separated and the exchange interaction J between the two radical is ~0 (situation a in Figure 21). Under these conditions, the hyperfine coupling of a ^{13}C nucleus can serve as a mechanism for ISC reorienting the electron spins from a triplet (↑↑) to a singlet (↑↓). Upon reencounter, the singlet geminate radical pairs recombine to form a ^{13}C enriched DBK. *The ^{12}C=O radical pairs cannot undergo ISC to form singlets and therefore either decarbonylate or escape from the micelle into the aqueous phase, but do not form DBK.*

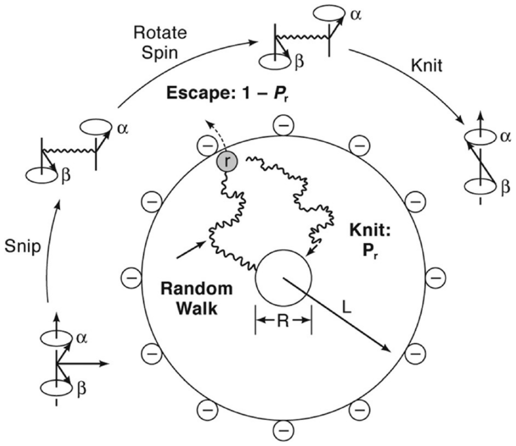


Figure 24. Micelle host of a radical pair operating as a "supramolecular spin ball" machine.

The MFE can be understood as an example of situation b in Figure 22. In this case the magnetic field strength exceeds that of the hyperfine coupling, and T_- and T_+ no longer can undergo ISC to singlets and combine to produce a cage product.

7D. Magnetic Isotope Effects on the Thermolysis of Anthracene Endoperoxides. Recall from the discussion of the thermolysis of endoperoxides,[3] that 9,10-anthracene endoperoxides underwent reaction through a biradical that decomposed to produce both $^1O_2$ and $^3O_2$, whereas thermolysis of 1,4-anthracene endoperoxides produced nearly exclusively $^1O_2$ through a concerted pathway (Figure 7). Since one pathway (path a) involves a biradical and the other (path e) does not, the MIE effect on the formation of $^1O_2$ should depend on magnetic isotopes only for the thermolysis of the 9,10-anthracene endoperoxides. The basis for this conclusion is that if the O atom of the biradical produced in path a is ^{16}O or ^{18}O, since both isotopes have nuclear spin of 0, they cannot influence the ISC of the biradical. However, if the O atom of the biradical produced in path a is ^{17}O then there is a possibility that ISC will be affected and thereby influence the relative yield of $^1O_2$ and $^3O_2$. Thus, ^{17}O will cause ISC to occur more rapidly than ^{16}O or ^{18}O! This means that if the reaction involves a biradical (BR), then there will be a separation of $^{16}O_2$ and $^{18}O_2$ (no effect on ISC) and $^{17}O_2$.

Furthermore, since 1,4-anthracene endoperoxides eliminate $^1O_2$, in a concerted reaction (path e), then there will be no difference in the separation of $^{16}O_2$, $^{17}O_2$ and $^{18}O_2$, since along the reaction path of a concerted reaction, the ^{17}O cannot influence ISC anywhere along the reaction coordinate, since at no point is there an odd electron character on the O atom.

The basis of the separation of $^{16}O_2$, $^{17}O_2$ and $^{18}O_2$ is shown schematically in Figure 25. The magnetic isotope ^{17}O, will influence the competition between the ISC step b and the elimination of $^1O_2$, which does not involve ISC. As endoperoxide molecules approach the BR structure, which crosses surface crossing between a singlet and triplet state, those possessing a magnetic ^{17}O nucleus will have a higher probability of undergoing ISC than molecules possessing a nonmagnetic ^{16}O or ^{18}O nucleus.

8. EXPANDING SUPRAMOLECULAR HOSTS: FROM LIQUIDS TO SOLID POROUS ZEOLITES AS HOSTS

The beauty of an effective working paradigm is that it allows the skilled user to see first what the paradigm allows with a wide scope of possibilities, *especially the subtle chemistry that occurs at the "edge" of the paradigm.* Others, who are not so skilled in paradigm exploitation may view an "edge" that is on the border of the paradigm as the result of something being

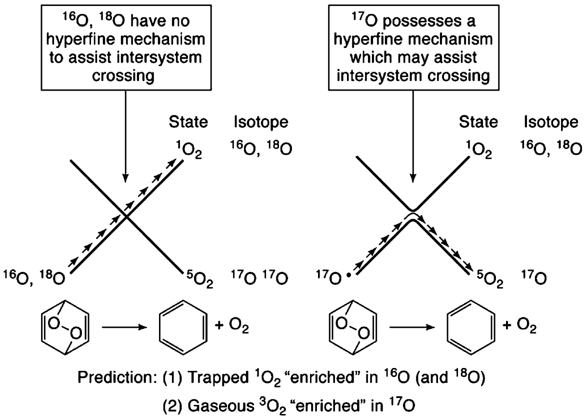


Figure 25. Schematic basis for the separation of $^{17}O_2$ from $^{16,18}O_2$ in the thermolysis of anthracene endoperoxides. In the scenario on the left, there is no mechanism for hyperfine coupled ISC so $^1O_2$ is the only product formed. In the scenario on the right, there is a mechanism (biradical formation as one C−O bond breaks to a much greater extent than the other).

outside of the paradigm (out of the box) and therefore an "extraordinary claim" that needs to be challenged! The skilled paradigm user understands the edge is still within the paradigm so the claim is not at all extraordinary, even thought to outsiders the chemistry may look very risky. For example, Figure 17 uses topological thinking to design a paradigm for supramolecular systems. From the general topological "circle" representing a supramolecular host, the chemist can translate and transform this abstract topological object into chemical objects that can serve as host (micelles, the internal surface of zeolites, the grooves of DNA, etc.). Since each of these vastly different chemical objects arise from a common topological origin, the skillful application of the paradigm for guest@host chemistry allows the chemist to take any of these systems and search for chemical structures that correspond to the topological structures, which will not be obvious by looking at the chemical structures.

As an example of an intellectual topological extension of the concept of supercages, let us consider two chemically appearing very different hosts[29−31] (Figure 17): porous solid zeolites and micelles. The former are porous solids filled with void space with rigid walls and an external surface and enormous internal surface. These spaces may be viewed as "supercages" or hosts for guests in photochemical reactions. A micelle is a single squishy liquid hydrophobic drop in an aqueous environment. We have seen how these hosts are supercages for guest molecules and allow the production of novel and "extraordinary" results for those not familiar with the underlying paradigm of supramolecular organic photochemistry.[31] Thus, the totality of micelles in an aqueous solution are analogous to the host spaces in porous solids. From the overlap of topologies we search for qualitatively common chemical features on systems that have been well established for micelles. For example, The cage effects and magnetic effects on the DBK family in micelles serve as inspiration in the search for other topologically analogous hosts (Figure 17) such as porous solids. Indeed, zeolites are outstanding hosts for observing cage effects and magnetic effects on the photochemistry of the DBK family (section 8A)!

Consider Figure 26, which schematically shows the structure and dimensions of the MFI family of zeolites as hosts and also shows the structure and dimensions of oMeDBK and pMeDBK as guests. The pores leading into the internal surface have a dimension of ~5.5 Å which will allow a molecule, such as benzene as a guest, to slither into the internal surface and fill the internal pore space. The internal pore space consists of "supercages" qualitatively analogous to the supramolecular hosts described above with diameters of ~9 Å. We shall describe briefly some examples of how the guest@zeolite

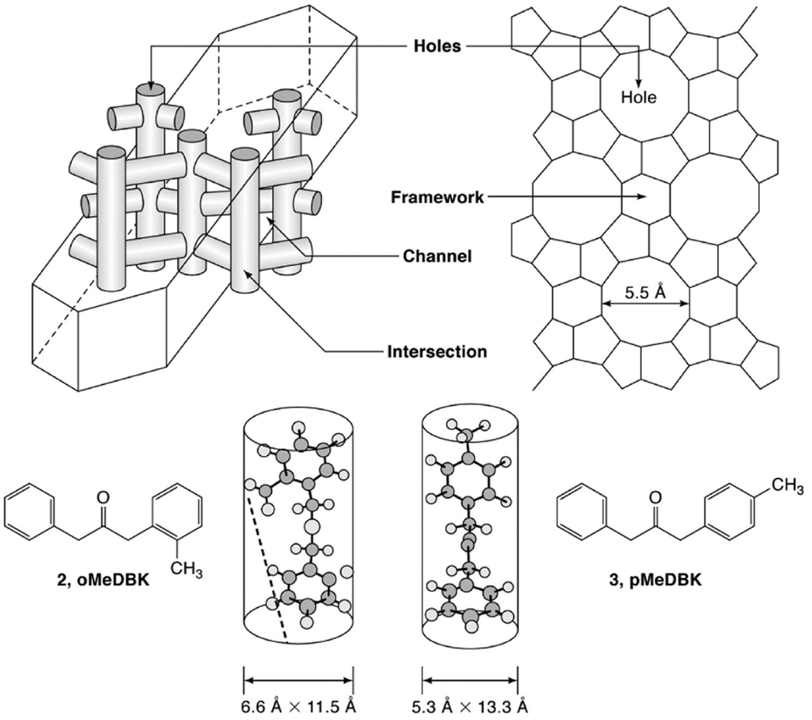


Figure 26. Top: Schematic description of a crystal of a MFI zeolite and the pore system of channels and intersections. Bottom: Dimensions of structures of oMeDBK and pMeDBK are compared to the pore size that allows entry into the internal surface of a MFI zeolite crystal.

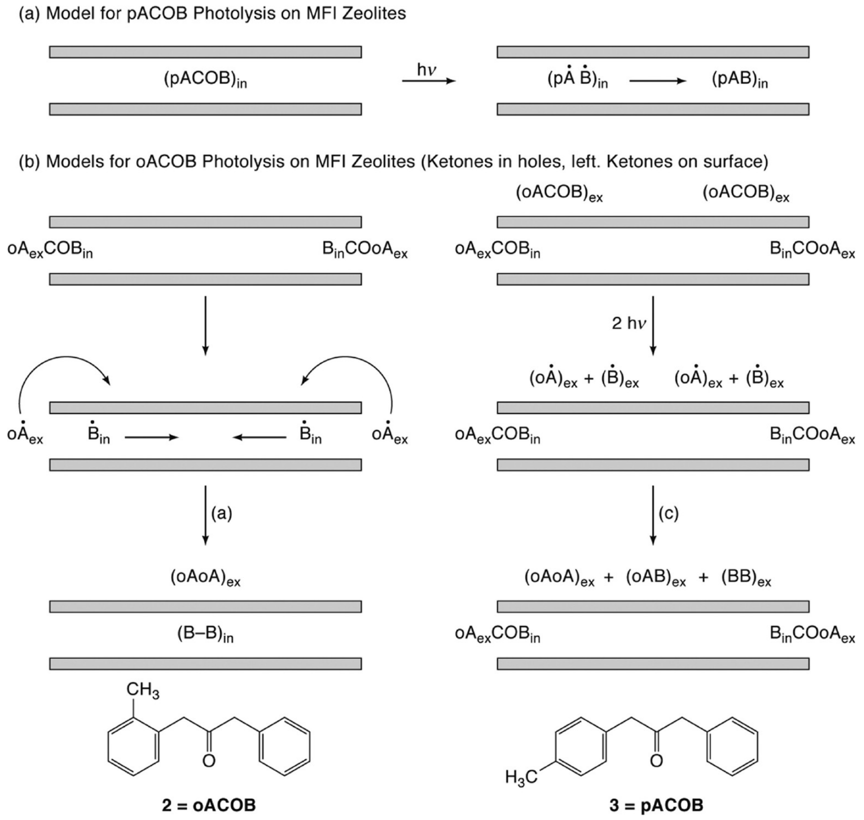


Figure 27. Schematic interpretation for the vastly different results in the cage effect for the photolysis of pACOB@MFI and oACOB@MFI. See text for discussion.

structures can be photolyzed and lead to product distributions that are completely different from those found when photolysis is conducted in solution or other supramolecular hosts. In addition, we will show examples of "supramolecular steric effects" that cause reactive carbon centered radicals to become kinetically persistent.

8A. Exemplars of Zeolite Host Control of Products Produced from Photolysis of DBK and Friends: MFI Zeolites As Hosts. The photolysis of oMeDBK@MFI (oACOB absorbed on a MFI zeolite, eq 9) absorbed on a MFI zeolite yields a profoundly different cage effect from that for the photolysis of pMeDBK@MFI (pACOB absorbed on a MFI zeolite, eq 10).

$$\text{pACOB@MFI} + h\nu \rightarrow \text{AB} \tag{9}$$

$$\text{oACOB@MFI} + h\nu \rightarrow \text{AA} + \text{BB} \tag{10}$$

Photolysis of pMeDBK@zeolite (pACOB, **3**, Figure 26) yields mainly the geminate coupling product AB (eq 6). *However, oACOB,* **2** *(Figure 26) yields mainly AA and BB* (eq 7). This amounts to a "negative cage effect" for the oMeDBK@zeolite complex, i.e., none of the geminate coupling product, AB is formed!

Figure 27 shows a schematic explanation of the results: (1) For pACOB the ketone is bound to the internal surface of the host. Photolysis results in decarbonylation with a geminate pair produced in the host supercage. A strong cage effect results. (2) oACOB has the smaller B moiety partially bound to the pore leading to the internal surface and the larger pA group extended to the external surface. Photolysis results in decarbonylation and the smaller B radical diffusing into the internal surface, where it only encounters other B radicals to form B−B product. The oA radical diffuses on the external surface and only encounters oA radicals to form oA−oA product. oA−B products are minimized because one of the radicals is confined to the external surface and the other to the internal surface.

8B. Exemplars of Zeolite Host Control of Products Resulting from Photolysis of DBK and Friends: FAU Zeolites As Hosts. We consider one more zeolite host (Figure 28), the faujasite (FAU) which has a larger pore opening (~8 Å) on its external surface and a spherical supercage host (~13 Å) in its internal surface. Both oMeDBK

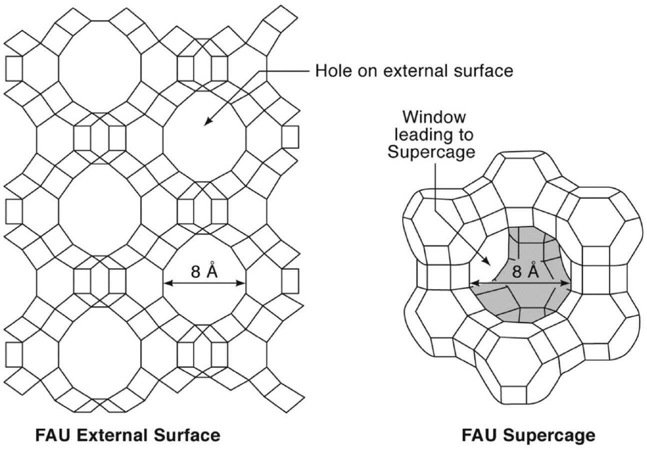


Figure 28. Schematic description of the external and internal surface of the fajausite (FAU) zeolite crystal. The supercages are roughly spherical of the internal surface are approximately 13 Å in diameter.

and pMeDBK can easily move past the pores on the external surface and pass into the supercages of the internal surface.

Understanding the paradigm of the supramolecular model of zeolite host led to the prediction of a photochemical "roach motel" reaction (Figure 29) in which a cyclic ketone, too large to be adsorbed into the internal surface is transformed into a linear chain biradical that can diffuse into the internal surface by photolysis. On adsorption to the supercage, the cyclic biradical undergoes cyclization to a cyclanone whose kinetic diameter (~15 Å) is too large for the species to escape from the pore (~13 Å) allowing exit from the supercage. Thus, like the roach motel bug catcher, "molecules can check in, but they can't check out!"

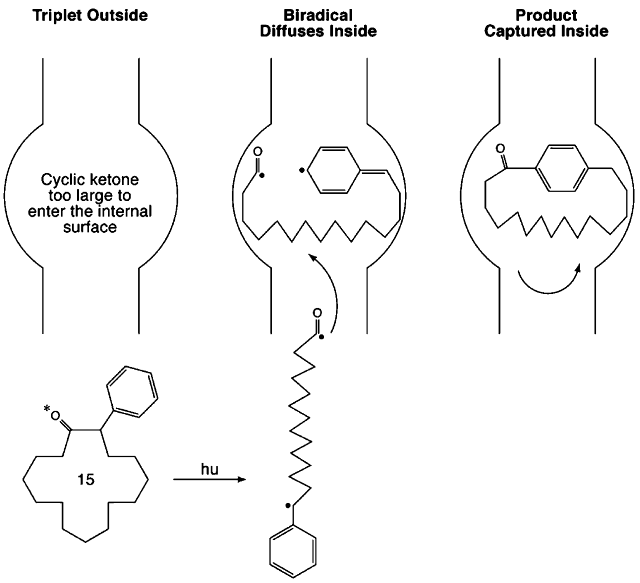


Figure 29. Schematic of the roach motel mechanism for molecules checking into zeolite hosts, but not able to check out!.

8C. Extension of Spin Chemistry to the Interconversion of Nuclear Spins. The critical ISC step interconverting singlet and triplet states is strictly forbidden in the absence of a "spin catalyst".[28] Consider Figure 30 for which a triplet state (↑↑) is converted into a singlet state (↑↓) or vice versa. Imagine that the green down spin (↓) on the left is a spin catalyst that makes the ISC allowed. The spin conservation rule states that the total number of spins up or down must be the same on both sides of the equation. On the left we have one spin down (↓) and two spins up (↑↑) and on the right-hand side of the equation we also have one spin down (↓) and two spins up (↑↑). So the overall spin angular momentum of the system is conserved and ISC is allowed because of the participation of the spin catalyst. *However, the presence of the spin catalyst is a necessary, but not a sufficient condition for effective spin catalysis of ISC.* As we have seen in the case of the magnetic isotope effect, certain other conditions must be met. There must be an interaction with the spin catalyst and it must be of the correct frequency.

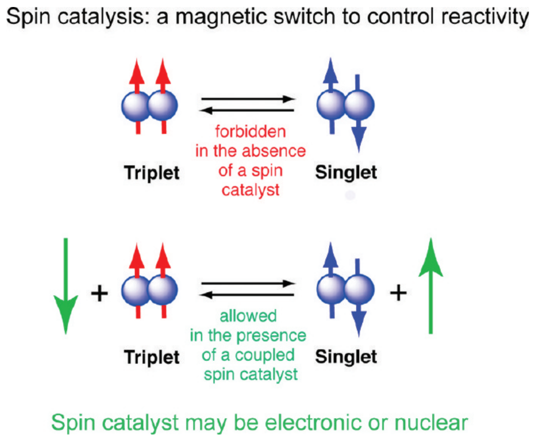


Figure 30. Schematic of spin catalysis of the intersystem crossing (ISC) of triplet and singlet states. The ISC shown at the top is strictly forbidden because spin angular momentum is not conserved (two spins up on the left and one up and one down on the right). The ISC shown at the bottom is catalyzed by the green spin so that there are two spins up on the each side of the equation.

Up to this point, we have been concerned with the spin chemistry determined by ISC of an *electronic triplet* and an *electronic singlet* state. The rules and ideas that we have discussed also apply to the ISC of a *nuclear triplet* and *nuclear singlet* state. Singlet and triplet nuclear spin states? Why not? Spin is spin, just like charge. Two different atoms with a charge of +1 have the same charge! Two nuclear spins can couple to each other to form nuclear singlet and nuclear triplet states. A classic example of this nuclear spin coupling is the H_2 molecule. The two protons of H_2 can couple to form a *nuclear singlet state* (↑↓) *and a nuclear triplet state* (↑↑)! We shall finish the scientific portion of this essay with a discussion of these nuclear spin states and their interconversion in a supramolecular system, $H_2@C_{60}$, and some related fullerenes.

9. SPIN CHEMISTRY GOES NUCLEAR: $H_2@C_{60}$ AND FRIENDS

The nuclear singlet (spins antiparallel) form of H_2 is termed "para-hydrogen", pH_2 (↑↓), and the nuclear triplet form of H_2 (spins parallel) is termed "ortho-hydrogen", oH_2 (↑↑). What are the chemical differences between these two species, what is the rate of their interconversion, and what does this rate depend on? To an organic chemist there is a profound difference between pH_2 (↑↓) and oH_2 (↑↑): *pH_2 (↑↓) is diamagnetic (nuclear spin are antiparallel and cancel) and does not possess a ^{1}H NMR signal, whereas oH_2 (↑↑) is paramagnetic (nuclear spins add to each other) and therefore possesses a ^{1}H NMR signal. This is quite remarkable and predicts that 100% pH_2 does not possess a ^{1}H NMR spectrum!* We shall see that this feature allows for a simple ^{1}H NMR analysis of the composition of pH_2 and oH_2 in any system under analysis. But first we shall review some of the profound quantum mechanical features of the nuclear spin isomers of H_2 which result from the Pauli principle (of all things!).

9A. Pauli Nuclear Spin Isomers of H_2. The rate of interconversion of the nuclear spin isomers pH_2 (↑↓) and oH_2 (↑↑) is exceedingly slow (half-life of years or longer!) and requires a spin catalyst (Figure 30) for the conversion to take place at a measurable rate.

Figure 31 displays the lowest energy rotational levels ($J = 0$ lowest energy level and $J = 1$ first excited rotation level) of H_2. We may well ask why are we considering the rotational states of a molecule? Organic chemists never worry about rotational states because they are all sort of merged into a continuum of states that cannot be separated and just serve as a junk energy sink. However, we shall now see that the rotational states become profoundly important when the Pauli Principle is considered for identical nuclei such as those of H_2.

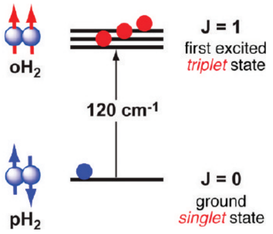


Figure 31. Energy levels for the ground and first excited rotational state of H_2. Note that the ground state ($J = 0$) is a nuclear singlet state and that the first excited rotational state ($J = 1$) is a nuclear triplet state.

Let us apply the Pauli Principle for exchange of two identical particles to the two protons of H_2. the Pauli Principle demands that the total wave function of a molecule must change sign when two identical particles (e.g., two electrons or two protons) are interchanged. As shown schematically in Figure 32, from simple symmetry arguments, since the lowest rotational level of H_2 ($J = 0$) has the symmetry of a s atomic orbital it is therefore symmetrical (**S**): thus, the spin function must be antisymmetrical (**A**) so that the total wave function changes sign upon interchange of the two protons. The singlet wave function is **A**, which means that pH_2 is the lowest rotational state of H_2. The first excited rotational state of H_2 ($J = 1$) has the symmetry of a p atomic orbital and is therefore antisymmetric (**A**). Thus, the nuclear spin wave function must be symmetric (**S**) and is the nuclear triplet state. This remarkable marriage of rotation and nuclear spin for H_2 molecules as the result of the Pauli Principle has a profound implication for its spin chemistry and magnetic spectroscopy of H_2 and of $H_2@C_{60}$.

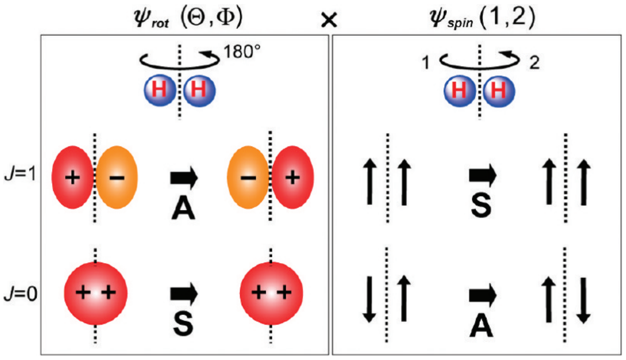


Figure 32. Schematic description of the effect on rotation about the H−H axis on the symmetry (**A**, asymmetric or **S**, symmetric) of the rotational wave function of H_2 (left) and the spin wave function (right) for the two lowest rotational levels ($J = 0$ and 1) of H_2. See text for discussion.

For example, pH_2 and oH_2 are constrained to rotate in a certain way depending on their spin because of the Pauli Principle, so that they can be termed "Pauli nuclear spin isomers". Because of the difficulties of interconverting both the spin and rotation of pH_2 and oH_2 the ISC of these two Pauli spin isomers is exceedingly slow and requires a spin catalyst (Figure 30) to occur at a measurable rate.

9B. The $H_2@C_{60}$ Complex: Can the H_2 Molecule Inside C_{60} Communicate with the Outside World? The spin catalysis of the interconversion of oH_2 and pH_2 has been studied[32] since the late 1920s right after the prediction of the existence of the two Pauli nuclear spin isomers of H_2. We decided to study the spin catalysis of the interconversion of the Pauli spin isomers of H_2 in a supramolecular system: *$H_2@C_{60}$*. This study was made possible by a splendid collaboration with Professors K. Komatsu and Y. Murata of the University of Kyoto. We were interested in exploring and understanding, in general, the mechanisms by which the H_2 inside C_{60} communicates with the outside world (Figure 33).

Figure 33. Can H_2 inside C_{60} communicate with the outside world?

9C. Synthesis of $H_2@C_{60}$ and $HD@C_{60}$. But where does $H_2@C_{60}$ come from? Figure 34 outlines the brilliant synthesis of $H_2@C_{60}$ of Komatsu and Murata.[33] The synthetic approach is termed "molecular surgery" that employs the following steps: (1) creating a hole on the C_{60} surface through cage opening reactions; (2) increasing the size of the hole until it is large enough to allow insertion of H_2 at high pressure and temperature and (3) surgically closing the hole to regenerate the intact C_{60} cage as a host with the H_2 molecule incarcerated as a guest. $HD@C_{60}$ (and $D_2@C_{60}$) can also be synthesized by an analogous procedure in which HD (or D_2) is substituted for H_2 in the insertion step.

9D. Running a Nuclear Spin Reaction in a Buckyball: The Holy Grail of an On−Off Switch of Massive Nuclear Polarization. Since $pH_2@C_{60}$ and $oH_2@C_{60}$ are two completely different substances (different substances that are composed of only one element are termed "allotropes", i.e., allotrope of carbon: graphite, diamond, C_{60}), their interconversion represents a true chemical reaction. By extension, the interconversion of $pH_2@C_{60}$ and $oH_2@C_{60}$ represents an example of a "nuclear spin reaction" within a buckyball. Figure 35 shows[32] how the % oH_2, at equilibrium, depends on temperature in the range 300K to 0 K: the ratio of $oH_2@C_{60}$ and $pH_2@C_{60}$ varies from ~75% $oH_2@C_{60}$ to 100% $pH_2@C_{60}$. At 77 K the boiling point of liquid nitrogen, the ratio of $pH_2@C_{60}$ and $oH_2@C_{60}$ is ~50/50.

We developed an efficient method[34,35] for the interconversion of the supramolecular allotropes $pH_2@C_{60}$ and $oH_2@C_{60}$ at 77 K. The method involves first, the dispersion of $pH_2@C_{60}$ and $oH_2@C_{60}$ on the zeolite NaY. The dispersion is necessary to allow each molecule of $pH_2@C_{60}$ and $oH_2@C_{60}$ to come in contact with the spin catalyst, triplet liquid oxygen, $^3O_2$. Under these conditions, the equilibrium mixture of 50/50 $pH_2@C_{60}$ and $oH_2@C_{60}$ is rapidly achieved. Rapid removal of the liquid $^3O_2$ spin catalyst leaves behind a stable equilibrium mixture of 50/50 $pH_2@C_{60}$ and $oH_2@C_{60}$ that can be extracted and analyzed.

^1H NMR analysis (Figure 35 insert and Figure 36) was selected to monitor the interconversion of $oH_2@C_{60}$ and $pH_2@C_{60}$. The NMR measurement takes advantage of the fact that pH_2 is "NMR silent" and oH_2 is "NMR active", so the NMR signal arises exclusively from oH_2 (which possesses a net spin of

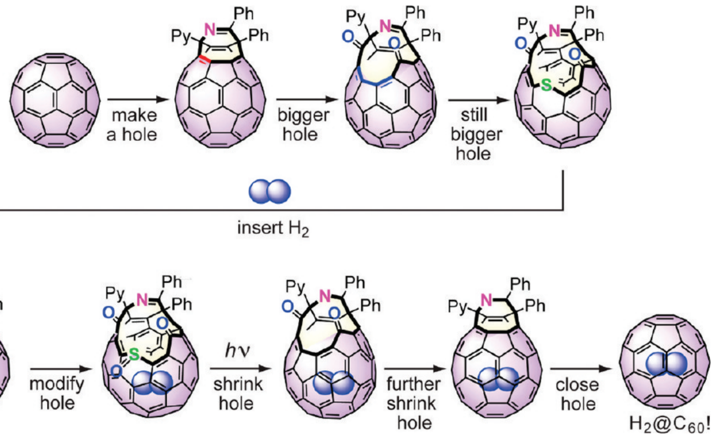


Figure 34. Molecular surgery (opening, guest insertion, and closing of the fullerene host) synthesis of $H_2@C_{60}$.

1 and therefore produces an NMR signal). The accuracy of the NMR was improved markedly by designing an internal standard for ^1H NMR analysis that would have a chemical shift close to that of $H_2@C_{60}$ and yet not run the risk of being converted to a new material at 77 K in the presence of a paramagnetic catalyst. Since H and D are *distinguishable* particles, HD is not required to follow the Pauli Principle coupling nuclear spins and rotational levels. The ^1H NMR of $HD@C_{60}$ is a triplet due to spin−spin coupling with D, which has a spin of 1.

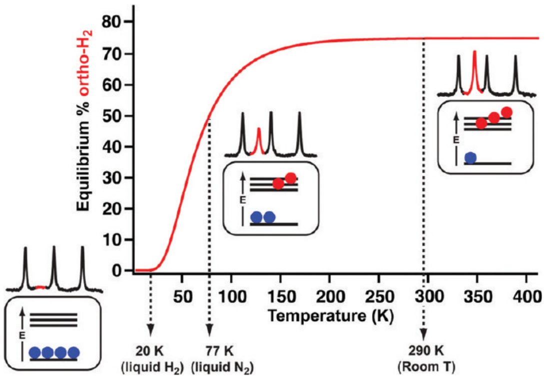


Figure 35. Temperature dependence of the % oH_2 in equilibrium with pH_2 as a function of temperature. See text for a discussion of the inserted ^1H NMR spectra.

As shown in an experimental example (Figure 36) in the ^1H NMR of $HD@C_{60}$ (black curves) each of the three ^1H NMR signals is resolved from that of $H_2@C_{60}$ (red curves). Since HD (H and D are not identical particles) is not subject to the Pauli restrictions of H_2 and the ^1H NMR intensity of HD will be proportional to the number of $HD@C_{60}$ molecules at all temperatures, then the ^1H intensity of *the signal from* $H_2@C_{60}$ *will be proportional to the number of* $oH_2@C_{60}$ *only*. Furthermore, it would be expected that the physical properties of $H_2@C_{60}$ and $HD@C_{60}$ are sufficiently similar so that the ratio of the two species should not change during the absorption/extraction on/from the zeolite or the enrichment process. Thus, if the experiment works as designed, at the time of NMR analysis, the signal of $HD@C_{60}$ should be exactly the same before and after the treatment of the sample with the paramagnetic catalyst, $^3O_2$ at 77 K: however, the $H_2@C_{60}$ should show a significant decrease in the ^1H NMR signal due to oH_2 as the result of the treatment. Comparison of the NMR intensities for $H_2@C_{60}$ and $HD@C_{60}$ at various times will therefore be a measure of the change in the percentage of $oH_2@C_{60}$ in the sample. In fact, all of these desirable features are achieved by the system, so we can determine the % pH_2 in any mixture of pH_2 and oH_2.

9E. Beyond $H_2@C_{60}$. Spin Catalytic Switches for Pauli Nuclear Spin Isomer Interconversion.

We have sought to develop spin catalysts for the reversible allotropic interconversion of $oH_2@C_{60}$ and $pH_2@C_{60}$ that can be turned on and off by the investigator. The strategy we have employed is to use the

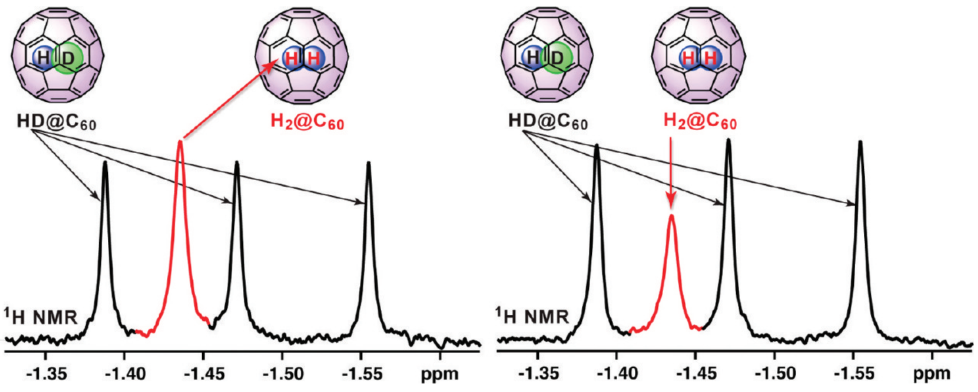


Figure 36. Initial ^1H NMR of a mixture of $oH_2@C_{60}$ and $HD@C_{60}$. The triplet black signals are from HD and the singlet red signal is from H_2. Left: before conversion with $^3O_2$ at 77 K. Right: after conversion with $^3O_2$ at 77 K. The relative signal from $oH_2@C_{60}$ has substantially decreased. See text for discussion.

C_{60} cage as a framework taking advantage of (1) reversible formation of the paramagnetic triplet state of C_{60}; (2) reversible electron transfer to the C_{60} cage to form the radical anion; and (3) synthetic methods that allow us to covalently attach spin catalysts such as nitroxides to the cage that can reversibly be interconverted to diamagnetic analogues. These possibilities are shown in Figure 37.

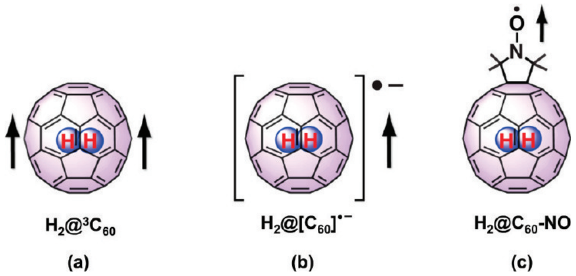


Figure 37. Possibilities for making the fullerene cage of C_{60} a spin catalyst: (a) formation of the paramagnetic triplet state of C_{60}; (b) formation of a radical cation of C_{60}; (c) covalent attachment of a stable radical such as a nitroxide to the fullerene cage.

Figure 38 shows schematically the specific situation for the fullerene triplet spin catalyst.[36] The idea is that the paramagnetism required for spin catalysis is only on when the C_{60} is in its triplet state. Since other fullerenes such as C_{70} have different lifetimes than C_{60} the extent of conversion may be controlled by photophysical parameter for different endofullerenes.

9F. Nitroxides as Switchable Spin Catalysts. A spin catalyst such as a nitroxide may be covalently attached to the fullerene cage of $H_2@C_{60}$. The catalyst is constantly acting on the nuclear spins of the incarcerated H_2 and will drive the system to equilibrium which will depend on temperature. At room temperature, nitroxides serve as paramagnetic spin catalysts for the backconversion of $pH_2@C_{60}$ to $oH_2@C_{60}$. We reasoned[35] that if a derivative of $H_2@C_{60}$ could be rapidly switched from a diamagnetic nitroxide precursor to a paramagnetic nitroxide, a "magnetic switch" for forward conversion ($pH_2@C_{60}$ to $oH_2@C_{60}$) at 77 K and back conversion ($pH_2@C_{60} \rightarrow oH_2@C_{60}$) at room temperature would be available. For the design of the spin catalyst switch we used the strategy of the convenient conversion of paramagnetic nitroxide to diamagnetic hydroxy amine (Figure 39) by phenylhydrazine and the reverse oxidation of hydroxamine to nitroxide by $Cu(OAC)_2$.

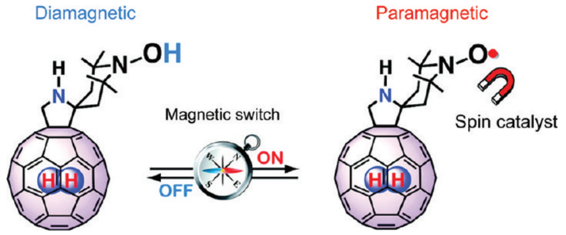


Figure 39. Magnetic switch for interconverting the nuclear spin isomers of $H_2@C_{60}$. A hydroxy amine (left) and nitroxide (right) are reversibly interconverted chemically.

These results showed that the rate of nuclear spin interconversion of encapsulated H_2 can be markedly increased by attaching the paramagnetic catalyst to the cage. Furthermore, comparison for a selected system of the catalyzed lifetime of (<90 s) with the uncatalyzed lifetime of <7.5 days (6.5×10^5 s) demonstrates that the rate of back conversion may be varied by <4 orders of magnitude by turning the catalyst on and off.

9G. Distance Dependence of Spin Catalysis. We have synthesized derivatives of $H_2@C_{60}$ with covalently attached nitroxides as spin catalysts for the conversion of $oH_2 \rightarrow pH_2$ inside the fullerene (Figure 40). A spacer separates the nitroxide from the fullerene cage and the incarcerated H_2 Figure 41. We have measured the rate of conversion of $oH_2 \rightarrow pH_2$ inside the fullerene and the conversion rates are in good agreement with theory.[37]

Figure 40. Schematic of the design of nitroxide spacers to detemine the spin dependence of the nitroxide spin catalysis of the interconversion of the Pauli spin isomers of $H_2@C_{60}$.

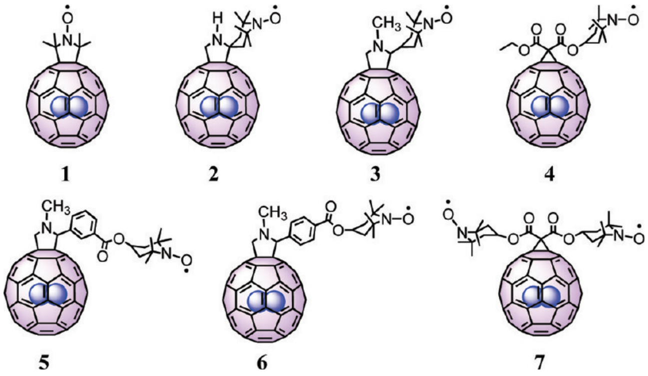


Figure 41. Structures of some nitroxide substituted $H_2@C_{60}$ derivatives.

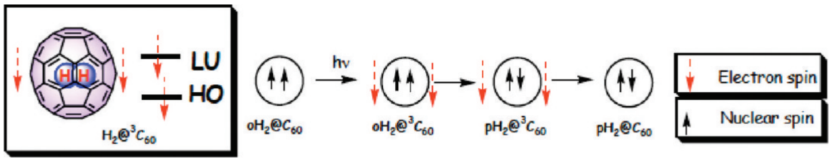


Figure 38. Triplet switch for the Pauli nuclear spin isomers of $H_2@C_{60}$. Schematic of the role of a spin catalyst (electron spin represented by a dotted red arrow) of the nuclear spin conversion of $oH_2@C_{60}$ to $pH_2@C_{60}$ (nuclear spins represented by solid arrows, circle representing the fullerene cage).

10. H_2O AS A HOST IN OPEN AND CLOSED FULLERENES

Striking as the fact that H_2 exists as two distinct Pauli nuclear isomers that are two completely separable compounds with different ^1H NMR spectra and other properties, *Pauli spin isomers exist for any system for which the symmetry is such that a rotation about a symmetry axis regenerates the same structure.* Thus,[38] *H_2O also exists as singlet (pH_2O) and triplet (oH_2O) Pauli nuclear spin isomers. pH_2O does not have an NMR spectrum, whereas oH_2O has an NMR singlet where H_2O is normally found* (Figure 42*)*. There is evidence in the literature that these two Pauli spin isomers can be separated in the vapor phase.[39] We are collaborating with Professor Murata of Kyoto University to investigate $H_2O@C_{60}$ to see if we can interconvert $oH_2O@_{60}$ into $pH_2O@C_{60}$. In this case we are anticipating that the complex structure of H_2O compared to H_2 may allow a "self catalysis" so that simply lowering the temperature to 4 K will provide the conditions for conversion.

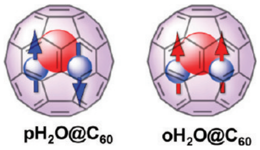


Figure 42. Pauli spin isomers of $pH_2O@C_{60}$ and $oH_2O@C_{60}$.

11. INTELLECTUAL SURVIVAL SKILLS. THE ROLE OF PARADIGMS, STRUCTURE, GEOMETRY, AND DYNAMICS IN DRIVING PROGRESS IN CHEMISTRY

Looking back over the past 50 years, I've discovered that studying paradigms, structure, and geometry have been very useful in understanding how to structure my approach to chemistry. I consider these "intellectual survival skills" that have been developed through evolution by the brain to assist in successful interactions with our environments. I'll describe in the next section the way I view chemical paradigms as both a driver and inhibitor of extraordinary chemistry. I'll also describe how intellectual processing of structure through geometry can be broken down into two essential forms, topological geometry (connections only between atoms) and Euclidian geometry (the orientation of atoms in space). Topological and Euclidian geometry, in my view, provide a fundamental basis for all of our ideas in structural chemistry.[40] Then beyond geometry, we add *dynamics (the motions of atoms in space that change bond angles and distances)*. The beauty of this approach is that it is completely general and applies not only to all areas of chemistry, but all areas of science.

11A. philosophy of Science and Scientific Paradigms. What Are Paradigms, Where Do They Come from, and How Do They Control Progress in Science and Chemistry? Throughout the history of science, and chemistry in particular, making a distinction between *revolutionary (extraordinary) science* and *pathological (nonsense) science* has never been completely clear.[41] As part of a self-analysis of my own intellectual development, I've wondered, though the years, if there was a cognitive process that I could develop that would allow me to distinguish clearly extraordinary science from nonsense and pathological science. Both extremes of the scientific intellectual spectrum from revolutionary science to pathological science can be characterized by some common traits such as the ability of a scientist or community of scientists to "think outside the *intellectual* box." But what is the intellectual box made of and what does thinking within the box mean? After years of exploring the philosophy of science I came up with some unifying concepts, namely *paradigms, structure, geometry and intellectual survival skills,* that made a lot of sense to me because they were completely consistent with my actual experience in dealing with chemists in all fields. These concepts also explained when my research was considered to be extraordinary and warned me when I should start thinking that it might be pathological!

A concept that caught my eye early on was put forth by Thomas Kuhn in his influential book[42] "The Structure of Scientific Revolutions": the concept was *scientific paradigms!* According to Kuhn, scientists (from this point on, let us confine the scientists under consideration to be us, chemists!) *share a set of governing beliefs and assumptions, or paradigms, that determine the way chemists intellectualize a research problem and cognitively analyze the problem.* In short, the set of chemical paradigms that form the intellectual and cognitive basis for doing research (or teaching, learning or any other intellectual processes) may be broadly defined as *"the characteristic set of governing beliefs and/or preconceptions (theoretical, instrumental, procedural and metaphysical) that is broadly shared and employed in every day research by a community of (organic, physical, theoretical, bio) chemists."* Thus, the ruling paradigms of chemistry determine the theory, the instruments, the kind of experiments, the interpretation of experiments, the class of arguments, etc., that a chemist uses in his/her everyday "normal science". By implicitly agreeing on the governing paradigms, tremendous time and effort is saved by avoiding arguments over fundamentals such as: *do molecules really exist? can molecules, if they really do exist, be described adequately by geometric structures? are there relationships between spectroscopy and these putative molecular structures? are there correlations between molecular structure and measurable properties? etc.* The paradigm considers these questions to be already answered completely and authoritatively. In this way chemists can make incredible intellectual and scientific penetration into the profound issues and challenges of the day by moving forward in their research without distractions. Paraphrasing Kuhn "if you are out of the paradigm, you are out of the intellectual box and you're wasting your time in your research."

Kuhn describes advances in research in *mature* sciences (e.g., physics, chemistry, or biology) as being performed in two phases. In one phase of a mature research, termed *normal science*, a community of scientists operates under the influence of a governing constellation of knowledge, theories, techniques, methods, and attitudes that are the community's paradigm. The latter is a *scientific constitution* that this community has agreed to obey as its highest authority for performing *legitimate* research. For example, chemists work under a paradigm assuming that all physical and chemical phenomena can be explained by the ideas implied by the existence of atoms and molecules, along with the implied substructure (nuclei and electrons) and implied supramolecular structure of molecules. *The acceptance of this paradigm defines the chemical community.* Indeed, the governing paradigm of the community defines what legitimate entities exist and which legitimate methods can be used for their investigation. Normal everyday research in chemistry is the investigation, within the constitution of the paradigm, of puzzles created by researchers to articulate and expand the chemical paradigm.

According to Kuhn, a *paradigm shift* is a quantum jump occurring through an intricate intellectual and social process required for the community to determine whether an extraordinary claim is revolutionary (perhaps worthy of wide acceptance and adoption perhaps recognition by a Nobel Prize) or if the claim is pathological (perhaps worthy of an Ig-Nobel Prize and the dust bin of scientific history!). Figure 43 shows schematically the procedural flow diagram of normal science and the branching points of extraordinary claims.

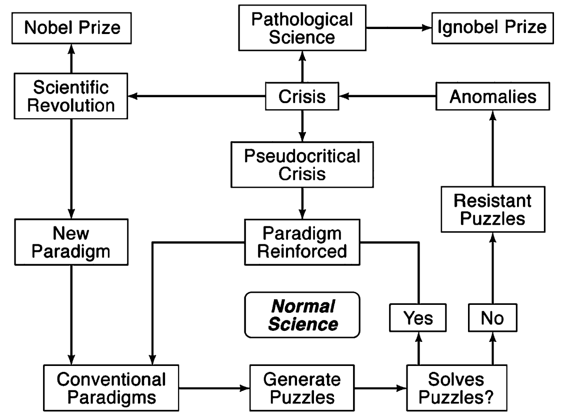


Figure 43. Schematic of Kuhn's theory of the role of "normal science" and "scientific revolutions" (paradigm shifts) in the development of science.

"Normal science" (Figure 43), what chemists do in their every day research, consists of generating "puzzles" based on expectations from the current ruling paradigms, solving the puzzles (as in students' Ph.D. research, for example), and thereby confirming and reinforcing the governing paradigm. However, from time to time, some puzzles are "anomalous" and become resistant to solution and, if sufficiently resistant to even the best practitioners of the community, may be considered as paradigm threatening anomalies by the community. Sometimes, these "anomalous results", unexplainable within a field's governing paradigm and important enough to cause true intellectual alarm within the community, can throw the field into crisis—an unpredictable state analogous to a catastrophe point in topological mathematics. Up to this point it is not at all clear whether the resistant puzzle and anomaly will eventuate into revolutionary (scientific revolution) science or into pathological science. In this preparadigm phase, there will be many irresolvable arguments about experiments, interpretations, etc., in the community.

Resolution of the crisis in Figure 43 can typically take one of three forms: (1) The revolutionary idea may be revealed as more apparent than real (it was in an improper interpretation of the paradigm, but now correctly interpreted, all is well, for example), and this "pseudocritical" state resolves to reinforce the original paradigm in the same way as ordinary science, although with more force because of the excursion; (2) the idea may foster a true Kuhnian revolution, and *a new paradigm shift occurs*; or (3) the idea may prove pathological, in which case only zealots continue to pursue it, and the paradigm structure is untouched.

As an example of how strongly new paradigms are resisted by the main line community, consider the following quote by Kolbe,[43] a great German chemist of the 1800s concerning a proposal for a paradigm that we absolutely take for granted: that molecules can be represented by atoms in 3D space. This intellectual concept was considered a pathological paradigm shift at the time it was presented and was passionately resisted and attacked by many chemists. Here's what Kolbe had to say about the idea of even discussing the positions of atoms in space:[43]

> *"It is typical of the present time, when there is so little criticism and so much hatred of criticism, that two practically unknown chemists, one from a veterinary college and the other from an agricultural institute, pass judgment on the loftiest problems of chemistry, those which will probably never be solved, particularly the question of the position of atoms in space, and they undertake to answer these problems with an impudence and assurance that absolutely astonish the true scientist. This idea is now brought forth again, out of the store room harboring the errors of the human mind; by pseudoscientists who try to smuggle it, like a fashionably dressed and freshly rouged prostitute, into good society, where it does not belong."*

And who were these two practically unknown chemists who proposed this pathological (in Kolbe's view) chemistry? None other than Le Bel and van't Hoff. Interestingly, van't Hoff was awarded the first Nobel Prize in Chemistry! Not for stereochemistry, of course, since the atoms in space paradigm was in its infancy in a preparadigm stage. Van't Hoff received the first Nobel Prize "in recognition of the extraordinary services he has rendered by the discovery of the laws of chemical dynamics and osmotic pressure in solutions", a field that he helped develop into a mature and governing paradigm during the late 1800s.

Consider the comment on the acceptance of new paradigms by Max Planck,[44] who caused perhaps the greatest paradigm shift of the last 100 years, quantum theory: "New scientific truth usually becomes accepted, not because opponents become convinced, but because opponents gradually *die,* and the rising generations are familiar with new truths from the onset."

Throughout the history of chemistry, such vitriolic attacks by a chemist on a colleague's claim of a new paradigm are common. However, they are rarely known to students. I've found that students really enjoy this "human" aspect of our science, and from time to time we go over the development of paradigms in fields of interest to show real examples of how paradigms are developed and the preparadigm phase progresses into a mature, governing paradigm or falls into the dustbin of pathological chemistry.

11B. Advice for the Aspiring Scientific Revolutionary. Clearly, scientific progress would be impossible if researchers always played it safely within a governing paradigm, ignoring or discarding unexpected or disturbing results or shying away from daring hypotheses that do not appear to be allowed by the governing paradigm. Some of today's most profound discoveries and most promising research subjects—manned space flight, wave-particle duality, C_{60} (buckminsterfullerene or "buckyball") molecules, high- temperature superconductivity—once struck mainstream scientific opinion as sheer pathological fantasy and unworthy of support or encouragement. There are some practical steps that a working researcher can take to reduce chances that today's "eureka!" will be tomorrow's Ig Nobel Prize:

(1) At the start of a research project, always generate and test several *possible and plausible* hypotheses to explain a result. Never get fixated on one pet hypothesis. Remember Chamberlin's warning: "The moment a

scientist has offered an original explanation for a phenomenon which seems satisfactory, at that moment affection for the intellectual child springs into existence. As the explanation grows into a definite theory parental affection cluster about the intellectual offspring. From this point there is then imminent danger of an unconscious selection and of a magnifying of phenomena that fall into harmony with the theory and support it, and an unconscious neglect of phenomena that fail of coincidence. Multiple hypotheses distribute the effort and divide the intellectual affections. The investigator becomes parent to a family of offspring hypotheses and by his parental relations to all is morally forbidden to fasten his/her affections unduly on any single one."

(2) Let the best available governing paradigm be your guide in interpreting your results.

(3) Be conservative about the concepts of statistical significance and margin of error, especially when analyzing phenomena on the threshold between signal and noise and particularly when the results appear to be extraordinary (chances are they are not!).

(4) If you believe that you have discovered a truly extraordinary phenomenon that represents a paradigm shift, reproduce, reproduce, reproduce. It is good practice to ask a reliable colleague to reproduce the result. If you can not reproduce, *never publish!*

(5) When possible, try to capture the phenomena of interest by two or more truly independent methods. If the results are consistent by two or more independent methods, you have paid "due diligence" and earned the right to claim that your observation is real. In this case, the community is likely to be forgiving because you gave it an honest shot.

(6) Discuss surprising (extraordinary) findings openly with peers (through both formal and informal channels, inside and outside one's own specialty) and make constructive use of the critiques that arise.

(7) If further studies convincingly falsify your hypothesis or any of your published results, and you are convinced also that you have made an error or misinterpretation, however innocently, acknowledge it. Blind leads and honest errors are nothing to be ashamed of; they're inseparable from the progress of science. After any number of pathological investigations, there's eventually one like quantum mechanics, which explained results that Newtonian theory could not explain, and revolutionized physics. The same communal corrective processes that falsified one theory verified the other; that is how science operates, and why it works so well.

It is important to understand that governing paradigms provide chemists with valuable intellectual tools to avoid pitfalls and to move rapidly in scientific activities. We need to remember that ruling paradigms are conservative and tend to *discourage* revolutionary science. Effectively, a paradigm serves as a barrier to caution the community to be very careful when presented with an extraordinary claim (statistically most of them will be modified or shown to be incorrect!). A good scientist often feels the essential tension between paradigmatic and pathological science, between the ordinary, normal, expected result and the extraordinary, amazing result. I hope that the readers of this perspective will find above discussion of paradigms to be a useful guide to in their own research to recognize and distinguish between science extraordinary and science pathological.

11C. Geometry and the Development of Paradigms of Molecular Structure of Organic Molecules. Consider the following process of cognitive and intellectual evolution from simple every day observations to the creation of wisdom from observations: observations → data → information → knowledge → intelligence → wisdom.

In a somewhat whimsical view, this cognitive evolution may be correlated with an increasing level of *cognitive survival skills.* I use the term "survival" deliberately here. I wish to evoke an image and analogy of the Darwinian notion of how organisms have struggled to adapt to their physical environment and develop biologically relevant survival skills. From the outset it seemed to me that the exhilaration that I experienced when learning a new subject or teaching students to learn or making a new discovery in the laboratory was akin to the satisfaction one feels when successfully developing a survival skill as described by Darwin's theory of natural selection. I therefore sought to explore the possible cognitive connections between "intellectual natural selection" the way chemists proceed from observations to wisdom.

Progressing from observations to wisdom implies an increasing level of intellectual development and cognitive structure. Observations refer to how our senses describe the world around us. Science begins with giving these observations some structure, which we can call "data". Data transform observations into a structure that is understood within the governing paradigms by the community of scientists in the field. Data are then transformed by the paradigm into information such as molecular structure. Molecular structure provides the doorway to knowledge. For example, though the paradigms of physical organic chemistry, molecular structures provide predictions of the physical and chemical properties associated with molecular structures. Knowledge is in itself not sufficient to "operate" successfully on the environment about us. Text books contain lots of chemical knowledge that students must deal with. To deal with knowledge, students must learn about the context in which molecular structures and properties are embedded. Finally, by learning context and gaining experience which provides *judgment within a context*, we can hope to use the intelligence to be successful in dealing with our environments and we and our students have achieved *wisdom*!

Thus, an "evolutionary" explanation of cognitive development shown above is that structure allows an individual to adapt to any new environments by allowing an understanding of experiences and by providing an increase in the individual's fitness to survive and to become more attractive as a possessor of valuable *intellectual genetic* material. The basic idea is simple, even naïve: nature, through evolution, makes us feel good when we develop any physical skills that allow us to act on our environment. By analogy, we feel an exhilaration when we develop new intellectual skills that allow us to interact more effectively with our environment. An organism is comfortable or "at cognitive equilibrium" in an environment to which it is adapted, but survival pressure serves as a driving force for the organism to feel uncomfortable or in cognitive disequilibrium in a new environment. This mechanism provides a motivation to develop new survival skills in order to survive in the new environment. Our model suggests that organisms are driven to adapt their knowledge in order to obtain a balance between the expectation produced by their intellectual processing and the

Table 2. Levels of Information Content Organized by Structural Representation, in Both Geometric and Chemical Senses

	geometry	chemistry
composition (topological)	number and kinds of mathematical elements in a set	number and kinds of atoms in a molecule
constitution (topological)	connectivity or neighborhood relationships of the elements in a set	connectivity of the atoms of a molecule
configuration (Euclidean)	representation of the elements that are neighbors of a given element in a set by a three-dimensional figure	3D representation of the atoms about a central atom
conformation (Euclidean)	representation of all of the elements of a set by a 3D figure	representation of a particular shape of a molecule
ceometric dynamics (Euclidean)	motion is not a fundamental component of geometrical systems	representation of the rates of the change in molecular shape (bond lengths and bond angles)

results of their experiences in acting on their environment. I use the term *intellectual closure* to describe the goal of the knowledge construction process that produces cognitive equilibrium. With closure comes the comfortable and gratifying feeling that one has adapted to the environment.

Chemists have used the ideas of geometry to develop structure as a powerful intellectual tool that has allowed our science to make remarkable progress over the last 150 years. Table 2 schematically displays the level of structural information that is commonly used in organic chemistry and how this structure is related to geometry. We start with molecular composition (number and kinds of atoms), and move to molecular constitution (on how the atoms are connected to one another). This is the highest level of *structural topological* information that chemists use to describe molecular structures. This is exactly the level implied by Lewis structures. It is important to realize that Lewis structures are topological objects and do not imply any stereochemistry! Topological objects do not have distance relationships or angle relationships between the elements (atoms) of the set. So we can now see that Kolbe's paradigm of structure was topological and to speak of atoms being oriented in space was pathological from the geometry point of view.

Topological structures can be represented in Euclidean space. When embedded in a space, we have the possibility of associating lengths and angles among the atoms of the molecule. Embedding a topological object in 3D space implies a *configuration*, a 3D representation of atoms about a single central atom. Finally, when we consider the entire molecule and a specific orientation of all of the atoms relative to one another, we are at the level of *conformation,* the overall shape of a molecule.

Composition, constitution, configuration and conformation are all geometric concepts that chemists have used to describe molecular structure. Chemist have added a new idea, that of motion of the atoms of a molecule that change bond lengths and bond angles. The motion is not a geometric idea, but strictly a very important chemical idea that is the basis of chemical dynamics.

Let us consider an example of toplogical thinking and extension addition of topological complexity in chemical terms. Let us start with the idea of a free electron and a free nucleus. Both are technically chemical objects, but not of great scope. If we "connect" or "bond" the electron to the nucleus, we have a "superelectron", *an atom behaves as a unit that has chemical value.* If we add more charge to the nucleus and more electrons, we extend the idea on connectivity of the group of electrons to the nucleus and to each other (electron correlation). If we now take these atoms (superelectrons) and connect them (chemically we assume *covalent connectivity*), we are at the level of a "superatom", *a molecule* which behaves as a unit and is the topological structure that chemists have dealt with so comfortably for over 100 years. Now if we go to the next level of connectivity (chemically we assume *noncovalent connectivity*), we are at the level of a "supermolecule," a group of molecules that behave as a unit. We then can imagine the next level of complexity involves aggregates of supermolecules, etc. to eventuate in very complicated chemical objects such as polymers and biomolecules.

12. THEORY OF COGNITIVE AND INTELLECTUAL DEVELOPMENT: PIAGET'S PARADIGM FOR TEACHING AND LEARNING

Since paradigms appear to me to be intimately involved in determining cognitive processes, I decided to explore the intellectual basis of why we accept them so readily and allow them to govern the way we do our science. My daughter, Cindy, in taking a course in the intellectual development of children, introduced me to the research of Piaget,[45] a psychologist who produced a theory that resonated with my recollection of my own intellectual development. Piaget's ideas are very pertinent to chemical education since they probe deeply into the growth and intellectual development of logical thought in adolescents and young adults. So I took a closer look at what Piaget had to say and see if it could be connected to my ideas on paradigms.

12A. Piaget and Chemical Education. A Theory of Knowledge Construction in Adolescents and Young Adults. Piaget proposed that learning processes in adolescents and young adults involve *constructing knowledge* within an intellectual structure that he termed *schema*, which seemed to me to be cogitatively analogous to governing paradigms. When learning is consistent with the schema, the individual feels a level of comfort because the intellectual system is in a state of equilibrium with his/her environment (as a chemist is comfortable with the governing paradigm when it works well in everyday research). Piaget used the term *assimilation* to describe knowledge that is accumulated, and that is consistent with the preexisting schema. When new information is consistent with consistent with what we know we reinforce the feeling of mental equilibrium during the assimilation process (see Figure 43 for reinforcing the governing paradigm). However, *when new ideas that are inconsistent with the governing schema are proposed,* they may cause cognitive disequilibria because they cannot be assimilated into the intellectual structures of the schema (see Figure 43 for the crisis in the governing paradigm). This uncomfortable feeling creates am essential intellectual and cognitive tension that is a driving force for resolution and closure (the good old comfortable feeling that we understand what is going on). When schemata are modified in an acceptable way, cognitive equilibrium returns. Piaget termed the process of changing schemata in reaction to a changing environment *accommodation* (see Figure 43 for reinforcing the governing paradigm). Thus, the learning process consisted of (1) assimilation of knowledge that is consistent with the individual's existing schema and (2) accommodation from time to time of new knowledge that is incompatible with previously existing schemata. Each new intellectual equilibrium brings the mind to a higher, more adaptive level and to a higher level of learning. If i replace Piaget's word *schema* with Kuhn's word *paradigm* I found an excellent "mapping" of one on to the other.

12B. Correlation between Piaget's Theory of Knowledge Creation and Kuhn's Paradigms. Applications to Chemical Education. In fact, Figure 44 shows the schematic correspondence between Kuhn's paradigms and normal and pathological science and Piaget's theory of knowledge creation in young adults (Figure 43). The two models are essentially congruent!

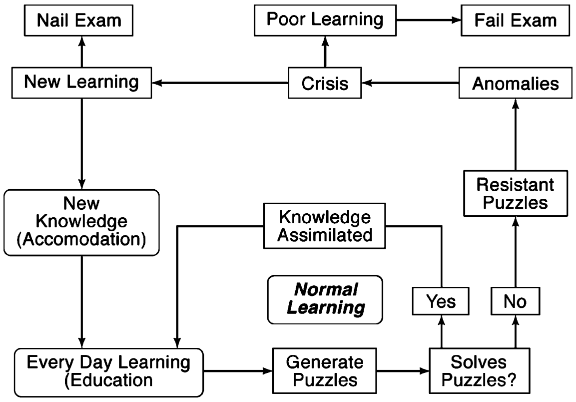


Figure 44. Schematic concept map of the process of everyday" learning and knowledge construction (Piaget's assimilation, Kuhn's "normal" science). See figure for the analogous schematic map of the process of "normal" science and paradigm construction and articulation. Also shown is the path to the development of extraordinary knowledge construction (Piaget's accommodation and new knowledge creation, Kuhn's "revolutionary" science and paradigm shift).

Research in chemical education in recent years has discovered a great deal about effective teaching and learning that serve as paradigms to instructors of undergraduates, especially faculty at research universities who teach large introductory courses. It would be unbecoming for a scholar to ignore significant research that is relevant to a major area of his or her discipline. Research scientists should be no more willing to fly blind in their teaching than they are in their scientific research, where no new investigation is begun without an extensive examination of what is already known.

In research, to cause a paradigm shift, a scholar must understand what the core of the community's governing paradigm is and attack it accordingly. In education, to change a student's preexisting knowledge (paradigms), an instructor must understand what the core of this preexisting knowledge is and attack it accordingly. *The most important single factor influencing student leaning is what the learner already "knows"*, i.e., the student's governing paradigms or in Piaget's terms, schemata. The instructor needs to probe what the learner believes he/she knows before the instructor can effectively change that knowledge. In a sense, students "know a lot", but unfortunately, much of what they "know" may not be so. Thus, an effective instructor of undergraduates needs not only sufficient scientific content knowledge on the one hand and pedagogical knowledge on the other hand, but also knowledge of the research showing the methods that reap benefits from the interplay between the two domains. We can consider preexisting knowledge as an example of an individual's cognitive paradigm. In this terminology, it is important to recognize the student's schema or the researcher's operating paradigm: by understanding the student's paradigm, one can use analogies to overlay new ideas and knowledge with preexisting knowledge. By understanding the student's paradigm, one can exploit effective learning techniques, i.e., either setting up cognitive dissonance by deliberately putting forth information that is in conflict with the student's preexisting beliefs, thus stimulating a cognitive context that seeks to remove the conflict, or using the paradigm to start from a point that has no conflict with preexisting knowledge and reinterpret the path to multiple conclusion.

12C. Essence of a Good Teacher and a Good Learner. My journey of self-reflection on teaching and learning probably had its origin with discussion that I had with Professor Gilbert Burford, one of my great undergraduate teachers and role models at Wesleyan University in Middletown, CT, my home town. During my exit interview as a senior, Professor Burford asked me what I thought it takes to be a good teacher. After a little reflection, my answer was something like "A good teacher can remember the difficulty and struggle that are involved in learning a new subject and can keep track of the intellectual tricks that build on things the student already understands in order to comprehend new knowledge. In this way, the teacher can retrace the path of thinking that was effective for him or her and hope that it will help students to learn." This idea, that I call the Burford principle of teaching, has been the bedrock for my writing, teaching, and research through the last half century.

13. SERENDIPITY: TEACHING PHOTOCHEMISTRY AT HARVARD AND DUPONT. ORIGIN OF THE BOOKS ON ORGANIC PHOTOCHEMISTRY

Let me finish Part II of this Perspective with a recollection of how I managed to produce a book on photochemistry at the same time I started my research career at Columbia. As a postdoc for Paul Bartlett at Harvard in 1963–1964, photochemistry was in a preparadigm stage and of great interest for organic chemistry because of its obvious potential for mechanistic studies and for novel synthetic applications. I was asked to present some seminars to the chemistry department on the basics of photochemistry. Wow! As I recall, in the audience were P. D. Bartlett, E. J. Corey, R. B. Woodward, R. Hoffman, and F. Westheimer. I used the Burford principle to put together several lectures. I kept the notes for these lectures figuring that they would be useful when I went to Columbia in the fall of 1964.

Then serendipity kicked in. I received an opportunity to develop a full course on organic photochemistry faster than I expected during my tenure as a postdoc at Harvard. My Ph.D. supervisor, George Hammond, had received an offer to teach a course on organic photochemistry at DuPont in Wilmington, DE, but he was unable to accept and recommended that DuPont invite me to teach the course. I was invited and accepted. I dug into my notes and decided to use the occasion of the course to penetrate deeply into all kinds of issues, which

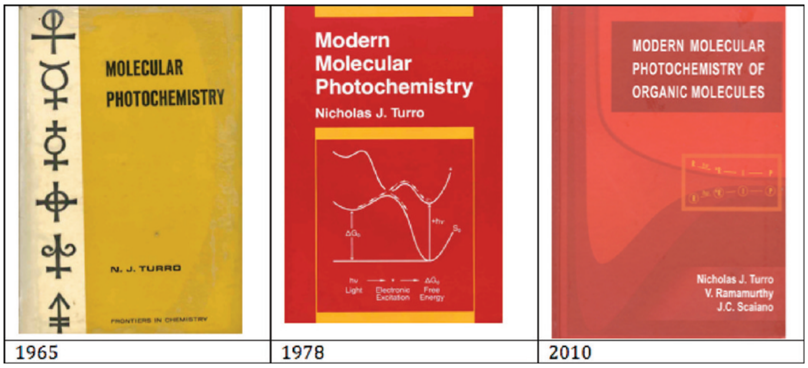


Figure 45. Textbooks on molecular photochemistry.

required me to create a detailed and expansive paradigm of organic photochemistry that would allow me to show the researchers at DuPont my path to understanding. The course was a fantastic experience, and the notes and suggestions and feedback from the students were used during my first year at Columbia as a basis for a textbook on organic photochemistry, *Molecular Photochemistry* (Figure 45, 1965).[16a] The rest, as the saying goes, is history. *Molecular Photochemistry* (Figure 45, 1978) was a success in revealing the paradigms of the emerging field of organic photochemistry. This text was followed, two decades later, by the publication of *Modern Molecular Photochemistry* in 1978.[16b] The latest version of the text, *Modern Molecular Photochemistry of Organic Molecules*, was published with two fabulous coauthors, Murthy Ramamurthury and Tito Scaiano in 2010 (Figure 45).[16c]

14. MY MUSE, SOUL MATE, AND INSPIRATION: SANDY AND ME

My muse and soul mate for nearly 70 years (that is right!) has been my wife Sandy. We met in kindergarten. Figure 46, left, shows a photo of Sandy and me at our marriage in 1960. Figure 46, right, shows a photo of Sandy and me at Columbia. Sandy has been by my side through thick and thin and serves to be my guide, help, support, and constant source of inspiration.

Figure 46. Left: Sandy and Nick at our marriage in 1960. Right: Sandy and Nick at Columbia.

15. MY MENTORS AND TEACHERS

I've been blessed with marvelous teachers in my formative high school and college years. These blessings were completed with the mentoring by two of the outstanding physical organic chemists of the 20th century: George Hammond as my Ph.D. supervisor and Paul Bartlett as my postdoctoral sponsor. I was also mentored by Peter Leermakers both as an undergraduate and at the start of my academic career. Peter was a brilliant chemist who died tragically in a car accident in his early 30s. In addition, I have enjoyed the last three decades of the wonderful mentoring of Anatoly Buchachenko, my "spin doctor" whose transfer of knowledge of spin chemistry to me has led to intellectual delights and major programs of my research program.

16. STUDENTS, POSTDOCS, VISITING SCHOLARS, AND COLLABORATORS

It is hard for me to believe the number of undergraduate students, graduate students, postdocs, and visiting scholars who have passed through my laboratory and made important contributions to my intellectual development while performing collaborative research (Figure 47). I estimate that I've sponsored 80 graduate students and 140 postdocs and over 200 undergraduates during my tenure at Columbia. We've had over 100 visitors come to Columbia to use the photochemical and ESR facilities.

Figure 47. The Turro research group is trained to exercise at the highest levels of professionalism.

Among the most delightful collaborations has been one with Lionel Salem and Bill Dauben. The three of us spent many stimulating and exciting hours, in 1973 and 1974, discussing and developing a "theory of organic photochemical reactions."

Visitors have provided the spice of cultural interchange in addition to excellent participation in collaborative research programs. I've strongly favored collaborative programs since I have found that by teaming up with experts in other fields I can take a student's attitude about new research and assimilate new knowledge much, much faster than if I tried to do so on my own. I do not have any detailed records of how many research collaborations that I have enjoyed in the last 50 years, but during the last 5 years, I have had the privilege of coauthoring publications with over 48 colleagues from institutions national and international.

17. COLLEAGUES AT COLUMBIA

One of the most important reasons for any success that I have had in my research at Columbia has been the fabulous colleagues that I have been blessed with during my tenure here. When I arrived at Columbia, the organic group was outstanding with giants in the field such as Cheves Walling, Ron Breslow, Gil Stork, and Tom Katz. Shortly after I arrived, Koji Nakanishi and Clark Still joined the faculty. Through casual and in depth conversations, Thursday evening seminars, and interactions with their students, I was immersed in a hot bed of constant stimulation dealing with the wonders of chemistry at many levels. Ideas could be presented in an atmosphere of scholars who sought to teach and learn together.

This group of fabulous chemists and colleagues has my thanks and gratitude for providing a nurturing environment in which I could flourish. Clearly, this was a case where it was very easy to "bloom where you were planted!"

18. FINAL THOUGHTS

I hope that the Perspective of the research physical organic chemistry, organic photochemistry, and spin chemistry that has been performed at Columbia since 1964 and the perceived philosophical of the intellectual development that served as the foundation of this research has been worth the effort for the reader. I certainly will be happy to receive comments, criticism, and questions on any of the material in the Perspective.

I close with some thoughts and musing about our noble, stimulating, and gratifying profession. We chemists deal with ideas which are the intellectual genetic material of teaching, learning, cognition and research. Chemists have sacred professional obligations to work with students and collaborators with whom the exchange this intellectual genetic material. We enjoy the exchange because we sense that the acquisition of new genetic material provides us with important survival skills in the same way that all living organisms derive survival skills through survival pressure.

We leave the readers, who have managed to make it this far (congratulations!) with an *exhortation* and with a *quote*.

The exhortation is: *"He who chooses to teach and conduct research must dare to never stop learning and remain a student forever!"*

The quote is from a beautiful piece of prose from a lecture given by Sir C. N. Hinschelwood on the occasion of the Centennial of the Chemical Society of London:[46]

> *"...Chemistry, that most splendid child of intellect and art. Chemistry provides not only a mental discipline, but an adventure and an aesthetic experience. Its followers seek to know the hidden causes which underlie the transformations of our changing world, to learn the essence of the rose's color, the lilac's fragrance and the oak's tenacity and to understand the secret paths by which the sunlight and the air create these wonders. And to this knowledge they attach an absolute value, that of truth and beauty. The vision of Nature yields the secret for power and wealth, and for this is may be sought by many. But it is revealed only to those who seek it for itself."*

■ AUTHOR INFORMATION

Corresponding Author

E-mail: njt3@columbia.edu.

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