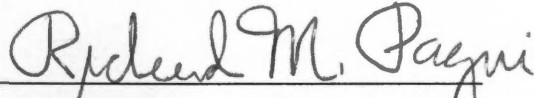
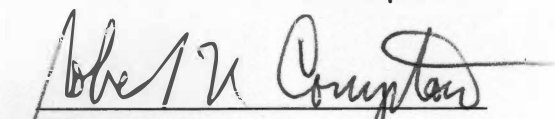


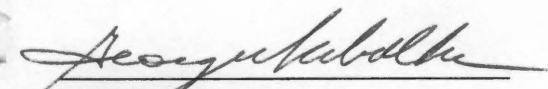
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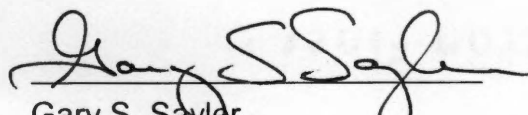
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PHOTOCHEMICAL REACTIONS OF OPTICALLY ACTIVE CHIRAL AND ACHIRAL ORGANIC MATERIALS

A Dissertation presented for the Doctor of Philosophy Degree

The University of Tennessee, Knoxville

Nicie Conley Murphy

December 2005

DEDICATION

The author wishes to dedicate this work to her parents, Gloria H. Curtis and Isaac L. Conley, Jr., and also to her wonderfully loving husband, Dexter D. Murphy. Without these individuals, this endeavor would not have come to fruition. Their encouragement, faith and love made this dream come true.

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ABSTRACT

Sodium chlorate, NaClO_3 , which crystallizes in the space group $P2_13$, forms optically active crystals upon crystallization although the molecule itself is achiral. NaClO_3 , has been shown to produce an asymmetric distribution of (+) and (-) crystals when crystallized from water while stirring. It has been discovered that beta or positron radiation can also induce asymmetric crystallization in NaClO_3 solutions. Like NaClO_3 , achiral 4,4'-dimethylchalcone crystallizes in enantiomeric forms in the space group $P2_13$. Kondepudi *et al.* provided evidence that stirred crystallizations of 4,4'-dimethylchalcone can induce a bimodal distribution of (+) and (-) crystals. The research presented in this dissertation offers results which show that beta radiolysis and linearly polarized and right- and left-circularly light also affect the crystallization of 4,4'-dimethylchalcone from ethyl acetate. These influences have been found to induce asymmetry in the crystals in unusual ways. The chirality of the crystals was determined via their reaction in water with pyridinium tribromide to yield the chiral compound 1,2-dibromo-4,4'-dimethylchalcone, thus allowing the chirality of the crystal to be propagated to molecular chirality. Benzil, and *N,N*-diisopropylbenzoylformamide are also achiral molecules that crystallize in the chiral space groups $P3_12_1$, and $P2_12_12_1$, respectively. It is possible with suitable reagents in water to convert the molecules in the crystals directly into chiral molecules. Only in the case of the chalcone, however, is asymmetric induction unequivocally observed.

Photoreactions initiated with circularly polarized light have been used for asymmetric synthesis, with mixed results. Reactions going through radical or ion pairs may offer a means to generate large enantiomeric excesses without degradation of the substrate. The photochemistry of racemic and resolved 2-iodooctane was previously studied by Gao *et al.* to give information on the dynamics of radical pair and ion pair intermediates as a function of solvent polarity and viscosity. By comparing the disappearance of the optically active substrate with its loss of optical activity, F , the fraction of the initially formed radical pair (RP) or ion pair (IP) resulting in product was determined for three solvents with differing polarities and viscosities. Gao *et al.* studied this effect in methanol, cyclopentane, 2-methyl-2-propanol and the gas phase. These F values will be valuable in assessing the photochemistry of 2-iodooctane in the same media with circularly polarized light.

So as to determine the full effect of polarity and viscosity on the photochemistry of 2-iodooctane, the results of an extension to this study are offered here. 2-Iodooctane was examined in acetonitrile and in aqueous acetonitrile solutions. The photochemistry of 2-deuterio-2-iodooctane was also studied. The photoreaction in acetonitrile occurred almost exclusively through heterolytic reactions with less than 1.6% occurring through homolytic reactions. A comparison of the disappearance of the optically active substrate with its loss of optical activity was done and F , the fraction of the initially formed radical pair or ion pair resulting in product, was determined for solvent mixtures. It was determined that reactions in non-polar solvents proceed via radical pairs while

reactions in more polar solvents proceed via either a mixture of ion pair and radical pair intermediates or exclusively through ion pairs. Reactions going through radical pairs have a greater tendency to escape the cage and react, thus larger F values are observed in these reactions. Viscosity does not correlate with the value of F , however. If the viscosity is high, fewer escape products are formed. Reactions in which the solvent polarity is high generate fewer escape products, have more intermediate returning to reactant, and have lower F values.

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Chapter I – Introduction

A. Chirality and Optical Activity

The terms chiral and chirality are common in modern chemistry. Chirality, meaning handedness, refers to the geometric property that is responsible for the nonidentity of an object with its mirror image.^[1] Two molecules that are mirror images of one another, but are not superimposable, are termed enantiomers. Such molecules lack symmetry elements such as a center, a plane, or an improper axis of symmetry and they share the common property of optical activity.^[1] Biot first formulated optical activity in 1812 after the observation by Arago (1811) that polarized light from the sun, upon passing through a quartz crystal, gave two solar images whose colors changed when the crystal rotated.^[2,3] Louis Pasteur (1848) linked molecular structure to optical activity while working with isostructural tartaric and racemic acids.^[3] He noticed that when in the form of tartaric acid, the natural product was optically active. Molecules that are optically active, have the ability to rotate the plane of monochromatic plane-polarized light. A collection of achiral molecules does not rotate light and is thus said to be optically inactive. Pasteur suggested correctly that the properties of the two crystalline forms also reflect the symmetry of the molecules themselves and that racemic acid was an equal mixture of the two molecular forms of tartaric acid.^[3] In Pasteur's experiments, the different isomers were identified by the direction in which they rotated plane-polarized light, but modern chemistry requires a more fundamental definition of configuration.^[3]

Jacobus Henricus van't Hoff and Joseph-Achille Le Bel (1874) independently proposed that carbon with four tetrahedrally disposed bonds could display handedness at the molecular level if the four bonds were to different atoms.^[3] Le Bel's theory also proposed that this concept could be extended to other atoms, and the formation of chiral compounds based on nitrogen, silicon, sulfur and phosphorus has verified his predictions. This new form of isomerism brought with it the problem of clearly designating the absolute configuration of the stereoisomer with which one is dealing. This problem involves the task of defining a standard orientation for the chiral center and describing a spatial relationship between the groups involved when the molecule is placed in the standard orientation. One of the first successful methods for designating the absolute configuration of chiral molecules was developed by Emil Fischer. The Fischer projection allowed the absolute configuration of many important molecules to be defined for the first time. By applying rules of sequence to the atoms based on atomic number, the Fischer projection allowed for the determination of a specific configuration of a molecule as D or L (see Figure 1-1). This two-dimensional representation of a three-dimensional molecule suffered in that it restricts the way in which comparisons between projections can be made. In a Fischer projection, all bonds are represented as horizontal or vertical lines and all horizontal bonds project forward. Therefore a Fischer projection cannot be rotated in the plane of the page as the orientation of bonds relative to one another can change, converting a molecule to its enantiomer. As the examples

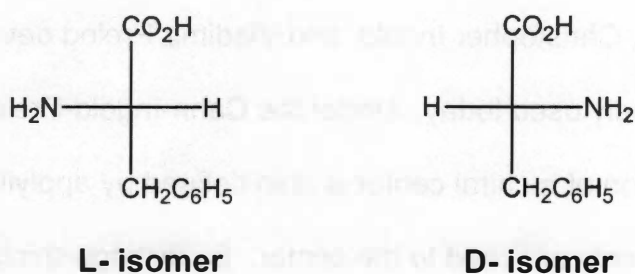


FIGURE 1-1 . Fischer Projections of Phenylalanine

of chiral molecules whose absolute configurations needed to be specified became more complex, the limitations of the Fisher system became more evident. R.S. Cahn, Christopher Ingold, and Vladimir Prelog developed the system that is routinely used today. Under the Cahn-Ingold-Prelog system, the absolute configuration of a chiral center is also defined by applying a series of rules to the substituents attached to the center. By distinguishing between the priorities of each atom attached to the stereocenter in the molecule, one can determine whether the stereochemistry there is *R* (Latin *rectus*, right) or *S* (Latin *sinister*, left). Any atom attached to the stereocenter has its own priority corresponding to its atomic number and thus allowing for comparisons. Not all chiral molecules possess chiral centers however, and the fact that the only requirement for chirality is that the molecule not be superimposable on its mirror image is often overlooked. There are several examples of chiral molecules for which the requirements of chirality are met without the presence of a chiral center. Each of the molecules in Figure 1-2 is chiral because the mirror symmetry of the molecule is broken. Based on the previous definition of chirality, each of these molecules will be able to rotate the plane of polarized light, thus rendering them optically active. Since the early experiments of Le Bel and Pasteur, there have been several attempts to explain how optical activity arises for a particular substance.^[2, 4, 5]

There are many molecules and objects in the physical world that are chiral. These examples range from items as simple as a glove designed to fit only one hand, to molecules as intricate as α -amino acids whose absolute configurations

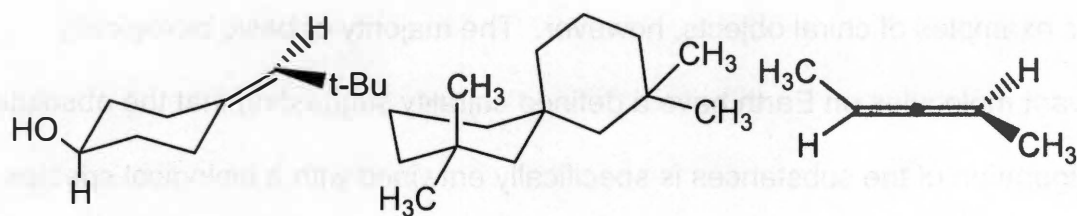


FIGURE 1-2. Examples of Chiral Molecules

are all the same. The applications of chiral research extend well beyond these basic examples of chiral objects, however. The majority of basic biologically relevant molecules on Earth have a defined chirality suggesting that the absolute configuration of the substances is specifically entwined with a biological species and with its molecular function. In many cases, molecules with the incorrect absolute configuration cannot even be digested, such as L-sugars or D-amino acids, and are therefore useless for human beings. Many pharmaceutical drugs display desired activity only as one of the two mirror-image forms. An opposing enantiomer is inactive and can be eliminated unmodified in a lucky situation. However some severe toxic effects are observed with the biologically “wrong” enantiomer. The drug thalidomide, shown in Figure 1-3, provides one of the most horrific examples of handedness being critical to function. While one form of the drug is a mild analgesic, the mirror image is a powerful teratogen, which results in babies being born without limbs. Sugars such as deoxyribose and ribose in DNA and RNA, respectively, that contain and transfer the genetic information are all right-handed and the 20 amino acids (except for glycine) that form the proteins that are essential for the structure and chemical transformations in cells also share a common relative configuration.^[6] The formation of enantiomerically enriched products from achiral precursors without the intervention of pre-existing optical activity is still a challenging opportunity for many scientists.

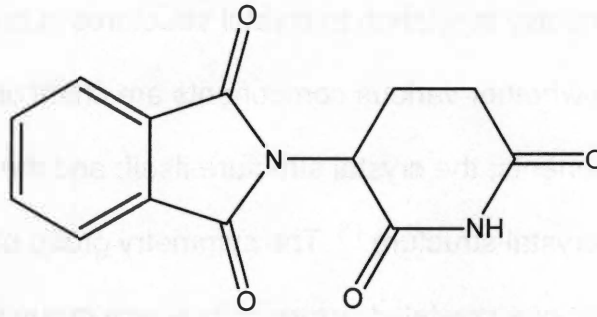


FIGURE 1-3. Molecular Structure of Thalidomide

In dealing with chirality in relation to crystal structures, it is essential to distinguish between whether various components are chiral or achiral, such as the molecular components; the crystal structure itself; and the symmetry group or space group of the crystal structure.^[7] The symmetry group of a molecule is its point group while that of a crystal structure is its space group.^[11] Molecules and crystals may be present in the form of mixtures. Enantiomeric mixtures of particular importance are those of compositions 100:0/R:S and 0:100/R:S and are described as enantiomerically pure. The equimolar composition of 50:50/R:S is described as racemic. By definition, all of the molecules in an enantiomeric mixture, be it enantiomerically pure, racemic, or of intermediate composition, are chiral. With regard to crystals, the solid-state mixture is characterized as having individual crystals that are enantiomerically pure, but the overall molecular composition of the crop is that of the racemate. The chirality sense of a molecule is specified by its absolute configuration.^[7] The chirality sense of a chiral crystal structure is specified by its absolute structure.^[7] For example, sodium chlorate (NaClO_3) is a compound whose individual ions are achiral; however, its crystals produced from an aqueous solution belong to the chiral space group $P2_13$ (see Figure 1-4).^[8, 9, 10] As a result, two types of crystals with enantiomeric lattices can be grown.^[9] Sodium chlorate crystals are isotropic which allows for the measurement of the optical activity of the crystal using traditional methods such as by polarimetry or carried out manually by using cross-polarizing paper. Optically active crystals have provided very useful environments for asymmetric synthesis, often yielding products with very high enantiomeric excesses (ee).

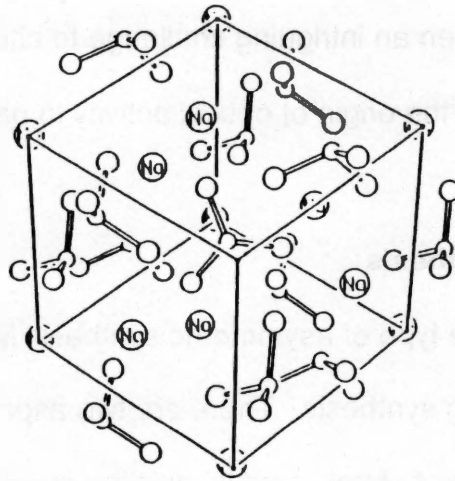


Figure 1-4. Unit Cell of Sodium Chlorate of the P2₁3 Space Group

Stereospecific solid-state chemical reactions of chiral crystals formed from achiral materials are defined as absolute asymmetric syntheses.^[1] Asymmetric synthesis starting from an achiral reagent, and in the absence of any external chiral agent, has long been an intriguing challenge to chemists and may also be central to the problem of the origin of optical activity in nature.

B. Asymmetric Synthesis

As mentioned, one type of asymmetric synthesis is the ability to control the chirality of crystals during synthesis. There are two aspects to this types of process: The generation of chiral crystals, and the chemically controlled solid-state reaction, which yields the chiral product. The chirality in solid-state asymmetric synthesis is introduced in the crystallization step; the chemical reaction then transforms the chirality of the crystal into that of the product. Chiral crystals, like any other asymmetric object, exist in two enantiomorphic equienergetic forms, but careful crystallization of the material can induce the entire ensemble of molecules to aggregate into one crystal of one handedness, presumably starting from a single nucleus.^[1, 13] In a typical crystallization, many enantiopure crystals of either kind grow, with their number and size reflecting the nature of nucleation and crystal growth. The resulting ee of the solid phase varies randomly. In this manner, a racemic liquid phase can be converted to a non-racemic solid phase.^[11] Processes that do not have a preference for the production of one or the other enantiomer can yet spontaneously produce a large excess of one of the two enantiomers. Crystallization depends on primary

nucleation, which occurs in two ways: heterogeneously, in which a foreign body such as a speck of dust in the solution induces crystallization of the solute, and homogeneously, where no foreign bodies induce crystallization.^[12] Primary nucleation seems to involve two events; an initial bringing together of solute molecules to form an amorphous-like droplet, which in the second step organizes itself into the crystallite.^[13, 14] If the first primary nucleating event yields a (+) crystal, an excess of (+) crystals in the dish is expected when crystallization is complete. Once the primary nucleus forms, it will generate more of the same kind of crystal by secondary nucleation, the formation of new crystal nuclei in the vicinity of the existing "parent" crystal.^[12, 13] Secondary nucleation can cause chiral autocatalysis.^[15, 16] In this process, the surface of a crystal in contact with fluid in motion generates new crystal nuclei.^[16] The primary and secondary nuclei, once formed, will continue to grow into larger crystals with the same chirality. Proliferation of crystals of a particular handedness must have the effect of suppressing the proliferation of crystals of opposite handedness, hence competition.^[16] The fidelity in which the secondary nucleation clones the parent crystal can be very high.^[17] Studies have shown, in the case of sodium chlorate, that only one in about two thousand secondary nuclei does not have the same structure as the parent crystal.^[17, 18] 1,1'-Binaphthyl, a chiral molecule shown in Figure 1-5, which forms chiral crystals, is an interesting case because it spontaneously resolves into homochiral crystals when crystallized in acetone, and forms racemic heterochiral crystals when crystallized from other solvents.^[13]

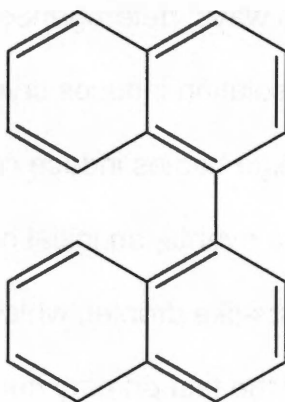


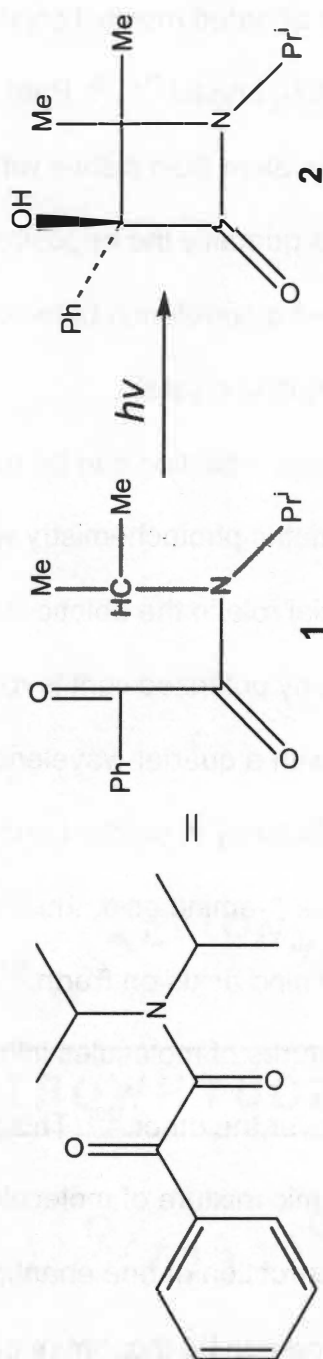
FIGURE 1-5. Molecular Structure of 1, 1'-Binaphthyl

Sodium chlorate, an example from the previous section, represents another interesting case. When crystallized from water, sodium chlorate yields large, well-formed colorless *d* and *l* crystals.^[13] When a sufficient number of crystallizations are performed, a 50:50 mixture of *d* and *l* crystals can be obtained.^[12, 13] Seeding aqueous sodium chlorate with either *d* or *l* sodium chlorate crystals yields *d* or *l* sodium chlorate crystals from the solution, respectively. It has been shown that stirring a sodium chlorate solution during crystallization yields either mostly *d* or *l* crystals, but the ee is approximately zero if the crystals from a large number of experiments are considered.^[12, 13, 16, 19] Since stirring is not a chiral perturbation, the direction of stirring is not correlated with the sign of the ee. Thus, in a given experiment one will obtain predominately *d* or *l* crystals, but one cannot predict which one of the crystals will predominate. This is an outcome of the fact that primary nucleation randomly gives a *d* or *l* crystallite. Secondary nucleation from the primary crystallite will ensure that the chirality of the initial crystal is maintained during the remainder of the crystallization. Chiral perturbations, however, may yield homochiral crystals in a controlled manner. D-Mannitol and D-sorbitol are polyhydroxy sugars derived from D-mannose and D-glucose, respectively. Crystallization of sodium chlorate from water containing the cosolute D-mannitol yields *d* NaClO₃ exclusively, while D-sorbitol has the opposite effect, yielding mostly *l* NaClO₃.^[13] Interestingly, the sugars D- and L- arabinose, and D-sucrose have no effect on the distribution of *d* and *l* sodium chlorate crystals.^[13]

Asymmetric synthesis can be realized in other ways as well. One can perturb the ee distribution of crystal growth using chiral particles.^[13] Spin-polarized electrons are generated in the beta decay of radioactive atoms.^[13] Beta particles are very energetic and mostly left-handed meaning that an observer would see the oncoming electrons spinning clockwise.^[13] This combination of translation and spin renders the electrons chiral. Positrons, or positively charged electrons, also resulting from radioactive decay, are also spin-polarized.^[13] Unlike beta particles, they are mostly right-handed. Beta particles have been shown to induce asymmetric crystallizations in a number of experiments. Akaboshi *et al.* found that irradiation of D- and L-alanine with internal or external beta radiation afforded an excess of radicals from the D enantiomer.^[13] Mahurin *et al.* discovered that when a room-temperature aqueous solution of NaClO₃ was exposed to beta particles from an Sr-90 source, NaClO₃ crystals were produced which were predominantly *d* with an ee of 32% (81% *d*, 19% *l*).^[12, 13] In a second set of experiments using a more energetic source of beta rays an overall ee of 47% was obtained (73.5% *d*, 26.5% *l*).^[12, 13] NaClO₃ crystallizations subjected to beta radiolysis had enantiomeric excesses of +100% four times more often than those with enantiomeric excesses of -100%.^[12, 13] The beta particles are approximately 80% left-handed and it has been rationalized that the more common left-handed electrons promote the preferential formation of (+) crystals, which then seed the solution to produce more of the same (+) crystals.^[13] By the same token, the less common right-handed electrons initiate the formation of (-) seed crystals. The details of how this result occurs are currently not known.

Mahurin *et al.* also found that NaClO₃ crystallizations subjected to positron exposure from a Na-22 source afforded mostly *l* crystals with an ee of 55% (77.5% *l*, 22.5% *d*) favoring the (-) crystal.^[12, 13] Petri dishes with 100% of the (-) were about four times more prevalent than dishes with 100% of the (+) crystals. The results with positrons were primarily the opposite of those obtained with beta particles. These results suggest a correlation between electron and positron helicity to the helicity of the resulting crystal.

Similarly, absolute asymmetric induction can be manipulated by photochemistry. Direct asymmetric photochemistry with circularly polarized light (CPL) may have played a crucial role in the abiotic synthesis of optically active molecules in nature.^[20] Circularly polarized light is readily generated from linearly polarized light in combination with a quarter wavelength plate. Photocyclization of **1** (see Figure 1-6) proceeds efficiently in sunlight and hydrolysis of the optically active **2** gives an optically active β -amino acid; thus possibly throwing light on the generation of optically active amino acids on Earth.^[21] It is well known that the photochemistry of racemic mixtures of molecules initiated with CPL can lead to an excess of one enantiomer over the other.^[20] This photochemistry can occur by photoequilibration of a racemic mixture of molecules without any loss of reactant or by the selective destruction of one enantiomer over the other.^[22] Photons moving in a straight line can be thought of as having right- or left-handed helicity and can thus also be called right- or left-circularly polarized light.^[32] These processes take advantage of the fact that the enantiomers have different absorptivities when exposed to left-circularly polarized light (LCPL) or

**FIGURE 1-6. Photocyclization of 1**

right-circularly polarized light (RCPL).^[22] These methods tend to have serious interferences, however. The first instance of asymmetric induction tends to generate low enantiomeric excesses because the differences in absorptivities are usually very small, while the sum of absorptivities is generally large.^[22] In the second case, very high enantiomeric excesses can be obtained but only at the expense of destroying most of the reactant. Only in the exceptional case where the difference in absorptivities is large is it possible to attain high ee's without too much of the reactant being consumed. There are several notable photoreactions in the literature initiated by CPL. Yuichi Shimizu studied the photochemistry of racemic tartaric acid with 351-nm CPL from a XeF excimer laser.^[23] Irradiation with RCPL led to a selective destruction of the L enantiomer, **8**, while concentration of the D enantiomer, **7**, changed little (see Figure 1-7).^[23] This led to a maximum enantiomeric excess of recovered tartaric acid of 7.5%. Irradiation with LCPL had essentially the opposite effect. These results revealed a clear correlation between enantioselection and the sense of the CPL.

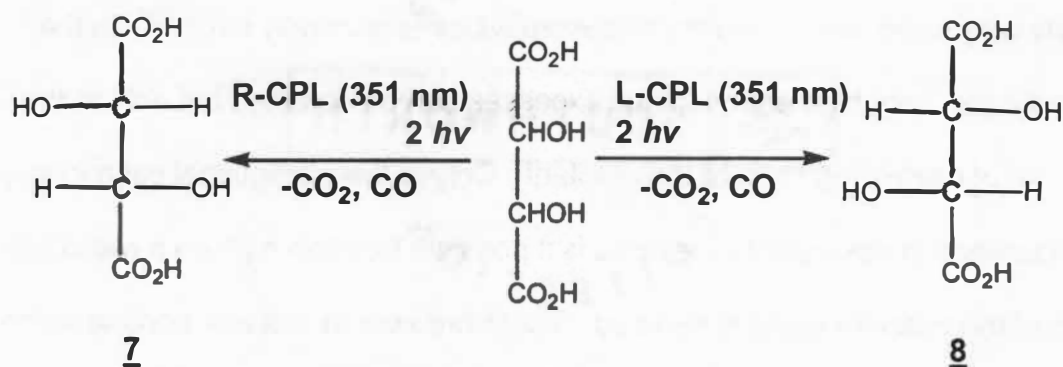


FIGURE 1-7. Racemic Tartaric Acid

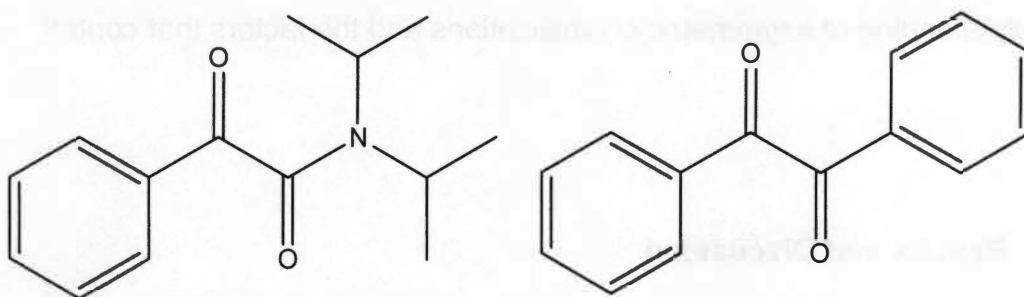
Chapter II – Asymmetric Crystallization of 4, 4'-Dimethylchalcone

A. Background

The study of the crystallization of achiral molecules that crystallize in chiral space groups is a topic of current interest and the manipulation of enantiomeric excesses in the same manner as those of the previous examples is of particular importance. Crystal enantiomeric excesses greater than 95% can easily be obtained in stirred crystallization of achiral compounds that crystallized in chiral forms such as with NaClO_3 .^[24] This phenomenon is not isolated; it can be expected to occur in all achiral compounds that crystallize in chiral forms. A stirred crystallization of chiral 1,1'-binaphthyl melt also spontaneously generates large enantiomeric excesses, often greater than 90%.^[17] These cases, however, are confined to the solid state in which the molecules in the crystal are achiral. To obtain molecular chiral asymmetry, Kondepudi *et al.* recognized that a procedure to convert the chirality of the crystal structure to molecular chirality would be necessary.^[24] This would be a means through which the crystal enantiomeric excesses of chiral crystals could be propagated through conversion of asymmetry of the crystalline state to that of molecules. Since optical activity of very small crystals is difficult to measure, especially if the crystals are not isotropic, a reaction which relates the crystal ee's of a crystalline powder to the ee of a molecule is useful because the latter could be readily measured using optical rotation.^[24] There are several ways in which chiral asymmetry present in a solid phase can be converted into molecular chirality. One way is through the chemical or photochemical conversion of chiral crystals into chiral molecules. In

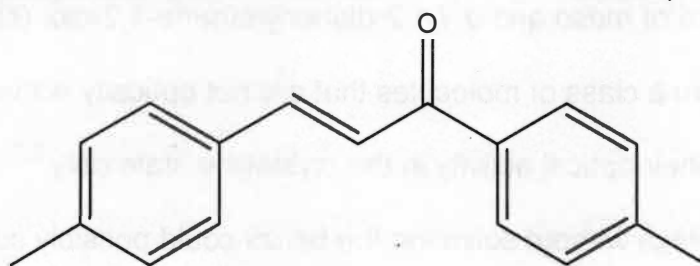
an attempt to discover new examples of crystal-to-molecule asymmetric induction, three cases were studied. Benzil, *N, N*-diisopropylbenzoylformamide, and 4,4'-dimethylchalcone, all shown in Figure 2-1, are achiral molecules that crystallize into enantiomeric forms of the chiral space groups $P3_12_1$ ^[25], $P2_12_12_1$ ^[1], and $P2_12_12_1$ ^[26] respectively. The crystals of these molecules are known to possess the property of birefringence, which is the double refraction of light when it is passed through the crystal. Because the crystals of these molecules are birefringent one cannot determine the optical activity by the traditional methods used in the case of NaClO_3 . The optical activity of these crystals has crystalline origin, and only a few exceptions such as camphor, are optically active in solution.^[27] A well-established procedure is to convert the molecules in the crystal directly into a chiral molecule using a suitable chemical reaction. A biphasic reaction will hopefully result in asymmetric induction, yielding an optically active molecule whose activity could be deduced by polarimetry.

Penzien and Schmidt contend that a gas-solid bromination of a single crystal of 4,4'-dimethylchalcone yields one of two possible enantiomorphous dibromides, thus achieving an asymmetric synthesis starting with optically inactive molecules.^[28] Using the method of Penzien and Schmidt, Kondepudi *et al.* found that spontaneous chiral symmetry breaking occurs in the stirred crystallizations of 4,4'-dimethylchalcone, as it does in the crystallization of NaClO_3 .^[24] These findings presented an opportunity to further study the spontaneous crystallization of 4,4'-dimethylchalcone in the manner of NaClO_3 . The investigations presented



***N*, *N*-Diisopropylbenzoylformamide, 3**

Benzil, 4



4, 4'-Dimethylchalcone, 5

FIGURE 2-1. Achiral Molecules from Chiral Space Groups

in this dissertation, and specifically in this chapter, are intended to provide a better understanding of asymmetric crystallizations and the factors that control them.

B. Results and Discussion

Commercially available, achiral **4** can easily be reduced in methanol to yield a diastereomeric mixture of *meso* and *d, l*-1,2-diphenylethane-1,2-diol (see Figure 2-2). Benzil belongs to a class of molecules that are not optically active in solution, but acquire their optical activity in the crystalline state only.^[27] A reduction that takes place without solvating the benzil could possibly succeed in transferring the optical activity of the crystal into that of the diol. When crystalline benzil is slurried with an aqueous solution of sodium borohydride, a rapid reaction ensues yielding the *meso* diol exclusively (see Figure 2-3 and 2-4). A comparison of the NMR spectrum of the product to published spectra of *meso* and racemic hydrobenzoin allowed for this determination. As the *meso* compound has no optical activity, this procedure cannot be used to convert the chirality of the benzil crystals into molecular chirality.

Next, **3** was examined. **3** is a crystalline solid prepared by the reaction of the acid chloride of benzoylformic acid with diisopropylamine (see Figure 2-5). When photolyzed it undergoes a Norrish II reaction to yield a chiral lactam, **9**, in high chemical and optical yields (see Figure 2-6).^[29, 30] In our hands, the photoreaction of the crystal proved to be very slow, and thus an alternate method of asymmetric induction was sought. When **3** was reduced with sodium

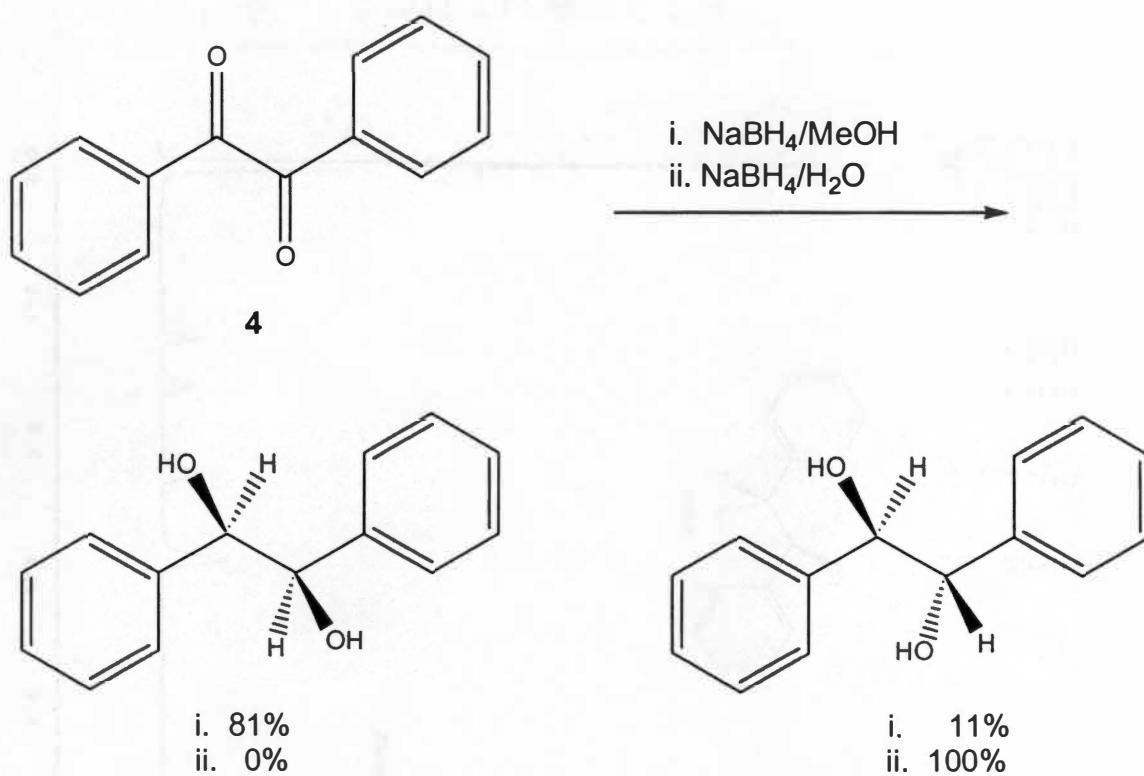


FIGURE 2-2. Reduction of Benzil, 4, in Methanol and Water

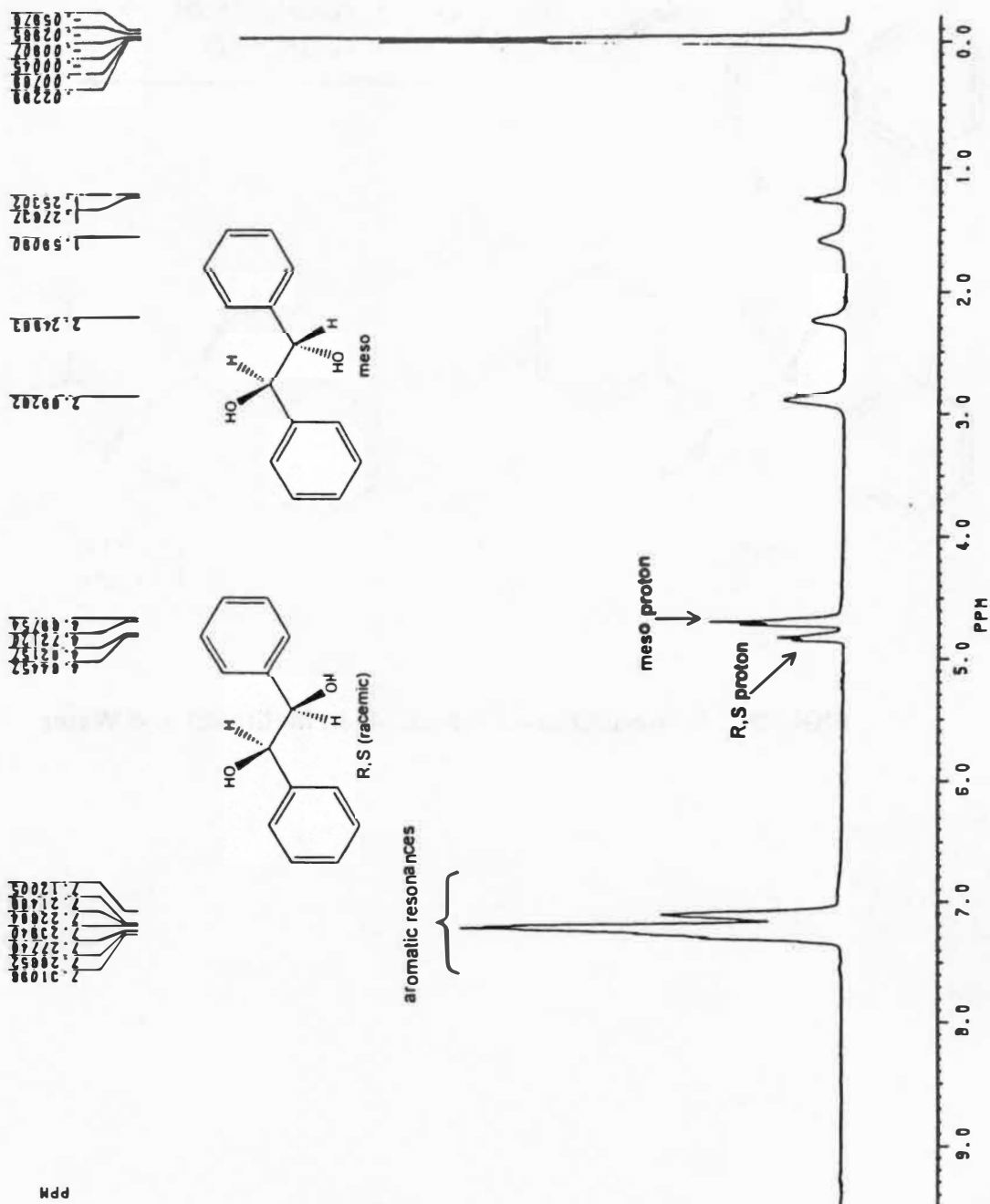


Figure 2-3. ^1H Proton NMR Spectrum of *Meso* and Racemic Hydrobenzoin from NaBH_4 Reduction in Methanol

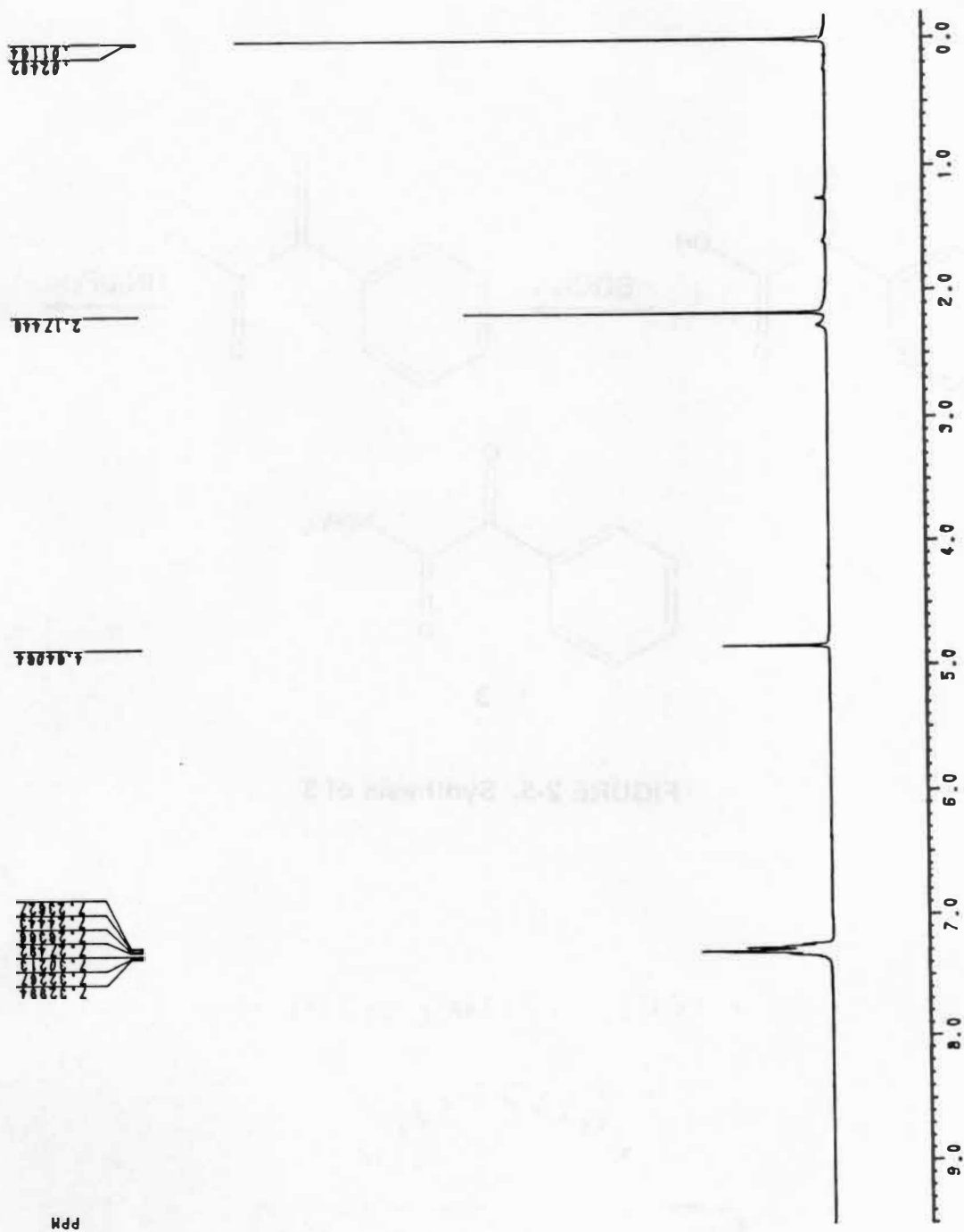


Figure 2-4. ^1H Proton NMR Spectrum of *Meso* Product from NaBH_4 Reduction in Water

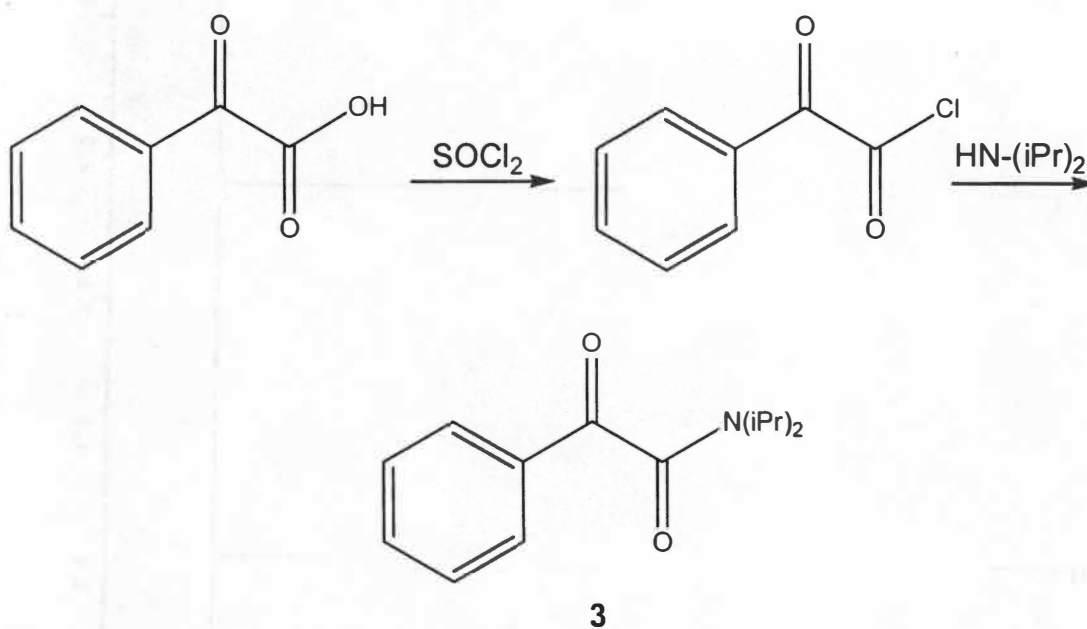


FIGURE 2-5. Synthesis of 3

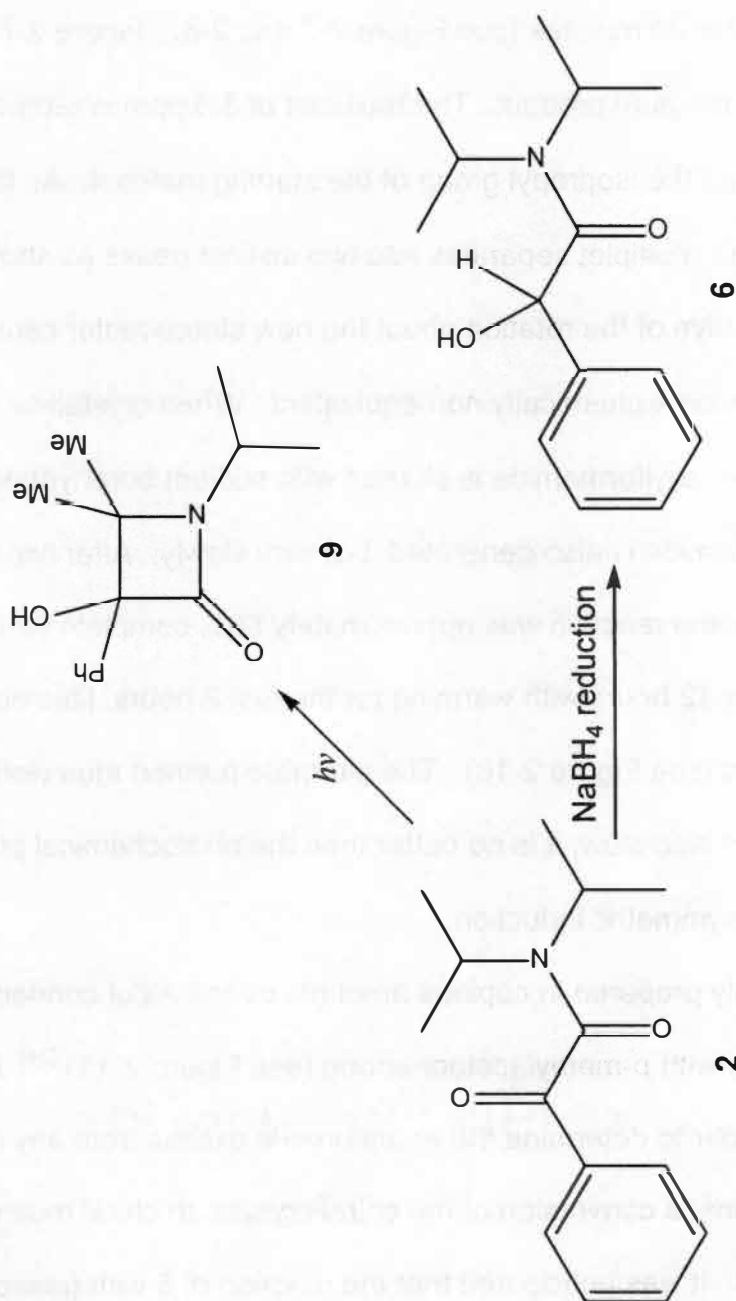


FIGURE 2-6. Photolysis and Reduction of 2

borohydride in methanol, chiral but racemic hydroxyformamide is generated in 90% yield after 20 minutes (see Figure 2-7 and 2-8). Figure 2-7 is the NMR spectrum of the pure product. The multiplet at 3.6 ppm is representative of the CH protons on the isopropyl group of the starting material. As the reaction proceeds, this multiplet separates into two distinct peaks as shown in Figure 2-8. This is indicative of the rotation about the new stereocenter causing the isopropyl groups to become chemically non-equivalent. When crystalline *N, N*-diisopropylbenzoylformamide is slurried with sodium borohydride in water, hydroxyformamide is also generated, but very slowly. After two hours at room temperature, the reaction was approximately 50% complete (see Figure 2-9). After another 12 hours with warming for the first 2 hours, little additional reaction had occurred (see Figure 2-10). The alternate method thus works but because its reaction is also slow, it is no better than the photochemical procedure as a method of asymmetric induction.

5 is readily prepared in copious amounts by the Aldol condensation of *p*-tolualdehyde with *p*-methylacetophenone (see Figure 2-11).^[24] As mentioned earlier, in order to determine the enantiomeric excess from any of the crystallizations, a conversion of the chiral crystals to chiral molecules must first be achieved. It was anticipated that the reaction of **5** with gaseous bromine as demonstrated by Penzien and Schmidt^[28] would accomplish this. However, all attempts to brominate the double bond of the chalcone using this procedure, resulted in a mixture of *erythro* and *threo* dibromides (see Figure 2-12, Figure 2-13 and Figure 2-14). The peaks located between 5.5-6.0 ppm in Figure 2-13 and

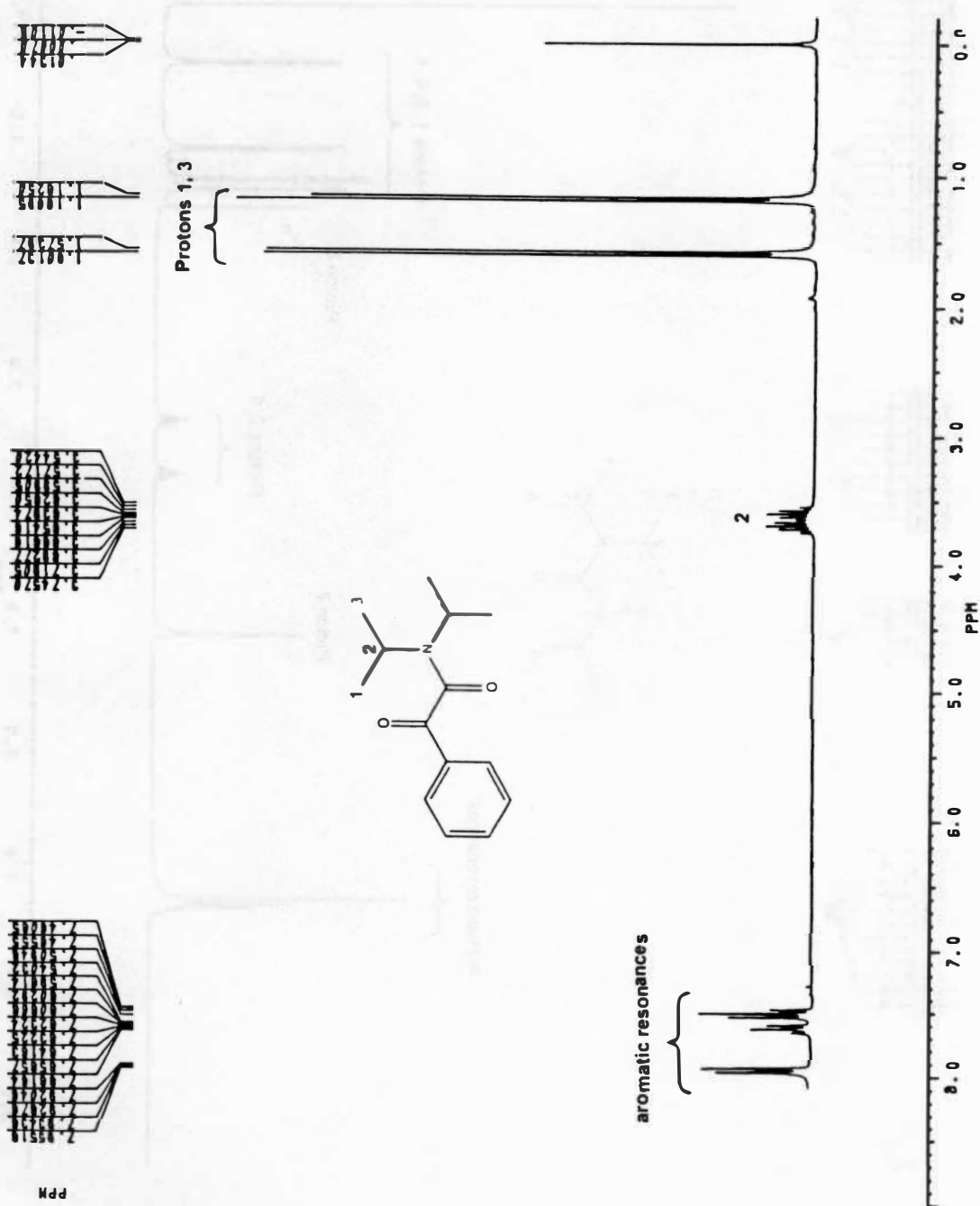


Figure 2-7. ^1H Proton NMR Spectrum of 3

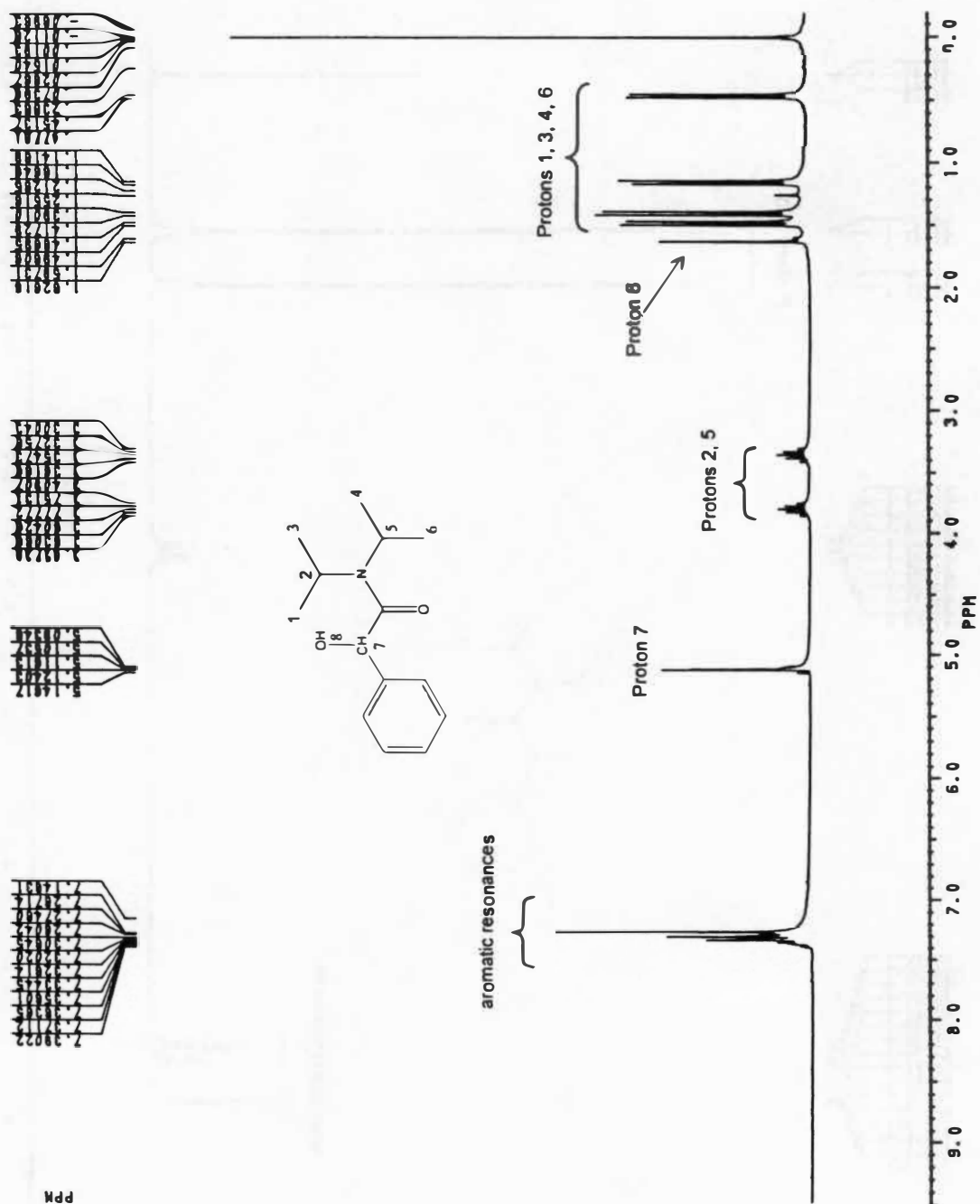
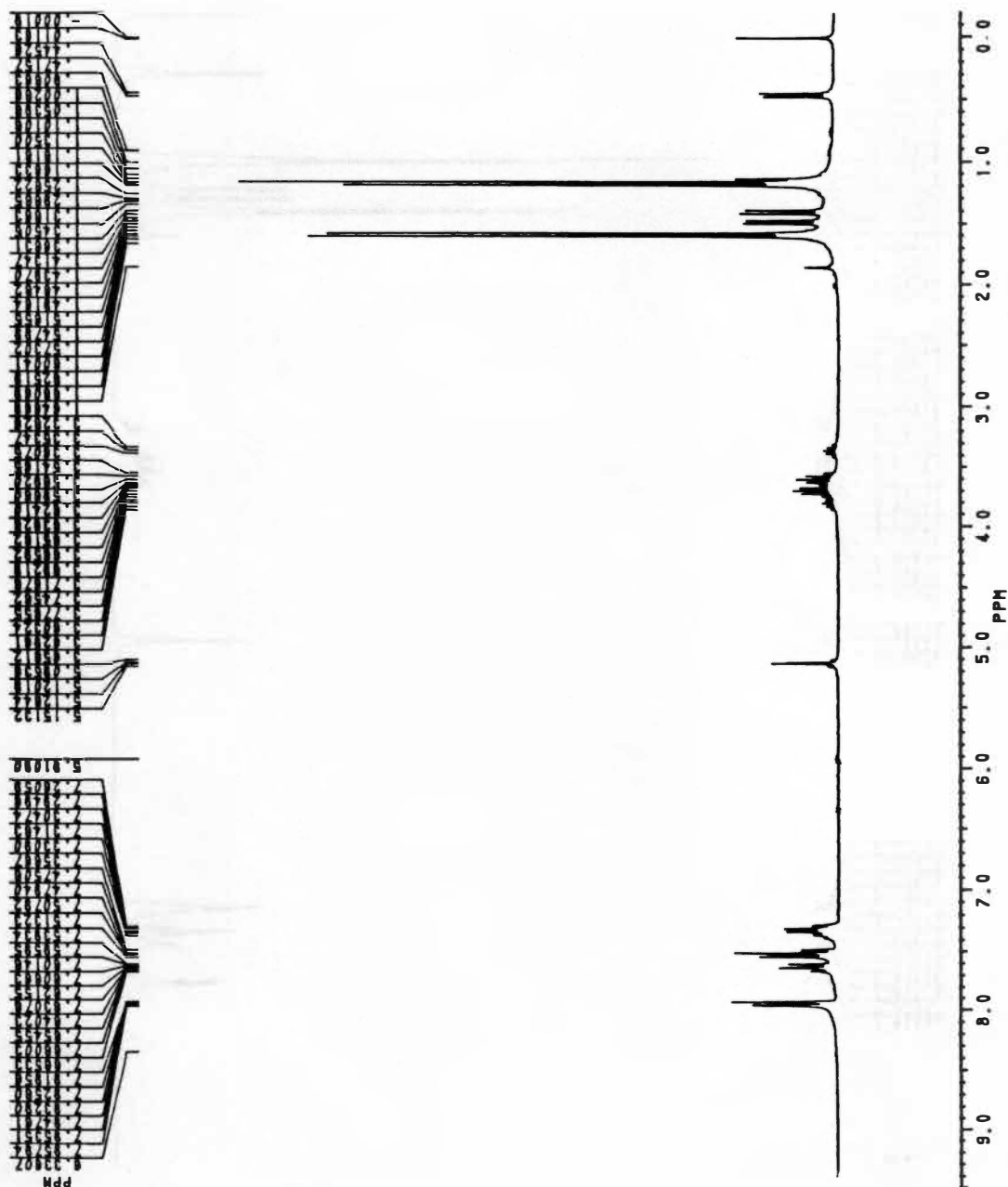


Figure 2-8. ^1H Proton NMR Spectrum of Product from Reduction of 3 in Methanol



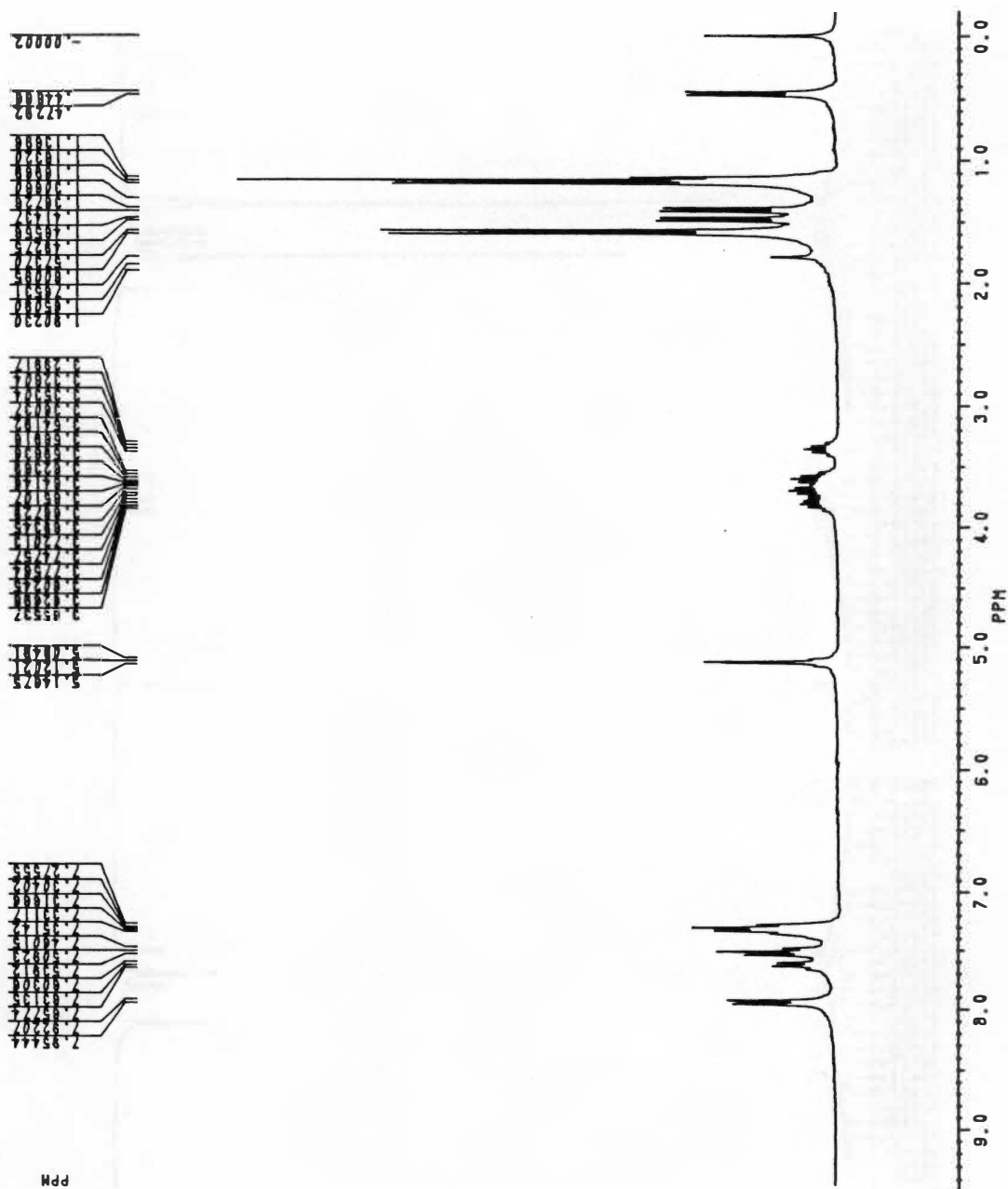


Figure 2-10. ^1H Proton NMR Spectrum of Product from Reduction of 3 after Additional 12 Hours with Warming

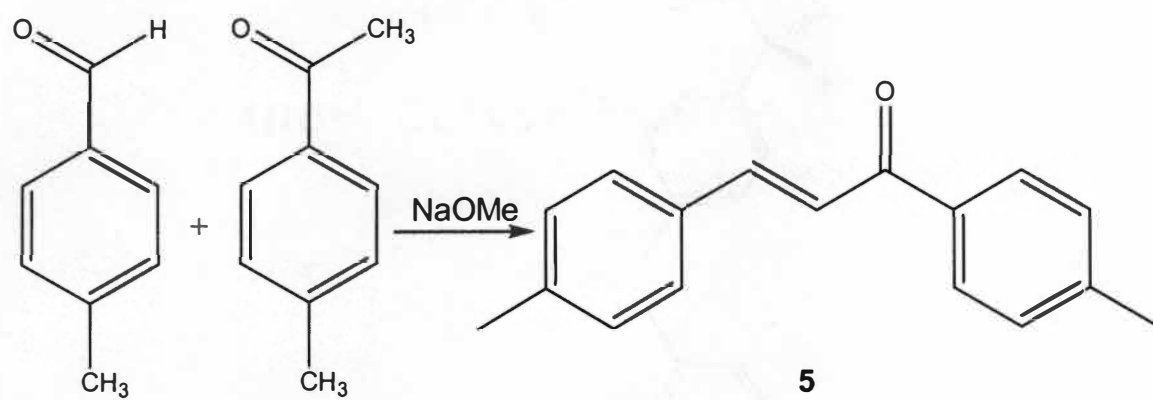


FIGURE 2-11. Synthesis of 5

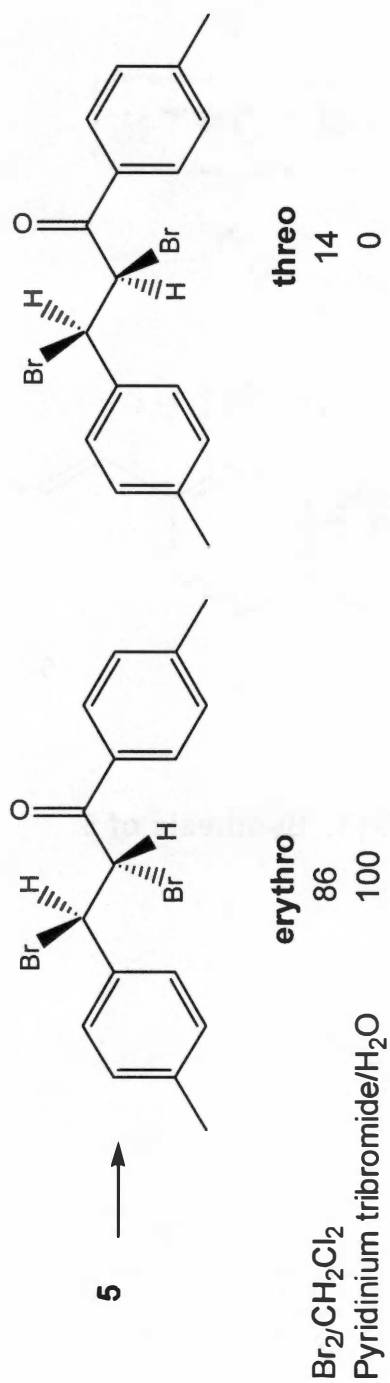


FIGURE 2-12. Bromination Reactions of 5

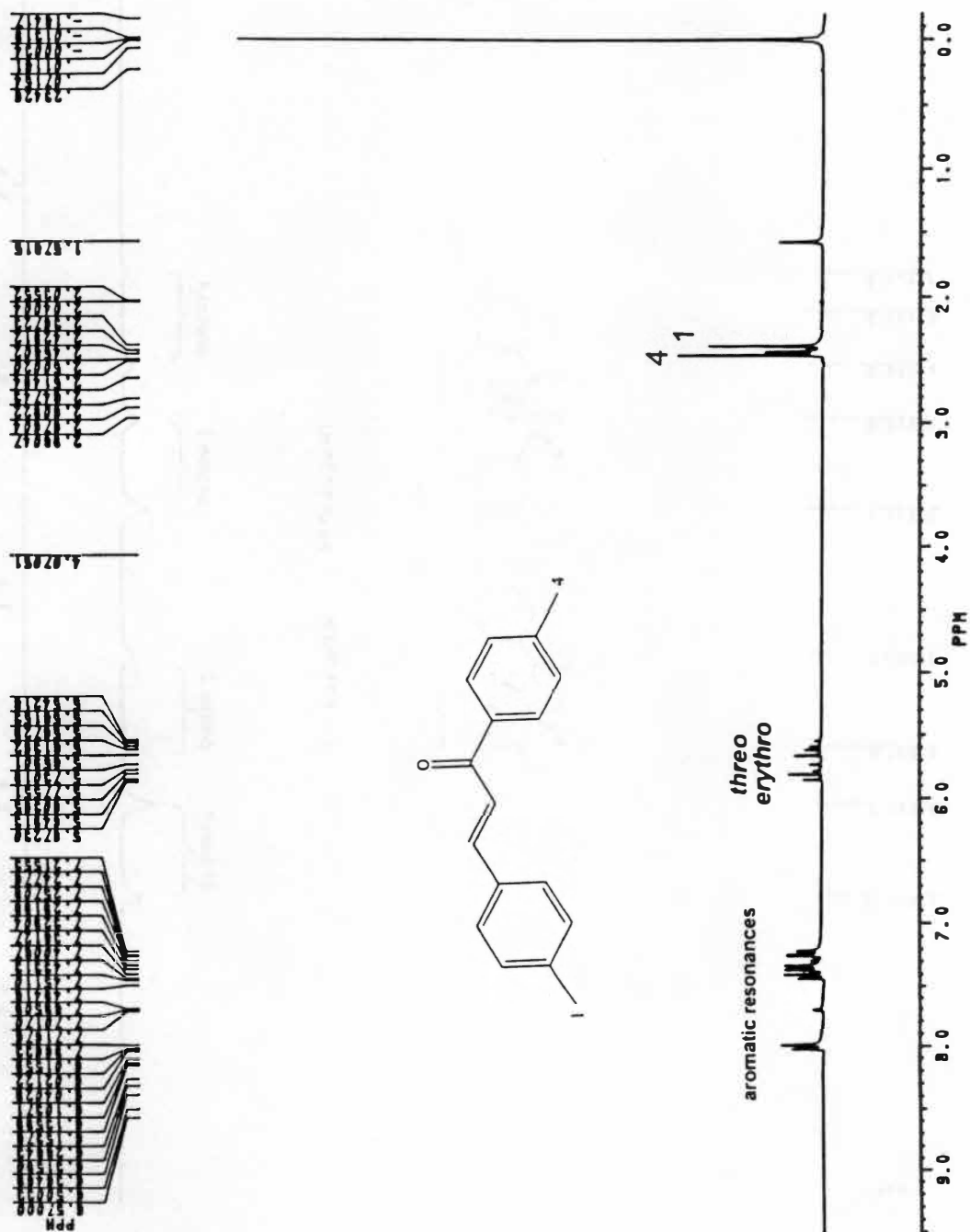


Figure 2-13. ^1H Proton NMR Spectrum of Brominated Product from Br_2 Reaction with Chalcone

Figure 2-14. Expanded Region of the ^1H Proton NMR Spectrum of Brominated Product from Br_2 Reaction with Chalcone

2-14 show the presence of the *erythro* and *threo* isomers in the reaction medium. As both forms may potentially contribute to the overall optical activity and unless that contribution is the same for each experiment, the results may not be interpretable. A more selective method employed by Toda *et al.* allowed for the bromination of the chalcone via a slurry in aqueous pyridinium tribromide where only the *erythro* dibromide from *anti* addition was formed (see Figure 2-15 and Figure 2-16).^[31] Since the crystals of 4,4'-dimethylchalcone are not isotropic, detecting the optical activity is not easy as it is in the case of sodium chlorate, however, the ee of the brominated chalcone will provide a method to estimate the ee of the crystalline phase of the chalcone.^[24]

Several types of crystallizations of 4,4'-dimethylchalcone were attempted so as to provide a basis of which types of perturbations induced chiral asymmetry and to determine the magnitude, if any, of the chiral induction. Crystals were grown by slow evaporation from ethyl acetate to dryness. The work of Kondepudi *et al.* was repeated with the stirred and unstirred crystallizations to provide a comparison to our work.^[24] Crystallization under beta particle conditions and crystallizations with intense linearly polarized light (LPL), RCPL and LCPL (1064nm) generated from a Nd-Yag laser were also examined. All crystallizations were completed using equimolar concentrations of ethyl acetate. Each experiment was compared using the specific rotation of the crystallized dibromide. Specific rotation, α , is easily calculated from the observed optical rotation using the formula $\alpha = \alpha_{\text{obs}} \div (l \times c)$ where α_{obs} is the observed optical rotation; l is the cell path length in dm; and c is the concentration in g/ml. A total

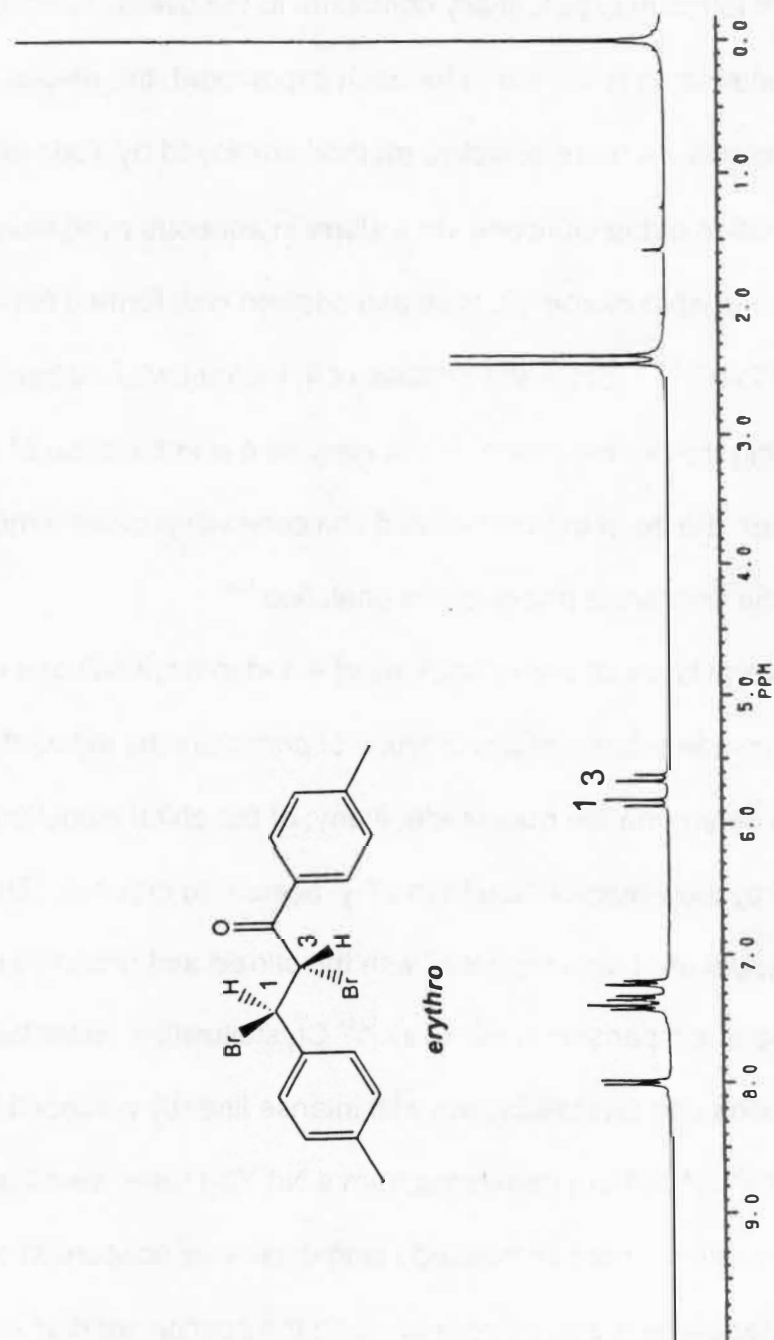


Figure 2-15. ¹H Proton NMR Spectrum of Brominated Product from Chalcone Slurry with Pyridinium Tribromide

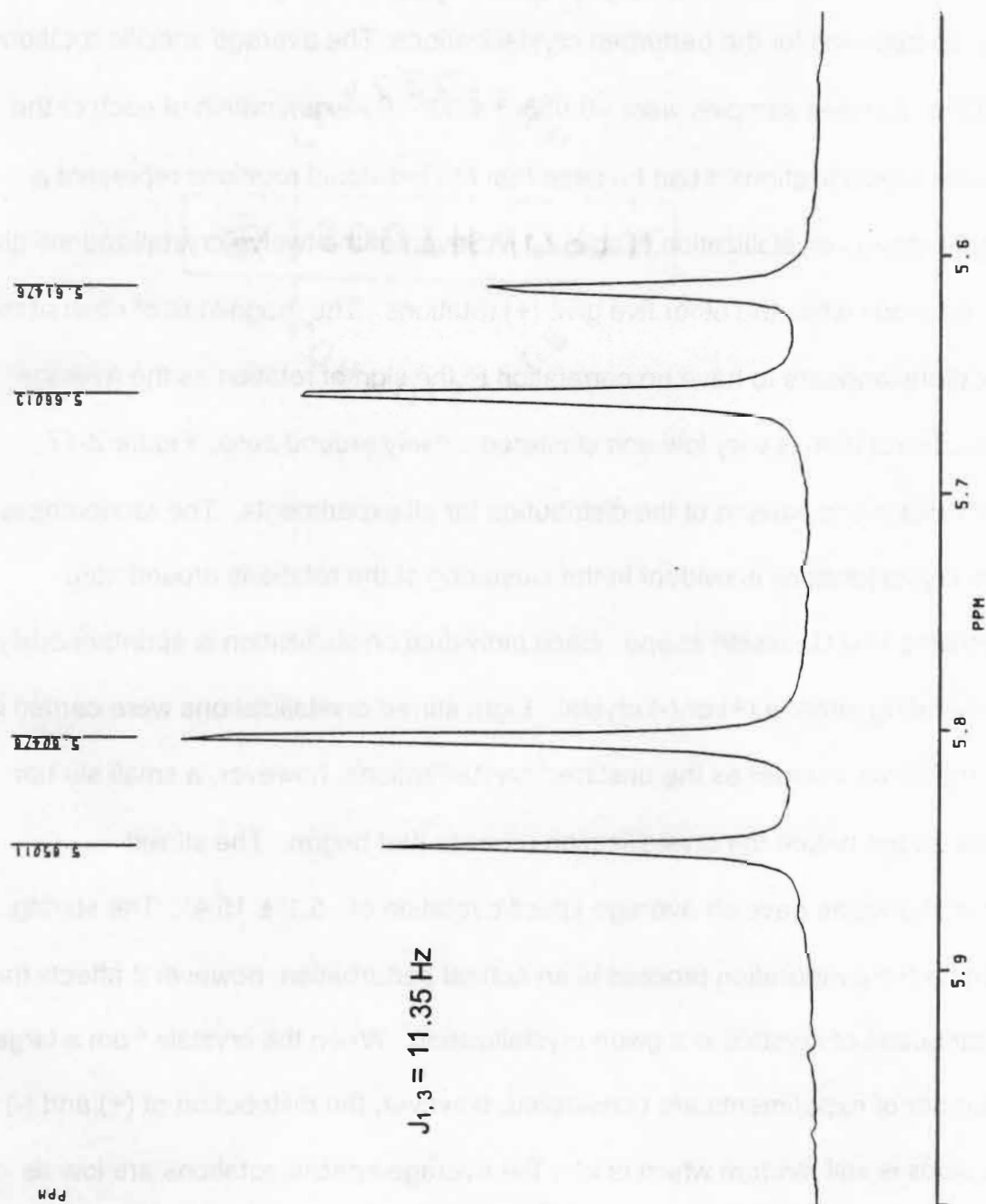


Figure 2-16. Expanded Region of ^1H Proton NMR Spectrum of Brominated Product from Chalcone Slurry with Pyridinium Tribromide

of twelve unstirred crystallizations were carried out. These experiments provide the comparison for the perturbed crystallizations. The average specific rotations for the unstirred samples were $-0.053^\circ \pm 4.60^\circ$. By examination of each of the twelve crystallizations it can be seen that the individual rotations represent a spontaneous crystallization (Table 2-1). Seven of the twelve crystallizations give (-) rotations while the other five give (+) rotations. The magnitude of each of the rotations appears to have no correlation to the sign of rotation as the average specific rotation is very low and clustered closely around zero. Figure 2-17 provides a comparison of the distribution for all experiments. The randomness of the crystallizations is evident in the clustering of the rotations around zero resulting in a Gaussian shape. Each individual crystallization is spontaneously generating either a (+) or (-) crystal. Eight stirred crystallizations were carried out in the same manner as the unstirred crystallizations; however, a small stir bar was added before the crystallization process had begun. The stirred crystallizations gave an average specific rotation of $-5.1^\circ \pm 15.4^\circ$. The stirring during the evaporation process is an achiral perturbation, however it affects the distribution of crystals in a given crystallization. When the crystals from a large number of experiments are considered, however, the distribution of (+) and (-) crystals is still random which is why the average specific rotations are low as compared to some of the individual values. The collision between the stir bar and the parent crystal does generate secondary nuclei.^[17] Stirred crystallization is an autocatalytic process that can result in chiral symmetry breaking with its

Table 2-1: Specific Rotations of Unstirred Crystallizations

Crystallization Number	Specific Rotation, α
Crystallization 1	-.50°
Crystallization 2	.20°
Crystallization 3	.89°
Crystallization 4	-4.7°
Crystallization 5	1.9°
Crystallization 6	10.3°
Crystallization 7	-3.4°
Crystallization 8	-8.4°
Crystallization 9	4.3°
Crystallization 10	-4.3°
Crystallization 11	-.89°
Crystallization 12	-.03°

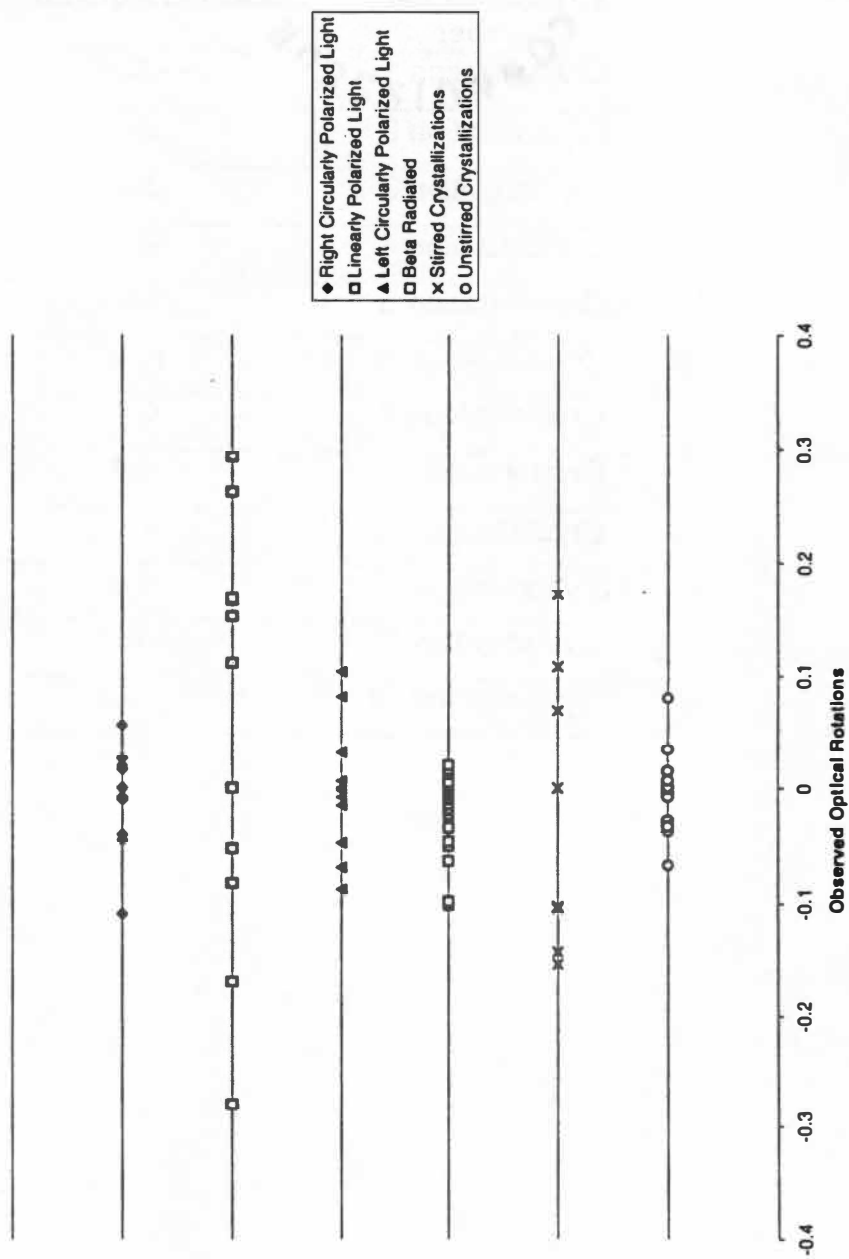


Figure 2-17. α Observed Distribution Chart for all Crystallization Experiments

characteristic bimodal distribution of crystal ee.^[17] Due to rapid secondary nucleation, the heat released may increase the temperature a little and decrease the primary nucleation rate thus decreasing the probability of generating new crystals through primary nucleation. Such suppression of primary nucleation by autocatalytic secondary nucleation will enhance the chances for a single crystal and its secondary nuclei to dominate the system and result in larger ee's. The largest rotation in magnitude regardless of sign for the stirred experiment was 21.8° as shown in Table 2-2. A comparison of the two experiments, show that the rotations for the stirred crystallizations have an increased bifurcation. The bimodal distribution of optical activity indicates that the occurrence of zero optical activity is a rare event, unlike the unstirred crystallizations and similar to those of sodium chlorate. These results are comparable to the work of Kondepudi *et al.*^[16, 24]

4,4'-Dimethylchalcone was crystallized also while being subjected to beta particles from an Sr-90 source. The beta particles were found to influence the rotations less significantly than the stirred crystallizations but had more of an affect on the crystallizations than if there were no perturbations. Twenty-eight crystallizations in the presence of beta particles afforded an average specific rotation of $-0.80^\circ \pm 5.16^\circ$ (see Table 2-3). The bifurcation here is less pronounced than what was observed in the stirred experiment, nevertheless, it affects the rotations more significantly than if there are no perturbations whatsoever. Thus, beta particles do not affect the enantiomeric excess of primary nucleation when averaged over many crystallizations. Beta particles do have an effect on the

Table 2-2: Specific Rotations of Stirred Crystallizations

Crystallization Number	Specific Rotation, α
Crystallization 1	-19.4°
Crystallization 2	-18.0°
Crystallization 3	8.7°
Crystallization 4	13.7°
Crystallization 5	21.8°
Crystallization 6	-13.2°
Crystallization 7	-12.9°
Crystallization 8	-13.0°
Crystallization 9	-13.2°

**Table 2-3: Specific Rotations for
Beta Radiation Crystallizations**

Crystallization Number	Specific Rotation, α
Crystallization 1	.63°
Crystallization 2	2.0°
Crystallization 3	-2.4°
Crystallization 4	-4.3°
Crystallization 5	1.8°
Crystallization 6	-1.0°
Crystallization 7	1.9°
Crystallization 8	-.89°
Crystallization 9	-2.9°
Crystallization 10	-1.8°
Crystallization 11	2.5°
Crystallization 12	1.8°
Crystallization 13	-8.0°
Crystallization 14	1.5°
Crystallization 15	-1.3°
Crystallization 16	-.63°
Crystallization 17	-6.3°
Crystallization 18	13.5°
Crystallization 19	-.25°
Crystallization 20	6.0°
Crystallization 21	-12.8°
Crystallization 22	-12.4°
Crystallization 23	-.58°
Crystallization 24	-2.3°
Crystallization 25	-2.9°
Crystallization 26	.38°
Crystallization 27	2.7°
Crystallization 28	3.5°

crystallizations in another way. As mentioned in the previous chapter, beta particles are very energetic. The Sr-90 source used generated 1.523×10^9 disintegrations per second with a particle energy of 0.546 MeV. The apparatus for the beta particle experiments is shown in Figure 2-18. When they impinge on the crystallizing medium, a complex chemistry is initiated and heat is dumped into the medium. Convection currents are created in the liquid, which facilitates secondary nucleation, similar to what is observed with stirring. Thermal stirring of the solution by the slowing down of beta particles is surely occurring and can act to propagate initial chiral bias initiated by the beta particles. It has also been proposed that the excess of L-electrons produced by beta decay emit left-handed electromagnetic radiation and this could cause the preferential decomposition of one stereoisomer in a racemate and leave a net excess of its enantiomer.^[6] It is necessary to note that the distribution of beta particle crystallizations is Gaussian as shown by Figure 2-17, however, the rotations center more to the left of zero unlike the stirred and unstirred crystallizations which center close to zero. This could be characteristic of the left-handed spin of the electrons emitted during the beta decay.

Crystallizations were next performed by photolysis under a 1064 nm Nd-Yag laser emitting linearly polarized light as well as crystallizations under left- and right-circularly polarized light. For each of these experiments, ten crystallizations were carried out. LCPL and RCPL influenced the optical activity of the chalcone crystal very little as compared to the stirred crystallizations. The average specific rotations from the data in Table 2-4 and Table 2-5 for the LCPL and RCPL

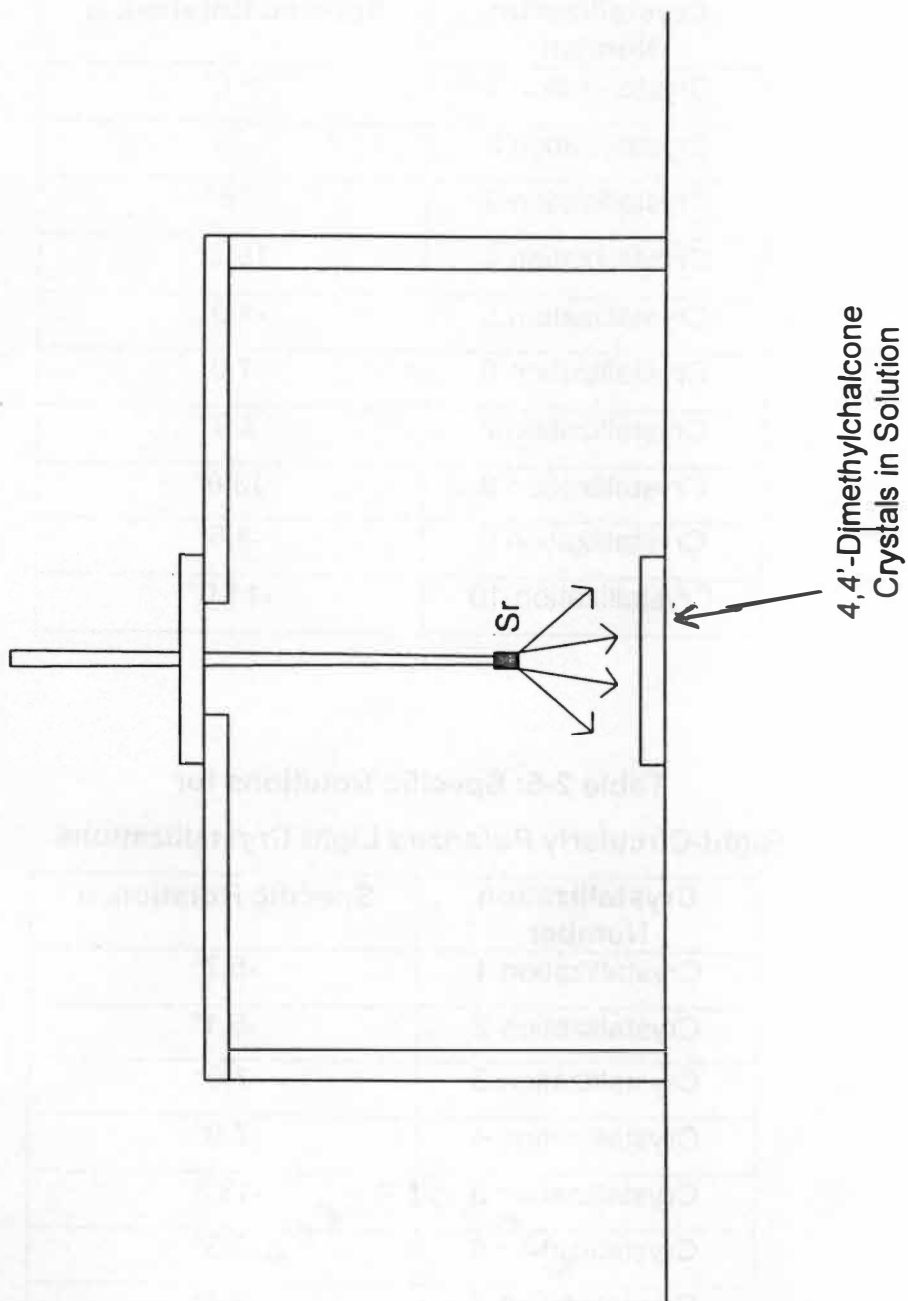


Figure 2-18. Apparatus for Beta Radiolysis Experiments

**Table 2-4: Specific Rotations for
Left-Circularly Polarized Light Crystallizations**

Crystallization Number	Specific Rotation, α
Crystallization 1	-6.0°
Crystallization 2	-.25°
Crystallization 3	.76°
Crystallization 4	10.3°
Crystallization 5	-1.9°
Crystallization 6	-1.0°
Crystallization 7	3.9°
Crystallization 8	13.0°
Crystallization 9	-8.6°
Crystallization 10	-11.0°

**Table 2-5: Specific Rotations for
Right-Circularly Polarized Light Crystallizations**

Crystallization Number	Specific Rotation, α
Crystallization 1	-5.7°
Crystallization 2	-5.1°
Crystallization 3	7.0°
Crystallization 4	7.0°
Crystallization 5	-13.8°
Crystallization 6	3.3°
Crystallization 7	2.4°
Crystallization 8	-1.3°
Crystallization 9	-1.0°
Crystallization 10	2.0°

crystallizations were $-0.08^{\circ} \pm 7.65^{\circ}$ and $-0.52^{\circ} \pm 6.38^{\circ}$ respectively. The distribution for the LCPL crystallizations are very similar to the unstirred crystallizations while the RCPL experiment is comparable to the results of the beta experiments. LCPL and unstirred crystallizations had distributions that centered at zero. However, the beta particle radiation experiment along with the RCPL experiment had distributions that leaned more to the left of zero indicating that the pattern may not be random or spontaneous for an individual crystallization. The stirred crystallizations resulted in larger specific rotations that were more bifurcated and thus the effect that stirring had on the crystallizing media was greater than that for both the LCPL and RCPL.

Most excitingly, linearly polarized light created a substantial effect on the specific rotations of the dibromide crystals. The specific rotations for this experiment are listed in Table 2-6. The specific rotation of greatest magnitude for LPL was 37.1° . This rotation is 30% larger in magnitude than the greatest in magnitude for the stirred experiments. The average specific rotation for these experiments were $7.2^{\circ} \pm 24.3^{\circ}$. As with the stirred experiments there is a bimodal distribution, however, the bifurcation is much larger. Stirring introduces chirally autocatalytic secondary nucleation that is able to amplify small initial asymmetry in the number of (+) and (-) crystals. A tentative assumption is that linearly polarized light encourages a similar process. Linearly polarized light results when there is a definite relationship between left- and right- circularly polarized beams.^[32] When LPL passes through a sample of resolved enantiomers, one component of the CPL may exhibit a greater or lesser speed

**Table 2-6: Specific Rotations for
Linearly Polarized Light Crystallizations**

Crystallization Number	Specific Rotation, α
Crystallization 1	-35.6°
Crystallization 2	37.1°
Crystallization 3	33.3°
Crystallization 4	21.3°
Crystallization 5	-21.4°
Crystallization 6	-6.6°
Crystallization 7	21.0°
Crystallization 8	19.2°
Crystallization 9	14.1°
Crystallization 10	-10.4°

than the other component.^[32] This difference gives rise to optical activity.^[32] The reason why RCPL and LCPL do not independently induce this effect cannot be explained by this theory, however. A more substantial theory to support the results of these experiments is based on the fact that linear and circular polarization both have been shown to have the opposite effect on the alignment of molecules.^[33] Garetz *et al.* discovered that upon inducing the nucleation of crystals of urea, they tended to be aligned with their needle axes parallel to the electric field direction of the LPL pulses.^[33] He suggested that this phenomenon was caused by the optical Kerr effect: The interaction between the electric field of light and the anisotropic polarizability of urea molecules causing them to align in the direction of the field.^[33] He further identified that for rod-like polarizability, LPL induces the molecules to align with their rod axes parallel to the applied field (arbitrarily called plane *z*), while CPL induces molecules to align with their rod axes in a perpendicular plane (arbitrarily called plane *xy*) (see Figure 2-19).^[33] For disk-like polarizability, LPL aligns the molecules with their disk axes perpendicular to the applied field, in the *xy* plane, while CPL aligns molecules with their disk axes parallel in the *z* direction, which is perpendicular to the *xy* plane.^[33] Thus linearly polarized fields are most effective in aligning molecules with rod-like polarizabilities, while circularly polarized fields are most effective in aligning molecules with disk-like polarizabilities.^[33] Rabinovich *et al.* determined using x-ray crystallography that the packing arrangement of 4, 4'-dimethylchalcone lies along a vertical axis (see Figure 2-20).^[34] Based on his results, the chalcone has a preference for rod-like alignment. Our own

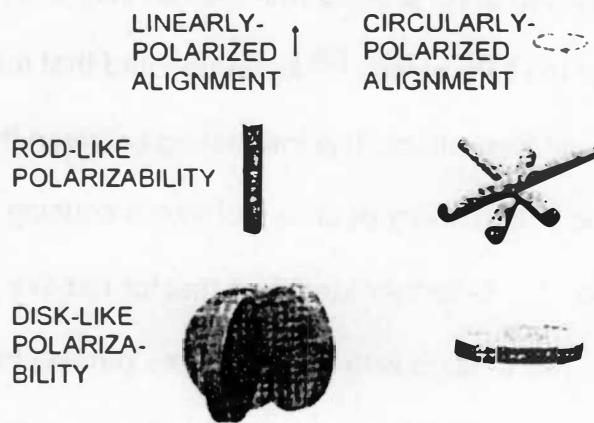


Figure 2-19. Types of Alignment for Polarized Light

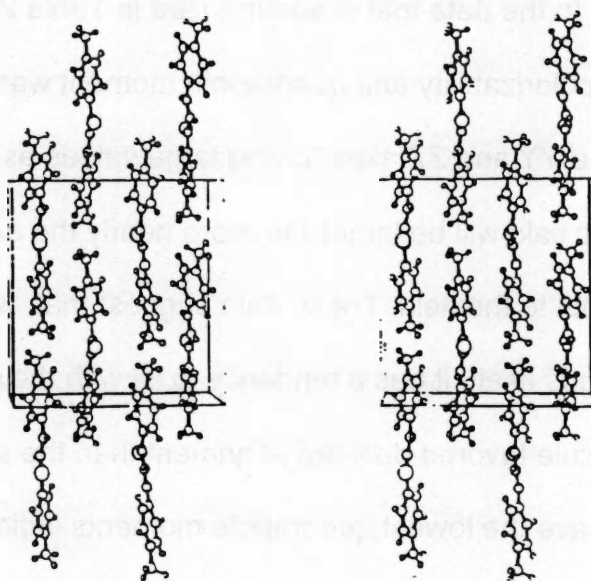


Figure 2-20. Packing Arrangement of 4, 4'-Dimethylchalcone

polarizability calculations were also done on 4,4'-dimethylchalcone so as to determine whether the molecule did in fact have preferential alignment and, if so, along which axis did it prefer to align. Based on the data collected, 4,4'-dimethylchalcone does indeed have a preference for how its crystals are arranged. According to the data that is summarized in Table 2-7, the plane in which the maximum polarizability and quadrupole moment was obtained was along axis XX with the YY and ZZ axes having large values as well. The moment induced by an electric field will be larger the more nearly the axes of greater polarizability lie parallel to the field. These data suggest that, when 4,4'-dimethylchalcone aligns itself, it has a tendency to lie with the plane parallel to the field. If the molecule favored disk-like alignment then the axes with highest polarizability would have the lowest quadrupole moments indicating that the molecule would have a greater propensity to align itself in a perpendicular plane. Thus it was confirmed that the chalcone was predisposed to align rod-like. Figure 2-21 shows the molecular orientation of 4,4'-Dimethylchalcone, from the calculations from Table 2-7, as it relates to the electric field. Based on these results a greater effect from LPL but not CPL can be explained. CPL causes a more random primary crystallite to form as it is not as effective at aligning the molecule in its preferred arrangement. The chalcone crystals prefer to align vertically therefore, upon photolysis with LPL, the first primary crystallite that is made will likely be less spontaneous causing greater enantiomeric excesses as a result.

TABLE 2-7: Polarizability Results of 4, 4'-Dimethylchalcone

Axis	Quadrupole Moment	Polarizability
XX	-77.2731	304.029
XY	-4.8091	-1.960
YY	-108.1762	175.799
XZ	1.3455	6.348
ZZ	-114.6497	81.606
YZ	.0188	-.004

Dipole Moment: X= -1.0079 Y= -3.8478 Z= 0.0644

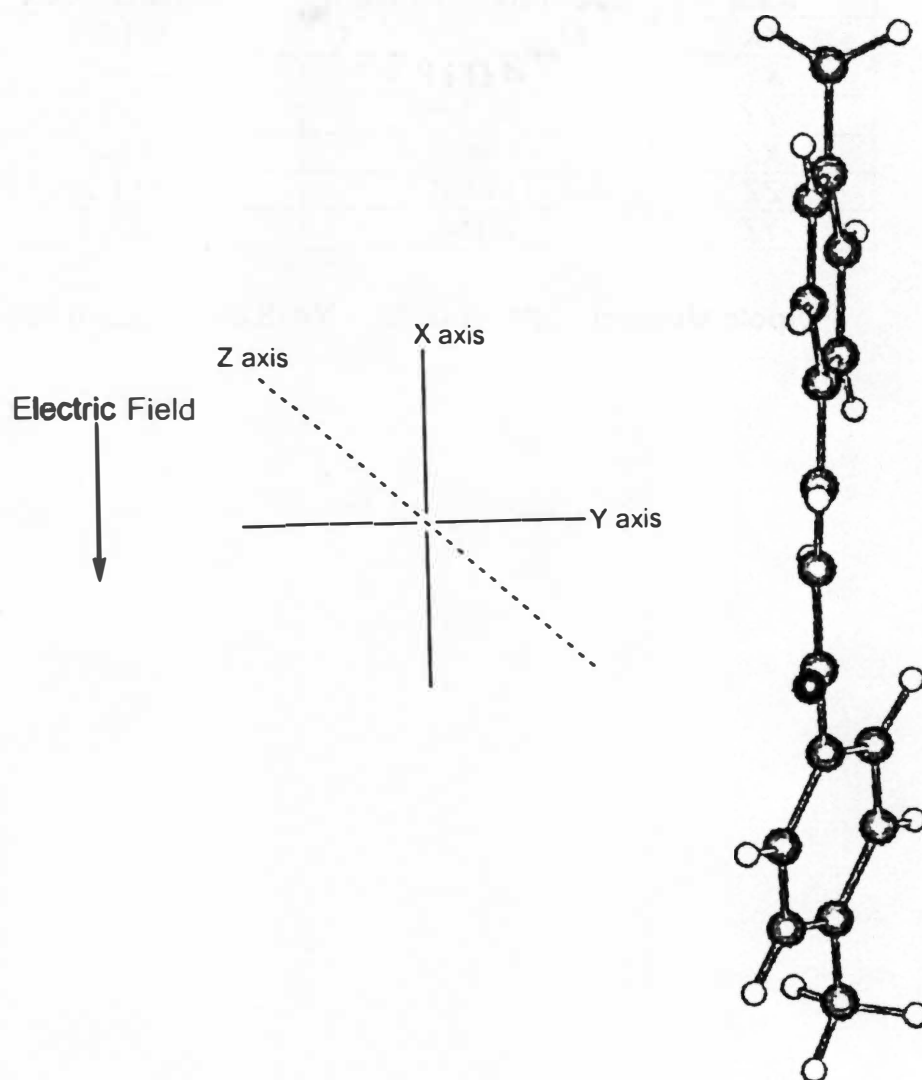


Figure 2-21. Molecular Orientation of 4, 4'-Dimethylchalcone

Steps were also taken to assure that no photochemical conversion of the chalcone material was occurring that would result in the increase in optical activity. To determine with certainty that no photoproducts were being synthesized during the photolyses, gas chromatography/mass spectrometry (GC/MS) and nuclear magnetic resonance (NMR) techniques were performed on control experiments with the 1064 nm laser using RCPL, LCPL, and LPL. The data collected indicated that no rearrangement of the chalcone or chalcone conversion to any other species was taking place. The spectra of the chalcone crystallizations were identical to the spectrum of pure chalcone before any experiments were attempted.

It was briefly postulated that more than one polymorph of the chalcone was formed during the crystallizations thus giving rise to these interesting results. This phenomenon occurs when more than one crystalline arrangement (space group) of the molecules exists in the solid state. If different polymorphs were present, each could potentially be more responsive to different types of light or particles and a *d* or *l* crystal could preferentially result. A solid-state NMR (see Figure 2-22) was collected for each crystallization of the chalcone crystal so as to detect the presence of polymorphs, if any. Sullivan *et al.* have recently determined the usefulness of SS-NMR in the detection of polymorphs of glycine so it was expected that if polymorphic structures were present that this method would suffice to acknowledge them.^[35] The solid-state NMR spectra obtained during the course of this research shows no evidence of the presence of other polymorphs for any of the different types of experiments conducted. Virtually no

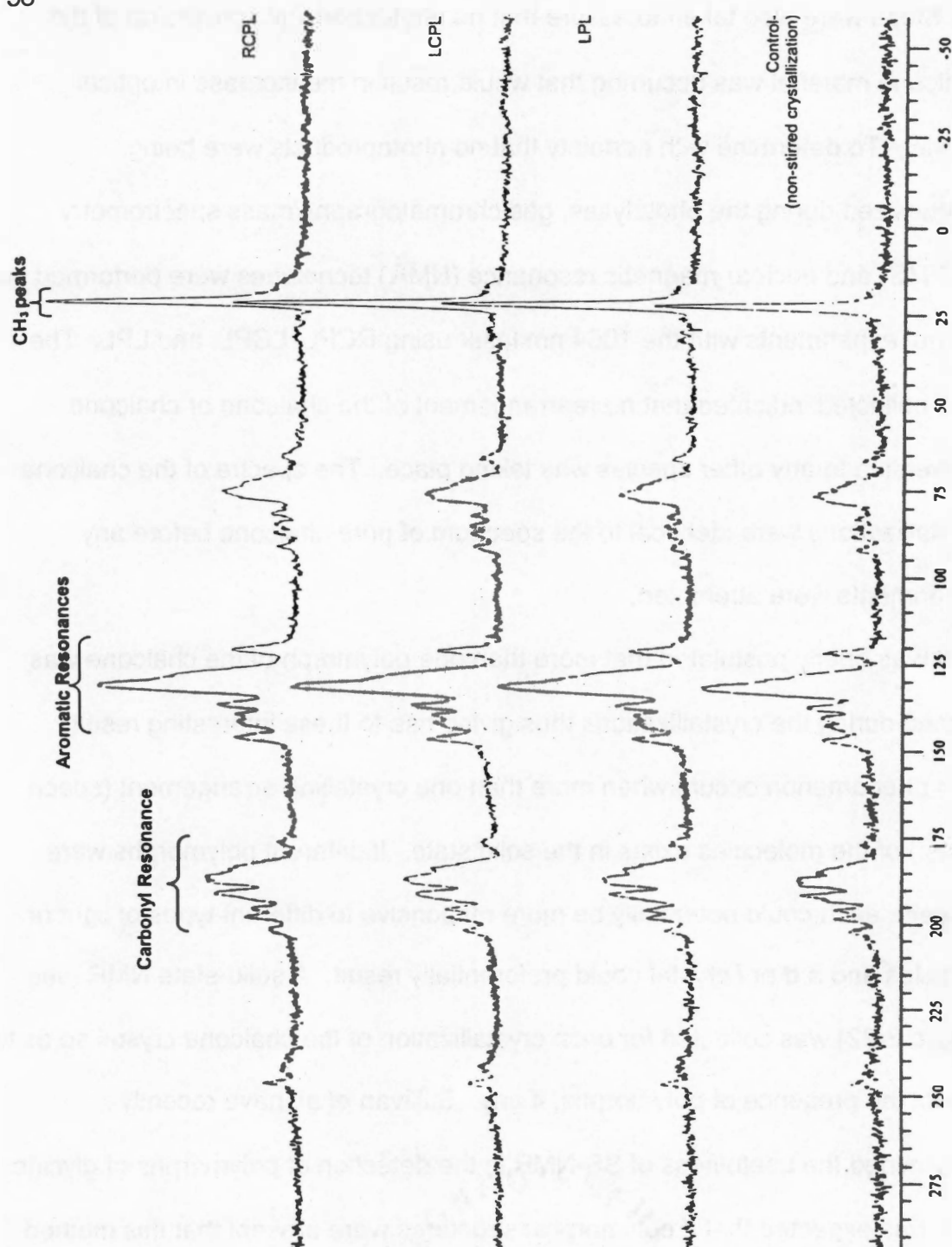


Figure 2-22. ^{13}C Solid-State NMR Spectrum of 4, 4'-Dimethylchalcone from Crystallization Experiments

difference is evident in the spectra for the crystals from the left-, right- and linearly polarized light experiments as compared to crystals that have not been subjected to any kind of perturbation.

C. Conclusions

This work has demonstrated that the manipulation of the optical activity of achiral molecules is possible using simple synthetic and photochemical methods. Stirred crystallizations of 4,4'-dimethylchalcone have been previously proven to induce chiral symmetry breaking, while unstirred crystallizations have little effect on the optical rotations of the molecule. Results have shown that right and left circularly polarized light, as well as beta radiation have a small effect on the enantiomeric excesses of the chalcone and are no better at inducing large enantiomeric excess than not stirring during crystallization. Linearly polarized light has been revealed to increase the bimodal distribution of the chalcone crystallizations and has a more substantial effect on the optical activity than even the stirred crystallizations. It has been suggested that the cause of this effect could be due to the optical Kerr effect. The anisotropic polarizability of the chalcone molecule causes a preferential alignment in the direction of the field when using LPL resulting in an increase of enantiomeric excesses. CPL does not influence alignment in the direction of the field and therefore no effect on the asymmetric induction. The process by which this occurs is random and spontaneous and the sign of optical activity cannot be predicted.

D. Experimental

General

Solution ^1H and ^{13}C NMR spectra were recorded on Brüker AC-250, and Varian 300 MHz instruments. CDCl_3 was used as solvents with 1% TMS ($\delta=0$) as the internal standard. Solid-state ^1H NMR spectra were recorded on a Brüker AMX 400 instrument. The standard was measured externally with a rotor filled with adamantane. Gas chromatography was carried out on a Hewlett-Packard (HP) 6890 instrument fitted with a HP 5973 mass spectrometer detector. The optical rotations were measured on a Perkin-Elmer 241 polarimeter with a Na 589 lamp using a 0.1dm path length cell. CH_2Cl_2 was used as the solvent for all polarimetry experiments. The Sr-90 beta source for the beta crystallizations resides at the Radiation Calibration Laboratory at Oak Ridge National Laboratory. Laser induced crystallizations were done with a 1064nm Nd-YAG laser. The laser was fitted with a quarter-wave plate to generate the circularly polarized light. The average power was 1 watt; peak power was 10^7 Js^{-1} .

Synthesis of *N, N*-Diisopropylbenzoylformamide

In a 250-ml round-bottomed flask equipped with a magnetic stir bar, 30 ml (0.5 mol) of thionyl chloride was added to 10 g (0.07 mol) of benzoylformic acid.^[21] The mixture refluxed for approximately 30 minutes at 80°C. Next, 15 ml of benzene was added to the reaction flask (to aid in removal of excess thionyl chloride) and subsequently distilled off. The reaction mixture was then cooled by the addition of 6 ml of diethyl ether. Very slowly, 20 ml (0.14 mol)

diisopropylamine was added to the reaction flask. The resultant mixture was recrystallized from benzene. The crystallization was left undisturbed for one day and gave flat, clear crystals in 55% yield. The crystals were dissolved in CDCl_3 with 1% TMS added as an internal standard for NMR analysis. δ_{H} (250 MHz; CDCl_3 ; Me_4Si) 8.0 (2H, m), 7.65 (2H, m), 7.5 (1H, m), 3.7 (1H, m), 1.6 (3H, d), 1.2 (3H, d).

Photolysis of *N,N*-Diisopropylbenzoylformamide

Crystals of recrystallized *N,N*-diisopropylbenzoylformamide were ground using mortar and pestle. The ground material was then placed in a small tube and photolyzed for 5 hours before agitating and then left overnight. After 28 hours reaction time, the resulting product was analyzed via NMR; no more than 5% of the starting material had reacted.

Reduction of *N,N*-Diisopropylbenzoylformamide

In Methanol

To 5.0 ml of methanol in a 25-ml round-bottomed flask immersed in an ice bath, 0.3 g (0.008 mol) of sodium borohydride was added. To this mixture, 0.5 g (0.002 mol) of the amide crystals was added. The reaction mixture was swirled for 5 minutes on ice and then refluxed gently for 10 minutes. Approximately 10 ml of water was added to quench the reaction. The product was extracted with methylene chloride and concentrated *in vacuo*. The resultant crystals were white and had a very fine consistency. The crystals were dissolved in CDCl_3 with 1%

TMS added as an internal standard for NMR analysis. The product was identified to be racemic hydroxyformamide. δ_{H} (250 MHz; CDCl_3 ; Me_4Si) 7.4 (5H, m), 5.1 (1H, s), 3.8 (1H, m), 3.4 (1H, m), 1.6 (1H, s), 1.4 (3H, d), 1.3 (3H, d), 1.2 (3H, d), 0.4 (3H, d).

In Water

To 5.0 ml of water in a 25-ml round-bottomed flask in an ice bath, 0.3 g (0.008 mol) of sodium borohydride was added. To this mixture, 0.5 g (0.002 mol) of the amide crystals was added. The reaction mixture was swirled for 5 minutes on ice. The amide crystals are insoluble in water. The product crystals were collected using a Büchner funnel. The crystals were analyzed via NMR spectroscopy. The solid product was dissolved in CDCl_3 with 1% TMS added as an internal standard for NMR analysis. The product was identified as hydroxyformamide with ample amounts of the starting material also present. The estimated ratio of reactant to product based on NMR interpretation is 85:15. δ_{H} (250 MHz; CDCl_3 ; Me_4Si) 8.1 (aromatic, m), 7.6 (aromatic, m), 7.5 (aromatic, m), 7.4 (aromatic, m), 5.1 (1H, s), 3.9 (1H, m), 3.8 (1H, m), 3.4 (1H, m), 1.6 (3H, d), 1.5 (3H, d), 1.4 (3H, d), 1.2 (3H, d), 0.5 (3H, d).

Synthesis of *Meso* and *d, l* -1,2-Diphenylethane-1,2-diol

In Methanol

To 10.5 g (0.05 mol) of benzil in a 250 ml round-bottomed flask, 100 ml of methanol was added and cooled to 0°C in an ice bath. Slowly, 2 g of sodium borohydride (dissolved in 50 ml of methanol) was added. The reaction mixture

refluxed at 65°C for approximately 10 minutes and left to stir at room temperature overnight. The solid product was dissolved in CDCl_3 with 1% TMS added as an internal standard for NMR analysis. The product was identified as a mixture of *meso* and *d,l*- isomers by NMR spectroscopy. δ_{H} (250 MHz; CDCl_3 ; Me_4Si) 7.4 (10H, m), 4.9 (*R,S* proton, 1H, d), 4.8 (*meso* proton, 1H, d), 2.1 (2H, s).

In Water

In a 250-ml round-bottomed flask, 2 g (0.05 mol) of sodium borohydride was dissolved in 75 ml of water. Next, 10.5 g (0.05 mol) of benzil, which is insoluble in water, was added with stirring using a magnetic stir bar. The mixture became frothy. Methanol (150 ml) was added to the flask after which the mixture was concentrated *in vacuo*. The solid material was dissolved in CDCl_3 with 1% TMS added as an internal standard for NMR analysis. The product was identified exclusively as the *meso* isomer by NMR spectroscopy. δ_{H} (250 MHz; CDCl_3 ; Me_4Si) 7.4 (10H, m), 4.9 (1H, s), 2.1 (1H, s).

Synthesis of 4, 4'-Dimethylchalcone^[24]

In a nitrogen-flushed three-neck 250-ml, round-bottomed flask equipped with two septum-sealed side arms and a magnetic stir bar, 1 g (0.04 mol) of Na metal was added slowly to 30 ml of HPLC grade methanol (H_2O content less than 0.01%) at 10°C. 4-Methylacetophenone (24 ml, 0.18 mol) was added to the sodium methoxide solution and allowed to swirl for 10 minutes. To this mixture, 21.6 ml (0.18 mol) of *p*-tolualdehyde was then added. The reaction mixture was

swirled on ice for 5 minutes and then brought slowly to room temperature. After standing overnight, the solid reaction product was filtered, washed with HPLC grade water until neutral, rinsed with chilled ethanol, and then air-dried.

Recrystallization from ethyl acetate gave 38 g (90% yield) of 4,4'-dimethylchalcone. The solid product was dissolved in CDCl_3 with 1% TMS added as an internal standard for NMR analysis. Experimental $M_p = 130^\circ\text{C}$.

Literature $M_p = 132^\circ\text{C}$.^[44] δ_c (250 MHz; CDCl_3 ; Me_4Si) 195.67, 190.05, 144.427, 143.439, 140.670, 135.736, 132.225, 129.839, 129.249, 126.579, 126.396, 121.497, 121.060.

Synthesis of 4,4'-Dimethylchalcone Dibromide

Gas Phase Bromination

Gas phase bromination was performed using a conventional Claisen distilling head equipped with two 25-ml flasks and a rubber septum. 2.0 g (0.008 mol) of powdered 4,4'-dimethylchalcone was placed in one of the flasks together with a magnetic stir bar to maintain the powder well mixed during the bromination reaction. The flask was partially immersed in a water bath and maintained at 30°C to prevent condensation of bromine on the solid during bromination.

Liquid bromine (0.70 ml, 0.014 mol) was added via syringe through the septum to the second flask. The system remained closed for 48 hours, during which time gaseous bromine diffused to the other flask through the connecting tube where it was adsorbed by and reacted with the chalcone crystals. After 48 hours, residual bromine was removed from the solid product under reduced pressure for 30

minutes. The solid material was dissolved in CDCl_3 with 1% TMS added as an internal standard for NMR analysis. Based on the resultant spectra, the product ratio of erythro to threo dibromides was estimated to be 85:14. δ_{H} (250 MHz; CDCl_3 ; Me_4Si) 8.0 (2H, m), 7.45 (4H, m), 5.7 (4H, dddd), 2.3 (3H, d), 2.2 (3H, d), 1.5 (impurity).

H_2O Suspension with Pyridinium Tribromide

In a 25 ml round-bottomed flask equipped with a magnetic stir bar, 1 g of powdered 4,4'-dimethylchalcone and 1 g (0.003 mol) of powdered pyridinium tribromide were slurried with 15 ml of HPLC grade H_2O for 1.5 hours at room temperature. The product was rinsed with water and vacuum filtered. The solid material was dissolved in CDCl_3 with 1% TMS added as an internal standard for NMR analysis. The erythro product was formed exclusively in 85% yield. δ_{H} (300 MHz; CDCl_3 ; Me_4Si) 8.0 (2H, d), 7.45 (4H, d), 7.35 (2H, d), 7.2 (2H, d), 5.75 (4H, dd), 2.45 (3H, s), 2.35 (3H, s); δ_{C} (300 MHz; CDCl_3 ; Me_4Si) 190.613, 145.263, 139.292, 135.409, 131.925, 129.676, 129.548, 129.014, 128.191, 50.062, 46.888, 21.294, 21.782.

Stirred and Unstirred Crystallizations

In a 25-ml Erlenmeyer flask, 0.5 g (0.002 mol) of recrystallized 4,4'-dimethylchalcone was dissolved in 0.5 ml of ethyl acetate at 75 °C using an H_2O bath. The solution was allowed to cool and evaporate to dryness while stirring with a magnetic stir bar for the stirred crystallizations and without stirring for the

unstirred experiments. Crystals were subsequently brominated using methods previously described.

Beta Radiolysis Crystallizations

4,4'-Dimethylchalcone (0.5 g, 0.002 mol) in a 25-ml beaker was dissolved in 0.5 ml of ethyl acetate at 75°C using a hot plate. The solution was allowed to cool and evaporate to dryness while being subjected to beta particles emitted from an Sr-90 source housed at Oak Ridge National Laboratory. Crystals were subsequently brominated using methods previously described.

Linearly Polarized and Circularly Polarized Light Crystallizations

4,4'-Dimethylchalcone (0.5 g, 0.002 mol) in a 25-ml Erlenmeyer flask was dissolved in 0.5 ml of ethyl acetate at 75°C using a hot plate. The solution was allowed to cool and evaporate to dryness while linearly and right- and left-circularly polarized light was impinged on the sample. Crystals were subsequently brominated using methods previously described.

Optical Activity Measurements

The optical rotations for all crystallizations were measured using a concentration of 0.079 g/ml of 4, 4'-dimethylchalcone dibromide in CH₂Cl₂. 0.158 g of the resulting bromide from each crystallization was dissolved in 2 ml of CH₂Cl₂ and then the optical rotation measured by polarimetry.

E. Materials

Solvents

Dichloromethane (methylene chloride), Fisher Chemical Company

Ethyl Acetate, Fisher Chemical Company

Water (HPLC grade), Fisher Chemical Company

Methanol (dry, HPLC grade), Fisher Chemical Company

Benzene, Fisher Chemical Company

Diethyl Ether, Aldrich Chemical Company

NMR Solvents

Chloroform-*d*, Aldrich Chemical Company

Gases

Nitrogen, Fisher Chemical Company

Reagents

Sodium metal, Aldrich Chemical Company

p-Tolualdehyde, Aldrich Chemical Company

4'-Methylacetophenone, Aldrich Chemical Company

Pyridinium Tribromide, Aldrich Chemical Company

Bromine, Aldrich Chemical Company

Thionyl Chloride, Aldrich Chemical Company

Benzoyl Formic Acid, Aldrich Chemical Company

Sodium Borohydride, Aldrich Chemical Company

Chapter III - The Photochemistry of Racemic and Resolved 2-Iodooctane

A. Background

It has been shown that photoreactions initiated with CPL may result in asymmetric induction. However, as mentioned earlier, these reactions offer certain disadvantages. Consider the hypothetical case of a racemate *R/S* undergoing a photochemical reaction with LCPL. Because the enantiomers have slightly different extinction coefficients, ϵ_R and ϵ_S , one enantiomer of the racemate will react faster than the other, thus leaving the substrate enriched in the less reactive stereoisomer.^[32, 36] The enantiomeric excess of recovered *R/S* approaches 100% as the time of the reaction increases; however, most of the substrate is destroyed before a large ee can be obtained.^[32,36] This is a consequence of the fact that the differences in extinction coefficients are usually small. There are several examples in literature that support this concept (see Figure 3-1). Photolysis of racemic camphor, **9**, with CPL, for example, afforded recovered camphor with an ee of 20% after 99% of the camphor had been degraded.^[37] Two-photon photochemistry of racemic tartaric acid, **10**, with CPL afforded a maximum ee for recovered tartaric acid of 7.5%.^[23, 38] Conversely, a system in which *R* and *S* of the mixture equilibrate photochemically but do not otherwise degrade would be ideal except that it has the negative effect of yielding very small ee's. For example, photoequilibration of (*E*)- and (*Z*)-cyclooctene, **11**, with CPL afforded (*E*) cyclooctene with a small enantiomeric enrichment.^[39] The first case, *R/S* → *P* is desirable because large ee values can be obtained regardless of the extinction coefficients but at the expense of degrading *R/S*

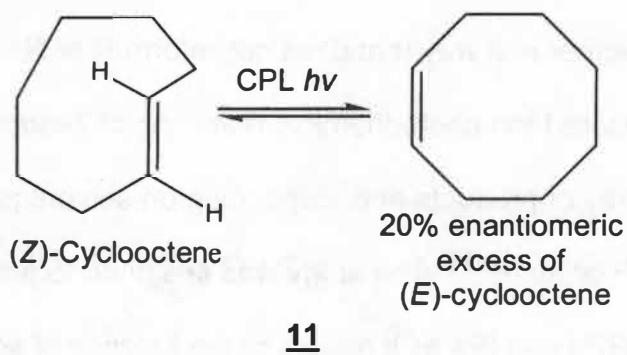
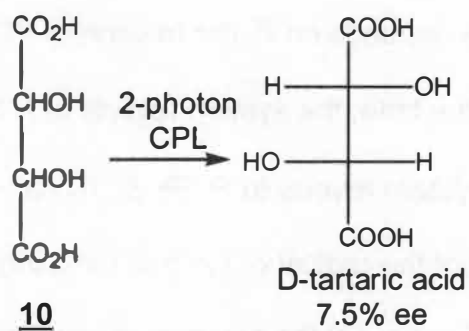
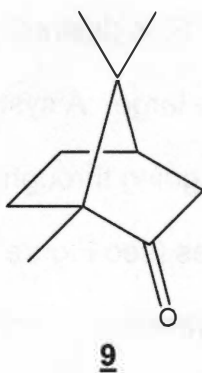


FIGURE 3-1. Photochemical Examples of Racemic Mixtures

significantly. The second case, $R \rightleftharpoons S$, is desirable because R/S is not degraded, but ee values will rarely be large. A system that possess the desirable attributes of both is ideal. Reactions going through radical pairs (RPs) and/or ion pairs (IPs) have features of both cases (see Figure 3-2). The enantiomers, R and S , photoequilibrate through the transient radical or ion pair (IN = intermediate) but ultimately yield products (P) through IN. It has been shown that the ee of recovered R/S depends on F , the fraction of IN that yields P. When $F = 1$, i.e., $IN \rightarrow P$ 100% of the time, the system reverts to $R/S \rightarrow P$. When $F = 0$, i.e., IN never yields P, the system reverts to $R \rightleftharpoons S$. IN can yield P in two ways: (1) by the two components of the radical or ion pair diffusing apart and then reacting with solvent, for example, and (2) the two components of the radical or ion pair reacting with one another in a way that does not reform R or S .

Gao *et al.* investigated the photochemical reactions of 2-iodooctane and found that they yield an array of products and, depending on solvent polarity, proceed through either an RP or an IP.^[36] The study was designed to provide information on the dynamics of RPs and IPs as it relates to the function of solvent polarity and viscosity. Once the effect of F on the lamp-induced photolysis of 2-iodooctane was determined then the effect of F using CPL can also be probed. The F values will be valuable in assessing the photochemistry of 2-iodooctane in the same media with circularly polarized light. This investigation included four phases of study in which the polarity and viscosity were varied so as to

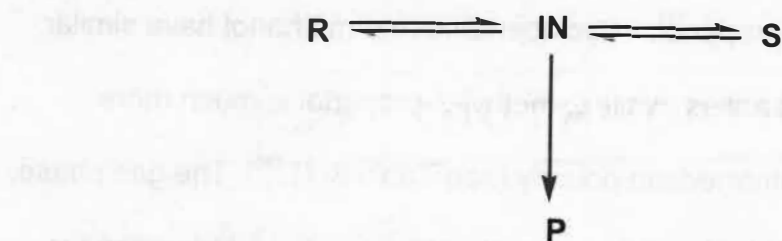


FIGURE 3-2. Equation of R/S to Product

determine the instances in which the F value parameter was affected. As reaction media for this study Gao *et al.* chose the gas phase, cyclopentane, methanol and 2-methyl-2-propanol. Cyclopentane and methanol have similar viscosities but different polarities, while 2-methyl-2-propanol is much more viscous and exhibits an intermediate polarity (see Table 3-1).^[36] The gas phase, which has no viscosity and is non-polar, was chosen because 2-iodooctane is volatile at room temperature. The photoproducts formed from the photoreactions in each of the four phases were examined and the mechanisms of the reactions were suggested.

Photolysis of racemic 2-iodooctane in the gas phase, where a radical pair yielding $F=1$ was expected, afforded six hydrocarbon products: 1-Octene, octane, (*E*)- and (*Z*)-2-octene, and *meso*- and *d,l*-7,8-dimethyltetradecane, the dimers of the two octyl radical (see Table 3-2 and Figure 3-3).^[36] Approximately 80% of the time the iodine atom dimerized to I_2 and 20% of the time it abstracted a hydrogen atom from C-1 or C-3 of the 2-octyl radical to form HI and the octenes (see Figure 3-4).^[36] In the gas phase there are no caged intermediates, thus the 2-octyl radical and iodine atom escape each other instantly resulting in large yields of dimers and I_2 . The photoreaction of 2-iodooctane in cyclopentane yielded the same six hydrocarbons as seen in the gas-phase plus iodocyclopentane and a considerable amount of I_2 . In cyclopentane, the two radicals are formed in a cage. The radicals can regenerate the reactant or produce HI and octenes and escape the cage. On the basis of the yields of the escape products, I_2 and the two dimethyltetradecanes, it is seen that about one-

Table 3-1. Properties of the Reaction Phases

Phase	$E_T(30)$	Viscosity/cp (25°C)	Bond Dissociation Energy (kcal/mol)	
			C-H	O-H
Gas	Low	Low		
Cyclopentane	31	0.416	94.5	
Methanol	55.4	0.551	94	104.4
2-Methyl-2-propanol	43.3	4.438	100.5	105.1
Acetonitrile	45.6	0.341	93	
Water	100	1.006		119

Table 3-2. Photoproducts and Yields (%) from the Photochemistry of 2-Iodooctane

	<i>Reaction Phase-- Racemic 2-Iodooctane</i>			
Photoproducts	Gas	Cyclopentane	Methanol	2-methyl-2-propanol
1-octene	22	12	4	54
octane	6	22	17	2
(<i>E</i>)-2-octene	4	29	10	28
(<i>Z</i>)-2-octene	4	14	6	16
7, 8-dimethyltetradecane				
isomer 1	21	4	1	
isomer 2	43	14	2	
unknown			7	
2-octanol			trace	trace
3-methoxyoctane			10	
2-methoxyoctane			38	
2-octanone			5	
Iodine	76 ^a	45 ^a	3 ^a	2 ^a
Hydrogen iodide	24 ^a	50 ^a	97 ^a	98 ^a
Dominant Intermediate	RP	RP	IP	RP

^aInferred from the amount of I₂ formed in the reaction.

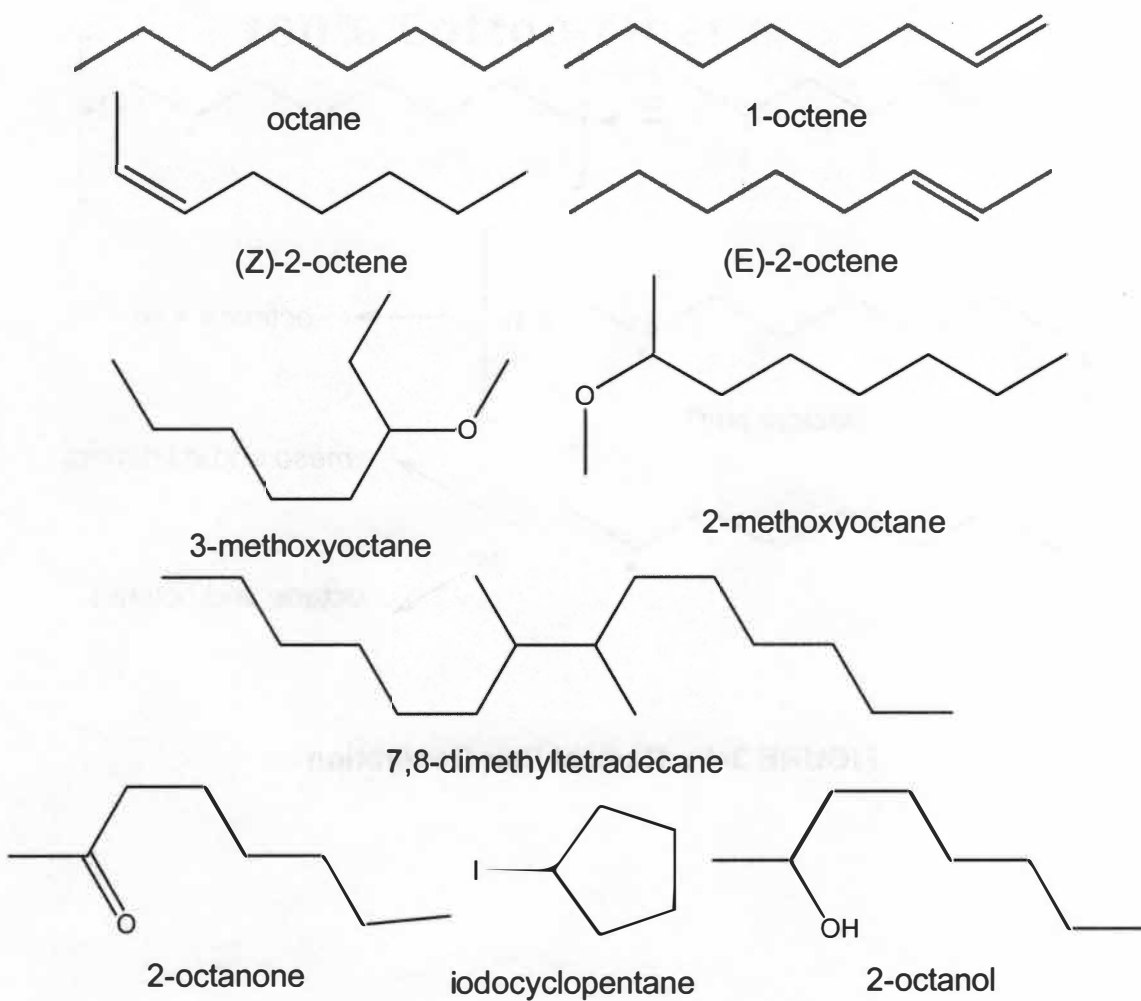


FIGURE 3-3. Major Photoreaction Products

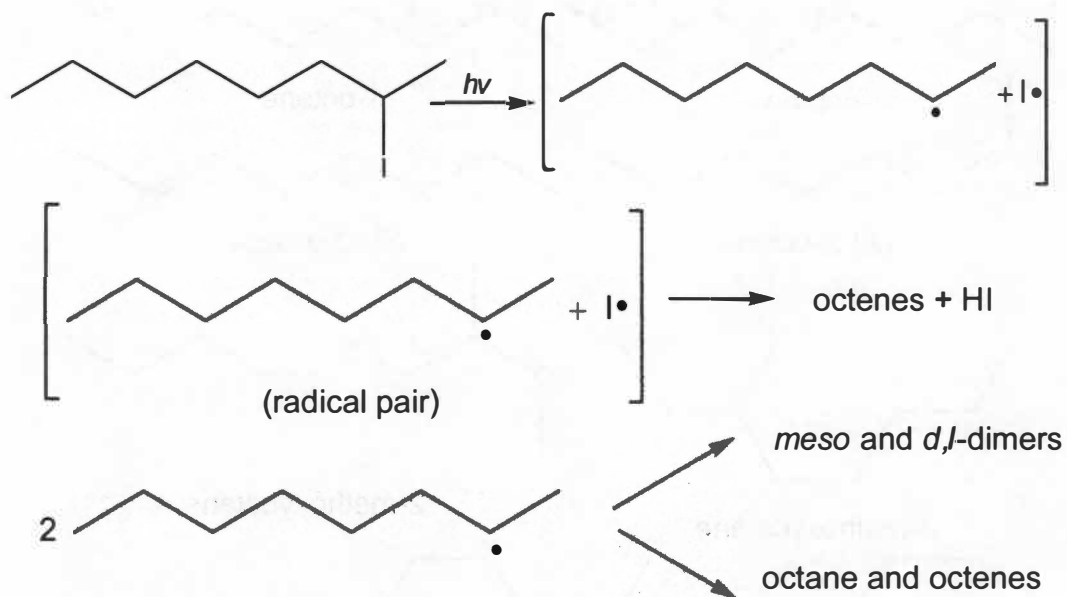


FIGURE 3-4 . Radical Pair Generation

half of the radical pairs escape into the bulk solvent.^[36] Reaction of 2-iodooctane in methanol yielded the six hydrocarbons as well. The reaction also yielded 2-methoxyoctane, which was the major product, 3-methoxyoctane, 2-octanol, 2-octanone and an unknown compound. The reaction in methanol proceeded mainly through the 2-octyl cation (53%) and another 20% occurring through the 2-octyl radical. The mechanism of the remaining 27% of the product is unclear because all of the octenes can be formed from the RP or IP (see Figure 3-5). Very little *meso*- and *d,l*-7,8-dimethyltetradecane are formed here, implying that little of the octane is formed by disproportionation of the 2-octyl radical. Most of the octane thus arises by the 2-octyl abstraction of a hydrogen atom from the solvent (see Figure 3-6). Unlike octane, the photoproducts 2- and 3-methoxyoctane, 2-octanol, and 2-octanone arise via heterolytic chemistry (see Figure 3-7). The 2-octanol is formed by the cleavage of 2-methoxyoctane by HI and then photooxidized by I₂ to form 2-octanone. The low yields of I₂ and the dimers suggest that very little of the radicals in the RP escape into the bulk solvent.^[36] Most of the ionic chemistry takes place within the IP and little of the relatively unstable 2-octyl cation and iodide escape into the bulk solvent. The photochemistry of the substrate in 2-methyl-2-propanol occurred completely through free radicals. No ion pairs are being formed here as evidenced by the absence of any ion pair products such as alcohols or oxygenated products. Very little dimers and I₂ are formed here, thus all the chemistry takes place in the RP and none of the products escape.

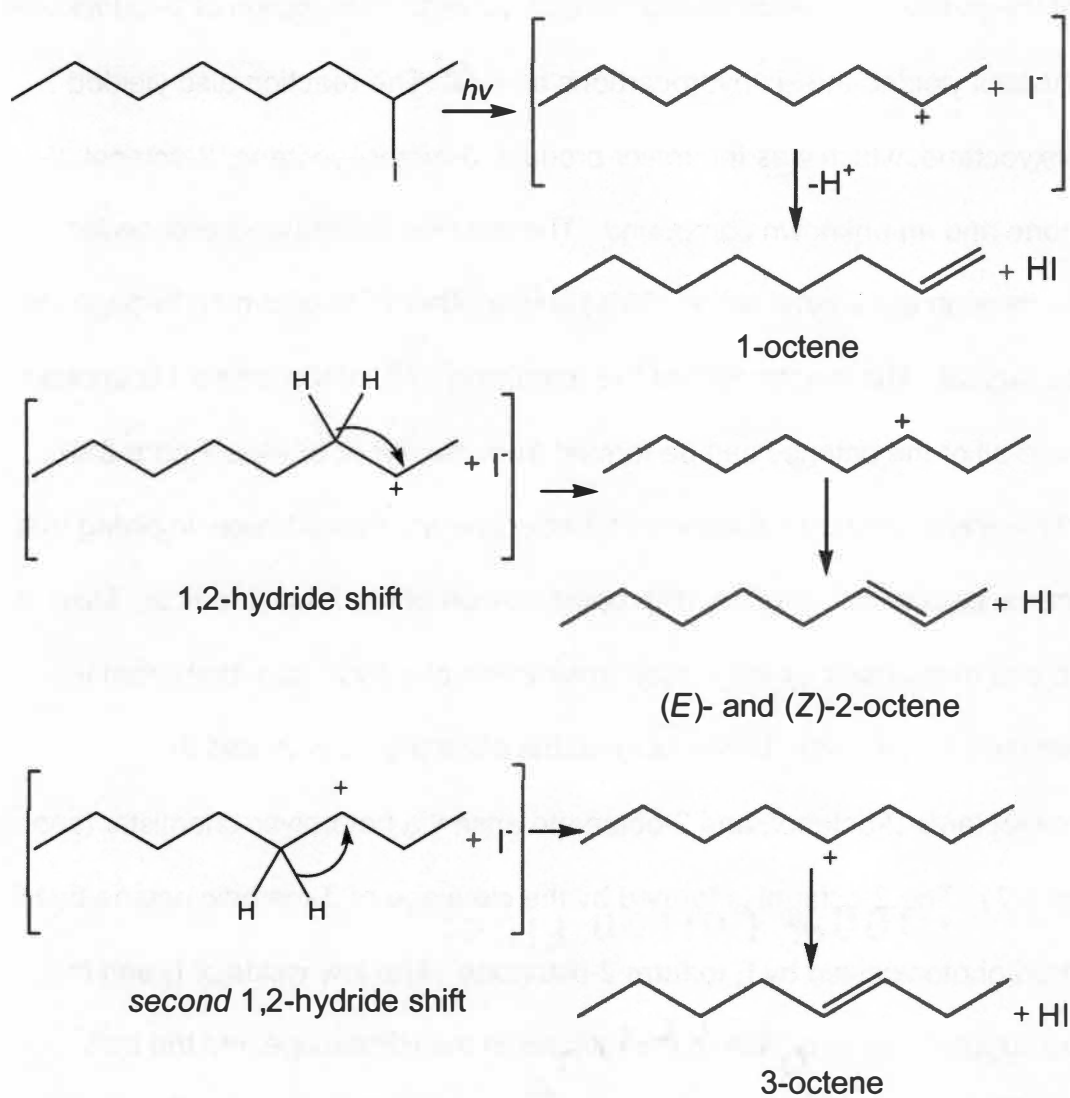


FIGURE 3-5. Octene Generation by Ionic Pair

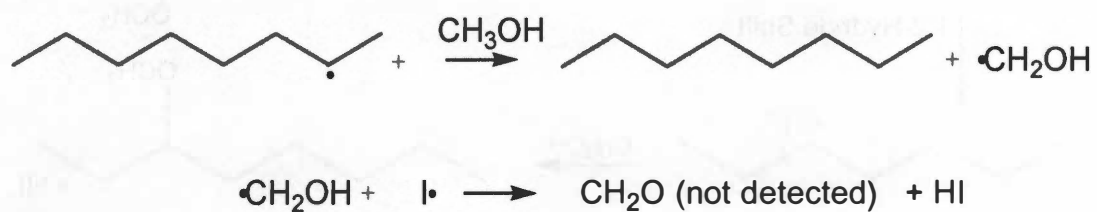


FIGURE 3-6. Generation of Octane via H-Abstraction from Solvent

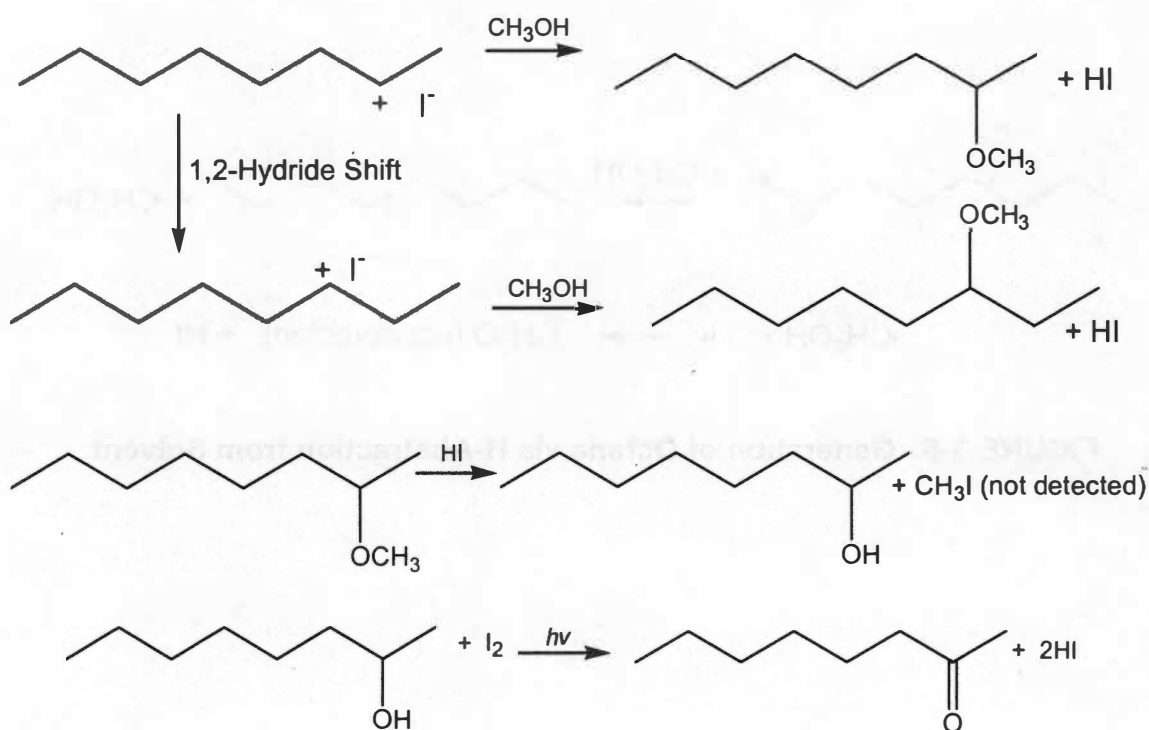


FIGURE 3-7. Heterolytic Reactions of 2-Iodooctane in Methanol

Gao *et al.* also studied the photochemistry of 2-deuterio-2-iodooctane in cyclopentane and methanol. The syntheses are shown in Figure 3-8. Interestingly, photolysis of 2-iodooctane- d_1 afforded much less octane (5%) than was seen in the nondeuterated case (22%), 47% of which contained no deuterium (see Table 3-3). This is consistent with the photoreaction yielding a small amount of the 2-octyl carbene (see Figure 3-9). Once formed the carbene could abstract hydrogen from the solvent to form octane or isomerize to (*E*)- and (*Z*)-2-octene, all with no deuterium. Unlike in cyclopentane, the photochemistry of 2-iodooctane- d_1 in methanol yields considerable amounts of octane, approximately 34% of which contains no deuterium.^[40] Some of the unlabeled (*E*)- and (*Z*)-2-octene must arise from the 2-octyl carbene. The rest arises from 1,2-hydride shifts starting from the 2-octyl cation. Neither 2-methoxyoctane nor 3-methoxyoctane has lost any deuterium, which is expected for their formation from the 2-octyl and 3-octyl cations, respectively.

Gao *et al.* also followed the photolysis of optically active (*R*)-2-iodooctane in methanol, cyclopentane, and 2-methyl-2-propanol by quantitative GC/MS and polarimetry as a function of time. Data analysis revealed F (methanol) = 0.60 ± 0.05 , F (cyclopentane) = 0.70 ± 0.12 , and F (2-methyl-2-propanol) = 0.74 ± 0.05 .^[36] The chemistry of all phases, except in methanol, where a sizeable fraction of the reaction proceeds through ion pairs, is dominated by free radicals. F is large in all cases through varying degrees of escape of the caged intermediates into the bulk solvent and reaction within the cage to form products

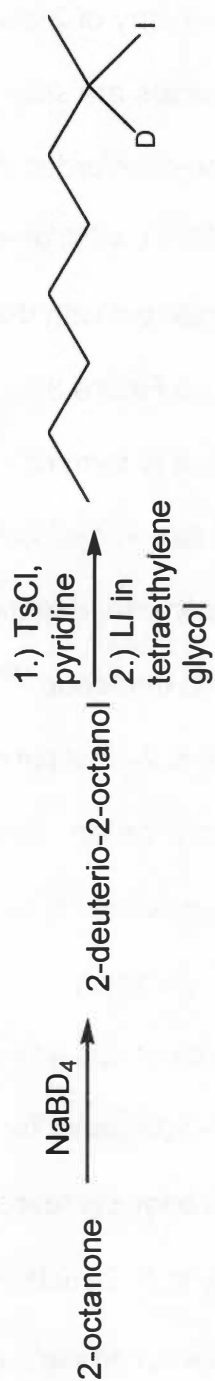


FIGURE 3-8. Synthesis of 2-Deuterio-2-Iodo-octane

Table 3-3. Percent Deuterium Content of Selected Photoproducts

Product	Photolysis of 2-Deuterio-2-Iodoctane			
	cyclopentane		methanol	
	d_1	d_0	d_1	d_0
1-octene	100	0	100	0
octane	53	47	66	34
(<i>E</i>)-2-octene	96	4	70	30
(<i>Z</i>)-2-octene	96	4	66	34
2-methoxyoctene			100	0
3-methoxyoctene			100	0

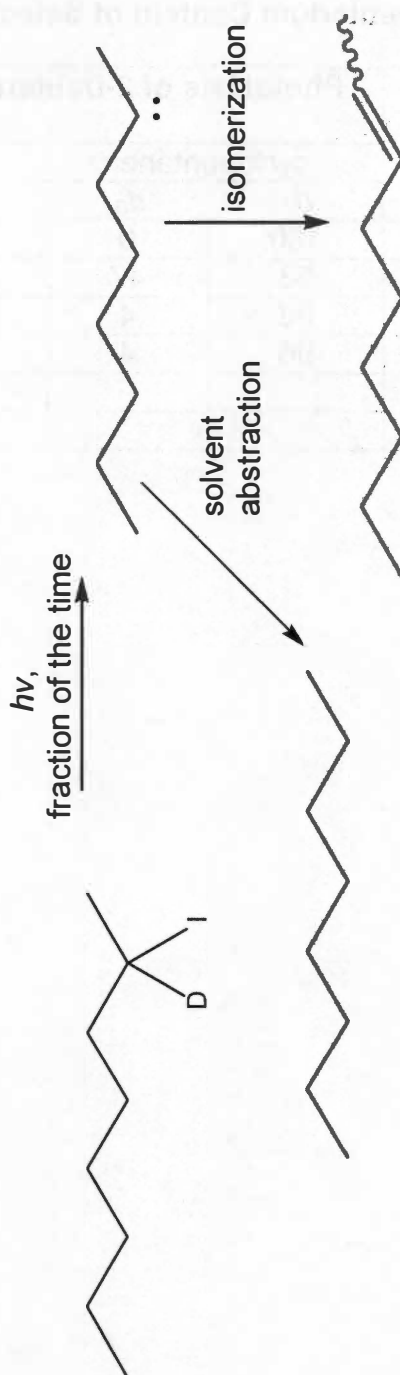


FIGURE 3-9. Carbene Reaction

other than the reactant. Escape of the radicals in the RP in cyclopentane is large, while very small in 2-methyl-2-propanol, reflecting the 10-fold difference in viscosity of the two media. The F value in methanol, a solvent with a viscosity similar to that of cyclopentane, is smaller than in the other two solvents. This is a reflection of the fact that the reaction in methanol is dominated by an IP, where escape of the ions likely does not occur.

Iodomethane and iodoethane are known to undergo homolytic cleavage of the C-I bond in the gas phase as a result of an $n \rightarrow \sigma^*$ transition (weak absorption at 270 nm).^[41] Similar behavior is observed for 2-iodooctane in the gas phase, where significant amounts of *meso*- and *d,l*-7,8-tetradecane are formed.

Comparable behavior is also seen for the substrate in the non-polar cyclopentane and the much more polar 2-methyl-2-propanol. Dimers are seen in cyclopentane, but not in the more viscous 2-methyl-2-propanol. It has been shown that dimers are not formed in the photochemistry of 1-iodooctane.^[40, 41] In cyclopentane, a small amount of carbene-derived products are formed. It has been shown that in the case of 1-iodooctane some 1-octyl carbene is formed; however, that the carbene does not arise in a concerted loss of HI, but instead may derive from the RP or IP.^[40] In methanol, considerably greater than half of the reaction occurs through an IP, with the rest through an RP. A small amount of the 2-octyl dimers are formed in methanol. 2-iodooctane affords more carbocation in methanol than does 1-iodooctane; the secondary 2-octyl cation is, of course, considerably more stable than the 1-octyl cation.^[36, 40, 41] The F values determined by Gao *et al.* have no correlation to solvent viscosity (see Table 3-

4).^[36] This is a consequence of the fact that the caged intermediates can not only reform the reactant and escape but also react within the cage to form the octenes. Table 3-4 does show however, that a correlation of the viscosity to the yield of dimers and I_2 exist. As the viscosity of the solvent increases, the yield of dimers approaches zero while as the viscosity decreases, the yield of dimers also increases. A higher viscosity hinders movement of the caged intermediates thus lowering the likelihood for escape to form the dimers.

So as to broaden the study of what solvent properties affect the F values and distributions of RPs and IPs, an extension of the Gao study was carried out using a different solvent. An ideal solvent will not absorb light in the 266 nm region and will not be halogenated as the number of expected photoproducts may increase due to the presence of the additional halogen. Acetonitrile was chosen based on its published values for viscosity and polarity. Acetonitrile has an intermediate polarity similar to that of 2-methyl-2-propanol; however, the viscosity is much lower than that of all the solvents previously used. The polarity and viscosity of acetonitrile is easily influenced by the addition of water, thus providing a simple method in which to manipulate the study. Water is miscible with acetonitrile and is very polar. Although viscosity is not correlated with F values, viscosity contributes a major effect on the products formed and whether they react within a cage or escape the cage.

This dissertation chapter will give a full account of the results of the photolyses of 2-iodooctane in acetonitrile/water as it compares to the results collected using the preceding solvents.

Table 3-4. Comparison of Viscosity to F and Yields of Dimers

Phase	Viscosity	<i>F</i>	% Yield- 7,8- dimethyltetradecane	I ₂
Gas	0	1	63	76
Cyclopentane	0.416	0.80	18	45
Methanol	0.551	0.60	3	3
2-Methyl-2-propanol	4.438	0.74	0	2

B. Results and Discussion

Racemic and resolved 2-iodooctane are easily prepared from the reaction of lithium iodide and the tosylate from racemic and resolved 2-octanol, respectively. (see Figure 3-10). 2-iodooctane is insoluble in water; therefore experiments that included water would be limited to those in which solubility was maximized. For this reason, experiments in 95%, 90%, 80% and 50% acetonitrile/water solution by volume were carried out. The 50% CH₃CN/water experiment was not included in the resolved study to determine *F* values because of the solubility of 2-iodooctane was too low. To determine the *F* values, the change of optical activity of the substrate and the loss of reactant versus time was done. Because 2-iodooctane is poorly soluble in 50% CH₃CN/H₂O, not enough optically active material could be dissolved to obtain meaningful optical rotations. Photolysis reactions in 100% acetonitrile were also attempted by rigorously removing traces of water by means of known experimental techniques. All attempts to completely remove water proved futile as the presence of certain photoproducts confirmed the existence of water in the reaction.

Based on the results of Gao *et al.*, a prediction of the behavior of the photolyses can be made. Reactions in acetonitrile/water mixtures where the polarity is higher than that of methanol should react mostly through ion pairs (see Table 3-5).^[45] Acetonitrile/water mixtures in which the polarity is lower than that of methanol may proceed through a mixture of radical and ion pairs. It is conceivable that, in the reactions in which radical pairs are formed, a mixture of photoproducts similar to those observed in methanol would be formed.

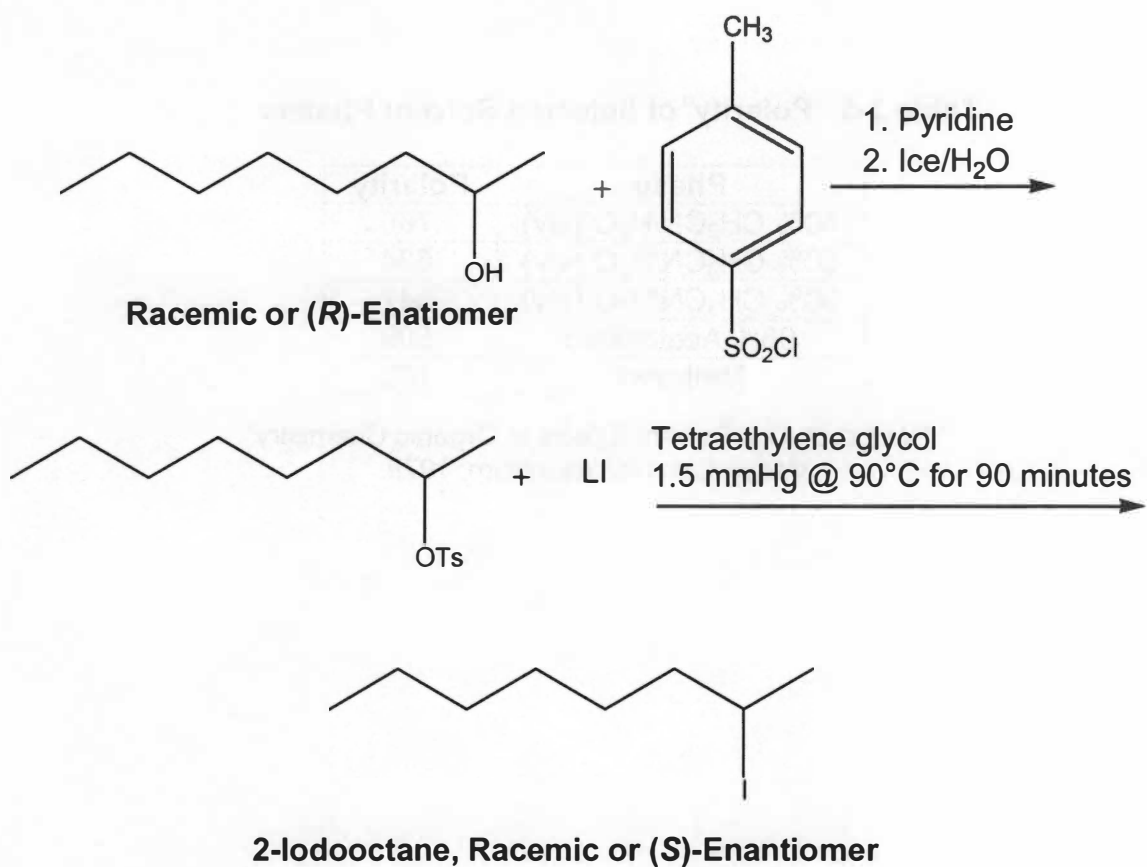


FIGURE 3-10 . Synthesis of Racemic and Resolved 2-Iodo-octane

Table 3-5. Polarity^a of Selected Solvent Phases

Phase	Polarity
50% CH ₃ CN/H ₂ O (v/v)	.766
80% CH ₃ CN/H ₂ O (v/v)	.634
90% CH ₃ CN/H ₂ O (v/v)	.547
95% Acetonitrile	.509
Methanol	.762

^a Reichardt, C., "Solvent Effects in Organic Chemistry",
Verlag Chemie, Weinheim, 1979.

In all acetonitrile/water experiments, the same photoproducts were formed, with the differences being in the relative amounts of each product (see Table 3-6 and Figures 3-11 and 3-12). 1-Octene, (*E*)- and (*Z*)-2-octene, 2-octanol, 2-octanone, and octane were present in all reaction mixtures similar to what was seen with the four solvents used by Gao *et al.* The presence of small amounts of octane indicates that some free radical reactions are occurring. 2-Octanol and 2-octanone are formed either directly or indirectly via ion pair reactions (see Figure 3-13). The 3- and 4-octanol products occur via hydride shifts from the 2-octyl cation to the 3-position and 4-position, respectively. 1-Octene, (*E*)- and (*Z*)-2-octene may form via RP or IP, as it has been shown in Figures 3-4 and 3-5. The 2-octenes may form in two ways: (1) by a 1,2-hydride shift from the 2-octyl cation, to form the 3-octyl cation followed by loss of a proton and (2) direct loss of a proton from carbon 3. Also present in these reaction mixtures was 3-octene, 3- and 4-octanol, and 2-, 3-, and 4-octylacetamide. 3-Octene is likely formed by a second hydride shift from the 2-octyl intermediate (either RP or IP). The octylacetamides are formed by the reaction of the alkyl cation with acetonitrile to form a new carbocation (see Figure 3-14); addition of water then generates the corresponding the acid amide. The assignments for the 2-, 3- and 4-octyl amides were made (1) based on the ion fragments given in the mass spectra; (2) gc retention times and (3) by comparison of the mass spectra of the amides to mass spectra of laboratory prepared 1-octylacetamide and 2-octylacetamide. An interesting observation of this experiment is that no dimers of the 2-octyl radical are produced at all in the reaction. This indicates that very little of the octane is

Table 3-6. Photoproducts and Relative Yields (%) from the Photochemistry of 2-Iodooctane (Expanded)

Photoproducts	Reaction Phase-- Racemic 2-Iodooctane							
	Gas	Cyclopentane	Methanol	2-methyl-2-propanol	Acetonitrile (5% H ₂ O)	Acetonitrile (10% H ₂ O)	Acetonitrile (20% H ₂ O)	Acetonitrile (50% H ₂ O)
1-octene	22	12	4	54	53.7	37.7	59.3	47.2
3-octene						0.7		0.8
octane	6	22	17	2	3.0	2.9	1.5	3.7
(E)-2-octene	4	29	10	28	16.2	17.8	20.7	21.1
(Z)-2-octene	4	14	6	16	7.1	8.3	9.2	10.3
7, 8-dimethyltetradecane								
isomer 1	21	4	1					
isomer 2	43	14	2					
Unknown			7		1.6	3.1	0.5	
4-octanol						0.6	1.7	1.9
3-octanol						1.6	1.4	5.3
2-octanol			trace	trace	7	17.2	2.2	5.2
3-methoxyoctane			10					
2-methoxyoctane			38					
2-octanone			5		0.8	0.7	1.6	1.8
4-octyl acid amide					2.0	1.0	0.4	0.5
3-octyl acid amide					3.5	2.2	0.4	0.7
2-octyl acid amide					5.1	6.2	1.1	1.2
Iodine	76 ^a	45 ^a	3 ^a	2 ^a	2 ^a	2 ^a	2 ^a	2 ^a
Hydrogen iodide	24 ^a	50 ^a	97 ^a	98 ^a	97	98 ^a	98 ^a	98 ^a
Dominant Intermediate	RP	RP	IP	RP	IP	IP	IP	IP

^aInferred from the amount of I₂ formed in the reaction.

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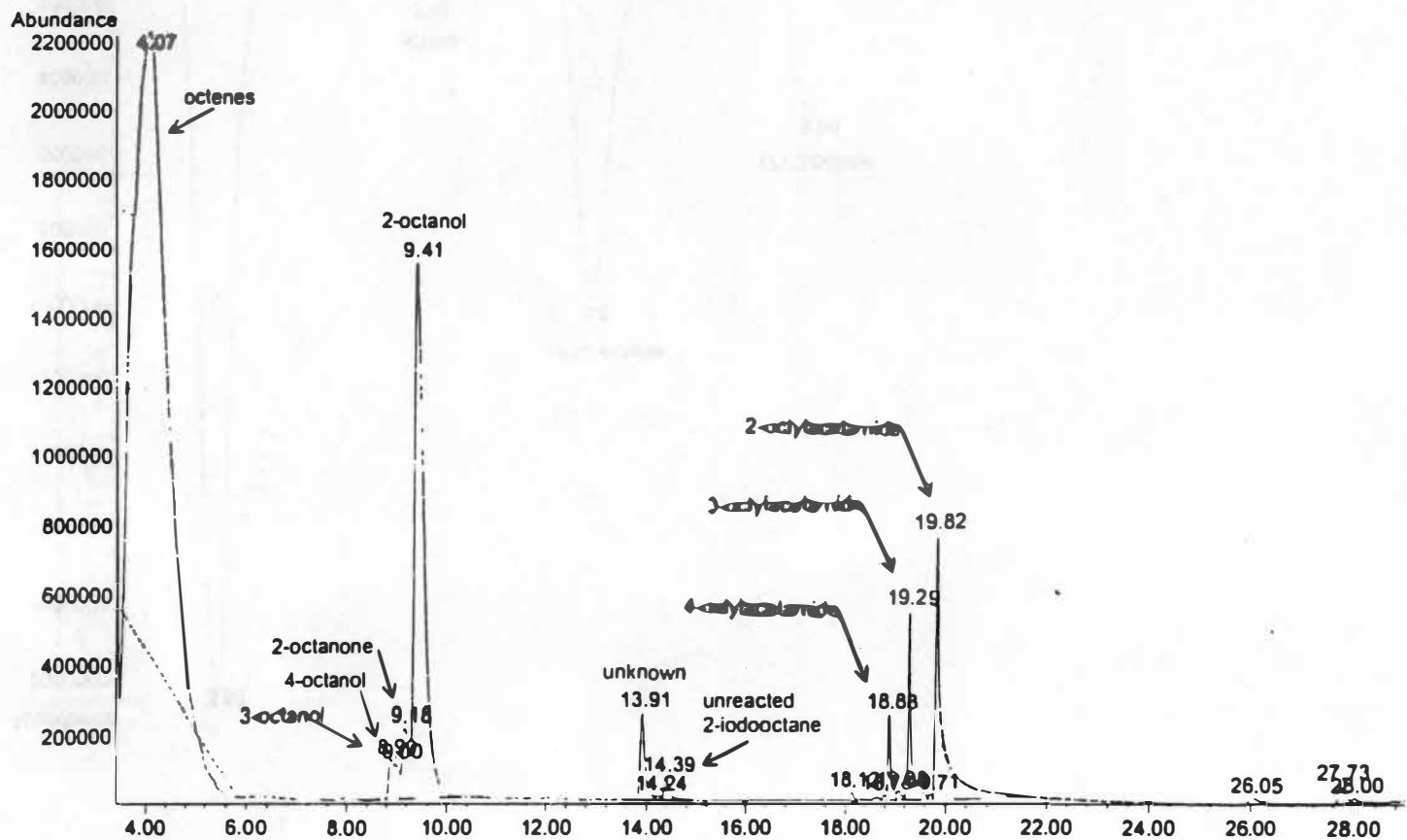
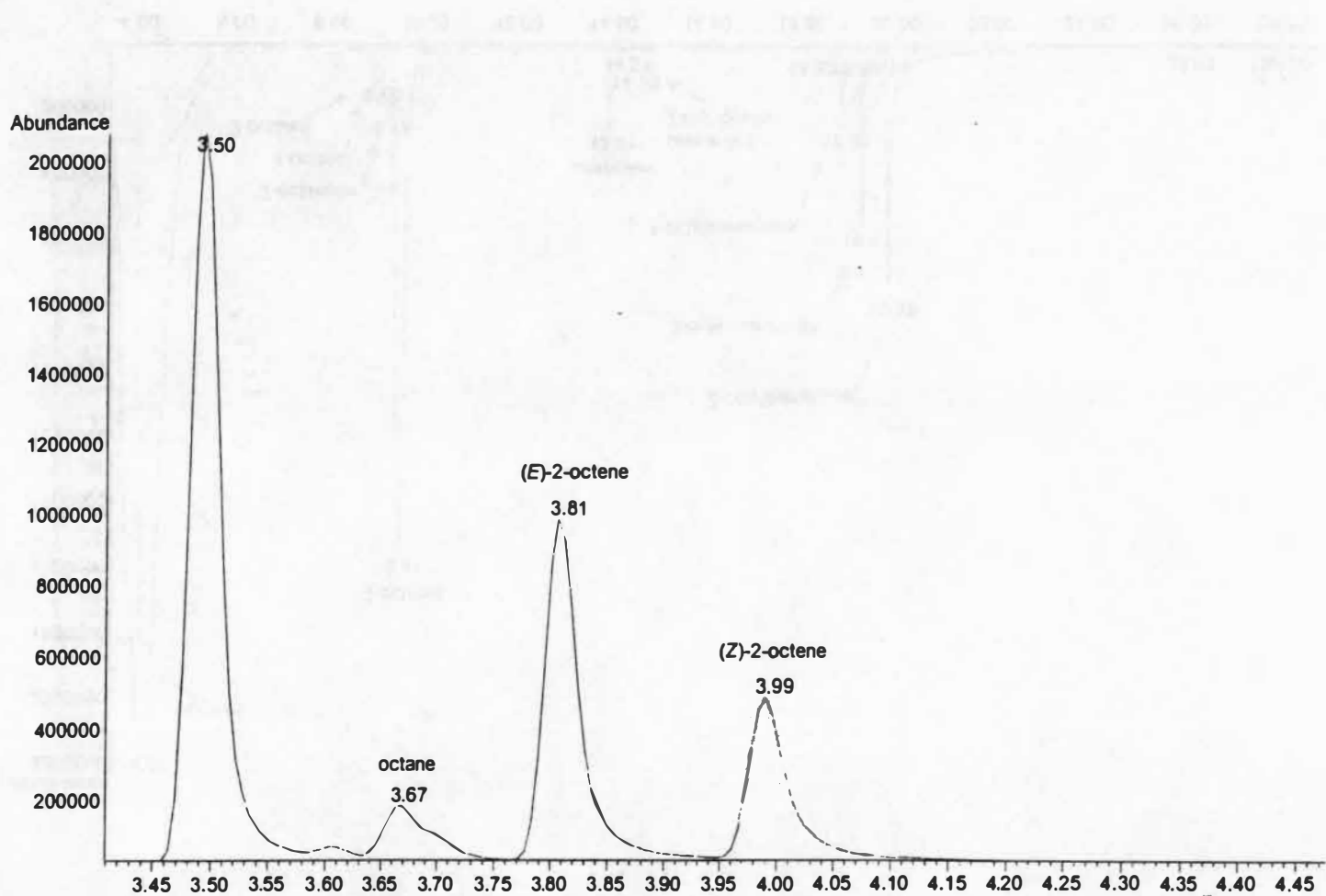


Figure 3-12. Gas Chromatogram of Reaction Products from Photolysis of 2-Iodooctane in 90% CH₃CN/H₂O (v/v) (Octene Region)



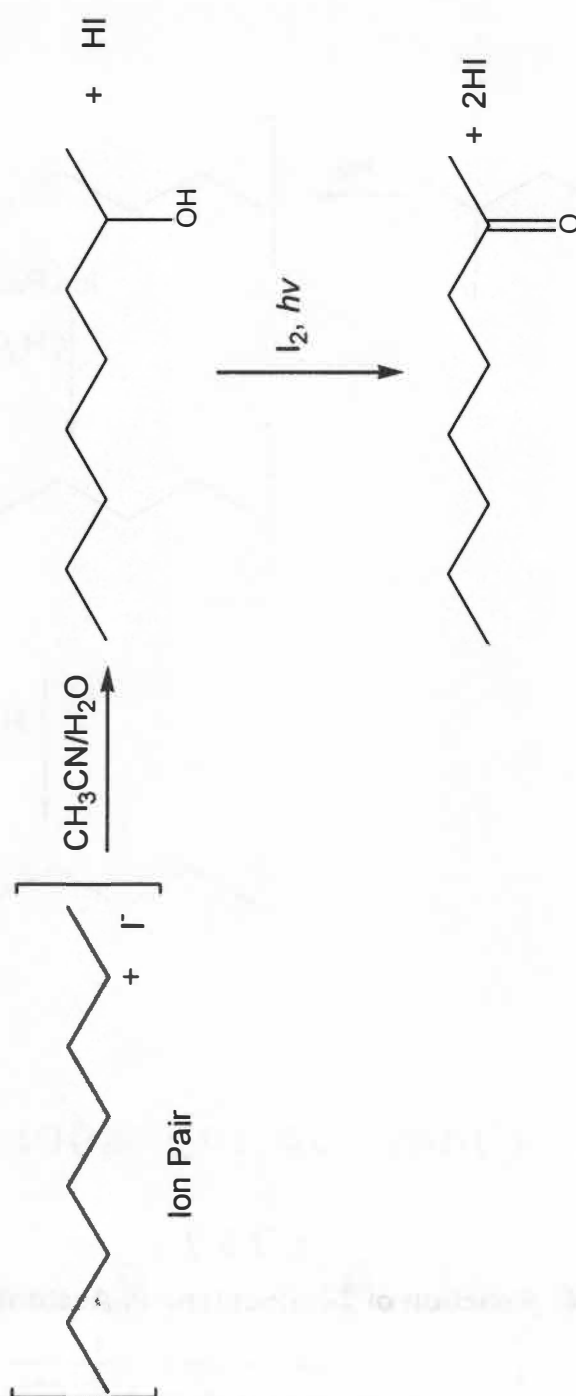


FIGURE 3-13. Synthesis of 2-Octanol and 2-Octanone

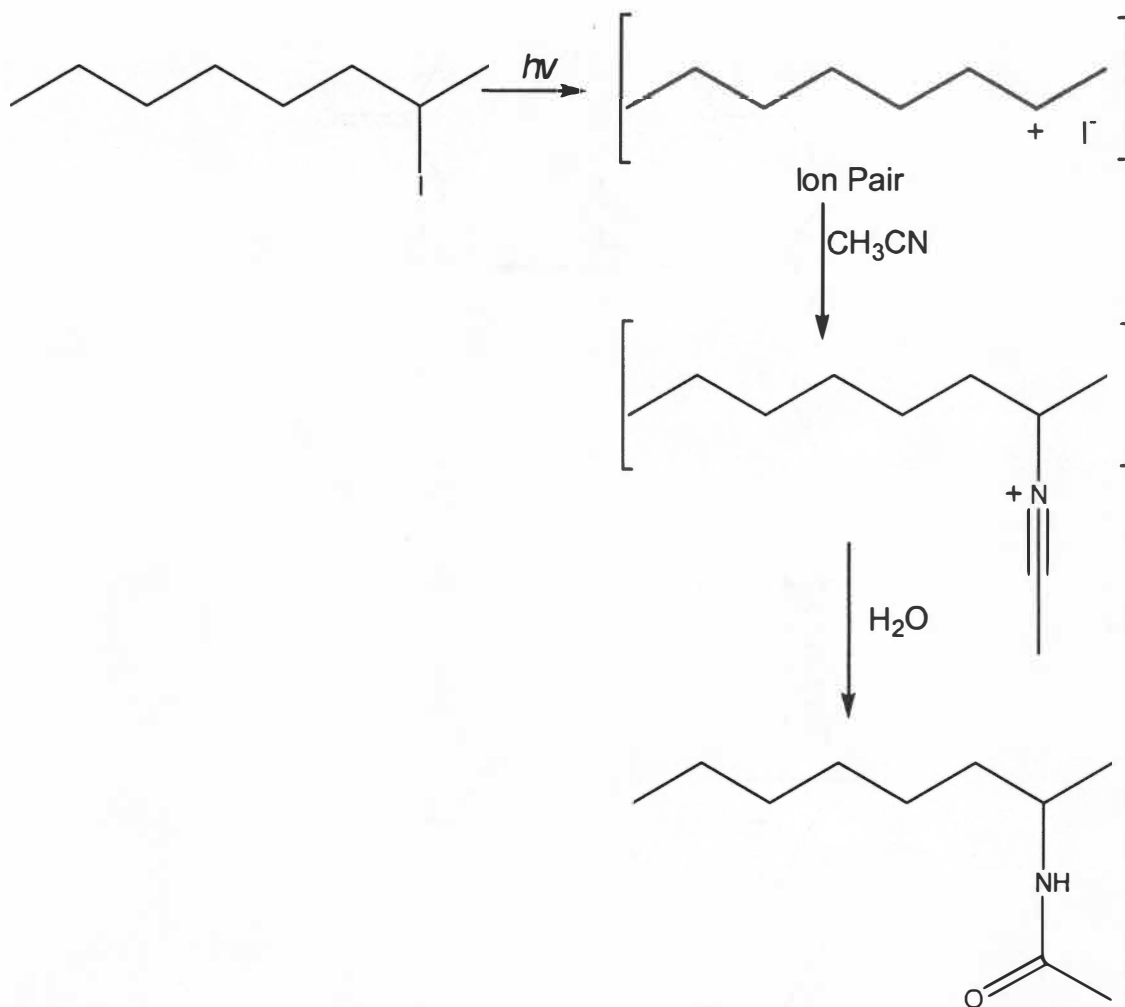


FIGURE 3-14. Reaction of 2-Iodooctane in Acetonitrile/Water

formed by the disproportionation of the 2-octyl radical. The octane present in the reaction must arise by the 2-octyl radical abstraction of the C-H hydrogen atom of acetonitrile. This is similar to what is seen for methanol. The bond dissociation energies of the C-H (see Table 3-1) on methanol and acetonitrile are characteristically low indicating that abstraction here is the most likely source of H. Water is least likely to supply an H as the bond dissociation energy for the O-H bond is large.

Based on the relative product yields for this experiment (Table 3-6), the dynamics of the RP and the IP can be analyzed for each of the acetonitrile/water experiments. In all cases the yield of octane is incredibly low and the dimers of the 2-octyl radical are non-existent. These facts indicate that a very low amount of radical pair is involved in the overall chemistry. Based on the absence of the dimers it can be assumed that the octenes are forming either in the radical pair cage or within the IP. It is unlikely that the octenes are forming via RP, as it was shown that escape is likely for solvents with low viscosity such as cyclopentane and acetonitrile, while escape is less likely for highly viscous solvents like 2-methyl-2-propanol. Escape in this manner would generate the dimers. Thus, it is likely that the octenes are being formed mainly within the IP. If this is the case, an average of only about 2% of the products are being formed via an RP mechanism. In all of the acetonitrile/water reactions there is a significant amount of octenes formed. It seems as though the octenes are formed in competition with the 2-octanol. When the yield of octenes is high, the yield of 2-octanol is low. The 95% acetonitrile/water experiment generates only 7% of 2-octanol

while the 90% reaction generates a far greater yield of 17.2%. Then, in the 80% reaction, the yield drops back down to 2.2%. A possible explanation is that in the 95% acetonitrile reaction, there isn't enough water in the reaction to generate high yields of the alcohol, however in the 90% reaction there is double the amount of water, therefore the alcohol is present in higher yields. In the 80% and 50% reactions, the ion pair is much better solvated, thus the ions may be longer lived, allowing for other reactions to compete generating lower yields of the alcohol.

The yields of HI and I₂ were not determined experimentally; instead their yields were estimated from the product distribution and hydrogen atom balance. Initially, attempts were made to quantify the HI and I₂ formed in the reactions. Experimental difficulties precluded this from being done. 2-Octanone can only be formed by the photooxidation of 2-octanol by I₂. Very small yields of 2-octanone were observed indicating that very little I₂ is being formed in the reaction. The I₂ that is formed is a byproduct of the disproportionation reaction to make octane and the octenes. This is an indication that some of the octane and octenes, albeit a very small percentage, are being formed via escape of the RP.

The chemistry of 2-iodooctane in acetonitrile/water mixtures is oddly similar to the behavior in 2-methyl-2-propanol although the viscosity and polarity of the two media differ immensely. Very little octane is formed in both media and there is no evidence of dimers in any of the product mixtures. It is an interesting observation that the 2-methyl-2-propanol reaction proceeded via an RP while the

results herein show that it is most likely that the acetonitrile reactions proceed via IPs.

The photochemistry of 2-deuterio-2-iodooctane was examined as well. The experiments were carried out in the same manner as those with the racemic substrate. Deuterium studies were conducted on the 90% and 50% acetonitrile/water experiments. The percent deuterium content in each product was determined by its mass spectrum using either the molecular ion peak when available or fragment peaks. The presence of deuterium in the product indicates that it was not formed via the 2-octyl carbene. It has been shown that carbenes are often observed in the photochemistry of alkyl halides.^[40, 41] The absence of deuterium confirms that a carbene is the source of the product (see Figure 3-15). Roughly 5% of 1-octene contains no deuterium and nearly 10% of the (*E*)- and (*Z*)-2-octenes are unlabeled (see Table 3-7). A small percentage of these products thus arises from the 2-octyl carbene, however the rest arises from the 2-octyl cation (see Figure 3-15). In both experiments, the deuterium content in the octylacetamides is relatively high. Approximately 11% of the 2-octylacetamide is formed by means of a carbene. This is due to the octyl carbene insertion into the C≡N bond. This reaction proceeds by way of a nitrile ylide intermediate formed by the addition of the octyl carbene to the acetonitrile solvent (see Figure 3-16).^[42, 43] This insertion of the carbene into the solvent was not seen when methanol was used as the solvent. Analysis of the mass spectrum of the 3-octylacetamide peak revealed no loss of deuterium. The mass

Table 3-7. Percent Deuterium Content of Selected Photoproducts in Acetonitrile

	<i>Photolysis of 2-Deuterio-2-Iodo-octane</i>			
	<u>90% CH₃CN</u>		<u>50% CH₃CN</u>	
	<i>d</i> ₁	<i>d</i> ₀	<i>d</i> ₁	<i>d</i> ₀
1-octene	95	5	95	5
(E)-2-octene	91	9	90	10
(Z)-2-octene	91	9	100	0
2-octanol	100	0	100	0
2-octyl acetyl amide	89	11	86	14

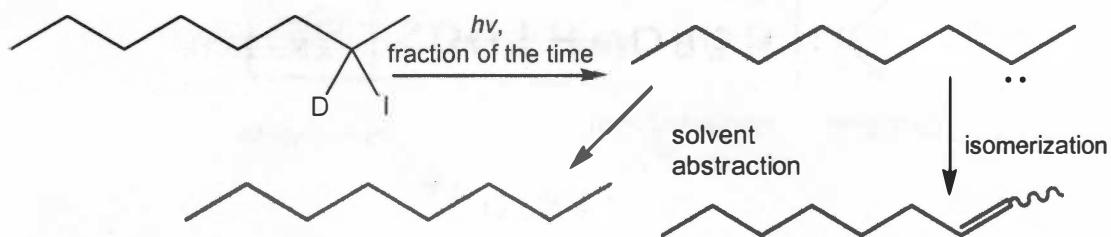
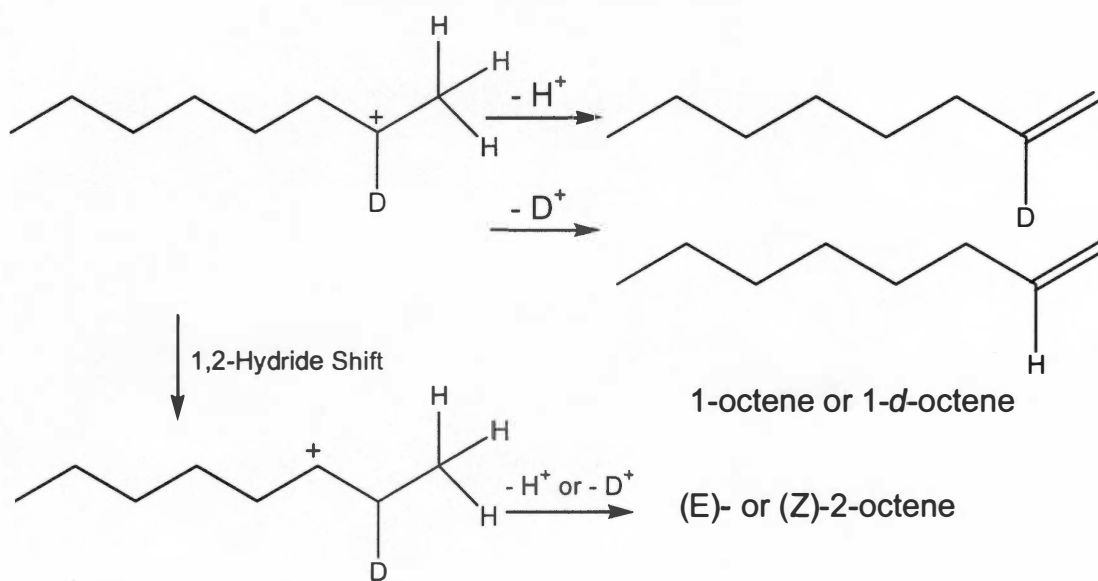
carbene reactions2-d-octyl cation reaction

FIGURE 3-15. Reactions of 2-D-2-Iodoctane

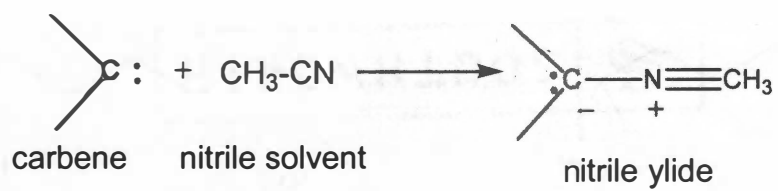


FIGURE 3-16. Formation of Nitrile Ylide

spectrum of the 4-octylacetamide show no loss of deuterium in the molecular ion peak, however, in fragment peaks there are peaks corresponding to M-1. It is likely that these peaks represent a rearrangement of some sort and are not representative of deuterium loss. Since the 4-octylcations comes from the 3-octylcation (3-amides has no loss of deuterium), it can be concluded that the 4-octylacetamide has no loss of deuterium as well. As expected, the 2-octanol has 100% deuterium as it is obtained completely through ion pairs.

Reactions in the absence of light were also carried out with racemic 2-iodooctane so as to determine if IPs (or RPs) dominate the reaction. These thermal reactions were allowed to stir for 3 weeks at room temperature in contrast to the 5 hours reaction time under the lamp. Reactions were done in 100% acetonitrile, and 95% and 90% acetonitrile/water solutions. In the 90% and 95% acetonitrile/water experiments there was, by visual inspection of the gas chromatogram, 96% unreacted starting material (see Table 3-8). No greater than 4% product was formed in either experiment. Based on gas chromatograph retention times and mass spectrum, the products were the three octenes and 2-octanol. The octenes were 38% of the product formed while 2-octanol was 63% of the product. In the 100% acetonitrile reaction, no alcohol is formed at all. Not less than 98% of the starting material was still present upon analysis. The octenes were formed in approximately 2% yield. The octylacetamides were not formed in any of the thermal reactions. Based on the previous arguments it is unlikely that the products are forming via an RP as there would likely not be enough energy imposed to create the intermediate. However, with the absence

**Table 3-8. Reaction Products and Relative Yields (%)
from the Thermal Reaction of 2-Iodooctane**

Photoproducts	Thermal Reaction Phase— 2-Iodooctane		
	100	95	90
octenes	2.0	1.5	2.5
4-octanol			
3-octanol			
2-octanol		2.5	2.5
2-octanone			
unreacted starting material	98.0	96.0	95.0

of the amides, the existence of ion pairs is questionable. A likely explanation of these products is that the octenes are generated by an E2 reaction of 2-iodooctane. 2-Octanol can as easily be formed by S_N2 reaction of 2-iodooctane.

If an optically active substrate reacts photochemically with unpolarized light according to Figure 3-2, it is easy to show that the disappearance of substrate, *i.e.* $[R] + [S]$, and the loss of optical activity, as measured by $[R] - [S]$ yields, respectively, $[R] + [S] = [R]_0 e^{-kFt}$ and $[R] - [S] = [R]_0 e^{-kt}$, where $[R] = [R]_0$ and $[S] = 0$ at $t=0$, k is the phenomenological rate constant, and F is the fraction of IN going to product (see Appendix). Plots of $\ln([R] + [S])/[R]_0$ and $\ln([R] - [S])/[R]_0$ versus time yield straight lines with slopes of kF and k , respectively. Plots of $([R] + [S])/[R]_0$ and $([R] - [S])/[R]_0$ versus time yield straight lines whose ratio of slopes yields F (see Figures 3-17 and 3-18).

Photolysis of optically active (*R*)-2-iodooctane in acetonitrile/water mixtures (95%, 90%, and 80%) were followed by quantitative GC/MS and polarimetry as a function of time. The data afforded linear plots for the first-half of the reaction for each experiment. As reaction times increase, the data deviates from linearity because the reaction is generating small amounts of HI, which in turn begins to racemize the starting material. From the slopes (see appendix for all plots), the F values obtained are $F(95\%) = 0.50 \pm 0.06$, $F(90\%) = 0.51 \pm 0.08$ and $F(80\%) = 0.62 \pm 0.04$. The photolysis reactions are deemed complete when rotations at or close to 0° are obtained because any unreacted 2-iodooctane will be racemic at this point.

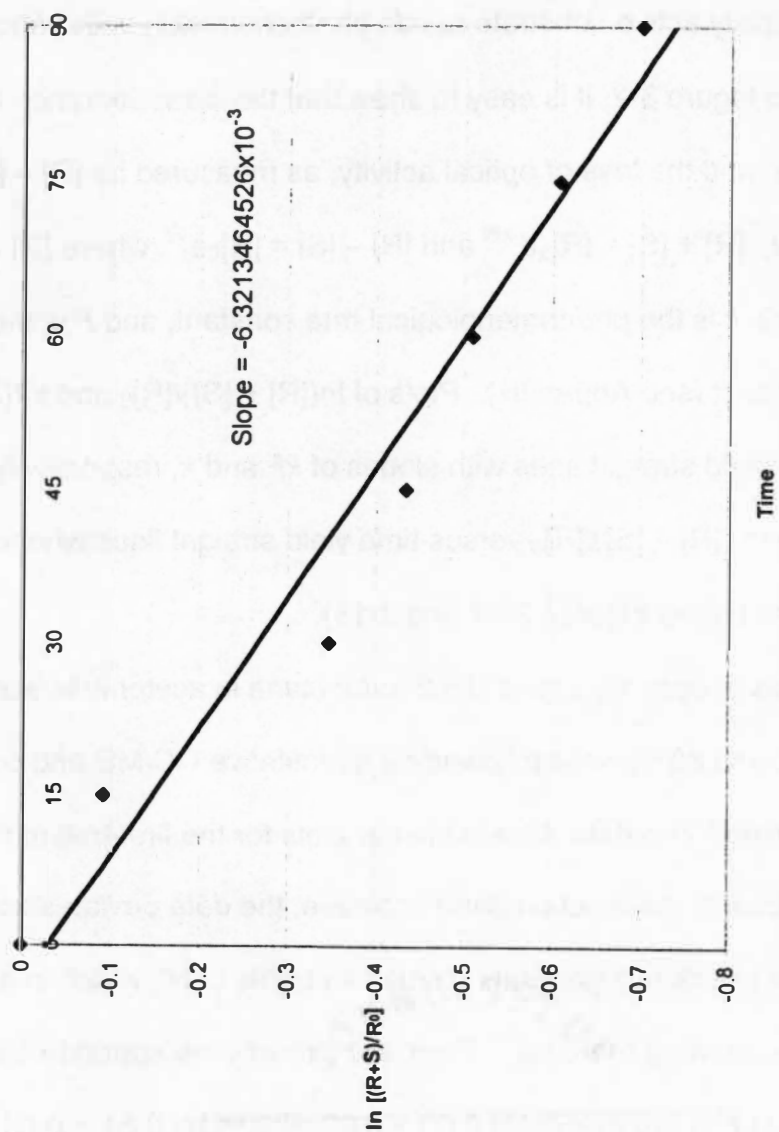


FIGURE 3-17. Plot of $\ln[(R+S)/R_0]$ vs. Time (95% Acetonitrile/Water)

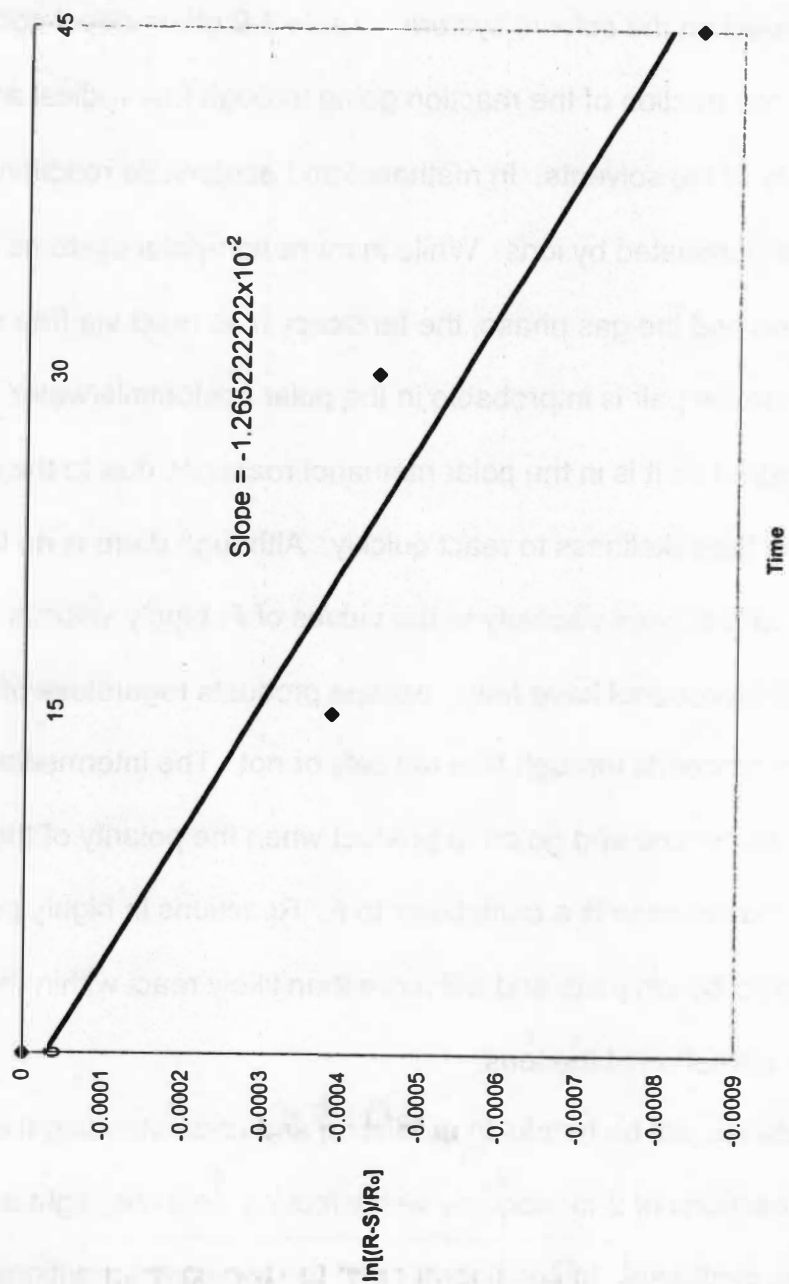


FIGURE 3-18. Plot of $\ln[(R-S)/R_0]$ vs. Time (95% Acetonitrile/Water)

Evaluation of the behavior of the radical and ion pair within the reactions can be made based on the solvent system. Table 3-9 offers direct comparison of the F values to the fraction of the reaction going through free radical and the polarity and viscosity of the solvents. In methanol and acetonitrile reactions, the chemistry is dominated by ions. While in more non-polar systems such as cyclopentane and the gas phase, the tendency is to react via free radicals. Escape of the ion pair is improbable in the polar acetonitrile/water reactions to the same extent as it is in the polar methanol reactions due to the instability of the ions and their likeliness to react quickly. Although there is no linear correlation with solvent viscosity to the values of F , highly viscous solvents such as 2-methyl-2-propanol have fewer escape products regardless of whether the mechanism proceeds through free radicals or not. The intermediate formed is more likely to escape and go on to product when the polarity of the solvent media is low and thus escape is a contributor to F . Reactions in highly polar solvents are dominated by ion pairs and will more than likely react within the cage due to Coulombic attraction of the ions.

The F values will be helpful in predicting and understanding the behavior of the photoreactions of 2-iodooctane with circularly polarized light as a method of asymmetric synthesis. In consideration of the two cases mentioned previously which can lead to an asymmetric synthesis, $R/S \rightarrow P$ and $R \rightleftharpoons S$, the F values determined here give tremendous insight. As mentioned, when $F = 1$ the

Table 3-9. Fractional Behavior of 2-Octyl Radical/Ion Pair

Phase	Fraction of Reaction that is Free Radical	F	Return to Reactant	Escape	Polarity	Viscosity
Gas	100%	1	0	100%	0	0
Cyclopentane	100%	0.80	0.20	50%	0.009	0.416
2-Methyl-2-propanol	100%	0.74	0.26	2%	0.389	4.438
80% CH ₃ CN/H ₂ O	2%	0.62	0.38	2% ^a	0.766	0.496
Methanol	20%-47%	0.60	0.40	3% ^a	0.762	0.551
90% CH ₃ CN/H ₂ O	2%	0.51	0.50	2% ^a	0.547	0.447
95% CH ₃ CN/H ₂ O	2%	0.50	0.50	2% ^a	0.509	0.415

^a From RP. Escape from IP unknown but assumed to be zero.

intermediates yield products 100% of the time reverting to $R/S \rightarrow P$; this system would give large ee's but while degrading the substrate. When $F = 0$, the intermediates never yield products because R and S photoequilibrate. The substrate does not degrade, however, ee's will be small. Thus it can be said that when $F = 0.5$, that 50% of the time the reactant is reformed and 50% of the time the system yields product. Theoretically this will allow for large ee's and for little degradation of product. According to this, investigations of asymmetric synthesis with CPL may be more successful if done with a very polar solvent. Also according to these findings, the gas phase will be the least successful of all solvent media in generating an asymmetric induction.

C. Conclusions

F , the fraction of intermediate that yields product, has contributions of both escape of the partners in the RP or IP into the bulk of the solvent and reaction within the RP or IP to yield products other than the substrate. For this reason, the F values derived from this experiment do not correlate with solvent viscosity. However, if the viscosity is exceptionally high, fewer escape products will be formed as a result. Reactions in which the solvent polarity is high will generate fewer escape products and have lower F values. Highly polar solvents generate ion pairs, which can then either react within the cage to make products or reversibly form the reactant. Less than 3% of each polar solvent has been shown to produce escape products. Non-polar solvents generate radical pair intermediates entirely. Whether or not non-polar solvents generate more escape

products based on low polarity or low viscosity has not been determined. The dynamics of radical and ion pairs have been thoroughly examined and the F values determined herein are suitable for application in future studies with circularly polarized light. Whether or not the experiments with CPL succeed, these studies have yielded valuable information into the nature of RPs and IPs.

D. Experimental

General

All gas chromatography was carried out on a Hewlett-Packard (HP) 6890 instrument fitted with a HP 5973 mass spectrometer detector. For the analysis of each photoreaction, two GC/MS experiments were performed. The resolution of the octene peaks was difficult to achieve using the traditional method. A small change to the ramp temperature in the chamber of the instrument was made which resulted in the separation needed for analysis. The optical rotations were measured on a Perkin-Elmer 241 polarimeter with a Na 589 lamp using a 0.1 dm path length cell. All rotations were measured using the neat product recovered from the photolysis. The photolyses reactions of 2-iodooctane were done using a Rayonet Reactor with four 2537 Å lamps with 35 W per lamp.

Synthesis of Racemic/Resolved 2-Iodooctane

To a stirred solution of (0.15 mol) *p*-toluenesulfonyl chloride in 150 ml of pyridine immersed in an ice-salt bath, 9 g (0.07 mol) of racemic or (*S*)-2-octanol was added. The mixture was allowed to stir on ice for approximately 8 hours and

then placed in the refrigerator for 2 days to ensure complete tosylation. The reaction can be followed by the development of color (pinkish red), followed by the separation of pyridine hydrochloride as long white needles. This precipitate will not form if the pyridine used is wet. When the reaction was complete, the entire mixture is poured over 300-400 g of ice and water. The product was next extracted twice with ether, and then washed with 1:1 hydrochloric acid solution (50 ml H_2SO_4 in 50 ml H_2O), then washed with water and dried with sodium sulfate. The ether was removed *in vacuo* and the tosylate was collected in 65% yield. The tosylate was then poured into a three-neck round-bottomed flask containing 100 ml of tetraethylene glycol. To this solution a 1 molar equivalent of lithium iodide powder was added and the product removed by distillation under 700 mTorr at 80°C for 2 hours. Racemic or (*R*)-2-iodooctane was collected in 40% yield. The product was determined to be at least 97% pure by GC/MS.

Synthesis of 2-*D*-2-iodooctane

To 20 ml (0.128 mol) of 2-octanone in 125-ml dry methanol stirring on ice, 1.5 g (0.036 mol) of sodium borodeuteride was added very slowly. The reaction was then refluxed at 40-45°C for 20 minutes. Afterwards, the reaction was allowed to stir for 24 hours before work-up. The methanol was then removed *in vacuo* and then the reaction mixture was quenched with water. Lastly the product was extracted with portions of methylene chloride. The deuterated alcohol was collected in 80% yield and the purity was determined to be 100% by GC/MS.

The alcohol was next converted to the alkyl halide by using the above procedure for the synthesis of racemic/resolved 2-iodooctane.

Synthesis of 1- and 2-octylacetamides

A 100-ml round-bottomed flask with 0.028 ml (0.39 mmol) of acetyl chloride was placed on ice. Very slowly and while stirring, 1.3 ml (0.008 mol) of either 1- or 2-octylamine was added to the flask. Upon addition of all the amine, after approximately 7 minutes, the mixture had developed into a clear, thick syrup. The syrup was then recrystallized from a 30% methanol/water solution and analyzed via GC/MS. The retention times and the mass spectrum of the laboratory prepared 2-octylacetamide allowed for the determination of 2-octylacetamide as one of the resulting products from the photoreactions. The 1-octylacetamide was shown not to be present as a product. The 3- and 4-octylacetamides were determined based on retention times and mass spectrum analysis as compared to the 2-octylacetamide.

Photolysis Reactions of Racemic and Deuterated 2-Iodooctane

All photolyses were carried out in the same general manner. However, due to solubility considerations, different concentrations for each experiment were used. All solutions were prepared by volume of acetonitrile to water. The deuterated experiments were carried out using only 90% and 50% acetonitrile/water solvents. For the 95% and 90% acetonitrile/water reactions, 0.65 g (0.003 mol) of 2-iodooctane was dissolved in 30 ml of solvent. For the 80%, 0.30 g (0.001

mol) of 2-iodooctane was dissolved in 50 ml of solvent and for the 50% acetonitrile/water experiments 0.15 g (0.62 mmol) of 2-iodooctane was dissolved in 80 ml of solvent. The reaction mixtures were sealed using parafilm in a transparent quartz tube and degassed for approximately 3 minutes with nitrogen gas. Each reaction was allowed to react for 4 hours. After the reaction was complete, the mixture was collected and injected neat into the GC/MS.

F Value Experiment

For each reaction, a measurement of the loss of optical activity with respect to time was done by polarimetry. Also, the disappearance of (*R*)-2-iodooctane was also followed as a function of time using GC/MS. For this experiment the concentrations were increased so as to get an appreciable optical rotation. This experiment was carried out using 95%, 90% and 80% acetonitrile/water solutions as the solvent media. For the 95% acetonitrile/water experiment, a concentration of 1.0 g (0.004 mol) of (*R*)-2-iodooctane in 20 ml solvent was used. For the 90% acetonitrile/water experiment, 1.30 g (0.005 mol) in 40 ml was used and for the 80% acetonitrile/water experiment, 1.0 g (0.004 mol) in 40 ml solvent was used.

For each experiment, the appropriate amount of (*S*)-2-iodooctane was dissolved in the appropriate solvent and a small aliquot was taken initially. This aliquot represented $t=0$. The reaction vessel was then degassed using nitrogen gas. After this point, the photolysis reaction began. Several aliquots were subsequently taken via syringe at 15 minute intervals *i.e.* $t=15$, $t=30$, *etc.* Each

aliquot was then analyzed using GC/MS and polarimetry. Once the rotation of the reaction reached zero, the experiment was over. The amount of (S)-2-iodooctane remaining in each aliquot was quantified using GC/MS and suitably plotted as a function of time. The rotations observed for each aliquot were also suitably plotted as function of time. The F values were determined mathematically based on the ratio of slopes of each experiment. For the mathematical details, please refer to the appendix.

Thermal Reactions

Each thermal reaction was conducted using the same concentrations mentioned above for the photolysis with the racemic material. Reactions in 100% acetonitrile, and 95% and 90% acetonitrile/water solutions were carried out. Each reaction was kept from all light sources by wrapping the round-bottom flask in aluminum foil. The reactions were allowed to stir for 3 weeks at room temperature before analysis was done. Each sample was injected neat into the GC/MS.

E. Materials

Solvents

Dichloromethane (methylene chloride), Fisher Chemical Company

Water (HPLC grade), Fisher Chemical Company

Methanol (dry, HPLC grade), Fisher Chemical Company

Pyridine, Aldrich Chemical Company

Diethyl Ether, Aldrich Chemical Company

Tetraethylene glycol, Aldrich Chemical Company

Acetonitrile (dry, HPLC grade), Aldrich Chemical Company

Gases

Nitrogen, Fisher Chemical Company

Reagents

1-Octylamine, Aldrich Chemical Company

2-Octylamine, Aldrich Chemical Company

(S)-2-Octanol, Aldrich Chemical Company

2-Octanol, Aldrich Chemical Company

2-Octanone, Aldrich Chemical Company

p-Toluenesulfonylchloride, Aldrich Chemical Company

Lithium Iodide, Aldrich Chemical Company

Sodium Borodeuteride, Aldrich Chemical Company

Acetyl Chloride, Aldrich Chemical Company

Sulfuric Acid, Fisher Chemical Company

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APPENDIX

Analysis of Data from the Photolysis of (R)-2-Iodoctane

The disappearance of the reactant was followed by GC/MS and corresponds to $[R] + [S]$. Because $[R] + [S] = [R]_0$ at $t=0$, one can then obtain $([R] + [S])/[R]_0$.

For the changes in optical rotation, the following equations are true.

$$f_R R_R + f_S R_S = R_{ob} \quad (1)$$

$$f_R + f_S = 1 \quad (2)$$

$$R_R = -R_S \quad (3)$$

$$R_R = R_{ob} \text{ at } t=0 \quad (4)$$

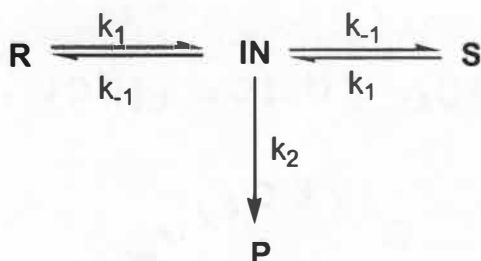
where f_R and f_S are the mole fractions of the two enantiomers, R_R and R_S are the optical rotations of the two enantiomers, and R_{ob} is the measured rotation.

Substituting equations (2) and (3) into (1) yields;

$$f_R = \frac{R_{ob} + R_R}{2R_R} \quad (5)$$

From this and $f_S = 1 - f_R$, one can easily calculate $([R] - [S])/[R]_0$.

Derivation of the theoretical equations for $[R] + [S]$ and $[R] - [S]$. You are given the system



where R and S are the enantiomers of the substrate, IN is the intermediate (RP or IP), and P is the product(s). If $[R] = [R]_0$ and $[S] = 0$ at $t=0$, and $F=k_2/(k_2 + 2k_{-1})$, one derives the following equations if the steady state approximation is applied to IN

$$\frac{d[R] - [S]}{dt} = -k([R] - [S]) \quad (6)$$

$$\frac{d[R] + [S]}{dt} = -kF([R] - [S]) \quad (7)$$

Thus,

$$\frac{\ln[R] + [S]}{[R]_0} = -k_1 F t \quad \text{and} \quad (8)$$

$$\frac{\ln[R] - [S]}{[R]_0} = -k_1 t \quad (9)$$

Suitable plots yield slopes whose ratio is F .

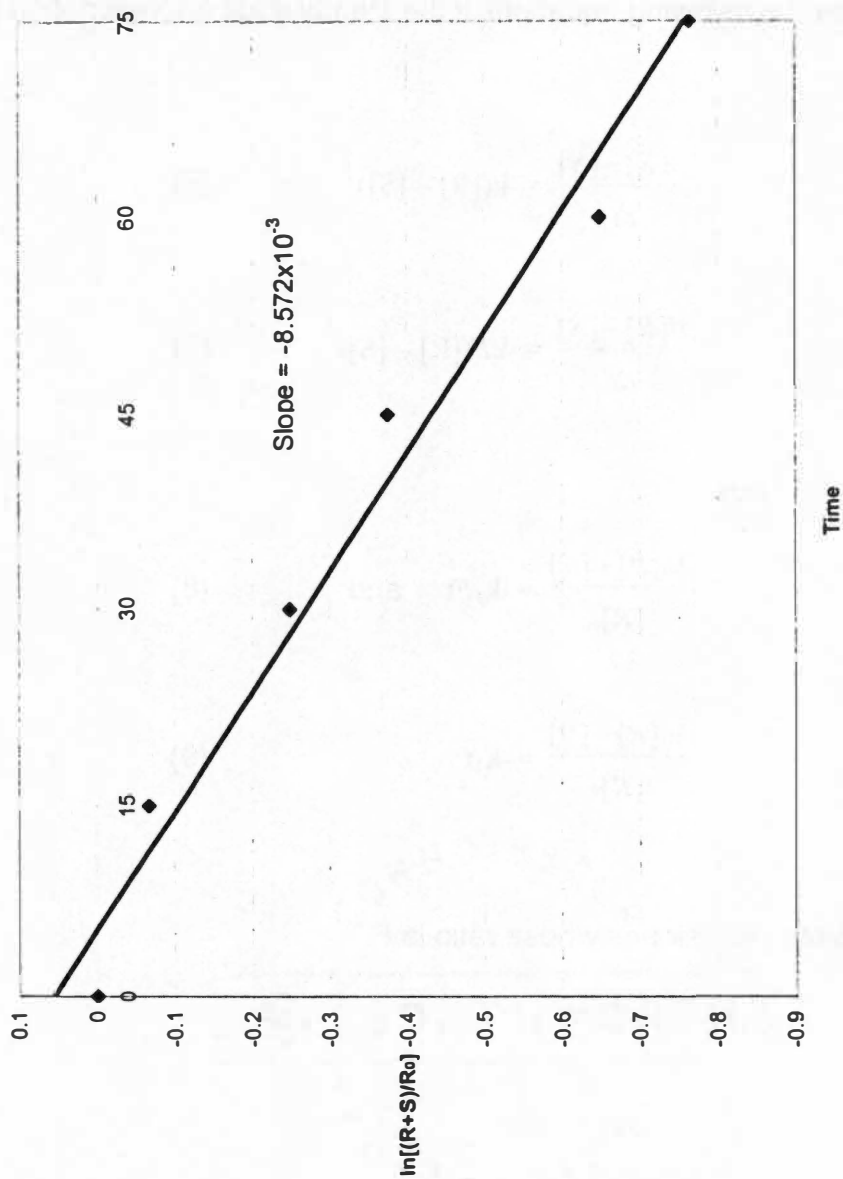


FIGURE A-1. Plot of $\ln[(R+S)/R_0]$ vs. Time (90% Acetonitrile/Water)

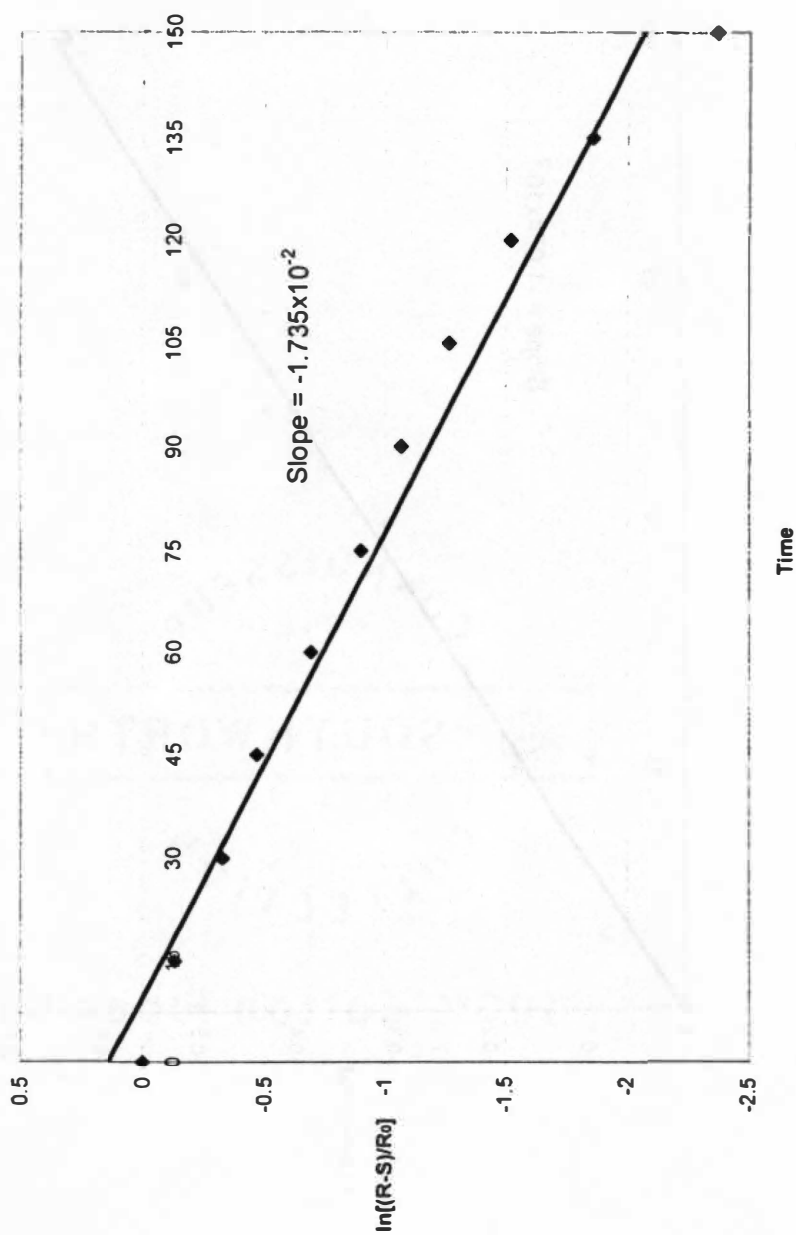


FIGURE A-2. Plot of $\ln[(R-S)/R_0]$ vs. Time (90% Acetonitrile/Water)

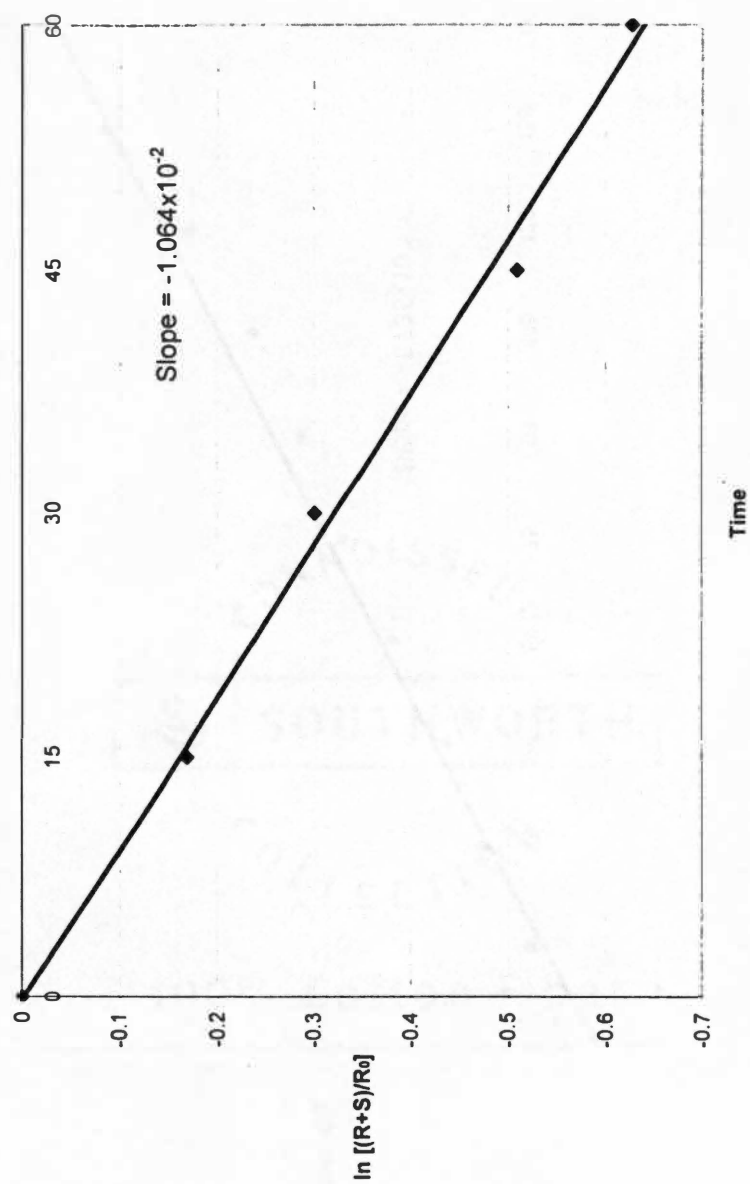


FIGURE A-3. Plot of $\ln[(R+S)/R_0]$ vs. Time (80% Acetonitrile/Water)

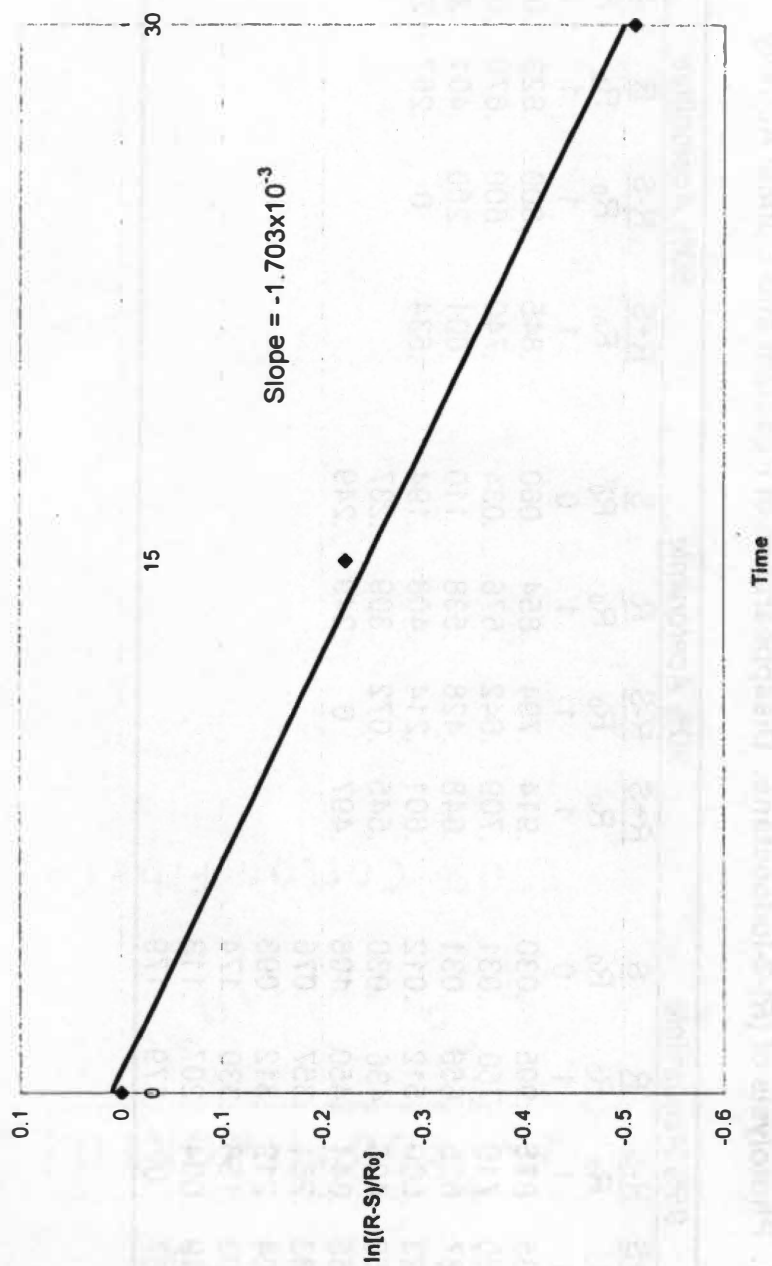


FIGURE A-4. Plot of $\ln[(R-S)/R_0]$ vs. Time (80% Acetonitrile/Water)

Table A-1. Photolysis of (*R*)-2-Iodoctane. Disappearance of Reactant and Optical Activity

Reaction Time	95% Acetonitrile				90% Acetonitrile				80% Acetonitrile			
	<u>R+S</u>	<u>R-S</u>	<u>R</u>	<u>S</u>	<u>R+S</u>	<u>R-S</u>	<u>R</u>	<u>S</u>	<u>R+S</u>	<u>R-S</u>	<u>R</u>	<u>S</u>
	R ₀	R ₀	R ₀	R ₀	R ₀	R ₀	R ₀	R ₀	R ₀	R ₀	R ₀	R ₀
0	1	1	1	0	1	1	1	0	1	1	1	0
15	.935	.875	.905	.030	.914	.794	.854	.060	.845	.800	.823	.023
30	.780	.719	.750	.031	.709	.642	.676	.034	.740	.600	.670	.070
45	.687	.625	.656	.031	.648	.428	.538	.110	.601	.200	.401	.201
60	.523	.500	.512	.012	.601	.214	.408	.194	.534	0	.267	.267
75	.466	.406	.436	.030	.545	.072	.309	.237				
90	.555	.344	.450	.106	.497	0	.249	.249				
105	.433	.281	.357	.076								
120	.404	.219	.312	.093								
135	.503	.156	.330	.174								
150	.319	.094	.207	.113								
165	.357	0	.179	.179								

Table A-2. Data from Acetonitrile/Water *F* Value Experiments

Reaction Time	95% Acetonitrile		90% Acetonitrile		85% Acetonitrile	
	observed optical rotation	percent remaining of starting material	observed optical rotation	percent remaining of starting material	observed optical rotation	percent remaining of starting material
0	-.032	100	-.014	99.63	-.005	100
15	-.028	93.49	-.011	31.09	-.004	84.52
30	-.023	78.00	-.009	70.64	-.003	74.00
45	-.020	68.67	-.006	64.61	-.001	60.10
60	-.016	52.25	-.003	59.88	.000	53.45
75	-.013	46.59	-.001	54.25		
90	-.011	55.46	.000	49.53		
105	-.009	43.27				
120	-.007	40.41				
135	-.005	50.26				
150	-.003	31.92				
165	.000	35.65				

**Table A-3. Photoproducts and Relative Yields (%)
from the Photochemistry of 2-*D*-Iodooctane**

Photoproducts	Reaction Phase— 2- <i>D</i> -Iodooctane	
	90 % CH ₃ CN/H ₂ O	50% CH ₃ CN/H ₂ O
1-octene	57.0	38
3-octene		
octane	4.0	2.6
(E)-2-octene	23.0	13.0
(Z)-2-octene	11.3	5.0
Unknown		13.0
4-octanol		
3-octanol		
2-octanol	2.0	16.0
2-octanone		4.0
4-octyl acid amide	0.3	1.3
3-octyl acid amide	0.4	2.6
2-octyl acid amide	2.0	4.5

VITA

Nicie Conley Murphy was born in Louisville, KY on November 21, 1978. She graduated from DuPont Manual Magnet High School in May 1996. In August 1996 she began college at Tennessee State University in Nashville where she majored in chemistry. In the summer of 1999, Nicie participated in a research program sponsored by the University of Florida that allowed her to do research at the University of Bordeaux, Paul Pascal Center of Research, in Bordeaux, France. She served as the Vice-president of the Chemistry Club in the year 1998-1999 and the President in 1999-2000. She became a member of Beta Kappa Chi National Scientific Honor Society and Golden Key National Honor Society in 1999. She was listed in Who's Who Among America's Colleges and Universities in 1999-2000. She graduated *cum laude* with her Bachelor of Science Degree in Chemistry in May 2000.

In August 2000, Nicie entered the University of Tennessee, Knoxville as a graduate student and Teacher's Assistant in the Department of Chemistry. She was honored with a Graduate Teaching Award in April 2005. Nicie defended her dissertation in September 2005. She received her Doctor of Philosophy Degree in Chemistry from the University of Tennessee, Knoxville in December 2005.

Nicie is a member of the National Organization for the Professional Advancement of Black Chemists and Chemical Engineers, the American Physical Society and Alpha Kappa Alpha Sorority, Incorporated.

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