

Conical Intersections in the Theory of Organic Singlet Photochemistry

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Background

Considerable progress has been made recently in the theory of photochemical reactions in the singlet state, due to improved understanding of the importance of conical intersections. The subject has a long history. Teller¹ pointed out in 1937 that in polyatomic molecules potential energy surfaces can cross (touch) even if the two states have the same symmetry. He suggested that this makes it much easier for internal conversion (IC) to occur in a polyatomic molecule than in diatomics. In his classic book on Quantum Chemistry published in 1957, Kauzmann² used this surface crossing model exclusively in his discussions of IC, and he suggested that "it is easy to believe that these cross-overs are not unusual in molecules." In the field of organic photochemistry, Zimmerman³ and Michl⁴⁻⁶ suggested that certain photoproducts originate from IC at a conical intersection of the S_1 and S_0 surfaces and introduced the terms "bi-funnel" and "funnel" for this topological feature. Michl and collaborators^{7,8} documented such features in *ab initio* calculations on a model four-electron, four-orbital system (H_4) and discussed the relevance to classical problems such as the photochemical conversion of butadiene to cyclobutene and bicyclobutane, and pericyclic photochemistry in general. Salem's diagrams⁹ illustrated the occurrence of conical intersections (surface "touchings" or "crossings") at symmetric geometries in the photochemistry of carbonyl compounds. Subsequently, geometries of symmetry-imposed conical intersections were computed for Schiff base syn-anti isomerization by Bonačić-Koutecký and Michl,¹⁰ using *ab initio* procedures, and the "3x3" model of biradicaloid electronic structure^{4,11,12} was elaborated¹³⁻¹⁵ to permit qualitative predictions of geometries at which S_1 - S_0 conical intersections take place. Yarkony¹⁶ and Ruedenberg¹⁷ identified conical intersection geometries in small molecules. Bernardi, Olivucci, and Robb's *ab initio* computations on the cycloaddition of two ethylenes¹⁸ and butadiene cyclization^{19,20} confirmed the validity of the old conjectures and simple models and showed the importance of full geometry optimization. The last named authors developed a simple "2x2" VB model that permits an easy visualization of the origin of the conical intersections.^{21,22} Detailed discussions of their nature and dimensionality have been provided (the set of points at which the two states touch is multidimensional).^{16-18, 22-25} Today, the widespread occurrence of conical intersections in organic molecules is generally acknowledged and is no longer a mystery and subject of conjectures, as it was a mere decade ago.

The importance of conical intersections in singlet photochemistry is due to their acting as funnels on the excited surface, which very efficiently return electronically excited molecules to the ground surface at geometries that might be difficult to reach in purely thermal processes. The initial absorption of a photon results in the generation of an excited state species (M^*). If radiationless decay from the first excited singlet S_1 to the ground state S_0 takes place at a local minimum (which might arise from an avoided touching of the S_1 and S_0 potential energy surfaces) and if the S_1 - S_0 energy gap at the position of this minimum is larger than a few kcal mol⁻¹, M^* will rapidly thermalize its vibrational motions and the IC probability will be determined by the Fermi Golden Rule. In this "wide gap" case, fluorescence, intersystem crossing, and possibly other processes will typically be competitive, and in this sense a wide-gap excited state minimum represents a "bottleneck"

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From the Executive Director

D.C. Neckers, Center for Photochemical Sciences

Several weeks ago, I presented a seminar at Hope College, where I first taught chemistry. I'm also an alumnus, so I took the opportunity to report on some work of particular interest to that institution done on the photochemistry of stable triphenylmethyl radicals. In a Ph.D. dissertation presented in the Center for Photochemical Sciences last fall, Alexandre Nikolaitchik investigated stable triphenylmethyl radicals of which benzophenone residues were part, identifying the excited states responsible for their photoreactivity.

The reason this work was of interest at Hope was because Moses Gomberg, a professor at the University of Michigan, was an important benefactor of Hope. A significant percentage of Hope's early chemistry library was given to them by his estate on the occasion of Professor Gomberg's death in 1947.

Gomberg's early work stimulated the idea that the photochemistry of derivatives of triphenylmethyl would be of continuing interest. In 1913, as part of his studies on molecules with trivalent carbon, Gomberg reported, in the experimental section of one of his papers, that α -naphthylidiphenylmethyl bleached with sunlight. Some 40 years later, Bob Letsinger, at Northwestern, analyzed the products of the bleaching of triphenylmethyl finding 9-phenylfluorene and triphenylmethane. This year, Nikolaitchik, using transient spectroscopy, GLC, HPLC, and several other techniques neither Gomberg nor Letsinger had at their disposal, identified the excited states, identified other products, and wrote still another mechanism for their formation.

Historical papers in science are a hobby of mine, and textbook authors often don't do great ideas justice. I often find that the first time an idea is written down, it is explained with much more clarity than one can find in later descriptions of the work. The ideas Gomberg described were carefully and clearly delineated. Of course to prove his point, he published all of his early papers twice--one time in *JACS* and as an identical translation in *Berichte*.

The value of Gomberg's work, of course, is today mainly confined to the experimental part of his papers. But this little seminar reminded me of the lasting impact of carefully done experiments and clearly thought out concepts.

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in the photochemical process. Radiationless decay of M^* at a funnel, i.e. a very weakly avoided or unavoided touching, is much faster than any possibly competing process. Thus, it represents no bottleneck, and implies that the IC process will be close to 100% efficient. The return to S_0 can occur on the timescale of a single vibration (i.e. the Landau-Zerner decay probability is nearly unity and the returning molecule keeps a memory of the direction from which it approached the funnel). This provides an opportunity for "direct"⁶ photochemical reactions, in which there is no vibrationally equilibrated intermediate between the initially excited state and the final ground state product.

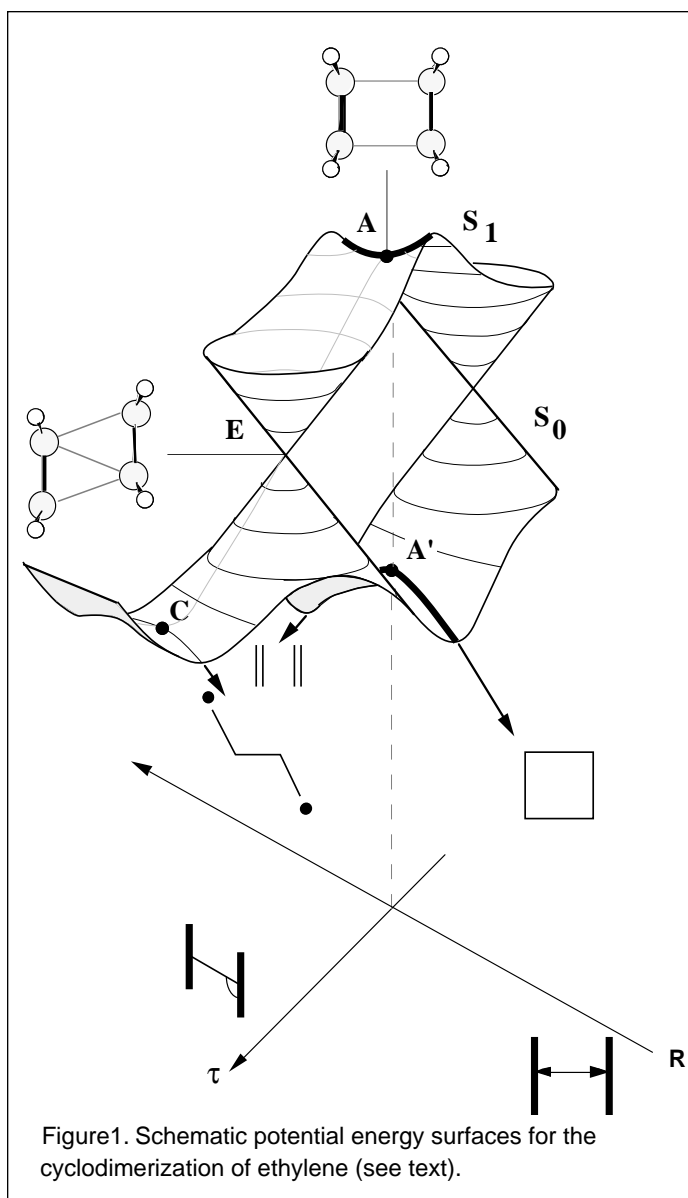
At times, the impression may have arisen that direct reactions are the only ones that can be concerted and stereospecific. This would be erroneous: there also are many that are not direct, and yet are concerted in the sense of moving atoms and breaking and making bonds in concert, thus conserving stereochemical information. This they can do regardless of whether they proceed through an intermediate such as an exciplex or excimer, particularly if they preserve cyclic bonding throughout.

The classical text-book view of photochemical reactions, mainly due to the work of van der Lugt and Oosterhoff,²⁶ assumed IC from a minimum in the excited state that was due to an avoided crossing. It was clear from the experimental evidence, such as the total absence of fluorescence from such minima, that the IC is extremely fast and that the degree of surface crossing avoidance cannot be high. Yet the calculations available at the time, which were forced to assume a fair degree of molecular symmetry all along the reaction path, predicted quite sizable gaps. Clearly, the

return took place from nearby locations of lower or no symmetry. Although some general hints as to the nature of the symmetry distortions involved were available from simple models and calculations, it was not clear just exactly what the return geometries were, and it was considered likely that the funnels involved were due to weakly avoided rather than true surface touchings (conical intersections).

The recent *ab initio* calculations have clarified the situation²⁷⁻³⁰ and similar results have now been obtained at the semiempirical level as well.³¹ A cut through a double cone yields an avoided crossing in a single dimension, unless it goes through its very tip. Thus, in a polyatomic molecule, there probably is a true conical intersection in the vicinity of any touching that is avoided along a particular one-dimensional coordinate. The simple 2x2 and 3x3 models and, more quantitatively, modern *ab initio* calculations tell us in which direction to go from the lowest energy point in the minimum in the symmetric reaction path to reach the (multidimensional) region of actual surface touching and efficient return to the ground state. This is the current text-book picture.³²

In Figure 1 we show an example in the schematic representation of the computed potential energy surface for the ground and excited (doubly excited covalent) electronic state for the cycloaddition of two ethylene molecules. The surface is plotted in two dimensions: the direction R corresponds to a synchronous formation of the two new σ bonds, and the direction τ corresponds to a rhomboidal distortion, which introduces a diagonal interaction into the pericyclic array of interacting orbitals. It is clear that the surface in the cutting plane R exhibits a local maximum on the ground state, A' , and a local minimum A on the excited state. This is in agreement with



the predictions of the Woodward-Hoffman or van der Lugt and Oosterhoff model. In contrast, in two dimensions one sees two conical intersections E or funnels at a rhomboidal geometry. The avoided crossing description of van der Lugt and Oosterhoff represents the zeroth order approximation; one merely has to move from a one dimensional model to a two dimensional one to turn the avoided crossing into the conical intersection or funnel. Such a conical intersection at a rhomboidal geometry was predicted and rationalized⁸ twenty years ago using the *ab initio* potential surface for H_4 , but the first *ab initio* verification of this for a real organic molecule had to wait 15 years for the development of the necessary computational tools.

Fast IC Processes Can Be Rationalized with a Conical Intersection Model

Using various laser spectroscopic techniques with a time resolution below the picosecond time scale, direct evidence is now accumulating that very fast IC processes and short excited state lifetimes are quite common. Femtosecond excited state lifetimes have been observed.^{33,34} Further, the presence of “thermally activated” fast radiationless decay channels, where radiationless decay competes with fluorescence, have also been studied in detail experimentally.³⁵ Recent *ab initio* computations²⁷⁻³⁰ show that such results can be explained in considerable detail with a model of fast decay through a conical intersection. The occasionally observed competition with fluorescence has been demonstrated to reflect the presence of an excited state energy barrier which separates a minimum in the lowest excited singlet M^* from the intersection structure.

VB and MO-CI Methods Provide Natural Models for Understanding Surface Touchings

In his 1969 paper,³⁶ Teller observed that there was no “natural model” that would enable one to say “in this molecule there must be a conical intersection.” Since then, considerable progress has been made on this front as well. The H_4 model^{7,8} accounts satisfactorily for the intersections seen in pericyclic reactions of conjugated hydrocarbons. The simple 2x2 VB model based upon two covalent structures^{21,22} turns out to be adequate to rationalize the structure of intersecting covalent states in polyenes and aromatic systems. The simple 3x3 MO-CI model based on one covalent and two ionic configurations provides an alternative rationalization and in addition permits a consideration of substituent effects.¹³⁻¹⁵ Results involving the crossing of covalent and ionic states are now becoming available.²⁹ Their modeling will be less simple and may require a larger configuration space, possibly the full 20x20 model introduced originally for H_4 .^{7,8} The photochemistry of carbonyl compounds has now been explored as well^{37,38} and it seems that simple VB models confirm and elaborate Salem’s results⁹ and permit an *a posteriori* understanding of the crossings in these surfaces as well.

The Validity of Woodward-Hoffmann Theory for Photochemistry

We have already discussed the fact that the conical intersection model is an evolution of previous concepts and methods rather than a revolution. Still, it is interesting to ask whether the validity of the rules used by the organic chemist based on Woodward-Hoffmann theory is challenged by new computational results.

In the photochemistry of polyenes, the original formulation of the WH rules³⁹ predicts the stereochemistry of the motion on the surface of the (HOMO-LUMO singly-excited ionic) $1B_2$ spectroscopic state. Van der Lugt and Oosterhoff²⁶ extended this model and suggested that along the “excited-state allowed stereochemical path” the $2A_1$ state has a minimum due to an avoided crossing, which provides an easy IC (“pericyclic minimum”), while such a minimum is absent on the “excited state-forbidden” path. Spectroscopic investigation³⁴ of short polyenes shows that after photoexcitation these systems decay from the $1B_2$ to a lower-lying doubly-excited ($2A_1$) state, as anticipated.²⁶ Why is the “disrotatory” stereochemistry predicted for the spectroscopic state of *s-cis* butadiene not lost on the $2A_1$ state? The standard answer to this question has been that the absence of a symmetry-imposed barrier in the $1B_2$ state enables the molecule to follow the allowed path, and that the $2A_1$ state guides it to the funnel, which lies in the allowed path. However, while a rigid disrotatory stereochemistry has been experimentally observed for the *s-cis* butadiene ring-closure, Leigh et al.⁴⁰ have demonstrated that the reverse photoreaction, the ring-opening of cyclobutene, occurs with a low degree of stereospecificity, and this is contrary to the simple classical expectations.

Computational investigation²⁸ shows that *s-cis*-butadiene $1B_2$ relaxation from the Franck-Condon region indeed involves a disrotatory motion of the terminal methylenes in agreement with the WH rules. Although both a disrotatory and a conrotatory path exist on the $2A_1$ potential energy surface and end in the same $2A_1/1A_1$ crossing, the disrotatory path is barrierless while the conrotatory path has a barrier, so the $2A_1$ potential energy surface indeed guides the molecule to the lowest energy point on the $2A_1$ state. This is not an ordinary minimum but a conical intersection, and is located at a geometry in which one of the terminal methylenes is 90° twisted. Upon return to the ground state,

relaxation to the *cis* and the *trans* isomers of the diene will therefore compete with disrotatory ring closure to cyclobutene. Photochemistry of *s-cis*-butadiene therefore involves competing stereospecific disrotatory ring closure and *cis-trans* isomerization, hardly a surprise to anybody. However, excitation of cyclobutene involves return through the same conical intersection, and leads to the same three species: the starting cyclobutene and the *cis* and *trans* isomers of the diene. Now, the ring opening reaction yields both the conrotatory and the disrotatory product, in apparent violation of the WH rules.

Structure and Dynamics

Current theoretical tools^{16,24,25} allow one to locate the lowest energy point on a multidimensional potential surface touching. Studies of the dynamics are needed before it becomes clear whether the molecule actually reaches such a lowest energy point or whether it decays to the lower electronic state immediately upon reaching the area of surface touching in the conical intersection. If the velocity of nuclear motion is sufficiently large, the system may decay to the ground electronic state close to the region of conical intersection but not exactly at a point of surface touching.

Here the first steps have been taken. While full quantum calculations are possible with a few nuclear degrees of freedom,⁴¹ it seems that semi-classical trajectories represent a feasible⁴² approach if all nuclear degrees of freedom are to be considered. There have been two studies where this approach has provided interesting insights. An examination of the S_1 state non-adiabatic dynamics in benzene⁴² gives new insight into the quantum yield of prefulvene, and a similar study of azulene³⁰ suggests that one may observe coherent vibrations on the ground state of azulene immediately after the IC.

What is New and What is Not New

Excited state chemical reactivity is controlled by barriers on the excited state branch of the reaction path, by the existence of funnels where efficient radiationless decay to the ground state can take place, and by barriers to reaction on the ground state branch of the reaction path. The concept of a funnel has been well established in mechanistic photochemistry for decades. What is new is that it has been demonstrated in many cases that this funnel takes the form of a conical intersection and that it can often occur far from idealized symmetric reaction path geometries. Thus "classical" mechanistic arguments about how photochemical reactions take place have been confirmed and refined. One of the basic properties expected of a funnel,⁴ branching to more than one product after return to the S_0 surface, has now been confirmed by theoretical studies.

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Photochemical Sciences Discussion List

Bob Midden, a principal in the Center for Photochemical Sciences, has established a photochemical sciences discussion group in conjunction with the American Society for Photobiology. Bob is the moderator of the list, which is hosted by Bowling Green State University. Discussion topics include photobiology, photochemistry and all other related photochemical sciences.

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Dynamics of Alkene Radical Cations

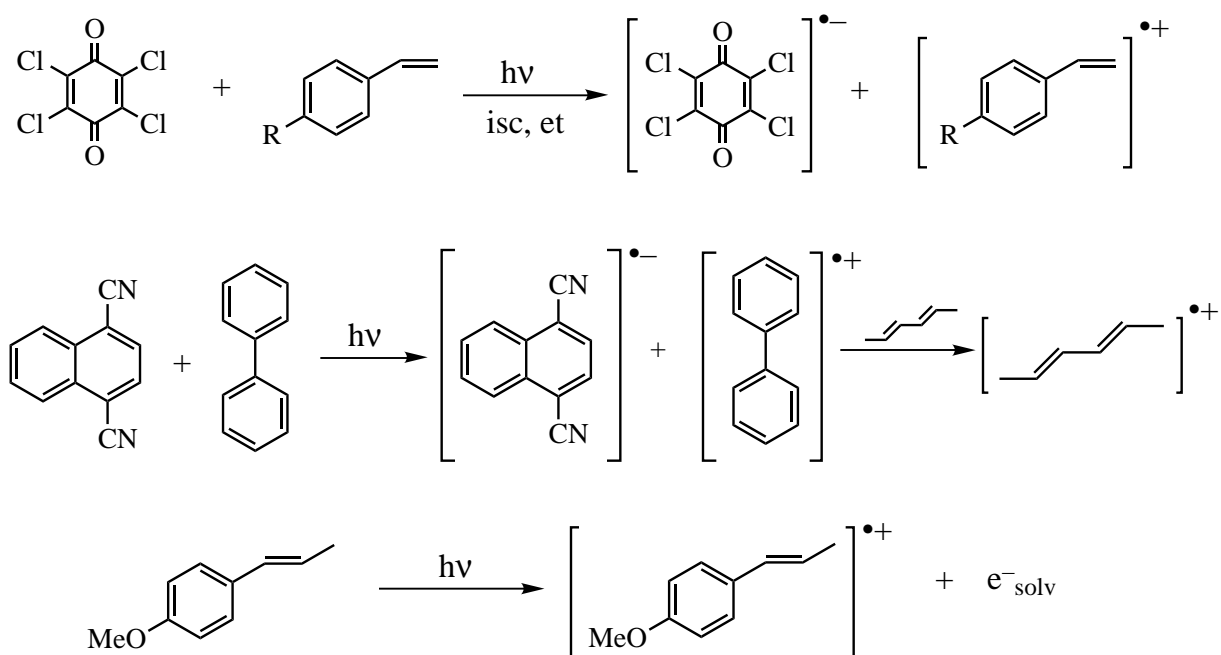
Linda J. Johnston, Steacie Institute for Molecular Sciences, National Research Council Canada

Introduction

The widespread importance of electron transfer reactions in chemistry and biology has led to increasing interest in the chemistry of radical ions.¹ Radical cations, in particular, have been the subject of a number of mechanistic studies and are now recognized as important intermediates in synthetic methodologies.²⁻⁵ Alkene radical cations undergo a variety of reactions such as addition of nucleophiles, deprotonation, electron transfer, *cis-trans* isomerization and cycloaddition reactions. This rich chemistry makes them particularly interesting substrates for studying the factors that control the competition between various reaction pathways. Such studies are essential in order to develop a detailed understanding of radical cation reactivity that will allow one to predict and control the chemistry of these important intermediates.

Despite the fact that alkene radical cations have been extensively studied in matrices and have been the subject of many mechanistic investigations, there was until very recently little absolute kinetic data for these species in solution under conditions comparable to those used in synthetic and mechanistic studies. We have used laser flash photolysis to generate and characterize a variety of arylalkene and conjugated diene radical cations.⁶⁻¹³ We have also obtained absolute kinetic data for their reactions with nucleophiles and for the initial step in the radical cation-initiated cyclobutane and Diels-Alder cycloaddition reactions. This work has led to detailed kinetic and mechanistic information that provides a quantitative basis for the rational development of synthetic strategies utilizing radical cation chemistry.

The most general method for generating radical cations for flash photolysis studies involves a photoinduced electron transfer reaction between a donor and an excited state acceptor (the photosensitizer) such as a cyanoaromatic or quinone to generate a radical cation/radical anion pair. The energetic requirements are determined by the Rehm-Weller equation which expresses the free energy for the electron transfer in terms of the available excited state energy, the redox potentials of the donor and acceptor and the Coulombic attraction energy gained by bringing the two



Scheme 1. Photochemical routes for generation of radical cations.

radical ions to the encounter distance.¹⁴ The yield of free radical cation from the original geminate radical ion pair is determined by the competition between back electron transfer and cage escape. Our work has typically used either triplet chloranil or a singlet dicyanoaromatic sensitizer with biphenyl as co-donor in polar solvents such as acetonitrile and 2,2,2-trifluoroethanol (TFE). These two techniques are illustrated in Scheme 1. Both systems overcome problems associated with the low yield of free radical ions that typically results from rapid in-cage back electron transfer for singlet ion pairs. Triplet chloranil is an attractive option in that it can oxidize a wider range of donors; however, the chloranil radical anion cannot be removed by oxygen-purging as can many other radical anions and may interfere with the spectra for the radical cations of interest. This problem can be overcome by using the dicyanoaromatic with biphenyl as co-donor, although this is limited to donors with oxidation potentials lower than biphenyl.

Photoionization provides an alternative photochemical method for generating radical cations in laser experiments (Scheme 1). Laser excitation of a wide range of easily oxidized substrates has been demonstrated to result in direct electron ejection to give a radical cation and the solvated electron. In most cases photoionization occurs from an upper excited state produced either directly by absorption of a single high energy photon or, more commonly, by sequential two-photon absorption. This method has the advantage of eliminating absorptions due to the sensitizer radical anion, since the solvated electron absorbs weakly in acetonitrile¹⁵ and can in any case be easily removed by oxygen or other scavengers. It is, however, not as widely applicable as photoinduced electron transfer. Nevertheless, it has been our experience that photoionization (where applicable) is the method of choice for the generation of radical cations for kinetic studies.

Radical cations are frequently identified on the basis of their characteristic UV-visible absorptions and the comparison of their spectra to those obtained in matrices at low temperature.¹⁶ For example, styrene radical cations have characteristic spectra with a maximum between 350-400 nm and a second weaker band between 500-600 nm. Conjugated diene radical cations also have two characteristic absorption bands in the 340-400 nm and 450-600 nm region. Thus, both classes of radical cations are amenable to spectroscopic and kinetic studies using laser flash photolysis techniques (Figure 1).^{6,13} In addition to their characteristic spectra, there are a number of other diagnostic tests that are commonly employed to identify these intermediates. For example, alkene radical cations generally react rapidly with nucleophiles (including solvent), react slowly, if at all, with oxygen, and can be readily scavenged by a donor with a lower oxidation potential than the precursor alkene. Many alkene radical cations have lifetimes in the microsecond range in solvents such as acetonitrile or aqueous acetonitrile, although some of the more reactive ones can only be observed on a nanosecond time scale in non-nucleophilic solvents such as TFE.

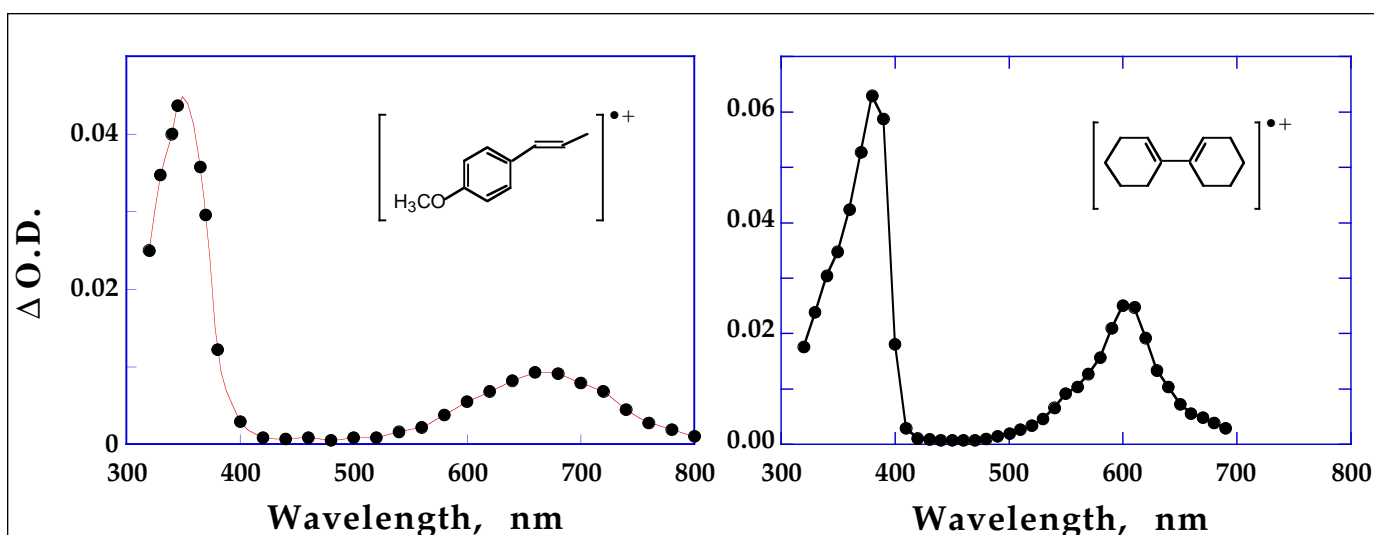
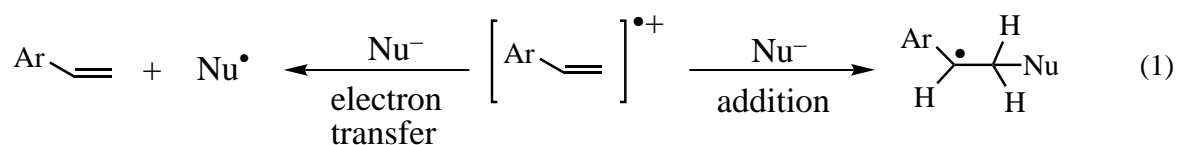


Figure 1. Transient absorption spectra of the trans-anethole and 1,1-bicyclohexene radical cations generated by photoionization and photosensitized electron transfer using 1,4-dicyanonaphthalene/biphenyl, respectively, in acetonitrile.

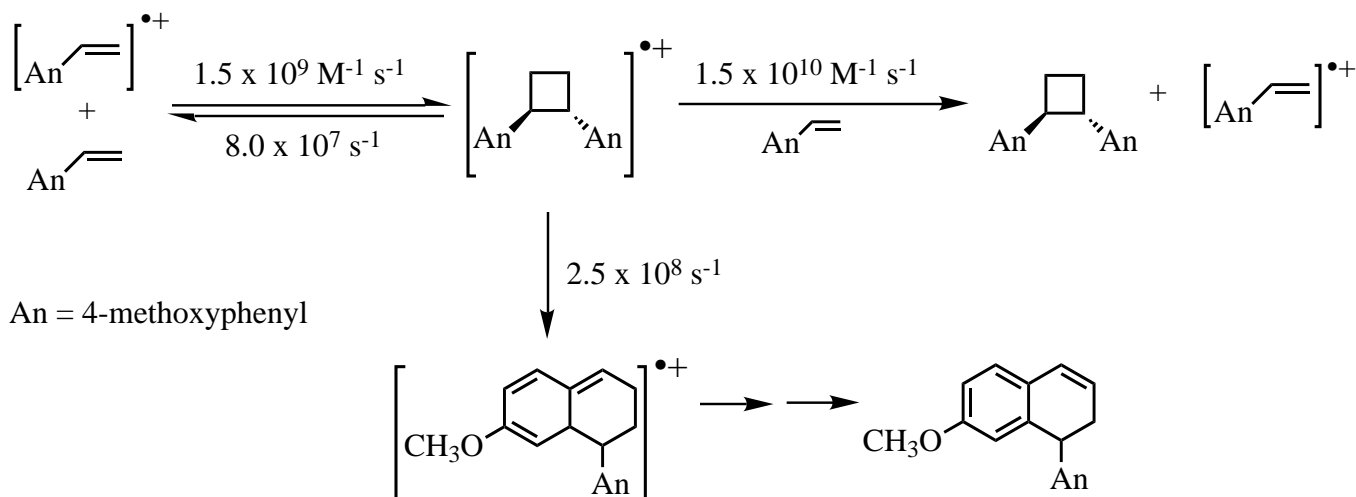
As noted above, radical cations exhibit behavior typical of other electrophilic species in that they react rapidly with nucleophiles such as anions, alcohols and amines. In general the reaction of a radical cation with a nucleophile can occur by either electron transfer, an energy wasting path that simply regenerates the starting alkene or diene, or by nucleophilic addition to give a radical (reaction 1). In the latter case the product radical leads to final products, either by typical radical chemistry such as disproportionation, coupling or abstraction reactions or by reduction to an anion followed by protonation. Reactions with alcohols occur exclusively via addition, since electron transfer is prohibitively endergonic for the arylalkene and diene radical cations that we have examined. In fact the discovery of the anti-Markovnikov addition of alcohols to diarylalkene radical cations by Arnold provided one of the first synthetically useful examples of radical cation chemistry.¹⁷ Rate constants for alcohol addition to styrene and 1,3-diene radical cations range from $\leq 10^5 - 10^8 \text{ M}^{-1}\text{s}^{-1}$ and demonstrate the steric and electronic effects of adding substituents to the aromatic ring and the double bond.^{6,13} For example, the rate constants for methanol addition to 4-substituted styrene radical cations decrease by almost 4 orders of magnitude in the order $\text{H} > \text{F} > \text{CH}_3 > \text{OCH}_3$. Similarly, the addition of two additional terminal methyl groups to the 2,4-hexadiene radical cation results in a decrease in rate constant for methanol addition of approximately 3 orders of magnitude.



Reactions with anionic nucleophiles occur with rate constants that are at or close to the diffusion-controlled limit in solvents such as acetonitrile.^{6,13} The competition between electron transfer and addition is in this case controlled largely by the redox properties of the alkene and the anion. In general, nucleophilic addition does not compete with electron transfer when the latter is exergonic by several kcal/mol. The reaction of the 4-methoxystyrene radical cation with azide provides a very nice illustration of this general trend.⁸ Azide reacts with the radical cation via electron transfer in acetonitrile but via addition in TFE; this is demonstrated unequivocally by the observation of the azide dimer radical anion ($\text{N}_6^{\bullet-}$) produced by addition of azidyl radical to excess azide in the electron transfer reaction and the product substituted benzyl radical in the case of addition. The change in reaction pathway from electron transfer to addition results from the substantial increase in oxidation potential for azide in TFE as compared to acetonitrile. In TFE addition can effectively compete with electron transfer, thus raising interesting possibilities for controlling chemoselectivity of radical cation reactions. Similarly, the rate constants for nucleophilic addition of anions and amines can be varied by as much as several orders of magnitude by changing the solvent from acetonitrile to aqueous mixtures; hydrogen bonding of the nucleophile is the major contributor to this effect.⁶

In the absence of added nucleophiles, the lifetimes for arylalkene and diene radical cations are largely determined by their reactions with the precursor alkene or diene. The addition of an alkene radical cation to its neutral precursor has been widely studied from a mechanistic point of view and provides the initial step in the radical cation chain reaction that leads to cyclobutane as well as rearranged products.^{2,3,18} The measured rate constants for the addition reaction are in the $10^8 - 10^{10} \text{ M}^{-1}\text{s}^{-1}$ range for a number of 4-substituted styrenes and 1,1-diarylethylenes.^{6,7,11} The mechanism for the radical cation-initiated dimerization of alkenes has been studied for almost thirty years, with considerable discussion as to whether the initial addition occurs in a concerted fashion to give an intact cyclobutane radical cation or in a stepwise fashion to generate a distonic acyclic radical cation. Depending on the particular alkene and the conditions used to generate the radical cation, there is compelling mechanistic evidence for both of these possibilities. Our recent studies of the radical cation-mediated dimerization of 4-methoxystyrene have used a combination of product studies and nanosecond and picosecond spectroscopy for both 4-methoxystyrene and its cyclobutane product to elucidate the reaction mechanism.⁷ The overall scheme is illustrated in Scheme 2; a long bond cyclobutane radical cation with a lifetime of 3 ns is proposed as the initial intermediate in the addition of radical cation to its neutral precursor; the same species can be produced from the cyclobutane by photosensitized electron transfer. The cyclobutane radical cation partitions between cleavage to regenerate the neutral styrene and its radical cation and rearrangement to a hexatriene radical cation that is the precursor to the dihydronaphthalene product. Reduction of the cyclobutane radical cation by excess 4-methoxystyrene in solution provides an alternate decay pathway under some conditions. The results clearly demonstrate that for this particular arylalkene the cyclobutane radical cation and

not the acyclic 1,4-radical cation is the primary intermediate, although it is not possible to conclusively eliminate the possibility that the latter plays a role in a later stage of the reaction.



Scheme 2. Mechanism for radical cation dimerization of 4-methoxystyrene.

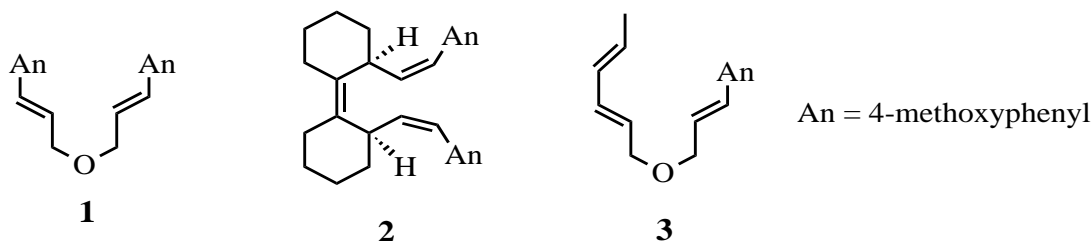
The addition of 1,3-diene radical cations to their precursor can yield either cyclobutane or Diels-Alder adducts. The latter are of particular interest since the radical cation-initiated Diels-Alder cycloaddition can be carried out under mild conditions for substrates that are typically unreactive in the conventional thermal Diels-Alder reaction.³ This fact, coupled with the frequently predictable and controllable stereochemistry and stereospecificity of these reactions, makes them attractive alternatives to the thermal Diels-Alder reaction. Our kinetic studies of 1,3-diene radical cations indicate that the initial addition of the radical cation to the neutral diene occurs with rate constants in the $10^8 - 10^9 \text{ M}^{-1}\text{s}^{-1}$ range, although plots of the observed rate constant for decay of the radical cation vs. [diene] level off at higher diene concentrations.¹³ This may result from regeneration of the initial radical cation via electron transfer or cleavage of the adduct radical cation. Product studies for 2,5-dimethyl-2,4-hexadiene indicate that the final product in the radical cation-mediated dimerization for this diene results from substantial rearrangement of the initial adduct radical cation. Both the observed rearrangement product and literature precedent are consistent with formation of a cyclobutane radical cation as the initial step.

The reactivity of styrene and diene radical cations toward other alkenes has also been examined.^{10,13} These cross-additions lead to either cyclobutane or Diels-Alder adducts, depending on the substrate, and have attracted considerable attention as synthetic tools, as noted above for the diene dimerizations. Knowledge of the relevant rate constants for the various steps is even more important in cross cycloadditions as the optimum concentrations and conditions must be chosen in order to minimize the amount of dimerization which, as noted above, occurs with relatively high rate constants. An extensive set of kinetic data for cycloaddition reactions of several styrene radical cations have been measured using laser flash photolysis. Some of the data for 4-methoxystyrene are summarized in Table 1, along with data for 2,4-hexadiene. Kinetic measurements for the latter are considerably more difficult. This is largely a reflection of the fact that the styrene data were obtained using photoionization to generate the radical cation. Most diene radical cations can only be produced in sufficient yield for kinetic measurements using photosensitized electron transfer. This limits the range of bimolecular reactions that can be examined since competition between the diene and the reactant for the sensitizer excited state is a complication, particularly in cases where the addition rate constants are slow. Nonetheless the data obtained so far illustrate the general trends and provide some of the first kinetic data for radical cation-initiated cross cycloadditions.

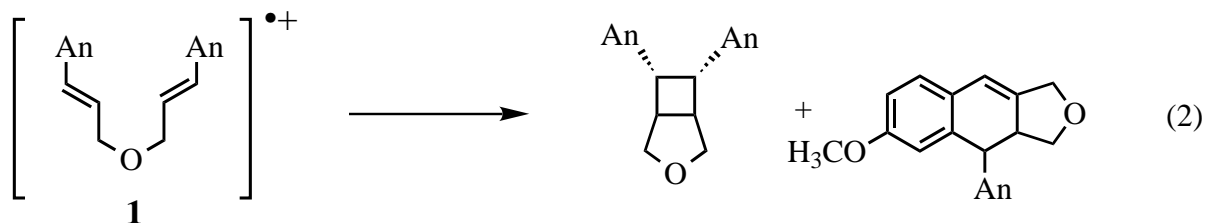
Table I. Rate constants for the initial step in the radical cation-mediated cycloaddition of 4-methoxystyrene and 2,4-hexadiene radical cations to alkenes in acetonitrile.^{10,13}

Alkene	$k_{\text{alkene}}, \text{M}^{-1}\text{s}^{-1}$	
	4-methoxystyrene ^{•+}	2,4-hexadiene ^{•+}
2-methyl-1-butene	1.5×10^6	9.8×10^7
3-methyl-2-pentene	7.2×10^5	8.3×10^6
ethoxyethene	3.2×10^9	7.0×10^7
1-ethoxy-1-propene	7.1×10^9	1.3×10^9
2,4-hexadiene	2.6×10^7	6.5×10^8
4-methoxystyrene	1.6×10^9	–

The radical cation-mediated cycloaddition chemistry of arylalkenes has recently been used by Bauld to design three intramolecular radical cation probes (1–3).¹⁹ The probe molecules all contain a β -alkyl-4-methoxystyrene moiety that undergoes an intramolecular cyclobutane or Diels-Alder reaction to give a single product under hole transfer catalysis conditions using triarylammonium salts. These probes have been used to test for the intermediacy of radical cations in the metalloporphyrin-catalyzed oxidations of alkenes. Their use as probes obviously requires accurate calibration of the rate constants for the initial cycloaddition reactions; estimates for the cyclization rate constants had originally been provided by an indirect approach using a competition kinetics method. A combination of nanosecond and picosecond laser flash photolysis has recently been used to provide absolute kinetic data for the rates of intramolecular cycloaddition of 1–3.^{11,12} Each of the three probe molecules yields a transient that can be assigned on the basis of its spectral characteristics and reactivity to a radical cation localized on the arylalkene moiety. The rate constants for decay of the initial radical cations thus provide a direct measure of the cyclization rate. Probes 1 and 3 cyclize rapidly with k_{cyc} values of 1.2×10^9 and $3 \times 10^8 \text{ s}^{-1}$ in acetonitrile, and the initial radical cation can only be detected in a picosecond experiment. By contrast, probe 2 has a much longer-lived radical cation, with $k_{\text{cyc}} = 3 \times 10^6 \text{ s}^{-1}$. Thus, these three probes cover a range of 3 orders of magnitude in time scale, making them ideal as a series of radical cation clocks or probes. In each case the rate constant measured by flash photolysis is faster than the original estimate, in some cases as a result of errors in rate constants used for calibration purposes.



Transient absorption measurements and product studies under photosensitized electron transfer conditions indicate that the chemistry for probe 1 is substantially more complicated than observed originally using a triarylammonium salt as the electron transfer catalyst. Transient experiments indicate the formation of a species consistent with a hexatriene radical cation, as observed for 4-methoxystyrene. Furthermore, product studies show the formation of two products, a cyclobutane and a dihydronaphthalene (reaction 2). There is no evidence for cleavage of the initial cyclobutane radical cation from 1, a reaction that is important in some other arylalkenes. Thus, it appears that the initial cyclobutane adduct radical cation formed by cyclization of $1^{\bullet+}$ can be reduced to cyclobutane or undergo a rearrangement that ultimately leads to a dihydronaphthalene product. The products will vary with reaction conditions, illustrating the importance of obtaining kinetic and mechanistic data under conditions as close as possible as those to be used for the probe reaction. The sensitivity of radical cation chemistry to the reaction conditions and method of generation of the radical cation may make the application of radical cation probes, at least those based on cycloaddition chemistry, somewhat less straightforward than is the case for radical reactions.



Kinetic and mechanistic data for reactions of arylalkene and diene radical cations provide essential background material for developing applications of radical cation chemistry. This data will eventually lead to a detailed understanding of radical cation chemistry that will permit one to predict and ultimately control the chemistry of these intermediates. In that regard a recent report of the construction of a bicyclic heteroatom-containing ring system by 1,5-cyclization of a diene radical cation, followed by intramolecular nucleophilic trapping, very nicely illustrates the potential of photoinduced electron transfer chemistry.²⁰

Acknowledgments

It is a pleasure to acknowledge the contributions of coworkers (listed in the references below) and colleagues at the NRC over the last few years. Particular thanks are due to Drs. Norman Schepp and Calvin Lew who were responsible for the majority of the work described herein.

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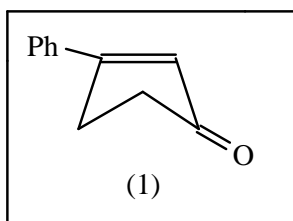
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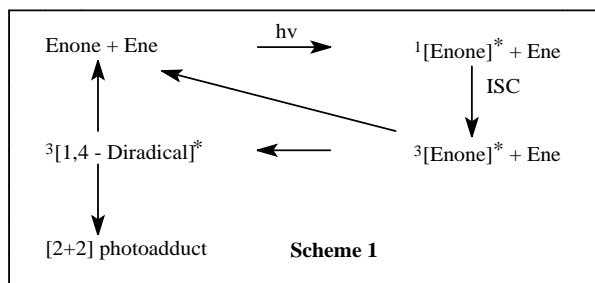
Photochemistry of Phenyl-Substituted Cyclic Enones

J.F. Daniel Kelly, John M. Kelly and T. Brian H. McMurry,
Department of Chemistry, Trinity College, Dublin, Ireland

The [2 + 2] - photocyclisation of enones and enes has attracted much attention both from a mechanistic point of view and also from its utility in chemical synthesis.¹⁻³ Our interest originally arose in the regiochemistry of intermolecular photocyclisations, and we chose to study 5-allyl-3-phenylcyclopentenones, as the phenyl substituent could be modified by electron donating and withdrawing groups and substituents could also be attached to the allyl side chain. In retrospect, the choice of a 3-phenylcycloalkenone chromophore was a happy one, as the compounds, and especially the 3-phenylcyclopentenone (**1**), turned out to have relatively long triplet state lifetimes in solution. Laser flash photolysis

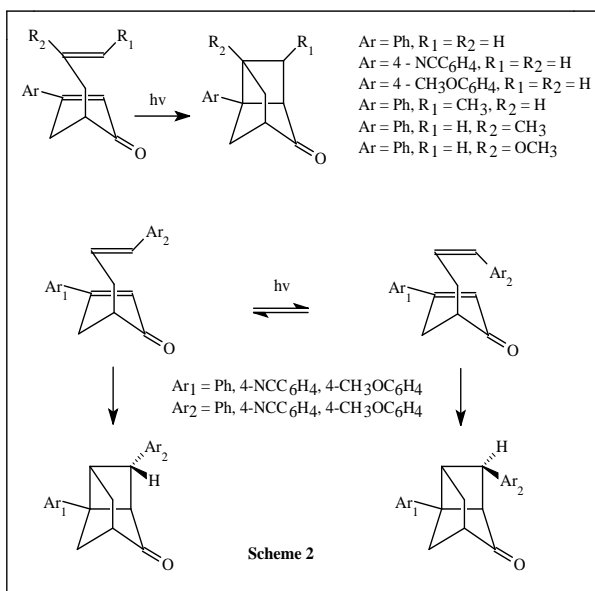


showed that the triplet state of **1**, which has a strong absorption band in the region 360-380 nm, decays with a lifetime of 20-50 microseconds (depending on solvent) at low concentrations.⁴ The compound phosphoresces in EPA glasses at 77 K.⁵ The decay, however, is not single exponential; the predominant two components appear to be associated with the decay in ether (25 ms) and alcohol (58 ms) domains in the frozen glass as decays with similar lifetimes are found in THF/ether glasses and ethanol glasses respectively.⁶ It has been suggested that the excited state, which is believed to be substantially $\pi\text{-}\pi^*$ in character, might resemble more the excited state of styrene rather than cyclopentenone.⁷ However, preliminary transient infra-red experiments reveal that the triplet excited state of **1** does not have a strong C=O stretching vibration above 1500 cm^{-1} ,⁸ behaviour which contrasts with that found for 4,4'-phenylbenzophenones, where the excited state is believed to be biphenyl-localised.⁹



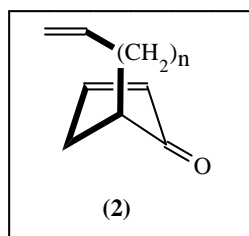
The reaction pathway for enone photocycloadditions originally proposed by Corey¹⁰ and supported by de Mayo¹¹ involved an exciplex intermediate. More recently Schuster² and Weedon¹² have provided evidence against the existence of such an exciplex and the generally accepted mechanism is shown in Scheme 1.

The regiochemistry of the intramolecular photocyclisations of arylcycloalkenones was found to be the same regardless of the substituents introduced (Scheme 2).¹³⁻¹⁵



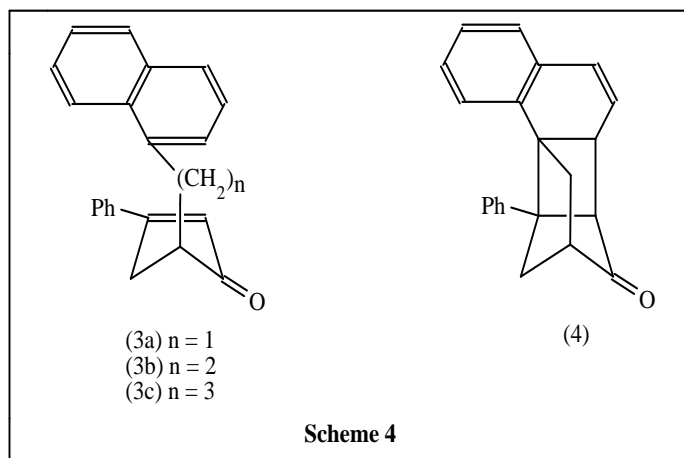
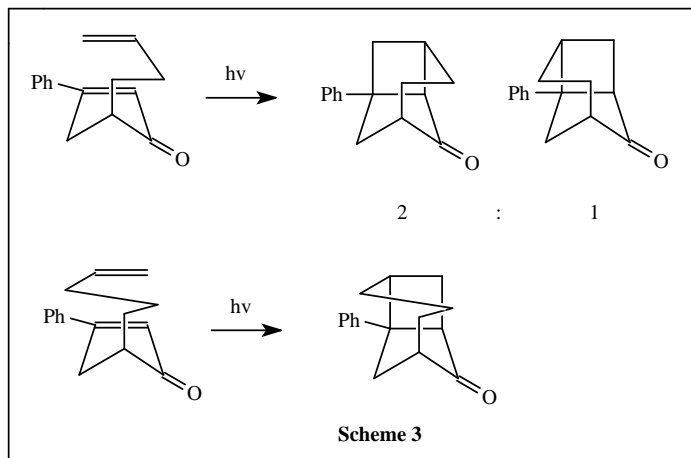
The question of the regiochemistry in related reactions has been addressed independently by Srinivasan¹⁶ and Hammond.¹⁷ They both pointed out that the products formed could be derived from intermediate di-radicals containing a five membered ring--the "rule of five". This concept was extended by Gleiter,¹⁸ who suggested that dienes with even number of atoms in the "linker" gave crossed products while those with an odd number of atoms in the "linker" gave straight products. He explained the results in terms of through-bond interactions. Our cases fit into his general rule if we consider the pathway highlighted in **2**.

We have extended our study in two directions. In the first, the substrate was modified by increasing the chain length of the 5-side chain containing a terminal alkene. This led to a dramatic change in regiochemistry (Scheme 3). Qualitatively the formation of monomeric products from compounds with butenyl side chains was slow, while the reaction of the compound with a pentenyl side chain was much faster.

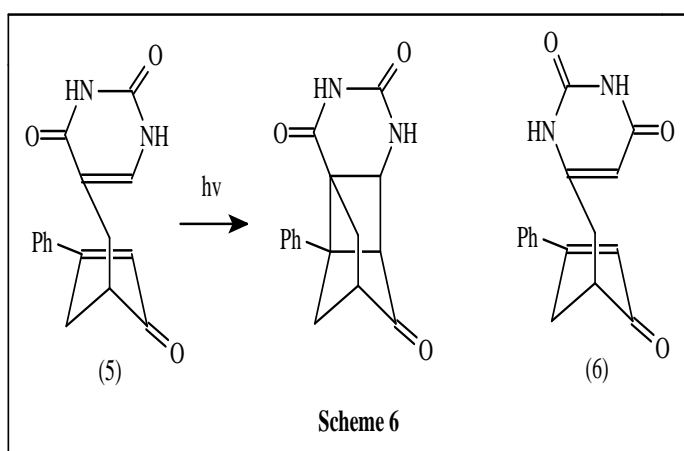
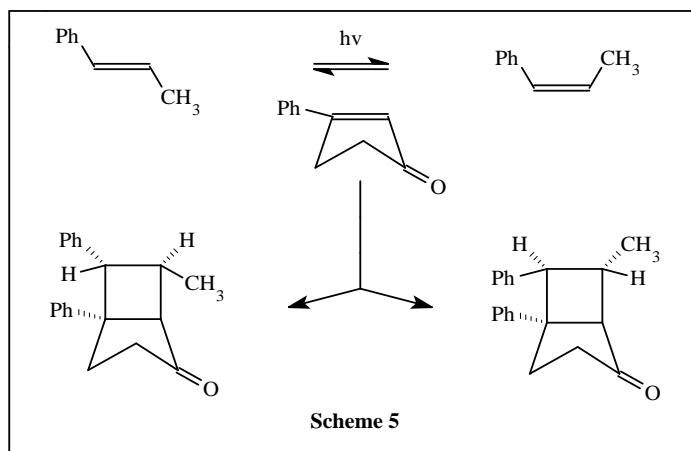


The other direction involved examining the addition of enone to aromatic double bonds.^{19,20} It was found that while 5-benzyl-3-phenylcyclopentenone gave no intramolecular photoadduct, such a product (**4**) was obtained from the 5-(1-naphthylmethyl) derivative (**3a**). The regio-chemistry of these reactions matched that of the 5-allyl analogues.

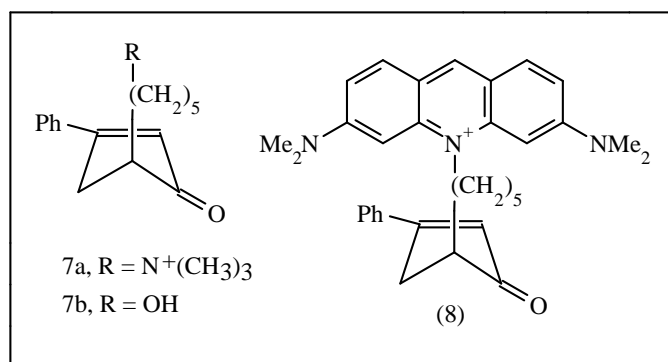
It was further observed that when the side chain was extended (i.e. **3b** and **3c**) no photoadduct could be detected. Instead low chemical yields of vinyl- and allyl-naphthalenes were detected in the complex mixture formed.²¹ Laser flash photolysis showed that the triplet excited state of **3b**, monitored in fluid solution, exhibits the spectral features expected for the separate enone and alkylnaphthalene moieties. This is consistent with rapid equilibration between their excited states which are estimated to differ by only 5 kJ mol⁻¹ in energy.^{6,22}



We have also examined a number of related intermolecular cycloadditions. Phenyl-propenes quench the triplet excited state of 3-phenylcyclopentenone **1** rapidly (e.g. $k_q = 2.2 \times 10^9 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ for the (*E*)-isomer) and 3-phenylcyclohexenone somewhat more slowly.⁴ The excited state of **1** is also efficiently quenched by its own ground state enone. Photolysis of either (*E*)- or (*Z*)-phenylpropene in the presence of 3-phenylcyclopentenone rapidly affords a mixture of the (*E*)- and (*Z*)-isomers and photoaddition products, which both have *trans*-phenyl and methyl groups, as if they are formed from the (*E*)-phenylpropene (Scheme 5).



It is well-known that other unsaturated carbonyl compounds such as psoralens²³ can add to pyrimidine bases in DNA. To test whether this is also the case for the phenylcyclopentenones, compounds **5** and **6** were initially synthesised. Intramolecular cycloaddition products were efficiently formed with the same regiochemistry as that found for the naphthalene derivatives (Scheme 6).²⁴ Laser flash photolysis studies demonstrated that although energy transfer between the enone and uracil moiety of these compounds is not energetically possible, the excited state is very efficiently deactivated.



A laser flash photolysis study of possible intermolecular quenching of enones **7a** and **7b** by thymine indicated that the rate constant for quenching was low ($k_q < 10^6 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$).²⁴ Currently experiments are underway with compound **8** which has been shown to bind strongly to DNA, presumably by intercalation.²⁴

In summary our studies with 3-phenylcycloalkenones show that they are a most useful class of compounds to study the factors affecting the mechanism of reaction and excited state reactivity of unsaturated ketones.

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Circular Dichroism Studies on Fullerenes and Related Derivatives

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Introduction

Chirality is one of the most pervasive elements of life, as most of the molecules synthesized by living organisms are optically active. Being related to the lack of symmetry, and particularly to the presence of asymmetric carbon atoms, chirality is strictly connected to the molecular geometry and, therefore, its manifestations have been exploited, in the past, to elucidate the intimate structure of a number of compounds. Circular dichroism (CD), in particular, represents an easy and widespread method to detect the optical activity of compounds by measuring the differential rotation of circularly polarized light when absorbed by an optically active sample.¹ Since this technique provides a set of complementary information on the excited states of a molecule with respect to conventional absorption techniques, it would be very appealing to detect the CD of large and symmetric molecules such as fullerenes, whose states are often electrically forbidden and therefore not detectable by normal spectroscopy. From a structural point of view, the states of a molecule are able to give a dichroic signal only if they bear simultaneously magnetic and electric transition moments. Among the recently synthesized fullerenes, only a few, like C_{76} , present natural optical activity,² their chirality being related not to a precise chiral centre, but to the overall symmetry, D_2 . On the other hand, the prototype and most studied of fullerenes, C_{60} , I_h point group, lacks any natural optical activity, but one can still make it chiral by using different chemical techniques (functionalization) or physical techniques (for example by imbedding C_{60} in a magnetic field or in the cavity of a chiral macrocycle).

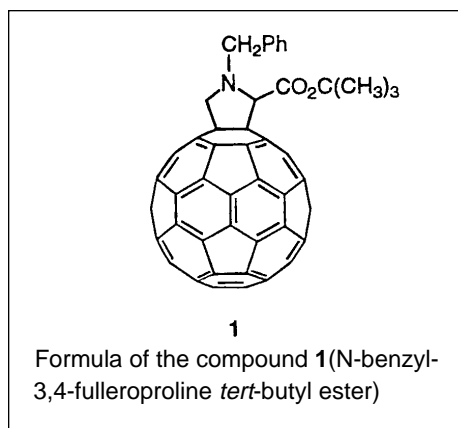
In this paper we present the results of our recent work on the chiroptical properties of buckminsterfullerene, C_{60} , by examining the natural CD of a recently synthesized class of artificial aminoacids (fulleroprolines), the induced CD (ICD) of this molecule when complexed by a cyclodextrin and when imbedded in a magnetic field (MCD). It was found that these kinds of artificially enhanced optical activity provide a wealth of information on the excited states of this molecule, allowing insight into its otherwise hidden states.

Natural Optical Activity of Fulleroprolines (Fpr)

One of the most exciting developments in the chemistry of fullerenes is the possibility of functionalizing them by adding some biologically active groups to the carbon clusters.³ The exact dimensional fit of these compounds with the

hydrophobic cleft of the active site of HIV-1 protease points to these compounds as possible inhibitors of this important enzyme.⁴ At the moment some classes of these compounds, obtained by adding chiral substituents like pyrrolidines and α -amino acid prolines to C_{60} , are being synthesized and actively studied in some Italian laboratories.⁵ From a structural point of view these compounds present the advantage of retaining the main electronic features of the parent carbon cluster, with the addition of two important new properties, such as solubility in polar solvents and optical activity. In fact a fairly intense rotatory power is detected for these compounds well below the region of the lowest permitted singlet of the parent C_{60} located at 326 nm.⁶ As an example of the interpretation of these CD spectra we describe the case of N-benzyl-3,4-fulleroproline *tert*-butyl ester (formula 1). The CD spectrum (Figure 1a) shows a specular pattern for the two enantiomers, with dichroic signals starting at ~ 700 nm and with a sharp peak at 428 nm. This maximum is displayed by all the Fpr examined⁶ and its sign can be taken as diagnostic of the absolute configuration of the C^α chiral centre, with a negative Cotton effect corresponding to the S configuration and a positive peak associated with the R configuration. This assignment, based on Nuclear Overhauser Effect (NOE) measurements, was nicely confirmed by a set of quantum mechanical calculations of the rotational strength of this compound, expressed by

$$R_{0a} = \text{Im} \langle \psi_0 | \mu | \psi_a \rangle \cdot \langle \psi_a | \mathbf{m} | \psi_0 \rangle \quad (1)$$



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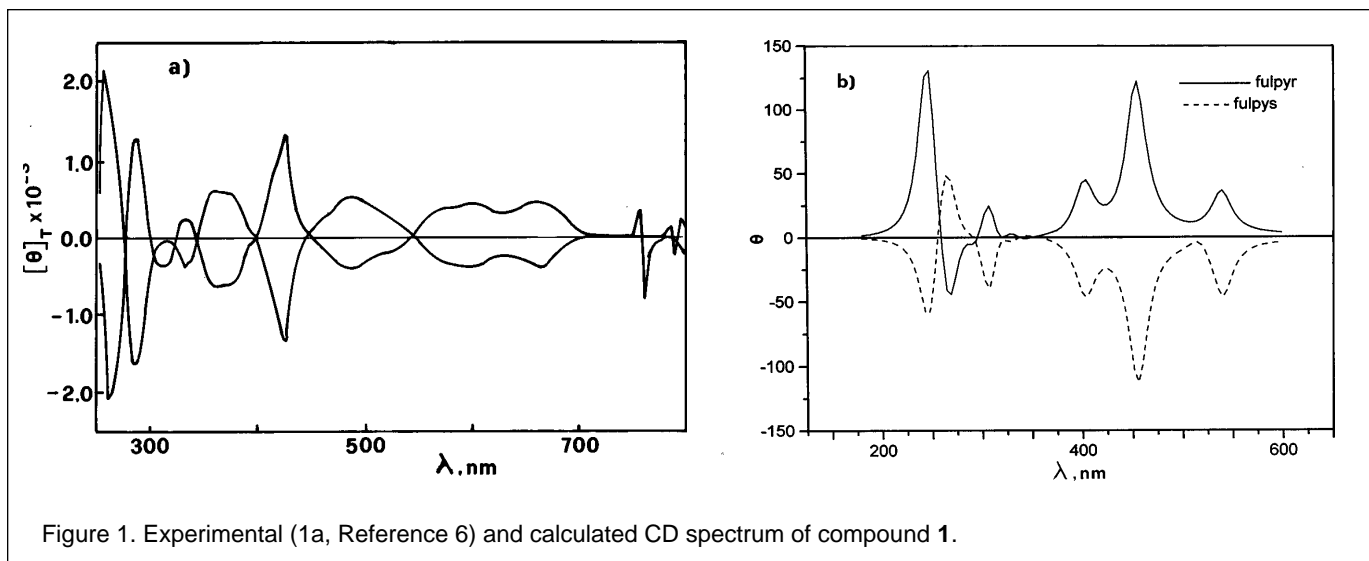


Figure 1. Experimental (1a, Reference 6) and calculated CD spectrum of compound 1.

where μ represents the electric dipole moment and \mathbf{m} the magnetic dipole moment. The quantities reported in Equation 1 were calculated using a CNDO/S Hamiltonian, with electric dipole integrals evaluated within the dipole velocity operator method and the magnetic dipole integrals evaluated in the complete angular momentum framework.⁷ The calculated rotatory powers so obtained were used to simulate the CD spectrum through a series of Gaussian bands centered on the calculated wavelengths with a procedure similar to that adopted for the CD spectrum of another Fpr characterized by 2,5-dioxopiperazine.⁶ The spectra for the diastereoisomers R and S, labeled fulpyr and fulpys respectively, are displayed in Figure 1b. While in C_{60} the low-lying excited singlets are forbidden both electrically and magnetically, the breaking of symmetry introduced by the proline substituents induces a number of optically active transitions below the threshold of the first allowed state. In particular, the first part of the CD spectrum, ranging from 700 to 500 nm, is attributed to a slight perturbation of G_g and T_{1g} states (the only ones which can bear a magnetic moment in the I_h point group), whereas the intense peak calculated at 455 nm (experimental 428 nm) is attributed to a larger perturbation of the prolinic π electrons in the extended π system of the carbon cluster. The breaking of symmetry induced by monofunctionalization of C_{60} is particularly effective in this region, and causes the emergence of an electrically and magnetically permitted state at 428 nm which is detected in all absorption and CD spectra of the compounds of this class. The fact that the calculation is able to reproduce a positive large signal for the R configuration and a specular negative signal for the S isomer offers a strong clue to the determination of the absolute configuration of this class of compounds. Since these newly synthesized Fpr are easily prepared and represent the ideal starting material for the synthesis of peptides with interesting biological activity, the possibility of separating the enantiomers and determining their absolute configurations provides an exciting development for future pharmaceutical applications of these compounds.

Induced Circular Dichroism (ICD) of C_{60} Included in Cyclodextrins

Another method to induce chirality in C_{60} is to surround the molecule with a chiral environment, e.g. forming a host-guest complex with cyclodextrins. Due to the large dimension of fullerene (diameter $\sim 7 \text{ \AA}$), only γ -CDx, the largest of the three cyclodextrins commonly used to this end, is able to form stable complexes with C_{60} . In fact, recently, the synthesis of such a stable complex with a 2:1 stoichiometry has been reported for the first time and the induced circular dichroism detected.⁸ In case of this kind of complexation, one can devise three mechanisms of generation of rotatory power: the mixing of electric and magnetic transition moments located on the guest (one electron mechanism), the coupling of electric moments placed one on the guest and the other on the host (dipole-dipole mechanism), and finally, the interaction between the electric moment of the guest and the magnetic moment of the host or vice versa (m - μ mechanism). In the case of cyclodextrin complexation of achiral guests, the second mechanism, governed by the interaction of the molecular electric dipole transition moments with those connecting the ground state to the high energy states of the macrocycle, appears the only effective one. As this term depends directly on the distance and on the angle between the dipole vectors involved, its calculation is very useful for investigating the structure of these supermolecules. To this aim a sequence of computational strategies was devised, starting from a Dynamic

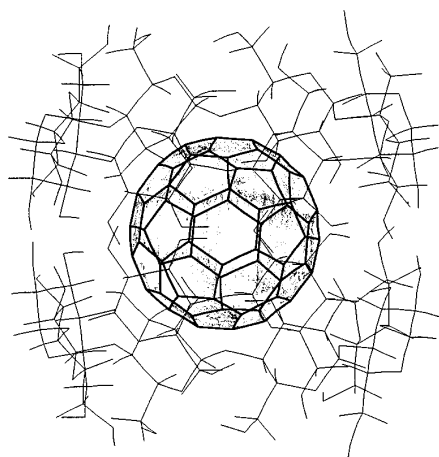


Figure 2. Low energy 1:2 complex of C_{60} and γ -CDx

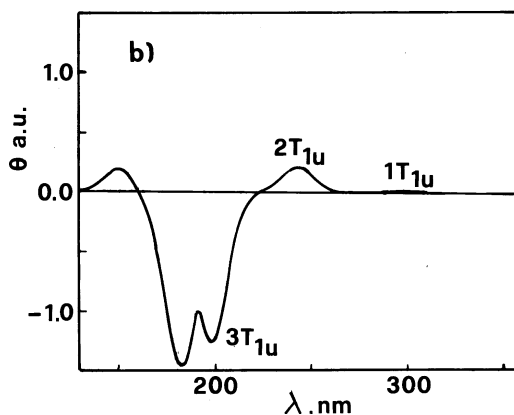
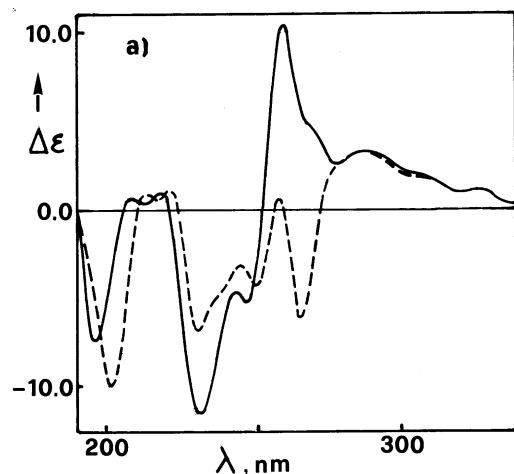


Figure 3a. Experimental ICD spectrum of the complex C_{60} - γ -CDx obtained in two different experimental conditions (see curves b and c of Figure 2 in Reference 8); 3b. calculated ICD spectrum for the complex of Figure 2.

Monte Carlo (DMC) procedure including solvent effects for the search of potential energy minima, followed by the calculation of the ICD within the Tinoco-Kirkwood framework⁹ in correspondence of the most stable structures found. This type of approach was recently applied to elucidate the complex geometry of several organic chromophores, like phenol and its derivatives, complexed by α and β cyclodextrins, and showed good correlation between structural and dynamic properties of these supermolecules and their photophysical and photochemical behavior.¹⁰ In the case of C_{60} + γ -CDx, the statistical treatment of the complexation pathway locates the lowest energy minima in correspondence of bicapped, symmetrical structures with the guest completely included within the cavity (Figure 2). The forces responsible for the stability of the complex are, in this case, the intermolecular hydrogen bonding between the adjacent secondary hydroxylic rims of the cyclodextrin unities, joined to a sizable Van der Waals host-guest interaction. The chirality induced in C_{60} by complexation in γ -CDx (Figure 3a) is revealed by a series of peaks corresponding to the three lowest permitted singlets, whereas no sizable optical activity is detected in the region of low-lying singlets below 2.3 eV⁸. The calculation (Figure 3b) reproduces the correct sequence of signs only for a few, very tight structures of the type displayed in Figure 2, although the rotatory power of the first permitted transition appears quite underestimated.¹¹ In particular, the largest positive band, corresponding to the second T_{1u} state at ~ 250 nm, is calculated with the right sign for very few low energy structures, whereas for looser or less symmetric complex geometries, the sign is calculated negative. This behavior is in agreement with the experimental results showing a negative peak in this region for looser, unstable complexes⁸ (dashed curve in Figure 3a), while tighter and more stable complexes obtained in more effective experimental conditions show a positive and large band in the same region (Figure 3a, solid curve). The conclusions reached for the structure of this complex are in full agreement with the results of an NMR analysis and show that the correct reproduction of the sign and size of the main bands of the ICD spectrum can be used to detect an effective molecular recognition.

Inclusion of Fullerene in a Magnetic Field: Magnetic Circular Dichroism (MCD)

The third approach used to make chiral the highly symmetric molecule of C_{60} is its inclusion in a magnetic field and the detection of the dichroism produced by the absorption of circularly polarized light. At variance with respect to the first method described above, where a chemical agent is used to induce a magnetic moment into the molecular eigenstates, in MCD the effect is purely physical, deriving from interaction of the electric field generated by the electrons of the molecule and the external magnetic field (Faraday effect).

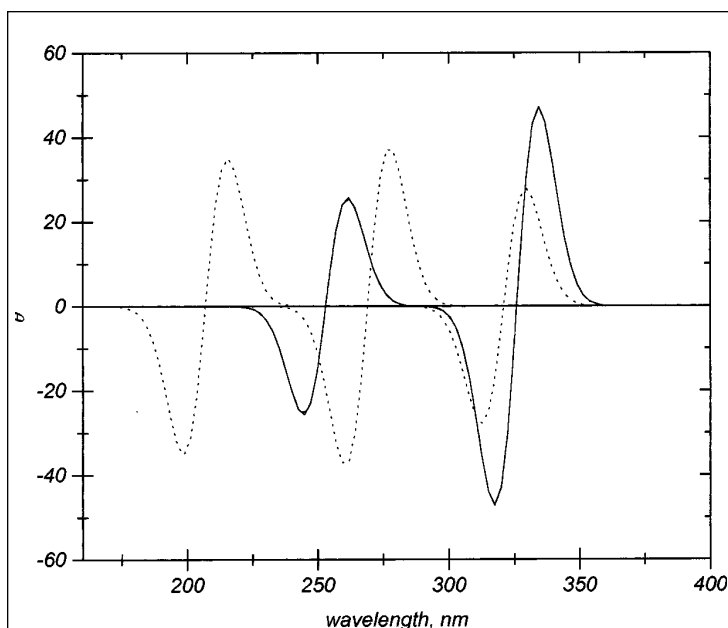


Figure 4. Experimental (solid curve, Reference 12) and calculated (dotted curve, only A terms reported) MCD spectrum of C_{60} .

For a closed shell molecule, an allowed transition in MCD can be characterized by two terms, A and B, the former pertinent to degenerate excited states and promptly recognized through its sigmoidal shape, and the second proper to all the excited states. The MCD spectrum of C_{60} , detected by Gasyna *et al.*¹² in Ar matrix at 5K, shows two intense bands dominated by A terms at 326 and 253 nm, in correspondence of the lowest absorbing states of T_{1u} symmetry. The calculation of the wavelengths of the lowest permitted states and of the relative magnitude of their A terms¹³ appears in fairly good agreement with the experiment (Figure 4). Particularly interesting is the optical activity shown by C_{60} in the region of ~ 600 nm, i.e. in a region with states forbidden by symmetry both electrically and magnetically. However some states can become permitted through vibronic coupling with the modes of suitable symmetry: a list of possible routes and vibrations involved in this process is reported in Reference 14. This spectral region includes also the state responsible for the vibronically induced fluorescence of this compound, a state of controversial attribution as far as the symmetry is concerned. In fact, at ~ 2.3 eV the calculations predict the presence

of three states of different symmetry, i.e. T_{1g} , T_{2g} and G_g . Calculation of vibronic activity of the modes in principle involved in the MCD spectrum, along with the evaluation of the magneto-optical constants pertinent to these states, and the good correspondence found for the modes detected in MCD and in fluorescence, indicate that the lowest state in C_{60} has T_{1g} symmetry and that the T_{1u} modes, particularly that of 1416 cm^{-1} , are the most active in inducing both dichroic absorption in a magnetic field and vibronically induced fluorescence.¹⁴

Conclusions

The study of fullerenes with all the implications of future development in material science or in biological chemistry cannot prescind from a detailed knowledge of the intimate electronic structure and from the knowledge of the properties of the excited states of these large carbon clusters. The study of circular dichroism, manifestation of an interplay of magnetic and electric properties of the molecular eigenstates, adds a number of pieces of information to those attained through conventional spectroscopy. We have shown that even for a very symmetric and achiral fullerene such as C_{60} one can obtain detailed information on these properties by inducing artificially a chiral response by means of physical or chemical devices. In the future, we plan to apply the same methodologies to the investigation of larger and more complicated fullerenes and fullero-derivatives of promising applicative interest.

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The Spectrum is a quarterly publication of the Center for Photochemical Sciences, Bowling Green State University, Bowling Green, OH 43403.

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