I. PHOTOINDUCED NUCLEOPHILIC ADDITION TO *s*-CIS NAPHTHALENONES

II. TANDEM DEALKOXYCARBONYLATION-MICHAEL ADDITION ROUTE TO CHROMANS

III. PHOTOENOLIZATION STUDIES OF HETEROAROMATIC COMPOUNDS

By

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CHAPTER 1

HISTORICAL BACKGROUND: PHOTOCATALYZED ADDITIONS TO CYCLIC α,β-ENONES

Introduction

This chapter presents an overview of the photochemical behavior of cyclic α,β-unsaturated ketones. The primary focus is on the photochemical addition of heteroatomic nucleophiles, in particular simple alcohols and water. Common photoadditions have been discussed in terms of mechanism and competing side reactions. Also included is a brief summary of photoreductions and important photorearrangements which include the aryl migration and the Type A rearrangement of cyclohexenones.

Possible Transition States Involved in Photoadditions

Nucleophilic addition to photochemically generated excited states has proven to be a very rich field of research. Some of the most widely studied systems have been the medium-sized (6-8 carbons) cycloalkenones. It is widely accepted that the mechanism leading to addition of alcohols and water to unsaturated enones involves either the π,π* triplet state[1] or the strained ground state isomer that results from decay of the excited state.[1-3] There is physical evidence that π,π* excitation of unsaturated cycloalkenones results in a short-lived twisted triplet state **2** which either (a) undergoes intersystem crossing to the ground state trans isomer **3** or (b) decays to the ground state cis isomer **1** as shown in Figure 1.[4-7] When considering the trans isomer, the geometry between the carbonyl and the α,β-double bond is orthogonal with the loss of conjugation. This

isomerization is directly affected by the ring size; thus, 2-cyclooctenone can readily isomerize while isomerization is not very favorable for 2-cyclohexenone. In order to

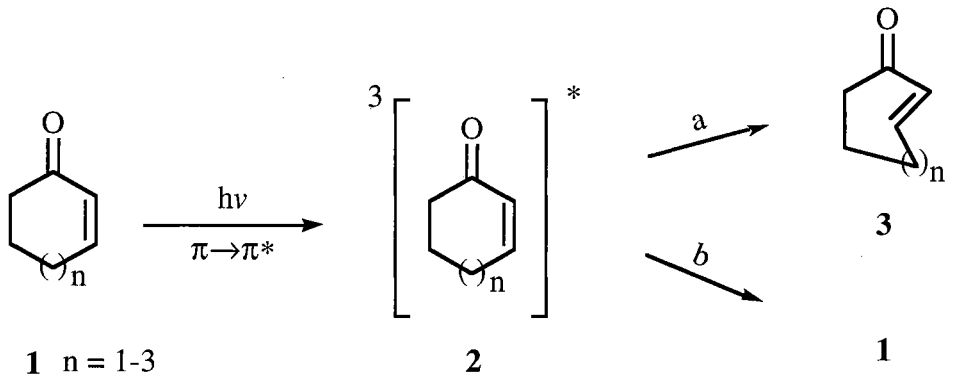
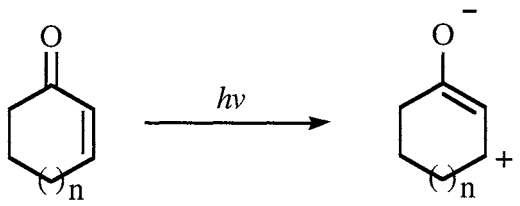


Figure 1. Cis-trans Isomerization of Cyclic Enones.

relieve the strain in the trans enone, the molecule can equilibrate back to the unstrained cis isomer. Alternatively, if an appropriate nucleophile such as water or alcohol is present, addition to the strained double bond to generate the less strained saturated system can occur.

Although not as widely accepted as the above scenario, a second mechanism involves a polar or zwitterionic state (i.e. **4**)[8,9] represented in Figure 2. Chapman introduced this concept,[10] but it is not entirely clear whether it is a ground state or an excited state species derived from π,π^* or n,π^* excitation. Since the proposal was advanced, little additional evidence has been reported to support the zwitterion.

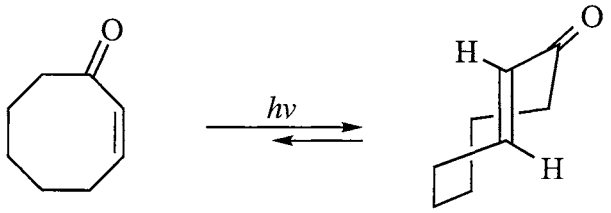


1 n = 1-3 **4**

Figure 2. Zwitterionic Transition State of Cyclic Enones.

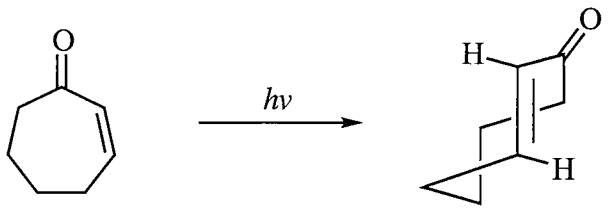
Photochemistry of Cycloheptenones and Cyclooctenones

Before discussing cyclohexenone photochemistry, it is important to first discuss the larger ring enones since a great deal of the pioneering work in photocatalyzed nucleophilic additions was performed on these systems. It was found that the alkene portion of the excited triplet state is analogous to the triplet state of an unconjugated alkene. When a dilute solution of 2-cyclooctenenone (**5**) in cyclohexane is irradiated at wavelengths greater than 300 nm, excitation to the triplet excited state allows for nearly unrestricted twisting of the α,β-bond, resulting in the trans isomer **6**. Once the trans isomer is formed, it is in photoequilibrium with its cis isomer. However, the smallest trace of mineral acid causes the equilibrium to rapidly shift back to the more stable cis double bond. This photoisomerization to the unstable trans isomer has been proven by both spectroscopic and chemical methods that are beyond the scope of this summary.[6]



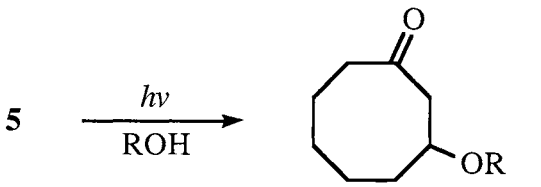
5 **6**

Shortly after the detection of trans cyclooctenone, Corey[11] and Eaton[7] independently reported that trans cycloheptenone **8** could be detected by irradiation of either a dilute solution or a thin film of *cis*-2-cyclohepten-1-one (**7**) at low temperatures. The major evidence for the trans cycloheptenone was based on the disappearance of the conjugated carbonyl and the appearance of a nonconjugated carbonyl in both the UV and IR spectra. It was suggested that since the carbonyl and the α,β-double bond have an orthogonal geometry in **8**, the spectral changes were explainable only if cis-trans isomerization had occurred.



7 **8**

Noyori and co-workers were the first to propose that the strained ground state intermediate **6** was responsible for the photoinduced alcohol addition to 2-cyclooctenone. Irradiation of **5** in the presence of methanol at room temperature for 30 min yielded 72% of 3-methoxycyclooctanone (**9a**). When **5** was irradiated in isopropanol under the same conditions, the reaction gave 3-isopropoxycyclooctanone (**9b**) in 43% yield after 2.5 h. In order to demonstrate that the strained ground state trans enone was responsible for the observed reaction, **5** was irradiated at -78 °C in an inert solvent for 15 min, then the cold photolysate was treated with excess methanol and warmed to room temperature while being kept in the dark. This dark reaction occurred in the same manner to give the addition products **9a** and **9b**. In a similar fashion, cyclooctenone was irradiated in isopropanol for 15 min at -78 °C and quenched in the dark with methanol. Upon warming, the reaction proceeded to give 97% of the methanol addition product and <1% of the isopropanol

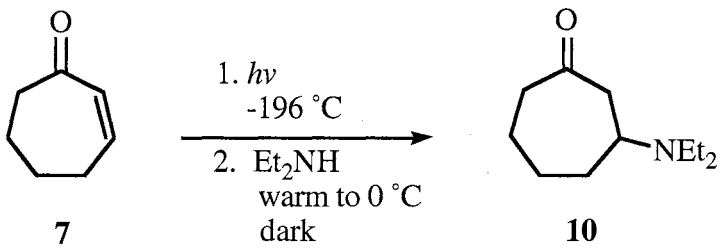


9a R = CH_3
9b R = $(CH_3)_2CH$

addition product. From these results, it was concluded that the reaction did not occur directly through the excited state to any great extent,[2] but rather a long-lived ground state intermediate was reacting with the nucleophiles. Later, Noyori and Katô found that other protic solvents such as water, diethylamine, and acetic acid also added to 2-cyclooctenone using the conditions described above.[12] It is important to note that in all cases addition occurred in a regiospecific manner, with the nucleophilic center forming a bond with the β-carbon of the enone analogous to that observed in a Michael-type reaction.

Although it was previously demonstrated that the strained trans isomer of 2-cyclohepten-1-one could be generated upon irradiation of *cis*-2-cyclohepten-1-one,[7,11] Noyori and Katô had difficulty showing that the ground state molecule was responsible for the observed addition of water and alcohols to this system.[3,12] In an attempt to prove this was the case, they irradiated a sample of *cis*-2-cyclohepten-1-one in an inert solvent at liquid nitrogen temperatures, turned off the lamp and quenched with methanol that was previously cooled to -78 °C. After gradual warming to room temperature, the only identifiable products were found to be dimers resulting from a [2+2] addition which often occurs as a side reaction in enone photochemistry.[13] Hart later suggested that these dimers were a direct result of a highly strained intermediate and have a greater tendency to dimerize than to add weakly nucleophilic alcohols.[14] By adding diethylamine, a stronger

nucleophile, to the cold photolysate and allowing the solution to warm to 0 °C, they were able to obtain **10** in a 25% yield. Using this methodology, it was confirmed that the photo-



7 **10**

induced nucleophilic addition to 2-cycloheptenones occurred in a manner similar to that observed for 2-cyclooctenones. Reduced stability caused by ring strain in the intermediate, however, was attributable to differences in the reactivity of the seven- and eight-membered cycloalkenones. It is of interest to note that irradiation of *cis*-2-cyclononenone resulted in a trans isomer that was sufficiently non-reactive to be isolated by normal procedures. This isomer was stable in methanol solution at room temperature and required heating to 100 °C for nucleophilic addition to occur.

Hart and co-workers[14] extensively studied the mechanism and resulting stereochemistry of the addition of alcohols to α,β-unsaturated cyclic enones. They determined that irradiation of both 2-cycloheptenone and 2-cyclooctenone in CH_3OD resulted in an addition product having the methoxy and the deuterium groups trans as shown in structures **13** and **14**. From the results of this study, it was ascertained that the reaction is not only regiospecific but also stereospecific. The regiospecificity was explained by a high degree of inductive polarization caused by the strained intermediate. This polarization causes nucleophilic attack to occur at the β-carbon to form the strained dipolar intermediates **11** and **12**. The observed stereospecificity was explained as follows. It was suggested that the deuterium could only be transferred to the same face as the nucleophile since the ring itself blocks attack from the opposite face. This transfer may

occur via a concerted four-centered transition state, or it may occur through an intermolecular transfer of a deuterium from another solvent molecule.

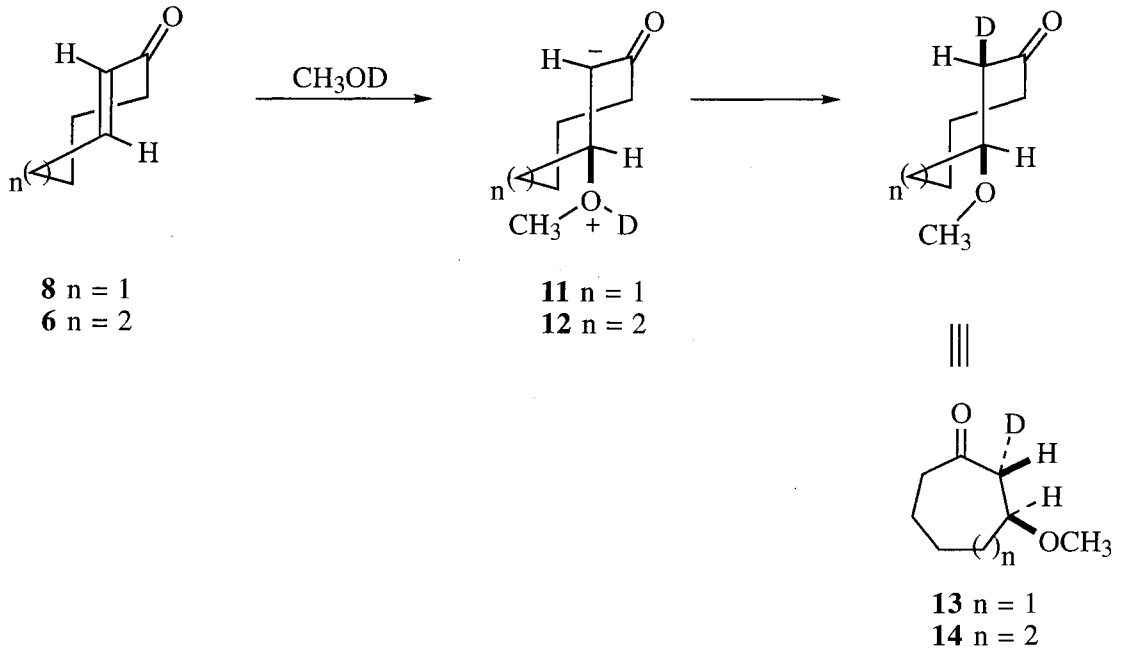
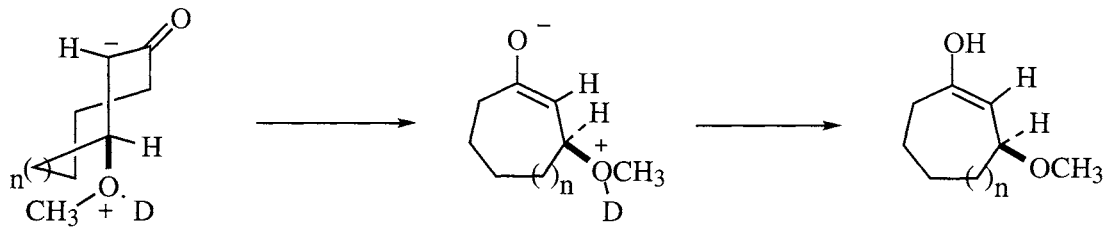


Figure 3. Mechanism of Photochemical Addition to Cycloalkenones.

An alternative mode of addition could also proceed to yield intermediates **11** and **12** which would relax to the conformationally favored enolates **15** and **16**. Deuteration at the oxygen would produce enols **17** and **18**, which could conceivably tautomerize to the keto forms **13** and **14**. It was deemed highly probable, however, that either deuteration of the enolates or ketonization of the resulting enols would lead to a mixture of both cis and trans addition products. Interestingly, base-catalyzed Michael addition of methanol to 2-cycloheptenone and 2-cyclooctenone also resulted in a trans relationship between the



11 n = 1
12 n = 2

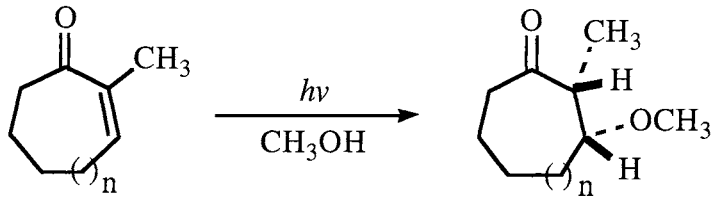
15 n = 1
16 n = 2

17 n = 1
18 n = 2

Figure 4. Alternative Mechanism of Photochemical Addition to Cycloalkenones.

methoxy and the deuterium groups. This thermal anti addition was explained by the principle of microscopic reversibility using antiperiplanar E2 elimination-addition of the alcohol as a descriptive mechanism which accounts for the observed results. A brief examination of the acid-catalyzed Michael addition showed no selectivity.

Hart and co-workers[15] also studied the effects of methyl substitution on the photoaddition process. They found that both 2-methyl-2-cycloheptenone (**19**) and 2-methyl-2-cyclooctenone (**21**) added methanol to give the expected *cis*-3-methoxy-2-methylcycloalkanones **20** and **22**, respectively. When the methyl group was moved to C-3, the reaction also proceeded to give the expected addition products. 2,3-Disubstituted



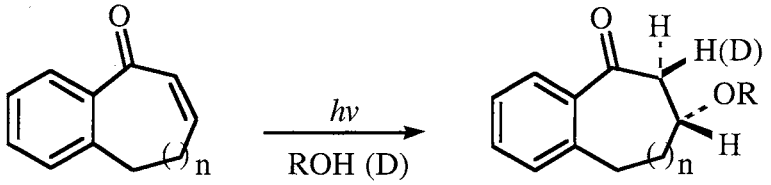
19 n = 1
21 n = 2

20 n = 1
22 n = 2

cyclooctenone, however, failed to add solvent under photochemical conditions. It was suggested that the non-reactivity of the tetrasubstituted double bond was a result of

increased strain due to the nonbonding interactions in the trans isomer. As a result, reversion back to the cis isomer occurred faster than addition of methanol. It is interesting that neither base-catalyzed nor acid-catalyzed addition of methanol was stereospecific when the double bond was substituted. The fact that stereospecificity was observed only in the photochemical reactions helped strengthen the argument for a concerted syn addition.

Hart also found that irradiation of benzocycloalkenones, such as **23** and **25**, in nucleophilic solvents showed reactivity parallel to that observed in the 2-cycloheptenones and 2-cyclooctenones.[14,16] As in all previously reported cases, the addition occurred to give the expected addition products **24** and **26**. The fused aromatic ring did not affect the reaction outcome.



23 n = 1
25 n = 2

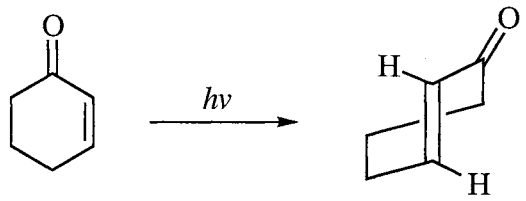
24 n = 1
26 n = 2

Photochemistry of Cyclohexenones

Among the enones, α,β-unsaturated cyclohexenones undoubtedly exhibit the most diverse photochemistry. The photoaddition of nucleophilic solvents to these systems is strikingly similar to seven- and eight-membered cyclic enones. The differences between these systems lie mainly in the increased ability for competing cyclodimerizations, free-radical solvent additions, and photorearrangements. These differences will be addressed where appropriate.

The detection of the isomerization of 2-cyclohexen-1-one (**26**) to ground state trans cyclohexenone **27** proved very elusive.[5,13,17,18] Schuster and co-workers used pulsed

laser excitation coupled with transient absorption spectroscopy in an attempt to detect a twisted ground state isomer or a trans cyclohexenone.[5] It was not clear from their results whether they succeeded in identifying the trans isomer, but they were able to determine that



26 **27**

a twisted π,π^* excited state, capable of producing the trans cyclohexenone, was present. Although not totally conclusive, Goldfarb also reported comparable results using laser photolysis and gas discharge flash photolysis.[17] Although the exact nature of the reactive species is still under investigation, many photochemical reactions of cyclohexenones are best explained by the trans isomerization hypothesis.

In an attempt to trap the trans isomer, Noyori and Katô photolyzed 2-cyclohexenone (**26**) using methanol as the solvent.[12] Although produced in low yield (0.7%), the isolation of 3-methoxycyclohexanone (**29**) indicated the possibility of intermediate **28** being the trans isomer **27**. The major products from the reaction proved to be the previously synthesized[19] [2+2] cyclodimers **30** and **31** which are commonly referred to as head-to-tail and head-to-head dimers, respectively. It was not indicated what intermediate was responsible for the dimers, but it is possible that the trans intermediate will yield the cis-fused dimers if epimerization at the α-carbon occurs after addition.

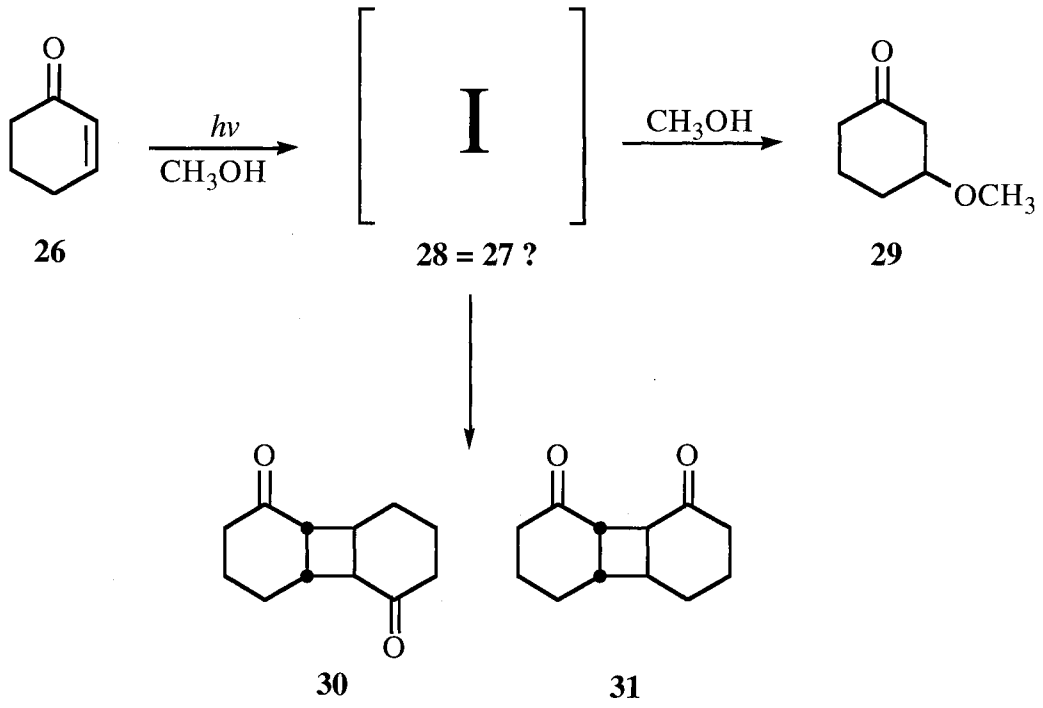


Figure 5. Photolysis of Cyclohexenone in Methanol.

While investigating 3-alkyl-2-cyclohexenones, Rudolph and Weedon found that irradiation of isophorone (**32**) in benzene with 10% methanol and catalytic acetic acid yielded a 3:1 mixture of the exocyclic deconjugated isomer **34** and the photoaddition product **35**. It was believed that acetic acid protonated the highly strained trans isomer to give carbocation **33** (or its enol tautomer) which then underwent alcohol addition or proton abstraction to give **34** and **35**.[20] In a recent publication, Schuster and co-workers reinvestigated this acid catalyzed addition using 3-methyl-2-cyclohexenone (**36**). Based on steady state and flash kinetic data, they concluded that the acid-catalyzed reaction which yielded **38** and **39** most likely proceeded through the enone triplet state and not through the trans isomer.[21]

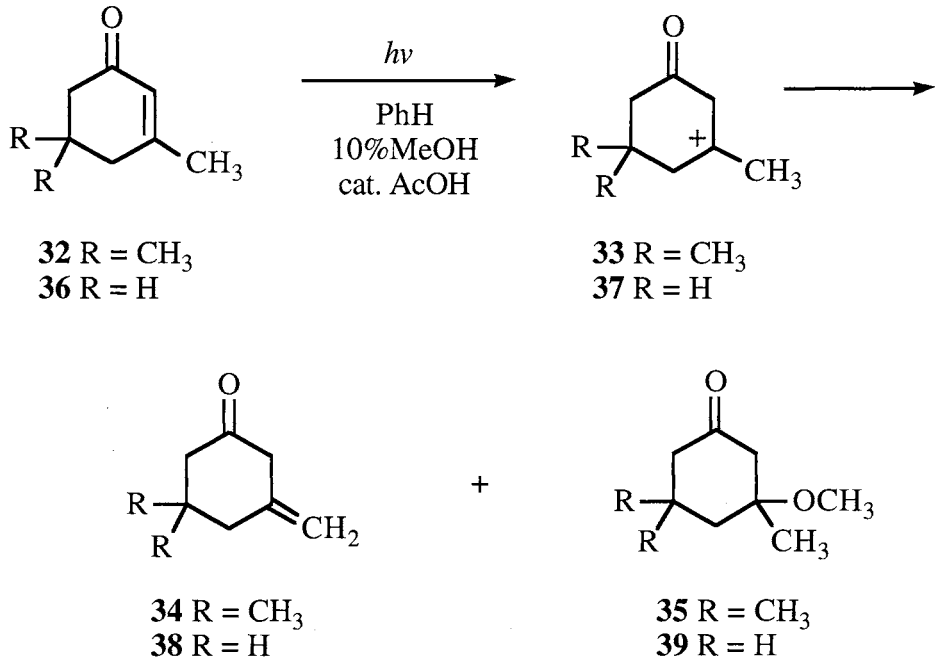


Figure 6. Acid-Catalyzed Photoaddition of Methanol to Cyclohexenones.

In a much earlier investigation of the reactivity of isophorone, Dauben found that irradiation of **32** in neutral *tert*-butyl alcohol gave only 4% of the addition product along with a crystalline [2+2] dimer as the major product.[22] It was not discussed whether the large size of the nucleophile resulted in the low yield of photoproduct, but it is possible that acid catalysis plays an important role in the addition process.

Most of the photoadditions of nucleophiles to cyclohexenones occur when the enone is part of a larger polycyclic system. One of the first examples of this type was the photoaddition of alcohols to Pummerer's ketone **40** described by Matsuura and Ogura.[8,9] When enone **40** was irradiated using methanol as a solvent, a crystalline methanol adduct was formed in 79% yield. X-ray and spectroscopic analyses indicated that the product was **41** resulting from alcohol addition. If the irradiation was done in isopropanol, photoaddition occurred to yield 37% of **42** at the expense of a competing rearrangement which yielded photoketone **43** in 22% yield. On the other hand, if the reaction was done in *tert*-butyl alcohol, only the rearrangement product **43** was isolated.

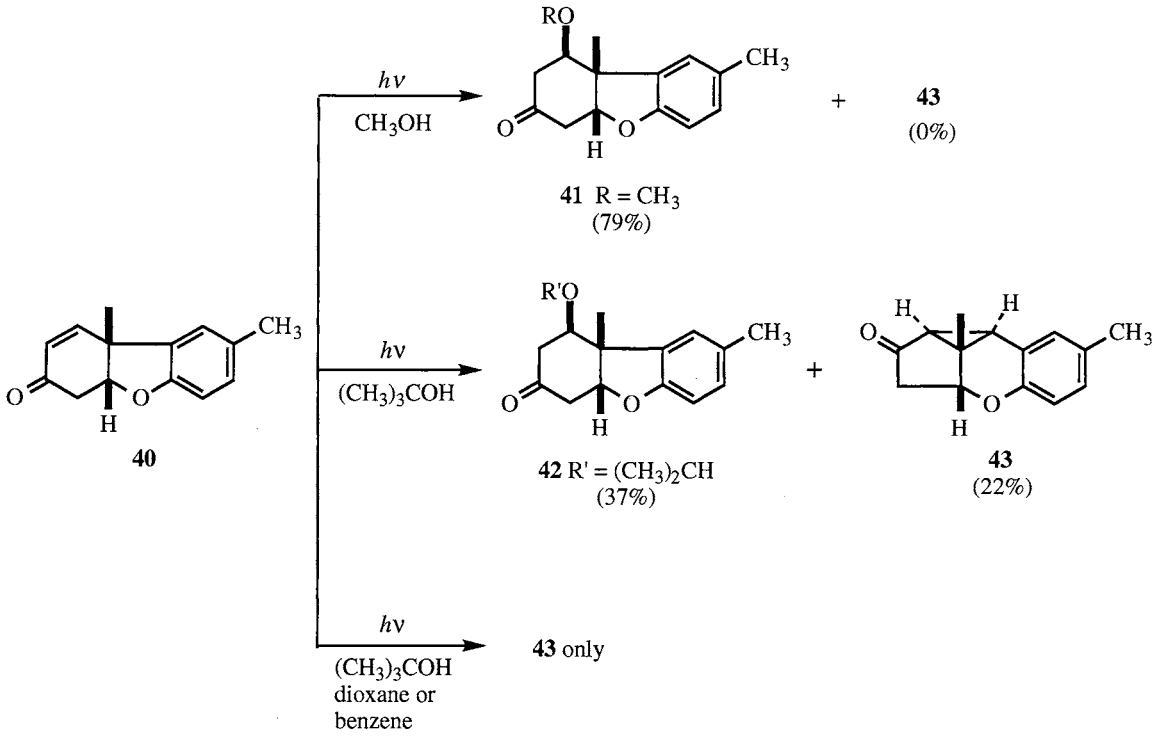
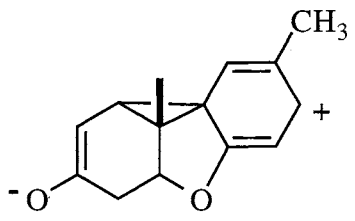


Figure 7. Photoaddition to Pummerer's Ketone.

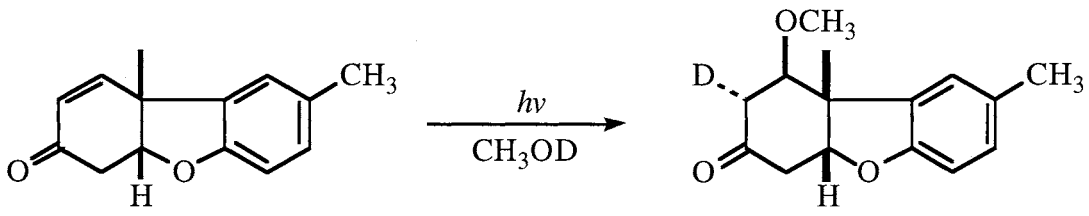
The competing rearrangement in isopropanol and *tert*-butyl alcohol was reported to be due to the steric hindrance in the bulky nucleophile. However, photolysis in dioxane and benzene also gave the rearranged product **43** in 31% and 72% yield, respectively. Three possible reaction mechanisms were proposed for the observed outcome. First, it was suggested that a phenonium ion such as **44** was produced upon n,π^* excitation of the enone. This transition state was then attacked by the nucleophilic solvent causing opening of the three-membered ring followed by protonation at the α-carbon to give compound **41**



44

or **42** depending on the solvent. The second possibility involved the π,π^* excited state. A zwitterionic transition state similar to that illustrated previously in Figure 2 was proposed, and it was assumed that attack occurred in a regiospecific fashion to the double bond. The third explanation made note of the close proximity of the enone to the benzene ring. It was suggested that this closeness resulted in an interaction which led to polarization of the enone such that the β-carbon was electron deficient. As a result of polarization, attack once again occurred at the β-carbon.

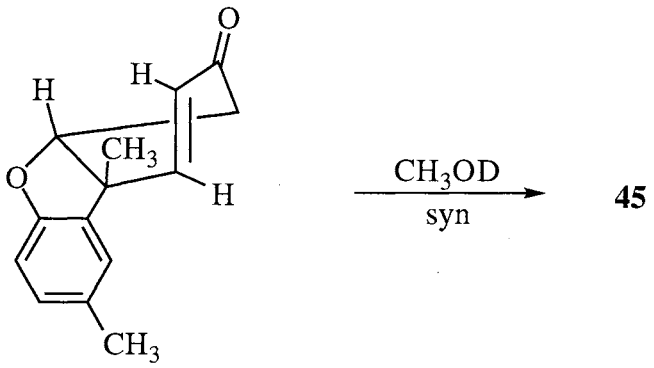
In an attempt to elucidate the exact mechanism of the photoaddition to Pummerer's ketone, Hart and co-workers studied the stereochemical outcome using deuterated methanol as the solvent.[14] They found that addition to the cyclohexenone ring of **40** occurred in a stereospecific manner giving a trans relationship between the deuterium and the methoxy group as shown in **45**. As Matsuura and Ogura had previously discovered, they also reported that the methoxy group and the angular methyl group end up cis to one



40 **45**

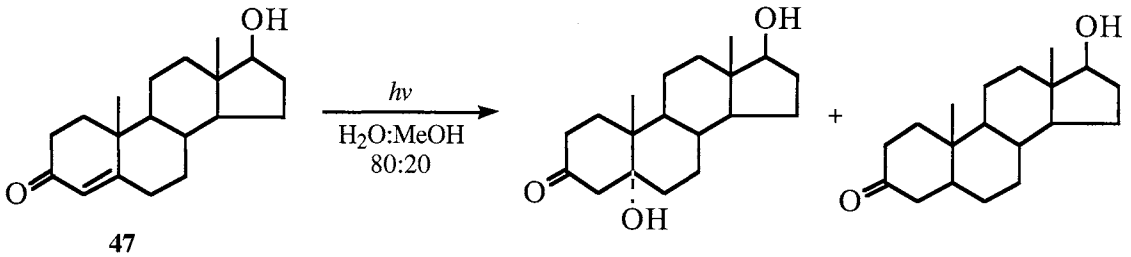
another. More importantly, it was found that the deuterium added to the congested concave face of the molecule. This latter finding suggested that the reaction proceeded through syn addition to the elusive trans double bond. Conformational analysis of the possible trans intermediate indicated that twisting of the double bond can occur only as shown in **46** because twisting in the other direction would result in an unfavorable steric effect between the double bond and the face of the phenyl and dihydrofuran rings. After addition occurs and the molecule relaxes, the products have the trans stereochemistry illustrated in **45**.

Schuster briefly studied the acid catalyzed addition of methanol to Pummerer's ketone and did not report any discrepancies in the reaction outcome.[21]



46

The photochemistry of steroids has proven to be a very active field of interest due to the physiological and pharmaceutical properties of these compounds. Filipescu and co-workers[23] investigated the addition of water to the enone moiety of androgenic steroids. They revealed that the steroids examined all reacted identically. Therefore, only testosterone **47** will be discussed. When dilute water-methanol (4:1) solutions (3×10^{-3} M) were irradiated for 90 seconds with a low pressure mercury lamp, the reaction proceeded with high efficiency to give the major photoaddition product **48** along with the reduced compound **49**. The authors suggested that the higher degree of reactivity observed in the polycyclic systems (when compared to smaller ring systems) was derived from the increased rigidity of the steroidal framework. Although they did not determine the stereochemistry of the added water, the zwitterionic transition state was favored as the explanation for the observed outcome.

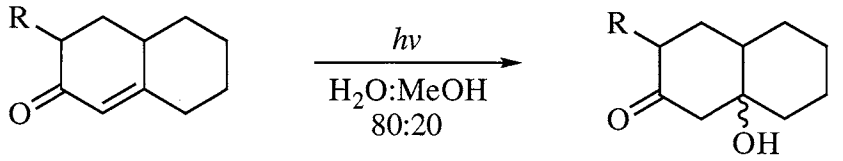


47

48
Major

49
Minor

As a comparison to the reactive A and B rings of the steroids, the same group investigated the reactivity of three different hexahydronaphthalenones. When irradiated under the same conditions, enones **50** and **52** reacted as expected to yield the hydrated products **51** and **53**. However, when the enone double bond was substituted with a methyl group at C-2, extended reaction times were required and more side-products were



50 R = H
52 R = CH_3

51 R = H
53 R = CH_3

produced. An attempt by Brown to synthesize the methanol addition products of **50** by photochemical methods was unsuccessful. Although trace amounts were detected by GC/MS, isolation of the addition products was not possible.[24,25]

Photoadditions that Produce Enol Intermediates

Although only ketone products were isolated from the previously discussed reactions, photochemical additions that proceed through a detected enol intermediate do have some precedent in the literature. Ramey and Gardner[1] found that irradiation of

1-acetylcyclohexene (**54**) in alcohol solvents gave the expected Michael-type adduct **56**. NMR analysis directly after irradiation, however, indicated the presence of a relatively long-lived enol which could be easily ketonized by gentle warming over 2 h. It was found that the hydrogen and the alkoxy moiety in the final product were ca. 80% trans. This latter finding suggested the possibility that initially two different enols **55a** and **55b** were formed, and ketonization occurred at different rates. The possible reactive species was not determined from the observed results, but it was suggested that the reaction may not involve the triplet-derived trans intermediate.

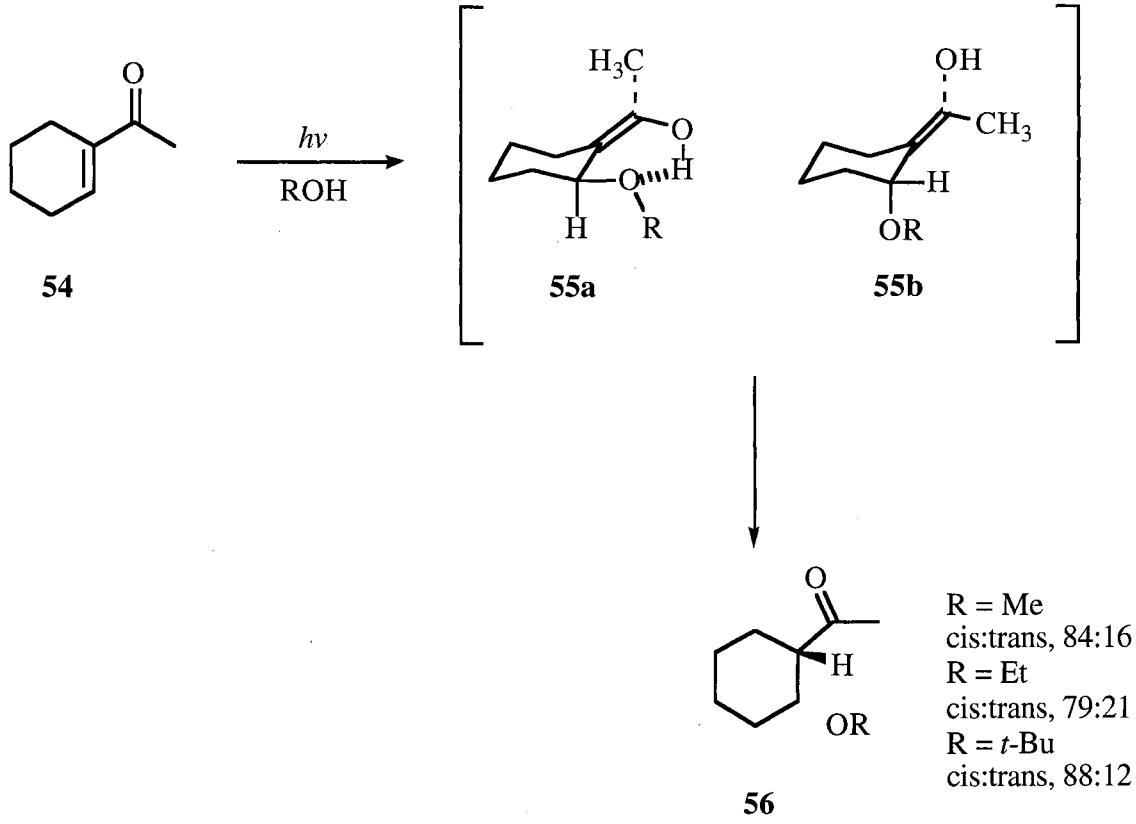


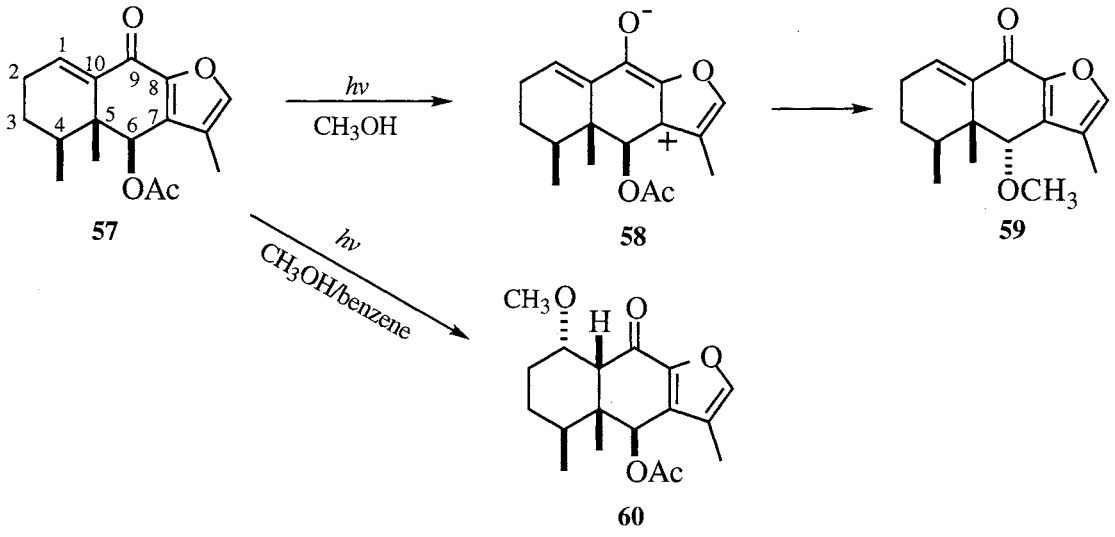
Figure 8. Photoaddition to 1-Acetylcyclohexene.

Photoaddition to *s*-Cis Enones

The photochemistry of *s*-cis enones has been very limited. Upon extensive review of the literature, only two examples of photochemical addition to *s*-cis α,β-unsaturated cyclic enones were found. All of the other examples reported incorporated *s*-trans enones

with the carbon-carbon double bond part of the same ring as the carbonyl. Therefore, research designed to study the photochemistry of *s*-cis enones may prove novel.

Rodríquez-Hahn and co-workers[26] examined the photoreactivity of decompostin (**57**) in various nucleophilic solvents. It was discovered that if **57** was irradiated in neat methanol, compound **59** was produced as the major product. This unexpected reactivity can be rationalized by stereospecific trapping of the zwitterionic intermediate **58** or possibly substitution with inversion of stereochemistry at C-6.[27] On the other hand, if **57** was irradiated in benzene containing 0.2% methanol, the expected addition occurred across the 1,10 double bond to give **60** in 95% yield as a crystalline product. Likewise, if the reaction was done using isopropyl alcohol or water in benzene, the addition occurred in the same manner to give analogous products. An explanation of the role of benzene in the reaction was not offered.

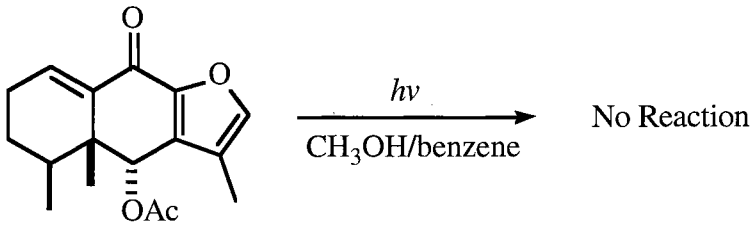


57 58 59 60

Figure 9. Photochemistry of Decompostin.

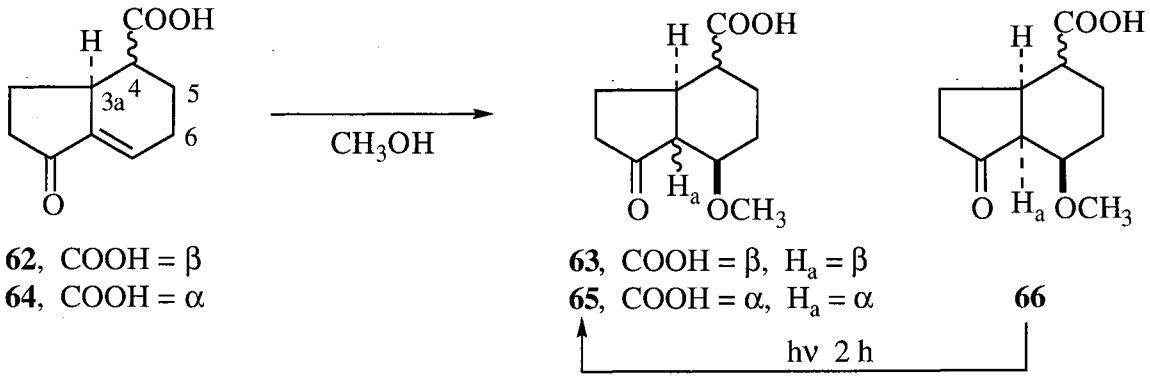
Although the mechanism for the addition was not studied in detail, X-ray analysis of the crystalline product confirmed the trans relationship of the substituents on the newly

formed chiral centers at C-1 and C-10 in **60**. This stereochemistry led the authors to suggest that the reaction proceeded by double bond isomerization followed by syn addition. It is interesting that when 6-*epi*-decompostin (**61**) was photolyzed under the same conditions, the reaction did not give any of the addition product but only starting material was isolated. The authors speculated that either the pseudo-axial acetate group or the methyl groups at C-4 and C-5 may be responsible for steric or electronic repulsion which blocks both sides from attack.



61

The second example of addition to an *s*-cis enone involves the diastereomeric 3a,4,5,6-tetrahydroindanones **62** and **64**.[28] When indanone **62** was irradiated in methanol, X-ray analysis of the isolated compound **63** showed that the most stable product had not only a cis relationship between

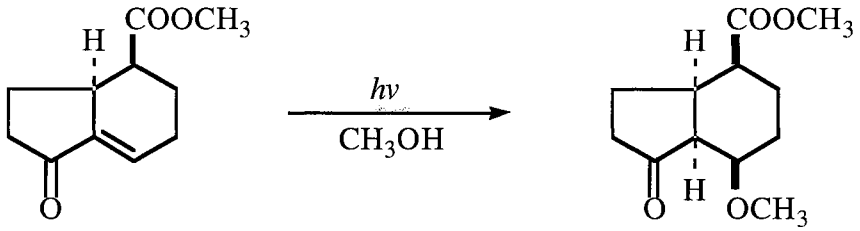


62, COOH = β
64, COOH = α

63, COOH = β, H_a = β
65, COOH = α, H_a = α

66

the added substituents but also a trans ring juncture. Photoaddition to compound **64** yielded a mixture of **65** and **66**. If the irradiation time exceeded 2 h, however, the cis-fused adduct converted entirely to **65** which had the trans ring juncture. In contrast, irradiation of the methyl ester of **62**, namely the tetrahydroindanone **67**, under the same conditions as above gave **68** which had the cis ring juncture and the trans relationship at the newly formed chiral centers. Although not mentioned by the authors, this finding suggests that the acidic conditions in the previous reactions have an effect on the outcome. It is



67 **68**

quite probable that under the acidic conditions the cis-fused adduct is initially formed, followed by epimerization at the α-carbon to give the thermodynamically favored compound. The overall interpretation of this study leads to the conclusion that once again isomerization, followed by syn addition, best describes the reaction mechanism even though it does not lead directly to the most stable isomer.

Photoreduction and Addition via Carbinols

Reduction is often observed upon photolysis of α,β-unsaturated enones in primary and secondary alcohols. Due to the wide number of examples in the literature, only a brief summary will be given. A review article by Schuster provides valuable insight on this subject and covers many of the important aspects that are beyond the scope of this review.[25]

Photoreductions are often a result of a free radical reaction in which the excited state of the enone abstracts a hydrogen from the solvent molecule. A study of the reductive ability of particular solvents indicates that the yield of reduction products is related to the C-H bond dissociation energy[29] of the solvent. Thus, when considering alcoholic solvents, the order of photoreduction can be summarized as follows: isopropanol > ethanol > methanol > *tert*-butyl alcohol.

In general, the reduction of cyclohexenones can occur to give secondary alcohols, pinacols, or saturated ketones, and the outcome appears to depend on whether the triplet state arises from n,π^* or π,π^* excitation. It is widely believed that the reduction of the carbonyl to give alcohols (secondary and pinacols) proceeds through initial hydrogen abstraction by the n,π^* excited state of the carbonyl oxygen[30] similar to mechanism (3) below. The resulting ketyl radical is then either attacked by a hydrogen donating species to yield a secondary alcohol or coupled with another ketyl radical to give a pinacol. By comparison, the mechanism for the reduction of the α,β-double bond is more complex. Although controversial, it has been reported that reduction of enols in isopropyl alcohol occurs by mechanism 1, via a π,π^* triplet state,[31] and mechanism 3, via an n,π^* triplet state.[32] In order to explain this reduction, three different mechanisms involving cyclohexenone **26** have been advanced (see Figure 10).

1) Hydrogen abstraction at the β-carbon generates the delocalized radical **69**. Hydrogen transfer from either isopropyl alcohol (IPA) or isopropyl radical (IPA•) can occur at the α-carbon to give saturated cyclohexanone **70** or at the oxygen to give enol **71** which then tautomerizes to the ketone.

2) Hydrogen abstraction at the α-carbon to give radical **72**, followed by hydrogen transfer to the β-carbon to provide **70**.

3) Hydrogenation of the carbonyl oxygen to give ketyl radical **73**, followed by hydrogen donation to the β-carbon of enol radical **74** and tautomerization of the resulting enol **71** to furnish cyclohexanone.

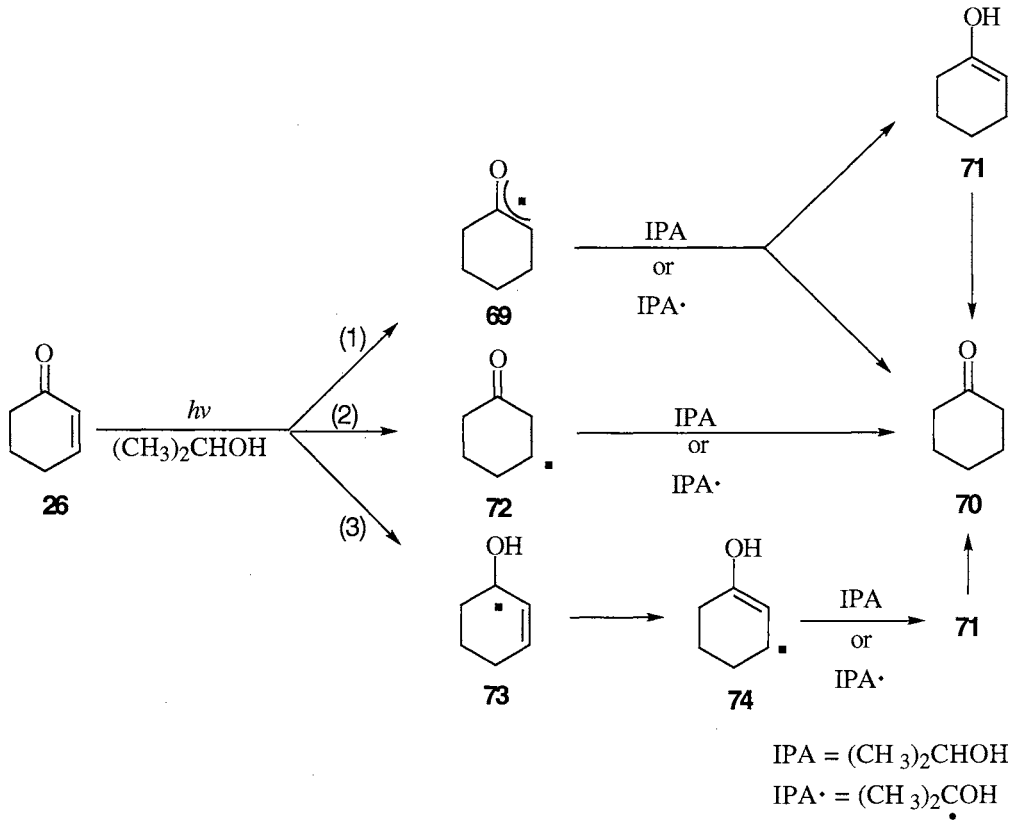
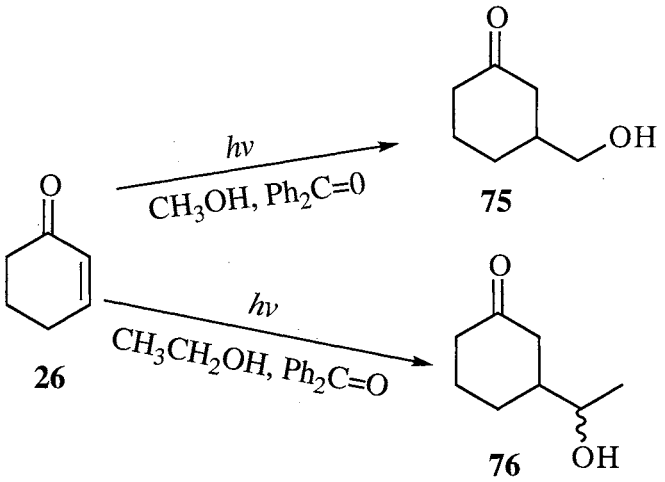


Figure 10. Photoreduction of Cyclohexenone.

Photoinduced conjugate addition of oxycarbinyl species to enones to produce alkylation products has also been reported in alcohol solvents. Benzophenone-sensitized irradiation of cyclohexenone in methanol proceeded slowly to yield keto alcohol **75** in 33% yield along with a large number of unidentified products. By comparison, the reaction performed in ethanol gave a mixture of epimers **76** in a much cleaner reaction.[33]

It appears that benzophenone plays an important role in this type of addition. Fraser-Reid and co-workers concluded that the triplet excited state of benzophenone initially abstracts a hydrogen from the alcohol to yield a ketyl radical which then undergoes

conjugate addition to the enone.[34] Without the benzophenone present, the reaction did not proceed to any significant extent.



Photorearrangements

Photorearrangements of 2-cyclohexen-1-ones constitutes one of the largest areas of study and many review articles have been written on this subject.[25,35,36] Two different photorearrangements, the Type A rearrangement and the aryl migration, are commonly encountered in the literature. A short summary of these processes follows.

Type A Rearrangements These rearrangements have been shown to occur with 4,4-dialkyl substituted cyclohexenones. One of the classical examples of a Type A rearrangement was reported by Chapman and co-workers.[10] It was found that irradiation of 4,4-dimethyl-2-cyclohexen-1-one (**77**) in *tert*-butyl alcohol resulted in the formation of bicyclic ketone **78** in 60% yield along with *ca.* 5% of 3-isopropyl-2-cyclopenten-1-one (**79**). The formation of **78** was easily explained using the zwitterionic transition state hypothesis as shown below. Compound **79** was found to be a secondary photoproduct. It was proposed that C_5 migrated to C_3, effectively contracting the ring. This was followed by migration of C_2 to C_4 to form the three-membered ring. Compound **79** was a result of hydride migration from C_3 to C_4 after ring contraction.

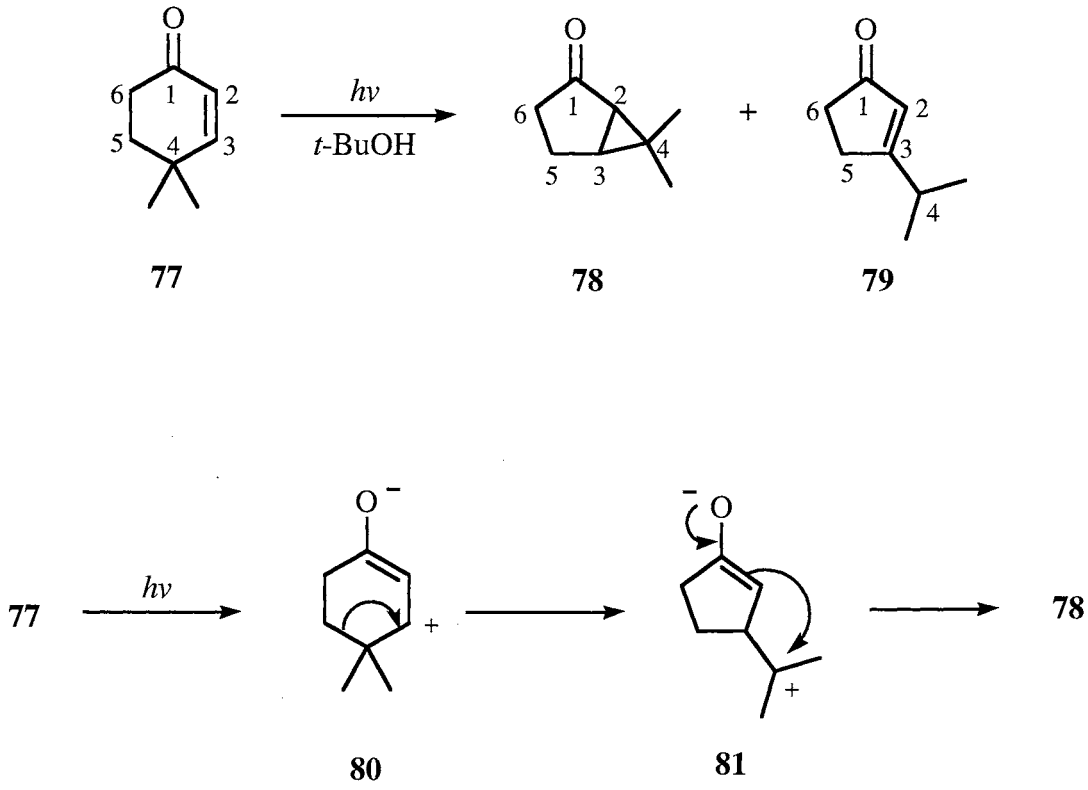
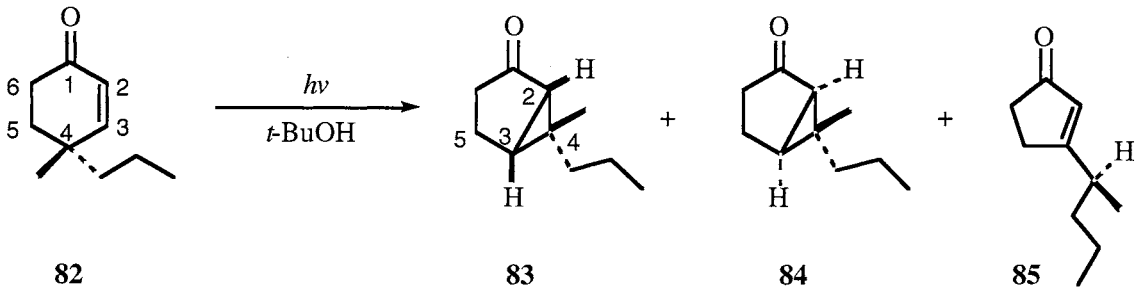


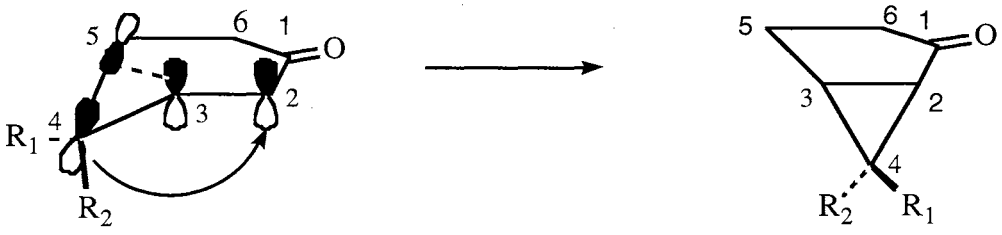
Figure 11. Zwitterionic Mechanism for Type A Rearrangement.

Much controversy over the exact mechanism involved in the Type A rearrangement exists in the literature.[37-39] Since it was discovered that the reaction proceeded in a stereospecific manner, the possibility of a concerted rather than a stepwise mechanism was advanced. To solve this problem, the optically active 4,4-disubstituted cyclohexenone **82** was studied.[39] It was found that irradiation of **82** in *tert*-butyl alcohol resulted in stereospecific formation of **83** and **84** as primary photoproducts with inversion of configuration at C_4 and retention of configuration at C_5.



82 83 84 85

From these results, it was proposed that the reaction followed a concerted pathway. The stereochemistry of the photoproducts suggested the reaction proceeded to give the same results as a $[\pi 2_a + \sigma 2_a]$ cycloaddition that involved antarafacial addition to both the C_2-C_3 π



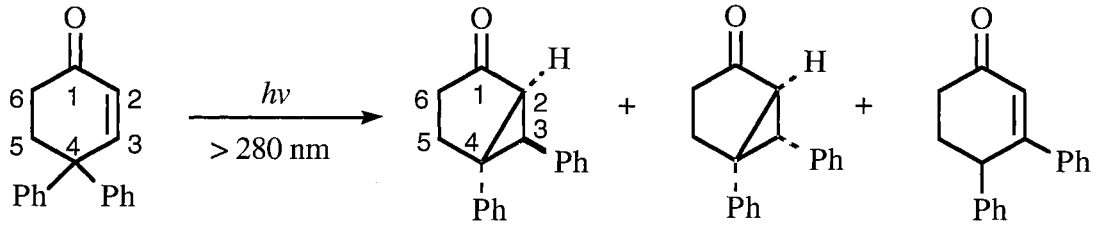
86 87

Figure 12. Concerted Mechanism for Type A Rearrangement.

bond and the C_4-C_5 σ bond of the twisted transition state **86**. The generation of **85** was also found to be a primary photoreaction, explainable by the concerted reaction hypothesis. The formation of this product proceeds through simultaneous ring contraction and hydrogen migration from C_3 to C_4 to invert the configuration at C_4.

Aryl Migration If the cyclohexenone is disubstituted with aromatic systems at C_4, then aryl migration is observed. The photochemistry of 4,4-diphenyl-2-cyclohexenone (**88**), as studied by Zimmerman,[40] undoubtedly represents the most well known rearrangement of this type. Upon irradiation of **88**, three photoproducts **89**, **90** and **91**

were isolated. Analysis of the reaction mixture at low conversion indicated that the [3.1.0]-bicyclohexanones were formed selectively, with the trans isomer **89** favored over the cis isomer **90** in a ratio of 140:1. Comparatively, extended irradiation resulted in a photoequilibrium favoring the cis over the trans isomer in a 57:43 ratio.



88 **89** **90** **91**

The mechanism of the rearrangement has received much attention and is, therefore, well understood.[40,41] Initially, the enone undergoes n,π^* excitation and intersystem crossing to give the triplet excited state. The pseudo axial phenyl group at C_4 then migrates to the odd electron center at the β-carbon. This migration is followed by electron demotion to the ground state and concomitant three ring formation to yield the bicyclohexanones. The formation of compound **91** is a result of hydride migration from C_3 to C_4 via the intermediate **92**.

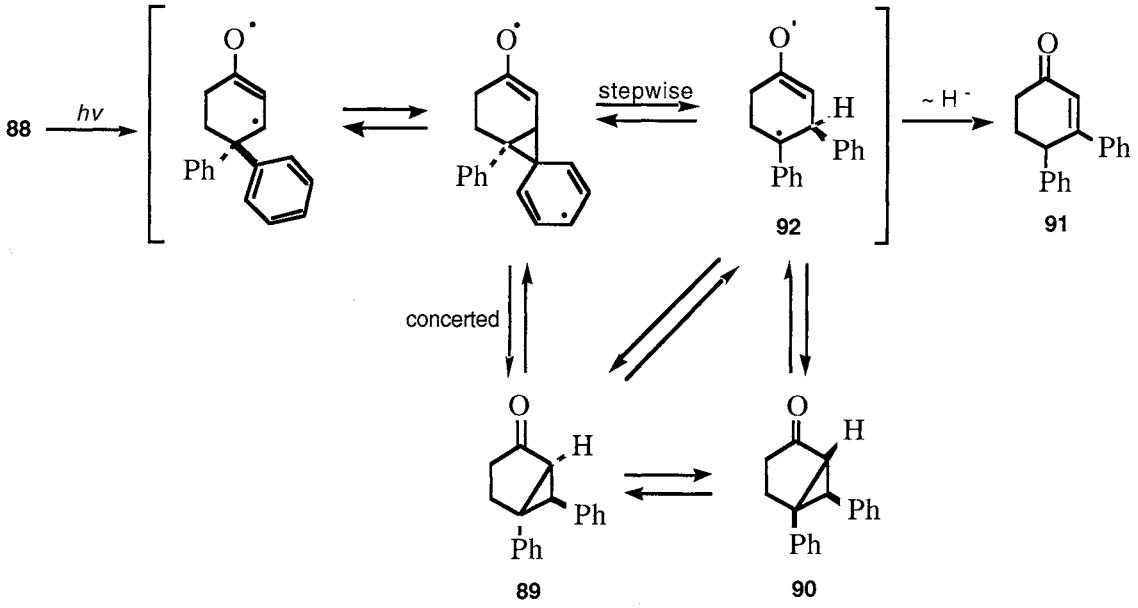
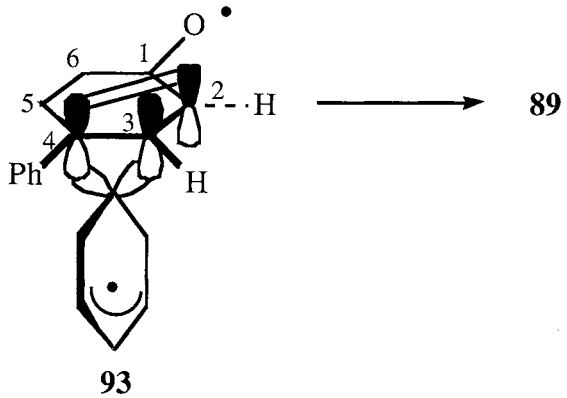
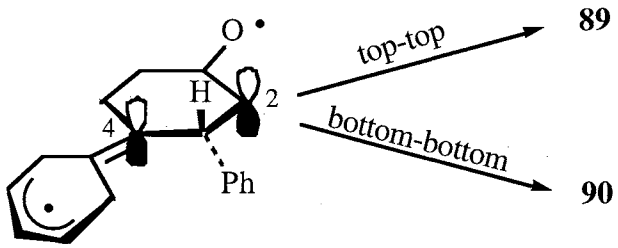


Figure 13. Mechanism for Aryl Migration.

Originally, the preference for the trans diphenyl isomer **89** was explained by a concerted process which led to inversion of configuration at C_4.[41] Migration of the C_4 phenyl to C_3 creates an incipient orbital at C_4 and is represented by transition state **93**. Cyclopropyl formation is allowed between this newly formed incipient orbital and the orbital at C_2 only if disrotatory rotation C_4-C_5 and C_1-C_2 bonds occurs. The cis isomer is explained by diradical closure of intermediate **92**.



An alternative mechanism describing the preference for the trans isomer has also been advanced.[42-44] First, the axial phenyl at C_4 migrates to C_3 resulting in diradical **94**. The three-membered ring can then be formed by overlap of either the bottom-bottom C_2-C_4 orbitals to form the cis isomer or top-top overlap of the C_2-C_4 orbitals to form the trans isomer. The trans isomer is believed to be preferred because it eliminates any interaction between the migrating phenyl and the delocalized phenyl in the transition state.



94

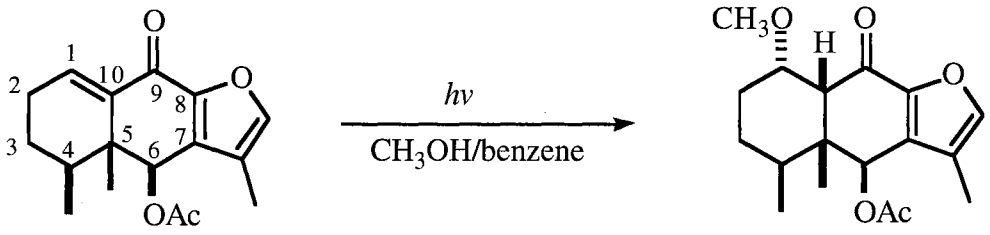
An extensive search of the available literature indicated that photorearrangements occur primarily in cyclohexenones containing *s*-trans α,β-enones. No mention of specific examples involving *s*-cis cyclic enones was found. Hence, further work investigating the rearrangement processes of these systems was required.

CHAPTER 2

THE PHOTOCHEMISTRY OF (±)-3,4,4a,5,6,7-HEXAHYDRO-4a-METHYL-1(2*H*)-NAPHTHALENONES

Introduction

One branch of our work has focused on studies involving photochemical reactions of *s*-cis-α,β-enones which have the unsaturated system extending over two rings. A review of the literature indicated that previous work in this field was very limited.[26,28] One of the few examples involved the photoaddition of oxygen nucleophiles to decompostin (**1**) described by Rodríquez-Hahn and co-workers.[26] These authors found that addition occurred in a stereospecific manner to give apparent trans addition of alcohol across the α,β-double bond.



1 **2**

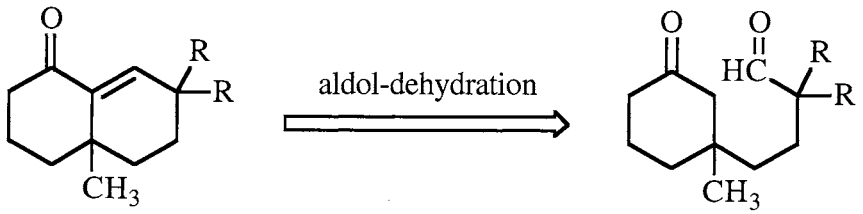
Literature precedent suggested that the observed stereochemistry in the adduct resulted from syn addition of the alcohol to the strained trans double bond that resulted

from irradiation.[12,14-16] In the current study, this reaction has been a valuable benchmark for the determination of product structures and reaction mechanism.

Our initial objective was to determine if photorearrangement would occur when the naphthalenone was disubstituted with either methyl or phenyl substituents at C-7. There were no reports in the literature of rearrangement or phenyl migration occurring in examples with the enone locked in an *s*-cis configuration. Early in the study, it was found that irradiation did not result in the predicted rearrangements; instead, in nucleophilic solvents, addition to the unsaturated system occurred to give either enols or ketones with the nucleophile adding to the β-position of the enone. Since many terpenes incorporate naphthalenones in their structure,[45,46] it is likely that photochemical functionalization of this ring system may prove useful in synthesis. Due to this possibility, we also synthesized the unsubstituted naphthalenone to determine if it could be functionalized using photoinduced additions. We report here the synthesis and photochemistry of three different (±)-3,4,4a,5,6,7-hexahydro-4a-methyl-1(2*H*)-naphthalenones.

Results

Synthesis of the Photochemical Substrates. Retrosynthetic analysis suggested that all three substrates could be constructed by intramolecular aldol condensation of the appropriate keto aldehyde **4** in the final step (Figure 14). Thus, using this methodology, compound **3a** was prepared in a 56% overall yield in two steps from 3-methyl-2-cyclohexen-1-one (Figure 15); **3b** was prepared in three steps from 3,3-dimethyl-4-penten-1-ol in an overall yield of 46% (Figure 16); **3c** was prepared in seven steps from 3-ethenyl-3-methylcyclohexanone in an overall yield of 48% (Figure 20).



3a R, R = H
3b R, R = CH_3
3c R, R = Ph

4a R, R = H
4b R, R = CH_3
4c R, R = Ph

Figure 14. Retrosynthetic Analysis of Desired Photosubstrates.

The synthesis of naphthalenone **3a** (Figure 15) started with the conjugate addition of the Grignard derived from 5-bromo-1-pentene (**5**) to 3-methyl-2-cyclohexen-1-one (**6**) to afford (±)-3-(4-pentenyl)-3-methylcyclohexanone (**7**)[47] in a yield of 73%. Ozonolysis of **7** in methanol at -78 °C, followed by reductive workup with dimethyl sulfide and acetic acid gave keto aldehyde **4a.** Condensative ring closure using *p*-toluenesulfonic acid in benzene generated the desired product. Purification by distillation gave (±)-3,4,4a,5,6,7-hexahydro-4a-methyl-1(2*H*)-naphthalenone (**3a**) in 76% overall yield from **7**. Refrigeration was required to prevent polymerization. This compound had been previously reported,[48-51] but the current synthesis is superior due to a shorter reaction scheme and a higher overall yield.

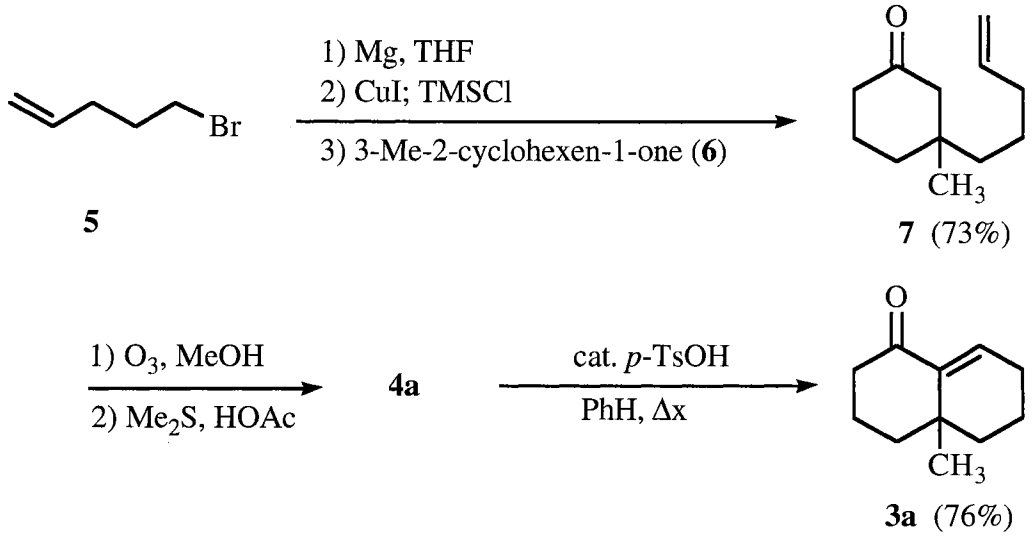


Figure 15. Synthesis of (±)-3,4,4a,5,6,7-Hexahydro-4a-methyl-1(2*H*)-naphthalenone.

To prepare **3b**, an analogous approach was followed (Figure 16). The synthesis of **3b** required preparation of the previously reported bromide **10**.[48] Modification of the literature preparation yielded **10** in an overall yield of 85% from 3,3-dimethyl-4-penten-1-ol **8** via mesylate **9**.[52] The bromide **10** was converted to the corresponding Grignard reagent and added to 3-methyl-2-cyclohexen-1-one (**6**) at -78 °C in the presence of copper(I) iodide and chlorotrimethylsilane.[47] This procedure resulted in conjugate addition of the organocopper species to the unsaturated ketone to afford (±)-3-(3,3-dimethyl-4-pentenyl)-3-methylcyclohexanone (**11**) in a yield of 72%. Ozonolysis of **11** in methanol at -78 °C, followed by reductive workup with dimethyl sulfide and acetic acid generated keto aldehyde **4b** which was treated directly with catalytic *p*-toluenesulfonic acid in refluxing benzene to give (±)-3,4,4a,5,6,7-hexahydro-4a,7,7-trimethyl-1(2*H*)-naphthalenone (**3b**) in a yield of 75% after purification by silica gel column chromatography. Interestingly, the product was formed with no detectable alkyl migration from the geminal dimethyl moiety.

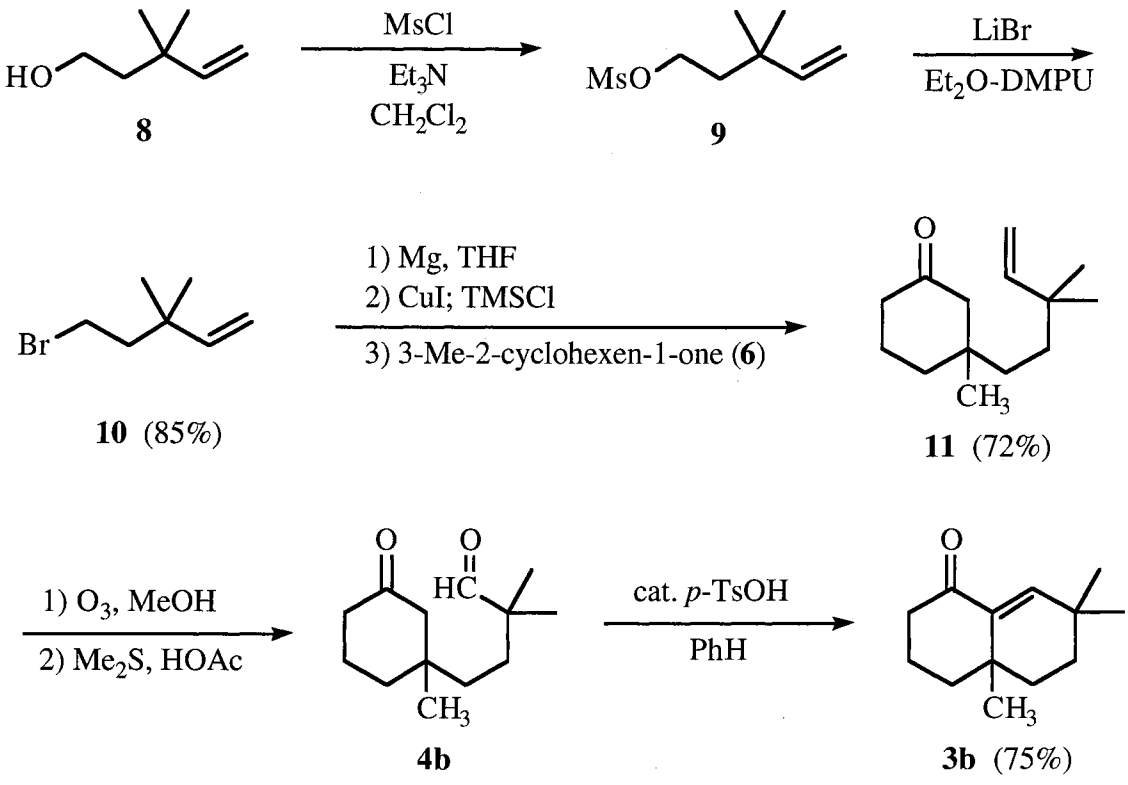


Figure 16. Synthesis of (±)-3,4,4a,5,6,7-Hexahydro-4a,7,7-trimethyl-1(2*H*)-naphthalenone.

Compound **4c** proved to be more synthetically challenging than **4a** and **4b** and required the development of a new approach. The following discussion summarizes our efforts to prepare **4c**. It was initially planned that **3c** would be prepared in the same manner as **3a** and **3b**. To test this strategy, a synthesis of 5-bromo-3,3-diphenyl-1-pentene (**12**), was developed in four steps from 1,1-diphenyl-1-propene (**15**) (Figure 17) with an overall yield of 52%.[53] The preparation of **15** was carried out by Grignard reaction involving **13** to give 1,1-diphenyl-1-propanol (**14**) which was dehydrated using phosphorous oxychloride in pyridine to yield **15**. The best yield of **14** in the Grignard reaction (88%) was realized by addition of phenylmagnesium bromide to propiophenone

(**13**). The dehydration proceeded in 90% yield to give **15**. Treatment of **15** with *n*-butyllithium at 0 °C followed by addition of 2 equivalents of ethylene oxide afforded 77% of 3,3-diphenyl-4-penten-1-ol (**16**), based upon a 72% conversion of **15** to its corresponding anion. GC and ^{1}H NMR analysis indicated that this alcohol contained less

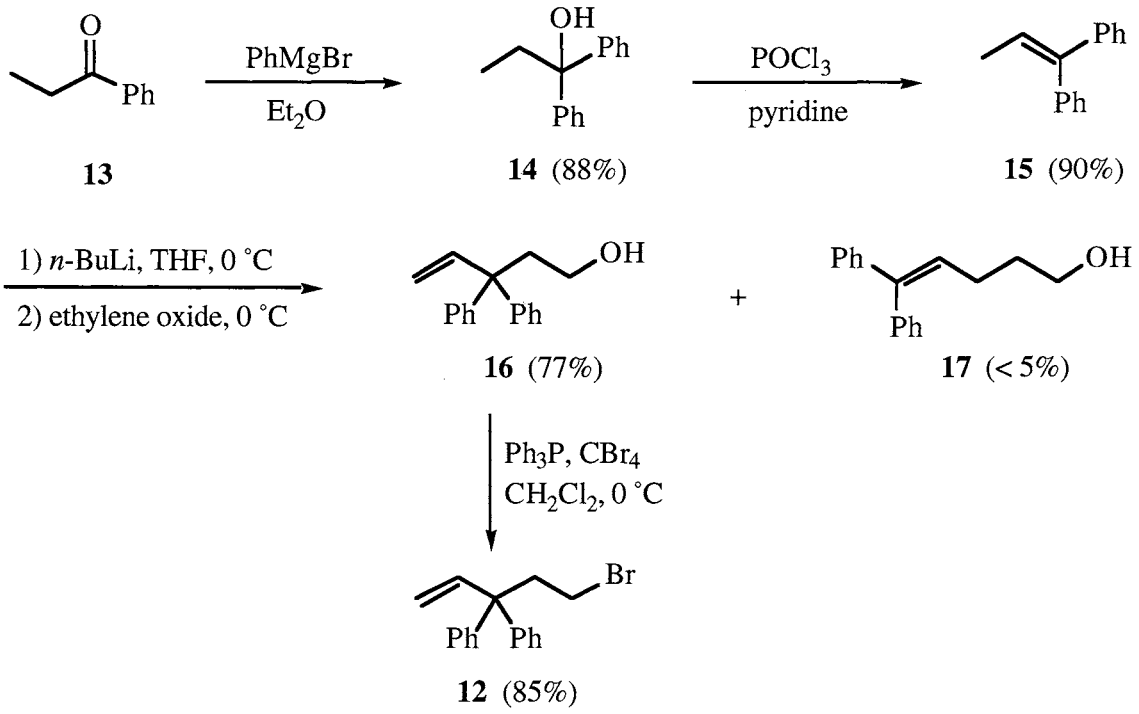
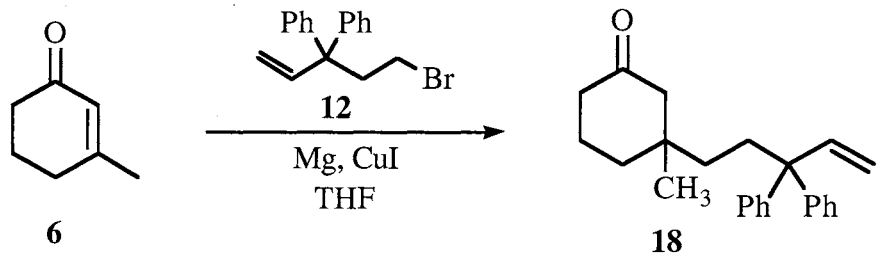


Figure 17. Synthesis of 5-Bromo-3,3-diphenyl-1-propene.

than 5% of the isomeric 5,5-diphenyl-4-penten-1-ol (**17**) which would result from the reaction at C-3 of the allylic system. The best ratio of C-1:C-3 addition product was achieved at 0° C, although the reaction typically proceeded to only *ca.* 70% conversion. Lower temperatures (-22 °C) slowed deprotonation of the alkene and suppressed the reaction with ethylene oxide; higher temperatures (35 °C) gave greater conversion to the anion but a significantly larger proportion (up to 20%) of C-3 addition. Alcohol **16** was converted directly to bromide **12** in 85% yield by treatment with triphenylphosphine and

carbon tetrabromide.[54] An alternative route via the mesylate of **16** gave inconsistent and generally unsatisfactory results.

Conjugate addition of **12** to 3-methyl-2-cyclohexen-1-one **6** using a copper-catalyzed Grignard reaction appeared to be a simple route to intermediate **18**.[55] However, the Grignard reagent was not only difficult to prepare, but competing side reactions presented additional difficulties (see Figure 18). The Grignard of bromide **12** could not be produced using standard conditions (Mg turnings, THF, reflux). Therefore, activated magnesium prepared according to the method of Rieke was utilized.[56] When the bromide



was exposed to Rieke magnesium at 0 °C for 30 min, followed by quenching with aqueous NH_4Cl, the isolated material consisted of a complex mixture which included the following: 22% of unreacted bromide **12**; 37% of 3,3-diphenyl-1-pentene (**19**) (quenched Grignard); 6% of 1,1-diphenylpropene (**15**) (fragmented Grignard); 20% of dimer **20**; and several unidentified minor compounds that could not be isolated in pure form. Using this methodology for the preparation of 3,3-diphenyl-4-pentenylmagnesium bromide, the reaction did not generate a significant amount of the desired product **18** when added to 3-methyl-2-cyclohexen-1-one (**6**).

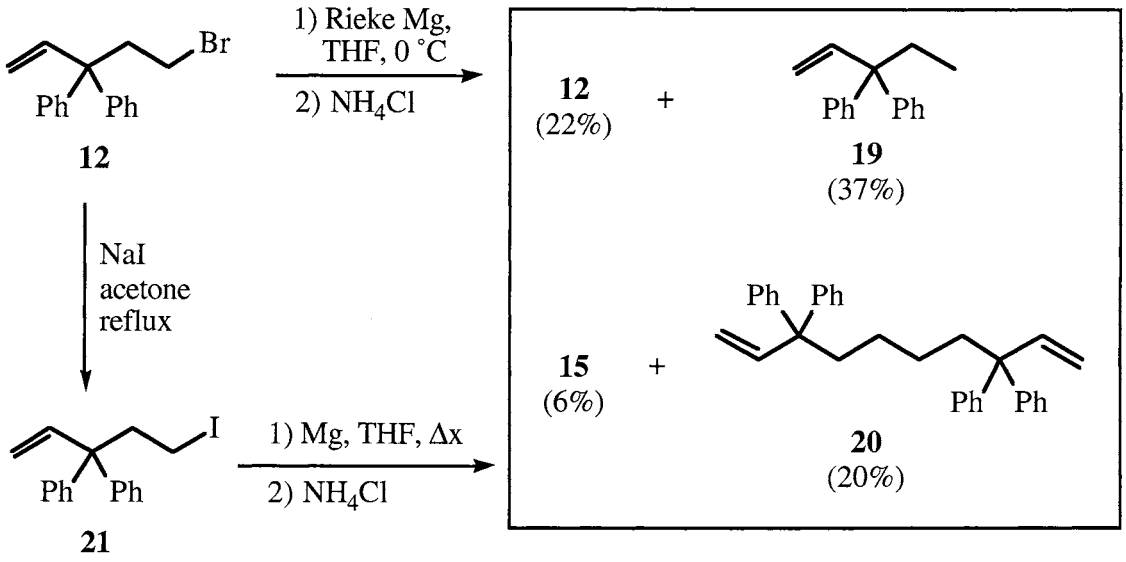


Figure 18. Reactions of 5-Halo-3,3-diphenyl-1-pentene Grignard Reagents.

The Grignard reaction was also attempted using standard conditions on 1-iodo-3,3-diphenyl-4-pentene (**21**) prepared from bromide **12** by the Finkelstein halide exchange. Refluxing **21** for 12 h over magnesium turnings in THF, followed by quenching with aqueous NH_4Cl also gave products similar to those obtained from use of Rieke magnesium (Figure 18) but in slightly different ratios, with the exception that no unreacted starting material was recovered. With these findings, an alternative route was sought.

Since it was known that under proper conditions the anion of 1,1-diphenylpropene (**15**) undergoes alkylation predominantly at the diphenyl-substituted carbon (C-1),[57,58] an alkylation route using the anion of **15** was envisioned. Following this lead, ketal bromide **24** was prepared as outlined in Figure 19. Anti-Markovnikov addition of HBr to the side chain double bond of 3-ethenyl-3-methylcyclohexanone (**22**)[47] was performed under photochemical conditions[59] to give 3-(2-bromoethyl)-3-methylcyclohexanone (**23**) in a yield of 83%. To optimize the yield, it was necessary to use commercial HBr.[60] Keto bromide **23** was then treated with ethylene glycol under acidic conditions to furnish ketal

24 in 98% yield. The alkylation was carried out by dropwise addition of **24** to the anion of 1,1-diphenylpropene (**15**) in the presence of TMEDA at 0 °C,[58] followed by quenching with aqueous NH_4Cl. Purification by silica gel chromatography provided **25** as the major compound. This outcome indicated that under these conditions the alkylation of ketal bromide **24** with diphenylpropene anion occurred predominately at (C-3).

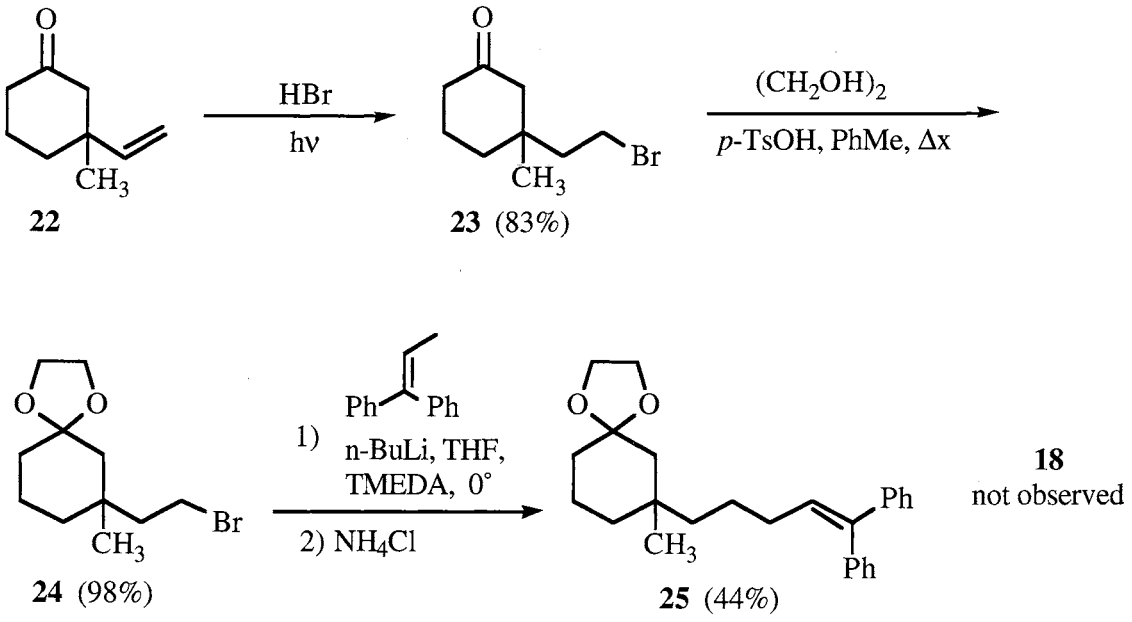
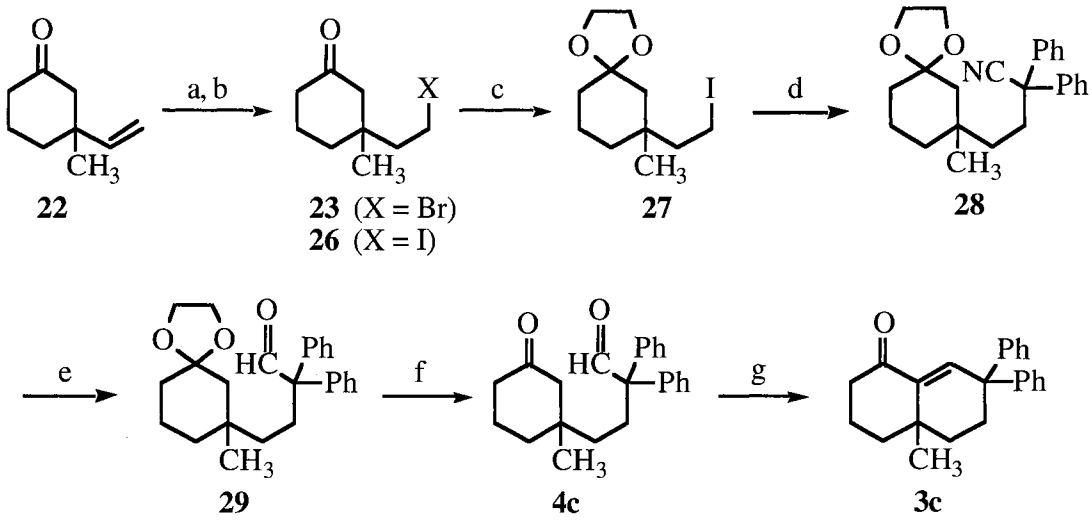


Figure 19. Attempted Synthesis of **18** by Alkylation of 1,1-Diphenylpropene Anion.

The successful synthesis of **4c** (Figure 20) began with 3-ethenyl-3-methylcyclohexanone (**22**). Photochemical addition of HBr yielded keto bromide **23** as described above. Halide exchange followed by ketone protection with ethylene glycol produced the iodo ketal **27** in 87% yield from **23**. Treatment of **27** with the anion of diphenylacetonitrile under phase-transfer conditions (KOH, MEK, reflux)[61] afforded the cyano ketal **28** in 81% yield; attempts to alkylate diphenylacetaldehyde directly using a

related phase-transfer protocol (NaOH, *n*-Bu_4NI, PhMe-H_2O, reflux; then H_3O^+)[62] afforded predominantly the O-alkylation product **30**. Nitrile reduction of **28** using DIBAL (-20→20 °C) provided ketal aldehyde **29** in 95% yield and treatment with PPTS in 9:1

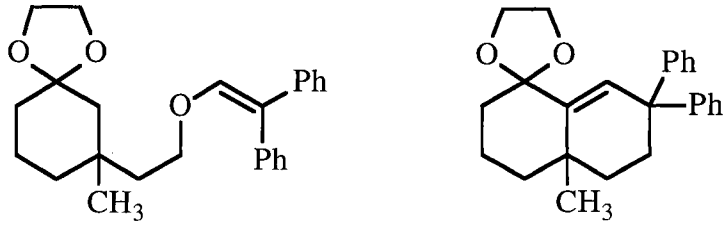


22 **23** (X = Br) **26** (X = I) **27** **28**

29 **4c** **3c**

(a) HBr, h ν, hexane, 83%; (b) NaI, acetone, 89%; (c) $(CH_2OH)_2$, *p*-TsOH, PhH, 98%; (d) Ph_2CHCN, KOH, MEK, 81%; (e) DIBAL, PhMe-hexane, 95%; (f) PPTS, 9:1 acetone-H_2O; (g) *p*-TsOH, PhMe, 86% from 29.

Figure 20. Synthesis of (±)-3,4,4a,5,6,7-Hexahydro-4a-methyl-7,7-diphenyl-1(2*H*)-naphthalenone.



30 **31**

Figure 21. By-products of Diphenyl Naphthalenone Synthesis.

acetone-H_2O gave **4c**. Final aldol closure with *p*-toluenesulfonic acid in refluxing toluene then afforded **3c** in an 86% yield from **29**. Interestingly, an attempted one-step deprotection-ring closure of **28** with *p*-toluenesulfonic acid in refluxing toluene containing added water proved less satisfactory, giving **3c** in a yield of 66% along with 18% of its ethylene ketal **31**. In this direct conversion of **28** to **3c**, it was necessary to add several drops of water in order to "jump-start" the initial deprotection. While ketal **31** was easily converted to the target naphthalenone (PPTS, acetone-H_2O, reflux), the overall yield by this route was slightly lower (81%). Final purification by silica gel column chromatography afforded the title compound as a stable, light yellow solid. Under optimum conditions, the seven step sequence required a minimum of purification steps and gave compound **3c** in an overall yield of 48%.

Exploratory Photochemistry of Substrates 3b and 3c and Structure Elucidation of Photoproducts. The first objective of this study was to determine the photoreactivity of naphthalenones **3b** and **3c** using conditions comparable to those reported for Type A rearrangements and aryl migrations.[40] In all of the examples, photolysis was done on degassed solutions in a Hanovia immersion apparatus using a Pyrex® filter and a 450-W medium pressure ultraviolet source. Reactions were monitored by TLC and IR until the conversion to product slowed.

Direct irradiation of compounds **3b** and **3c** in benzene led to recovery of starting material after 15 h, and it was concluded that the photosubstrates were photochemically inactive in benzene. Direct irradiation of **3b** in *tert*-butyl alcohol led to the formation of one photoproduct at 80% conversion after 4.5 h. Isolation using preparative silica gel thin layer chromatography provided enol **32** in 81% yield based on 80% conversion. There was no indication of other products according to GC or TLC analysis. It was, therefore, concluded that Type A rearrangement of **3b** was not favorable under these conditions. Since it was difficult to prevent the *tert*-butyl alcohol from freezing during the reaction,

approximately 10% benzene was added to the solution. This change of solvent conditions resulted in a longer reaction time (8 h) and a lower yield of 45%. These observations may derive from significant absorbance of light by the benzene and correspondingly less excitation of the naphthalenone π system.

By analogy to the previous literature,[8,12,14-16,26,28] the expected product from **3b** was a β-alkoxy ketone **33**; however, it was possible if ketone **33** was initially formed, tautomerization on mildly acidic silica gel during purification could conceivably generate the enol. IR and ^{1}H NMR analyses of the crude reaction mixture confirmed this hypothesis. The IR spectrum revealed a strong hydroxyl stretch at 3279 cm^{-1} and a strong absorbance

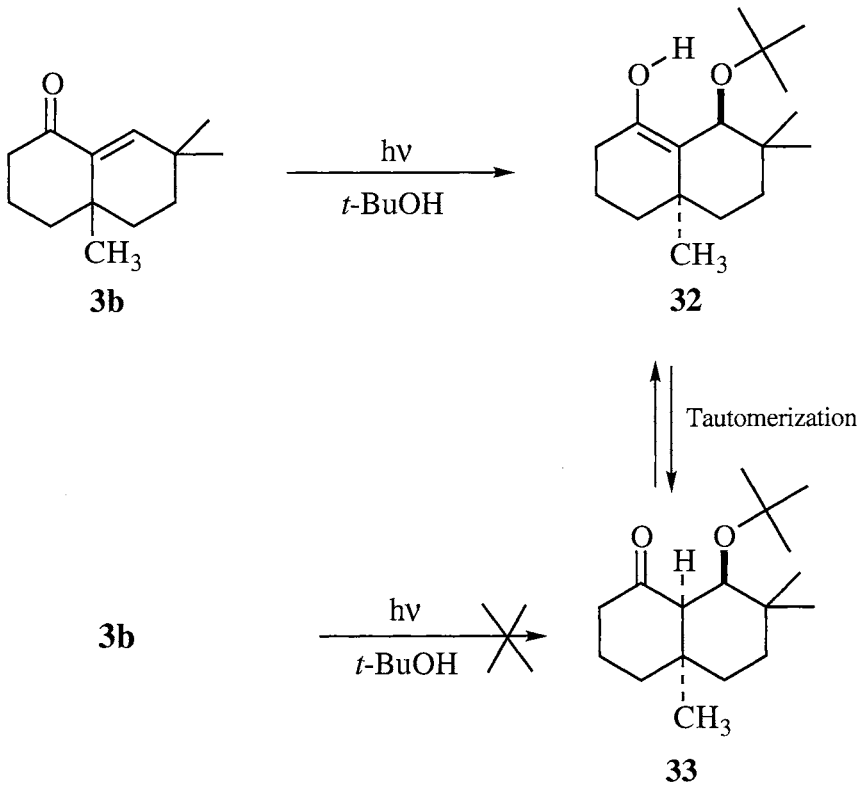
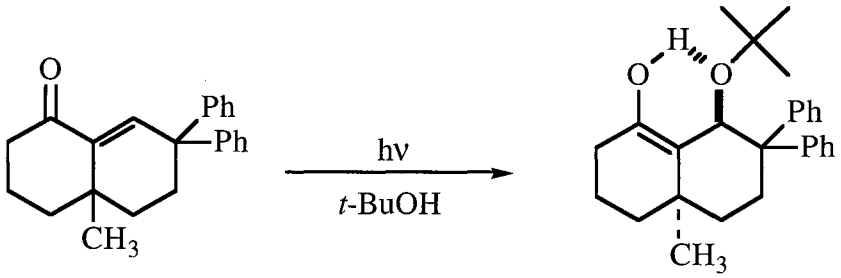


Figure 22. Photoreactivity of **3b** in *tert*-Butyl alcohol.

at 1675 cm^{-1}, both due to the enol.[63] The NMR absorption at 9.25 ppm further suggested an enol product. There was no evidence of a ketone as the initial product based on the spectra of the crude photolysate.

It was not possible to determine the relative configuration of the stereocenters at C-4a and C-8 of the enol product by spectroscopy. This problem was resolved when it was found that a similar photoaddition of *tert*-butyl alcohol took place using compound **3c**. Irradiation of **3c** in neat *tert*-butyl alcohol for 30 h provided compound **34** in high yield (81%). If the compound was irradiated in *tert*-butyl alcohol and benzene, the isolated yield increased to 91% and the reaction time decreased to 18 h. IR and NMR analysis of the crude photolysate indicated that an enol was the initial product formed. Purification on silica gel and slow recrystallization from ether provided a crystalline sample of enol **34**. The availability of a crystalline enol allowed for determination of the enol stereochemistry by single crystal X-ray analysis.



3c **34**

Figure 23. Photoreactivity of **3c** in *tert*-Butyl Alcohol.

The projection view in Figure 24 shows the molecular structure of **34** with the numbering scheme. The cyclohexane ring adopts a pseudo-chair conformation with the *tert*-butoxy group at C-8 occupying a pseudo-equatorial site. Internal hydrogen bonding

between the enol hydroxyl group and the ether oxygen is also evident by the planar geometry of these functional groups. The angular methyl group occupies a pseudo-axial site with respect to the cyclohexane rings and it is trans to the *tert*-butoxy substituent at C-8. The phenyl rings at C-7 are aligned in such a way as to minimize interaction with the other substituents.

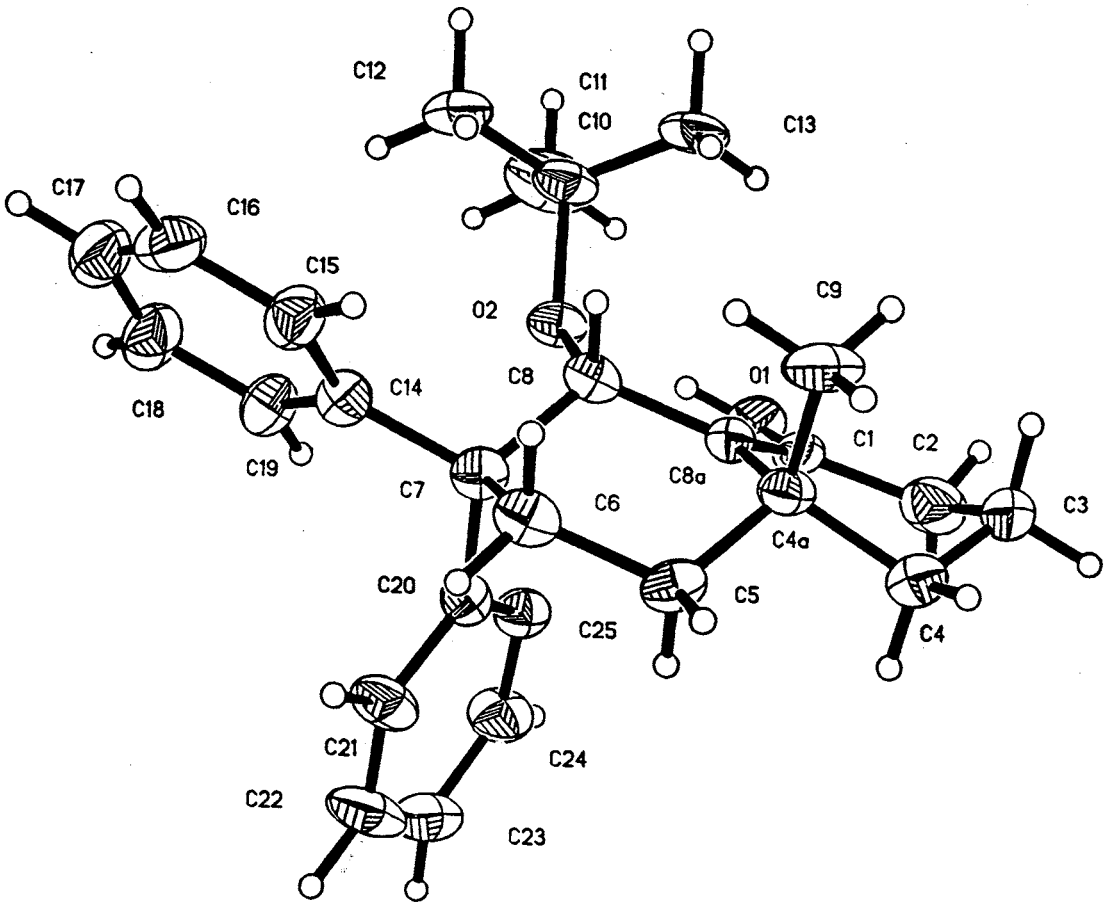
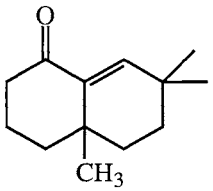
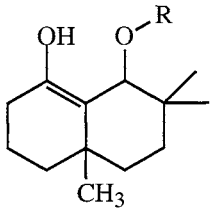
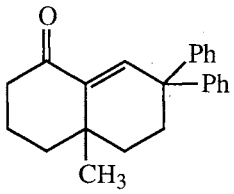
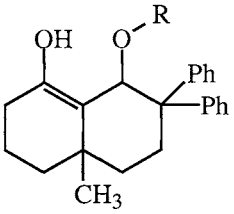


Figure 24. Projection View of Compound **34**.

To determine if photoreduction[31,64,65] was possible in these types of systems, substrates **3b** and **3c** were irradiated in isopropanol and methanol. It was found that these alcohols added to the β-carbon of the unsaturated system in the same manner as *tert*-butyl alcohol to give the enol as the initial photoproduct. The results of irradiation of **3b** and **3c** in isopropanol and methanol are compiled in Table 1. The assumption had to be made that the stereochemistry of the products **35-38** is the same as that found by the X-ray analysis

Starting enone	Solvent	Conversion[a] %	Yield[b] %	Adduct
 **3b**	*i*-PrOH	90	55	 **35** R = $CH(CH_3)_2$ **36** R = CH_3
	MeOH	40	enol tautom-erizes readily	
 **3c**	*i*-PrOH	95	81	 **37** R = $CH(CH_3)_2$ **38** R = CH_3
	MeOH	70	78	

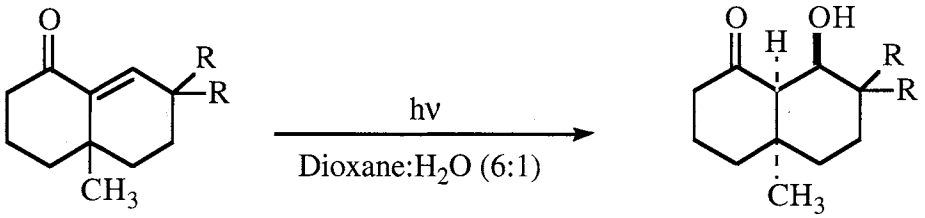
[a] Conversion based on isolated material. [b] Yield based on conversion.

Table 1. Results of Isopropyl Alcohol and Methanol Addition to **3b** and **3c**.

of **34** described above. When substrate **3b** was irradiated in methanol the resulting enol could not be isolated in pure form due to tautomerization when placed on silica gel, but it

was clear from the NMR analysis of the crude product that the enol was present as the major product. When irradiated in either isopropanol or methanol, **3b** gave trace amounts of an insoluble product. Although not identified, it was speculated that these solids are a result of a competing [2+2] dimerization which is often seen in photochemistry of α,β-unsaturated cyclic enones.[13]

It was also of interest to determine if water added in an analogous manner to give a stable product. When compound **3b** was irradiated in dioxane-H_2O (6:1), the reaction was complete in 11 h. Crude ^1H NMR analysis indicated that addition of water had occurred, but the enol proton was not present. This suggested that either the addition of water occurs directly to give ketol **39**, or enol formation is followed by rapid ketonization. Purification on silica gel produced β-hydroxy ketone **39** in 63% yield (88% conversion) as a stable crystalline compound (Figure 25).



3b R = CH_3
3c R = Ph

39 R = CH_3
40 R = Ph

Figure 25. Addition of H_2O to **3b** and **3c**.

Photoaddition of water to compound **3c** also occurred across the alkene double bond to furnish β-hydroxy ketone **40** in 38% yield based on 50% conversion after 30 h. The naphthalenone appeared to be much less reactive than compound **3b** under these conditions. Moreover, the extended photolysis time resulted in several by-products not

observed in the other reactions. It is possible that these products are the result of competing photochemical fragmentation and polymerization processes but, due to the complexity of the mixture, isolation of individual products was not attempted.

From the previous X-ray structure of **34**, it was known that the photoaddition of the nucleophile occurred such that the substituent at C-8 and the angular methyl group were trans to one another in the final product. It was believed that comparison of the coupling constants between the protons attached to C-8 and C-8a would help elucidate the stereochemical relationship between these hydrogens, and thus, the overall stereochemistry of the molecule. At room temperature, this proved futile for **39** due to conformational mobility in the ring system which broadened the NMR signals.[66] However, this mobility suggested that the ring juncture was cis-fused.[13,51,66,67] At 70 °C, the coupling of the C-8a proton was found to be 4.76 Hz, but the signal for the proton on C-8 was still broadened. This coupling constant implied an equatorial-axial[63] interaction which could only be explained if the hydroxy substituent at C-8 was trans diaxial with respect to the proton at C-8a. Examination of models indicated that this stereochemistry and conformation was possible in the adduct with both the cis and trans fused ring juncture. Fortunately, this problem was solved by X-ray analysis of a single crystal of compound **39**.

Figure 26 shows the molecular structure of **39** with the numbering scheme. X-ray crystallographic analysis confirmed the trans relationship between the proton at C-8a and the hydroxy substituent at C-8. It is clear that the cyclohexane ring is cis fused to the cyclohexenone ring which adopts a pseudo-chair conformation. As previously discovered for **34**, the angular methyl group has a trans relationship with the substituent at C-8.

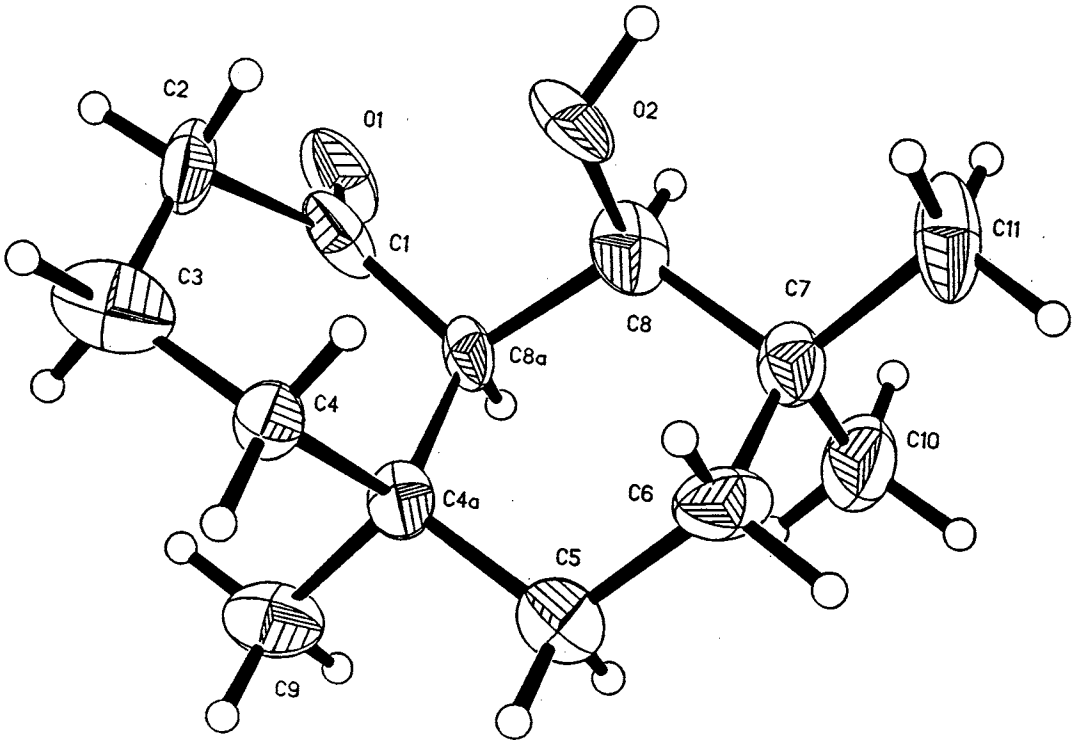


Figure 26. Projection View of Photoadduct **39**.

Surprisingly, the ^{1}H NMR of compound **40** was not broadened; therefore, coupling constants could be determined for the protons on C-8 and C-8a. These constants were found to be 2.7 Hz which indicated that the stereochemistry of compound **40** was likely the same as that determined for **39**. Although the relative stereochemistry could not be determined by the coupling constants alone, it can be assumed that both naphthalenones react by the same mechanism and thus give the same stereochemistry in the product.

Attempted Photolysis of Compound 3a. Photolysis of the unsubstituted naphthalenone **3a** in alcoholic solvents using the above conditions did not proceed cleanly. Solvent addition products were not isolated, but GC analysis indicated a mixture of several volatile compounds and a significant amount of polymeric material was also isolated from the reaction. This non-reactivity toward nucleophiles may be due to low absorbance of light at the wavelength used or possibly due to competing photoreactions. Further study of this compound was not pursued.

Tautomerization of the Photoproducts. Upon purification of photoproduct **36**, it was found that extended contact with mildly acidic silica gel resulted in tautomerization to give β-methoxy ketone **41**. This indicated that the hydrogen bonded enol structure was not thermodynamically stable in all cases. In order to determine the tendency toward tautomerization, the above photoproducts, with the exclusion of the β-hydroxy naphthalenones **39** and **40**, were placed on silica gel preparative thin layer chromatography plates and allowed to stand for 3 h - 3 days.

The results varied depending on the size of the alkoxy moiety and the substitution at C-7. It was found that *tert*-butoxy adduct **32,** along with all of the diphenyl substituted photoproducts (**34**, **37**, and **38**), did not tautomerize after several days on silica gel. ^{1}H NMR analysis of the crude isolated substance in all cases indicated that only the enol was present after exposure to silica gel. The stability of these adducts can best be explained by referring to molecular models and the X-ray projection view in Figure 24. Large alkoxy groups prefer to adopt the pseudo-equatorial conformation not only because of the favorable hydrogen bonding between the ether oxygen and the enol hydrogen, but also because tautomerization would require a very unfavorable eclipsing interaction between the axial substituent at C-7 and the alkoxy group at C-8 in the enol to ketone transition state. It is also clear that the group at C-8 occupies the axial position in the keto tautomer, which in the case of the larger substituents is conformationally unfavorable[68] and places this group

on the sterically crowded concave face of the molecule. In cases where tautomerization does occur, any steric interaction between the carbonyl oxygen and the ether oxygen is minimized when the group at C-8 occupies the axial position.

In photoadducts of **3b** that have smaller sterically hindered alkoxy groups (**35** and **36**), tautomerization occurs readily to give **41** and **42**, respectively (Figure 27). Surprisingly, the isopropoxy adduct **35** of the dimethyl-substituted naphthalenone undergoes tautomerization while the isopropoxy adduct **37** of the diphenyl-substituted naphthalenone prefers the enol form. This difference suggests that the geminal methyls at C-7 do not restrict rotation about C-7-C-8 as much as the phenyls at C-7. A reasonable explanation for this observance can be rationalized by examination of the X-ray structure of adduct **34** (Figure 24). The orientation of the axial phenyl group at C-7 is such that tautomerization would require the alkoxy substituent at C-8 to rotate past the edge of the phenyl ring causing an unfavorable interaction.

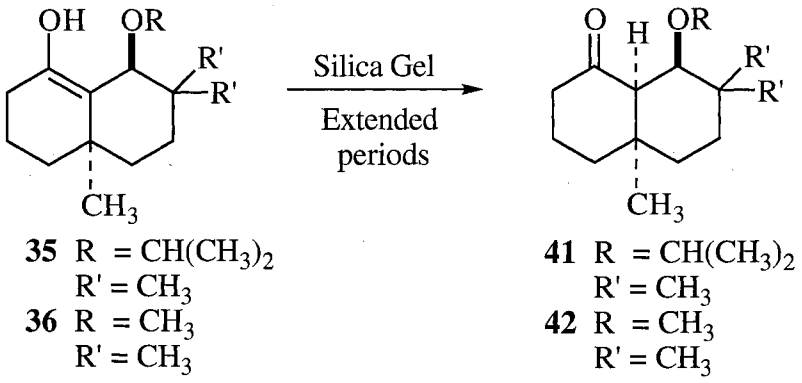


Figure 27. Enol-keto Tautomerization of Photoproducts.

Upon tautomerization, the proton at C-8a can conceivably bond to either the α or β face of the molecule. The overall stereochemistry of the keto tautomers can be determined

using the same rationale used for the hydroxy adducts **39** and **40**. Since it was already shown from X-ray analysis of **34** that the reaction proceeded to give a trans relationship between the C-8 substituent and the angular methyl group, a NOESY experiment was performed to determine the relationship between the protons at C-8 and C-8a of the isopropoxy adduct **35**. Irradiation of the signals centered at 2.34 and 3.22 ppm clearly showed cross peaks in the contour diagram (Figure 28). These cross peaks confirmed that the protons at C-8 and C-8a are in close proximity to one another which is only possible for the cis ring juncture. Thus, the overall stereochemistry for the tautomerization products was found to be the same as the water addition products described above.

It is important to note that upon tautomerization a small amount of naphthalenone **3b** was recovered. This suggests that elimination of the alcohol from the photoadduct is possible under the mildly acidic conditions. Assuming that the elimination mechanism occurs through a diaxial antiperiplanar geometry, the stereochemical assignment of C-8 and C-8a is correct.

Attempted Michael Additions. It was important to establish that the addition was proceeding through the photochemical route and not through a thermal Michael addition. Thus, the possible base-catalyzed addition of methanol was examined. Both compounds **3b** and **3c** were stirred at room temperature in a 0.09 M $NaOCH_3$ solution in methanol for 10 days. GC and IR analyses of aliquots taken at various intervals indicated that no addition occurred in either case. Boeckman previously reported[50] that weakly nucleophilic anions add reversibly to compound **3a**. Unfortunately, the equilibrium is unfavorable for addition due to either peri interactions in the product and/or interactions of the incoming nucleophile with the angular methyl group. Compound **3a** was not tested to determine its reactivity under Michael conditions because of Boeckman's findings and the possibility of polymerization.[50,51] It was concluded from this brief examination of base-catalyzed

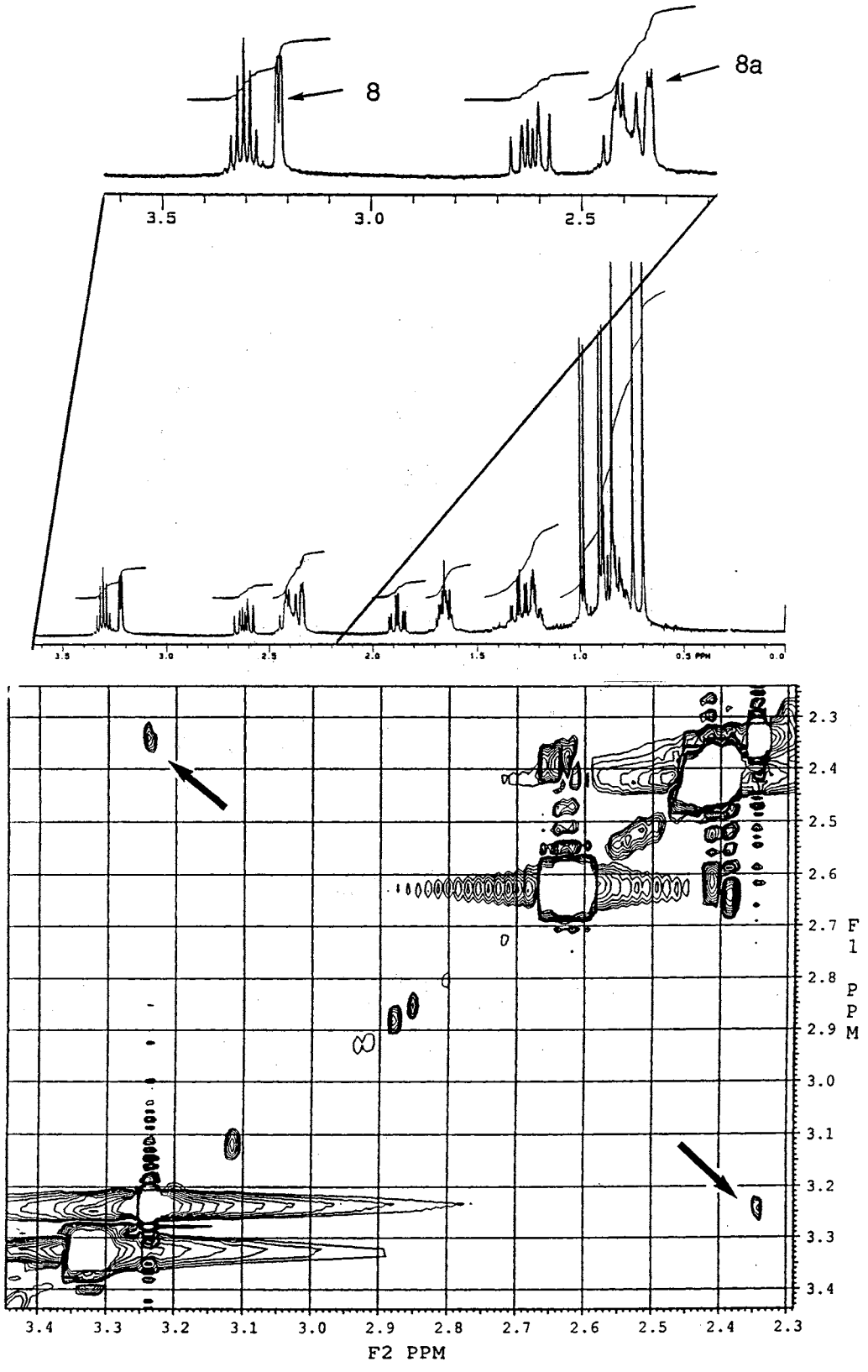
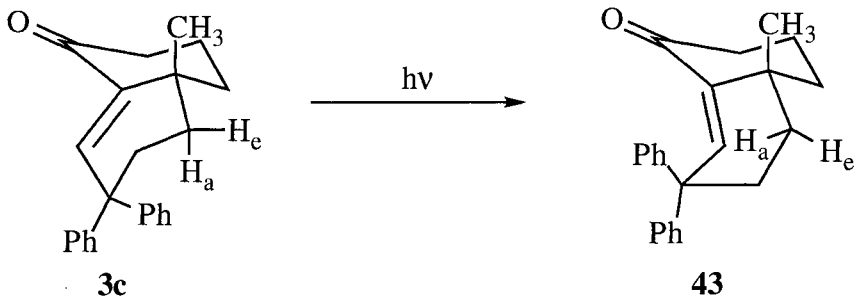


Figure 28. NOESY Spectrum for Compound **35**.

Michael conditions that functionalization of the compounds in question with oxygen nucleophiles takes place only by photoinduced addition to the double bond.

Mechanistic and Interpretative Discussion. Photolysis of **3b** and **3c** in alcoholic solvents gave unexpected enol products as the primary photoproducts in all of the cases studied. These results can be explained by mechanisms advanced previously. Irradiation of the enone results in excitation and intersystem crossing to a π,π^* triplet state. The resulting excited enone then underwent twisting about the C_α-C_β bond in order to minimize the electron-electron repulsion between the unpaired electrons. Once a critical geometry is reached, radiationless decay occurs to the give the ground state trans enone.[69] In the current substrates **3b** and **3c**, it appears that radiationless decay occurs fast enough so that cis-trans isomerization supersedes any migration or rearrangement pathway. This isomerization, using compound **3c** as an example, is formulated in Figure 29.



3c **43**

Figure 29. Cis-trans Isomerization of Naphthalenone **3c**.

The strained trans isomer **43** is highly susceptible to nucleophilic attack which provides for relief of strain. The observed regioselectivity can be explained by the polarizing effect of the carbonyl. Although the extended π system no longer has effective overlap of the electrons, the inductive effect of the carbonyl allows for an electropositive

center at the β-carbon. Thus, nucleophilic solvents tend to attack at this position. This rationale has been previously utilized to explain photoinduced addition of nucleophiles to other α,β-cycloalkenones.[6,7,11,12,14]

Examination of the final products in all cases studied clearly shows that the alkoxy group at C-8 and the angular methyl have a trans relationship to one another. This would suggest that the nucleophile must approach the strained trans intermediate **43** on the same face occupied by the angular methyl group; subsequent conformational relaxation of the adduct gives the trans relationship of the two groups. Although a severe 1,3-non-bonded interaction of the nucleophile with the angular methyl group would be expected, the close proximity of the pseudo axial proton (H_a) to the reactive center effectively blocks attack from the other face of the intermediate forcing addition to occur on the same face as the angular methyl group.

In the current study, there are two different products observed depending on the nucleophile, 1) enol formation with alcohol addition and 2) ketone formation with water addition. Both the enol and the keto products can be explained by initial formation of a dipolar intermediate **44** upon attack of the nucleophile (see Figure 30).[14] Intermediate **44** relaxes conformationally, resulting in delocalization of charge to form enolate **45**. Protonation at the oxygen would give the enol **46**. If alcohol is the addend, this enol is stable due to hydrogen bonding. In the case of water addition, only the ketone is isolated. This suggests that either the α-carbon of enolate **45** is directly protonated to give **47** or tautomerization of the enol intermediate occurs readily before isolation of the crude photoproduct can be achieved. If the latter occurs, the relatively small size of the hydroxyl substituent allows for eclipsing in the transition state in order to obtain the thermodynamic ketone product.

If water addition does occur through the enol intermediate, it must be assumed that tautomerization occurs selectively to give the trans relationship between the proton at C-8a and the hydroxyl group at C-8. Examination of models supports the likelihood of selective

protonation at the α-carbon. Due to the steric bulk of the system, protonation would not likely occur on the congested concave face of intermediate **45**. The selective tautomerization is also supported in the tautomerization of alcohol adducts. Although not all the enol photoproducts tautomerize when exposed to silica gel (see above), those that do must also undergo stereospecific protonation at the ring juncture which can be rationalized using the same arguments.

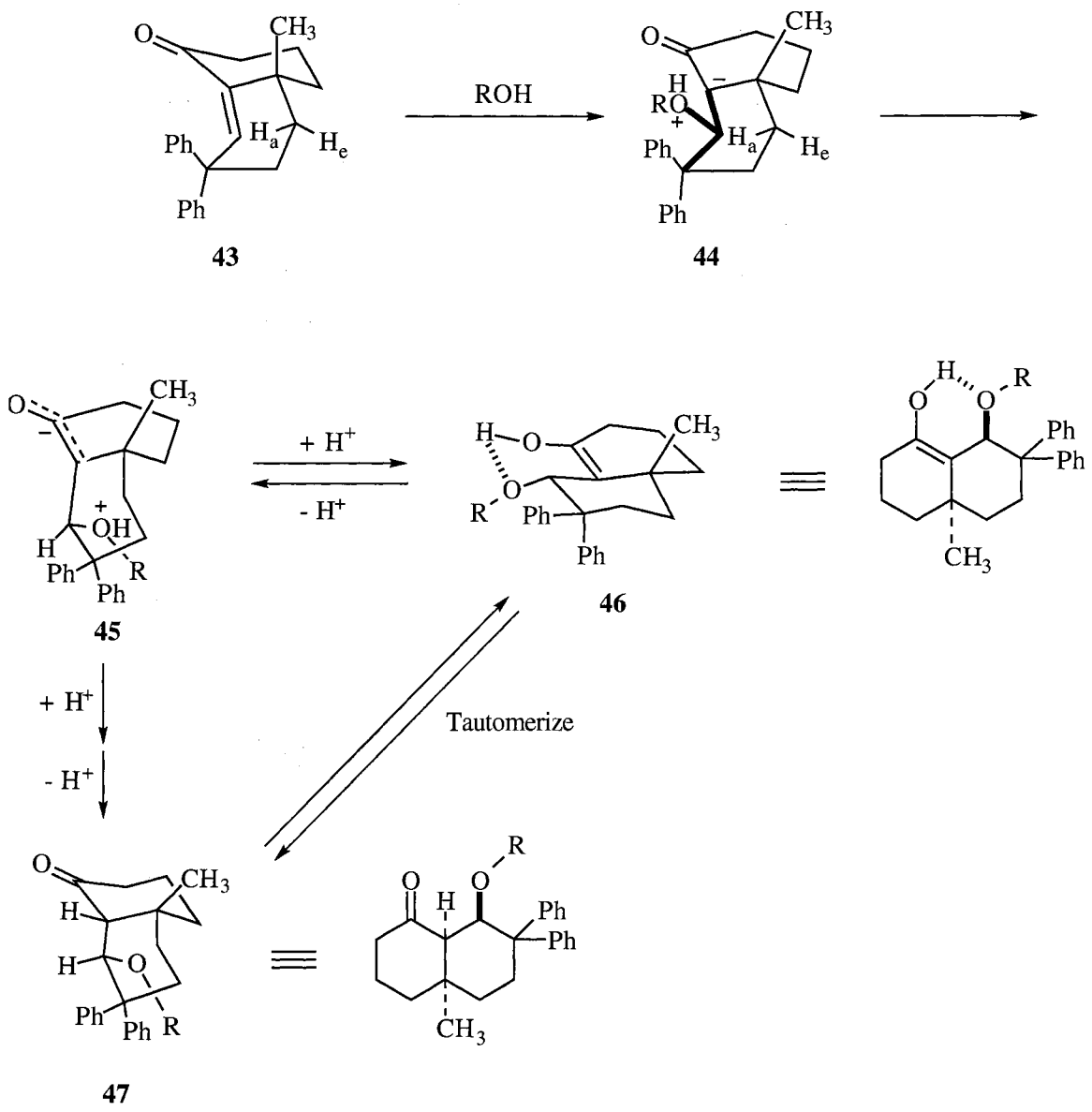


Figure 30. Mechanism of Photoaddition to Naphthalenone **3c**.

One cannot discount the possibility of a zwitterionic intermediate as the reactive species in the addition.[10] Irradiation of the molecule would result in the dipolar intermediate **48** (Figure 31). The nucleophilic solvent would then attack the positively charged β-carbon resulting in a delocalized species **45**. In this alternative mechanism, the orientation of the alkoxy group in **45** can be explained due to guidance of the incoming nucleophile by the angular methyl group. The remainder of the mechanism follows that depicted in Figure 30.

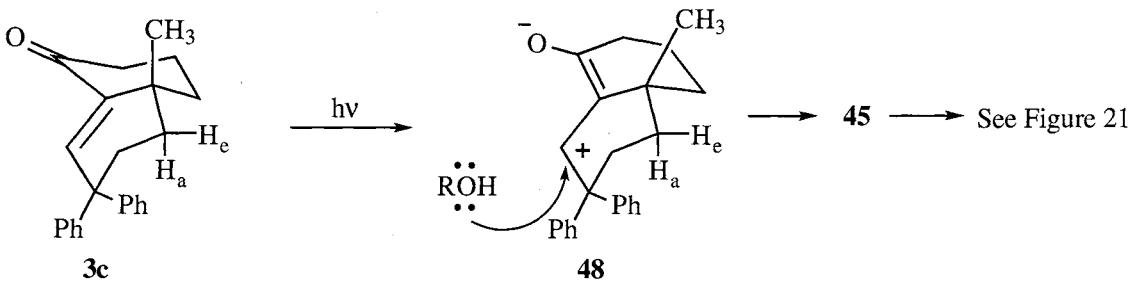


Figure 31. Alternative Mechanism for Photoaddition to Naphthalenone **3c**.

Conclusion

Photolysis of 7,7-disubstituted-(±)-3,4,4a,5,6,7-hexahydro-4a-methyl-1(2*H*)-naphthalenones **3b** and **3c** in nucleophilic solvents results in addition to the α,β-unsaturated system. If alcohols are used as the solvent, a hydrogen bonded enol ether results as the primary product. In cases where tautomerization is allowed, β-alkoxy ketones are formed readily upon exposure to silica gel. If water is used as the nucleophile, photolysis results in β-hydroxy ketones as the isolated products. It is not clear whether an

enol is initially formed, followed by rapid tautomerization, or the ketone is the initial photoproduct. Our observations support the alternative mechanism advanced previously by Hart.[14] In all the cases tested, a stereospecific and regiospecific nucleophilic addition occurred. The stereochemistry can be explained by an initial photochemically-induced isomerization to the strained trans intermediate followed by addition of the solvent to the least hindered face of the molecule and conformational relaxation to relieve the strain.

When photolysis is done in benzene, no reaction is observed and >80% of the starting materials are recovered. Thus, these naphthalenones are photochemically inert in benzene. The naphthalenones are also unreactive under standard base-catalyzed Michael conditions. Functionalization using photoinduced addition of oxygen nucleophiles was very dependable and thus has potential as a useful synthetic strategy.

Experimental

THF was distilled from $LiAlH_4$; triethylamine was distilled from CaH_2 and stored over 4Å molecular sieves; isopropyl alcohol and *tert*-butyl alcohol were distilled from CaH_2; benzene was purified according to the procedure of Zimmerman and Bunce;[70] DMPU was stored over 4Å molecular sieves. Copper(I) iodide (CuI) was purified using a combination of the procedures reported by Dieter[71] and Kauffman.[72] CuI (13.0 g, 68.3 mmol) was dissolved in boiling, saturated KI (130 g KI / 100 mL of H_2O), then cooled, diluted with H_2O to precipitate the salt, and filtered. The solid was washed sequentially with H_2O, EtOH, EtOAc, Et_2O, and pentane, and then dried under vacuum for 24 h. Other reagents were used as received. All reactions were run under dry N_2 in oven-dried glassware. Reactions were monitored using one of the following methods: (1) TLC on hard-layer silica gel GF plates (Analtech) using UV detection or (2) capillary GC with FI detection (SE-30 column, 6 m x 0.25 mm i.d., 0.25 μm film thickness) programmed between 50-300 °C. The NH_4Cl, 1 M HCl, $NaHCO_3$, 5% $Na_2S_2O_3$, and NaCl used in workup procedures refer to aqueous solutions. Preparative separations were performed

using one of the following methods: (1) PTLC on 20-cm x 20-cm silica gel GF plates (Analtech) or (2) column chromatography on silica gel (Grace, grade 62, 60-200 mesh) containing UV-active phosphor (Sylvania no. 2282); band elution was monitored using a hand-held UV lamp. IR spectra are referenced to polystyrene. Unless otherwise indicated ^{1}H NMR and ^{13}C NMR spectra were run in $CDCl_3$ at 400 and 100 MHz, respectively, and are referenced to internal Me_4Si. High resolution mass spectra (HRMS, EI/DP) were obtained at 70 eV. Elemental analyses were ± 0.3%.

(±)-3-(4-Pentenyl)-3-methylcyclohexanone (7). This compound was prepared using an adaptation of the procedure reported by Paquette and Poupart.[47] To a vigorously stirred suspension of 1.45 g (60.4 mmol) of magnesium turnings in 2 mL of dry THF was added 5 mL of a solution consisting of 8.00 g (53.7 mmol) of 5-bromo-1-pentene in 15 mL of THF. Once the reaction started, the remainder of the bromide was added over a 25 min period at a rate which maintained a gentle reflux. The reaction was heated at reflux for an additional 2 h. The resulting gray solution was diluted with 10 mL of dry THF, cooled to -5 °C, and treated with 4.85 g (25.5 mmol) of purified CuI. The deep blue solution was stirred for 10 min and then cooled to -78 °C. A solution of 2.66 g (3.10 mL, 24.5 mmol) of chlorotrimethylsilane in 5 mL of THF was added dropwise during 20 min followed, in a like manner, by a solution of 2.56 g (2.63 mL, 23.3 mmol) of 3-methyl-2-cyclohexen-1-one (**6**) in 5 mL of THF. The resulting green solution was stirred for 1.5 h during which time the reaction became blue again. The reaction was quenched by sequential addition of 5 mL of MeOH and 3 mL of 25% H_2SO_4, warmed to room temperature, stirred for 2 h, then filtered through Celite® and concentrated under vacuum. The residue was diluted with 100 mL of ether and 50 mL of water and the resulting solution was filtered through Celite® a second time. The layers were separated and the ether layer was washed with H_2O (3x), $Na_2S_2O_3$ (1x), and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum. The product was purified by short path distillation to give 3.06 g (17.0 mmol, 73%) of **7** as a colorless liquid, bp 64-65 °C (0.5

mm Hg). IR (thin film) 3082, 1716, 1644, 1381, 997, 919 cm^{-1}; ^1H NMR δ 5.78 (ddt, 1 H, J = 17.1, 10.3, 6.7 Hz), 4.99 (d, 1 H, J = 17.1 Hz), 4.94 (d, 1 H, J = 10.3 Hz), 2.27 (t, 2 H, J = 6.6 Hz), 2.19 (AB d, 1 H, J = 13.5 Hz), 2.10 (AB d, 1 H, J = 13.5 Hz), 2.02 (q, 2 H, J = 6.9 Hz), 1.86 (m, 2 H), 1.63 (m, 2 H), 1.56 (m, 1 H), 1.36 (m, 2 H), 1.26 (m, 2 H), 0.92 (s, 3 H); ^{13}C NMR δ 211.9, 138.4, 114.4, 53.5, 40.8 (2), 38.3, 34.0, 24.8, 22.5, 21.9; HRMS *m/e* for $C_{12}H_{20}O$ calcd 180.1514, found 180.1512.

(±)-3,4,4a,5,6,7-Hexahydro-4a-methyl-1(2*H*)-naphthalenone (3a). A solution of 4.75 g (26.4 mmol) of **7** in 150 mL of MeOH at -78 °C was treated with ozone until the solution turned a light blue color. The reaction was quenched at -78 °C with a solution of 7.62 g (9.00 mL, 122.5 mmol) of dimethyl sulfide and 1 mL of acetic acid, warmed to room temperature, and stirred for 12 h. The solvent was removed under vacuum and the crude product was dissolved in ether and washed with H_2O (4x) and NaCl (1x). The ether layer was dried ($MgSO_4$) and concentrated under vacuum to give the crude keto aldehyde **4a** which was used without further purification.

The intermediate aldehyde was dissolved in 125 mL of benzene, 50 mg of *p*-TsOH was added, and the solution was heated under reflux using a Dean-Stark apparatus to separate water from the reaction. GC analysis indicated that the reaction was complete after 4 h. The cooled reaction mixture was washed with $NaHCO_3$ (1x) and NaCl (1x) and then dried ($MgSO_4$) and concentrated under vacuum to afford a yellow oil. The product was purified by distillation to give 3.33 g (20.3 mmol, 77%) of **3a** as colorless liquid, bp. 76-77 °C (0.5 mm), [lit[50] bp 72 °C (0.3 mm)]. Refrigeration was required to prevent polymerization. UV (EtOH) 240 nm (ε 1700), 315 (90); IR (thin film) 1675, 1620, 1375 cm^{-1}; ^1H NMR δ 6.43 (m, 1 H), 2.54 (dm, 1 H, J = 17.0 Hz), 2.28 (m, 1 H), 2.19 (m, 2 H), 1.98 (m, 1 H), 1.88 (m, 1 H), 1.67 (m, 3 H), 1.60 (tt, 2 H, J = 14.2, 3.3 Hz), 1.42 (m, 1 H), 0.86 (s, 3 H); ^{13}C NMR δ 203.2, 144.4, 133.4, 40.2, 38.6, 37.5, 35.3, 25.7, 25.3, 19.0, 17.5; HRMS *m/e* for $C_{11}H_{16}O$ calcd 164.1201, found 164.1202.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.49; H, 9.76. Found: C, 80.35; H, 9.73.

5-Bromo-3,3-dimethyl-1-pentene (10). This bromide was prepared from 3,3-dimethyl-4-penten-1-ol (**8**)[48] by conversion to its mesylate (**9**) and nucleophilic displacement by bromide ion. The mesylate was prepared by the general procedure of Crossland and Servis.[52] A solution of 25.6 g (0.22 mol) of **8** and 33.4 g (46.0 mL, 0.33 mol) of triethylamine in 600 mL of CH_2Cl_2 was stirred at -5 °C while a solution of 27.7 g (18.7 mL, 0.24 mol) of methanesulfonyl chloride in 25 mL of CH_2Cl_2 was added during 45 min. The reaction was stirred for 15 min and transferred to a separatory funnel containing a mixture of H_2O and crushed ice. The layers were separated, and the organic layer was washed with ice cold H_2O (2x), 10% HCl (1x), $NaHCO_3$ (1x), and NaCl (1x), then dried (Na_2SO_4). Concentration under vacuum at 30-35 °C afforded 42.3 g (0.22 mol, 100%) of the crude mesylate **9** which was used without further purification. IR (thin film) 3084, 1643, 1354, 1181 cm^{-1}; ^1H NMR δ 5.76 (dd, 1 H, J = 17.4, 10.8 Hz), 5.00 (d, 1 H, J = 10.8 Hz), 4.97 (d, 1 H, J = 17.4 Hz), 4.20 (t, 2 H, J = 7.5 Hz), 2.99 (s, 3 H), 1.79 (t, 2 H, J = 7.5 Hz), 1.06 (s, 6 H); ^{13}C NMR δ 146.4, 111.7, 67.6, 40.6, 37.3, 35.5, 36.8.

To a stirred suspension of 94.5 g (1.10 mol) of lithium bromide in 400 mL of anhydrous ether was added 100 mL of dry DMPU dropwise with stirring followed by 42.3 g (0.22 mol) of **9**. The reaction was stirred at reflux for 24 h, then cooled to 0 °C, cautiously treated with 100 mL of H_2O, and transferred to a separatory funnel. The layers were separated, and the ether layer was washed with H_2O (2x), 10% HCl (2x), $NaHCO_3$ (1x), and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum. The crude product was distilled through a 15-cm Vigreux column to afford 32.9 g (0.19 mol, 85% from **8**) of **10** as a colorless oil, bp 53-56 °C (25 mm Hg) [lit[48] 56-57 °C (18 mm Hg)]. IR (thin film) 3084, 1643, 1372, 1361, 1001, 915 cm^{-1}; ^1H NMR δ 5.73 (dd, 1 H, J = 17.5, 10.8 Hz), 4.98 (d, 1 H, J = 10.8 Hz), 4.94 (d, 1 H, J = 17.5 Hz), 3.29 (m, 2 H),

1.91 (m, 2 H), 1.02 (s, 6 H); ^{13}C NMR δ 146.5, 111.7, 45.9, 37.8, 29.3, 26.5; HRMS *m/e* for $C_7H_{13}{}^{79}Br$ calcd 176.0201, found 176.0188.

Anal. Calcd for $C_7H_{13}Br$: C, 47.45; H, 7.34. Found: C, 47.29; H, 7.32.

(±)-3-(3,3-Dimethyl-4-pentenyl)-3-methylcyclohexanone (11). This compound was prepared using an adaptation of the procedure reported by Paquette and Poupart.[47] To a vigorously stirred suspension of 1.40 g (58.3 mmol) of magnesium turnings in 2 mL of dry THF was added 5 mL of a solution consisting of 9.00 g (50.8 mmol) of bromide **10** in 15 mL of THF. Once the reaction started, the remainder of the bromide was added over a 25 min period at a rate which maintained a gentle reflux. The reaction was heated at reflux for an additional 2 h. The resulting gray solution was diluted with 10 mL of dry THF, cooled to -5 °C, and treated with 4.59 g (24.1 mmol) of purified CuI. The deep blue solution was stirred for 10 min and then cooled to -78 °C. A solution of 2.52 g (2.94 mL, 23.2 mmol) of chlorotrimethylsilane in 5 mL of THF was added dropwise during 20 min followed, in a like manner, by a solution of 2.42 g (2.49 mL, 22.0 mmol) of 3-methyl-2-cyclohexen-1-one (**6**) in 5 mL of THF. The resulting green solution was stirred for 1.5 h during which time the reaction became blue again. The reaction was quenched by sequential addition of 5 mL of MeOH and 3 mL of 25% H_2SO_4, warmed to room temperature, stirred for 2 h, then filtered through Celite® and concentrated under vacuum. The residue was diluted with 100 mL of ether and 50 mL of water and filtered through Celite® a second time. The layers were separated and the ether layer was washed with H_2O (3x), $Na_2S_2O_3$ (1x), and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum. The product from two runs was combined and purified by short path distillation to give 6.60 g (31.8 mmol, 72%) of **11** as a colorless liquid, bp 69-74° C (0.5 mm Hg). IR (thin film) 3080, 1720, 1643, 1382, 1362, 1001, 911 cm^{-1}; ^{1}H NMR δ 5.70 (dd, 1 H, J = 17.4, 10.8 Hz), 4.91 (d, 1 H, J = 10.8 Hz), 4.88 (d, 1 H, J = 17.4 Hz), 2.26 (t, 2 H, J = 6.7 Hz), 2.16 (AB d, 1 H, J = 13.4 Hz), 2.09 (AB d, 1 H, J = 13.4 Hz), 1.84 (quintet, 2 H, J = 6.5 Hz), 1.60 (m, 1 H), 1.53 (m, 1 H), 1.28-1.12

(complex, 4 H), 0.97 (s, 6 H), 0.89 (s, 3 H); ^{13}C NMR δ 212.1, 148.1, 110.6, 53.8, 40.9, 38.2, 36.1, 35.8, 37.7, 35.6, 26.6 (2), 24.9, 22.0; HRMS *m/e* for $C_{14}H_{24}O$ calcd 208.1828, found 208.1826.

Anal. Calcd for $C_{14}H_{24}O$: C, 80.77; H, 11.53. Found: C, 80.56; H, 11.48.

(±)-3,4,4a,5,6,7-Hexahydro-4a,7,7-trimethyl-1(2*H*)-naphthalenone (3b). A solution of 5.50 g (26.4 mmol) of **11** in 150 mL of MeOH at -78 °C was treated with ozone until the solution turned a light blue color. The reaction was quenched at -78 °C with a solution of 7.62 g (9.00 mL, 122.5 mmol) of dimethyl sulfide and 1 mL of acetic acid, warmed to room temperature, and stirred for 12 h. The solvent was removed under vacuum and the crude product was dissolved in ether and washed with H_2O (4x) and NaCl (1x). The ether layer was dried ($MgSO_4$) and concentrated under vacuum to give the crude keto aldehyde **4b** which was used without further purification.

The aldehyde was dissolved in 125 mL of benzene, 50 mg of *p*-TsOH was added, and the solution was heated under reflux using a Dean-Stark apparatus to separate water from the reaction. GC analysis indicated that the reaction was complete after 4 h. The cooled reaction mixture was washed with $NaHCO_3$ (1x) and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum to afford a yellow oil. The product was purified by chromatography on a 50-cm x 3-cm silica gel column eluted with 5% ether in hexane. Band 2 afforded 3.82 g (19.9 mmol, 75%) of **3b** as a pale yellow oil which slowly crystallized on standing, mp 24-26 °C. UV (*t*-BuOH) 252 nm (ε 2500), 320 (95); IR (thin film) 1693, 1628 cm^{-1}; ^{1}H NMR δ 6.14 (s, 1 H), 2.55 (ddt, 1 H, J = 16.9, 5.1, 2.0 Hz), 2.28 (ddd, 1 H, J = 16.9, 12.6, 7.6 Hz), 1.99 (m, 1 H), 1.88 (m, 1 H), 1.78-1.40 (complex, 6 H), 1.07 (s, 3 H), 1.02 (s, 3 H), 1.00 (s, 3 H); ^{13}C NMR δ 203.4, 142.5, 141.9, 40.4, 38.8, 35.8, 35.4, 32.8, 32.5, 29.9, 28.3, 25.2, 19.2; HRMS *m/e* for $C_{13}H_{20}O$ calcd 192.1514, found 192.1513.

Anal. Calcd for $C_{13}H_{20}O$: C, 81.25; H, 10.42. Found: C, 80.99; H, 10.40.

1,1-Diphenyl-1-propanol (14). This alcohol was prepared by reaction of 0.35 mol of propiophenone (**13**) with 0.40 mol of phenylmagnesium bromide (88%) in ether according to the procedure described by Ottenbrite and co-workers,[73] mp 90-91 °C, (lit[73] mp 90-92 °C). Other workers have prepared this compound by reaction of phenylmagnesium bromide with ethyl propionate (60%)[74] and addition of ethylmagnesium bromide to benzophenone (87%).[75,76] IR (thin film) 3530, 1602, 1498, 750, 700 cm^{-1}; ^1H NMR δ 7.41 (d, 4 H, J = 7.3 Hz), 7.30 (m, 4 H), 7.20 (t, 2 H, J = 7.0 Hz), 2.31 (q, 2 H, J = 7.3 Hz), 2.05 (bs, 1 H), 0.87 (t, 3 H, J = 7.3 Hz); ^{13}C NMR δ 146.9, 128.1, 126.7, 126.1, 78.4, 34.4, 8.1; HRMS *m/e* for $C^{15}H^{16}O$ calcd 212.1201, found 212.1202.

1,1-Diphenyl-1-propene (15). To a stirred 0-5 °C (ice bath) solution of 43.0 g (0.20 moles) of **14** in 400 mL of pyridine was added 62.9 g (38.2 mL, 0.41 mol) of phosphorous oxychloride dropwise during 30 min. The mixture was heated at reflux for 2 h, cooled to room temperature, poured onto 1 kg of crushed ice, and extracted with ether (3 x 250 mL). The combined ether extracts were washed with 1 M HCl (3 x 300 mL), H_2O, $NaHCO_3$, and NaCl, then dried ($MgSO_4$) and concentrated under vacuum. The crude alkene was purified by chromatography on a 30-cm x 6-cm silica gel column eluted with hexanes. Concentration of the eluent gave 35.2 g (0.18 mol, 90%) of **15** as a clear oil which crystallized to a white solid, mp 46-47 °C, (lit[77] mp 49 °C). IR (thin film) 1598, 1495, 1360, 755, 699 cm^{-1}; ^1H NMR δ 7.40-7.18 (complex, 10 H), 6.18 (q, 1 H, J = 7.0 Hz), 1.76 (d, 3 H, J = 7.0 Hz); ^{13}C NMR δ 142.9, 142.4, 140.0, 130.0, 128.1, 128.0, 127.2, 126.8, 126.7, 124.2, 15.7; HRMS *m/e* for $C_{15}H_{14}$ calcd 194.1095, found 194.1090.

3,3-Diphenyl-4-penten-1-ol (16). To a magnetically stirred solution of 5.82 g (30.0 mmol) of **15** in 15 mL of THF at 0 °C (ice-salt bath) was added 20.3 mL of 1.5 M *n*-butyllithium (30.5 mmol) dropwise during 15 min. The reaction was stirred for 15 min and a solution of 2.64 g (3.00 mL, 60 mmol) of ethylene oxide in 10 mL of THF was

added dropwise. The reaction was stirred for 10 min, then quenched at 0 °C with 20 mL of saturated NH_4Cl, diluted with 200 mL of H_2O, and ether extracted (2 x 100 mL). The combined ether extracts were washed with NH_4Cl, H_2O, and NaCl, then dried ($MgSO_4$) and concentrated under vacuum. The crude alcohol was purified by chromatography on a 50-cm x 2.5-cm silica gel column. Elution with hexane yielded 0.78 g (4.0 mmol, 13.4%) of unreacted **15**; 5% ether in hexane removed several minor side products; 10% ether in hexane gave 3.96 g (16.6 mmol, 55.5%, 77% based on 72% conversion) of alcohol **16** as a colorless viscous oil which crystallized to a white solid, mp 54-55 °C. IR (thin film) 3415, 3080, 3060, 3025, 1635, 1600, 1498, 1030, 920, 758, 702 cm^{-1}; ^1H NMR δ 7.31-7.18 (complex, 10 H), 6.44 (dd, 1 H, J = 17.5, 10.7 Hz), 5.21 (d, 1 H, J = 10.7 Hz), 4.87 (d, 1 H, J = 17.5 Hz), 3.53 (m, 2 H), 2.60 (t, 2 H, J = 7.3 Hz), 1.60 (bs, 1 H); ^{13}C NMR δ 146.4, 144.3, 128.2, 128.1, 126.2, 114.2, 60.0, 52.4, 41.2; HRMS *m/e* for $C_{17}H_{18}O$ calcd 238.1356, found 238.1351.

Anal. Calcd for $C_{17}H_{18}O$: C, 85.71; H, 7.56. Found: C, 85.63; H, 7.59.

5-Bromo-3,3-diphenyl-1-pentene (12). To a magnetically stirred 0-5 °C (ice bath) solution of 2.00 g (8.40 mmol) of **16** and 3.41 g (10.4 mmol) of carbon tetrabromide in 15 mL of CH_2Cl_2 was added portionwise 3.37 g (12.8 mmol) of triphenylphosphine during 45 min. The reaction was stirred for an additional 5 min, 2 g of silica gel was added, and the mixture was concentrated under vacuum. The product was purified by silica gel column chromatography using increasing concentrations of ether in hexanes. Band 2 afforded 2.15 g (7.14 mmol, 85%) of **12** as a colorless oil. IR (thin film) 3075, 3050, 3020, 1630, 1595, 1490, 1000, 920, 753, 698 cm^{-1}; ^1H NMR δ 7.29-7.15 (complex, 10 H), 6.37 (dd, 1 H, J = 17.5, 10.7 Hz), 5.25 (d, 1 H, J = 10.7 Hz), 4.92 (d, 1 H, J = 17.5 Hz), 3.13 (m, 2 H), 2.85 (m, 2 H); ^{13}C NMR δ 145.4, 143.3, 129.8, 128.3 (2), 128.1 (2), 127.2, 126.5, 114.5, 54.4, 42.1, 29.3; HRMS *m/e* for $C_{17}H_{17}{}^{79}Br$ calcd 300.0514, found 300.0513.

Anal. Calcd for $C_{17}H_{17}Br$: C, 67.77; H, 5.65. Found: C, 67.96; H, 5.78.

(±) -3- (2- Bromoethyl) -3- methylcyclohexanone (23). This compound was prepared using an adaptation of the procedure described by Molander and McKie.[59] A solution of 1.10 g (7.97 mmol) of 3-ethenyl-3-methylcyclohexanone (**22**)[47] in 150 mL of spectrophotometric-grade hexane was placed in a 175-mL quartz tube equipped with a magnetic stirrer. The reaction vessel was positioned adjacent to a Hanovia immersion well, and the solution was purged with N_2 for 15 min prior to starting. The reaction was irradiated (450-W medium pressure mercury vapor lamp, Vycor filter) while dry commercial HBr gas was bubbled through the solution at a moderate rate. The reaction was monitored by GC until all of the starting material had been consumed. Excess HBr was removed by purging the reaction with N_2 for 15-30 min. The crude reaction mixture was washed with H_2O (2x), 5% $Na_2S_2O_3$ (1x), $NaHCO_3$ (1x), and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum. The resulting dark brown oil was purified by silica gel column chromatography using 10% ether in hexanes. Band 2 afforded 1.44 g (6.61 mmol, 83%) of **23** as a pale yellow oil which slowly crystallized upon standing, mp 24-26°C. IR (thin film) 1720, 1386 cm^{-1}; ^1H NMR δ 3.37 (m, 2 H), 2.30 (t, 2 H, J = 6.8 Hz), 2.23 (AB d, 1 H, J = 13.6 Hz), 2.14 (AB d, 1 H, J = 13.6 Hz), 1.90 (m, 4 H), 1,64 (m, 2 H), 0.97 (s, 3 H); ^{13}C NMR δ 210.9, 53.2, 45.2, 40.8, 39.7, 35.7, 27.6, 24.5, 21.9; HRMS *m/e* for $C_9H_{15}{}^{79}BrO$ calcd 218.0307, found 218.0307.

When the above procedure was scaled up to 7.90 g (57.2 mmol) of 3-ethenyl-3-methylcyclohexanone in 1 L of hexane using a Hanovia immersion apparatus, the yield of **23** was lowered to 58%.

(±)-7-(2-Bromoethyl)-7-methyl-1,4-dioxaspiro[4.5]decane (24). A mixture of 8.57 g (39.0 mmol) of **23** and 2.92 g (50.3 mmol) of ethylene glycol in 200 mL of benzene was treated with 50 mg of *p*-TsOH and heated under reflux for 12 h using a Dean-Stark apparatus to collect the H_2O produced. The cooled reaction mixture was washed with $NaHCO_3$ (2x) and NaCl (1x), then dried ($MgSO_4$) and concentrated under

vacuum to give 10.1 g (35.5 mmol, 98%) of ketal **24** as a light brown oil. This product was pure by NMR analysis and was used without further purification. IR (thin film) 1380 cm^{-1}; ^1H NMR δ 3.91 (s, 4 H), 3.38 (m, 2 H), 2.04 (dt, 1 H, J = 12.3, 5.4 Hz), 1.92 (dt, 1 H, J = 12.3, 5.4 Hz), 1.62 (m. 2 H), 1.57 (m, 2 H), 1.51 (AB d, 1 H, J = 13.8 Hz), 1.42 (AB d, 1 H, J = 13.8 Hz), 1.27 (m, 2 H), 0.99 (s, 3 H); ^{13}C NMR δ 108.9, 64.1 (2), 45.4, 44.6, 37.1, 36.0, 34.8, 29.3, 25.9, 19.5; HRMS *m/e* for $C_{11}H_{19}{}^{79}BrO_2$ calcd 262.0568, found 262.0565.

(±)-3-(2-Iodoethyl)-3-methylcyclohexanone (26). A solution of 8.53 g (39.1 mmol) of **23** and 30.0 g (200 mmol) of NaI in 500 mL of acetone was heated at reflux for 24 h. The crude reaction mixture was cooled, concentrated under vacuum, diluted with H_2O, and extracted with ether (3x). The combined ether extracts were washed with 5% $Na_2S_2O_3$ (1x) and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum to give 9.24 g (34.7 mmol, 89%) of compound **26** as a dark yellow oil. This material was pure by NMR analysis and was used without further purification. IR (thin film) 1713, 1382 cm^{-1}; ^1H NMR δ 3.14 (m, 2 H), 2.29 (t, 2 H, J = 6.9 Hz), 2.21 (AB d, 1 H, J = 13.6 Hz), 2.12 (AB d, 1 H, J = 13.6 Hz), 1.98 (m, 2 H), 1.89 (m, 2 H), 1.62 (m, 2 H), 0.95 (s, 3 H); ^{13}C NMR δ 210.9, 52.6, 46.9, 41.0, 40.8, 35.3, 24.1, 21.8, -1.3; HRMS *m/e* for $C_9H_{15}IO$ calcd 266.0169, found 266.0167.

(±) -7- (2-Iodoethyl) -7- methyl -1,4- dioxaspiro[4.5]decane (27). A solution of 9.60 g (36.1 mmol) of **26** and 2.60 g (41.9 mmol) of ethylene glycol in 250 mL of benzene was treated with 50 mg of *p*-TsOH, and the solution was heated under reflux for 12 h using a Dean-Stark apparatus to collect the H_2O produced. The cooled reaction mixture was washed with $NaHCO_3$ (2x) and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum to give 11.0 g (35.5 mmol, 98%) of ketal **27** as a light brown oil. This product was pure by NMR analysis and was used without further purification. IR (thin film) 1380 cm^{-1}; ^1H NMR δ 3.91 (s, 4 H), 3.16 (m, 2 H), 2.08 (dt, 1 H, J = 12.8, 5.1 Hz), 1.95 (dt, 1 H, J = 12.8, 5.1 Hz), 1.62 (m, 2 H), 1.57 (m, 2 H), 1.51 (AB

d, 1 H, J = 13.8 Hz), 1.50 (AB d, 1 H, J = 13.8 Hz), 1.28 (m, 2 H), 0.97 (s, 3 H); ^{13}C NMR δ 108.9, 64.0 (2), 47.1, 44.1, 37.3, 36.7, 34.7, 25.4, 19.4, 1.0; HRMS *m/e* for $C_{11}H_{19}IO_2$: calcd 310.0431, found 310.0428.

(±) -7- (3- Cyano -3,3- diphenylpropyl) -7- methyl -1,4- dioxaspiro-[4.5]decane (28). The phase-transfer alkylation procedure of Adelstein and co-workers[61] was used. A mixture of 10.8 g (34.8 mmol) of **27**, 6.72 g (34.8 mmol) of diphenylacetonitrile, and 2.50 g (44.6 mmol) of pulverized KOH in 150 mL of MEK was heated under reflux with vigorous stirring. After 12 h, GC analysis indicated that a significant amount of starting material remained. An additional 1.00 g (17.9 mmol) of pulverized KOH was added and heating was continued for another 12 h. The mixture was cooled, the solution was filtered from the solid KOH using excess MEK, and the filtrate was concentrated under vacuum. The residue was taken up in ether and washed with 1 M HCl (1x), $NaHCO_3$ (1x), 5% $Na_2S_2O_3$ (1x), and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum. The product was purified by chromatography on an 80-cm x 2.5-cm silica gel column eluted with 15-25% ether in hexanes. Band 3 yielded 10.5 g (28.1 mmol, 81%) of compound **28** as a pale yellow oil. IR (thin film) 3061, 3029, 2242, 1599, 1493, 1360, 753, 699 cm^{-1}; ^1H NMR δ 7.41-7.26 (complex, 10 H), 3.89 (m, 4 H), 2.34 (m, 2 H), 1.59-1.23 (complex, 10 H), 0.99 (s, 3 H); ^{13}C NMR δ 140.5, 140.2, 128.8, 128.7, 127.8, 126.9, 126.8, 122.4, 109.2, 64.1, 63.9, 51.8, 44.5, 38.1, 37.4, 34.8, 34.3, 34.1, 25.3, 19.5; HRMS *m/e* for $C_{25}H_{29}NO_2$ calcd 375.2200, found 375.2187.

Anal. Calcd for $C_{25}H_{29}NO_2$: C, 80.00; H, 7.73. Found: C, 79.91; H, 7.71.

Attempted Phase-Transfer Alkylation of Diphenylacetaldehyde with Iodo Ketal 27: (±)-7-(2-(2,2-Diphenylethenoxy)ethyl)-7-methyl-1,4-dioxa-spiro[4.5]decane (30). The phase-transfer conditions of Buschmann and Zeeh[62] were used. A mixture of 170 mg (0.55 mmol) of **27**, 130 mg (0.66 mmol) of diphenylacetaldehyde, 66 mg (1.65 mmol) of finely ground NaOH, and 5 mg of

tetrabutylammonium iodide was placed in a round-bottomed flask containing 0.25 mL of toluene and 0.25 mL of H_2O. This reaction mixture was stirred and heated at reflux for 4 h, then cooled to room temperature, and extracted with ether (2x). The combined organic extracts were washed with 1 M HCl (1x), H_2O (1x), and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum. The product was purified by PTLC eluted with 10% ether in hexanes. The slowest moving band yielded 80 mg (0.21 mmol, 38.5%) of compound **30** as a light yellow oil. IR (thin film) 3080, 3054, 3026, 1634, 1598, 1496, 1381, 766, 698 cm^{-1}; ^1H NMR δ 7.32 (d, 2 H, J = 8.4 Hz), 7.24-7.10 (complex, 8 H), 6.42 (s, 1 H), 3.91 (t, 2 H, J = 7.4 Hz), 3.81 (m, 4 H), 1.75 (dt, 1 H, J = 13.9, 7.2 Hz), 1.63 (dt, 1 H, J = 13.9, 7.2 Hz), 1.54 (m, 2 H), 1.48 (m, 2 H), 1.46 (AB d, 1 H, J = 13.6 Hz), 1.38 (AB d, 1 H, J = 13.6 Hz), 1.28-1.17 (complex, 2 H), 0.93 (s, 3 H); ^{13}C NMR δ 145.5 (2), 140.8, 137.8, 129.8, 128.3, 128.2, 127.8, 126.3, 126.2, 119.9, 109.1, 70.4, 64.0 (2), 45.0, 40.8, 37.6, 34.8, 34.7, 33.8, 26.3, 19.6; HRMS *m/e* calcd for $C_{25}H_{30}O_3$: 378.2196, found 378.2177.

Anal. Calcd for $C_{25}H_{30}O_3$: C, 79.36: H, 7.94. Found: C, 79.33; H, 7.93.

(±)-7- (3- Formyl -3,3- diphenylpropyl) -7- methyl -1,4- dioxaspiro-[4.5]decane (29). A solution of 2.48 g (6.61 mmol) of **28** in 100 mL of CH_2Cl_2 was cooled to -20 °C and treated with 9.92 mL (9.92 mmol) of a 1 M solution of DIBAL in hexane over 30 min. After the addition was complete, stirring was continued for 2.5 h during which time the reaction warmed to 20 °C. The reaction was cooled to -20 °C and carefully quenched with 50 mL of 50% (w/w) aqueous citric acid. Stirring was continued until the two immiscible phases became clear. The organic layer was separated, washed with H_2O (2x) and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum to yield 2.37 g (6.27 mmol, 95%) of **29** as a viscous, colorless oil that was pure by GC and NMR. This product was used without further purification. IR (thin film) 3086, 3059, 3025, 2818, 2716, 1722, 1599, 1493, 756, 701 cm^{-1}; ^1H NMR δ 9.78 (s, 1 H), 7.36 (t, 4 H, J = 7.4 Hz), 7.30 (m, 2 H), 7.19 (m, 4 H), 3.89 (m, 2 H), 3.83 (m, 2 H), 2.26 (m, 2 H),

1.58-0.84 (complex, 10 H), 0.95 (s, 3 H); ^{13}C NMR δ 199.0 140.1, 140.0, 129.2, 128.7, 128.6, 127.2, 109.3, 64.1, 63.8, 63.6, 44.5, 37.3, 37.1, 34.9, 34.5, 27.9, 25.0, 19.6; HRMS *m/e* for $C_{25}H_{30}O_3$ calcd 378.2196, found 378.2199.

(±) - 4- (1- Methyl -3- oxocyclohexyl) -2, 2- diphenylbutanal (4c). A solution of 2.35 g (6.22 mmol) of **29** and 1.04 g (4.14 mmol) of PPTS in 75 mL of 9:1 acetone-H_2O was heated at reflux for 36 h. The solution was cooled and concentrated under vacuum. The resulting oily residue was triturated with ether (3x) and decanted away from the solid PPTS. The combined ether extracts were washed with H_2O (3x) and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum to yield 1.97 g of **2** containing *ca.* 10% of an impurity (by GC). A small amount of sample was purified for analytical purposes using PTLC eluted with 5% ether in hexanes. The remainder of the material was used without further purification. IR (thin film) 3086, 3058, 3026, 2828, 2709, 1722, 1714, 756, 701 cm^{-1}; ^{1}H NMR δ 9.79 (s, 1 H), 7.37 (t, 4 H, J = 7.3 Hz), 7.31 (m, 2 H), 7.17 (t, 4 H, J = 7.8 Hz), 2.30-2.16 (complex, 4 H), 2.12 (AB d, 1 H, J = 13.4 Hz), 2.07 (AB d, 1 H, J = 13.4 Hz), 1.76 (m, 2 H), 1.60 (m, 1 H), 1.53 (m, 1 H), 1.01 (t, 2 H, J = 7.3 Hz), 0.90 (s, 3 H); ^{13}C NMR δ 211.9, 198.3, 139.9, 139.6, 128.9, 128.8, 127.4, 63.4, 53.7, 40.9, 38.5, 35.9, 35.5, 27.6, 24.5, 21.9; HRMS *m/e* for $C_{23}H_{26}O_2$ calcd 334.1934, found 334.1928.

Anal. Calcd for $C_{23}H_{26}O_2$: C, 82.63; H, 7.78. Found: C, 82.41; H, 7.80.

(±)-3,4,4a,5,6,7-Hexahydro-4a-methyl-7,7-diphenyl-1(2*H*)-naphthalenone (3c). Route A. A solution of 1.96 g of crude **4c** and 50 mg of *p*-TsOH in 100 mL of toluene was heated under reflux in a 250-mL round-bottomed flask equipped with a Dean-Stark apparatus to collect the H_2O that was produced. After 12 h, the crude reaction mixture was cooled to room temperature, washed with $NaHCO_3$ (2x), H_2O (1x), and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum. The oil was eluted through a small plug of silica gel using 5% ether in hexanes to give 1.68 g (5.32 mmol, 86% from **29**) of **3c** as a yellow oil which crystallized on standing. Slow recrystallization from ether

gave an analytically pure sample, mp. 120-122 °C. UV (*t*-BuOH) 254 nm (ε 2429), 320 (120); IR (thin film) 3082, 3057, 3022, 1685, 1626, 1598, 1495, 1379, 762, 703 cm^{-1}; ^1H NMR δ 7.30-7.13 (complex, 10 H), 6.76 (s, 1 H), 2.64 (ddt, 1 H, J = 16.9, 5.1, 2.0 Hz), 2.37 (m, 3 H), 2.03 (qt, 1 H, J = 13.2, 4.4 Hz), 1.90 (m, 1 H), 1.69 (AB d, 1 H, J = 13.6 Hz), 1.60 (m, 3 H), 1.13 (s, 3 H); ^{13}C NMR δ 203.5, 249.0, 247.1, 144.6, 138.3, 127.8, 128.5, 128.3, 127.7, 126.5, 126.4, 49.4, 41.0, 38.9, 36.2, 35.4, 32.0, 25.3, 19.7; HRMS *m/e* for $C_{23}H_{24}O$ calcd 316.1828, found 316.1826.

Anal. Calcd for $C_{23}H_{24}O$: C, 87.34; H, 7.59. Found: C, 87.22; H, 7.61.

Route B. A mixture of 2.00 g (5.29 mmol) of **29**, 50 mg of *p*-TsOH, 150 mL of toluene, and 0.25 mL of H_2O was stirred and heated under reflux for 24 h using a Dean-Stark apparatus to collect H_2O from the reaction. The mixture was cooled to room temperature, washed with $NaHCO_3$ (2x) and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum. Purification on a 95-cm x 2.5-cm silica gel column eluted with 5-10% ether in hexanes afforded 1.10 g (3.48 mmol, 66%) of **3c** as a light yellow oil which crystallized on standing. The physical and spectral data matched those given above. Also isolated from this reaction was 0.35 g (0.97 mmol, 18%) of ethylene ketal **31**. IR (thin film) 3083, 3057, 3022, 1598, 1490, 756, 700 cm^{-1}; ^1H NMR δ 7.23 (m, 8 H), 7.16 (m, 2 H), 6.27 (s, 1 H), 3.94 (m, 1 H), 3.88 (t, 2 H, J = 6.1 Hz), 3.76 (m, 1 H), 2.36 (ddd, 1 H, J = 13.3, 10.1, 5.8 Hz), 2.23 (dm, 1 H, J = 12.5 Hz), 1.94 (m, 2 H), 1.72 (dd, 1 H, J = 13.3, 4.5 Hz), 1.64 (m, 1 H), 1.53 (dm, 1 H, J = 12.5 Hz), 1.41 (m, 2 H), 1.25 (s, 3 H), 1.24 (m, 1 H); ^{13}C NMR δ 149.9, 148.1, 140.7, 129.1, 128.3, 128.1, 127.9, 127.4, 125.7, 108.5, 64.9, 63.4, 49.2, 41.1, 37.9, 37.3, 35.9, 32.2, 24.8, 19.5; HRMS *m/e* for $C_{25}H_{28}O_2$ calcd 360.2090, found 360.2088.

Anal. Calcd for $C_{25}H_{28}O_2$: C, 83.33; H, 7.78. Found: C, 83.08; H, 7.81.

(±)-3,4,4a,5,6,7-Hexahydro-4a-methyl-7,7-diphenyl-1(2*H*)-naphthalenone (3c) from Ethylene Ketal 31. A solution of 350 mg (0.97 mmol) of **31** and 100 mg (0.40 mmol) of PPTS in 10 mL of 9:1 acetone-H_2O was heated under reflux

for 36 h. Reaction mixture was cooled and concentrated under vacuum. The resulting oily residue was triturated with ether (3x) and decanted away from the solid PPTS. The combined ether extracts were washed with H_2O (3x) and NaCl (1x), then dried ($MgSO_4$), and concentrated under vacuum to yield 260 mg (0.82 mmol, 84.5%) of **3c** as pale yellow crystals which were pure by GC and NMR. When these crystals were combined with those from route B, the yield of **3c** was increased to 81%.

Attempted Preparation of 3-(3,3-Diphenyl-4-pentenyl)-3-methylcyclohexanone Using the Grignard of Bromide 12. The activated magnesium was prepared by the method of Rieke[56] and the conjugate addition was attempted as reported by Helquist.[55] A suspension of 0.61 g (15.6 mg atom) of freshly cut potassium, 0.72 g (7.56 mmol) of dry $MgCl_2$, and 0.83 g (5.00 mmol) of dry KI in 30 mL of THF was stirred at reflux for 3 h. The resulting dark gray solution was cooled to room temperature and then to -20 °C. To this solution 1.51 g (5.03 mmol) of bromide **12** in 5 mL of THF was added dropwise over 10 min. Stirring was continued for 20 min; then the reaction mixture was cooled to -78 °C. A solution of containing 0.34 g (1.66 mmol) of cuprous bromide-dimethyl sulfide complex in 4 mL of dimethyl sulfide was added dropwise over 3 min, followed by stirring for 1 h. A solution of 3-methyl-2-cyclohexen-1-one (**6**) in 6 mL of THF was added slowly over 30 min. Stirring was continued for 9 h at -78 °C. After this time, the reaction mixture was warmed to 0 °C and quenched using NH_4Cl. The reaction vessel was opened to the air, and the mixture was vigorously stirred at room temperature for 3 h. The mixture was taken up in ether and washed with H_2O (2x) and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum. The product was purified by chromatography on an 80-cm x 2.5-cm silica gel column eluted with 0-15% ether in hexanes. IR and NMR analysis of the different bands indicated that the desired product was not obtained.

Preparation of 3,3-Diphenyl-1-pentene (19) and 3,3,8,8-Tetraphenyldeca-1,9-diene (20). If the bromide **12** was added to Rieke magnesium

and quenched after 30 min, the following compounds were isolated upon workup and purification on PTLC eluted with 5-15% ether in hexanes.

Band 1 gave 5-bromo-3,3-diphenyl-1-pentene (**12**) in 22% yield. Spectral analysis agreed with an authentic sample.

Band 2 gave 1,1-diphenylpropene (**15**) in 6% yield. Spectral analysis agreed with an authentic sample.

Band 3 gave 3,3-diphenyl-1-pentene (**19**) in a yield of 37%. IR (thin film) 3086, 3026, 1599, 756, 699 cm^{-1}; ^1H NMR δ 7.35-7.15 (complex, 10 H), 6.45 (dd, 1 H, J = 17.5, 10.7 Hz), 5.18 (d, 1 H, J = 10.7 Hz), 4.77 (d, 1 H, J = 17.5 Hz), 2.30 (q, 2 H, J = 7.40 Hz), 0.77 (t, 3 H, J = 7.40); ^{13}C NMR δ 146.7, 144.5, 128.6, 128.0, 127.8, 126.8, 126.7, 125.8, 124.0, 114.2, 53.9, 31.3, 9.3.

Band 4 gave 3,3,8,8-tetraphenyldeca-1,9-diene (**20**) in a yield of 20%. IR (thin film) 3086, 3025, 1599, 756, 699 cm^{-1}; ^1H NMR δ 7.36-7.07 (complex, 20 H), 6.41 (dd, 2 H, J = 17.5, 10.7 Hz), 5.16 (d, 2 H, J = 10.7 Hz), 4.72 (d, 2 H, J = 17.5 Hz), 2.16 (m, 2 H), 1.26 (m , 2 H), 1.10 (m, 2 H), 0.86 (m, 2 H); ^{13}C NMR δ 146.9, 144.8, 128.5, 127.8, 125.8 (2), 114.1, 53.6, 38.8, 25.6.

Attempted Preparation of 3,3-Diphenyl-1-pentenylmagnesium Iodide from 21. The Grignard was prepared using standard conditions. A solution of 0.50 g (1.44 mmol) of iodide **21** in 6 mL of THF was added dropwise to a 0.04 g (1.66 mmol) of freshly ground Mg metal suspended in 2 mL of THF. After the addition was complete, the reaction mixture was stirred at reflux for 12 h. The reaction mixture was cooled to room temperature, quenched with NH_4Cl and extracted with excess ether. The organic layer was washed with H_2O (2x), NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum. GC analysis indicated approximately the same ratio of **15**, **19**, and **20** that was found when the bromide was reacted with Rieke magnesium; there was no unreacted iodide detected.

Attempted Alkylation of Bromide 24 with the Anion of 1,1-Diphenylpropene: (±)-7 - (5,5-Diphenyl-4-pentenyl) -7- methyl-1,4-dioxa-spiro[4.5]decane (25). The alkylation conditions of Tanaka were used.[57,58] A solution of 0.16 g (0.82 mmol) of 1,1-diphenylpropene (**15**) and 0.09 g (0.12 mL, 0.77 mmol) of TMEDA in 10 mL of THF was cooled to 0 °C and stirred for 15 min. To this solution, 0.60 mL (0.80 mmol) of 1.33 M *n*-BuLi in hexanes was slowly added. The resulting dark red solution was briefly stirred before dropwise addition of 0.20 g (0.76 mmol) of bromoketal **24** in 5 mL of THF. Over a 4 h period, the reaction gradually warmed to room temperature and the deep red color dissipated. The reaction was quenched with NH_4Cl and extracted with excess ether. The organic layer was washed with H_2O (2x) and NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum. Purification by PTLC gave compound **25** in 44% yield as a viscous colorless oil. IR (thin film) 3086, 3056, 3026, 1636, 1599, 1496, 1375, 767, 698 cm^{-1}; ^1H NMR δ 7.38-7.16 (complex, 10 H), 6.08 (t, 1 H, J = 7.4 Hz), 3.89 (m, 4 H), 2.07 (m, 2 H), 1.59 (complex, 6 H), 1.46 (AB d, 1 H, J = 14.2 Hz), 1.39 (AB d, 1 H, J = 14.2 Hz), 1.25 (complex, 4 H), 0.98 (s, 3 H); ^{13}C NMR δ 143.6, 142.1, 141.0, 130.6, 128.8, 128.7, 127.9, 127.5, 127.4, 110.2, 64.8, 64.6, 45.5, 43.1, 37.9, 37.8, 35.5, 35.2, 31.2, 26.2, 24.7, 20.4.

General Procedure for the Exploratory Photolysis of Naphthalenones 3a, 3b, and 3c. A 10^{-3} M solution of the naphthalenone in the appropriate solvent was purged with dry nitrogen gas for 30 min in a 200 mL flask equipped with a drying tube, Pyrex filter, and a 450-W medium pressure ultraviolet source housed inside a Hanovia immersion apparatus. After degassing for 30 min, the solution was irradiated for 4.5-30 h. The reactions were monitored by either GC, TLC, or IR and were stopped when further progress was no longer detected. For reactions performed in alcohol solvents, concentration under vacuum yielded the crude photolysate which was purified using silica gel PTLC eluted with 5-10% ether in HPLC grade hexane. For reactions performed in dioxane-water (6:1), isolation was achieved by concentrating under vacuum, extracting

with excess ether, washing the extract with NaCl (1x), then drying ($NaSO_4$) and concentrating under vacuum. Purification was done using silica gel PTLC eluted with 10-20% ether in hexane.

Attempted Photolysis of Naphthalenone 3a in Alcohol Solvents. A solution of 100 mg (0.61 mmol) of **3a** in 175 mL of *tert*-butyl alcohol was irradiated for 10 h. After 10 h, GC analysis indicated that 75% of the starting material had been consumed. The reaction had proceeded to give eight products along with a polymeric material. Upon attempted purification using silica gel PTLC, further decomposition of the products occurred and isolation of purified photoproducts was not possible. Irradiation in both isopropanol and methanol gave comparable results. Due to these unsatisfactory observations, examination of compound **3a** was discontinued.

(±)-8-*tert*-Butoxy - 2,3,4,4a,5,6,7,8 - octahydro - 4a,7,7 - trimethyl-1-naphthol (32). A solution of 100 mg (0.52 mmol) of **3b** in 175 mL of *tert*-butyl alcohol was irradiated for 4.5 h until the reaction had reached 80% conversion (GC). The photolysate was isolated and purified to give 89.0 mg (0.33 mmol, 80% based on 80% conversion) of **32** as a colorless, viscous oil. If irradiation was done in *tert*-butyl alcohol containing 10% benzene the reaction time was extended to 8.5 h and the yield was lowered to 45% based on 80% conversion. IR (thin film) 3279, 1675, 1380, 1369 cm^{-1}; ^1H NMR δ 9.25 (s, 1 H), 3.95 (s, 1 H), 2.02 (m, 2 H), 1.64-1.41 (complex, 5 H), 1.39-1.20 (complex, 3 H), 1.23 (s, 9 H), 1.07 (s, 3 H), 0.93 (s, 3 H); ^{13}C NMR δ 148.1, 108.8, 79.4, 75.7, 40.4, 38.1, 37.5, 36.7, 36.6, 29.4, 28.6, 27.4 (2), 24.5, 18.8 (2) 18.5; HRMS *m/e* for $C_{17}H_{30}O_2$ calcd 266.2246, found 266.2240.

(±)-8-*tert*-Butoxy - 2,3,4,4a,5,6,7,8 - octahydro-4a-methyl -7,7- di-phenyl-1-naphthol (34). A solution of 100 mg (0.32 mmol) of **3c** in 175 mL of *tert*-butyl alcohol was irradiated for 30 h until conversion to product slowed (TLC). ^1H NMR and IR analysis of the crude photolysate indicated the presence of an enol. Purification afforded 100 mg (0.25 mmol, 81%) of **34** as a white precipitate, mp 164-167 °C. Slow

recrystallization from ether gave an analytically pure sample. If irradiation was done in *tert*-butyl alcohol containing 10% benzene, the reaction time was only 18 h and the isolated yield was increased to 91%. IR (thin film) 3246, 1672, 1599, 1494, 1395, 1372, 755, 697 cm^{-1}; ^1H NMR δ 9.62 (s, 1 H), 7.45 (d, 2 H, J = 7.7 Hz), 7.28 (complex, 8 H), 4.33 (t, 1 H, J = 2.2 Hz), 2.72 (dt, 1 H, J = 13.8, 3.3 Hz), 2.30 (dt, 1 H, J = 6.9, 4.1 Hz), 2.05 (dm, 1 H, J = 17.0 Hz), 1.96 (dm, 1 H, J = 17.0 Hz), 1.63 (m, 1 H), 1.52 (m, 1 H), 1.43 (dm, 1 H, J = 12.9 Hz), 1.34 (dt, 1 H, J = 13.3, 3.4 Hz), 1.23 (s, 3 H), 1.12 (m, 2 H), 0.75 (s, 9 H); ^{13}C NMR δ 147.8, 147.4, 144.6, 129.8, 129.4, 127.6, 127.1, 125.9, 125.5, 109.8, 80.4, 77.4, 56.3, 40.1, 37.6, 36.2, 33.7, 29.3, 26.3, 24.8, 18.2; HRMS *m/e* for $C_{27}H_{34}O_2$ calcd 390.2559, found 390.2561.

(±)- 2,3,4,4a,5,6,7,8-Octahydro - 8 - isopropoxy -4a,7,7- trimethyl-1-naphthol (35). A solution of 100 mg (0.52 mmol) of **3b** in 175 mL of isopropanol was irradiated for 7 h. ^1H NMR and IR analysis of the crude photolysate indicated the presence of an enol. Purification afforded 65.0 mg (0.26 mmol, 55% based on 90% conversion) of **35** as a viscous, colorless oil. IR (thin film) 3297, 1678, 1382, 1373 cm^{-1}; ^1H NMR δ 9.23 (s, 1 H), 3.82 (s, 1 H), 3.69 (septet, 1 H, J = 6.2 Hz), 2.03 (m, 2 H), 1.61 (m, 2 H), 1.45 (m, 2 H), 1.32-1.17 (complex, 4 H), 1.22 (d, 3 H, J = 6.2 Hz), 1.21 (d, 3 H, J = 6.2 Hz), 1.05 (s, 3 H), 0.96 (s, 3 H), 0.88 (s, 3 H); ^{13}C NMR δ 148.2, 107.2, 86.3, 74.5, 40.5, 38.5, 37.5, 36.2, 29.4, 27.8, 24.7, 22.4, 21.1, 18.7, 18.2; HRMS *m/e* for $C_{16}H_{28}O_2$ calcd 252.2089, found 252.2086.

A trace amount of insoluble material was also isolated but the mass spectrometer was not available for analysis. It is believed that this material is a [2+2] dimerization product.

(±)-2,3,4,4a,5,6,7,8,- Octahydro -8- methoxy -4a,7,7- trimethyl-1-naphthol (36). A solution of 100 mg (0.52 mmol) of **3b** in 175 mL of HPLC grade methanol was irradiated for 10 h. ^1H NMR and IR analysis of the crude photolysate indicated the presence of an enol; however, isolation of a pure sample was not possible

due to rapid tautomerization. Partial spectra for the crude sample: IR (thin film) 3340, 1673, 1382 cm^{-1}; ^1H NMR (C_6D_6) δ 8.92 (s, 3 H), 3.50 (m, 1 H), 3.10 (s, 3 H), no other peaks are interpretable. A trace amount of insoluble material was also isolated but the mass spectrometer was not available for analysis. It is believed this material results from a [2+2] dimerization.

(±) - 2,3,4,4a,5,6,7,8- Octahydro -8- isopropoxy-4a - methyl - 7,7 - diphenyl-1-naphthol (37). A solution of 100 mg (0.32 mmol) of **3c** in 175 mL of isopropanol was irradiated for 10 h. ^1H NMR and IR analysis of the crude photolysate indicated the presence of an enol. Purification afforded 88.0 mg (0.24 mmol, 81% based on 95% conversion) of **37** as a viscous, colorless oil. IR (thin film) 3265, 3086, 3056, 3021, 1670, 1599, 1495, 1385, 1374, 755, 698 cm^{-1}; ^1H NMR δ 9.73 (s, 1 H), 7.42 (d, 2 H, J = 8.0 Hz), 7.30-7.12 (complex, 8 H), 4.32 (t, 1 H, J = 2.3 Hz), 2.70 (td, 1 H, J = 13.5, 2.3 Hz), 2.41 (septet, 1 H, J = 6.2 Hz), 2.20 (dt, 1 H, J = 13.9, 3.3 Hz), 2.09 (dm, 1 H, J = 17.0 Hz), 1.98 (dm, 1H, J = 17.0 Hz), 1.70 (m, 1 H), 1.57 (m, 1 H), 1.41 (dm, 1 H, J = 12.9 Hz), 1.32-1.21 (complex, 3 H), 1.23 (s, 3 H), 1.04 (d, 3 H, J = 6.2 Hz), 0.79 (d, 3 H, J = 6.2 Hz); ^{13}C NMR δ 147.8, 147.5, 143.9, 129.6, 128.9, 127.7, 127.4, 126.1, 125.6, 108.5, 87.0 75.2, 56.0, 39.9, 37.2, 35.8, 33.3, 29.2, 25.0, 22.3, 20.1, 18.1; HRMS *m/e* for $C_{26}H_{32}O_2$ calcd 376.2402, found 376.2408.

(±)-2,3,4,4a,5,6,7,8-Octahydro-8-methoxy-4a-methyl-7,7-diphenyl-1-naphthol (38). A solution of 100 mg (0.32 mmol) of **3c** in 175 mL of HPLC grade methanol was irradiated for 10 h. ^1H NMR and IR analysis of the crude photolysate indicated the presence of an enol. Purification afforded 60.0 mg (0.17 mmol, 78% based on 70% conversion) of **38** as a viscous, colorless oil. IR (thin film) 3284, 3086, 3056, 3023, 1670, 1599, 1496, 1375, 756, 698 cm^{-1}; ^1H NMR δ 9.24 (s, 1 H), 7.41 (d, 2 H, J = 8.1 Hz), 7.31-7.14 (complex, 8 H), 4.26 (t, 1 H, J = 2.4 Hz), 2.89 (s, 3 H), 2.60 (dt, 1 H, J = 13.9, 3.5 Hz), 2.22 (td, 1 H J = 14.0, 3.5 Hz), 2.10 (dm, 1 H, J = 17.0 Hz), 2.01 (dm, 1 H, J = 17.0 Hz), 1.70 (m, 1 H), 1.58 (m, 1 H), 1.43 (m, 1 H), 1.35-1.21

(complex, 3 H), 1.22 (s, 3 H); ^{13}C NMR δ 147.5, 147.4, 143.4, 129.6, 128.6, 127.7, 127.5, 126.1, 125.8, 106.8, 91.6, 60.36, 55.9, 39.8, 37.2, 35.7, 33.8, 29.0, 25.3, 18.1; HRMS *m/e* for $C_{24}H_{28}O_2$ calcd 348.2089, found 348.2059.

(±)-3,4,4a,5,6,7,8,8a-Octahydro-8-hydroxy-4a,7,7-trimethyl-1(2*H*)-naphthalenone (39). A solution of 100 mg (0.52 mmol) of **3b** in 175 mL of dioxane-H_2O (6:1) was irradiated for 11 h. ^{1}H NMR and IR analysis of the crude photolysate indicated the presence of a keto alcohol. Purification afforded 61.0 mg (0.29 mmol, 63% based on 88% conversion) of **39** as a white solid, mp 96-99 °C. A small amount was slowly recrystallized from ether to obtain a crystal for X-ray analysis. IR (thin film) 3449, 1692, 1382 cm^{-1}; ^{1}H NMR (C_6D_6, 70 °C) δ 3.40 (bs, 1 H), 2.44 (quintet, 1 H, J = 7.8 Hz), 2.17 (d, 1 H, J = 4.8 Hz), 2.14 (m, 1 H), 1.93 (m, 1 H), 1.69-1.50 (complex, 3 H), 1.32 (m, 2 H), 1.12-0.95 (complex, 3 H), 0.87 (s, 3 H), 0.80 (s, 3 H), 0.78 (d, 3 H, J = 1.7 Hz); ^{13}C NMR (C_6D_6, 70 °C) δ 215.3, 77.5, 58.4, 41.7, 36.2, 34.3, 32.1, 29.3, 27.1, 25.5, 20.9 (2); HRMS *m/e* for $C_{13}H_2O_2$ calcd 210.1620, found 210.1611.

(±)-3,4,4a,5,6,7,8,8a-Octahydro-8-hydroxy-4a-methyl-7,7-diphenyl-1(2*H*)-naphthalenone (40). A solution of 100 mg (0.32 mmol) of **3c** in 175 mL of dioxane-H_2O (6:1) was irradiated for 30 h. ^{1}H NMR and IR analysis of the crude photolysate indicated the presence of a keto alcohol. Purification afforded 20.0 mg (0.06 mmol, 38% based on 50% conversion) of **40** as a white oil. IR (thin film) 3533, 3088, 3056, 3031, 1694, 1599, 1494, 1318, 751, 701 cm^{-1}; ^{1}H NMR δ 7.52-7.12 (complex, 10 H), 4.80 (bs, 1 H), 2.86 (td, 1 H, J = 13.6, 3.2 Hz), 2.69 (m, 2 H), 2.55 (td, 1 H, J = 12.4, 6.5 Hz), 2.35 (t, 2 H, J = 14.8 Hz), 1.87 (m, 2 H), 1.53 (dt, 1 H, J = 14.0, 3.2 Hz), 1.20 (m, 2 H), 1.11 (d, 1 H, J = 12.4 Hz) 0.78 (s, 3 H); ^{13}C NMR δ 216.2, 145.8, 144.0, 128.9, 128.7, 127.2, 127.1, 126.6, 126.0, 73.6, 56.9, 51.1, 40.5, 35.3, 34.4, 31.3, 29.4, 24.3, 20.3; HRMS *m/e* for $C_{23,}H_{26}O_2$ calcd 334.1933, found 334.1918.

General Procedure for Tautomerization of Enol Photoproducts to Keto Products. To initiate tautomerization the appropriate enol was taken up in CH_2Cl_2

and placed on a silica gel PTLC plate. This was allowed to stand for 4 - 72 h at which time the product was removed from the silica gel by extraction with ether. NMR analysis indicated product was greater than 90% ketone with a small amount of the starting enone **3b** present; no further purification was required.

(±) - 3,4,4a,5,6,7,8,8a-Octahydro-8-isopropoxy - 4a,7,7 - trimethyl-1(2*H*)-naphthalenone (41). A small amount of **35** was placed on PTLC silica gel for 3 days then removed by extracting with ether. IR (thin film) 1699, 1383, 1369 cm^{-1}; ^1H NMR (C_6D_6) δ 3.31 (septet, 1 H, J = 6.1 Hz), 3.22 (dd, 1 H, J = 4.1, 1.5 Hz), 2.62 (dt, 1 H, J = 15.6, 10.5 Hz), 2.41 (m, 2 H), 2.34 (dm, 1 H, J = 4.1 Hz), 1.88 (td, 1 H, J = 13.9, 4.3 Hz), 1.65 (m, 2 H), 1.30 (td, 2 H, J = 13.9, 4.3 Hz), 1.23 (m, 2 H), 0.99 (d, 3 H, J = 6.1 Hz), 0.90 (d, 3 H, J = 6.1 Hz), 0.85 (s, 3 H), 0.75 (s, 3 H), 0.70 (s, 3 H); ^{13}C NMR (C_6D_6) δ 214.4, 82.1, 73.0, 58.9, 41.6, 36.7, 36.5, 35.0, 32.3, 30.6, 30.1, 28.9, 25.3, 23.5, 21.5, 21.4.

(±)-3,4,4a,5,6,7,8,8a-Octahydro-8-methoxy-4a,7,7-trimethyl-1(2*H*)-naphthalenone (42). A small amount of crude **36** was placed on PTLC silica gel and allowed to stand for 3 h. The sample was then isolated by extracting with ether. IR (thin film) 1698, 1385 cm^{-1}; ^1H NMR (C_6D_6) δ 2.94 (s, 3 H), 2.86 (d, 1 H, J = 4.0 Hz), 2.43 (m, 3 H), 2.27 (m, 1 H), 1.83 (td, 1 H, J = 13.8, 4.7 Hz), 1.64 (m, 2 H), 1.40-1.13 (complex, 4 H), 0.84 (s, 3 H), 0.73 (s, 3H), 0.65, (s, 3 H); ^{13}C NMR (C_6D_6) δ 213.7, 88.7, 57.9, 40.6, 36.1, 34.7, 32.7, 31.6, 30.0, 29.7, 28.0, 24.5, 23.4, 21.1.

Attempted Base-Catalyzed Michael Addition of Methanol to 3b and 3c. A solution of **3b** (80.0 mg, 0.33 mmol) in 6.5 mL of a 90.0 mM methanolic sodium methoxide was stirred at room temperature, and the reaction was followed by GC and TLC. After 10 days, there was no indication of a Michael adduct so the reaction was discontinued. The reaction was also attempted using **3c** (100 mg, 0.32 mmol) in 6.5 mL of 90.0 mM methanolic sodium methoxide with similar results.

Single Crystal X-ray Structure Determination of (±)-8-*tert*-Butoxy-2,3,4,4a,5,6,7,8-octahydro-4a-methyl-7,7-diphenyl-1-naphthol (34). A single crystal of **34** was mounted on a Syntex P3 automated diffractometer. Unit cell dimensions (Table 3) were determined by least squares refinement of the best angular positions for 58 independent reflections ($2\theta > 9.99°$) during normal alignment procedures using molybdenum radiation (λ = 0.71073 Å). Data (7973 independent points after removal of space group forbidden and redundant data) were collected at room temperature using a variable scan rate, θ-2θ scan mode and a scan width of 1.2° below $K\alpha_1$ and 1.2° above $K\alpha_2$ to a maximum 2θ value of 45°.[64] Backgrounds were measured at each side of the scan for a combined time equal to the total scan time. The intensities of three standard reflections were remeasured every 97 reflections. As the intensities of these reflections showed less than 6% variation, corrections for decomposition were deemed unnecessary. Data were corrected for Lorentz, polarization, and background effects. After removal of redundant and space forbidden data, observed reflections [3116] were used for solution of carbon and oxygen positions of the structure by direct methods.[78] Refinement of scale factor, positional and anisotropic thermal parameters for all non-hydrogen atoms was carried out to convergence. Hydrogen positions were calculated using a C-H distance of 0.97 Å and appropriate geometry. All hydrogen atoms were included in the final refinement with isotropic thermal parameters but with fixed positional and thermal parameters. A difference Fourier synthesis revealed no electron density of interpretable level. Scattering factors were taken from the International Tables.[79]

The final cycle of refinement [function minimized $\Sigma(|F_o|-|F_c|)^2$] leading to a final agreement factor, R = 0.0613 [$R = (\Sigma| |F_o| - |F_c| | / \Sigma|F_o|) \times 100$]. In the final stages of refinement, a weight of $\sigma^2(F) + 0.0008F^2$ was used, R_w = 0.1180. Appendix B, lists bond angles and distances, positional parameters, and final anisotropic thermal parameters for **34**.

Single Crystal X-ray Structure Determination of (±)-3,4,4a,5,6,7,8,8a - Octahydro - 8 - hydroxy - 4a,7,7 - trimethyl - 1(2*H*)-naphthalenone (39). A single crystal of **39** was mounted on a Syntex P3 automated diffractometer. Unit cell dimensions (Table 3) were determined by least squares refinement of the best angular positions for 51 independent reflections ($2\theta > 10.2^{\circ}$) during normal alignment procedures using molybdenum radiation (λ = 0.71073 Å). Data (4450 independent points after removal of space group forbidden and redundant data) were collected at room temperature using a variable scan rate, θ-2θ scan mode and a scan width of 1.2° below $K\alpha_1$ and 1.2° above $K\alpha_2$ to a maximum 2θ value of 50°.[64] Backgrounds were measured at each side of the scan for a combined time equal to the total scan time. The intensities of three standard reflections were remeasured every 97 reflections. As the intensities of these reflections showed less than 6% variation, corrections for decomposition were deemed unnecessary. Data were corrected for Lorentz, polarization, and background effects. After removal of redundant and space forbidden data, observed reflections [3788] were used for solution of carbon and oxygen positions of the structure by direct methods. Refinement of scale factor, positional and anisotropic thermal parameters for all non-hydrogen atoms was carried out to convergence.[78] Hydrogen positions were calculated using a C-H distance of 0.97 Å and appropriate geometry. All hydrogen atoms were included in the final refinement with isotropic thermal parameters but with fixed positional and thermal parameters. A difference Fourier synthesis revealed no electron density of interpretable level. Scattering factors were taken from the International Tables.[79]

The final cycle of refinement [function minimized $\Sigma(|F_o|-|F_c|)^2$] led to a final agreement factor, R = 0.0509 [$R = (\Sigma| |F_o| - |F_c| | / \Sigma|F_o|) \times 100$]. In the final stages of refinement, a weight of $\sigma^2(F) + 0.0008F^2$ was used, R_w = .1045. Appendix B lists bond angles and distances, positional parameters, and final anisotropic thermal parameters for **39**.

Acknowledgments Support for this work was provided by UCER. Partial support by NSF (CHE-8718150) for our NMR facility and (BSS-8704089) for our high resolution mass spectrometer is also appreciated.

CHAPTER 3

RING CLOSURES BY TANDEM DEALKOXYCARBONYLATION-MICHAEL ADDITION REACTIONS

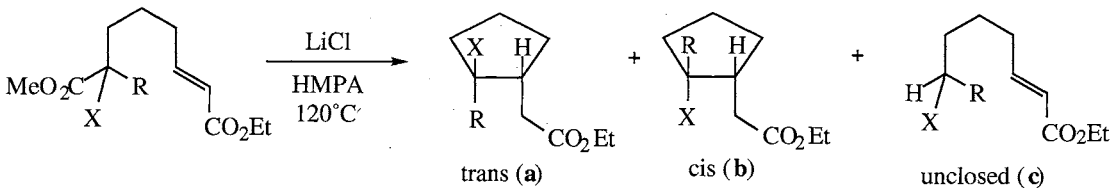
Introduction

This chapter presents an overview of the utility of tandem dealkoxycarbonylation-Michael addition reactions in the synthesis of cyclic compounds. This methodology is relatively new and therefore literature precedent is limited. To date, these tandem reactions have been used to synthesize five- and six-membered carbocycles, oxygen heterocycles, and spiranes. The reaction has also been reported in a novel ring expansion procedure.

Preparation of Carbocyclic Compounds

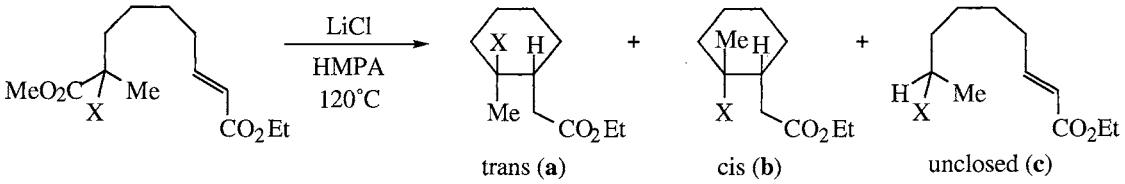
Bunce and co-workers[80] found that highly functionalized cyclopentane- and cyclohexaneacetic esters were easily prepared using the tandem dealkoxycarbonylation-Michael addition strategy. Ring-closure substrates were chosen such that nucleophilic cleavage and decarboxylation of an activated methyl ester produced a stabilized carbanion which then underwent Michael addition to a strategically placed acrylate acceptor. In general, treatment of the substrates with four equivalents of lithium chloride in hexamethylphosphoramide (HMPA) at 120 °C for 4 h gave the desired compounds in moderate to excellent selectivity (3:1-99:1) with the favored isomer possessing a trans relationship between the electron-withdrawing group and the acetic ester side chain. Due to the potential hazards associated with the use of HMPA,[81] 1-methyl-2-pyrrolidinone (NMP), 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU), and 1,3-dimethyl-2-imidazolidine (DMEU) were explored as alternative solvents. Although these solvents

sometimes gave better selectivities, HMPA was a superior solvent for a larger number of examples. The results of the cyclizations using HMPA are summarized in Table 2 and Table 3.



substrate	R	X	product	(a) : (b) : (c)	yield, (%)
1	Me	CO_2Et	**2**	74 : 26 : 0	64
3	Me	COMe	**4**	93 : 7 : 0	94
5	Me	COPh	**6**	89 : 11 : 0	78
7	Me	SO_2Ph	**8**	99 : 1 : 0	91
9	Me	CN	**10**	77 : 23 : 0	67

Table 2. Synthesis of Cyclopentaneacetic Esters by the Tandem Dealkoxycarbonylation-Michael Reaction.



substrate	X	product	(a) : (b) : (c)	yield, (%)
11	CO_2Et	**12**	40 : 10 : 26	Complex mixture
13	COMe	**14**	64 : 12 : 24	55
15	COPh	**16**	74 : 2 : 24	76
17	SO_2Ph	**18**	80 : 5 : 15	82
19	CN	**20**	69 : 15 : 16	45

Table 3. Synthesis of Cyclohexaneacetic Esters by the Dealkoxycarbonylation-Michael Reaction.

The mechanism for the reaction (Figure 32) involves selective attack of the nucleophilic chloride ion at the methyl carbon of the methyl ester. This is expected based on the relative reactivity of methyl versus ethyl substrates in the S_N2 reaction. At the high temperatures of the reaction, loss of the methyl group as methyl chloride initiates decarboxylation to give the stabilized carbanion which is predisposed for Michael addition to the pendant acrylate ester.

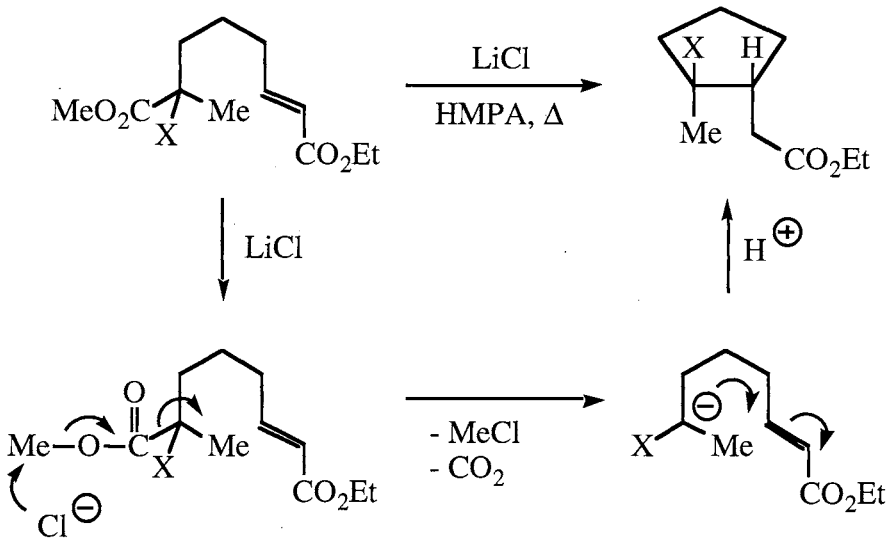


Figure 32. Mechanism of Dealkoxycarbonylation-Michael Reaction.

It was found that the reaction worked best for the preparation of cyclopentane derivatives. The cyclization of cyclohexyl derivatives resulted in lower yields and higher recovery of uncyclized material. The formation of six-membered rings by this methodology was limited to only precursors which produce tertiary carbanions upon dealkoxycarbonylation. Formation of five-membered rings occurred from either secondary or tertiary carbanions. It was suggested that the difference in reactivity was due to electronic, torsional, and entropic factors.

In order to understand the trans selectivity of the ring closure, steric and electronic effects were discussed. If the functional group X is sterically smaller than methyl,[82,83] then analysis of the possible transition states leading to ring closure indicated an unfavorable 1,3-interaction in the transition state leading to the trans isomer (Figure 33). Thus, other non-steric factors must govern the stereochemical outcome of the ring closure.

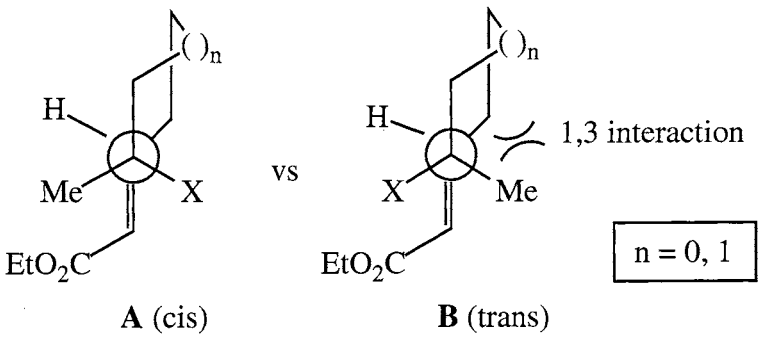


Figure 33. Steric Interactions in the Transition States for Ring Closure.

It was suggested that secondary orbital interactions similar to those invoked to explain the Diels-Alder reaction play an important role. It was previously reported that these interactions may influence similar ring closures.[84] In a compact chair transition state, overlap of the HOMO of the enolate (Michael donor) and the LUMO of the *s*-cis α,β-unsaturated ester (Michael acceptor) may effectively stabilize the transition state which leads to the trans product (Figure 34).[38,85-91]

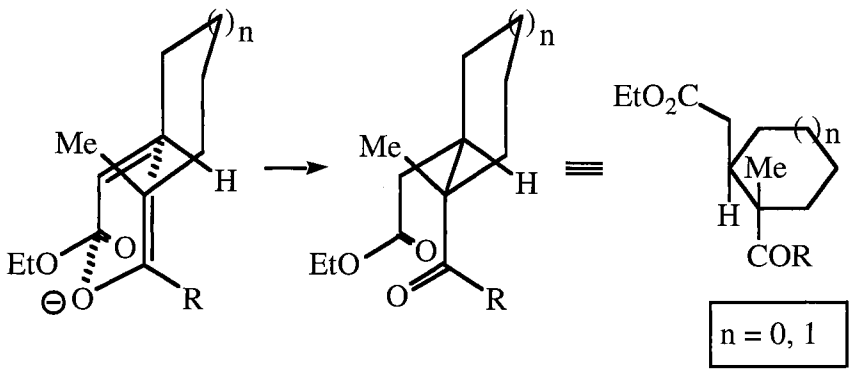
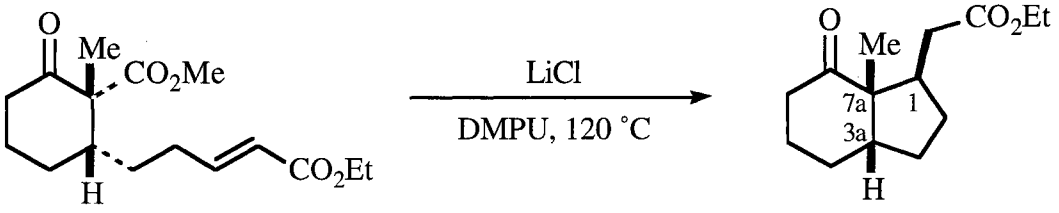


Figure 34. Compact Chair Transition State for Ring Closure.

This tandem cyclization has also been reported for the synthesis of a fused-ring bicyclic compound.[92] Treatment of cyclohexanone diester **21** with lithium chloride in DMPU afforded the keto ester **22** which is an important structural motif in many natural products.[93,94] The reaction proceeded to give the previously reported all-cis arrangement at C(1), C(3a), and C(7a) in high selectivity (>20:1). The observed outcome can be explained by the same rationale used for the monocyclic systems. The potential use of this reaction in the synthesis of many diverse and challenging compounds is clearly evident from this example.



21 **22**

Preparation of Oxygen Heterocycles

The synthesis of highly functionalized tetrahydrofuran and 2*H*-tetrahydropyran derivatives via the dealkoxycarbonylation-Michael addition reaction is currently under investigation.[95] Two examples of this reaction are illustrated below. These reactions proceeded in the same manner as that discussed for the carbocycles. First, methyl displacement by chloride ion gave the carboxylate which spontaneously decarboxylated to give the stabilized carbanion. This carbanion added in Michael fashion to the pendant α,β-unsaturated ester to close the ring.

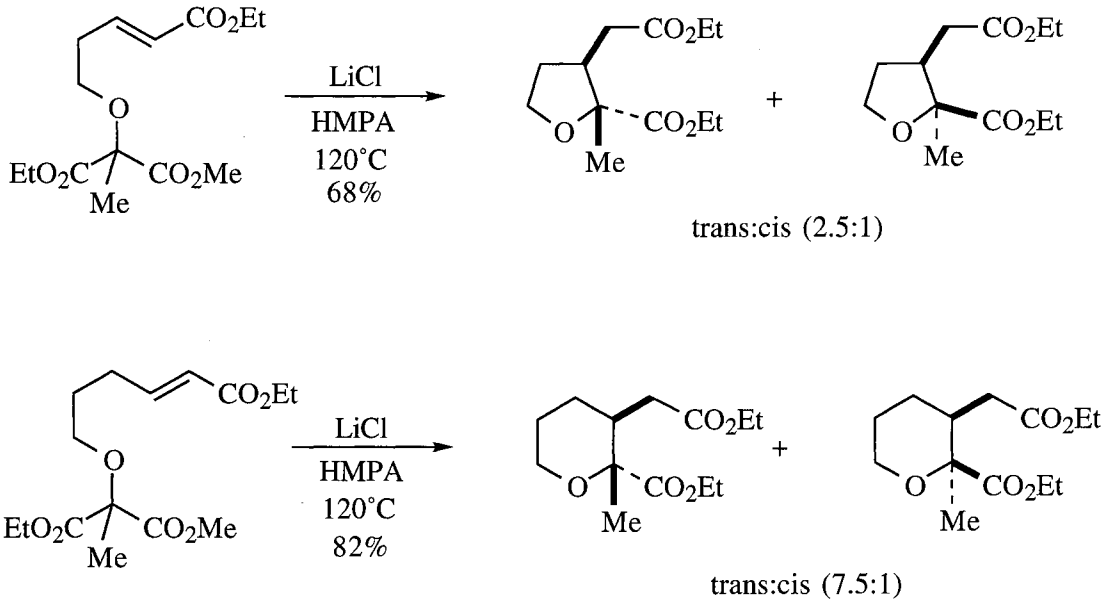


Figure 35. Oxygen Heterocycles by the Tandem Dealkoxycarbonylation-Michael Reaction.

The structures of the isolated products were characterized by comparison to those ring-closed products prepared in the carbocycle series. As found in the carbocycle study,

the carboalkoxy groups attached to C-2 and C-3 are trans to one another and it is believed that the same electronic factors govern the outcome. Interestingly, it was noted that the trans selectivity of the six-membered rings was generally superior to that found in the monocyclic carbocycles while the five-membered ring closures showed a decrease in selectivity. This lower selectivity can be attributed to the shorter carbon-oxygen bonds (1.43 Å versus 1.54 Å for the carbon-carbon bonds).[96] The shorter bonds result in a smaller ring which would cause greater strain in the transition state leading to closure of the five-membered ring. Thus, optimum alignment of the orbitals would be more difficult to achieve and selectivity would decrease.

Preparation of Spirocyclic Compounds

Functionalized spiranes have been prepared by Bunce and co-workers[97] using a dealkoxycarbonylation-Michael addition sequence. Treatment of the appropriate cycloalkanone diester with excess lithium chloride in HMPA at *ca.* 100 °C resulted in chemoselective cleavage of the methyl ester and decarboxylation to give the expected carbanion. Once again, addition of the generated anion to the β-center of the unsaturated ester closed the ring. This methodology proved most efficient in the synthesis of spiranes that required the closure of five- and six- membered rings (see Figure 36). If the side chain was decreased in length such that a four- membered ring was possible, the reaction did not proceed to give any cyclic product; only decarboxylated material was isolated. This likely results from reversibility of the Michael addition which would tend to disfavor the closure of the strained cyclobutane.[98,99]

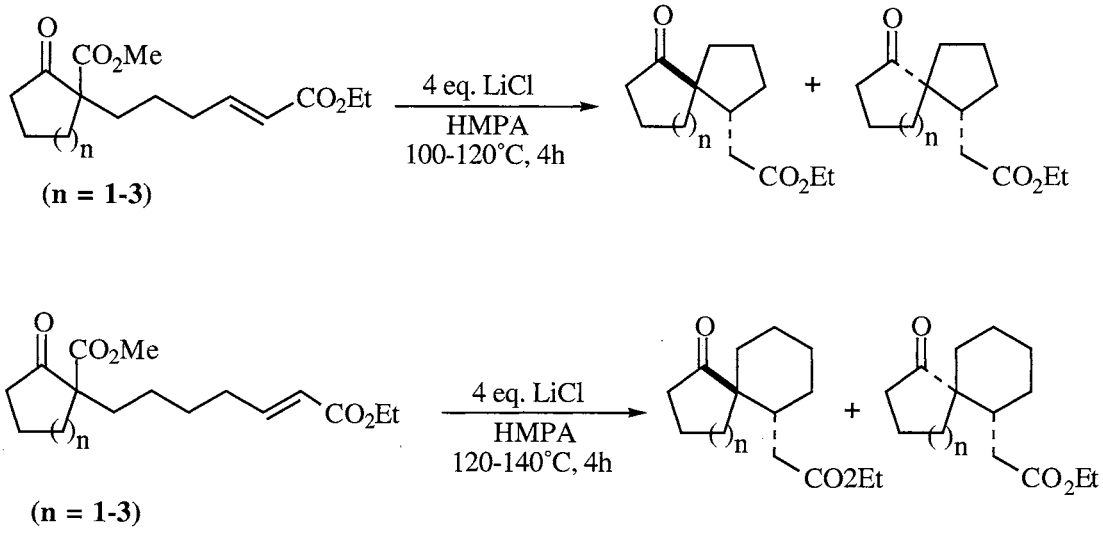
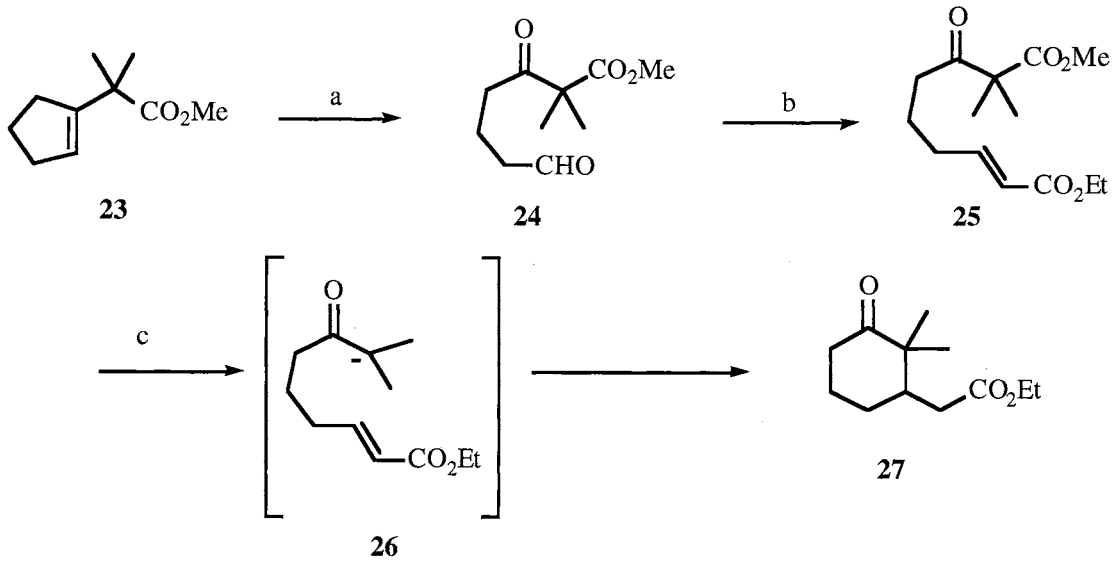


Figure 36. Spirocycles by the Tandem Dealkoxycarbonylation-Michael Reaction.

Ring Expansion

The tandem dealkoxycarbonylation-Michael addition has also been utilized as the key step in a novel ring expansion protocol for the synthesis of functionalized cyclohexaneacetic esters.[100] For example, keto ester **27** can be prepared in three steps in an overall yield of 43% starting from cyclopentene acetic ester **23**. The ring expansion procedure started with ozonolytic cleavage of the carbon-carbon double bond to yield keto aldehyde **24**. Chemoselective Wittig olefination formed the acrylate ester selectively at the aldehyde carbonyl to give the cyclization substrate **25**. Heating at 120 °C with four equivalents of lithium chloride in HMPA generated the ketone-stabilized carbanion **26** which underwent the expected cyclization to close the ring.



(a) O_3, CH_2Cl_2, -78 °C, Me_2S, -78 → 0 °C; (b) $Ph_3P{=}CHCO_2Et$, PhH, 80 °C; (c) LiCl, HMPA, 120 °C.

Figure 37. Ring Expansion Based on the Tandem Dealkoxycarbonylation-Michael Reaction.

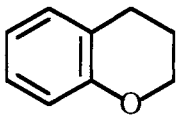
It was reported that the reaction proceeded best to form six-membered rings. Five-membered rings were also available using this methodology but yields were very low. The observed results can be rationalized in terms of Baldwin's rules for ring closure.[101] The six-membered ring cyclizes through a favorable 6-[*enolendo*]-*exo-trig* transition state while the five-membered ring must cyclize by an unfavorable 5-[*enolendo*]-*exo-trig* transition state. For the five-membered ring the planarity of the enolate distorts the geometry of the transition state such that the reaction is unfavorable. It was also suggested that the five-membered ring formation was disfavored due to possible reversibility of the Michael reaction.[98,99]

CHAPTER 4

A TANDEM DEALKOXYCARBONYLATION MICHAEL ADDITION ROUTE TO CHROMAN DERIVATIVES

Introduction

Many natural products incorporate the chroman ring system **1** and, thus, access to chromans is an important goal in organic synthesis.[102-113] Recently, Aukrust and Skattebol[103] successfully synthesized the naturally occurring chroman derivative, robustadial A. They obtained the chroman skeleton by preparing the corresponding



1

chromanone in one step using known procedures and treating the chromanone with methallylzinc bromide to reduce the carbonyl. Baker and Deshpande[104] reported the availability of chiral substituted chroman rings that are structurally related to calophyllum coumarins. Their strategy involved treating the appropriate *ortho*-alkenylphenol with mercuric acetate followed by $NaBH_4$ reduction. Three different groups independently reported a tandem dehydration-Diels-Alder reaction for the construction of the chroman ring system. These groups generated an *o*-quinone methide by thermal dehydration of *o*-hydroxy benzyl alcohols, and this reactive species underwent an intramolecular Diels-Alder

cyclization. Many other approaches to these heterocyclic systems can be found in the current literature. As an extension of our work on tandem reactions, the use of a tandem dealkoxycarbonylation-Michael addition reaction has been developed as a synthetic route to highly functionalized chromans.

Previous work in this laboratory has demonstrated that methyl esters that are activated toward decarboxylation by an electron withdrawing group readily undergo dealkoxycarbonylation to give a stabilized anion when heated in the presence of lithium chloride or lithium iodide in polar aprotic solvents. This anion can then be trapped by a Michael addition to a pendant acrylate ester to form the cyclized product.[80,92,95] Until now, only monocyclic heteroaromatic systems have been explored. The current chapter describes the preparation of chromans using this methodology.

Results

Synthesis of Cyclization Substrates. The syntheses for the substrates **7** and **14** are illustrated in Figures 38 and 39, respectively. The synthesis of cyclization substrate **7** began with esterification of 2-hydroxyphenylacetic acid (**2**) in boiling ethanol containing catalytic sulfuric acid to give **3** in 84% yield.[114] The phenolate anion was then generated using sodium hydride and subsequently treated with allyl bromide to furnish ester **4** in a yield of 91%. Treatment of the ester with two equivalents of LDA followed by addition of methyl chloroformate furnished diester **5** in 62% yield.[115] Methylation of the active methine carbon in **5** using sodium hydride and 1.4 equivalents of methyl iodide gave **6** in 89% yield.[116] Finally, the acrylate ester moiety was introduced by (1) ozonolysis of **6** with reductive workup and (2) Wittig olefination[117,118] to give the cyclization substrate **7** in a yield of 52% for the two steps.

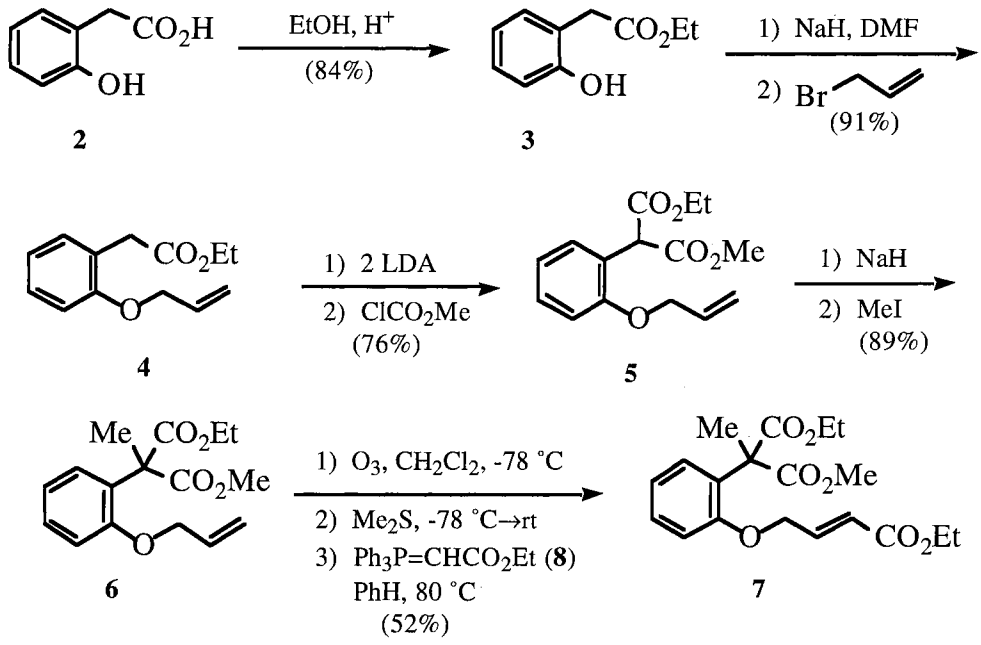


Figure 38. Synthesis of Cyclization Substrate **7**.

The synthetic route (Figure 39) to prepare cyclization substrate **14** started by generating the phenolate anion of 2-allylphenol (**9**) and treating with chloro diester **11** which was easily prepared using the general method of Budesinsky and co-workers.[119] The etherification proceeded to give diester ether **12** in an overall yield of 88% starting from **9**. Methylation of **12** was achieved as described above (NaH, DMF, excess MeI) to give compound **13** in 90% yield. The final conversion of **13** to **14** was effected by an ozonolysis-Wittig sequence which gave the target compound in a yield of 55%. Both substrates **7** and **14** were readily available by the described routes without any notable difficulties.

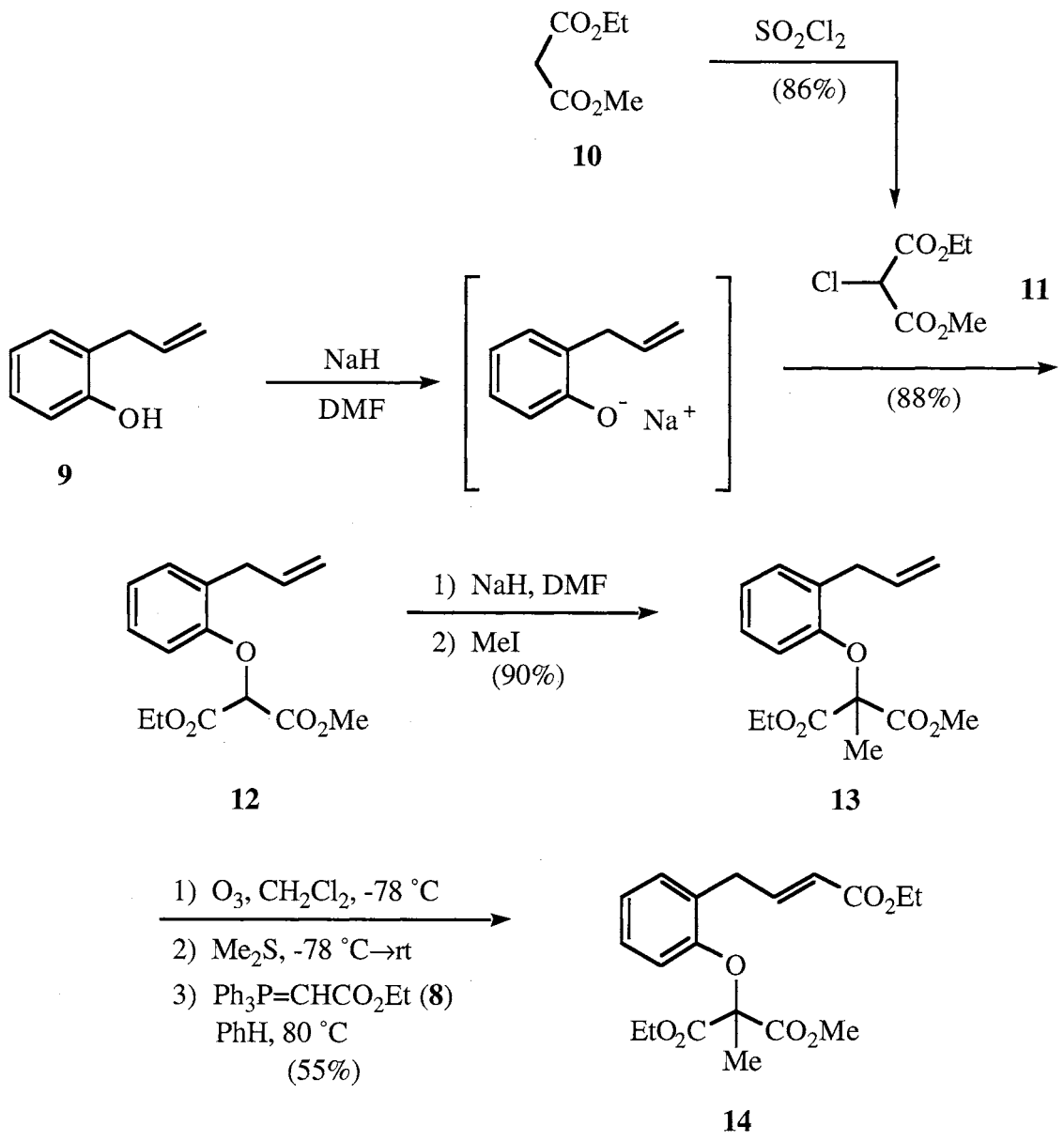
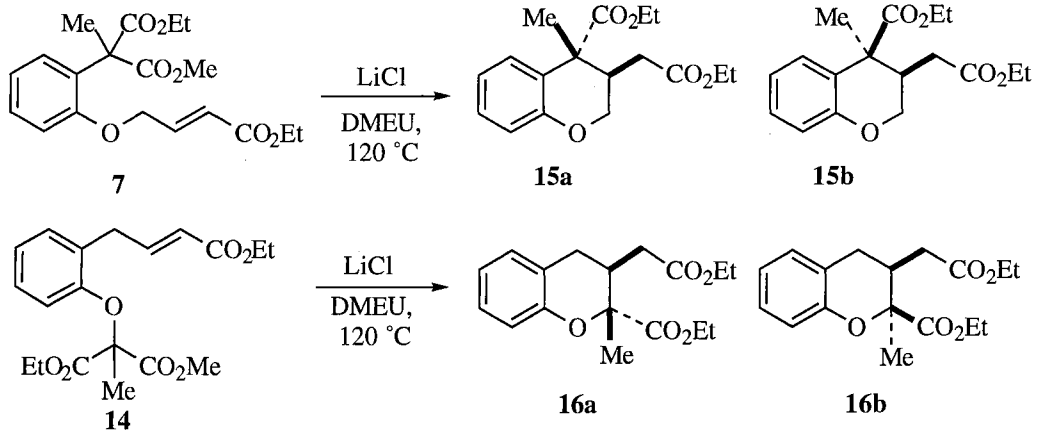


Figure 39. Synthesis of Substrate **14**.

Cyclization of Substrates 7 and 14. The results of the tandem dealkoxycarbonylation-Michael addition for compounds **7** and **14** are summarized in Table 4. To successfully cyclize **7,** the reaction was run at 120 °C in DMEU using four equivalents of anhydrous lithium chloride. Formation of the trans and cis 3,4,4-trisubstituted chromans, **15a** and **15b**, proceeded smoothly in 8 h. GC analysis indicated that the reaction gave two major isomers in the ratio of approximately 8:1, but upon

purification only a 6:1 ratio was obtained with trans being the major isomer. Reaction of substrate **14** on the same scale at 120 °C also went to completion in 8 h. GC analysis indicated the presence of two major isomeric products **16a** and **16b** in a ratio of 3:1 along with three minor products. Upon purification, only the major trans product could be isolated free of contamination in a yield of 54%. None of the minor products could be isolated pure enough for NMR analysis.

Previous cyclizations using this methodology required the use of HMPA as the solvent to obtain optimum results; however, higher selectivity (6:1) was observed when DMEU was used for the closure of compound **7**. When the reaction was run in HMPA, the selectivity determined by GC was only 3:1. On the other hand, the selectivity for the ring closure of **14** in HMPA was 3:1 which was the same when using DMEU as the solvent. Due to the hazards associated with the use of HMPA,[81] it is evident that DMEU is a superior solvent for these reactions.



Starting material	Products	a:b[a]	yield, %[b]
7	**15**	**8:1**	**89**
14	**16**	**3:1**	**54[c]**

[a] Product ratios determined by GC of crude product. [b] Yield refers to isolated purified products. [c] Only trans product was isolated in pure form.

Table 4. Results of Tandem Cyclizations of **7** and **14**.

The mechanism of the reaction involves nucleophilic attack by chloride ion at the methyl ester to generate methyl chloride and the carboxylate anion which spontaneously decarboxylates to an ester-stabilized anion. The reaction sequence is then terminated by a Michael addition to the pendant acrylate moiety (see Figure 40). In both cases the methyl ester was chemoselectively cleaved to initiate the reaction. It is well-documented[120] that methyl reacts thirty times faster than ethyl in the S_N2 reaction; thus, the observed selectivity would be expected.

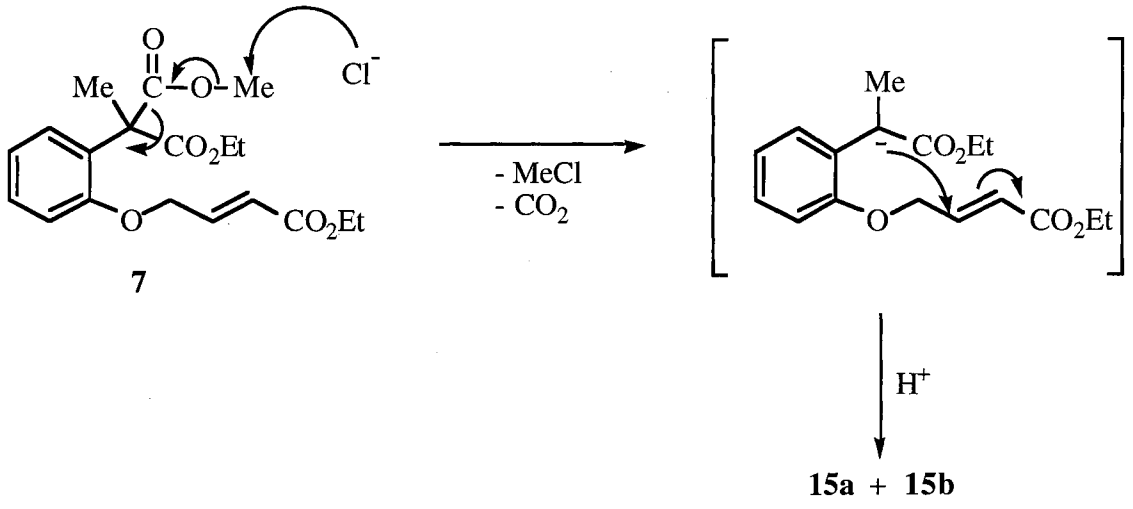
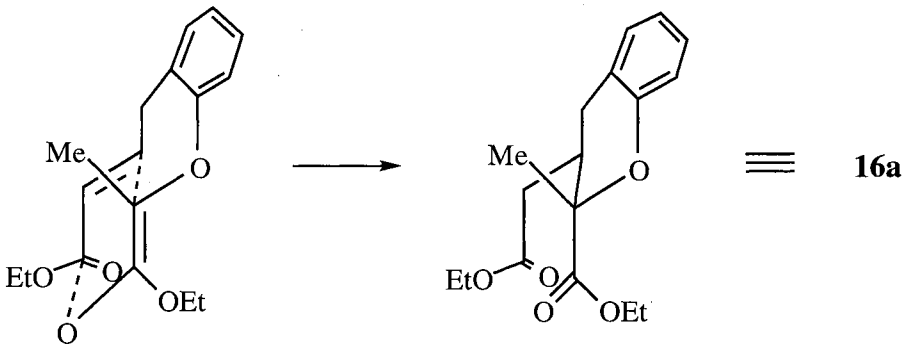


Figure 40. Mechanism of the Dealkoxycarbonylation- Michael Ring Closure of Substrate **7**.

The structures of the cyclized products were assigned by comparison to those encountered in the simple carbocycle series.[80] In both cases, it was established that the isomer having the ethoxycarbonyl group trans to the acetic ester residue was the major product. The previously reported rationale used to explain this selectivity can be applied to

the chroman systems as well. Analysis of the steric interactions which develop during the ring closures indicate that steric factors have a minimal effect on the outcome of these reactions. Instead, electronic factors are believed to be responsible for the observed outcome. Calculations suggest[84] that overlap between the HOMO of the enolate and LUMO of the *s*-cis α,β-unsaturated ester stabilizes a chair-like transition state leading to the trans product (Figure 41).



14

Figure 41. Transition State for the Ring Closure of Chromans.

In summary, a new route to highly functionalized chroman derivatives using a tandem dealkoxycarbonylation-Michael addition strategy has been developed and optimized. The method is simple and leads selectively to compounds with potentially valuable substitution patterns. Application of this procedure may prove useful in the synthesis of a wide variety of benzo-fused heterocycles.

Experimental Section

THF was distilled from $LiAlH_4$; DMF was distilled from BaO and stored over 4Å molecular sieves; HMPA and DMEU (1,3-dimethyl-2-imidazolidinone) were stored over 4Å molecular sieves. Other reagents were used as received. All reactions were run under dry N_2 in oven-dried glassware. Reactions were monitored using one of the following methods: 1) TLC on hard layer silica gel GF plates (Analtech) using UV detection or 2) capillary GC with FI detection (SE-30 column, 6 m x 0.25 mm i.d., 0.25 μm film thickness) programmed between 50-300 °C. The saturated NH_4Cl, 0.5 M-1 M HCl, 0.02M NaOH, 5% $Na_2S_2O_3$, saturated $NaHCO_3$, and saturated NaCl used in workup procedures refer to aqueous solutions. Preparative separations were performed using one of the following methods: 1) PTLC on 20-cm x 20-cm silica gel GF plates (Analtech), 2) flash chromatography[121] on silica gel (Grace, grade 62, 60-200 mesh) containing UV-active phosphor (Sylvania no. 2282), or 3) flash vacuum chromatography[122] on silica gel (60-200 mesh) containing UV-active phosphor; in each case, band elution was monitored using a hand-held UV lamp. IR spectra are referenced to polystyrene. ^1H NMR and ^{13}C NMR were measured in $CDCl_3$ at 400 and 100 MHz, respectively, and are referenced to internal Me_4Si. High resolution mass spectra (HRMS, EI/DP) were obtained at 70 eV. Elemental analyses were ± 0.3%.

Ethyl (2-Hydroxyphenyl)ethanoate (3). The procedure of Offe and Jatzkewitz[114] was used. To a mixture of 400 mL of absolute ethanol and 12.5 mL of concentrated sulfuric acid was added 25.0 g (0.160 mole) of 2-hydroxyphenylacetic acid. The reaction was heated under reflux for 8 h, then cooled, concentrated, diluted with water, and extracted with ether (3x). The combined ether extracts were washed with H_2O, $NaHCO_3$, and NaCl, then dried ($MgSO_4$) and concentrated under vacuum. Vacuum distillation of the resulting oil afforded 24.8 g (0.140 moles, 84%) of **3**, bp 83-85 °C (0.5 mmHg) [lit[114] bp. 149-151 °C (18 mmHg)]; IR (thin film) 3407, 1714, 1604, 1509, 1370, 754 cm^{-1}; ^1H NMR δ 7.63 (br s, 1 H), 7.15 (t, 1 H, J = 7.7 Hz), 7.09 (d, 1 H, J =

6.9 Hz), 6.86 (m, 2 H), 4.18 (q, 2 H, J = 7.1 Hz), 3.66 (s, 2 H), 1.27 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 173.9, 155.1, 130.9, 129.0, 120.6, 117.2, 61.7, 37.6, 13.9; HRMS *m/e* for $C_{10}H_{12}O_3$ calcd 180.0787, found 180.0793.

Ethyl (2-(2-Propenoxy)phenyl)ethanoate (4). To a suspension of 2.00 g (25.0 mmol) of oil-free sodium hydride in 50 mL of DMF at 20 °C (water bath) was added a solution of 9.00 g (50.0 mmol) of ethyl (2-hydroxyphenyl)ethanoate in 25 mL of DMF. The reaction was stirred for 15 min and a solution of 6.66 g (55.0 mmol) of allyl bromide in 25 mL of DMF was added dropwise over 30 min. The reaction was heated at 50 °C (oil bath) for 8 h, then cooled, added to saturated NH_4Cl, and extracted with ether (3x). The combined ether extracts were washed with H_2O and NaCl, then dried ($MgSO_4$) and concentrated under vacuum. Final purification by vacuum distillation gave 9.96 g (45.3 mmol, 91%) of **4** as a colorless oil, bp. 95-96 °C (0.5 mmHg); IR (thin film) 3077, 1736, 1648, 1370, 996, 923, 755 cm^{-1}; ^{1}H NMR δ 7.22 (m, 2 H), 6.90 (t, 1 H, J = 7.5 Hz), 6.83 (d, 1 H, J = 8.4 Hz), 6.00 (ddt, 1 H, J = 17.3, 10.6, 4.9 Hz), 5.40 (d, 1 H, J = 17.3 Hz), 5.23 (d, 1 H, J = 10.6 Hz), , 4.51 (d, 2 H, J = 4.9 Hz), 4.13 (q, 2 H, J = 7.1 Hz), 3.63 (s, 2 H), 1.23 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 171.1, 156.4, 133.1, 130.8, 128.3, 123.4, 120.5, 116.7, 111.5, 68.5, 60.4, 36.1, 14.0; HRMS *m/e* for $C_{13}H_{16}O_3$ calcd 220.1100, found 220.1089.

(±)-Ethyl Methyl (2-(2-Propenoxy)phenyl)propanedioate (5). The general procedure of Rathke and Deitch[115] was used. LDA (50 mmol) was generated at -78 °C in 75 mL of THF from 5.25 g (7.27 mL, 52.0 mmol) of diisopropylamine and 31.3 mL of 1.6 M *n*-butyllithium (50.0 mmol) in hexanes. To the stirred solution of LDA was added a solution of 5.50 g (25.0 mmol) of ethyl (2-(2-propenoxy)phenyl)ethanoate in 25 mL of THF dropwise during 15 min. The mixture was stirred at -78 °C for 15 min, and a solution of 2.36 g (1.93 mL, 25.0 mmol) of methyl chloroformate in 10 mL of THF was added dropwise over 10 min. The reaction was stirred for 10 min at -78 °C and quenched with 50 mL of 1 M HCl. The mixture was warmed to 20 °C, the organic layer was

separated, and the aqueous phase was extracted with ether (2x). The combined organic extracts were washed with H_2O, $NaHCO_3$, and NaCl, then dried ($MgSO_4$) and concentrated under vacuum. The product from two runs was purified by chromatography on a 100-cm x 2.5-cm silica gel column eluted with increasing concentrations of ether in hexanes. Band 2 afforded 8.62 g (31.0 mmol, 62%) of **5** as a light yellow oil. IR (thin film) 1744, 1735, 1656, 1377, 996, 930, 755 cm^{-1}; ^1H NMR δ 7.28 (m, 2 H), 6.96 (t, 1 H, J = 7.5 Hz), 6.87 (d, 1 H, J = 8.1 Hz), 6.00 (ddt, 1 H, J = 17.3, 10.6, 6.6 Hz), 5.39 (d, 1 H, J = 17.3 Hz), 5.25 (d, 1 H, J = 10.6 Hz), 5.14 (s, 1 H), 4.54 (d, 2 H, J = 6.6 Hz), 4.21 (q, 2 H, J = 7.1 Hz), 3.74 (s, 3 H), 1.25 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 169.0, 168.4, 155.8, 132.8, 129.3, 129.2, 122.0, 120.8, 117.0, 111.8, 68.8, 61.5, 52.5, 51.3, 13.9; HRMS *m/e* for $C_{15}H_{18}O_5$ calcd 278.1154, found 278.1159.

(±)-Ethyl Methyl Chloropropanedioate (11). This compound was prepared by the method of Budesinsky and co-workers.[119] A neat sample of 33.8 g (20.1 mL, 0.25 mol) sulfuryl chloride was added to 36.5 g (0.25 mol) of ethyl methyl malonate at 60-70 °C (oil bath) during 1 h. The reaction was stirred at 60-70 °C for 1 h then heated to 160 °C for 10 min. The crude reaction mixture was vacuum distilled through a 30-cm Vigreux column to afford 38.7 g (0.22 mole, 86%) of **11** as a colorless oil, bp. 88-89 °C (2 mmHg); IR (thin film) 1762, 1367 cm^{-1}; ^1H NMR δ 4.88 (s, 1 H), 4.30 (q, 2 H, J = 7.1 Hz), 3.85 (s, 3 H), 1.32 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 165.0, 164.4, 63.2, 55.1, 53.7, 13.8; HRMS *m/e* for $C_6H_9{}^{35}ClO_4$ calcd 180.0190, found 180.0174.

(±)-Ethyl Methyl (2-(2-Propenyl)phenoxy)propanedioate (12). To a suspension of 1.00 g (25.0 mmol) of oil-free sodium hydride in DMF was added a solution of 3.01 g (22.5 mmol) of 2-allylphenol in 10 mL of DMF. To the clear solution was added a solution of 4.50 g (25.0 mmol) of ethyl methyl chloropropanedioate in 10 mL of DMF. The reaction was stirred for 1 h at room temperature and for 6 h at 60 °C, then cooled, quenched with saturated NH_4Cl, and extracted with ether (3x). The combined ether extracts were washed with H_2O, 0.02 M NaOH (until the washes were colorless),

H_2O, and NaCl, then dried ($MgSO_4$) and concentrated under vacuum. The resulting oil was flash chromatographed on a 100 cm x 2.5 cm column of silica gel eluted with increasing concentrations of ether in hexane. Band 2 gave 5.50 g (19.8 mmol, 88%) of **12** as a light yellow oil. IR (thin film) 1773, 1751, 1648, 1370, 996, 916, 755 cm^{-1}; ^1H NMR δ 7.15 (m, 2 H), 6.98 (t, 1 H, J = 7.4 Hz), 6.74 (d, 1 H, J = 8.1 Hz), 6.03 (ddt, 1 H, J = 17.0, 10.1, 6.8 Hz), 5.20 (s, 1 H), 5.09 (d, 1 H, J = 17.0 Hz), 5.05 (d, 1 H, J = 10.1 Hz), 4.30 (q, 2 H, J = 7.1 Hz), 3.84 (s, 3 H), 3.51 (d, 2 H, J = 6.8 Hz), 1.29 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 166.2, 165.6, 154.7, 136.6, 130.3, 129.9, 127.2, 122.6, 115.6, 112.3, 77.0, 62.3, 53.0, 34.2, 13.9; HRMS *m/e* for $C_{15}H_{18}O_5$ calcd 278.1154, found 278.1144.

Representative Procedure for the Methylation of Propanedioate Esters: (±)-Ethyl Methyl Methyl(2-(2-propenoxy)phenyl)propanedioate (6). The general procedure of Inomata and co-workers[116] was used. To a suspension of 0.60 g (25.0 mmol) of oil-free sodium hydride in 25 mL of DMF was added a solution of 6.95 g (25.0 mmol) ethyl methyl (2-(2-propenoxy)phenyl)propanedioate in 25 mL of DMF. The mixture was stirred for 30 min, and then 4.97 g (2.18 mL, 35.0 mmol) of methyl iodide was added dropwise. The reaction was heated at 50 °C (oil bath) for 12 h, then cooled, poured into 0.5 M HCl, and extracted with ether (3x). The combined extracts were washed with H_2O, 5% $Na_2S_2O_3$, and NaCl, then dried ($MgSO_4$) and concentrated under vacuum. Final purification by chromatography on a 75-cm x 2.5-cm silica gel column eluted with increasing concentrations of ether in hexanes afforded 6.50 g (22.3 mmol, 89%) of **6** as a light yellow oil. IR (thin film) 1750, 1744, 1648, 1370, 996, 930, 755 cm^{-1}; ^1H NMR δ 7.25 (t, 1 H, J = 8.2 Hz), 7.08 (d, 1 H, J = 7.7 Hz), 6.93 (t, 1 H, J = 7.7. Hz), 6.90 (d, 1 H, J = 8.2 Hz), 5.96 (ddt, 1 H, J = 17.3, 10.6, 4.9 Hz), 5.37 (d, 1 H, J = 17.3 Hz), 5.25 (d, 1 H, J = 10.6 Hz), 4.52 (m, 2 H), 4.22 (m, 2 H), 3.73 (s, 3 H), 1.84 (s, 3 H), 1.24 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 172.0, 171.3, 155.8, 132.8, 129.0, 128.7,

127.0, 120.7, 117.0, 112.4, 69.0, 61.5, 57.7, 52.6, 21.7, 13.8; HRMS *m/e* for $C_{16}H_{20}O_5$ calcd 292.1311, found 292.1306.

(±)-Ethyl Methyl Methyl(2-(2-propenyl)phenoxy)propanedioate (13). 4.76 g (16.3 mmol, 90%); IR (thin film) 1746, 1635, 1367, 988, 909, 751 cm^{-1}; ^1H NMR δ 7.17 (d, 1 H, J = 7.4 Hz), 7.08 (m, 1 H), 6.98 (t, 1 H, J = 7.4 Hz), 6.78 (d, 1 H, J = 8.1 Hz), 5.99 (ddt, 1 H, J = 17.0, 10.1, 6.8 Hz), 5.06 (d, 2 H, J = 17.0 Hz), 5.04 (d, 1 H, J = 10.1 Hz), 4.27 (q, 2 H, J = 7.1 Hz), 3.82 (s, 3 H), 3.46 (d, 2 H, J = 6.8 Hz), 1.72 (s, 3 H), 1.25 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 169.7, 168.9, 152.3, 136.8, 132.1, 130.3, 126.8, 123.0, 117.3, 115.6, 82.6, 62.3, 53.1, 34.4, 20.2, 13.9; HRMS *m/e* for $C_{16}H_{20}O_5$ calcd 292.1311, found 292.1304.

(Carbomethoxymethylene)triphenylphosphorane (8).[123,124] To a solution of 262 g (1.00 mol) of triphenylphosphine in 400 mL of benzene was added 167 g (111 mL, 1.00 mol) of ethyl bromoacetate dropwise with stirring. The reaction refluxed gently during the addition and was heated at reflux for an additional 12 h. The reaction was cooled and the phosphonium salt filtered and washed with ether under aspirator vacuum. The salt was allowed to air dry for 24 h. The yield of (carbomethoxymethyl)triphenyl phosphonium bromide was 416 g (0.97 mol, 97%).

The dried salt was divided into two equal portions and each was dissolved in 2 L of H_2O in a 4 L Erlenmeyer flask equipped with an overhead stirrer. To each dissolved portion was slowly added a solution of 1 M aqueous NaOH until a pH of 8 was reached. The resulting white ylide was filtered under aspirator vacuum and washed with 8-10 L of water. Air was drawn through the ylide for 2 h, the solid was transferred to a crystallizing dish, and air dried for 2 days. The solid was then placed in a dessicator over KOH pellets and further dried under vacuum for 2 days prior to use. The yield of **8** was 292 g (0.84 mol, 87%)

Representative Ozonolysis-Wittig Procedure: (±)-Ethyl Methyl (*E*)-(2-(3-Ethoxycarbonyl-2-propenoxy)phenyl)methylpropanedioate (7). A

solution of 5.50 g (18.8 mmol) of ethyl methyl methyl(2-(2-propenoxy) phenyl)propanedioate in 200 mL of CH_2Cl_2 was cooled to -78 °C and treated with ozone until the solution turned a light blue color. The reaction was quenched at -78 °C with 2.34 g (2.75 mL, 37.6 mmol) of dimethyl sulfide, warmed to room temperature, stirred for 3 h, and concentrated under vacuum. To the resulting yellow oil was added 150 mL of benzene and 9.48 g (27.3 mmol) of (carbomethoxymethylene)triphenylphosphorane. The solution was heated under reflux for 12 h, then cooled and concentrated to give a brown semisolid mass. The residue was loaded onto a 5-cm x 5-cm plug of silica gel in a sintered glass frit, and 1 L of 20% ether in hexanes was poured through under aspirator vacuum. Concentration of the filtrate afforded the crude triester as a light yellow oil. The crude product was flash chromatographed on a 100-cm x 2.5-cm silica gel column eluted with increasing concentrations of ether in hexane. Band 3 gave 3.48 g (9.78 mmol, 52%) of **7** as a light yellow oil. IR (thin film) 1742, 1730, 1659, 1367, 972, 751 cm^{-1}; ^1H NMR δ 7.27 (t, 1 H, J = 7.7 Hz), 7.12 (d, 1 H, J = 7.7 Hz), 7.02 (dt, 1 H, J = 15.8, 3.9 Hz), 6.98 (t, 1 H, J = 7.7 Hz), 6.86 (d, 1 H, J = 7.7 Hz), 6.15 (dt, 1 H, J = 15.8, 2.2 Hz), 4.71 (m, 2 H), 4.23 (m, 4 H), 3.75 (s, 3 H), 1.86 (s, 3 H), 1.30 (t, 3 H, J = 7.1 Hz), 1.25 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 171.8, 171.1, 166.1, 155.3, 141.9, 129.0, 128.9, 127.3, 121.7, 121.3, 112.6, 67.1, 61.6, 60.5, 57.5, 52.6, 21.8, 14.1, 13.8; HRMS *m/e* for $C_{19}H_{24}O_7$ calcd 356.1522, found 356.1508.

Anal. Calcd for $C_{19}H_{24}O_7$: C, 64.04; H, 6.74. Found: C, 63.92; H, 6.71.

(±) - Ethyl Methyl (*E*) - (2-(3-Ethoxycarbonyl-2-propenyl) phenoxy) methyl propanedioate (14). IR (thin film) 1746, 1714, 1651, 1367, 980, 751 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.12 (m, 3 H), 6.98 (t, 1 H, J = 7.4 Hz), 6.77 (d, 1 H, J = 8.2 Hz), 5.82 (d, 1 H, J = 15.5 Hz), 4.27 (q, 2 H, J = 7.1 Hz), 4.16 (q, 2 H, J = 7.1 Hz), 3.82 (s, 3 H), 3.60 (d, 2 H, J = 6.8 Hz), 1,75 (s, 3 H), 1.26 (t, 3 H, J = 7.1 Hz), 1.24 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 169.5, 168.5, 166.6, 152.6, 147.0, 130.7, 129.5, 127.5, 123.0,

122.1, 116.8, 82.6, 62.3, 60.6, 53.1, 33.0, 20.5, 14.2 13.8; HRMS *m/e* for $C_{19}H_{24}O_7$ calcd 356,1522, found 356.1509.

Anal. Calcd for $C_{19}H_{24}O_7$: C, 64.04; H, 6.74. Found: C, 63.85; H, 6.75.

Representative Procedure for the Tandem Dealkoxycarbonylation-Michael Reaction: (3*R,4*R**)-Ethyl 3,4-Dihydro-2-ethoxycarbonyl-2-methyl-2*H*-1-benzo-pyran-3-acetate (15a).** The general procedure of Bunce and co-workers[80] was used. A solution of 356 mg (1.00 mmol) of ethyl methyl (*E*)-(2-(3-ethoxycarbonyl-2-propenoxy)-phenyl)methylpropanedioate and 170 mg (4.00 mmol) of LiCl in 15 mL of DMEU was heated for 8 h in an oil bath that had been preheated to 120 °C (± 5 °C). The reaction was cooled, added to 0.5 M HCl, and extracted with ether (3x). The combined organic layers were washed with 0.5 M HCl, H_2O, and NaCl, then dried ($MgSO_4$) and concentrated under vacuum. The crude product was purified by chromatography on a 50-cm x 1-cm column of silica gel, eluted with increasing concentrations of ethyl acetate in hexanes, to afford 232 mg (0.79 mmol, 76%) of **15a** and 40 mg (0.13 mmol, 13%) of the 3*R**,4*S** isomer (**15b**). The spectral data for the major 3*R**,4*R** isomer were: IR (thin film) 1730, 1589, 1494, 1377, 754 cm^{-1}; ^1H NMR δ 7.12 (m, 2 H), 6.88 (t, 1 H, J = 6.9 Hz), 6.82 (d, 1 H, J = 8.0 Hz), 4.24 (dd, 1 H, J = 11.1, 3.2 Hz), 4.16 (m, 4 H), 3.97 (dd, 1 H, J = 11.1, 8.7, Hz), 3.15 (m, 1 H), 2.36 (dd, 1 H, J = 16.0, 4.1 Hz), 2.20 (dd, 1 H, J = 16.0, 10.2 Hz), 1.49 (s, 3 H), 1.27 (t, 3 H, J = 6.9 Hz), 1.21 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 175.1, 171.8, 153.0, 128.4, 128.1, 124.7, 120.7, 117.0, 65.7, 61.4, 60.7, 46.8, 35.6, 32.1, 22.0, 14.1, 14.0; HRMS *m/e* for $C_{17}H_{22}O_5$ calcd 306.1468, found 306.1459.

Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.67; H, 7.19. Found: C, 66.54; H, 7.18.

The spectral data for the minor 3*R**,4*S** isomer (**15b**) were: IR (thin film) 1730, 1590, 1492, 1374, 755 cm^{-1}; ^1H NMR δ 7.20 (d, 1 H, J = 7.8 Hz), 7.14 (t, 1 H, J = 7.1 Hz), 6.87 (m, 2 H), 4.29-4.08 (complex, 6 H), 2.53 (dd, 1 H, J = 15.9, 2.8 Hz), 2.47 (m, 1 H), 2.20 (dd, 1 H, J = 15.9, 10.2 Hz), 1.60 (s, 3 H), 1.28 (t, 3 H, J = 7.2 Hz),

1.21 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 174.0, 171.8, 153.8, 128.2, 128.0, 124.7, 120.7, 117.4, 66.0, 61.2, 60.8, 45.5, 38.9, 32.5, 25.3, 14.2, 14.1; HRMS *m/e* for $C_{17}H_{22}O_5$ calcd 306.1468, found 306.1452.

Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.67; H, 7.19. Found: C, 66.39; H, 7.16.

(2*R,3*S**)-Ethyl 3,4-Dihydro-4-ethoxycarbonyl-4-methyl-2*H*-1-benzopyran-3-acetate** (**16a**): 165 mg (0.54 mmol, 54%); IR (thin film) 1735, 1594, 1490, 1375, 751 cm^{-1}; ^{1}H NMR δ 7.12 (t, 1 H, J = 6.9 Hz), 6.98 (d, 1 H, J = 7.1 Hz), 6.88 (m, 2 H), 4.16 (m, 4 H), 2.91 (m, 2 H), 2.59 (d, 2 H, J = 17.5 Hz), 2.15 (dd, 1 H, J = 16.3, 9.5 Hz), 1.55 (s, 3 H), 1.25 (t, 3 H, J = 7.1 Hz), 1.20 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 173.0, 172.5, 153.2, 129.9, 127.6, 120.9, 118.7, 116.5, 79.9, 61.5, 60.7, 33.3, 33.1, 28.5, 21.9, 14.2, 14.0; HRMS *m/e* for $C_{17}H_{22}O_5$ calcd 306.1468, found 306.1463.

Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.67; H, 7.19. Found: C, 66.47; H, 7.17.

The minor 2*R**,3*R** isomer (**16b**) could not be isolated free of contamination.

Acknowledgments Support for this work was provided by the Oklahoma Center for the Advancement of Science and Technology (HR1-035) and the NIH Biomedical Research Support Program (SO7 RR07077025). Partial support by NSF (CHE-8718150) for our NMR facility and (BSS-8704089) for our high resolution mass spectrometer is also appreciated.

CHAPTER 5

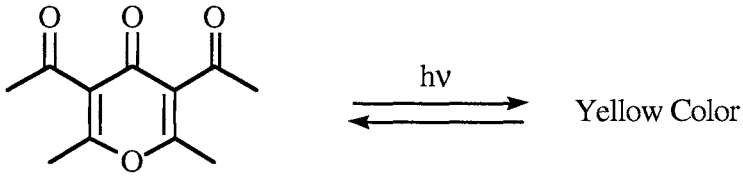
HISTORICAL BACKGROUND: PHOTOENOLIZATION AS A SYNTHETIC TOOL

Introduction

This chapter presents a brief overview of the photoenolization reaction of carbonyl compounds in organic synthesis. Attention has been focused on photoenolizations that are coupled with a Diels-Alder reaction to terminate the sequence. This methodology has been used as a synthetic approach to several useful compounds. Specific examples have been chosen from the literature to illustrate these applications.

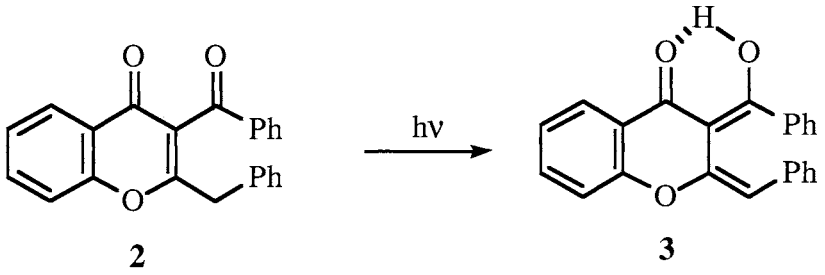
Photoenolization

The phenomenon of photoenolization was first reported by Collie[125] in 1904 when he observed a brilliant yellow color upon exposing crystals of the pyrone **1** to sunlight. It was noted that the color faded upon melting the crystals or dissolving them in a solvent. Ullman and co-workers later reported the same color change using the pyrone **2** and came to the conclusion that a dienol species **3** resulted from the irradiation.[126]



White

1



2 3

It is widely agreed that the process of photoenolization occurs by the steps outlined in Figure 42 for 2-methylbenzophenone (**4**). Irradiation into the n,π* UV absorption band leads to an excited singlet state which rapidly undergoes intersystem crossing to the n,π* triplet. This triplet state is responsible for 1,5-hydrogen abstraction from the alkyl substituent at the *ortho*-position to yield the dienol. The resulting dienol is a highly reactive species and is often referred to as an *ortho*-quinodimethane intermediate.[127]

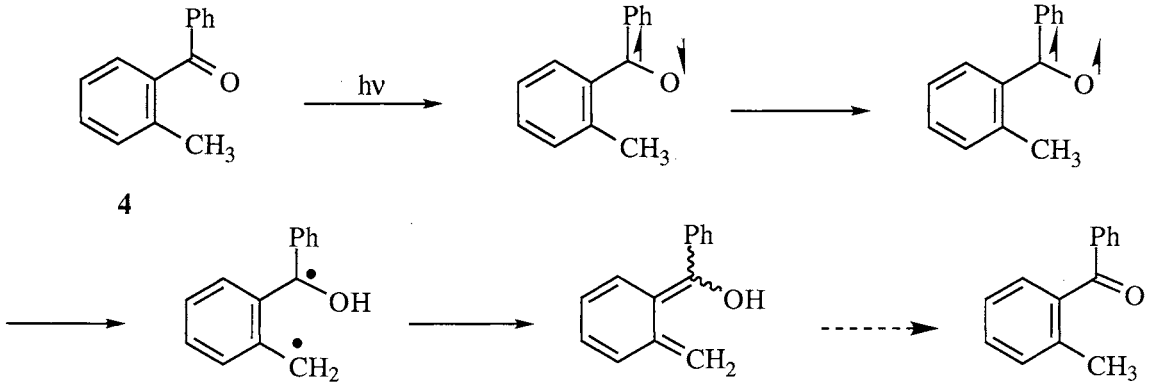
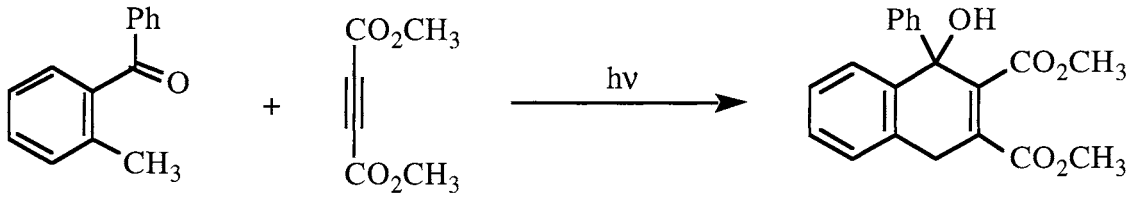


Figure 42. Mechanism for Photoenolization

Although reported before the exact mechanism of photoenolization was known, Yang and Rivas[128] illustrated that the ground state dienol was indeed a likely intermediate in the photolysis of 2-methylbenzophenone (**4**). They found that if irradiation was performed in the presence of dienophiles such as dimethyl acetylenedicarboxylate (**5**), an adduct **6,** which was explainable by a typical Diels-Alder reaction, was produced. Others



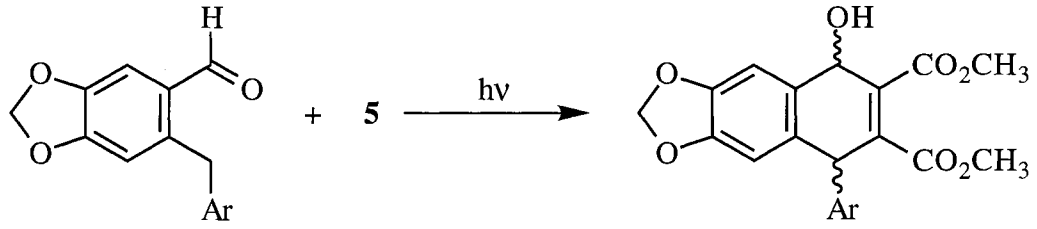
4 **5** **6**

reported that irradiation of 2-methylbenzophenone in the presence of dienophiles also yielded adducts that were readily explained by invoking a ground state dienol intermediate.[129,130] These reactions are not limited to ketones; it was found that 2-methylbenzaldehyde underwent the same type of reaction with maleic anhydride.[131]

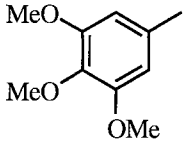
Synthetic Applications

The trapping of photoenols with Diels-Alder dienophiles has been utilized in the preparation of several polycyclic systems. The main advantage of this reaction is the ease of accessibility of the precursors; however, possible photochemical side reactions place limits on its usefulness. Sammes and co-workers[132] were able to employ this reaction for the preparation of a family of lignans. Photocyclization was accomplished using either **7a**

or **7b** in the presence of dimethyl acetylenedicarboxylate (**5**) to give the initial photoproducts **8a** or **8b**. Although **8a** and **8b** were unstable, manipulation of these photoproducts allowed the generation of the final desired compounds. It was reported that the solvent played an important role in the reaction. When the reaction was performed in dioxane the reaction proceeded as desired; however, the use of benzene or acetone was reported without explanation to be detrimental to the reaction outcome.

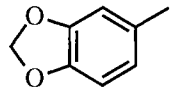


7a Ar =

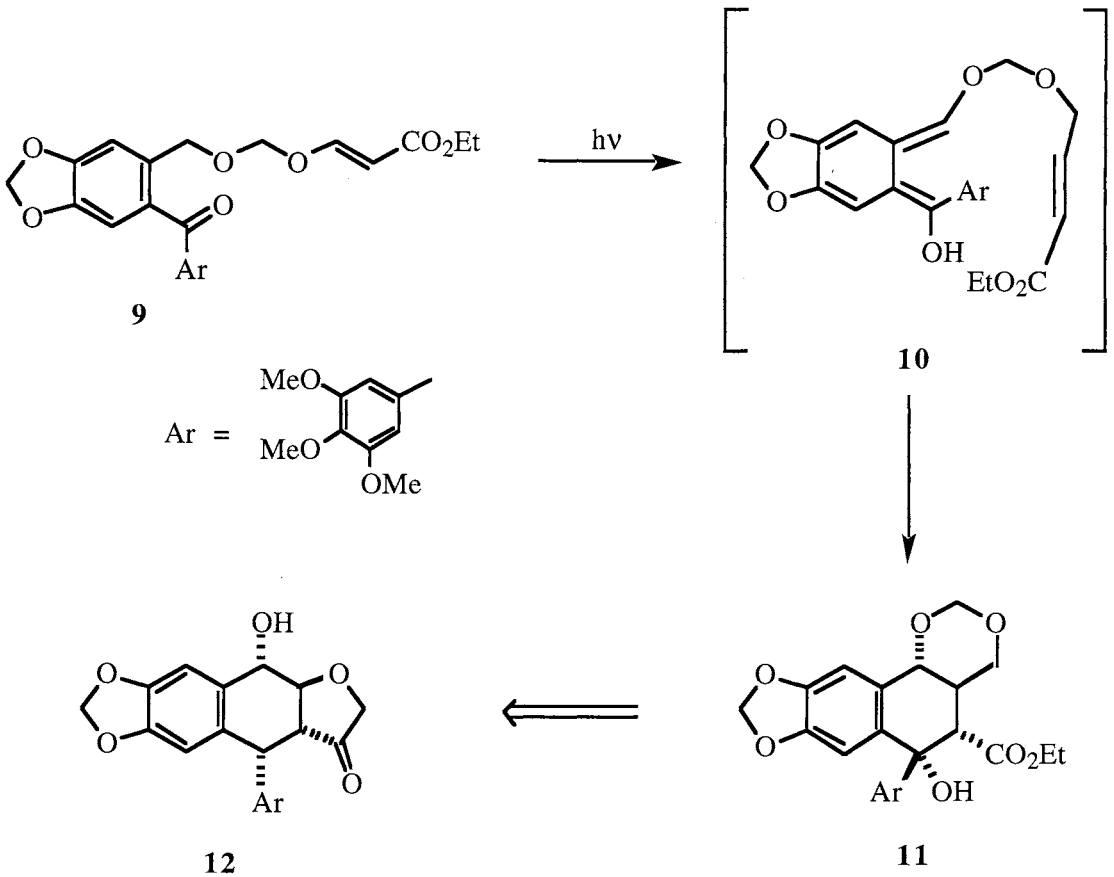


8a
8b

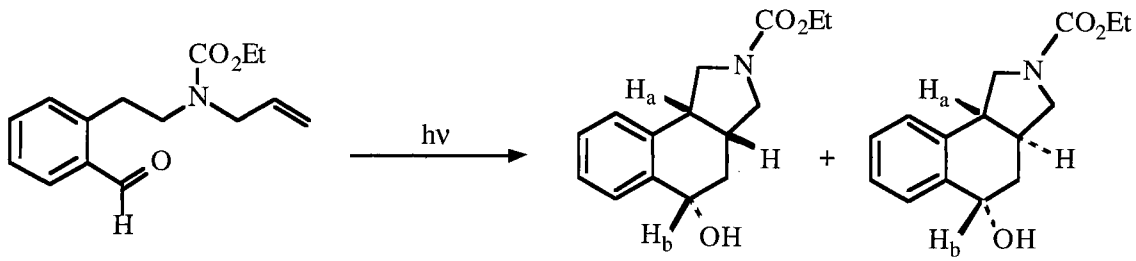
7b Ar =



Kraus and Wu reported a formal synthesis of the biologically active podophyllotoxin **12** which involved a similar strategy using an intramolecular approach.[133] Photoenolization of the diaryl ketone **9** proceeded by abstraction of the benzylic hydrogen atom to give intermediate **10** which subsequently cyclized to the hydroxy ester **11**. This compound was further reacted to give target molecule **12**.

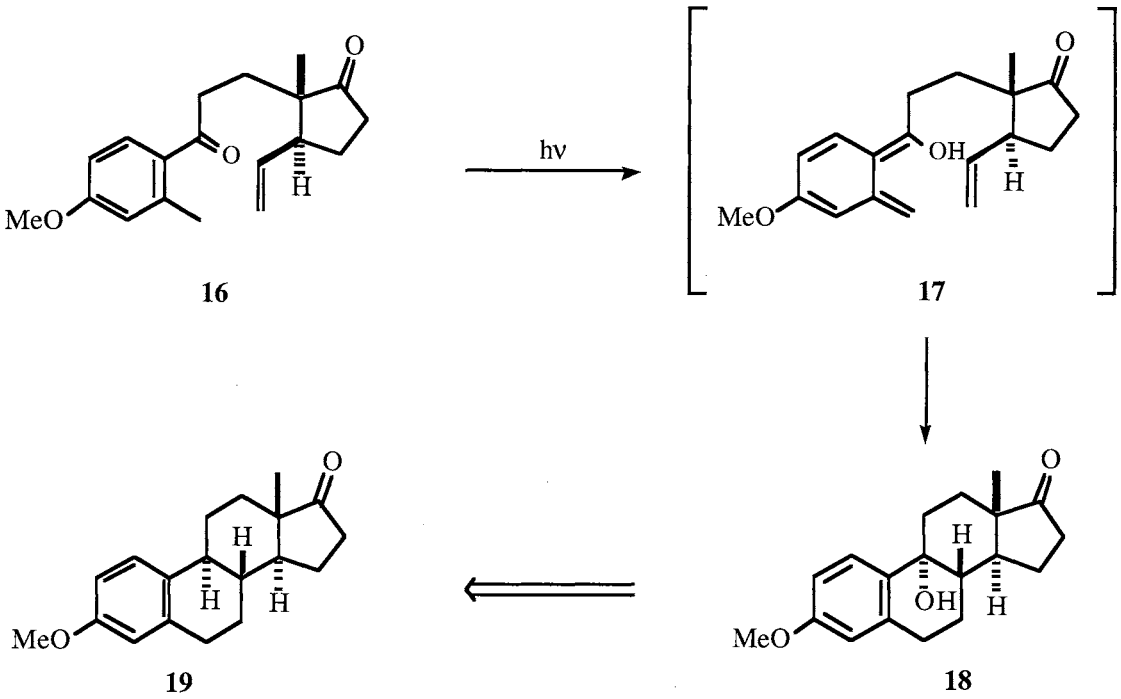


In a study involving the potential for the synthesis of nitrogen heterocycles, Oppolzer and Keller found that photolysis of aldehyde **13** in toluene resulted in an intramolecular Diels-Alder addition to furnish two adducts **14** and **15** in a 3:1 ratio. In order to determine the product stereochemistry, double resonance NMR analysis was performed, and it was found that the relationship between H_a and H_b was cis in both products. This finding led the authors to propose that the major product resulted from *endo* addition of the dienophile while the minor product was produced from *exo* addition.



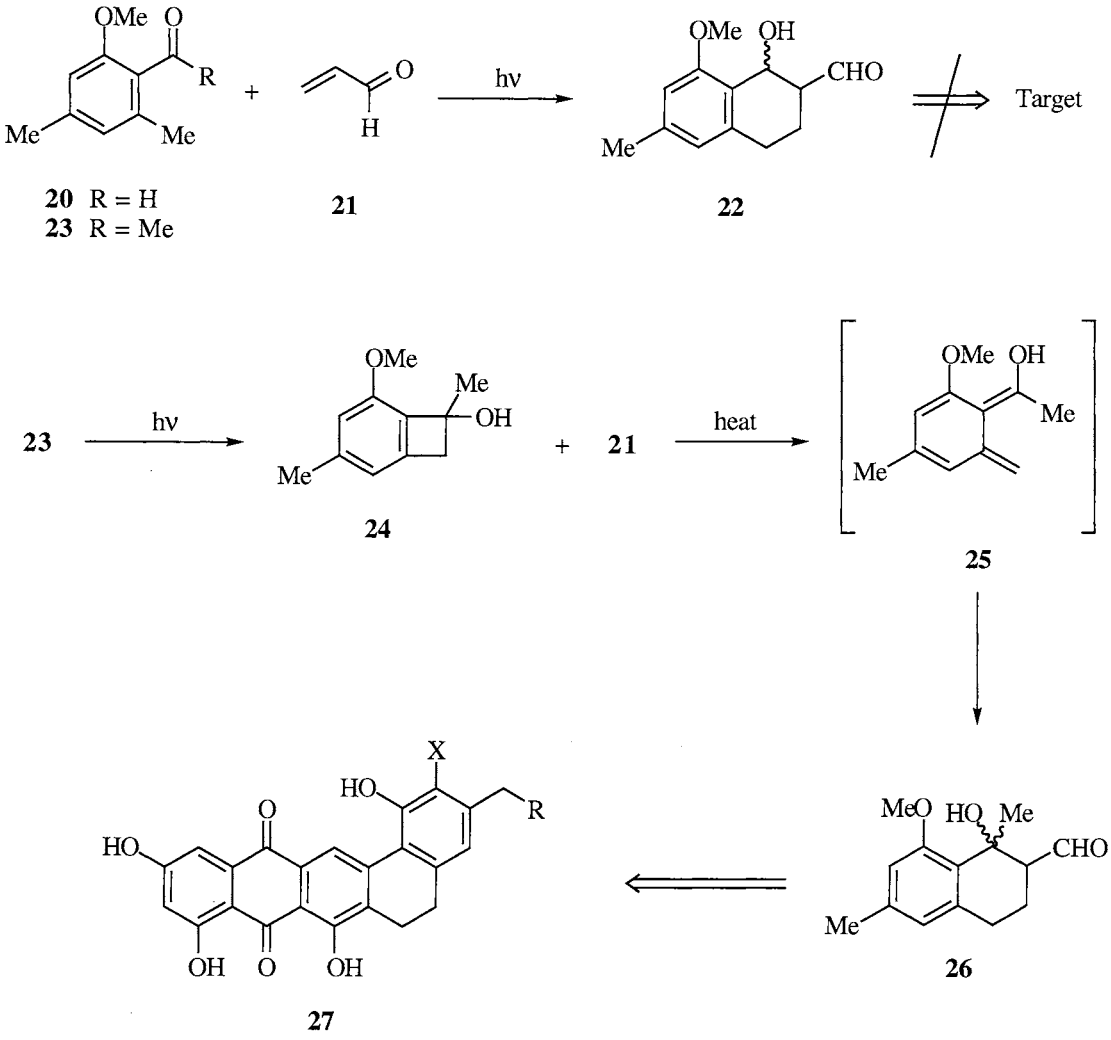
13 *endo* **14** *exo* **15**

In a novel synthesis of (±)-estrone (**19**), a tandem photoenolization-Diels-Alder reaction played a pivotal role.[134] The photolysis substrate **16** was easily obtained in four steps from inexpensive starting materials. Upon irradiation in methylcyclohexane, pyridine, and mesitol at 98 °C, photoenol **17** was produced and readily underwent cycloaddition to the pendant double bond to give the unstable steroid alcohol **18** in 61% yield. Three simple steps then afforded the racemic steroid **19**. Although lacking extensive detail, the authors did point out that the photochemical reaction proceeded with extremely high regioselectivity and diastereoselectivity.



16 **17** **19** **18**

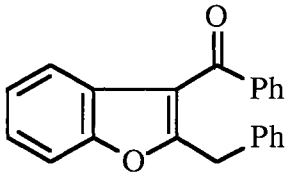
In an attempt to synthesize angularly fused quinone natural products,[135] aldehyde **20** was irradiated with acrolein (**21**) to give the expected photoproduct **22** in 85% yield. When compound **22** could not be further converted to the target compound, a related photochemical method was utilized as the key step. Irradiation of ketone **23** in the presence of acrolein gave benzocyclobutanol **24** by electrocyclization of the initial



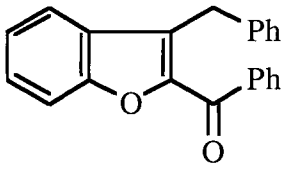
photoenol. Heating of cyclobutenol **24** in the presence of acrolein (**21**) readily underwent cyclobutene opening and cycloaddition to furnish product **26**. This adduct was then carried on to the desired target molecule **27**. The formation of cyclobutanols is a common occurrence in photoenolization reactions. However, they can often be thermally ring-opened to the dienol and trapped as a Diels-Alder adduct. A review article by Sammes gives valuable information concerning these types of reactions.[136]

Photoenolization of Heteroaromatic Compounds

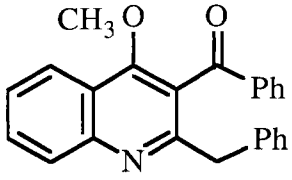
Although a review of the literature indicated that photoenolization of heteroaromatic compounds has apparently not been used in synthesis, a brief mention of the reactivity of such compounds is necessary. Among oxygen heterocycles, benzofurans such as **28** and **29** have been reported to undergo photoenolization.[126] It was found that irradiation of an ether solution of these compounds at -50 °C resulted in a bright yellow color which is characteristic of the enol. On the other hand, when irradiation was done at room temperature, a color change was not observed. It was concluded from deuterium exchange studies that enolization did occur at room temperature but reketonization occurred at a very rapid rate. In the same study, quinoline **30** did not change color or exchange deuterium, and thus it was considered to be a non-reactive substrate.



28



29



30

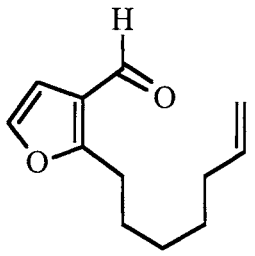
CHAPTER 6

PHOTOENOLIZATION STUDIES OF NITROGEN AND OXYGEN HETEROAROMATIC COMPOUNDS

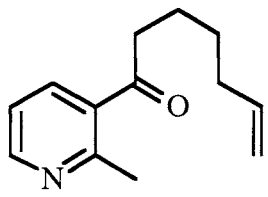
Introduction

A recent project in our group required the synthesis of fused ring nitrogen and oxygen aromatic compounds for thermochemical studies. A review of the literature[133-135,137] indicated that photoenolization coupled with an intramolecular Diels-Alder reaction allows for the preparation of polycyclic systems similar to those sought in the current study with the exception that heteroaromatic substrates had not yet been reported. This cyclization technique would not only afford the compounds needed for the thermochemical study, but it would also provide heterocyclic compounds that may be attractive as potential biologically active molecules.

For preliminary investigations, two different heteroaromatic substrates were synthesized and photolyzed. The compounds selected for this study consisted of furan derivative **1** and pyridine derivative **2**. The expected photocyclization is illustrated in detail



1



2

for compound **1** in Figure 43. It was proposed that irradiation in the n,π* absorption band would result in excitation and intersystem crossing to give the triplet excited state represented as **3**. Hydrogen abstraction from the adjacent methyl group would generate the *ortho*-quinodimethane-type intermediate **4**. This reactive species should readily undergo intramolecular cycloaddition with the pendant alkene to give the partially hydrogenated heteroaromatic **5**. The driving force for the reaction is probably the rearomatization of the system.

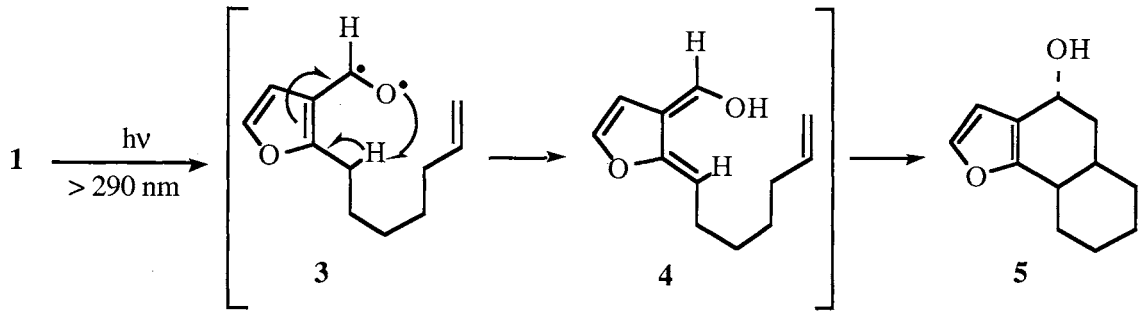
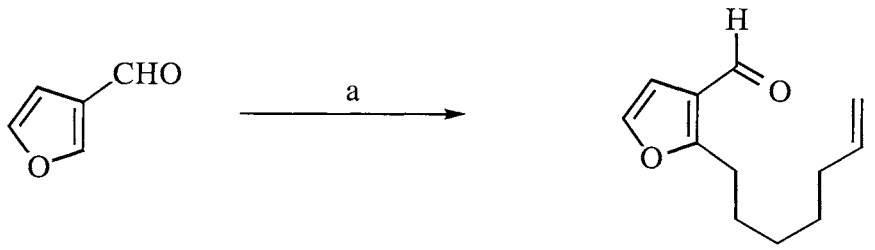


Figure 43. Mechanism for the Photoenolization-Diels-Alder Reaction of Heteroaromatic Compounds.

Results

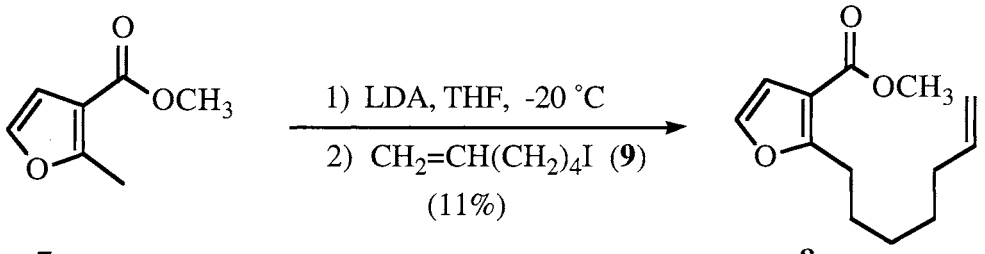
Synthesis of the Photochemical Substrates. For this study, a furan derivative **1** and a pyridine derivative **2** were selected as test cases for the tandem photoenolization-Diels-Alder reaction. Initially, it was believed that 2-(6-heptenyl)-3-furaldehyde (**1**) could be made by direct alkylation of 3-furaldehyde (**6**) using lithium *N,N,N'*-trimethylethylenediamine. Similar alkylations have been reported by Comins and Killpack[138] using methyl iodide as the alkylating agent. These authors noted that metallation was directed to the C-2 position of the furan due to the coordinating ability of the amine. Subsequent electrophilic attack then occurred predominantly at this position.



6 **1**

a) 1 eq. lithium *N, N, N'*-trimethylethylenediamine, THF-hexane, -78 °C; 2 eq. *n*-BuLi, -78 °C; 3 eq. $CH_2=CH(CH_2)_5I$

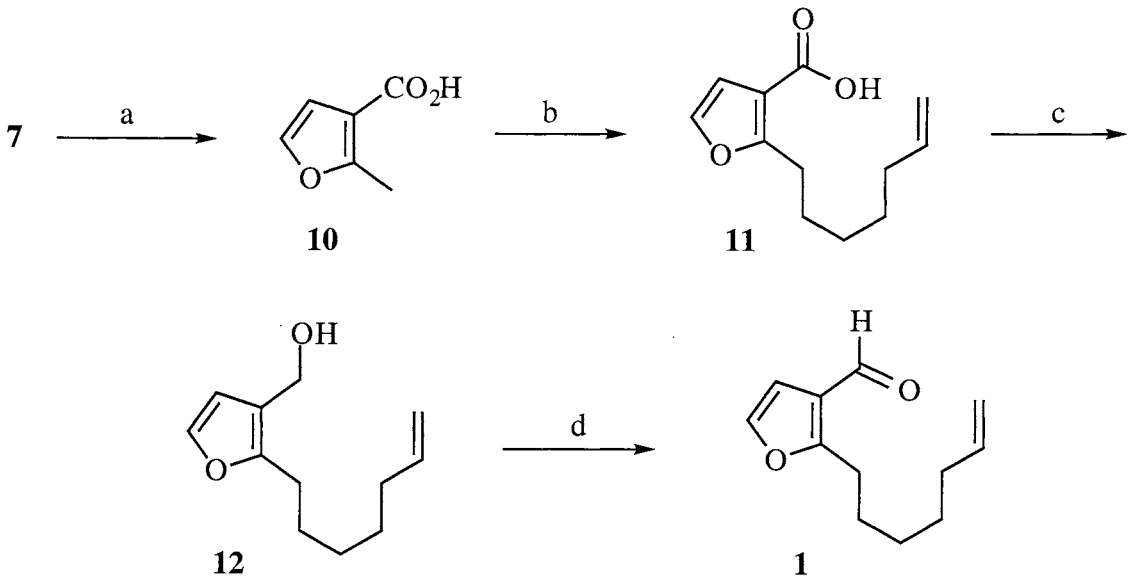
When these conditions were applied to the preparation of the hexenyl analogue of **1**, the alkylation was not reproducible. Therefore, a new synthetic route for **1** was devised proceeding through methyl 2-(6-heptenyl)-3-furancarboxylate (**8**) was devised. Starting with methyl 2-methyl-3-furan carboxylate (**7**), alkylation[139] was accomplished using LDA and 6-iodo-1-hexene (**9**) at -78 °C. Although furan ester **8** was isolated, the yield was extremely low (11%) due to competing polymerization of the starting material. This route was clearly unsuitable for the preparation of the large amounts of the ester that would be required.



7 **8**

The successful route (Figure 44) to **1** started with the previously reported 2-methyl-3-furoic acid[140] (**10**) which could be easily obtained by base hydrolysis (KOH, EtOH, reflux) of ester **7**. Using the alkylation procedure reported by Keay,[141] treatment of **10**

with 2 eq. of *n*-BuLi followed by addition of 1.3 eq. 6-iodo-1-hexene (**9**) at -20 °C gave 2-(6-heptenyl)-3-furoic acid (**11**) in 85% yield. The acid was reduced with $LiAlH_4$ at 0 °C to furnish alcohol **12** in a yield of 62%. Collin's oxidation[139] of **12** then yielded compound **1** in 43% yield. The synthesis of furaldehyde **1** was thus easily realized in three steps with an overall yield of 23% starting from acid **10**. This strategy should prove valuable for other target 3-furaldehydes that require alkyl substitution at C-2 of the furan ring.

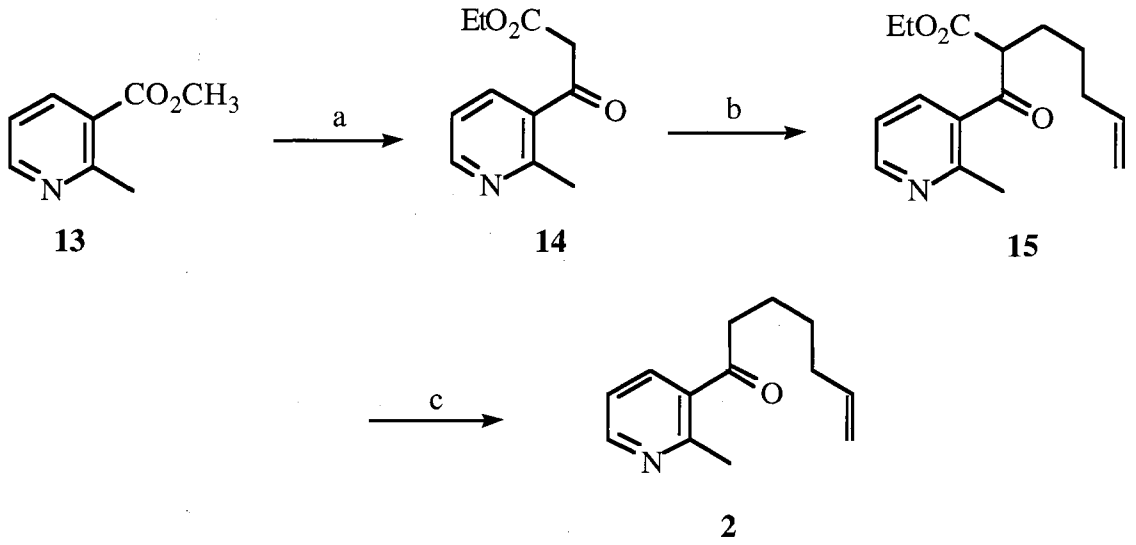


a) KOH, EtOH, 78 °C b) 2 eq. *n*-BuLi, THF, -20 °C; 1.3 eq. $CH_2=CH(CH_2)_4I$ (**9**), THF, 36 h, rt (85%) c) $LiAlH_4$, Et_2O, -20 →25 °C (62%) d) CrO_3, pyridine, CH_2Cl_2, 0 °C (43%)

Figure 44. Synthesis of 2-(6-Heptenyl)-3-furaldehyde.

The preparation of pyridine **2** is outlined in Figure 45. Condensation of methyl 2-methyl-3-pyridinecarboxylate (**13**) with ethyl acetate in the presence of NaH gave the 3-pyridinoylacetate derivative **14** as a mixture of both the keto and the enol tautomers. Treatment of this crude mixture with NaH followed by alkylation with 5-bromo-1-pentene yielded the alkylated keto ester **15**. Once again the reaction mixture was carried on without further purification to avoid decomposition of the sensitive pyridine derivative. Hydrolysis

and of **15** decarboxylation of the resulting acid to give **2** was accomplished by refluxing **15** in a 1:1 volume ratio of glacial acetic acid and 1 M hydrochloric acid. Purification by silica gel chromatography afforded 1-(2-methylpyridinyl)-6-hepten-1-one (**2**) in an overall yield of 11% from **13**. It is evident that the synthesis of compound **2** is not very efficient, and thus, if large amounts of material is needed, an alternate method would be required.



13 **14** **15** **2**

a) 1.7 eq. NaH, EtOAc, reflux b) NaH, DMF; $CH_2=CH(CH_2)_3Br$
c) 1:1 glacial AcOH:1 M HCl, 100 °C

Figure 45. Synthesis of 1-(2-Methylpyridinyl)-6-hepten-1-one.

Exploratory Photochemistry of Compound 1. Direct irradiation of a 10^{-2} M solution of **1** was performed in either degassed benzene or 1,4-dioxane through Pyrex® using a 450-W medium pressure ultraviolet source. The reaction was followed by TLC or IR until all of the starting material had been consumed. When 1,4-dioxane was used as the solvent, the reaction was complete after 4 h. IR analysis of the crude reaction mixture showed the presence of a hydroxyl, suggesting that the reaction had possibly gone to the desired product **5**. However, the sample was not easily dissolved in any common solvent ($CHCl_3$, CH_2Cl_2, hexane, ether, acetone) which suggested the formation of a polymer.

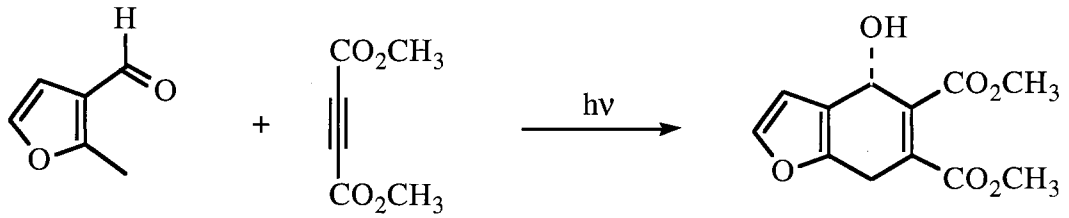
The sample was centrifuged to remove the insoluble impurity, and the remaining soluble material was purified on silica gel. The NMR spectrum of the major component showed several very broad peaks in the aliphatic region and no peaks in the aromatic region. This indicated that fragmentation of the side chain may have occurred. Irradiation using benzene as the solvent resulted in the same outcome.

Exploratory Photochemistry of Compound 2. Compound **2** was photolyzed under the same conditions as described for substrate **1**. It was noted that upon irradiation for 1 h in 1,4-dioxane the solution turned a very bright yellow color and, upon standing, the color diminished. Thus, it was possible that photoenolization had occurred. After irradiating for 6.5 h, IR analysis indicated the presence of a hydroxyl group, but a large quantity of insoluble precipitate was formed upon addition of ether. This precipitate was believed to be polymeric material. The crude reaction mixture was centrifuged to remove this substance and the remaining material was purified using thin layer silica gel chromatography. Proton NMR analysis of the major product showed only three very broad peaks centered around 1.7 ppm. The lack of aromatic signals suggested that the substrate had fragmented upon irradiation. The same results were observed using benzene as the solvent.

It was concluded from the results of photolyses that the expected cyclization did not occur for either compound **1** or **2**. Competing photoreactions appeared to dominate under the conditions prescribed in the literature for similar cyclizations of carbocyclic systems.[132,133] Thus, further work to develop better reaction conditions is required.

Future Work. Studies need to be designed to investigate the energy needed for photoenolization to occur with a minimum of competing reactions. In this area, a different wavelength of light and/or a less intense power source such as a Rayonet® reactor may be helpful. It is also possible that using a photosensitizer to transfer the required energy to the photochemical substrate would allow for the desired reaction to occur.

Rather than using compounds **1** and **2** for the optimization studies, a simpler and more available system could be utilized. One such compound would be 2-methyl-3-furaldehyde (**16**) which could be prepared by the method of Scarpa.[142] Irradiation of this compound in the presence of a dienophile such as dimethyl acetylenedicarboxylate (**17**) could be used to determine if an intermolecular Diels-Alder reaction is possible. Once optimum conditions are found in this case, the intramolecular ring closure of compounds such as **1** and **2** could be reinvestigated.



16 **17** **18**

Experimental

THF was distilled from $LiAlH_4$; DMF was distilled from BaO and stored over 4Å molecular sieves. Benzene was purified according to Zimmerman and Bunce.[70] The 1,4-dioxane was spectrophotometric grade obtained from Aldrich. Other reagents were used as received. All reactions were run under dry N_2 in oven-dried glassware. Reactions were monitored using one of the following methods: 1) TLC on hard layer silica gel GF plates (Analtech) using UV detection or 2) capillary GC with FI detection (SE-30 column, 6 m x 0.25 mm i.d., 0.25 μm film thickness) programmed between 50-300 °C. The saturated NH_4Cl, 1 M and 6 M HCl, 1 M NaOH, 5% $Na_2S_2O_3$, saturated $NaHCO_3$, and saturated NaCl used in the workup procedures refer to aqueous solutions. Preparative separations were performed using one of the following methods: 1) PTLC on 20-cm x 20-cm silica gel GF plates (Analtech), 2) flash chromatography[121] on silica gel (Grace, grade 62, 60-200

mesh) containing UV-active phosphor (Sylvania no. 2282); in each case, band elution was monitored using a hand-held UV lamp. IR spectra are referenced to polystyrene. ^{1}H NMR and ^{13}C NMR were measured in $CDCl_3$ at 400 and 100 MHz, respectively, and are referenced to internal Me_4Si.

Methyl 2-(6-Heptenyl)furan-3-carboxylate (8). This compound was prepared according to the procedure reported by Trahanovsky and Leung. [139] To a solution of 12.1 g (120 mmol) of diisopropylamine in 150 mL of THF at -78 °C was added 85 mL of a 1.3 M solution of *n*-BuLi solution in hexanes (111 mmol). After 2.5 h at -78 °C, a solution of 9.66 g (69.0 mmol) of methyl 2-methyl-3-furancarboxylate (**7**) in 50 mL of THF was added slowly. The reaction mixture was stirred at -78 °C for 2.5 h, and a solution of 13.2 g (62.9 mmol) of 6-iodo-1-hexene (**9**) in 25 mL of THF was added dropwise. After stirring for an additional 1.5 h, the reaction was quenched by addition of water at -78 °C. The quenched solution was warmed to room temperature and extracted with CH_2Cl_2 (2x). The combined extracts was washed with NaCl (2x), filtered through Celite®, then dried (Na_2SO_4) and concentrated under vacuum. Purification was done by chromatography on a 110-cm x 2.5-cm silica gel column eluting with 5% ether in hexanes. Band 2 afforded 1.66 g (7.47 mmol, 11%) of **8**. IR (thin film) 3076, 1715, 1640, 911 cm^{-1}; ^{1}H NMR δ 7.18 (d, 1 H, J = 2.0 Hz), 6.54 (d, 1 H, J = 2.0 Hz), 5.67 (ddt, 1 H, J = 17.1, 10.3, 6.7 Hz), 4.87 (d, 1 H, J = 17.1 Hz), 4.84 (d, 1 H, J = 10.3 Hz), 3.74 (s, 3 H), 1.89 (m, 2 H), 1.63-1.49 (complex, 4 H), 1.31-1.07 (complex, 4 H); ^{13}C NMR δ 166.4, 164.5, 140.4, 138.9, 114.2, 114.1, 110.3, 51.2, 37.5, 33.8, 33.5, 28.7, 26.8, 15.2.

2-Methyl-3-furoic acid (10). This compound was prepared from the ethyl ester **7** according to the method reported by Gilman.[140] No exceptions were noted and the reaction proceeded as described.

2-(6-Heptenyl)-3-furoic acid (11). The procedure of Keay[141] was used. A solution of 5.78 g (45.9 mmol) of 2-methyl-3-furoic acid (**10**) in 200 mL of THF was

cooled to -20 °C, and 70.4 mL (91.5 mmol) of a 1.3 M solution of *n*-BuLi in hexanes was added dropwise over 40 min. The resulting red solution was allowed to stir for 1 h and was treated by dropwise addition of a solution of 12.47 g (59.4 mmol) of 6-iodo-1-hexene (**9**) in 85 mL of THF. The reaction mixture was stirred at room temperature for 36 h and then quenched with 25 mL of H_2O. The crude reaction mixture was basified with 1 M NaOH and washed with excess ether. The aqueous layer was acidified to pH 3-4 using 1 M HCl followed by extraction with excess ether. The ether extract was washed with NaCl (2x), then dried (Na_2SO_4) and concentrated under vacuum to give 8.11 g (39.0 mmol, 85%) of a dark brown oil. The crude product was greater than 90% pure and was used without further purification. IR (thin film) 3300-2500, 1685, 1642, 1598, 911 cm^{-1}; ^1H NMR δ 10.8 (bs, 1H), 7.27 (d, 1 H, J = 2.1 Hz), 6.68 (d, 1 H, J = 2.1 Hz), 5.80 (ddt, 1 H, J = 17.1, 10.2, 6.8 Hz), 4.99 (d, 1 H, J = 17.1 Hz), 4.96 (d, 1 H, J = 10.2 Hz), 3.01 (t, 2 H, J = 7.5 Hz), 2.06 (m, 2H), 1.69 (quintet, 2 H, J = 7.5 Hz), 1.44-1.32 (complex, 4 H); ^{13}C NMR δ 169.9, 164.9, 140.6, 138.9, 114.3, 112.5, 110.8, 33.6, 28.6, 28.5, 27.7, 27.6.

2-(6-Heptenyl)-3-(hydroxymethyl)furan (12). The general procedure of Trahanovsky and Leung[139] was used. To a suspension of 0.40 g (10.0 mmol) of $LiAlH_4$ in 12 mL of ether at 0 °C was added dropwise a solution of 2.23 g (10.0 mmol) of 2-(6-heptenyl)furoic acid (**11**) in 18 mL of ether. The mixture was stirred for 4 h with gradual warming to room temperature. The reaction mixture was cooled back to 0 °C and cautiously quenched with 0.40 mL of H_2O, 0.40 mL of 1 M NaOH, and enough H_2O to produce a granular precipitate. The resulting suspension was filtered through Celite® and then through $MgSO_4$. GC indicated the product was >90% pure. Chromatography on a 75-cm x 1.5-cm silica gel column eluting with 90% hexane containing 9% EtOAc and 1% EtOH did not purify the compound. It was therefore carried on without further purification. The yield was 1.20 g (6.20 mmol, 62%) of **12** as a light brown oil. IR (thin film) 3363, 3076, 1640, 911 cm^{-1}; ^1H NMR δ 7.25 (d, 1 H, J = 1.8 Hz), 6.35 (d, 1 H,

J = 1.8 Hz), 5.79 (ddt, 1 H, J = 17.2, 10.2, 6.7 Hz), 4.98 (d, 1 H, J = 17.2 Hz), 4.94 (d, 1 H, J = 10.2 Hz), 4.45 (s, 2 H), 2.62 (t, 2 H, J = 7.4 Hz), 2.05 (m, 2 H), 1.62 (quintet, 2 H, J = 7.6 Hz), 1.39 (m, 2 H), 1.32 (m, 2 H); ^{13}C NMR δ 153.4, 140.7, 139.1, 118.8, 114.5, 110.9, 56.5, 33.8, 28.8, 28.7, 28.6, 26.1.

2-(6-Heptenyl)-3-furaldehyde (**1**). This compound was prepared by the method of Trahanovsky and Leung.[139] To a vigorously stirred suspension of 11.6 g (116 mmol) of CrO_3 in 275 mL of CH_2Cl_2 at 0 °C was slowly added 18.6 g (19.0 mL, 246 mmol) of pyridine. To the resulting dark brown solution was added a 25-mL CH_2Cl_2 solution of 3.75 g (19.3 mmol) of 2-(6-heptenyl)-3-(hydroxymethyl)furan (**15**) all in one portion. After stirring for 20 min, the tarry mixture was treated with excess ether and worked up as reported by Ratcliffe[143] to give the crude product as a brown oil. The oil was purified by chromatography on a 30-cm x 1.5-cm silica gel column eluting with 5% ether in hexanes. Band 2 gave 1.60 g (8.30 mmol, 43%) of **1** as a pale yellow oil. UV (cyclohexane) 224 nm (ε 3822), 253 (3828), 290 (900); IR (thin film) 3126, 3076, 2859, 2739, 1686, 1640, 911 cm^{-1}; ^{1}H NMR δ 9.94 (s, 1 H), 7.31 (d, 1 H, J = 2.2 Hz), 6.69 (d, 1 H, J = 2.2 Hz), 5.77 (ddt, 1 H, 17.1, 10.3, 6.8 Hz), 4.99 (d, 1 H, J = 17.1 Hz), 4.96 (d, 1 H, J = 10.3 Hz), 2.95 (t, 2 H, J = 7.6 Hz), 2.05 (m, 2 H), 1.74 (quintet, 2 H, 7.6 Hz), 1.40 (m, 4 H); ^{13}C NMR δ 184.7, 166.0, 142.0, 138.5, 122.3, 114.4, 107.8, 33.4, 28.3 (2), 28.0, 26.6.

Ethyl 2-Methyl-3-pyridinoylcarboxylate (**14**). This compound was prepared by the method of Wenkert and co-workers.[144] To a suspension of 4.45 g (111 mmol) of NaH (60% dispersion in mineral oil) in 10 mL of THF was added 10.0 g (60.6 mmol) of methyl 2-methyl-3-pyridinecarboxylate (**13**) and 23 mL of EtOAc all in one portion. The initial reaction was exothermic and an insoluble precipitate was formed. This mixture was heated at reflux for 3 h, then cooled to room temperature. The crude reaction mixture was transferred to a separatory funnel containing ice water and extracted with ether. The aqueous solution was brought to pH 6-7 using 6 M HCl, then saturated with

NaCl and extracted exhaustively using CH_2Cl_2. The combined extracts were washed with NaCl, then dried (Na_2SO_4) and concentrated under vacuum to give 9.05 g of the β-ketoester as a keto-enol mixture in greater than 80% purity according to GC and NMR. The crude product was carried on to the next reaction without further purification. IR (thin film): 3400, 1740, 1690 cm^{-1}.

Ethyl 2-((2-Methylpyridinyl)oxomethyl)-6-heptenoate (15). To a suspension of 0.38 g (9.5 mmol) of NaH (60% dispersion in mineral oil) in 10 mL of DMF was added 1.79 g of crude ethyl 2-methyl-3-pyridinoylcarboxylate (**14**) in 30 mL of DMF at room temperature. After addition was complete, solution of 5-bromo-1-pentene in 10 mL of DMF was added dropwise and the reaction mixture was stirred for 20 h at room temperature. The crude reaction mixture was neutralized using 1 M HCl, saturated with NaCl, and extracted with excess ether. The combined ether extracts were dried (Na_2SO_4) and concentrated under vacuum to yield 1.98 g of crude oil that was carried on to the next step without further purification. A small amount was purified for characterization purposes using PTLC eluted with 15-25% ether in hexanes. IR (thin film) 3075, 1744, 1695, 1640 cm^{-1}; ^{1}H NMR δ 8.60 (dd, 1 H, J = 4.8, 1.7 Hz), 7.95 (dd, 1 H, J = 7.8, 1.7 Hz), 7.25 (dd, 1 H, J = 7.8, 4.8 Hz), 5.76 (ddt, 1 H, J = 17.1, 10.3, 6.8 Hz), 5.01 (d, 1 H, J = 17.1 Hz), 4.96 (d, 1 H, J = 10.2 Hz), 4.18 (t, 1 H, J = 7.1 Hz), 3.68 (s, 3 H), 2.71, (s, 3 H), 2.09 (m, 2 H), 1.97 (m, 2 H), 1.45 (m, 2 H); ^{13}C NMR δ 197.7, 169.8, 158.2, 151.2, 137.6, 135.6, 132.4, 120.6, 115.0, 56.3, 52.3, 33.2, 28.0, 26.5, 23.9.

1-(2-Methylpyridinyl)-6-hepten-1-one (2) To 8.80 g of crude ethyl 2-((2-methylpyridinyl)oxomethyl)-6-heptenoate (**15**) was added 75 mL of glacial acetic acid and 75 mL of 1 M HCl. The solution was stirred at 100 °C for 18 h then cooled to room temperature, neutralized using 1 M NaOH and extracted with excess ether. The ether extracts were washed with H_2O, NaCl, then dried (Na_2SO_4) and concentrated under vacuum. The product was purified by chromatography on a 60-cm x 2.5-cm silica gel

column eluted with 15-25% ether in hexanes. Band 2 yielded 1.31 g (6.50 mmol, 11% from **13**) of **2** as a colorless oil. UV (cyclohexane) 255 nm (ε 2039), 322 (ε 188); IR (thin film) 2958, 1690, 1581, 1563, 1435, 1373 cm^{-1}; ^1H NMR δ 8.58 (dd, 1 H, J = 4.8, 1.5 Hz), 7.88 (dd, 1 H, J = 7.8, 1.6 Hz), 7.22 (dd, 1 H, 7.8, 4.8 Hz), 5.82 (ddt, 1 H, J = 17.2, 10.3, 6.7 Hz), 5.02 (d, 1 H, J = 17.2 Hz), 4.98 (d, 1 H, J = 10.3 Hz), 2.89 (t, 2 H, J = 3.2 Hz), 2.71 (s, 3 H), 2.15 (m, 2 H), 1.73 (quintet, 2 H, J = 7.4 Hz), 1.47 (quintet, 2 H, J = 7.4 Hz); ^{13}C NMR δ 203.5, 157.6, 150.9, 138.3, 135.7, 133.4, 120.7, 114.8, 41.4, 33.5, 28.4, 24.3, 23.6.

Representative Procedure for the Exploratory Direct Photolysis of Compound 1.

A. In 1,4-Dioxane: A solution of 100 mg (0.52 mmol) of 2-(6-heptenyl)-3-furaldehyde (**1**) in 20 mL of degassed 1,4-dioxane in a Pyrex® reaction vessel equipped with a water-cooled cold finger was irradiated with a 450-W medium pressure ultraviolet source. The reaction was followed using TLC and IR until the starting material was no longer detected (4 h). The solution was concentrated under vacuum and $CHCl_3$ was added. A precipitate formed which was removed by centrifugation. The soluble material was purified by PTLC eluted with increasing amounts of EtOAc in hexanes. The slowest moving band contained the major product as a brown solid. The IR (thin film) showed a strong band at 3405 cm^{-1}; no other peaks were informative. The ^1H NMR showed three very broad signals centered around 3.60, 2.05, 1.25 and no significant peaks in the aromatic range.

B. In Benzene: The irradiation was done under the same conditions as above. A reaction time of 8 h was required. Comparison of the R_f of the major product with the isolated product from the 1,4-dioxane solution indicated that they were the same. Therefore, purification was not attempted.

Representative Procedure for the Exploratory Photolysis of Compound 2.

A. In 1,4-Dioxane. A solution of 90 mg (0.44 mmol) in 10 mL of degassed 1,4-dioxane in a Pyrex® reaction vessel was irradiated with a 450-W medium pressure ultraviolet source. The reaction was monitored using TLC and IR. After 1 h, the solution had turned a bright yellow color and upon standing this color dissipated. After irradiating for 6.5 h, TLC indicated complete consumption of the starting ketone. The solution was concentrated under vacuum and $CHCl_3$ was added. The mixture was centrifuged to remove the insoluble impurities, and the supernatant solution was purified using PTLC eluted with increasing amounts of EtOAc in hexanes. The slowest moving band was the major product. The IR (thin film) showed a strong band at 3270 cm^{-1}; no other peaks were informative. The ^1H NMR showed broad signals centered about 0.95, 1.23, and 1.6 with no significant peaks in the aromatic region.

B. In Benzene. The reaction was done in the same manner and the major compound had the same R_f value as the product isolated from the above reaction.

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APPENDIX A

TABLES OF CRYSTALLOGRAPHIC DATA FOR (±)-8-*tert*-BUTOXY-2,3,4,4a,5,6,7,8-OCTAHYDRO-4a-METHYL-7,7-DIPHENYL-1-NAPHTHOL (**34**)

TABLE 5

CRYSTAL DATA FOR **34**

Formula	$C_{27}H_{34}O_2$
M. W.	390.5 g mole^{-1}
a	19.54 (2) Å
b	14.288 (10) Å
c	18.048 (16) Å
α	90°
β	116.10(7)°
γ	90°
V	4527(7) Å^3
F(000)	1696
μMoKa	0.07 mm^{-1}
λMoKa	0.71073 Å
D_{calc}	1.146 Mg/m^3
Z	8
Meas refl	7973
Obs refl	3116
R	6.13%
R_W	11.80%
G. O. F.	1.25
Space Group	$P2_1/c$

TABLE 6

BOND ANGLES FOR COMPOUND **34**

Atoms	Angle (°)
C(8)-O(2)-C(10)	118.5(5)
O(1)-C(1)-C(2)	109.8(8)
O(1)-C(1)-C(8A)	124.6(9)
C(2)-C(1)-C(8A)	125.6(9)
C(1)-C(2)-C(3)	111.5(9)
C(2)-C(3)-C(4)	109.6(8)
C(3)-C(4)-C(4A)	110.9(6)
C(4)-C(4A)-C(5)	107.2(6)
C(4)-C(4A)-C(8A)	112.5(7)
C(5)-C(4A)-C(8A)	107.3(7)
C(4)-C(4A)-C(9)	108.8(8)
C(5)-C(4A)-C(9)	109.8(7)
C(8A)-C(4A)-C(9)	111.2(6)
C(4A)-C(5)-C(6)	114.4(6)
C(5)-C(6)-C(7)	113.1(7)
C(6)-C(7)-C(8)	103.6(7)
C(6)-C(7)-C(14)	111.7(7)
C(8)-C(7)-C(14)	109.4(6)
C(6)-C(7)-C(20)	107.5(6)
C(8)-C(7)-C(20)	114.9(7)
C(14)-C(7)-C(20)	109.6(7)
O(2)-C(8)-C(7)	111.1(6)
O(2)-C(8)-C(8A)	112.5(6)
C(7)-C(8)-C(8A)	113.5(6)
C(1)-C(8A)-C(4A)	120.4(9)
C(1)-C(8A)-C(8)	125.2(8)
C(4A)-C(8A)-C(8)	114.4(7)
O(2)-C(10)-C(11)	100.9(6)
O(2)-C(10)-C(12)	109.8(7)
C(11)-C(10)-C(12)	111.9(9)
O(2)-C(10)-C(13)	110.2(7)
C(11)-C(10)-C(13)	111.3(8)
C(12)-C(10)-C(13)	112.2(8)
C(7)-C(14)-C(15)	122.5(9)
C(7)-C(14)-C(19)	119.3(8)
C(15)-C(14)-C(19)	118.3(10)
C(14)-C(15)-C(16)	121.7(10)
C(15)-C(16)-C(17)	120.5(11)
C(16)-C(17)-C(18)	118.3(11)
C(17)-C(18)-C(19)	120.6(11)
C(14)-C(19)-C(18)	120.7(9)
C(7)-C(20)-C(21)	118.4(8)
C(7)-C(20)-C(25)	124.5(6)
C(21)-C(20)-C(25)	117.0(7)
C(20)-C(21)-C(22)	121.5(9)
C(21)-C(22)-C(23)	120.9(9)

C(22)-C(23)-C(24)	118.3(9)
C(23)-C(24)-C(25)	119.8(9)
C(20)-C(25)-C(24)	122.4(7)
C(8')-O(2')-C(10')	117.0(6)
O(1')-C(1')-C(2')	108.8(8)
O(1')-C(1')-C(8A')	124.0(7)
C(2')-C(1')-C(8A')	127.2(8)
C(1')-C(2')-C(3')	111.3(8)
C(2')-C(3')-C(4')	108.9(8)
C(3')-C(4')-C(4A')	111.8(7)
C(4')-C(4A')-C(5')	107.7(6)
C(4')-C(4A')-C(8A')	111.3(7)
C(5')-C(4A')-C(8A')	108.1(7)
C(4')-C(4A')-C(9')	108.3(7)
C(5')-C(4A')-C(9')	110.1(7)
C(8A')-C(4A')-C(9')	111.4(6)
C(4A')-C(5')-C(6')	113.7(6)
C(5')-C(6')-C(7')	112.5(7)
C(6')-C(7')-C(8')	103.3(6)
C(6')-C(7')-C(14')	107.9(6)
C(8')-C(7')-C(14')	117.5(7)
C(6')-C(7')-C(20')	111.2(6)
C(8')-C(7')-C(20')	108.3(6)
C(14')-C(7')-C(20')	108.5(7)
O(2')-C(8')-C(7')	110.9(6)
O(2')-C(8')-C(8A')	112.3(6)
C(7')-C(8')-C(8A')	113.5(6)
C(1')-C(8A')-C(4A')	120.4(7)
C(1')-C(8A')-C(8')	125.7(7)
C(4A')-C(8A')-C(8')	113.9(7)
O(2')-C(10')-C(11')	102.7(6)
O(2')-C(10')-C(12')	109.5(8)
C(11')-C(10')-C(12')	109.4(6)
O(2')-C(10')-C(13')	112.8(6)
C(11')-C(10')-C(13')	111.2(9)
C(12')-C(10')-C(13')	110.9(7)
C(7')-C(14')-C(15')	124.7(9)
C(7')-C(14')-C(19')	117.6(8)
C(15')-C(14')-C(19')	117.6(9)
C(14')-C(15')-C(16')	119.6(11)
C(15')-C(16')-C(17')	122.5(11)
C(16')-C(17')-C(18')	117.3(11)
C(17')-C(18')-C(19')	121.1(13)
C(14')-C(19')-C(18')	121.8(10)
C(7')-C(20')-C(21')	119.1(7)
C(7')-C(20')-C(25')	122.2(7)
C(21')-C(20')-C(25')	118.6(7)
C(20')-C(21')-C(22')	119.9(8)
C(21')-C(22')-C(23')	120.9(9)
C(22')-C(23')-C(24')	119.7(8)
C(23')-C(24')-C(25')	119.4(10)
C(20')-C(25')-C(24')	121.5(9)

TABLE 7

BOND LENGTHS FOR COMPOUND **34**.

Atoms	Distance (Å)
O(1)-C(1)	1.375 (11)
O(2)-C(8)	1.447 (9)
O(2)-C(10)	1.502 (8)
C(1)-C(2)	1.493 (16)
C(1)-C(8A)	1.333 (13)
C(2)-C(3)	1.526 (15)
C(3)-C(4)	1.511 (13)
C(4)-C(4A)	1.536 (14)
C(4A)-C(5)	1.536 (10)
C(4A)-C(8A)	1.531 (11)
C(4A)-C(9)	1.544 (11)
C(5)-C(6)	1.525 (14)
C(6)-C(7)	1.559 (11)
C(7)-C(8)	1.560 (10)
C(7)-C(14)	1.536 (14)
C(7)-C(20)	1.533 (11)
C(8)-C(8A)	1.524 (13)
C(10)-C(11)	1.484 (13)
C(10)-C(12)	1.479 (16)
C(10)-C(13)	1.485 (14)
C(14)-C(15)	1.367 (14)
C(14)-C(19)	1.384 (14)
C(15)-C(16)	1.382 (16)
C(16)-C(17)	1.377 (18)
C(17)-C(18)	1.392 (17)
C(18)-C(19)	1.383 (16)
C(20)-C(21)	1.389 (10)
C(20)-C(25)	1.372 (13)
C(21)-C(22)	1.379 (14)
C(22)-C(23)	1.362 (17)
C(23)-C(24)	1.406 (13)
C(24)-C(25)	1.368 (12)
O(1')-C(1')	1.398 (11)
O(2')-C(8')	1.455 (8)
O(2')-C(10')	1.471 (10)
C(1')-C(2')	1.485 (11)
C(1')-C(8A')	1.316 (13)
C(2')-C(3')	1.534 (15)
C(3')-C(4')	1.526 (16)
C(4')-C(4A')	1.529 (9)
C(4A')-C(5')	1.536 (14)
C(4A')-C(8A')	1.532 (10)
C(4A')-C(9')	1.547 (12)
C(5')-C(6')	1.516 (10)

C(6')-C(7')	1.561 (11)
C(7')-C(8')	1.558 (13)
C(7')-C(14')	1.533 (12)
C(7')-C(20')	1.557 (9)
C(8')-C(8A')	1.515 (10)
C(10')-C(11')	1.519 (12)
C(10')-C(12')	1.514 (12)
C(10')-C(13')	1.496 (14)
C(14')-C(15')	1.371 (13)
C(14')-C(19')	1.388 (16)
C(15')-C(16')	1.393 (16)
C(16')-C(17')	1.369 (22)
C(17')-C(18')	1.366 (19)
C(18')-C(19')	1.369 (16)
C(20')-C(21')	1.380 (12)
C(20')-C(25')	1.382 (12)
C(21')-C(22')	1.391 (11)
C(22')-C(23')	1.370 (16)
C(23')-C(24')	1.378 (16)
C(24')-C(25')	1.382 (12)

TABLE 8

POSITIONAL PARAMATERS FOR COMPOUND **34**

Atom	x	y	z	U(eq)
O(1)	-103(3)	23(4)	3831(3)	64(3)
O(2)	549(2)	817(3)	3005(3)	47(2)
C(1)	-505(4)	844(7)	3713(5)	51(4)
C(2)	-964(5)	821(7)	4189(5)	77(5)
C(3)	-1268(5)	1790(8)	4243(5)	81(5)
C(4)	-1618(4)	2237(7)	3397(5)	64(4)
C(4A)	-1015(4)	2391(5)	3080(5)	47(4)
C(5)	-1441(4)	2537(6)	2143(5)	50(4)
C(6)	-929(4)	2572(5)	1705(5)	54(4)
C(7)	-449(4)	1665(5)	1825(5)	49(4)
C(8)	10(4)	1582(5)	2780(4)	45(4)
C(8A)	-493(4)	1542(6)	3229(5)	46(4)
C(9)	-551(4)	3277(6)	3492(6)	71(4)
C(10)	1364(4)	1004(7)	3601(6)	61(4)
C(11)	1669(5)	37(7)	3782(7)	106(6)
C(12)	1737(4)	1562(7)	3192(6)	85(5)
C(13)	1401(4)	1470(7)	4354(5)	77(5)
C(14)	107(4)	1756(6)	1436(5)	51(4)
C(15)	399(5)	2598(7)	1355(5)	64(5)
C(16)	914(5)	2664(8)	1024(6)	70(5)
C(17)	1154(5)	1874(10)	769(6)	83(6)
C(18)	848(5)	1015(8)	834(6)	76(5)
C(19)	331(5)	960(7)	1165(5)	61(5)
C(20)	-1007(4)	860(6)	1411(5)	48(4)
C(21)	-1527(5)	957(7)	589(5)	65(4)
C(22)	-2024(5)	246(9)	169(6)	86(5)
C(23)	-2021(5)	-578(8)	549(7)	79(6)
C(24)	-1477(5)	-700(6)	1372(6)	69(5)
C(25)	-1004(4)	23(6)	1785(5)	52(4)
O(1')	5202(3)	-26(4)	4004(3)	67(3)
O(2')	4571(2)	747(3)	2561(3)	43(2)
C(1')	5616(4)	806(7)	4268(5)	54(4)
C(2')	6042(4)	790(7)	5181(5)	76(5)
C(3')	6388(5)	1750(8)	5522(5)	88(5)
C(4')	6747(4)	2148(7)	4990(5)	70(4)
C(4A')	6153(4)	2315(6)	4102(4)	47(4)
C(5')	6581(4)	2440(6)	3569(5)	53(4)
C(6')	6062(4)	2476(6)	2651(5)	53(4)
C(7')	5580(4)	1565(5)	2328(4)	42(3)
C(8')	5119(4)	1511(5)	2845(4)	40(3)
C(8A')	5617(4)	1476(5)	3767(5)	42(4)
C(9')	5709(4)	3219(6)	4082(5)	66(4)
C(10')	3785(4)	965(6)	2413(5)	53(4)
C(11')	3422(4)	3(6)	2291(6)	73(5)

C(12')	3397(4)	1523(6)	1623(5)	76(5)
C(13')	3746(4)	1468(7)	3120(5)	72(5)
C(14')	6130(4)	759(6)	2418(5)	50(4)
C(15')	6223(5)	-21(6)	2897(6)	71(5)
C(16')	6751(7)	-701(7)	2941(7)	95(6)
C(17')	7177(5)	-634(9)	2512(8)	98(7)
C(18')	7083(5)	149(9)	2043(7)	82(6)
C(19')	6564(5)	823(7)	1984(5)	69(5)
C(20')	5006(4)	1658(6)	1402(5)	47(4)
C(21')	4757(4)	860(6)	927(5)	54(4)
C(22')	4230(5)	929(8)	103(5)	71(5)
C(23')	3948(4)	1780(9)	-246(6)	76(5)
C(24')	4194(5)	2582(8)	223(6)	79(5)
C(25')	4722(4)	2513(7)	1040(5)	61(4)
H(1A)	194	76	3603	80
H(2A)	-649	595	4735	80
H(2B)	-1388	402	3933	80
H(3A)	-854	2173	4608	80
H(3B)	-1642	1758	4452	80
H(4A)	-1855	2822	3407	80
H(4B)	-2006	1824	3028	80
H(5A)	-1750	3090	2025	80
H(5B)	-1777	2013	1918	80
H(6A)	-587	3091	1927	80
H(6B)	-1232	2681	1126	80
H(8A)	303	2147	2961	80
H(9A)	-875	3814	3397	80
H(9B)	-277	3168	4074	80
H(9C)	-197	3388	3265	80
H(11A)	2199	17	4165	80
H(11B)	1376	-283	4015	80
H(11C)	1595	-264	3277	80
H(12A)	2262	1687	3557	80
H(12B)	1706	1233	2715	80
H(12C)	1464	2142	3025	80
H(13A)	1920	1589	4739	80
H(13B)	1130	2053	4194	80
H(13C)	1166	1076	4606	80
H(15A)	264	3149	1565	80
H(16A)	1091	3262	934	80
H(17A)	1524	1906	556	80
H(18A)	989	463	632	80
H(19A)	140	362	1230	80
H(21A)	-1519	1517	299	80
H(22A)	-2393	324	-395	80
H(23A)	-2382	-1061	261	80
H(24A)	-1437	-1291	1642	80
H(25A)	-654	-50	2356	80
H(1'A)	4908	24	3491	80
H(2'A)	6451	345	5348	80
H(2'B)	5700	595	5404	80
H(3'A)	6753	1714	6091	80
H(3'B)	5985	2163	5478	80
H(4'A)	7100	1689	4977	80

H(4'B)	7025	2710	5230	80
H(5'A)	6908	1906	3669	80
H(5'B)	6896	2989	3737	80
H(6'A)	6357	2585	2352	80
H(6'B)	5722	2995	2553	80
H(8'A)	4823	2075	2734	80
H(9'A)	5334	3333	3527	80
H(9'B)	5462	3155	4436	80
H(9'C)	6060	3733	4267	80
H(11D)	3657	-344	2797	80
H(11E)	2883	44	2122	80
H(11F)	3511	-309	1871	80
H(12D)	2882	1678	1509	80
H(12E)	3683	2089	1686	80
H(12F)	3397	1164	1174	80
H(13D)	3980	1078	3600	80
H(13E)	4023	2045	3212	80
H(13F)	3229	1597	3013	80
H(15B)	5956	-62	3232	80
H(16B)	6789	-1261	3252	80
H(17B)	7541	-1107	2555	80
H(18B)	7379	213	1739	80
H(19B)	6495	1357	1635	80
H(21B)	4933	260	1180	80
H(22B)	4080	371	-227	80
H(23B)	3567	1803	-809	80
H(24B)	4013	3177	-36	80
H(25B)	4880	3070	1370	80

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

TABLE 9

ANISOTROPIC THERMAL PARAMETERS FOR COMPOUND **34**

Atom	U11	U22	U33	U23	U13	U12
O(1)	53(3)	64(4)	66(4)	17(3)	19(3)	21(3)
O(2)	35(2)	42(3)	51(3)	8(3)	6(2)	3(3)
C(1)	31(4)	76(7)	39(5)	2(5)	9(4)	11(5)
C(2)	66(6)	98(9)	52(6)	-5(6)	13(5)	13(6)
C(3)	47(5)	145(11)	51(6)	-9(6)	20(5)	-15(7)
C(4)	44(5)	82(7)	64(6)	-1(5)	22(5)	-10(6)
C(4A)	38(4)	45(5)	51(5)	-2(4)	13(4)	-10(5)
C(5)	37(4)	40(5)	67(6)	13(4)	18(4)	6(5)
C(6)	53(5)	43(5)	54(5)	7(4)	13(4)	2(5)
C(7)	45(4)	43(5)	54(5)	9(4)	18(4)	5(5)
C(8)	44(4)	35(5)	45(5)	7(4)	11(4)	-2(4)
C(8A)	37(4)	57(6)	41(5)	1(4)	14(4)	-3(5)
C(9)	37(4)	64(6)	93(7)	-4(4)	10(5)	-22(6)
C(10)	38(4)	67(7)	58(6)	5(5)	1(5)	-10(5)
C(11)	77(7)	80(8)	112(9)	4(6)	-2(7)	-7(7)
C(12)	39(5)	123(9)	82(7)	-21(6)	15(5)	-22(7)
C(13)	31(4)	112(9)	60(6)	- 5(5)	-7(4)	-13(6)
C(14)	51(5)	48(6)	53(5)	5(5)	23(4)	10(5)
C(15)	60(6)	71(7)	67(6)	-2(5)	32(5)	13(6)
C(16)	53(6)	74(8)	76(7)	-13(6)	20(5)	10(6)
C(17)	59(6)	118(10)	73(7)	8(7)	31(5)	25(8)
C(18)	58(6)	96(9)	84(7)	19(6)	40(6)	10(7)
C(19)	64(5)	55(7)	76(6)	6(5)	40(5)	8(5)
C(20)	49(5)	48(6)	47(5)	9(5)	20(4)	-1(5)
C(21)	52(5)	73(7)	48(6)	17(5)	1(5)	4(5)
C(22)	53(6)	99(9)	66(7)	12(7)	-11(5)	-16(8)
C(23)	45(5)	83(9)	94(9)	2(6)	16(6)	-39(7)
C(24)	68(6)	54(6)	79(7)	-21(5)	25(6)	-21(6)
C(25)	46(5)	48(6)	59(6)	3(5)	20(4)	-3(5)
O(1')	56(3)	67(4)	67(4)	-17(3)	16(3)	15(3)
O(2')	32(3)	42(3)	52(3)	-4(3)	15(2)	-6(3)
C(1')	38(4)	71(7)	51(6)	-9(5)	19(4)	-1(6)
C(2')	40(5)	119(9)	57(6)	-16(6)	10(5)	22(6)
C(3')	57(6)	149(11)	45(6)	-19(7)	11(5)	-6(7)
C(4')	41(4)	101(8)	53(6)	-23(5)	8(4)	-16(6)
C(4A')	37(4)	48(6)	49(5)	-6(4)	12(4)	-12(4)
C(5')	45(4)	55(6)	60(6)	-10(4)	23(4)	-13(5)
C(6')	55(5)	48(6)	56(6)	-5(4)	26(4)	-2(5)
C(7')	42(4)	38(5)	42(5)	1(4)	14(4)	-5(4)
C(8')	38(4)	33(5)	47(5)	-7(4)	16(4)	-6(4)
C(8A')	34(4)	42(5)	44(5)	-6(4)	13(4)	0(4)
C(9')	49(5)	64(7)	68(6)	-6(5)	9(5)	-21(5)

C(10')	47(5)	59(6)	49(5)	-3(5)	17(4)	-10(5)
C(11')	36(4)	81(7)	92(7)	-20(5)	19(5)	-19(6)
C(12')	40(4)	91(8)	82(7)	8(5)	12(5)	-4(6)
C(13')	37(4)	111(8)	72(6)	1(5)	27(4)	-15(6)
C(14')	44(4)	48(6)	54(6)	-7(5)	19(4)	-16(5)
C(15')	94(7)	37(6)	90(8)	12(6)	49(6)	5(6)
C(16')	93(8)	53(8)	120(10)	32(7)	31(8)	7(7)
C(17')	34(5)	93(10)	149(12)	19(6)	24(7)	-38(9)
C(18')	52(6)	96(9)	107(9)	-2(7)	41(6)	-35(8)
C(19')	66(6)	68(7)	73(7)	0(6)	31(5)	-11(6)
C(20')	36(4)	49(6)	53(6)	-4(4)	18(4)	6(5)
C(21')	38(4)	57(6)	53(6)	-9(4)	6(4)	-7(5)
C(22')	75(6)	81(8)	47(6)	-16(6)	18(5)	-8(6)
C(23')	37(5)	122(10)	55(6)	-14(6)	7(5)	7(8)
C(24')	79(7)	80(8)	69(7)	-8(6)	25(6)	23(7)
C(25')	54(5)	66(7)	54(6)	-4(5)	15(5)	3(5)

The anisotropic displacement exponent takes the form:

$-2\pi^2(H^2A^{*2}U_{11} + ... + 2HKA^*B^*U_{12})$

APPENDIX B

CRYSTALLOGRAPHIC DATA FOR (±)-2,4,4a,5,6,7,8,8a-OCTA-HYDRO-8-HYDROXY-4a,7,7-TRIMETHYL-1(2*H*)-NAPHTHALENONE (**39**)

TABLE 10

CRYSTAL DATA FOR COMPOUND **39**

Formula	$C_{13}H_{22}O_2$
M. W.	210.31 g $mole^{-1}$
a	24.149 (5) Å
b	6.2080 (10) Å
c	17.525 (3) Å
α	90°
β	114.450 (10) °
γ	90°
V	2445.3 (8) $Å^3$
F(000)	928
μMoKa	11.28 cm^{-1}
λMoKa	0.71073 Å
D_{calc}	1.142 Mg/m^3
Z	8
Meas refl	4450
Obs refl	3799
R	5.09%
R_W	10.45%
G. O. F.	.647
Space Group	Cc

TABLE 11

BOND ANGLES FOR COMPOUND **39**

Atoms	Angle (°)
O(2)-C(8)-C(7)	113.3(13)
O(2)-C(8)-C(8A)	106.7(13)
C(7)-C(8)-C(8A)	113.0(10)
C(4)-C(4A)-C(5)	108.4(13)
C(4)-C(4A)-C(9)	114.1(13)
C(5)-C(4A)-C(9)	105.7(13)
C(4)-C(4A)-C(8A)	111.5(12)
C(5)-C(4A)-C(8A)	108.8(12)
C(9)-C(4A)-C(8A)	108.2(12)
C(98A)-C(94A)-C(99)	110.3(13)
C(98A)-C(94A)-C(95)	110.6(11)
C(99)-C(94A)-C(95)	108.9(12)
C(98A)-C(94A)-C(94)	110.3(11)
C(99)-C(94A)-C(94)	102.7(12)
C(95)-C(94A)-C(94)	113.8(13)
C(93)-C(94)-C(94A)	114.6(13)
C(5)-C(6)-C(7)	111.6(13)
C(97)-C(96)-C(95)	111.9(13)
C(94A)-C(95)-C(96)	112.5(12)
C(910)-C(97)-C(96)	109(2)
C(910)-C(97)-C(911)	110.3(14)
C(96)-C(97)-C(911)	109.6(14)
C(910)-C(97)-C(98)	111(2)
C(96)-C(97)-C(98)	107.5(13)
C(911)-C(97)-C(98)	109.3(13)
C(8)-C(8A)-C(1)	109.2(10)
C(8)-C(8A)-C(4A)	114.9(11)
C(1)-C(8A)-C(4A)	109.6(12)
C(91)-C(98A)-C(94A)	115.7(11)
C(91)-C(98A)-C(98)	108.6(12)
C(94A)-C(98A)-C(98)	115.9(13)
C(93)-C(92)-C(91)	115.4(13)
O(1)-C(1)-C(2)	122(2)
O(1)-C(1)-C(8A)	115(2)
C(2)-C(1)-C(8A)	122(2)
C(8)-C(7)-C(10)	111.5(12)
C(8)-C(7)-C(6)	111.4(13)
C(10)-C(7)-C(6)	107.5(14)
C(8)-C(7)-C(9)	111(2)
C(10)-C(7)-C(9)	104.2(14)
C(6)-C(7)-C(9)	111.4(14)
O(92)-C(98)-C(98A)	107.2(14)
O(92)-C(98)-C(97)	109.4(13)
C(98A)-C(98)-C(97)	114.1(13)
C(6)-C(5)-C(4A)	116.7(11)
C(4A)-C(4)-C(3)	111.2(13)

C(2)-C(3)-C(4)	113.3(11)
C(94)-C(93)-C(92)	111.9(12)
O(91)-C(91)-C(98A)	128(2)
O(91)-C(91)-C(92)	117(2)
C(98A)-C(91)-C(92)	115.5(14)
C(1)-C(2)-C(3)	113.8(14)

Table 12

BOND DISTANCES FOR COMPOUND **39**

Atoms	Distance (Å)
C(8)-O(2)	1.43(2)
C(8)-C(7)	1.48(2)
C(8)-C(8A)	1.57(2)
C(4A)-C(4)	1.51(2)
C(4A)-C(5)	1.54(2)
C(4A)-C(9)	1.55(2)
C(4A)-C(8A)	1.566(14)
O(92)-C(98)	1.41(2)
C(94A)-C(98A)	1.50(2)
C(94A)-C(99)	1.56(2)
C(94A)-C(95)	1.51(2)
C(94A)-C(94)	1.54(2)
C(94)-C(93)	1.47(2)
C(6)-C(5)	1.54(2)
C(6)-C(7)	1.54(2)
C(96)-C(97)	1.53(2)
C(96)-C(95)	1.53(2)
C(97)-C(910)	1.49(2)
C(97)-C(911)	1.53(2)
C(97)-C(98)	1.54(2)
C(8A)-C(1)	1.54(2)
C(98A)-C(91)	1.46(2)
C(98A)-C(98)	1.52(2)
C(92)-C(93)	1.50(2)
C(92)-C(91)	1.57(2)
C(1)-O(1)	1.25(2)
C(1)-C(2)	1.45(3)
C(7)-C(10)	1.54(2)
C(7)-C(9)	1.56(2)
C(4)-C(3)	1.57(2)
O(91)-C(91)	1.17(2)
C(3)-C(2)	1.51(2)

TABLE 13

POSITIONAL PARAMETERS FOR COMPOUND **39**

Atom	x	y	z	U(eq)
C(8)	3018(8)	2431(26)	7391(10)	48(4)
C(4A)	2508(8)	2174(26)	5777(10)	48(4)
O(92)	4631(7)	4731(20)	3352(9)	79(4)
C(94A)	5302(9)	2798(23)	5043(11)	51(4)
O(2)	3187(7)	211(15)	7513(10)	67(3)
C(94)	5208(8)	5189(23)	5206(12)	47(4)
C(6)	1922(9)	1829(27)	6768(12)	60(4)
C(96)	5859(8)	3177(30)	4079(12)	69(5)
C(95)	5876(8)	2370(28)	4911(11)	58(4)
C(97)	5366(10)	2088(28)	3369(12)	58(4)
C(8A)	3033(7)	3087(28)	6533(10)	62(5)
C(98A)	4780(8)	1966(23)	4332(10)	47(4)
C(92)	4121(8)	4768(28)	4663(11)	67(5)
C(1)	3632(8)	2382(34)	6485(12)	56(5)
C(7)	2439(9)	2882(29)	7468(11)	55(4)
C(10)	2421(9)	2015(31)	8283(10)	90(6)
C(98)	4773(9)	2526(29)	3483(12)	65(5)
C(99)	5332(9)	1684(30)	5852(12)	70(5)
C(5)	1922(8)	2489(29)	5922(12)	72(5)
O(1)	4042	3728(27)	6741	107(5)
C(4)	2586(9)	-200(25)	5659(13)	71(5)
C(9)	2451(10)	3574(30)	5023(11)	79(5)
O(91)	3769(3)	1364(25)	4123(4)	83(4)
C(3)	3189(8)	-650(26)	5539(11)	58(4)
C(93)	4653(9)	5637(28)	5341(13)	86(6)
C(91)	4196(8)	2444(34)	4358(11)	65(5)
C(9)	2343(10)	5363(24)	7510(14)	72(5)
C(911)	5342(9)	3064(25)	2557(12)	78(5)
C(910)	5486(10)	-272(31)	3384(14)	105(7)
C(2)	3724(8)	243(35)	6222(11)	82(6)
H(8A)	3319(8)	3249(26)	7801(10)	80
H(92A)	4458(7)	4958(20)	2841(9)	80
H(2A)	3362(7)	-38(15)	8021(10)	80
H(94A)	5176(8)	5931(23)	4711(12)	80
H(94B)	5547(8)	5755(23)	5642(12)	80
H(6A)	1550(9)	2155(27)	6824(12)	80
H(6B)	1975(9)	296(27)	6815(12)	80
H(96A)	6232(8)	2843(30)	4027(12)	80
H(96B)	5810(8)	4713(30)	4056(12)	80
H(95A)	5940(8)	841(28)	4933(11)	80
H(95B)	6197(8)	3011(28)	5354(11)	80
H(8AA)	2996(7)	4624(28)	6477(10)	80
H(98A)	4777(8)	423(23)	4370(10)	80
H(92B)	4091(8)	5696(28)	4211(11)	80

H(92C)	3764(8)	4936(28)	4779(11)	80
H(10A)	2488(9)	490(31)	8289(10)	80
H(10B)	2732(9)	2673(31)	8735(10)	80
H(10C)	2044(9)	2285(31)	8333(10)	80
H(98B)	4476(9)	1666(29)	3084(12)	80
H(99A)	5393(9)	163(30)	5822(12)	80
H(99B)	5657(9)	2290(30)	6298(12)	80
H(99C)	4966(9)	1931(30)	5938(12)	80
H(5A)	1605(8)	1717(29)	5519(12)	80
H(5B)	1830(8)	3997(29)	5852(12)	80
H(4A)	2280(9)	-521(25)	5140(13)	80
H(4B)	2529(9)	-1117(25)	6065(13)	80
H(9A)	2145(10)	3060(30)	4533(11)	80
H(9B)	2357(10)	5010(30)	5139(11)	80
H(9C)	2825(10)	3580(30)	4947(11)	80
H(3A)	3175(8)	-190(26)	5010(11)	80
H(3B)	3244(8)	-2184(26)	5564(11)	80
H(93A)	4627(9)	7138(28)	5455(13)	80
H(93B)	4664(9)	4821(28)	5812(13)	80
H(9D)	2658(10)	6027(24)	7955(14)	80
H(9E)	2334(10)	5951(24)	7000(14)	80
H(9F)	1969(10)	5636(24)	7570(14)	80
H(91A)	5724(9)	2826(25)	2518(12)	80
H(91B)	5040(9)	2353(25)	2111(12)	80
H(91C)	5261(9)	4582(25)	2532(12)	80
H(91D)	5492(10)	-984(31)	3874(14)	80
H(91E)	5161(10)	-821(31)	2922(14)	80
H(91F)	5854(10)	-532(31)	3308(14)	80
H(2B)	3877(8)	-729(35)	6677(11)	80
H(2C)	4024(8)	421(35)	5989(11)	80

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

TABLE 14

ANISOTROPIC THERMAL PARAMETERS FOR COMPOUND **39**

Atom	U11	U22	U33	U23	U13	U12
C(8)	42(6)	51(10)	32(6)	-11(7)	-8(5)	1(7)
C(4A)	47(7)	57(9)	26(5)	2(7)	-5(5)	-26(8)
O(92)	95(8)	112(10)	32(4)	28(6)	26(5)	13(9)
C(94A)	85(10)	26(8)	49(7)	12(7)	32(7)	20(8)
O(2)	88(7)	43(6)	63(6)	9(5)	20(5)	35(6)
C(94)	33(6)	54(9)	50(7)	-20(7)	12(5)	-11(7)
C(6)	84(10)	43(10)	64(9)	-1(9)	39(8)	13(9)
C(96)	38(7)	90(13)	74(10)	29(10)	17(7)	-1(9)
C(95)	61(8)	53(10)	56(8)	-3(8)	17(6)	-16(8)
C(97)	82(10)	44(10)	58(8)	1(9)	38(8)	12(10)
C(8A)	42(7)	91(12)	34(6)	18(8)	-8(5)	-35(8)
C(98A)	84(9)	28(7)	36(6)	-4(6)	30(6)	12(7)
C(92)	80(10)	72(12)	70(9)	-8(10)	53(8)	14(10)
C(10	54(9)	64(12)	43(8)	-3(9)	7(6)	-14(10)
C(7)	52(7)	57(10)	41(7)	9(8)	1(6)	3(9)
C(10)	82(9)	135(16)	42(7)	14(10)	10(6)	15(11)
C(98)	97(11)	43(11)	70(9)	17(8)	50(8)	-5(9)
C(99)	77(10)	44(9)	72(9)	15(8)	7(8)	0(9)
C(5)	54(8)	65(12)	71(10)	8(9)	-9(7)	19(9)
O(1)	104(9)	145(13)	80(8)	-45(10)	41(7)	-67(11)
C(4)	103(11)	43(10)	61(9)	17(8)	25(8)	-13(10)
C(9)	123(13)	73(11)	34(7)	12(8)	22(8)	-5(11)
O(91)	67(7)	132(12)	43(6)	-29(8)	11(5)	-44(9)
C(3)	87(10)	55(10)	50(8)	1(8)	46(7)	6(9)
C(93)	82(12)	58(11)	89(11)	-2(10)	-2(9)	-35(10)
C(91)	61(9)	103(15)	29(7)	-10(9)	13(6)	-34(11)
C(9)	93(11)	38(10)	76(10)	-24(9)	19(9)	-11(10)
C(911)	136(13)	44(9)	97(11)	-5(9)	92(10)	-17(10)
C(910)	134(15)	110(15)	99(13)	28(12)	74(11)	62(13)
C(2)	47(8)	126(17)	50(8)	21(11)	-10(6)	-8(11)

The anisotropic displacement exponent takes the form:

$-2\pi^2(H^2A^{*2}U_{11} + ... + 2HKA^*B^*U_{12})$

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VITA

Rodney Shawn Childress

Candidate for the Degree

of Doctor of Philosophy

Thesis: I. PHOTOINDUCED NUCLEOPHILIC ADDITION TO *s*-CIS NAPHTHALENONES II. TANDEM DEALKOXYCARBONYLATION-MICHAEL ADDITION ROUTE TO CHROMANS III. PHOTOENOLIZATION STUDIES OF HETEROAROMATIC COMPOUNDS

Major Field: Chemistry

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