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Photogeneration and Chemistry of *o*-Quinone Methides

by

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ABSTRACT

The photochemistry of several *o*-hydroxybenzyl alcohols has been studied in aqueous alcohol solution. The aim of this investigation is to achieve a comprehensive understanding of the photochemical behaviour of these substrates in aqueous solution, which may involve synthetically and biochemically important *o*-quinone methides (*o*-QM) as critical intermediates.

In general, photolysis of these compounds in aqueous alcohol solutions results in an efficient photosolvolysis to give the corresponding ethers. Photolysis of the substrates in the presence of electron-rich dienophiles results in a regiospecific [4 + 2] Diels-Alder type addition, to give the corresponding 2-substituted chroman derivatives in good yields, implicating the involvement of *o*-QM intermediates. Product quantum yield measurements indicate that the formation of *o*-QM's is very efficient. It is estimated that $\Phi_p = 0.29$ for formation of the parent *o*-QM (**1**) and $\Phi_p = 0.58$ for formation of the phenyl substituted *o*-QM (**113**), from the corresponding benzyl alcohols in 50% CH_3CN-H_2O. The mechanism of reaction is believed to involve adiabatic deprotonation of the phenol form of the substrate upon excitation to S_1, to generate the phenolate ion in the singlet excited state, which subsequently reacts by dehydroxylation, to give the reacting *transoid-o*-QM. The *transiod-o*-QM is then trapped by alcohol to give a Michael type addition product, or trapped by H_2O to regenerate the starting material. It will also react with electron-rich dienophiles in a formal *endo* addition manner to give the corresponding [4 + 2] cycloaddition products.

The photosolvolytic behaviour of *o*-aminobenzyl alcohol has also been studied in aqueous solution over a range of pH and in moderately concentrated aqueous H_2SO4. Although reactive at all pH's studied, clean solvolytic reaction was observed only when $pH < pK_a$. The reaction in acidic medium is believed to proceed *via* adiabatic deprotonation of the protonated substrate in S_1 to give the excited free amine, which subsequently dehydroxylates to give protonated *o*-QMI (or dehydrates to give free *o*-QMI) as the reactive intermediate. Nucleophilic attack by added ROH gives the photosolvolytic product.

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TABLE OF CONTENTS

Preliminary Pages

List of Tables

List of Figures

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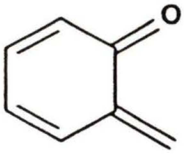
To my wife, Fenglin Yu, and our son, the little Harvey

1. Introduction

1.1 Quinone Methides

Quinone methides are derived from quinones by replacement of one of the carbonyl oxygens by a methylene or substituted methylene group. They are also known as methylenequinones or quinone methines. They are labile organic compounds belonging to the class of unsaturated conjugated ketones. The study of these substances has developed vigorously during the past decades primarily owing to their unique structure, high reactivity, and the role which they play in many chemical and biological reactions.[1-5]



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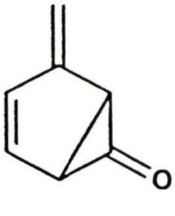

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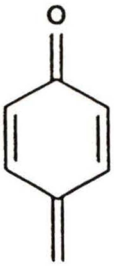

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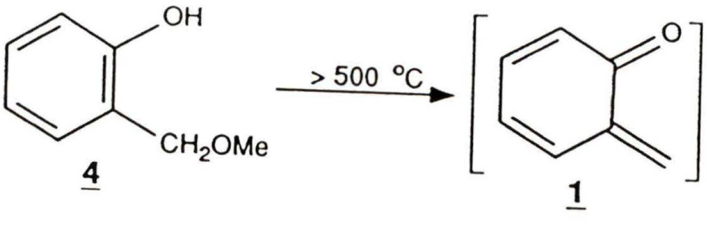
There are three structural isomers of simple quinone methides, namely, *ortho*-quinone methide (**1**) (*o*-QM, 6-methylenecyclohexa-2,4-dienone), *meta*-quinone methide (**2**) (*m*-QM, 4-methylene-2-oxo-bicylco[3.1.0]hexa-5-ene) and *para*-quinone methide (**3**) (*p*-QM, 4-methylenecyclohexa-2,5-dienone). The *p*-QM's are believed to be involved in many biochemical processes and hence have been intensively studied during the last three decades.[4,5] Like the corresponding *m*-quinonedimethanes,[6] *m*-QM's can apparently exist only as biradical intermediates with very short lifetimes.[4] Hitherto their chemistry has not been well documented. The *o*-QM's are also believed to be involved in some biochemical processes as well as being useful in organic synthesis.[1-4,7-15] Therefore the generation and chemistry of *o*-QM's have drawn much attention from both synthetic and mechanistic organic chemists in recent years.[7-30] In the following text we will discuss only *o*-QM's unless otherwise indicated.

1.2 Chemical Properties of *o*-Quinone Methides

1.2.1 General Reactivity

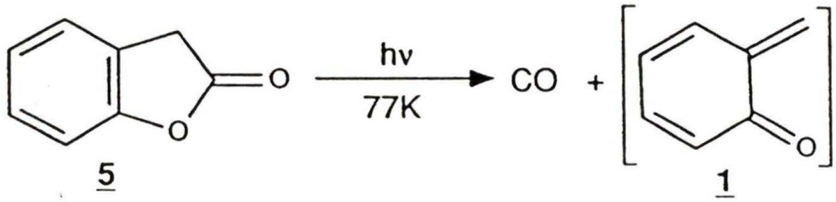
Simple *o*-QM's are unstable molecules that self-condense spontaneously. Some of them are nevertheless sufficiently stable, in dilute solution or at low temperature, to allow studies of their properties. The parent member of the *ortho* series, **1**, has been matrix isolated[31] by flash vacuum thermolysis (FVT) of *o*-(methoxymethyl)phenol (4) (eq. 1).



(1)

On warming to -50 °C, the pyrolysate liquifies and appears quite stable. The liquid then spontaneously trimerizes to a solid upon further warming to -20 °C. Chapman and McIntosh[32] successfully recorded the

IR spectrum of **1**, by irradiation of benzofuran-2(3*H*)-one (**5**) (eq. 2) at 77 K in a low-temperature IR cell. Attempts to isolate more stable *o*-QM's have also succeeded. Nakayama *et al.*[33] isolated compounds **6a-6c**, which are thermally stable. For example, **6c** melts at 284-285 °C without decomposition. Koutek and co-workers[34] obtained pure **7**, while **8** exists only in solution as an equilibrium mixture with its dimer. Arduini and co-workers[35] obtained **10** by oxidation of **9** with Ag_2O (eq. 3). Recrystallization of crude **10** from Et_2O affords a pale orange crystal. The X-ray structural analysis of **10** indicates a *transoid*-configuration for the α,β-unsaturated ketone moiety.



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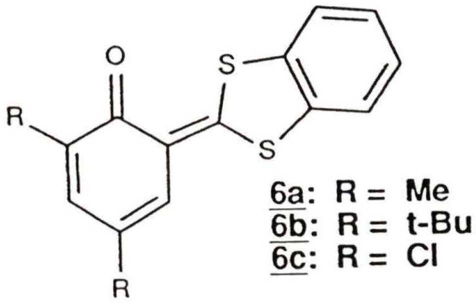
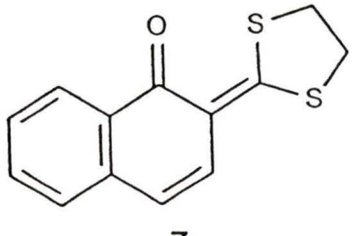


6a: R = Me
6b: R = t-Bu
6c: R = Cl



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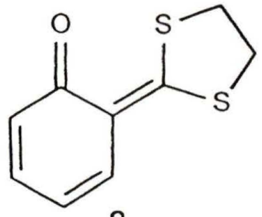

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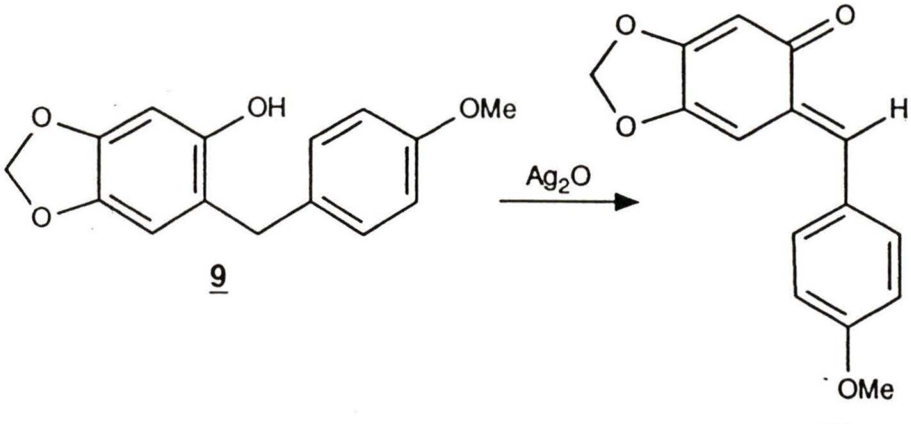
o-QM's are in general much more reactive than simple α,β-unsaturated ketones, owing to the additional driving force for transformation of their high energy quinoid structures into more stable benzenoid products which characterizes all their reactions.[36, 37] The typical reactions of *o*-QM's include:[37] 1,4-addition



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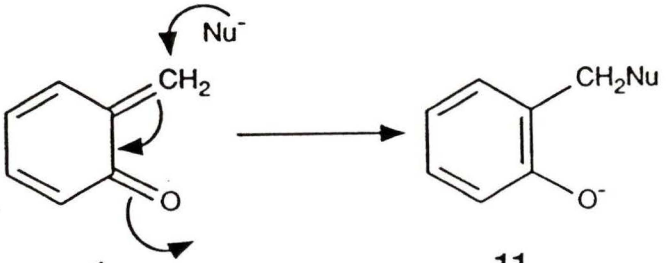
(3)

to afford phenol products;[38, 39] reaction with dienophiles as electron-deficient "dienes" in a Diels-Alder type cycloaddition to give benzoheterocycles;[40] and in the absence of a suitable trapping agent, self-condense to give the dimer, the trimer, and even oligomers.[41]

1.2.2 1,4-Addition

By virtue of the conjugated system, the *o*-QM's have two reaction centres: a nucleophilic centre at the oxygen of the carbonyl, and an electrophilic center at the carbon of the methylene unit. Depending on the nature of the attacking agent, the reaction can be directed initially to either of the centres indicated. In both cases, the result of the reaction is the same 1,4-addition with formation of phenol derivatives. Naturally, the reactions with electrophiles, *e.g.*, hydronium ion, begin with attack on the electronegative oxygen atom of the carbonyl group. Thus the reaction of *o*-QM's with protic acids, *e.g.*, acetic acid, can be assumed to involve the electrophilic attack of proton on the oxygen atom in the primary step.[39]

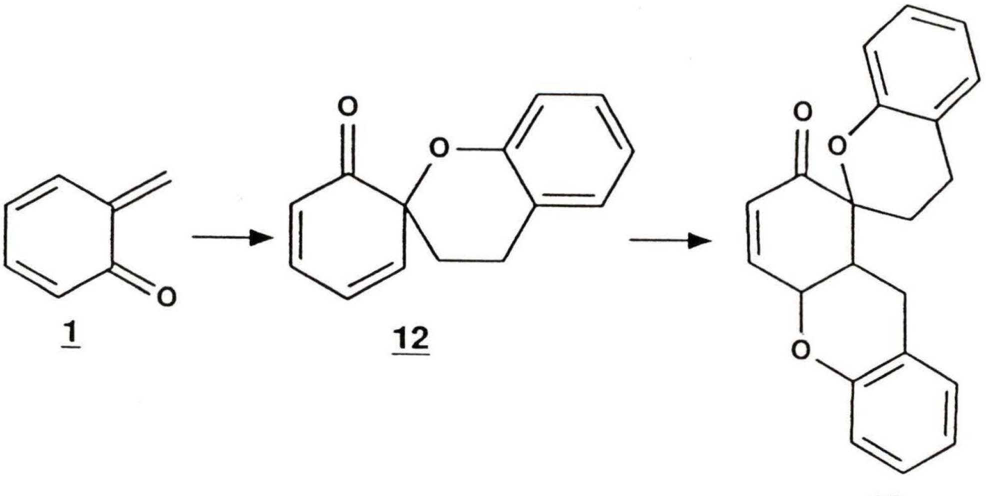


1 11 (4)

However, the most characteristic and most common reaction of *o*-QM's (and all quinone methides in general) is the susceptibility to attack by nucleophiles at the methylene carbon atom (eq. 4).[2, 4, 38] Nucleophiles involved in this process include alcohols, amines, Grignard reagents, metal hydrides, phenols, thiourea, water, cyanides, and active methylene compounds.

1.2.3 [4 + 2] Cycloaddition

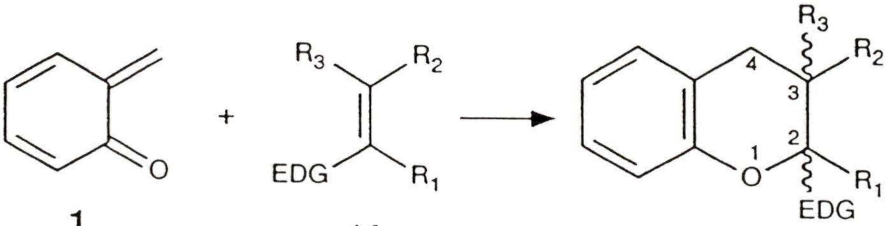
It was recognized as early as 1907[42] that *o*-QM's gave dimers and/or



1 12 13 (5)

trimers by a Diels-Alder [4 + 2] type reaction, in which one molecule adds across a double bond of another (eq. 5). Attempts to isolate **12** and dimers of other simple *o*-QM's were unsuccessful, due to their ready ability to give the trimer **13**. Although there are several possible isomers of **13**, independent results from three groups[41, 43, 44] have shown that, for **1** and its simple derivatives, only trimer **13** has been observed.

Just as in their self-condensation, so too will *o*-QM's react with electron-rich dienophiles, to give chroman derivatives (eq. 6).[2,4,9,11,27] The Diels-Alder type

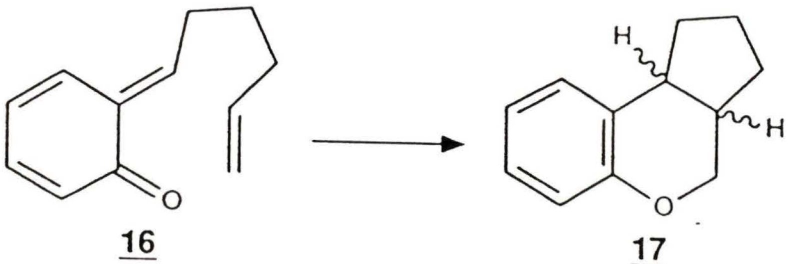


1 14 15 (6)

EDG: electron-donating group

adducts **15** are found to be completely regiospecific (the EDG ends up at the 2-position).[2,4,9,11,18,27,32] This can be explained in terms of the frontier molecular orbital interaction of the LUMO of *o*-QM (as the "diene") and the HOMO of the electron-rich alkene (*vide infra*).[45] *o*-QM's in general do not react with electron-deficient alkenes such as methyl acrylate, maleic anhydride, and acrylonitrile, whereas they do react with electron-rich alkenes. That is, *o*-QM's preferentially behave as "electron-deficient dienes". Therefore, the reaction of *o*-QM's with "dienophiles" may be regarded as an example of an "inverse-electron-demand" Diels-Alder reaction.

Unlike the intermolecular reaction, however, *o*-QM's do react with alkenes substituted with mildly electron-releasing (alkyl) or electron-withdrawing substituents when carried out intramolecularly (eq. 7).[46] This intramolecular reaction is a versatile method for assembling complex polycyclic structures in a single step which has been found useful in organic synthesis, especially in natural product and biomimetic syntheses. Other intramolecular type reactions involving *o*-QM intermediates, as for examples, the isomerization to the alkenyl phenols,[47] the electric ring closure to give chromenes,[48] the ring closure followed by a sigmatropic [1,7]-H shift to afford xanthenes,[49] have also been documented.



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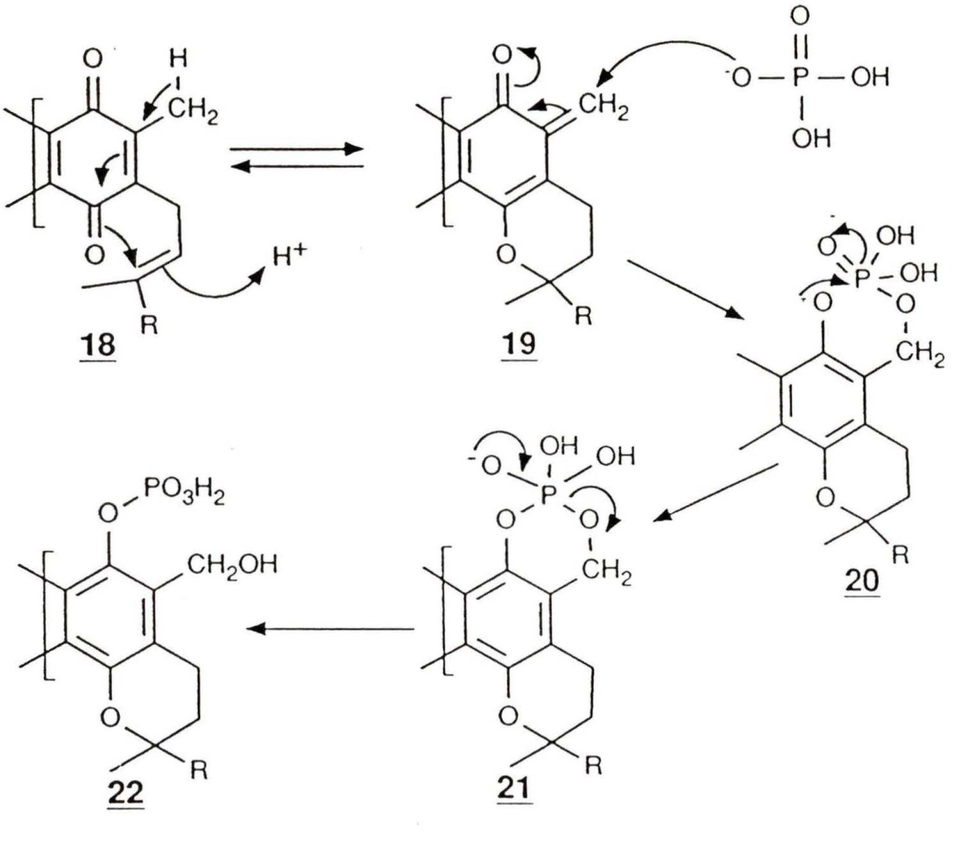
1.3 *o*-Quinone Methides as Biochemical Intermediates

o-QM's are suspected to be reactive intermediates in many biochemical processes, in which they are thought to arise either by tautomeric rearrangement of a quinone or by oxidation of phenols.[4,6,53] The participation of quinones in the vital processes of electron transport along the respiratory chain and in the phosphorylations which accompany oxidation has been well documented.[4,50,51] A theory for the reaction cycle operating during oxidative phosphorylation of Vitamin K and relative compounds has been suggested by Vilkas and Lederer,[50] as shown by eq. 8. Quinones of this series (partial structure **18**), in the presence of

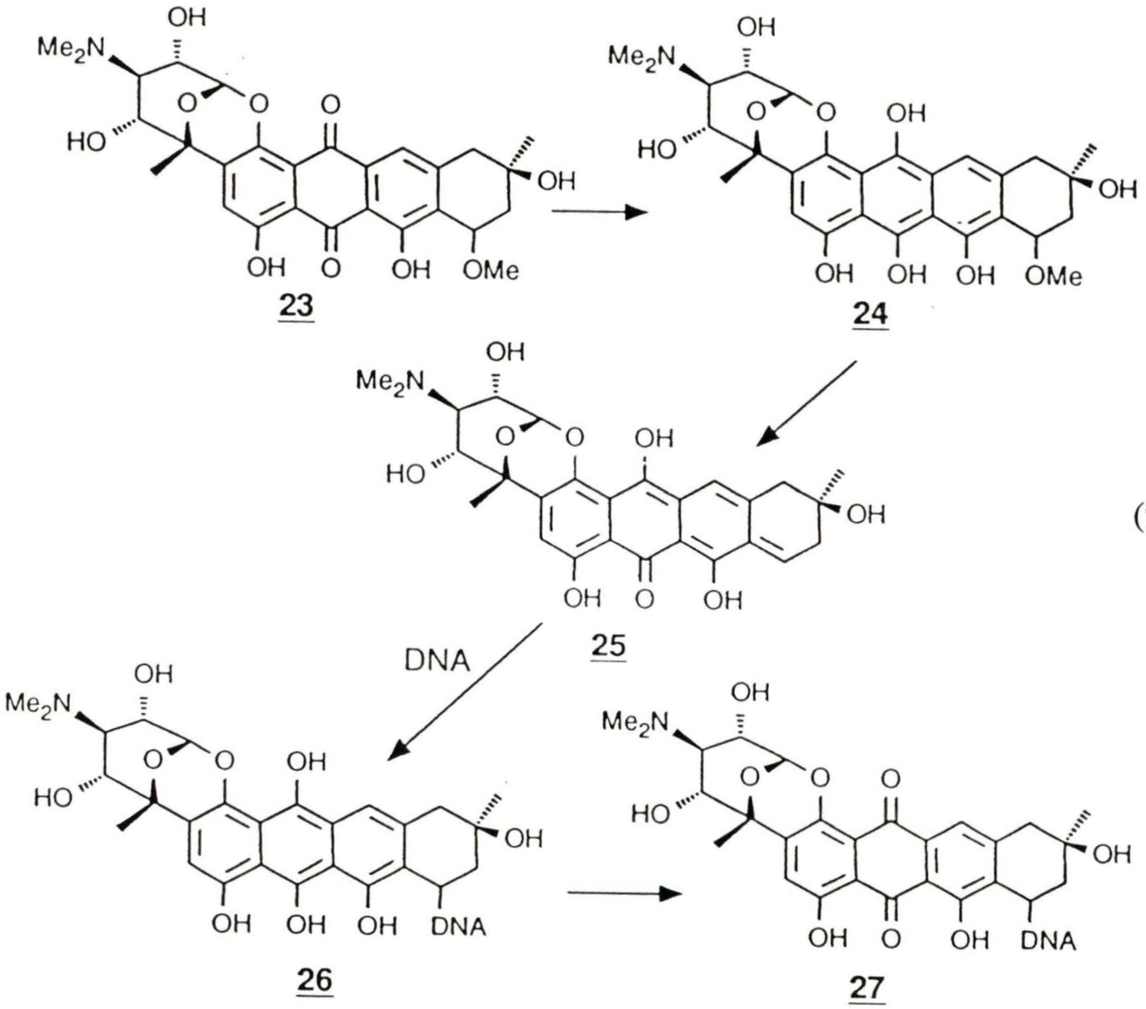


(8)

hydronium ion, rearrange to *o*-QM's (partial structure **19**). Nucleophilic attack of **19** by phosphate anion at the terminal methylene group affords **20**, which then undergoes intramolecular migration of the phosphate group to the phenolic oxygen by way of the cyclic phosphate **21**, to give the active quinol phosphates **22**. The ease of transformation from **18** to **19** is apparent from the ready formation of *o*-

QM-type dimers.[50, 51] In addition, *o*-QM **19** of Vitamin K and uniquinone series has been trapped by dienophiles.[51]

Based on earlier work of Lin and Sartorelli,[52] Moore[53] developed a theory of bioreductive alkylation to rationalize the biological activity of quinoid



(9)

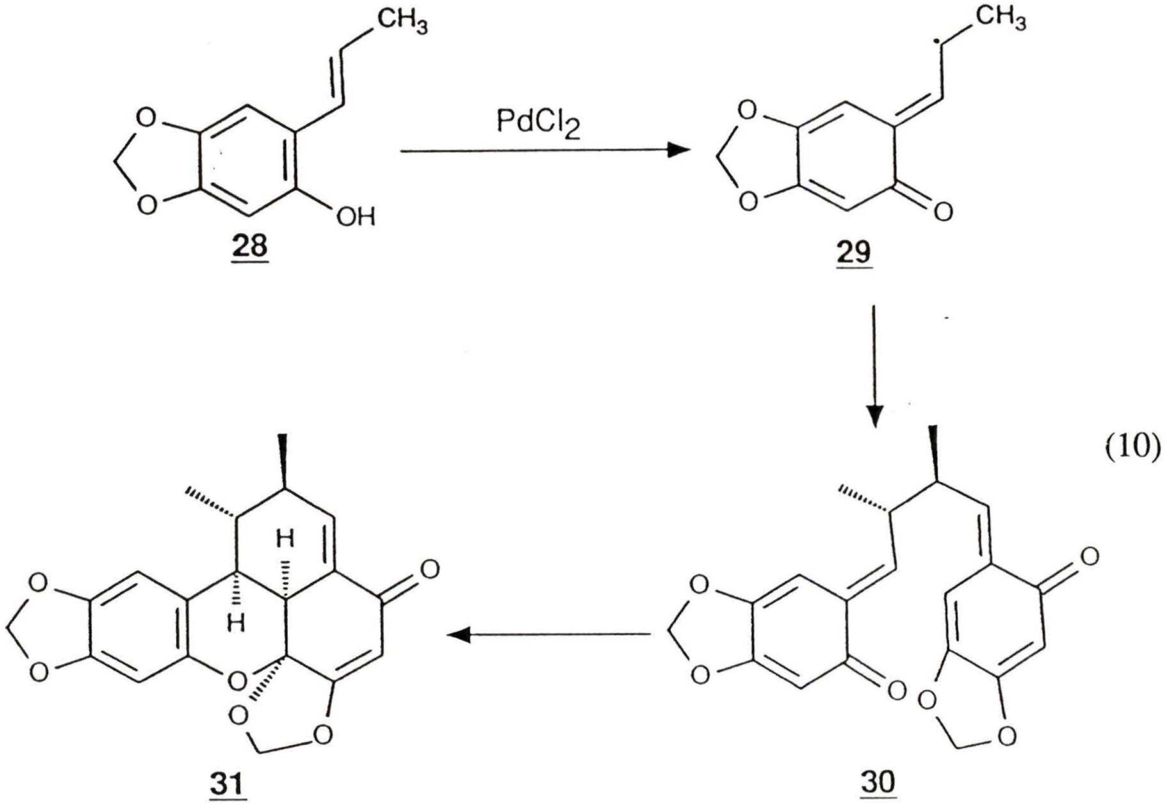
antitumour compounds. This theory calls for several hundred structurally similar anthracyclines to derive their antitumour activity via the same general type of process: reduction of a quinone to a hydroquinone followed by the loss of leaving group at the benzylic position, usually a sugar, to afford an *o*-QM. The *o*-QM then act as an electrophile towards some critical cellular macromolecule such as DNA, to afford a new hydroquinone which then undergoes oxidation back to a quinone. The tumour cell toxicity is proposed to result from the reaction of the *o*-QM with a nucleophilic site in DNA. This process is illustrated for menogaril (**23**) in eq. 9. Convincing evidence has been provided for the intermediacy of *o*-QM's in the chemistry of some of these antitumour compounds.[54] Study on the chemistry and mode of the action of these compounds have also provided indirect evidence for the alkylation of DNA.[55]

1.4 *o*-Quinone Methides in Synthesis

o-QM's are important intermediates in synthesis. They undergo inter- and intramolecular Diels-Alder reactions, to furnish polycyclic oxygen heterocycles,[9-11,20-27] ring closure to give chromenes,[58] and very easy Michael addition to afford *ortho*-substituted phenols.[17] Summarised below are some elegant syntheses which required the use of an *o*-QM in a crucial step.

1.4.1 Total Synthesis of Carpanone

Carpanone (**31**), a lignan obtained from the bark of the carpano tree, poses a significant synthetic challenge. The molecule possesses no element of symmetry and has five contiguous asymmetric centres. In the presence of $PdCl_2$, phenol **28** is oxidized to give radical **29**. Two molecules of **29** are then coupled together to afford bis-*o*-QM 30, which then undergoes *in situ* intramolecular Diels-Alder reaction to furnish **31** (eq. 10).[59] The total yield of crystalline **31** is 46%. The intermediate bis-*o*-QM **30** was not detected even at the early stage of the reaction, indicating that the intramolecular Diels-Alder reaction is fast. This elegant synthesis introduces five contiguous asymmetric centres with the correct relative stereochemistry in a single step with high yield. Moreover, this approach has particular appeal because it may be related to the biosynthesis of **31**: in the biochemical system, **31** may also be synthesized with simple coupling of **29**, which is formed by the oxidation of carpacin or its demethylated derivative **28**.[60,72] A similar synthetic approach to carpanone by oxidative coupling of phenols, using



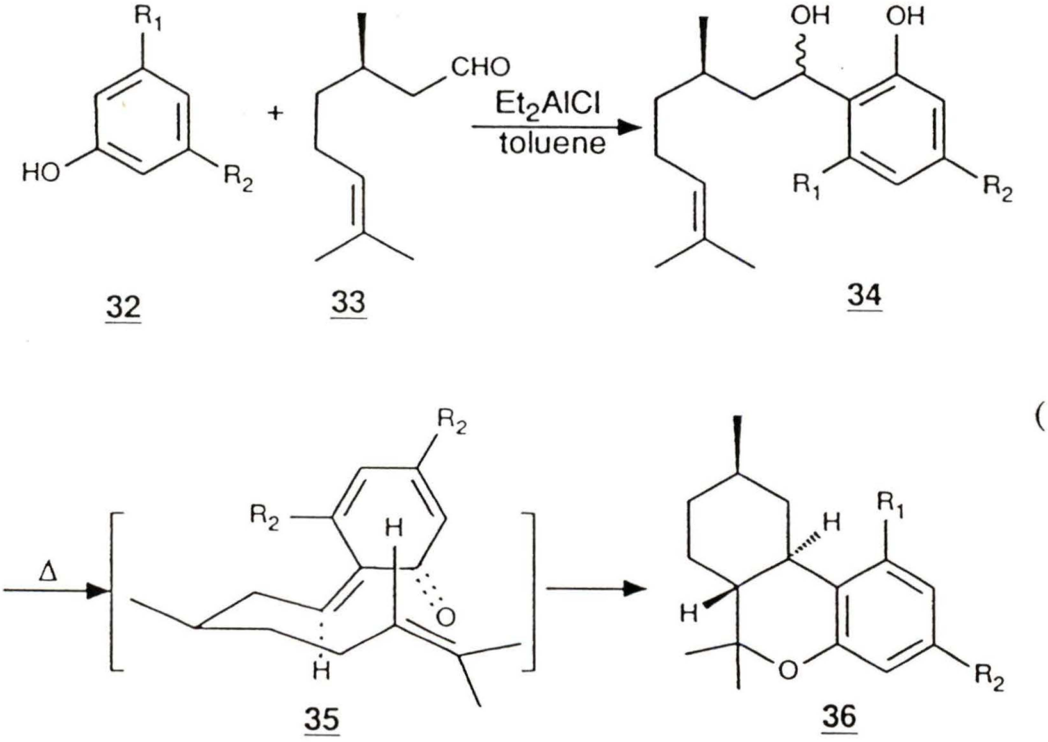
28 29 30 31

(10)

Cobalt(II) bis(3-salicylideneaminopropyl)amine as catalyst, has also been achieved by Matsumoto and Kuroda.[72]

1.4.2 Synthesis of Hexahydrocannabinol (HHC)

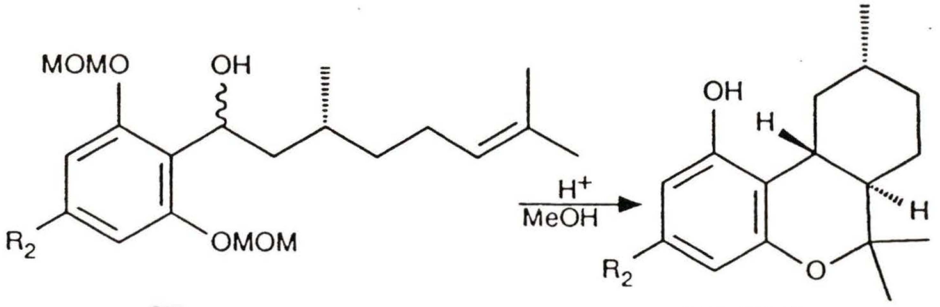
HHC (**36**, R_1 = OH, R_2 = C_5H_{11}) is an unnatural, psychotropically active compound closely related to natural cannabinoids which has been the focus of recent synthetic attention. Several elegant syntheses of HHC and relatives based on the intramolecular cycloaddition of *o*-QM's have been documented.[9,26,28,61]



(11)

Casiraghi and co-workers[61] have reported a simple entry to both enantiomers of HHC and their relatives. The key step involves Et_2AlCl-assisted coupling of suitable phenols **32** with (*R*)-(+)- or (*S*)-(-)-citrinellal (**33**), to afford the *o*-

hydroxybenzyl alcohol **34**, which in the presence of Lewis acid Et_2AlCl, undergoes dehydration to give the *o*-QM **35**. Subsequent *in situ* regio- and stereospecific intramolecular Diels-Alder reaction gave enantiomerically pure **36** (R_1 = OH, R_2 = C_5H_{11}) with a reasonable yield (≥ 50%) (eq. 11). The formation of a single diastereomer in the intramolecular Diels-Alder reaction is consistent with the cycloaddition reaction proceeding through a preferred *exo* transition state from a chair conformation possessing an equatorial methyl substituent. Lu *et al.*[9] have



37

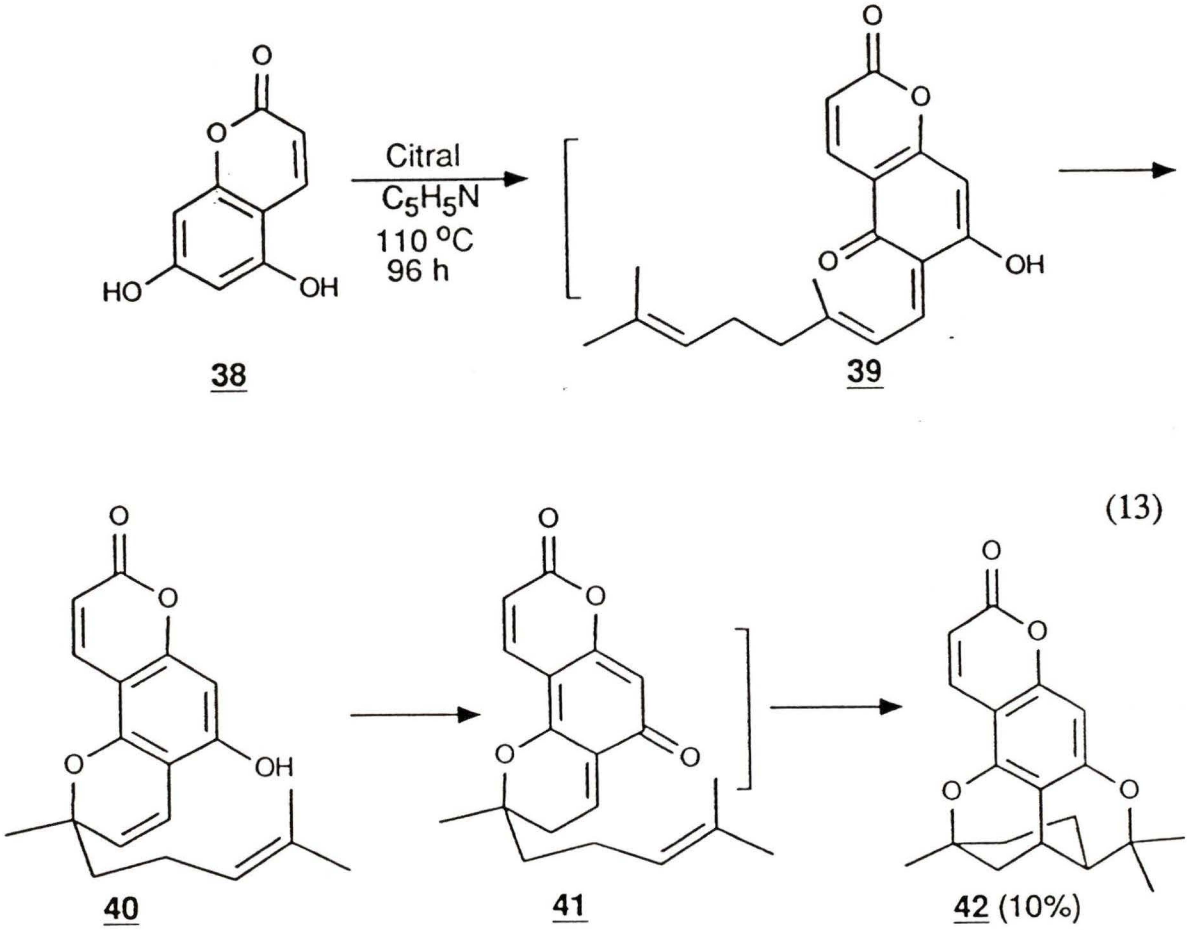
36 (93%)

(12)

reported a similar procedure under milder conditions. When treated with 0.5 equivalent of *o*-toluenesulfonic acid in methanol at reflux, the protected phenol **37** dehydrates to afford *o*-QM **35**, which then gives **36**, in 93% yield (eq. 12).

1.4.3 Biomimetic Total Synthesis of (±)-Deoxybruceol

A two-step biomimetic total synthesis of (±)-deoxybruceol (**42**) has been reported.[62] The second step of this synthesis is the condensation of 5,7-dihydroxycoumarin (**38**) with citral in the presence of pyridine (eq. 13). This stereospecific reaction can be rationalized as follows. The first reaction of **38** with citral is a condensation to give *o*-QM **39**, which then undergoes an electrocyclic ring closure to afford **40**. The *o*-hydroxystyrene moiety of chromene **40** then undergoes a [1,5]-hydrogen shift to give the isomeric *o*-QM **41**, which then undergoes an intramolecular Diels-Alder reaction to furnish **42** in 10% yield. This mechanism is reasonable since the chromene intermediate **40** has been isolated and thermally converted to **42**.[63]



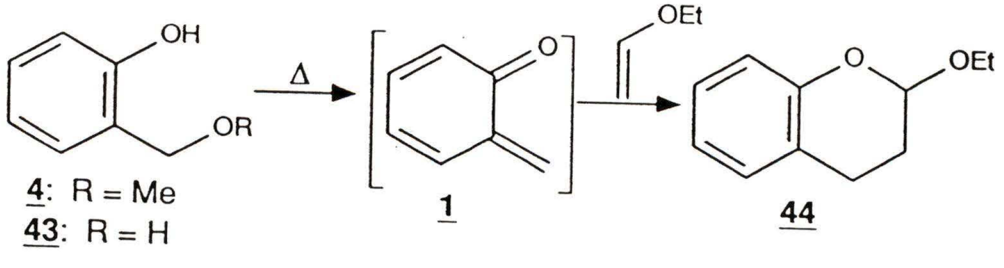
(13)

1.5 Thermal Generation of *o*-Quinone Methides

The methodologies for the thermal generation of *o*-QM's have been intensively studied. The various methods reported (some already discussed above) includes dehydration of *o*-hydroxybenzyl derivatives, elimination of Mannich bases, oxidation of substituted *o*-alkylphenols, desilylation of disilylated *o*-hydroxybenzyl alcohols, Lewis acid catalyzed dethiolation of *o*-(α-(alkylthio)alkyl)phenols, and thermolysis of 2-phenyl-4*H*-1,3,2-benzodioxaborins and *o*-(α-benzotriazolylalkyl)phenols.

1.5.1 Dehydration of *o*-Hydroxybenzyl derivatives

This is a classic and probably the most widely used method for generating *o*-QM's. Both thermal and Lewis acid promoted dehydration have been well documented.[9,26,27,40,41,43,31,64-69] Pyrolysis of both *o*-hydroxybenzyl alcohol (**43**) and *o*-(methoxymethyl)phenol (**4**) at 500-650 °C gives *o*-QM **1**. The formation of **1** has been shown by its matrix isolation,[64] trapping by CO,[65] and isolation of its trimer.[67] A typical thermal dehydration procedure has been discussed by Arduini

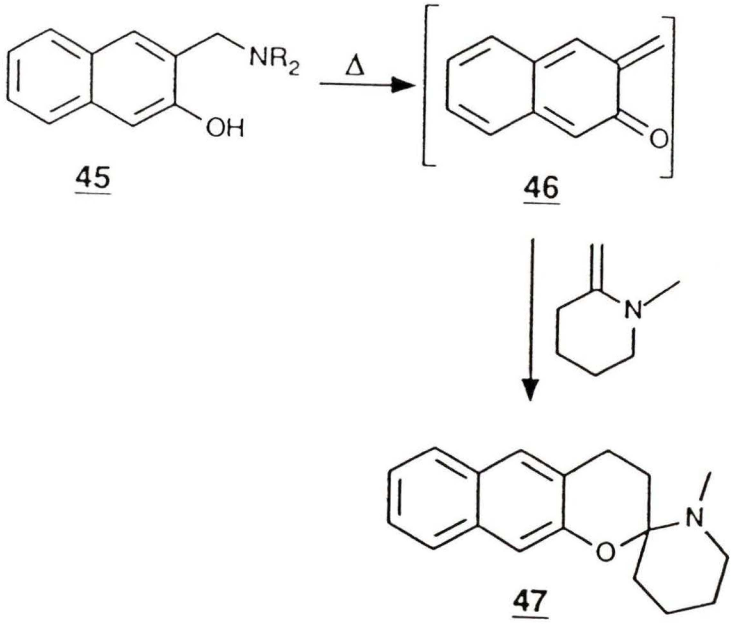


(14)

and co-workers.[27] A hexane solution of *o*-hydroxybenzyl alcohol **43** was sealed in thick tube and heated at 170 °C for 24 hours. In the presence of ethyl vinyl ether, over 50% of **43** was converted to the corresponding chroman derivative **44**, indicating the formation of *o*-QM **1** (eq. 14). The acid-promoted dehydration of *o*-hydroxybenzyl derivatives under milder conditions to generate *o*-QM's has been utilized by Lu and co-workers to synthesize HHC (eq. 12).[9]

1.5.2 Elimination of Phenol Mannich Bases

Mannich bases of benzophenols are thermally unstable and decompose to give an amine and an *o*-QM.[73] von Strandtman and co-workers[70] have demonstrated the reaction by refluxing Mannich base **45** in dry dioxane in the presence of enamines. *o*-QM **46** was trapped by the enamine, to give benzopyran **47** (eq. 15). Balasubramanian and Selvaraj[71] have also shown that the thermal

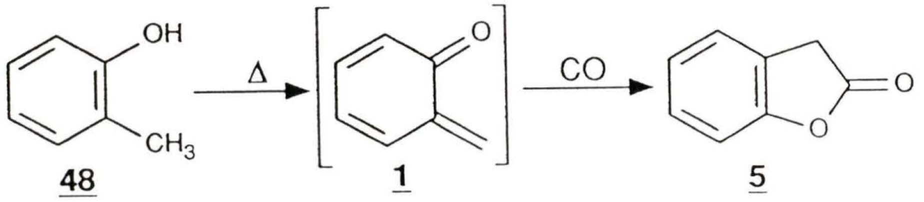


(15)

elimination of Mannich bases of β-naphthol affords the corresponding *o*-QM's. However, their attempts to generate *o*-QM's from Mannich bases of simple and substituted phenols were not successful. They attributed this to the greater thermal stability of simple phenolic Mannich bases compared to that of β-naphthol Mannich bases.

1.5.3 Oxidation of *o*-Alkylphenols

When *o*-cresol (**48**) and $Co_2(CO)_8$ were shaken in a stainless steel tube with CO at 300 °C and 1000 atmospheres for 9.5 hours, **48** was converted to benzofuran-2(3*H*)-one (**5**) (eq. 16).[65] In this reaction, **48** is oxidized by $Co_2(CO)_8$ to afford **1**, which is then trapped by CO *in situ*, via a [4 + 2] type reaction to give



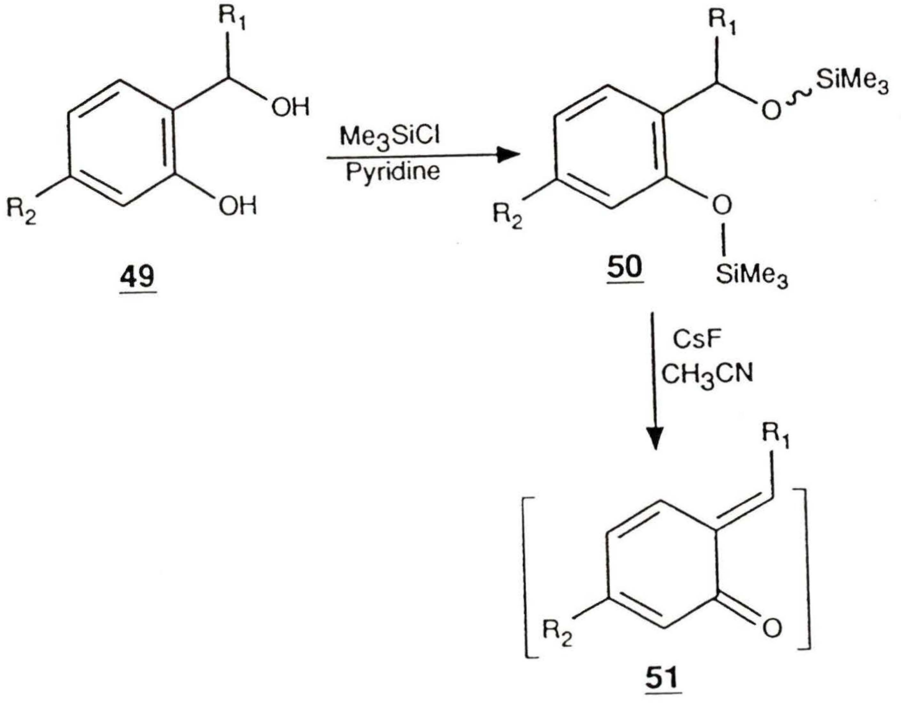
(16)

5. Bolon [40,43] then developed a general method for *o*-QM generation based on this reaction under milder conditions. When substituted *o*-cresols are refluxed in benzene or toluene together with Ag_2O, they are oxidized to the corresponding *o*-QM's, which have been trapped by alkenes as well as by nucleophiles. The most significant application of this method is the oxidative phenolic coupling approach to carpanone (eq. 10).[36,72] Generation of *o*-QM's by oxidation of *o*-alkylphenols

with DDQ has also been reported.[24]

1.5.4 Desilylation of Disilylated *o*-Hydroxybenzyl Alcohols

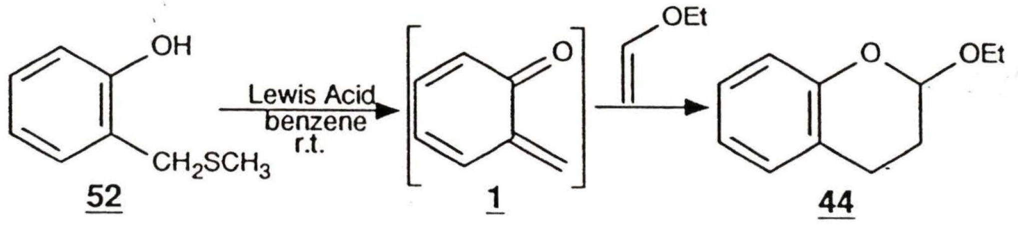
Marino and Dax[28] have demonstrated the generation of *o*-QM's via fluoride-induced desilylation of disilyl derivatives **50** of *o*-hydroxybenzyl alcohols **49**. This procedure is quite simple, although the reaction time is very long (40 hours). In a typical procedure, **49** was bisilylated with Me_3SiCl and pyridine in refluxing benzene. The entire reaction mixture was then added dropwise to a suspension of CsF in refluxing CH_3CN. The heterogeneous reaction mixture was then refluxed further under an argon atmosphere to afford *o*-QM's **51** (eq. 17). HHC (**36**) has also been synthesized by this method with very high yield (80-90%).[28]



(17)

1.5.5 Lewis Acid Catalyzed 1,4-Dethiolation of *o*-(1-(Alkylthio)-alkyl)phenols

Sato and co-workers[15,17,18,23] have recently shown a simple and mild procedure for generation of *o*-QM's from readily available *o*-(1-(alkythio)alkyl)-phenols (**52**) by a novel 1,4-elimination process (eq. 18). In this procedure, **52** is stirred in dry benzene together with Lewis acid (≥ 1 equiv.) at room temperature to generate *o*-QM's, which, again, are trapped *in situ* with alkenes to afford chromans. It has been shown that the Lewis acid catalyzes both the dethiolation and the Diels-Alder reaction. One of the shortcomings is that this procedure produces one equivalent of thio-byproduct, which results in a stench. Furthermore, the Lewis acid used can initiate polymerization of alkenes, which reduces the yield of the desired chroman product as well as introducing difficulty in product separation.



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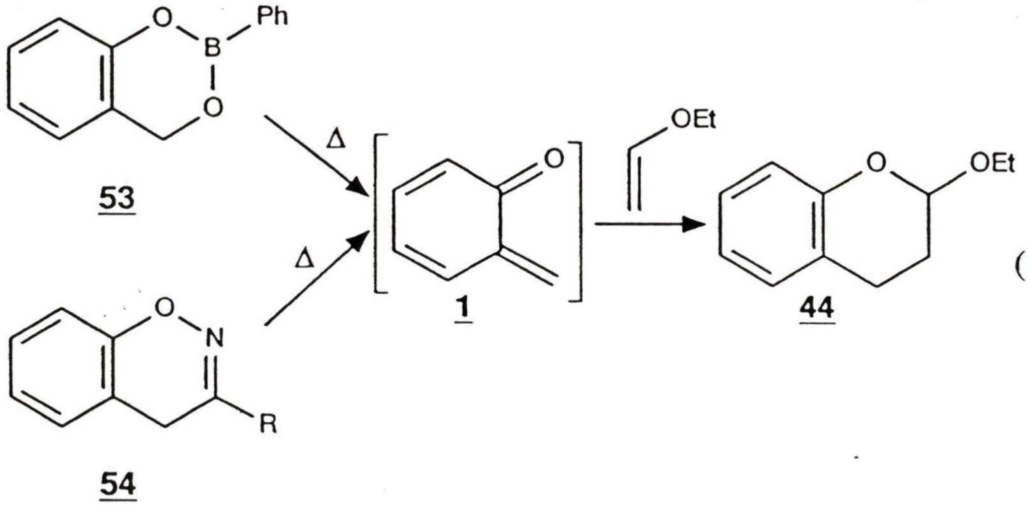
1.5.6 Other Methodologies

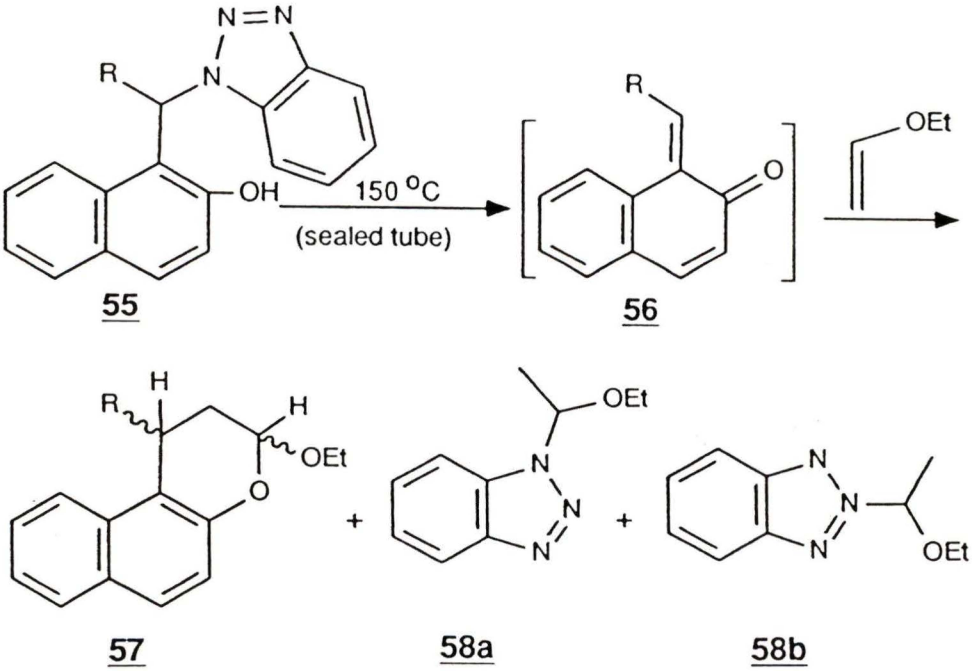
Thermolysis of 2-phenyl-4*H*-1,3,2-benzodioxaborins (53) and 4*H*-Benzoxazines (54). Thermolysis of both **53** and **54** generates the corresponding *o*-QM's.[11,16] The formation of **1** has again been demonstrated by the fact that, in



(19)

the presence of an electron-rich alkene, both compounds yield the corresponding chroman product (**44**) in moderate to good yield (up to 83%) (eq. 19).

Thermolysis of *o*-(α-Benzotriazolylalkyl)phenols (55). When heated at



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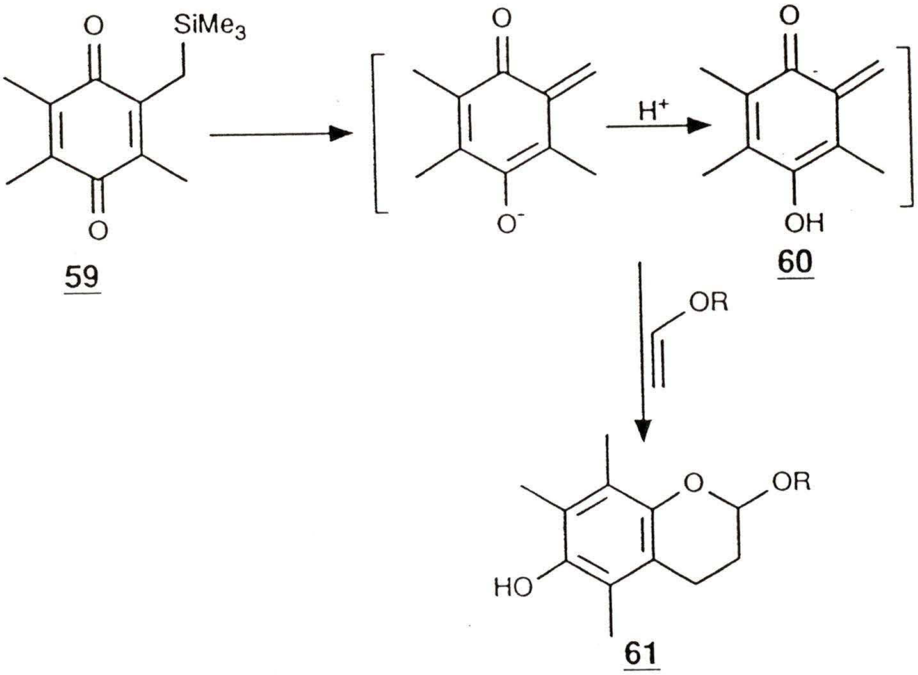
150 °C in a sealed tube, **55** decomposes to afford *o*-QM **56**, which can be trapped with alkenes to give the corresponding chroman derivatives (**57**) in high yield (≥ 82%) (eq. 20).[8] However, the reaction time was not reported. Two by-products, **58a** and **58b**, were also formed.

Desilylation of ((Trimethylsilyl)methyl)-1,4-benzoquinones (59). When heated at reflux in protic solution, **59** desilylates to give **60**, which can be trapped by nucleophiles as well as by electron-rich alkenes (eq. 21).[14]



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Other methods for generating *o*-QM's, for example, the thermal 1,5-hydrogen shift of an *o*-hydroxystyrene,[74] the thermal dissociation of spirochromene dimer,[75] the thermal cheletropic extrusion of carbon monoxide, carbon dioxide or sulfur dioxide,[76-77] have also been reported.

1.5.7 Summary

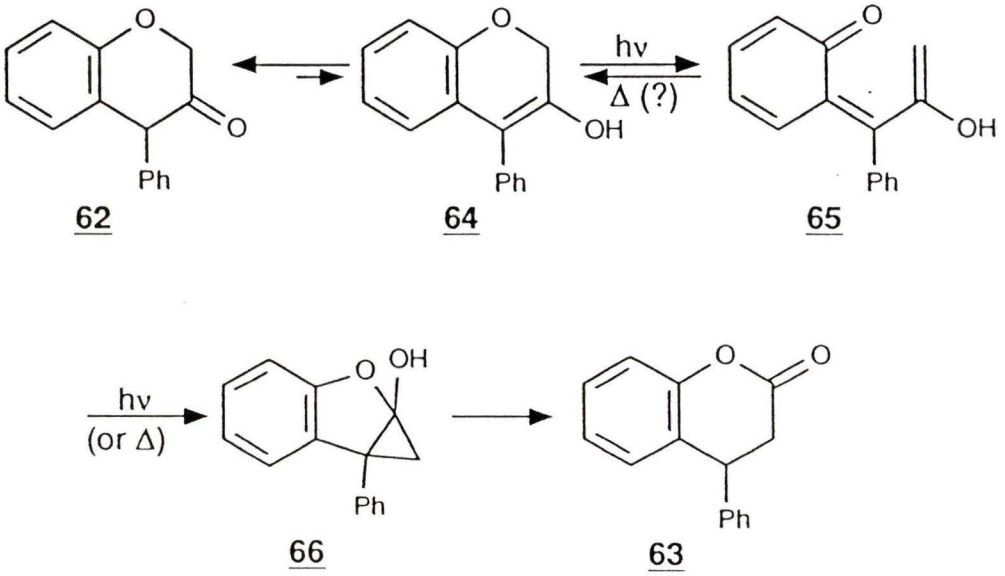
Methodologies for generating *o*-QM's have received a great deal of attention owing to their increased use in organic synthesis. A variety of methods for the thermal generation of *o*-QM's have now been reported. However, these reactions are generally carried out under harsh conditions, *i.e.*, high temperature, very long reaction time, and/or high pressure, to generate the high energy quinoid structures. Although some of the reactions can be carried out under relatively mild conditions, they are often accompanied by side products and/or cause side reactions which make the reaction less useful. Hence additional methods for generation of *o*-QM's are still desirable.

1.6 Photochemical Generation of *o*-Quinone Methides

Unlike the thermal generation methodology, the photochemical generation of *o*-QM's has not been well documented. Only several examples have been reported.

Decarbonylation of Benzofuran-2(3*H*)-one (5). Photolysis of **5** to give **1** is the classic example for photogeneration of *o*-QM's (*vide supra*, eq. 2).[32] The involvement of *o*-QM in this reaction has been shown by its matrix isolation, trapping with nucleophiles as well as by electron-rich alkenes.[32,78,79] The photolysis can be carried out in both organic and aqueous solutions and is very clean, producing only CO as the by-product. The reaction also appears quite efficient, although the quantum yield has not been reported.

Photoisomerization of 4-Substituted 3-Chromanones (62). Padwa and co-workers[80] have shown that **62** isomerizes to 4-substituted dihydrocoumarins (**63**) upon photolysis. This reaction has been shown to take place *via* the prior enolization of **62** to its enol tautomer **64**, which undergoes photochemical ring opening to *o*-QM **65**. Subsequent photochemical *supra-antara* cycloaddition of **65** gives **66**, which then ring opens to afford **63** (eq. 22). The quantum yield of this reaction is again not available. Moreover, due to the complexity of this reaction, **62** can hardly be used as a general *o*-QM precursor.



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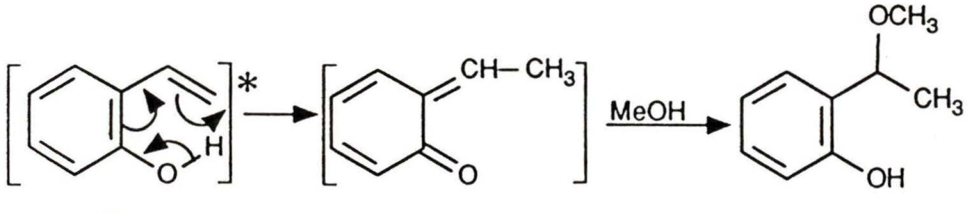
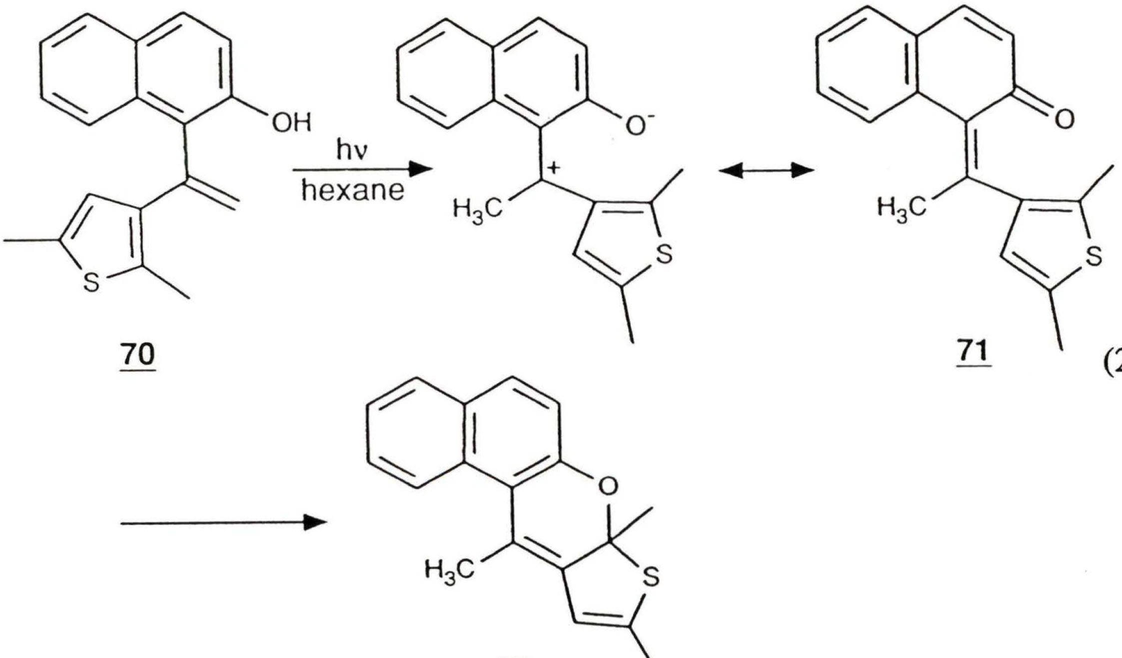
Excited State Intramolecular Proton Transfer of *o*-Hydroxystyrenes. Gutsche and Co-workers[79] have shown that **67**, upon photolysis in methanol solution, give *o*-hydroxybenzyl methyl ether (**69**). This reaction has been rationalized as due to intramolecular proton transfer of **67** in the excited state to



67 68 69 (23)

give *o*-QM intermediate **68**, which is then trapped by methanol to afford **69** (eq. 23). This mechanism has been verified by Kalanderopoulos and Yates.[81,82] They



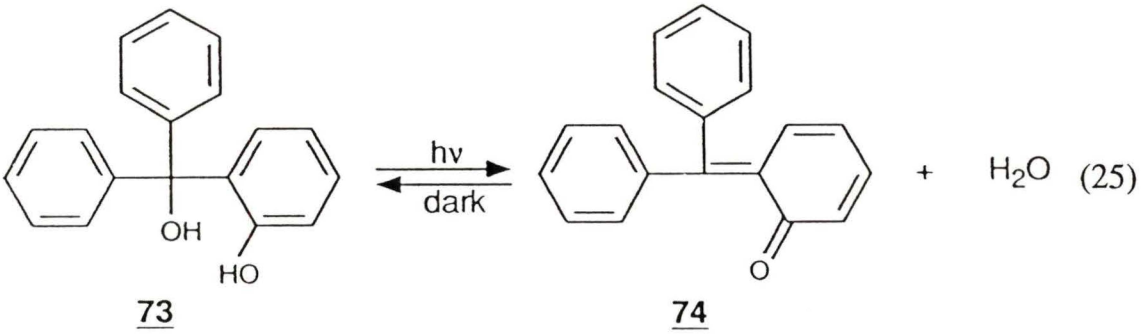
70 71 (24)

72

have shown that **67** adds H_2O efficiently on photolysis, with high quantum yield, especially at low pH (Φ up to 0.41).

A similar excited state intramolecular proton transfer reaction which affords *o*-QM has been reported by Uchida and Irie.[57] Upon photolysis, **70** undergoes the intramolecular proton transfer to generate *o*-QM **71**, which then undergoes a thermal electrocyclic ring closure, to give the coloured product **72**, with high overall quantum efficiency (Φ = 0.2) (eq. 24).

Photodehydration of *o*-Hydroxybenzyl Alcohols. At room temperature, **73** shows photochromism in several solvent systems. The chemistry of the photochromism is based upon the formation of colored *o*-QM **74** from photoexcited **73**, which is colourless (eq. 25).[83] At room temperature, **74** is stable in saturated hydrocarbons, while in other solvents, *e.g.*, CH_3CN, CH_2Cl_2, Et_2O, it will recombine with H_2O to go back to **73**. Wan and co-workers[103] have shown that, when photolyzed in aqueous solution, **43** undergoes a similar photodehydration, to give **1**, which then is trapped by methanol via 1,4-addition, to afford **4** (*vide infra*).



o-QM intermediates are also believed to be involved in the photochemistry of 4-

acetoxy-2*H*-chromene[84] and duroquinone.[85]

This thesis will explore the mechanistic details of the photodehydration of selected *o*-hydroxybenzyl alcohols and *o*-aminobenzyl alcohol, since it is anticipated that such systems will provide a general route to *o*-QM's. The crucial step of this reaction is believed to be dehydroxylation from the S_1 state of the starting material. Therefore, the photodehydroxylation of benzyl derivatives will be discussed briefly in next section.

1.7 Photodehydroxylation of Benzyl Derivatives

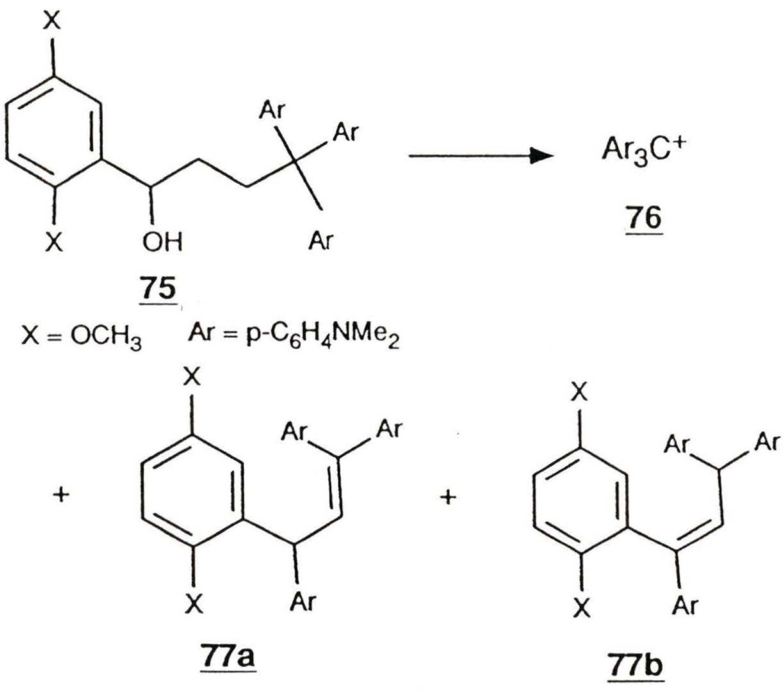
While bond homolyses resulting from photoactivation of molecules are well recognized and well studied phenomena, bond heterolyses *via* photolysis have been considerably less well studied.[92-94] This is mainly due to the fact that much of the earlier work in organic photochemistry was carried out in the gas phase or in nonpolar solvents, conditions unlikely to favour bond heterolysis to give ion pairs, over the corresponding homolysis to give radical pairs. In more polar solvents, where ions and ion pairs can be solvated, this disparity can be reduced or turned about, and, like thermal activation, photoactivation may then lead to heterolysis rather than homolysis.[94]

Since the early report by Zimmerman and Sandel[87] on the photosolvolysis of benzyl derivatives ($ArCH_2$-X) in nucleophilic solvents, there has been considerable interest in this system. Photosolvolysis reactions involve a formal heterolytic cleavage of a σ bond between a carbon and a heteroatom such as oxygen, sulfur, nitrogen or halogen. The carbocationic species generated is then

$$\begin{tikzcd} ArCH_2\text{-}X \arrow[r, "h\nu"] & ArCH_2^+ \quad + \quad X^- \arrow[d, "Sol\text{-}H"] \\ & ArCH_2\text{-}Sol \quad + \quad HX \end{tikzcd} \qquad (26)$$

trapped by the nucleophilic solvent present to afford the solvolysis product (eq. 26).[87-93]

It is well known that hydroxide ion (HO^-) is not a very good leaving group



75 76

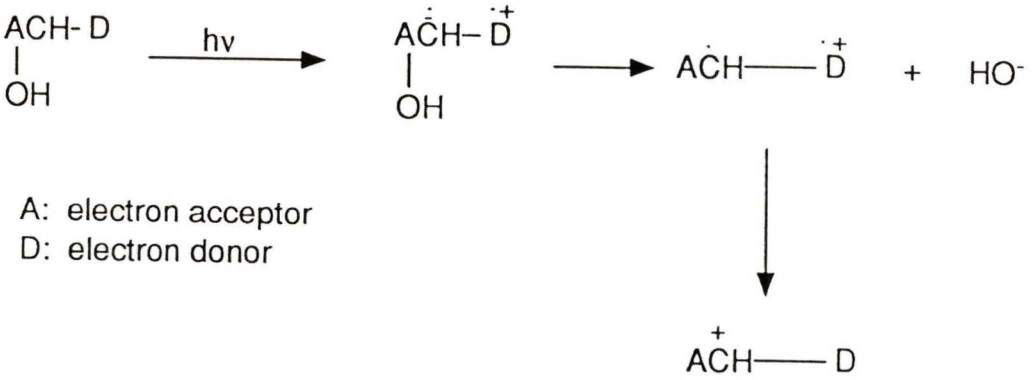
X = OCH_3 Ar = p-$C_6H_4NMe_2$

77a 77b

(27)

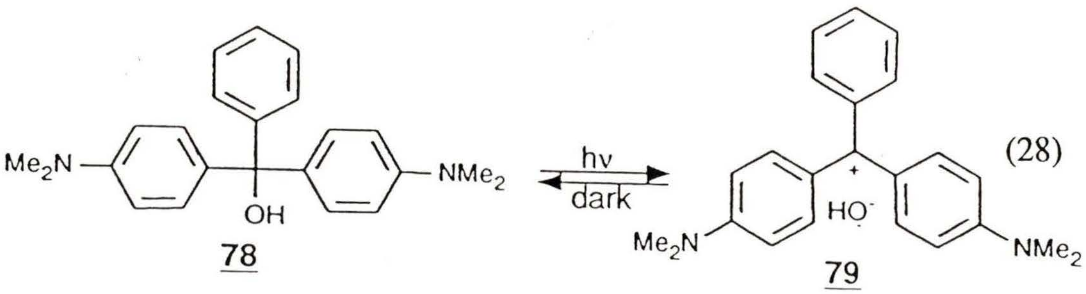
in ground state solvolysis reactions. However, on coordination with a proton (H^+), its basicity is decreased and becomes a good leaving group.[86] This is probably of greatest importance in the solvolysis of alcohols, since there are very few instances of direct heterolysis of R-OH to give the carbocation R^+ and HO^-. Recently it has been shown that hydroxide ion behaves as a good leaving group in excited state photosolvolysis reactions, which are known as photodehydroxylation.[92, 93]

The first example of photodehydroxylation of benzyl derivatives was reported by Ullman and co-workers.[95] They reported that certain benzyl alcohols, when irradiated in methanol, gave products (substitution, fragmentation and rearrangement) resulting from heterolysis of the carbon-oxygen bond. More specifically, photolysis (>300 nm) of compound **75** gave crystal violet cation **76** and the rearranged olefins **77a** (38%) and **77b** (40-50%) (eq. 27). Further results on related system suggested that both an electron acceptor (phenyl) and donor (dimethylamino) groups are required for the photodehydroxylation. An electron-transfer mechanism was proposed for the fragmentation via the singlet excited state (**Scheme 1.1**). That is, the photogenerated radical ion pair (after electron transfer) undergoes loss of hydroxide ion, resulting in the carbocation.



Scheme 1.1

Triarylmethyl leuco derivatives are well known photochromic molecules, which dissociate into ion pairs under UV-irradiation with production of intensely coloured triarylmethyl cations, which revert back to **78** on standing (eq. 28).[96] Mechanistic investigations of various derivatives have shown that the dissociation proceeds very rapidly (within 40 ns) with high quantum yield.[96,97] Irie[98] has reported the observation of an increase of pH, from 5.4 to 10.0, when diamino-substituted triarylmethanol **78** was photolyzed in aqueous solution. After removal of light, the pH returns to its initial value within 15 minutes. Other derivatives of **78** have shown similar increases in pH on photolysis.[99] In this reaction, the triarylmethanol functions as a light-induced hydroxide ion emitter. The driving force for this reaction is the formation of the exceptionally stable triaryl carbocation **79**.



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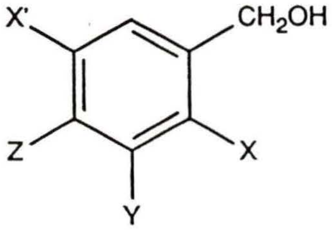
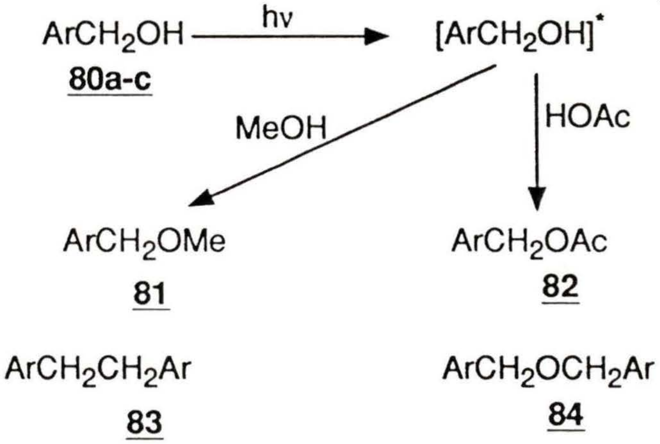
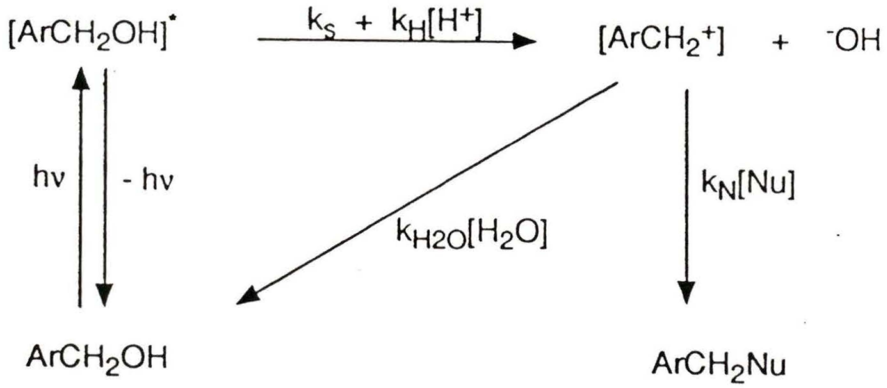
In recent years, Wan and co-workers,[100-109] in a series of studies, have shown that many *simple* benzyl alcohol derivatives undergo efficient photochemical dehydroxylation (solvolysis) in aqueous solution to give corresponding benzyl cations, which could be subsequently trapped by external nucleophiles. Photolysis of methoxybenzyl alcohols (**80a-80c**) in methanol-water or acetic acid-water solution results in the formation of methyl ether (**81**) or acetate products (**82**) (eq. 29). Only small amounts of dimeric products (**83** or **84**) were observed.[100] Photolysis of **80d** under similar conditions, however, results in recovery of 90% or more of the starting material; the corresponding methyl ether, or acetate was not observed. The relative efficiencies for formation of **81** or **82** for **80a-80c** are dependent on pH with quantum efficiencies increasing with decreasing pH. Moreover, the relative quantum yield for methyl ether formation increases in a manner that is complementary to the fluorescence quenching. This observation



80a: X = OCH_3; X' = Y = Z = H
80b: Y = OCH_3; X = X' = Z = H
80c: Y = X' = OCH_3; X = Z = H
80d: Z = OCH_3; X= X' = Y = H (29)

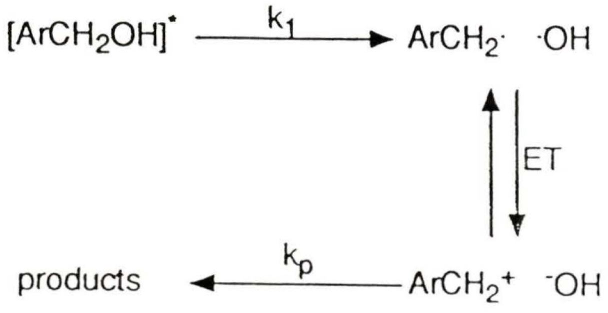


strongly indicates a mechanism involving benzyl cation formation as the primary photochemical step from the singlet excited state. Based on the above observations, the authors proposed a mechanism for the photodehydroxylation of methoxybenzyl alcohols (**Scheme 1.2**). The primary photochemical step involves proton-assisted cleavage of the benzylic-OH bond, to generate the corresponding benzyl cations $ArCH_2^+$. This intermediate may return to the starting material or else is trapped by external nucleophiles other than water (*e.g.*, MeOH or HOAc). For benzyl alcohol **80d** the results suggest that simple acid-catalyzed benzyl cation formation is not an important pathway. The possibility that the primary step involves homolytic cleavage followed by rapid electron transfer (**Scheme 1.3**) can be ruled out. The observation of acid-catalyzed formation of methyl ether products can be explained by this alternative mechanism if the k_p step is assumed to be acid-catalyzed. However, this scheme cannot account for hydronium ion quenching of fluorescence from these benzyl alcohols concurrent with acid-catalyzed methyl



Scheme 1.2

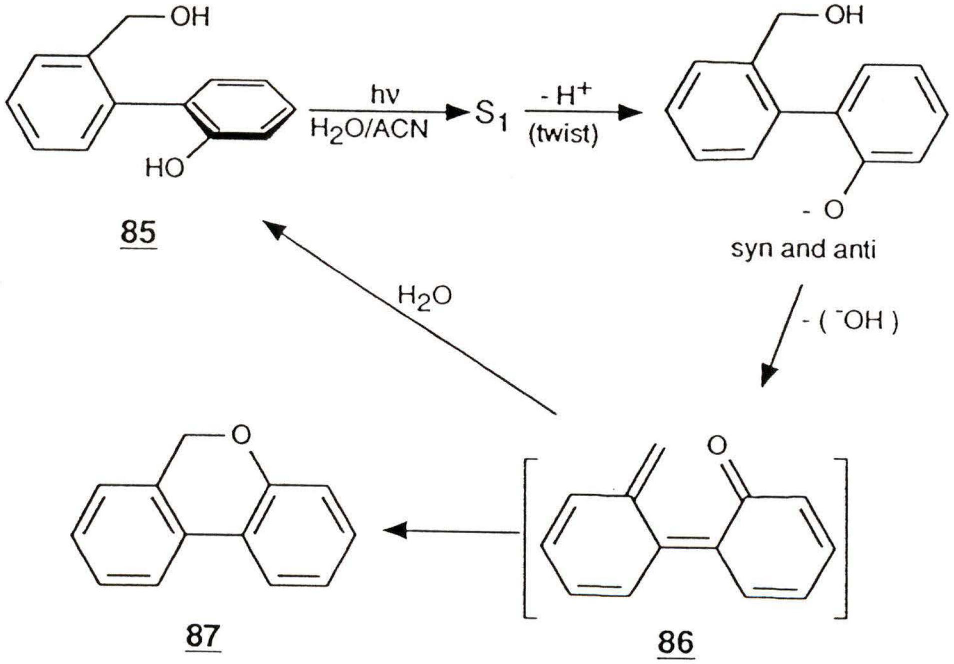
ether formation since the primary step (k_1 step) is unimolecular and, more importantly, does not require proton assistance. Subsequent studies by Wan and co-workers[102-104] corroborate these initial observations. Recent investigations employing laser flash photolysis, of substrates initially studied by the Wan group, have shown that the primary intermediate is indeed a carbocation in at least two examples.[110-113] The mechanism involving initial C-OH heterolysis from S_1 is now well established.



Scheme 1.3

Recently, Wan and Hall[105] reported the photosolvolysis of simple arylmethanols. The results show that all of these simple compounds photosolvolyze only in the presence of acid (pH < 3) and are photostable in neutral solution. It would appear that without methoxy substituents, simple aryl groups do not have sufficient electron-donating power to effect photosolvolysis with a poor leaving group such as hydroxide ion. However, these substrates show substantial photosolvolytic reactivity in acid solution of pH 2 or lower. This indicates that there is a degree of charge polarization in the excited singlet states of these systems which, in the presence of sufficient acid as catalyst, can initiate C-OH bond heterolysis. Thus simple arymethyl carbocations can be photogenerated cleanly.

Wan and co-workers[107] have reported the photocyclization of 2-(2'-hydroxyphenyl)benzyl alcohol (**85**) and derivatives in aqueous solution to give dibenzopyrans (**87**) (eq. 30). The primary photochemical step is believed to involve a very fast twisting of the biphenyl to a more planar geometry which is probably concerted with deprotonation of the phenol moiety. This is followed by a dehydroxylation step, to generate the biphenyl-*o*-QM (**86**), which is facilitated by the electron-rich phenolate ion and increased electronic communication through the biphenyl ring system. Subsequent eletrocyclic ring closure gives the observed **87**.



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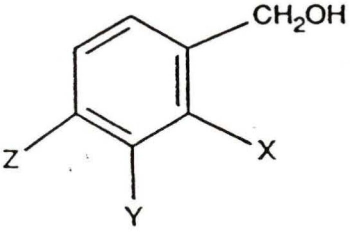
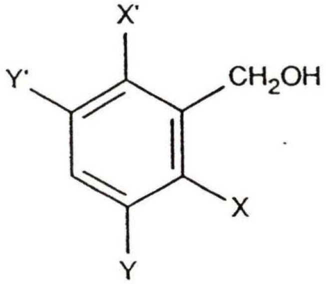
The presence of methanol in the solvent results in the trapping of **86**, to give the corresponding methyl ether products. Otherwise, trapping by water leads back to



	X	Y	Z
80a:	OCH_3	H	H
80b:	H	OCH_3	H
80d:	H	H	H
43:	OH	H	H
88:	H	OH	H



	X	X'	Y	Y'
89a:	H	H	OCH_3	OCH_3
89b:	OCH_3	H	OCH_3	H
89c:	OCH_3	OCH_3	H	H

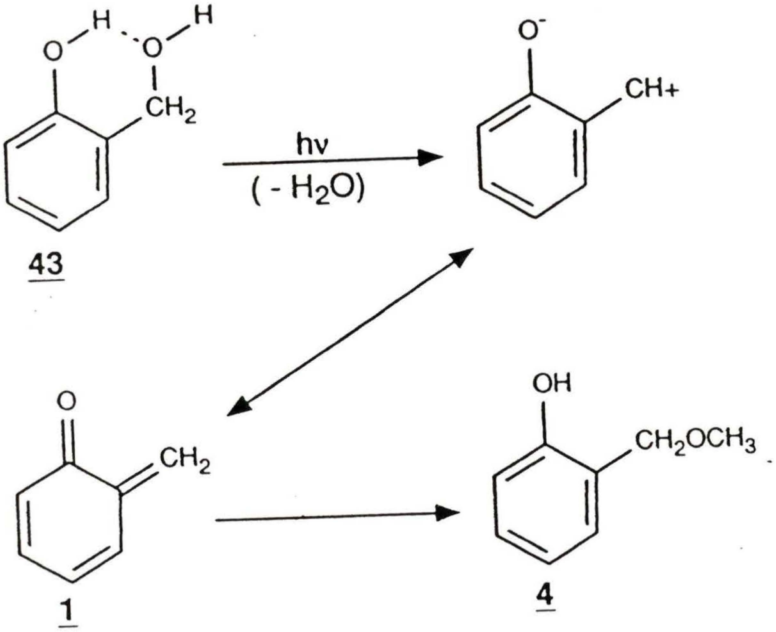
Table 1.1 Quantum yields for methyl ether formation of benzyl alcohols in 50% MeOH-H_2O solution

Compound	Quantum Yield(Φ)	Relative Reactivity
80a	0.058	0.19
80b	0.01	0.03
80d	0.00	0.00
43	0.30	0.97
88	0.02	0.0
89a	0.025	0.081
89b	0.18	0.58
89c	0.31	1.00

substrate.

In another related study Wan and Chak[103] investigated the acid catalyzed photodehydroxylation of several methoxy-, dimethoxy- and hydroxy-substituted benzyl alcohols (**80a, 80b, 80d, 43, 88, 89a-89c**) in aqueous solution. The product quantum yields for photolysis in 50% MeOH-H_2O show that disubstituted methoxy benzyl alcohols are in general more reactive than the corresponding monosubstituted derivatives (**Table 1.1**). It has been suggested that the relative magnitudes of the quantum yields of these benzyl alcohols reflects their relative kinetic reactivity.[103] It has also been suggested that analogous to the situation in ground state, substituent effects in the S_1 state are additive.[103]

As seen from **Table 1.1**, the photodissociation efficiency of *o*-hydroxybenzyl alcohol (**43**) is about five times higher than that of **80a**, a closely related analog. Although this greatly enhanced reactivity observed for **43** may well be due to electronic factors (*i.e.*, a better electron-donating group in *o*-OH compared with *o*-OMe in S_1), a more reasonable explanation lies in the close proximity of the phenolic OH with respect to the departing benzylic hydroxy group. It is well known that phenols ($pK_a \approx 10$ in the ground state) become much more acidic in the excited singlet state ($pK_a \approx 3$),[115] and the close proximity of this acidic proton in S_1 may result in intramolecular catalysis of photodehydroxylation, as shown by eq. 31. In this mechanism, the departure of hydroxide ion from **43** is facilitated by proton-assistance from the phenolic OH, presumably via a hydrogen bonded species, resulting in the elimination of water rather than a higher energy species in



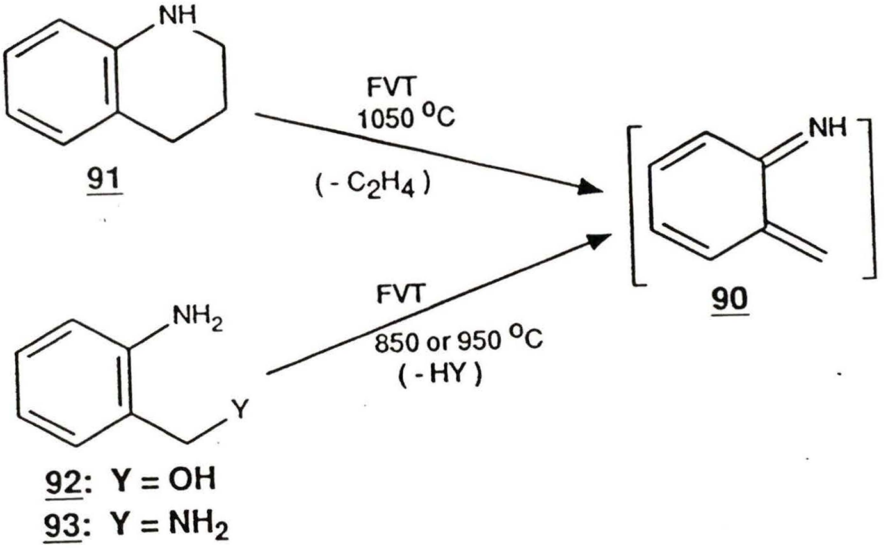
(31)

hydroxide ion. A photocondensation reaction resulting in the formation of phenol-formaldehyde type oligomers was observed when the photolysis was carried out at high pH in the absence of MeOH.[116] It has already been shown that heavily subsituted derivatives of **1** with long lifetimes may be photogenerated in hexane (*vide supra*, eq. 28).[83]

1.8 *o*-Quinone Methide Imines (*o*-QMI)

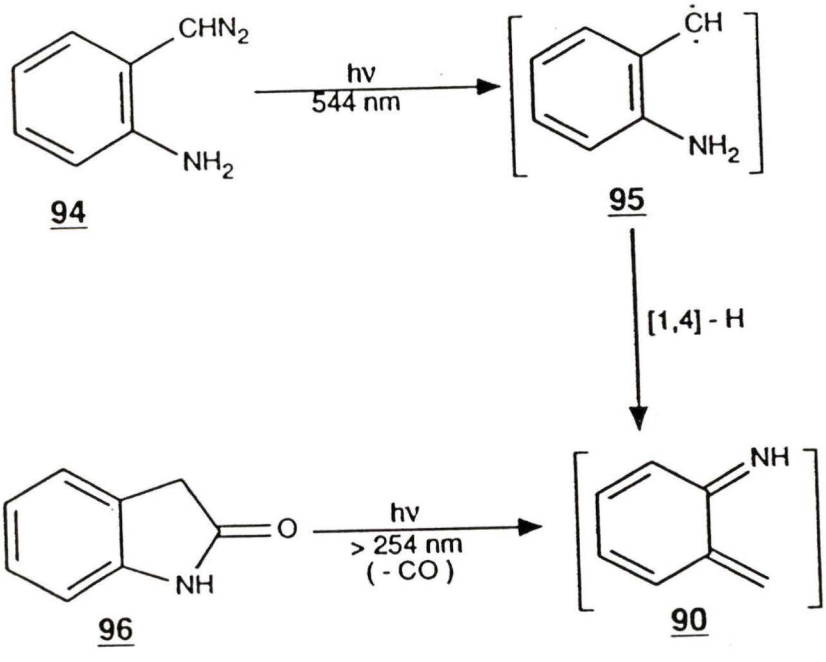
Unlike the *o*-QM's, only a few routes have been reported for the generation of *o*-QMI's. Therefore, utilization of *o*-QMI in organic synthesis has been limited. 6-Methylene-2,4-cyclohexadien-1-imine (**90**), the parent *o*-QMI, has been generated and matrix isolated from tetrahydroquinoline (**91**) or *o*-aminobenzyl derivatives (**92**, **93**) via flash vacuum thermolysis (FVT) by several groups (eq. 32).[117-121] FVT of

1-allylbenzotriazoles and dihydrobenzoxaines to generate ***o*-QMI** derivatives has also been reported.[120] Sander and Morrawietz[117] have shown that photolysis of



(32)

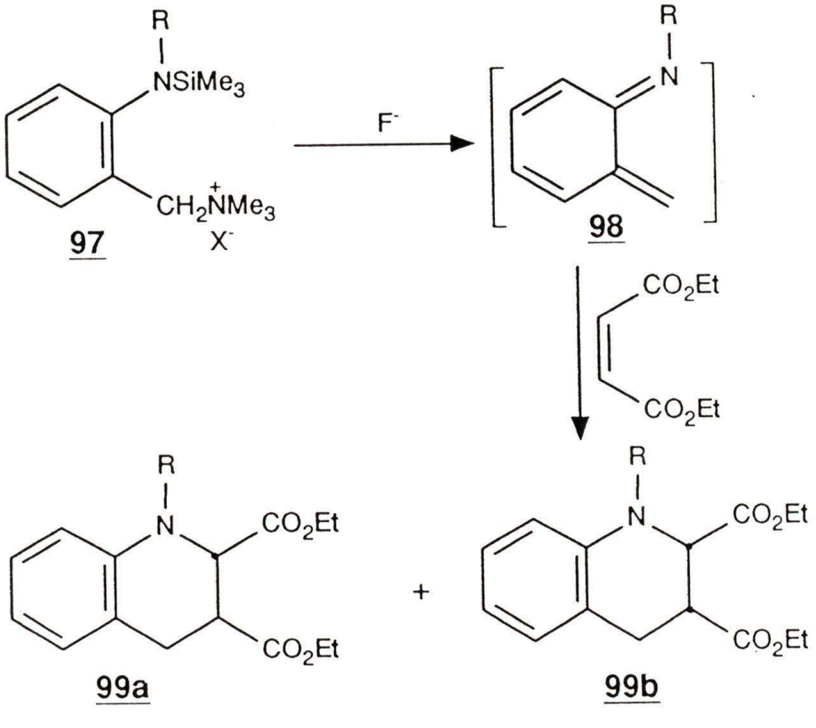
o-aminophenyldiazomethane (**94**) with visible light (λ = 544 nm) gave *o*-aminophenylcarbene (**95**), which then undergoes [1,4]-H shift to afford **90** (eq. 33).



(33)

Short wavelength (λ = 254 nm) photolysis of 2-indolinone (**96**) also produces **90** in very low efficiency.[117]

Ito and co-workers[29,122,123] have reported that the fluoride anion induced 1,4-elimination to *o*-(N-(trimethylsilyl)-N-alkylamino)-benzyltrimethylammonium halide (**97**) provides a new and versatile generation of *o*-QMI derivatives (**98**) (eq. 34). Interestingly, attempts to trap *o*-QMI derivatives intermolecularly with electron rich-dienophiles all met with failure. However, *o*-QMI's do react with electron-deficient dienophiles intermolecularly to give the corresponding tetrahydroquinoline derivatives (**99a, 99b**).[29,123]



(34)

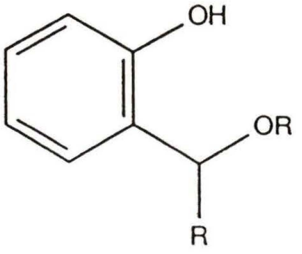
1.9 Proposed Research

As discussed in section 1.7, the efficient and clean photosolvolysis of **43** in aqueous solution imply the involvement of the parent *o*-QM (**1**) as intermediate. Therefore, a detailed study of the photochemistry of **43** and derivatives in aqueous solution may result in the developement of a general and mild photochemical method for generating *o*-QM intermediates. This is appealing since it will enable the reactivity of these intermediates to be probed under controlled conditions at ambient temperature, either via classical photochemical techniques, or by laser flash photolysis. Therefore, the photosolvolysis and possible photocycloaddition reactions of several *o*-hydroxybenzyl alcohols will be studied in this work. The involvement of *o*-QM intermediates will be demonstrated by trapping with electron-rich dienophiles. The regiospecificity and diastereoselectivity, as well as the question of concerted vs stepwise mechanism of the [4 + 2] reaction will also be addressed. Quantum efficiencies for formation of products will be measured. A working mechanism will be proposed based on product studies and the fluorescence measurements. The photosolvolytic behavior of *o*-aminobenzyl alcohol (**92**) will also be studied in aqueous solution over a range of pH and in moderately concentrated H_2SO_4 solution in the hope that the corresponding *o*-QMI (**90**) is also photogenerated for this closely related molecule.

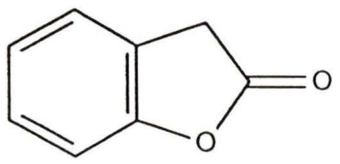
2. Photogeneration and Trapping of *o*-Quinone Methides from *o*-Hydroxybenzyl Alcohols in Aqueous Solution

2.1 Product Studies

The photochemical reactions of *o*-hydroxybenzyl alcohols **43, 100** and **101** with nucleophiles and electron-rich dienophiles in aqueous solution were studied. For comparison, the photochemical behaviour of *o*-hydroxystyrene (**67**) and benzofuran-2(3*H*)-one (**5**) under identical conditions were also studied. Compound **5** and *o*-hydroxybenzyl alcohol (**43**) were commercially available. α-Methyl-*o*-hydroxybenzyl alcohol (**100**) was prepared *via* $NaBH_4$ reduction of 2'-hydroxyacetophenone. α-phenyl-*o*-hydroxybenzyl alcohol (**101**) was prepared from 2-hydroxybenzaldehyde and phenyl lithium. Styrene **67** was prepared *via* thermal decomposition of 2-hydroxycinnamic acid.[124]



43: R = H
100: R = Me
101: R = Ph



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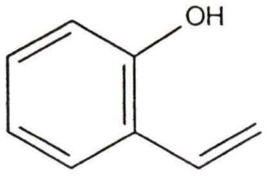
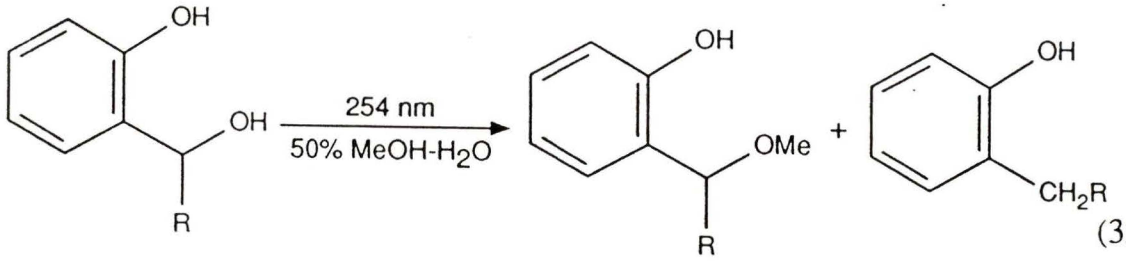


67

2.1.1 Photomethanolysis

Although *o*-hydroxybenzyl alcohols underwent photomethanolysis in several solution systems, *e.g.*, pure MeOH, CH_3CN-MeOH and MeOH-H_2O, a maximum in reaction efficiency was observed at ≈ 50% MeOH-H_2O (*v*/*v*) mixture. This is consistent with Wan and Chak's previous results from methoxy-substituted benzyl alcohols.[103] Therefore, product studies for the photomethanolysis were carried out in 50% MeOH-H_2O (*v*/*v*) mixture. Irradiation (254 nm) of an argon purged solution of *o*-hydroxybenzyl alcohol (**43**) (4.0 × 10^{-3} **M**) in a Rayonet RPR 100 photochemical reactor at ≈ 15 °C gave only one product at low conversion (*i.e.*, < 15%) (eq. 35). The product was isolated by preparative TLC (silica gel, CH_2Cl_2)



(35)

43: R = H
101: R = Ph

4: R = H
102: R = Ph

48: R = H
103: R = Ph

and characterized as *o*-(methoxymethyl)phenol (**4**) by ^{1}H NMR (methoxy singlet at δ 3.4 and benzylic methylene at δ 4.6) and mass spectroscopy (observation of $M^+ + 1$ peak). Photolysis of **101** under the same conditions gave the corresponding methyl ether **102** (methoxy singlet at δ 3.4 and benzylic methine singlet at δ 5.7) (eq. 35). No dimeric product, which may be formed *via* initial C-OH bond homolytic cleavage, was observed for either **43** or **101**, indicating that C-OH bond homolytic cleavage in the above systems can be neglect. Control experiments performed in the absence of light did not give any observable reaction.

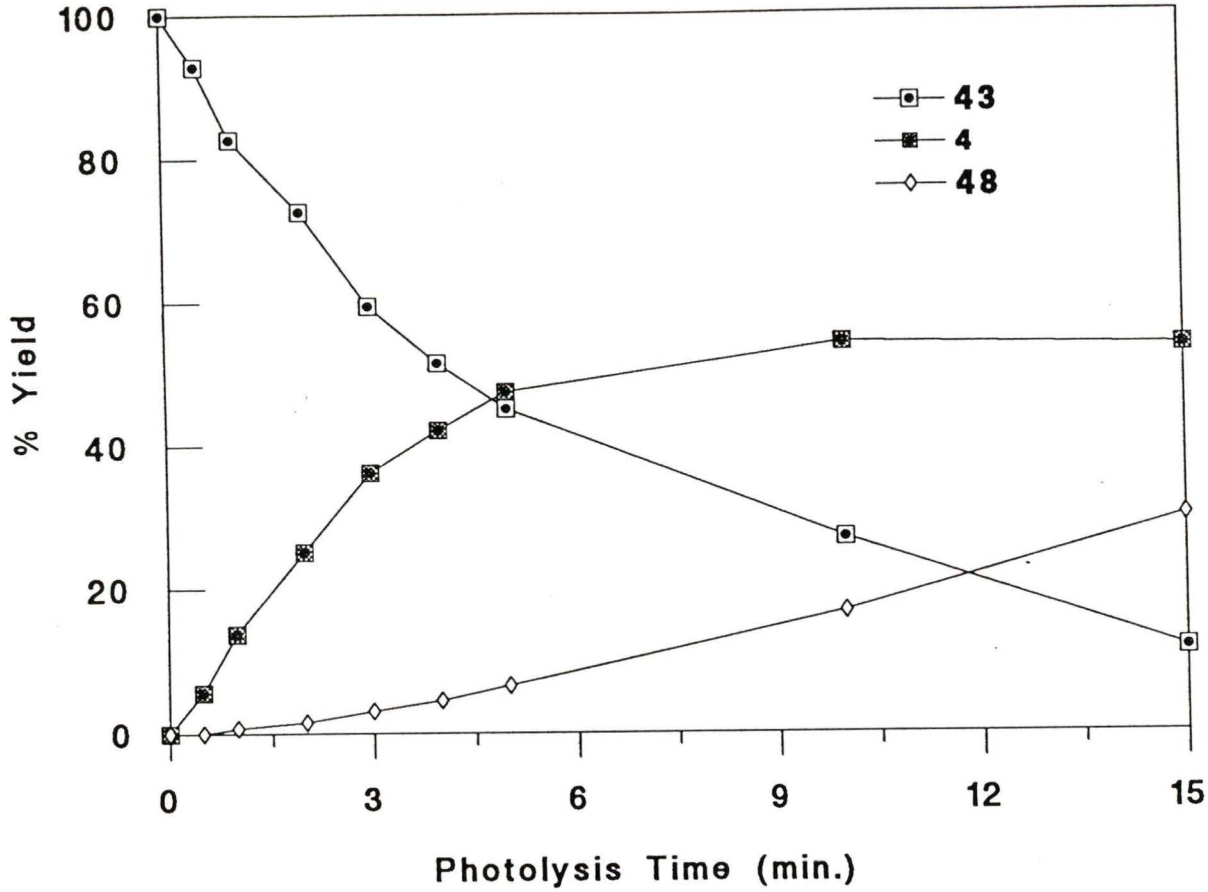
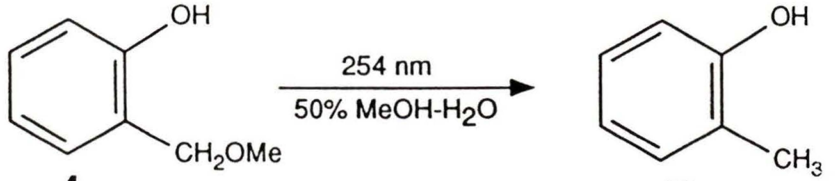


Figure 2.1 Plot of conversion of **43** to **4** and **48** on photolysis in 50% MeOH-H_2O as a function of photolysis time

On further photolysis to greater than 15% conversion, the secondary "reduced" products were observed, *i.e.*, *o*-cresol (**48**) for **43** and 2-(benzyl)phenol (**103**) for **101**. The yields of "reduced" products increased with further photolysis (**Figure 2.1**). That **48** and **103** are secondary photochemical products, formed *via* photolysis of the corresponding ether products **4** and **102**, was shown by independent photolysis of **4** in 50% MeOH-H_2O which gave **48** exclusively (eq. 36).

As discussed in Section 1.8, two plausible mechanisms may account for the

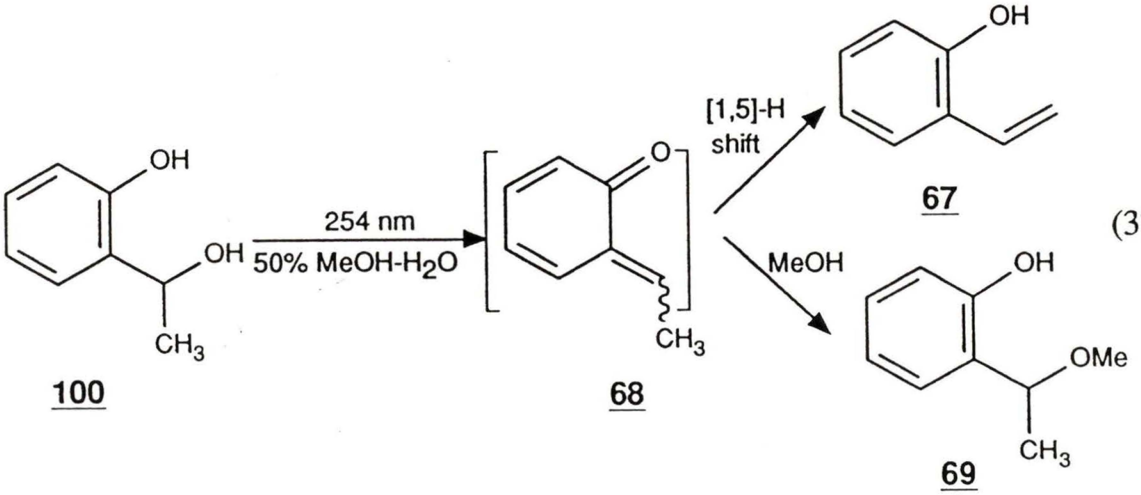


4 **48** (36)

photosolvolysis of *o*-hydroxybenzyl alcohols.[103] Upon irradiation, the substrate in S_1 may either dehydroxylate to give a carbocation, which is subsequently trapped by MeOH, to give the corresponding methyl ether products (*vide supra*, **Scheme 1.2**), or, taking advantage of the enhanced acidity of phenolic proton in the excited state, dehydration to afford *o*-QM (**1**), which then reacts with MeOH *via* a Michael type 1,4-addition to give the same ether products (*vide supra*, eq. 31). The second mechanism seems more reasonable. However, at this stage, the two mechanisms are not differentiable with the data at hand.

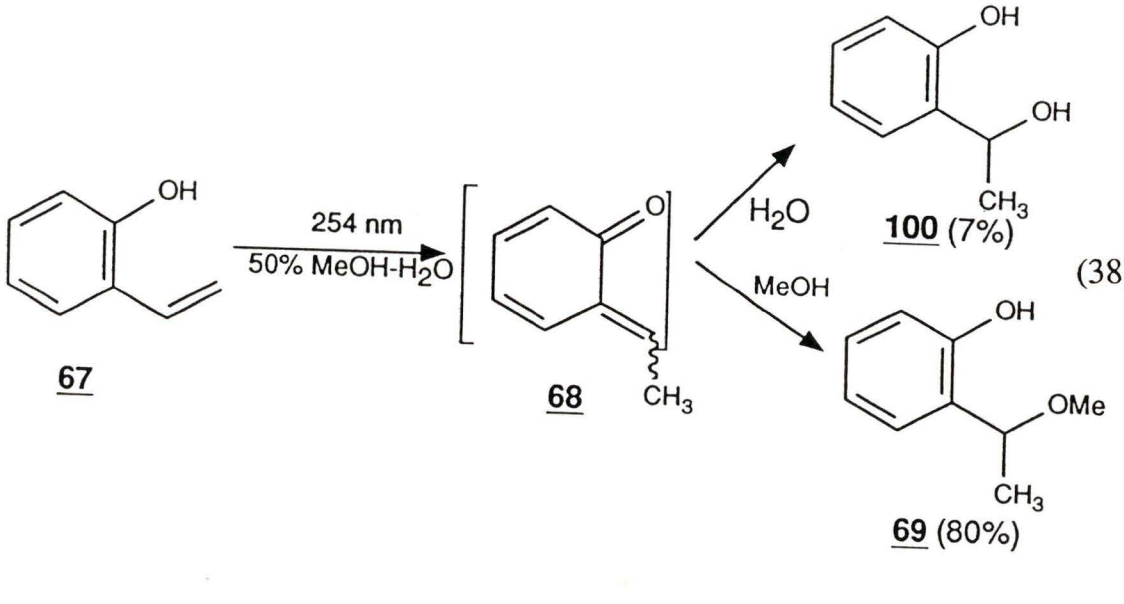
The photomethanolysis efficiency for **101** was found to be about two times as that for **43** by ^{1}H NMR analysis. This can be attributed to either the increased stability of the α-phenyl substituted *o*-QM or of the phenyl substituted carbocation. Evidence favoring the formation of *o*-QM will be presented throughout this work (*vide infra*).

Photolysis of an argon purged 50% MeOH-H_2O solution of **100** gave **69** as the major product in low-conversion. Monitoring the reaction by UV-Vis suggested that styrene **67** was also formed in a trace amount. In this reaction,



(37)

excitation of benzylic alcohol **100** gives *o*-QM **68**, which then either proceeds *via* a [1,5]-hydrogen shift to give *o*-hydroxystyrene **67**, or is trapped by the surrounding solvent molecules to give the ether product **69** (eq. 37). Photolysis of **67** in 50%



(38)

MeOH-H_2O solution gave **69** as the only product in low-conversion. On extended photolysis, **100** was formed as a minor product (eq. 38). The relative yields of **69** to **100** reflect the relative nucleophilicity of MeOH vs. H_2O (*vide infra*).[125]

Neither the dimers nor the trimers of *o*-QM's were observed for the *o*-hydroxybenzyl alcohols discussed above on photolysis in both CH_3CN-H_2O and MeOH-H_2O solutions. This not surprising, considering that both MeOH and H_2O are weakly nucleophilic, but are present in large excess. Therefore, they will react with the *o*-QM's preferentially to give the ether products or regenerate the starting materials, respectively.

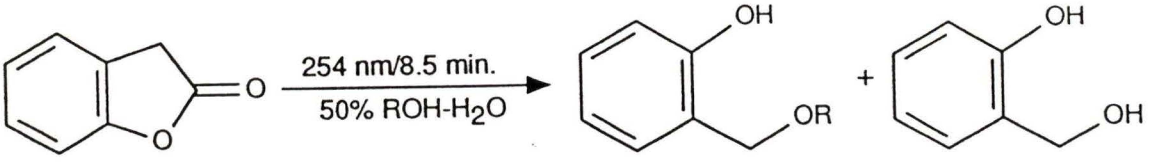
2.1.2 Relative Nucleophilicity Between Alcohols and Water

o-Hydroxybenzyl alcohols were also found to undergo photosolvolysis in other aqueous alcohol solutions. The yields of the corresponding ethers decreased with increasing branching of the alkyl group of the alcohols, as shown by **Table**

Table 2.1 Yields of ethers $ArCH_2OR$ on photolysis of **43** and **5** in ROH-H_2O^a

ROH	yield of $ArCH_2OR$ (%)^b	
	43^c	**5**^{d}
MeOH	60	60 (4)^e
EtOH	45	50 (18)^e
2-PrOH	30	31 (34)^e
t-BuOH	10	12 (59)^e

[a] 50% ROH-H_2O (*v*/*v*) at pH 7.
[b] calculated by ^{1}H NMR integration; estimated error ± 15% of quoted value.
[c] photolyzed at 254 nm for 10 min.
[d] photolyzed at 254 nm for 8.5 min.
[e] yield of **43**, see eq. 39.



5

4: R = CH_3
104: R = Et
105: R = 2-Pr
106: R = t-Bu

43

(39)

2.1. Photolysis of **5** is known to give **1** (*vide supra*).[32] Thus, irradiation of **5** in 50% ROH-H_2O gave **43** and the corresponding ethers (eq. 39). In this reaction, the yield of ethers decreased from 60% in MeOH-H_2O to 12% in *t*-BuOH-H_2O and yield of **43** increased from 4% in MeOH-H_2O to 59% in *t*-BuOH, while the overall conversion of **5** remained essentially unchanged at 65-70% (**Table 2.1**). This result, which reflects the relative nucleophilicity of alcohols, is consistent with that observed for photolysis of **43**. In aqueous alcohol solution, the only reaction channels for **1** generated from **5** are trapping by the alcohol and by H_2O. Moreover, the overall photodecarbonylation efficiency of **5** was shown to be independent of solvent. Therefore, the ratio of the yields of ether to that of **43** reflects the relative nucleophilicity of the corresponding alcohol vs. H_2O towards **1**. Considering that alcohols and H_2O are in large excess (hence their concentration can be regarded as constant during the reaction) and employing steady-state assumption for **1** in low conversion, the relative reactivity is given by eq. 40, where k_{ROH} and k_{H2O} are the biomolecular rate constants for reaction of ROH and H_2O

with **1**, respectively. Thus k_{ROH}/k_{H2O} is a measure of the relative reactivity of ROH

$$\frac{k_{ROH}}{k_{H_2O}} = \frac{[ArCH_2OR][H_2O]}{[43][ROH]} \tag{40}$$

vs H_2O towards **1**. Taking the reactivity of MeOH as 1.0, values for different alcohols are calculated and given in **Table 2.2**. The relative reactivity of MeOH

Table 2.2 Relative reactivity of nucleophiles with *o*-QM **1** and carbocations in aqueous solution

Nucleophile	Relative Reactivity (k_{ROH}/k_{MeOH})		
	o-QM (**1**) (from **5**)	2,6-DMB$^+$ [a] (from **89c**)	Ph_2CH^+ [b] (from Ph_2CHCl)
MeOH	1.0	1.0	1.0
EtOH	0.78[c]	--	0.71[g]
2-PrOH	0.26[c]	0.3[e]	0.26[g]
H_2O	0.08[c]	--	0.1[g]
t-BuOH	0.04[c]	--	0.06[g]
EVE	23.0[d]	< 0.03[f]	0.1[g]

[a] 2,6-DMB$^+$: 2,6-dimethoxybenzyl cation; photogenerated from **89c** in aqueous solution.[103].

[b] data from ref. 125.

[c] in ROH-H_2O-CH_3CN; ratio of ROH to H_2O were chosen so that both products had ≥ 5% yield.

[d] k_{EVE}/k_{MeOH}, in 0.15 **M** EVE in 20% MeOH-CH_3CN.

[e] in 50% ROH-H_2O.

[f] in 0.15 **M** EVE in 20% 2-PrOH-H_2O.

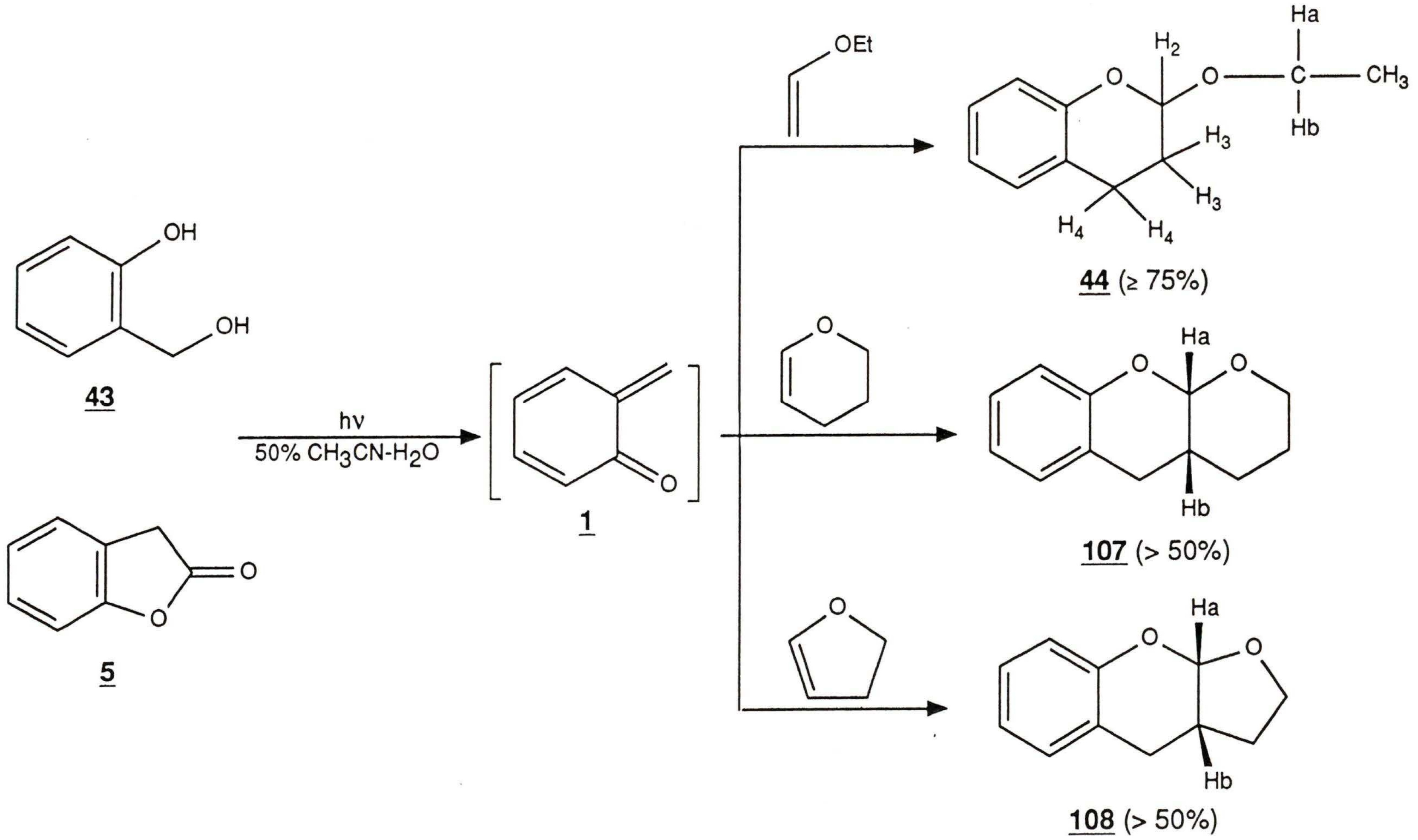
[g] in CH_3CN.

vs EVE is given by k_{EVE}/k_{MeOH}, which is calculated from the data of photolysis of

5 in 0.15 **M** EVE in 20% MeOH-CH_3CN. For comparison, the relative reactivities of ROH *vs* EVE toward 2,6-dimethoxybenzyl cation (2,6-DMB^+), which was photogenerated from 2,6-dimethoxybenzyl alcohol (**89c**) in aqueous solution,[103] were also measured and listed in **Table 2.2**. The values for reaction of Ph_2CH^+ photogenerated from Ph_2CHCl in CH_3CN by laser flash photolysis were calculated from reported data.[125]. The nucleophilicity of the alcohols towards both *o*-QM **1** and PH_2CH^+ decreases by a factor of about 20 from MeOH to *t*-BuOH. The nucleophilicity of H_2O was previously assumed to be about approximately the same as that of MeOH.[103,125] However, the above results show that the nucleophilicity of H_2O, is about 10 fold less than that of MeOH, ranging between 2-propanol and *t*-butanol. Interestingly, although ethyl vinyl ether (EVE) reacts with both carbocations and *o*-QM (**1**), the relative reactivities are very different. EVE is about 300 time more reactive than H_2O towards *o*-QM (**1**) and less reactive towards the two benzylic carbocations. This implies that EVE reacts with *o*-QM (**1**) and benzylic carbocations *via* different mechanisms (*vide infra*).

2.1.3 [4 + 2] Cycloaddition

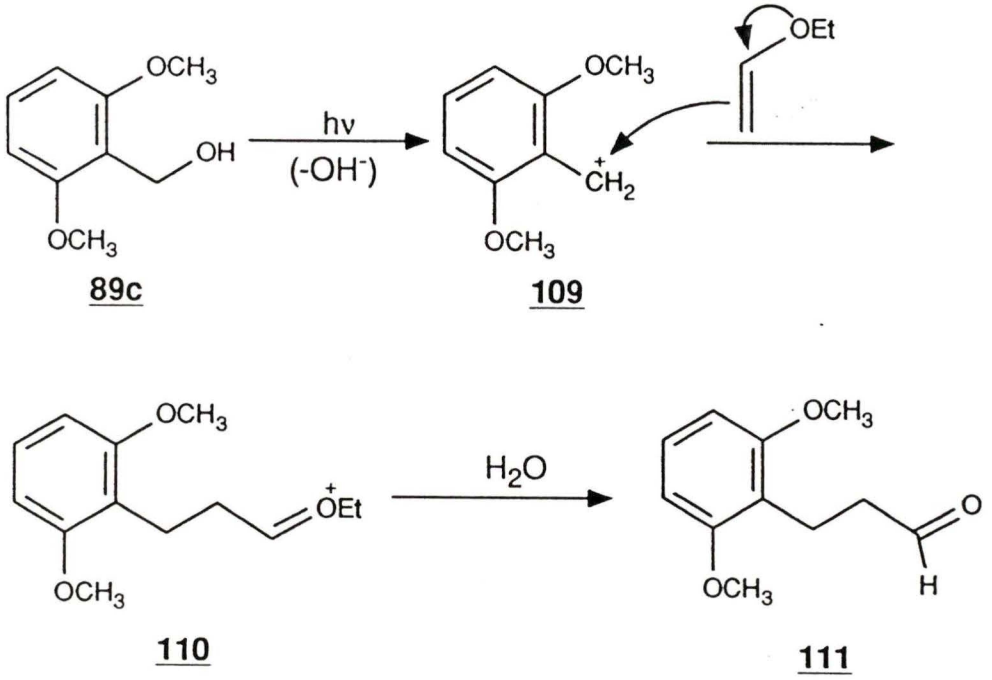
The photosolvolysis of *o*-hydroxybenzyl alcohols in aqueous solutions has been discussed in the above sections. Although this reaction may be rationalized as *via o*-QM intermediates, direct evidence for involvement of *o*-QM's has not been presented. Electron-rich alkenes, *e.g.*, vinyl ethers, are known to trap *o*-QM's in a Diels-Alder type [4 + 2] cycloaddition, to give 2-alkyloxy substituted chromans (*vide supra*).[2,4,9,11,18,27,32] Thus, photolysis of the parent *o*-hydroxybenzyl alcohol (**43**) in the presence of various vinyl ethers was studied. For comparison, lactone **5**, a well-known photochemical precursor of **1**,[32] was also studied under identical conditions. Photolysis of an argon purged 50% CH_3CN-H_2O (*v*/*v*) solution of **43** (4.0×10^{-3} **M**), in the presence of EVE (0.10 **M**), at ≈ 15 °C gave 2-ethoxychroman (**44**) as the only product in high yield (≈ 75% in one hour photolysis for **43, Scheme 2.1**). A control experiment carried out in the absence of light showed that no "dark" reaction was observable for similar periods of time. Irradiation of **5** under identical conditions also gave **44** as the only product. The product was isolated by preparative TLC and its structure was established by 250 MHz ^{1}H NMR, using chemical shifts and coupling constants, which were obtained from references,[11,17,18,27] for the assignments (H_2: δ 5.26, triplet, $J_{2,3} = 2.92$; H_3: δ 1.95-2.10 multiplet; H_a and H_b: δ 3.83-3.97, 3.57-3.71, multiplets). Similarly, photolysis of aqueous CH_3CN solutions of **43** and **5** in the presence of dihydropyran and dihydrofuran gave the expected tetrahydropyranobenzopyran **107** and tetrahydrofuranobenzopyran **108 (Scheme 2.1)** with the same regiospecificity, with > 50% yield in one hour photolysis. As expected for a cycloaddition reaction, only *cis*-fused ring products were obtained (assigned by the coupling constants between H_a and H_b: H_a δ 5.32, doublet, $J_{a,b} = 2.60$ Hz for **107**, δ 5.24, doublet, $J_{a,b}$ = 4.8 Hz for **108**). Thus the *o*-QM's are probable intermediates in the


OH
OH
43
5
O
O
hν
50% CH_3CN-H_2O
O
1
OEt
O
O
O
H_2
O
C
Ha
Hb
CH_3
H_3
H_3
H_4
H_4
44 (≥ 75%)
Ha
O
O
Hb
107 (> 50%)
Ha
O
O
Hb
108 (> 50%)

Scheme 2.1

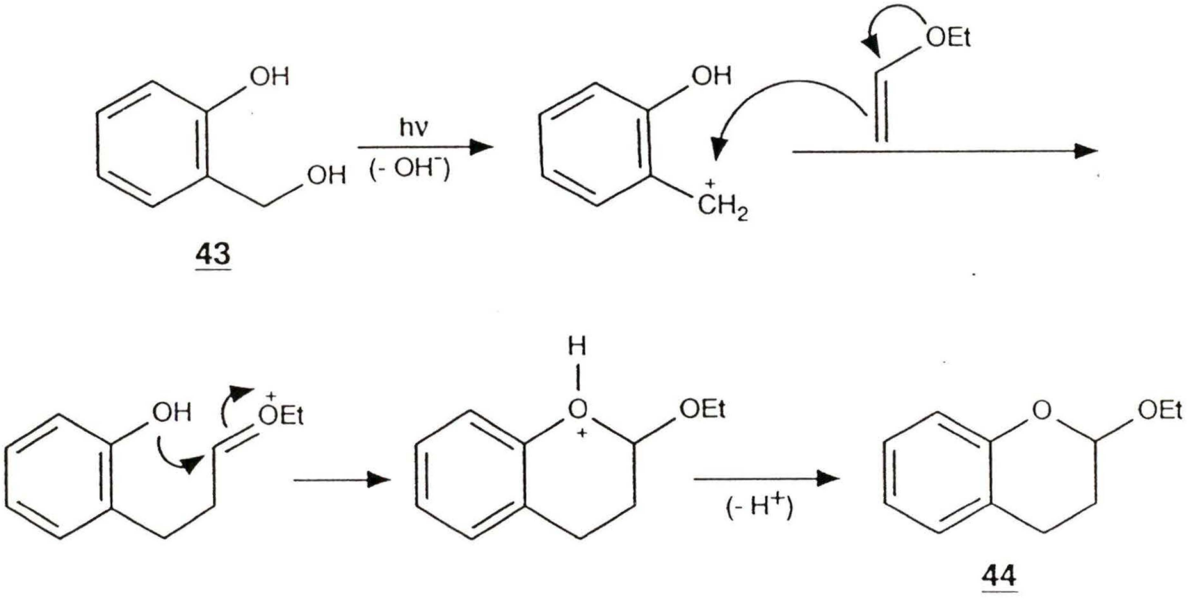
photochemistry of *o*-hydroxybenzyl alcohols in aqueous solution was established.

Photolysis of an argon purged 50% CH_3CN-H_2O solution of 2,6-dimethoxybenzyl alcohol (**89c**), which has approximately the same photochemical

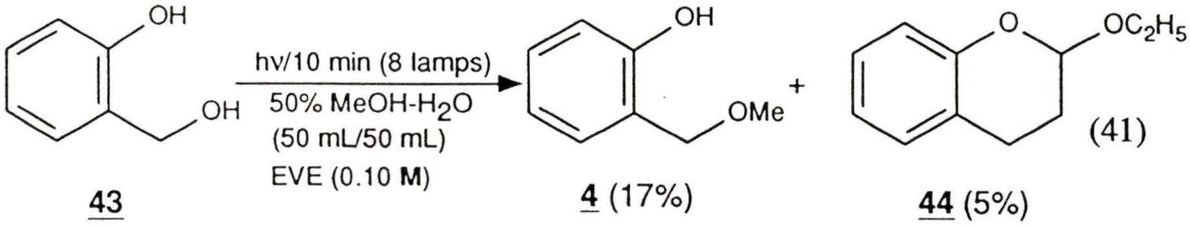


Scheme 2.2

reactivity as **43** towards alcohol nucleophiles in aqueous solution,[103] gave aldehyde product **111**, in the presence of 0.10 **M** EVE. The structure of **111** was assigned by ^1H NMR (triplet at δ 9.8 for the aldehyde proton; doublet of triplet at δ 2.55 for protons α to the carbonyl; and triplet at δ 2.95 for the benzylic protons). This reaction can only be rationalized as *via* a step-wise pathway, as shown by **Scheme 2.2**. Upon irradiation, **89c** dehydroxylated to give benzylic carbocation **109**,[103] which then reacts with EVE to afford **110**, which hydrates *in situ* to give **111**. The occurrence of this reaction implys that **43** and **5** may also undergo a similar step-wise pathway to give **44**, as shown by **Scheme 2.3**. The step-wise mechanism can account for the regiospecific formation of the 2-substituted chroman products. However, the step-wise mechanism can not explain the high efficiency for formation of **44**. As already discussed in the previous section, EVE is approximately as reactive as H_2O toward carbocations in aqueous solutions. The above step-wise mechanism would predict a very low-efficiency for formation of **44** from **43** in aqueous solution which is inconsistent with what is observed. Photolysis of **43** in aqueous MeOH solution, however, has shown that EVE can even compete with MeOH efficiently (eq. 41). The high efficiency for trapping by EVE is consistent with the involvement of an *o*-QM intermediate (*vide supra*). Therefore, one can confidently conclude that the step-wise pathway is at best a

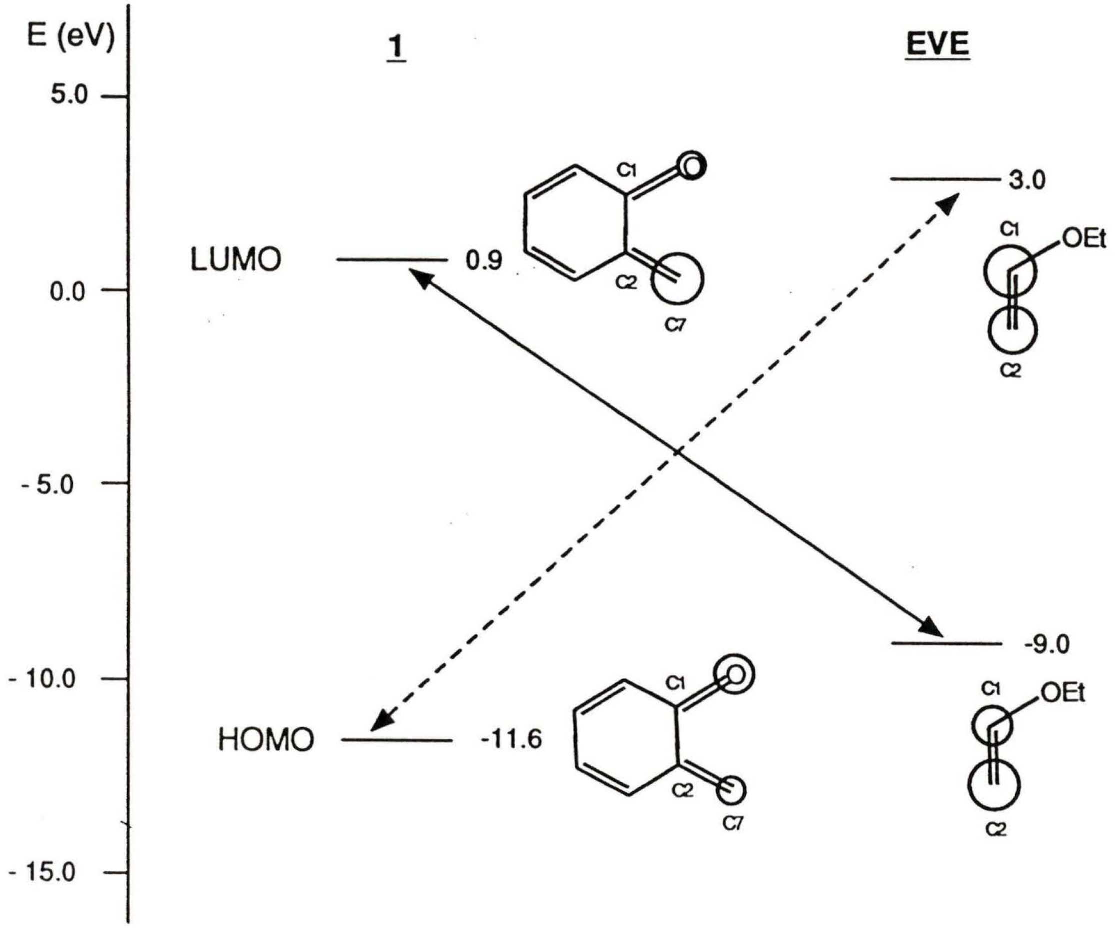


Scheme 2.3



minor pathway for the photocycloaddition of *o*-hydroxybenzyl alcohols with "electron-rich dienophiles" in aqueous solution.

Consistent with previous reports,[2,4,11,17,18,27,32] *o*-QM **1** generated from **43** and **5** reacts with dienophiles in a totally regiospecific manner. This can be explained in terms of frontier molecular orbital interactions.[45,127,128] The frontier molecular orbitals of **1** and EVE are schematically shown by **Figure 2.2**. The molecular orbital coefficients are calculated by Hückel Molecular Theory (HMO). The energies of the orbitals, based on the CNDO/2 calculation, are adopted from literature.[45,129] According to Frontier Molecular Orbital (FMO) theory, which states that *those orbitals will interact most which overlap best and are closest in energy*.[130] Therefore, the [4 + 2] cycloaddition between **1** and EVE will be controlled by the interaction of the LUMO of **1** and the HOMO of EVE, as shown by the solid arrow in **Figure 2.2**. FMO theory also indicates that the large-large (overlap of C(7) of **1** with C(2) of EVE) and small-small (overlap of O of **1** with C(1) of EVE) interactions are the most favorable overlap,[127,128,130] thus predicting the experimentally observed regiospecificity of the above reaction.



1

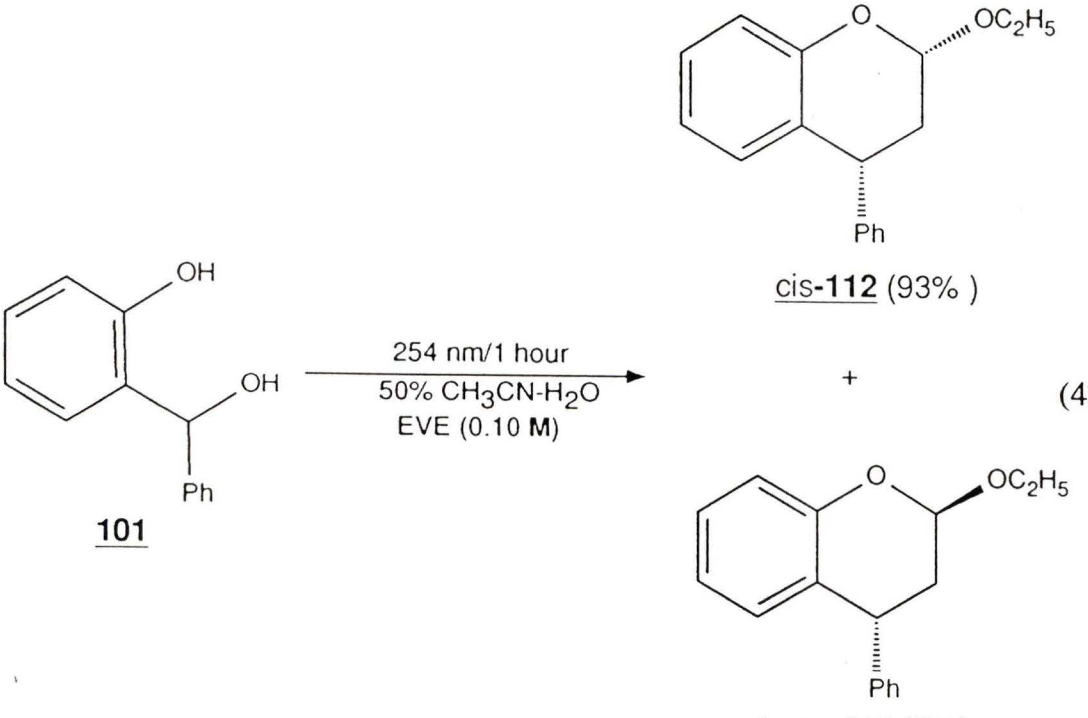
	HOMO	LUMO
O	-0.539	-0.294
C(7)	0.287	-0.705
C(6)	0.483	0.170
C(5)	0.107	-0.350
C(4)	-0.415	-0.128
C(3)	-0.370	0.365
C(2)	0.181	0.084
C(1)	0.198	0.329

EVE

	HOMO	LUMO
O	-0.397	0.233
C(2)	0.756	0.632
C(1)	0.521	-0.739

Figure 2.2 Frontier molecular orbital coefficients (from HMO) and energies (from CNDO/2) for **1** and EVE

FMO theory groups the Diels-Alder reaction into three categories:[126-128] the "direct" Diels-Alder reaction, in which the dominant interaction occurs between the HOMO of the diene and the LUMO of the dienophile, which requires an electron-rich diene and an electron-deficient dienophile; the "neutral" Diels-Alder reaction, in which both HOMO and LUMO of the diene and the dienophile should be considered, which takes place between ordinary conjugated alkenes; and the "inverse" reaction, in which the dominant interaction occurs between the LUMO of the diene and HOMO of the dienophile, which requires an electron-deficient diene and an electron-rich dienophile. Thus FMO theory also explains why **1** is trapped only by electron-rich alkenes.[131,132]



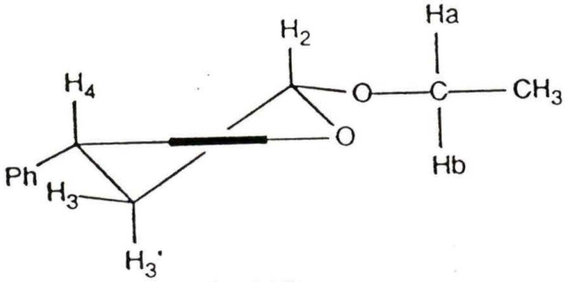
101

cis-**112** (93%)

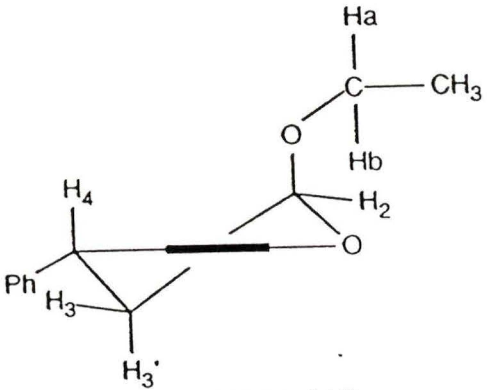
trans-**112** (7%)

(42)

Photolysis of an argon purged 50% CH_3CN-H_2O solution of **101**, in the presence of 0.10 **M** EVE, at ≈ 15 °C for one hour, gave two diastereomers of the corresponding chromans, *i.e.*, *cis*-**112** and *trans*-**112**, with a combined yield of



cis-**112**



trans-**112**

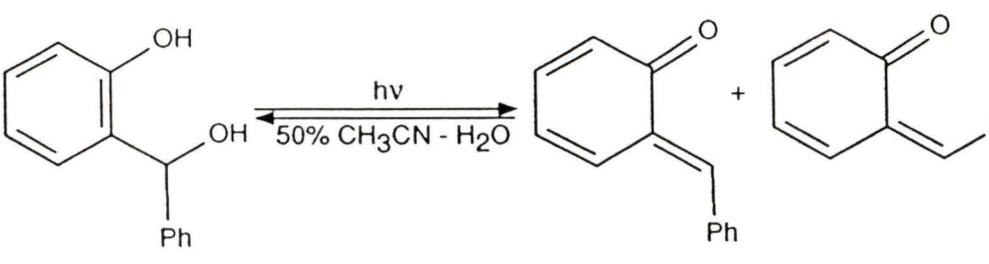
Table 2.3 Characteristic ^1H NMR data for *cis*-**112** and *trans*-**112**

		H_2	H_3	H_3'	Ha/Hb	CH_3
cis-**112**	found	δ 5.25 $J_{2,3}$=2.45 $J_{2,3'}$=8.48	δ 2.38 $J_{3,3'}$=13.34 $J_{3,4}$=6.50	δ 2.17 $J_{3',4}$=11.2	δ4.06/3.66	δ1.25
	reported[a]	5.23 $J_{2,3}$=2.80 $J_{2,3'}$=8.40	2.37 $J_{3,3'}$=13.00 $J_{3,4}$=6.50	2.17 $J_{3',4}$=10.50	4.06/3.66	1.26
trans-**112**	found	5.32 $J_{2,3}$=2.81 $J_{2,3'}$=2.81	2.27 $J_{2,3}$=13.54 $J_{2,3'}$=5.96	2.11 $J_{3',4}$=11.92	3.90/	1.20
	reported[a]	5.25 $J_{2,3}$=2.80 $J_{2,3'}$=2.80	2.22 $J_{3,3'}$=13.00 $J_{3,4}$=6.30	2.10 $J_{3',4}$=11.30	3.90/3.64	1.20

[a] from ref. 27.

100% (eq. 42). The products were isolated as the diastereomeric mixture by preparative TLC and characterized by GC-MS and 360 MHz ^{1}H NMR without further separation. The ^{1}H NMR signals were assigned by comparison with reported data.[27] The characteristic chemical shifts and coupling constants of *cis*-**112** and *trans*-**112** are listed in **Table 2.3**. As shown by eq. 42, this reaction is very clean with no side product being observed, even up to 100% conversion. The reaction is also efficient as it is quantitatively complete in one hour of photolysis. Although both *cis*-**112** and *trans*-**112** were observed, the maximum yield of *trans*-**112** is only 7%. By comparison, analogous thermal reaction of **101** at 180 °C gave *trans*-isomer in 25% yield along with 75% of *cis*-isomer.[27] Thus, the photochemical method provides a diastereoselective method to furnish *cis*-4-substituted chromans. The observed high diastereoselectivity of this reaction is consistent with a concerted cycloaddition mechanism.

Photolysis of **101** can in principle results in the formation of *o*-QM's in both

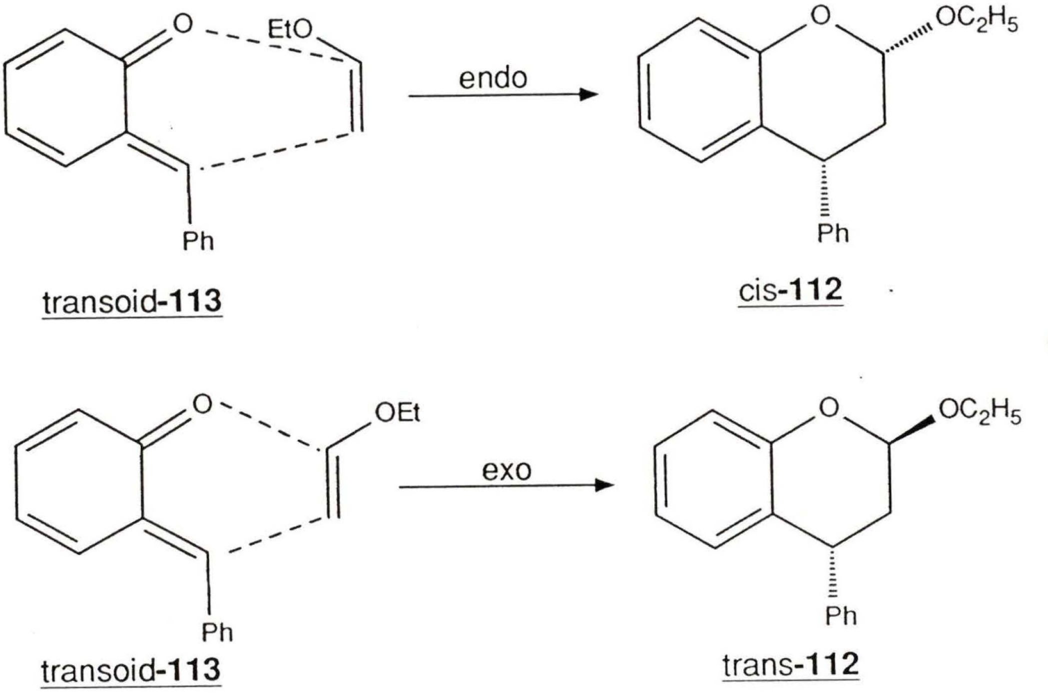


(43)

101 transoid-**113** cisoid-**113**

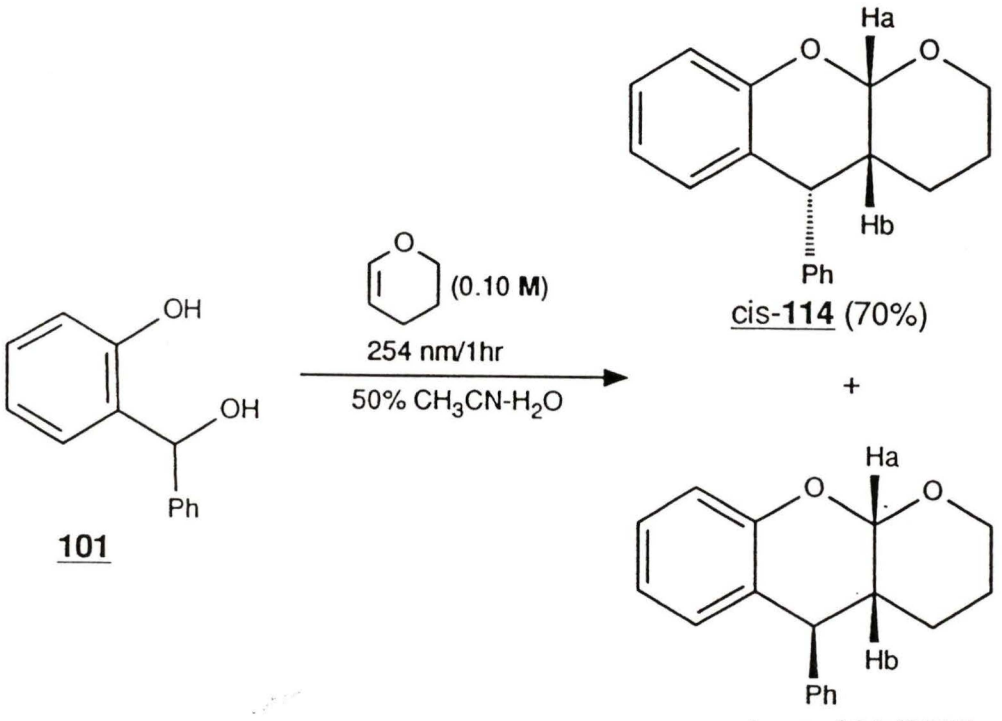
cisoid- and *transoid*-configurations (eq. 43). The *transoid*-*o*-QM is more stable for steric reason. In addition, it has been reported that *cisoid*-α,β-unsaturated carbonyl compounds have very low reactivity in cycloadditions.[133] Thus, it is reasonable to assume that *transoid*-**113** is formed predominantly from **101**.

Transoid-**113** may react with EVE in either *endo* or *exo* manner. The *endo*-addition affords *cis*-**112**, while *exo* affords *trans*-**112** (eq. 44). The observed high yield of *cis*-**112** implies that the *endo*-addition dominates in this reaction. The high *endo* selectivity in this reaction may be rationalized in terms of secondary attractive interaction between the ethereal oxygen and the diene moiety.[8,11,27]



(44)

Photolysis of **101** in the presence of dihydropyran also gave two tetrahydropyranobenzopyrans, *cis*-**114** and *trans*-**114** (eq. 45). The *cis*-isomer was again the major product. This observation is consistent with an *endo*-addition mode.



101

cis-114 (70%)

trans-114 (30%)

(45)

2.2 Product Quantum Yields

Photochemical efficiencies may be quantified in terms of a product quantum yield (Φ_p), which, by definition, is the moles of photochemical product formed for each mole of photon absorbed (eq. 46).[134] Selected product quantum yields (Φ_p)

$$\phi_p = \frac{Moles\text{-}of\text{-}product\text{-}formed}{moles\text{-}of\text{-}photon\text{-}absorbed} \qquad (46)$$

for photosolvolysis of **43** and **101** and for the formation of **44** and **112** were measured and listed in **Table 2.4**. The Φ_p's for the photomethanolyses of **43** and **102** in 50% MeOH-H_2O and the Φ_p's for the formation of **44** and **112** in 50%

CH_3CN-H_2O with 0.14 **M** EVE were measured on an optical bench utilizing a mercury arc lamp in conjunction with a monochromator to obtain an excitation wavelength of 280 nm. Samples (5.00×10^{-3} **M** substrate) were irradiated in 3 mL quartz cuvettes at ambient temperature while purged with argon. The light intensities were measured with potassium ferrioxalate ($K_3[Fe(C_2O_4)_3]{\bullet}3H_2O$) chemical actinometer.[135,136] The product yields were measured by GC. Φ_p's for the photosolvolysis of **43** in other aqueous alcohol solutions were also measured using ^1H NMR integration for calculating product conversions, and the

Table 2.4 Product quantum yields (Φ_p) for photosolvolysis of **43** and **101** and for formation of **44** and **112**

Substrate	Nucleophile	Product	Φ_p
43	MeOH	**4**	0.23 ± 0.03
	EtOH	**104**	0.18 ± 0.03[a]
	2-PrOH	**105**	0.12 ± 0.03[a]
	t-BuOH	**106**	0.040 ± 0.005[a]
	EVE	**44**	0.080 ± 0.005[b]
101	MeOH	**102**	0.46 ± 0.03
	EVE	**112**	0.27 ± 0.03[b,c] (0.25 ± 0.03)[b,d]

[a] by ^1H NMR integration, using the photolysis of **43** in 50% MeOH-H_2O as reference, estimated.
[b] measued in 50% CH_3CN-H_2O with 0.14 **M** EVE.
[c] total quantum yield for formation of *cis*- and *trans*-**112**.
[d] Φ_p for *cis*-**112.**

photomethanolysis of **43** in 50% MeOH-H_2O ($\Phi_p = 0.23 \pm 0.03$) as a secondary actonometric standard. The results in **Table 2.4** show that the photochemical reactivity of **101** in aqueous solution is about 2-3 times that of **43**. This may well be rationalized as due to the enhanced stability of **113** resulting from the increased conjugation available in the α-phenyl group.

As expected, in the dilute EVE concentration region, a rapid increase in Φ_p for the formation of **44** in 50% CH_3CN-H_2O was observed on increasing the EVE concentration (**Figure 2.3**). However, Φ_p levelled off at 0.10 **M** EVE and remained

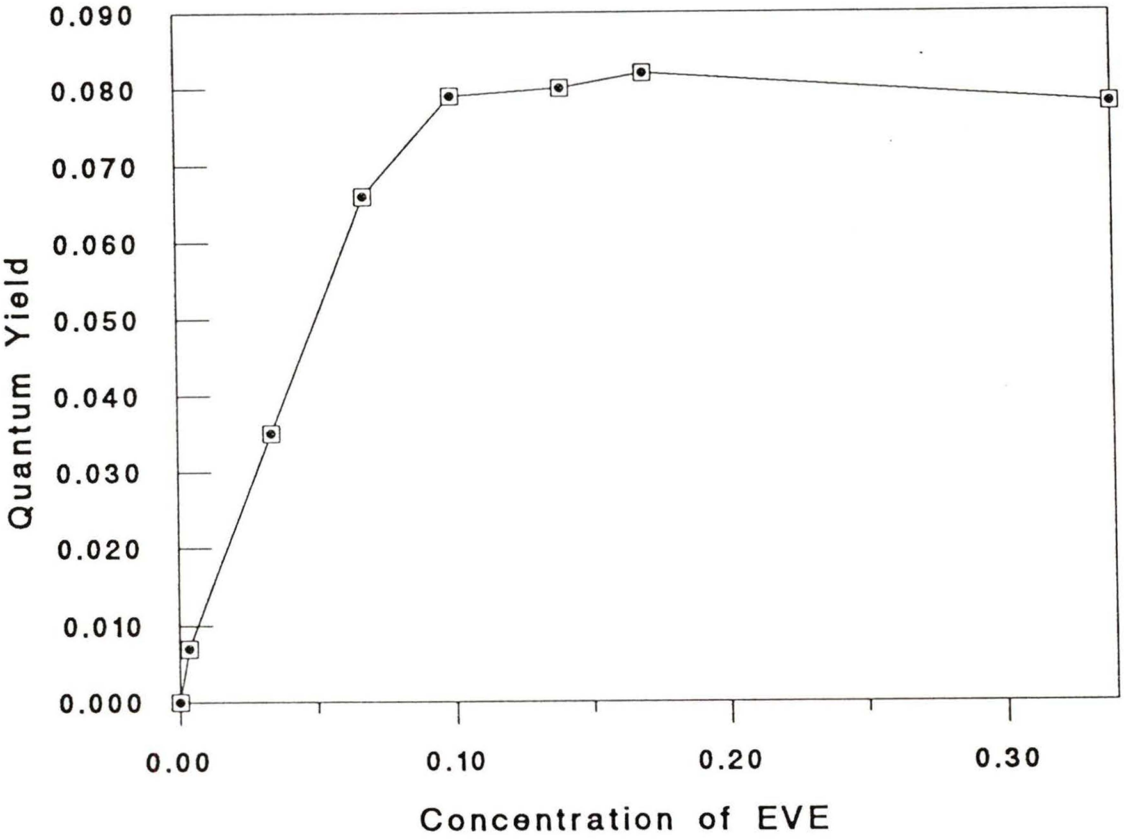


Figure 2.3 Product quantum yields (Φ_p) for the formation of **44** as a function of concentration of EVE in 50% CH_3CN-H_2O

unchanged up to 0.34 **M** EVE. Φ_p's at higher EVE concentration were not measured due to solubility problems. The only reaction channels for *o*-QM's in aqueous CH_3CN solution containing EVE are trapping by EVE to afford **44**, and reaction with H_2O to give back the starting material. Thus, increasing the EVE concentration will increase the observed photochemical efficiency for formation of **44**. On the other hand, increasing the EVE concentration also results in the increase of the fraction of light absorbed by the EVE at 280 nm, resulting in apparent decrease in efficiency for formation of **44**. Competition between the above two effects leads to the observed Φ_p-EVE concentration curve of **Figure 2.3**.

Previous discussion has shown that EVE is about 23 times more reactive than MeOH towards **1** in aqueous solution. However, the Φ_p for formation **44** (0.080) is only about one third of that for photomethanolysis of **43** (0.23) (**Table 2.4**). This disparity is due to that Φ_p was measured in aqueous solution. Although the reactivity of H_2O towards *o*-QM (**1**) is relatively very low, the concentration of H_2O is over 200 times higher than that of EVE. The hugh concentration difference enables H_2O to compete with EVE efficiently enough to reduce the Φ_p for the formation of **44**. In addition, absorption of light by EVE at 280 nm can also reduce the quantum efficiency for formation of **44**.

Employing steady-state assumption for **43*** (or **101***) and **1** (or **113**), the Φ_p for photomethanolysis in aqueous MeOH solution is given by eq. 47,[103] where Σk_d represents the sum of all deactivational process of S_1 not leading to solvolysis, k_{H2O}

$$\phi_p=(\frac{k_{MeOH}[MeOH]}{k_{MeOH}\ [MeOH]+k'_{H_2O}[H_2O]})\times(\frac{k_{H_2O}}{\sum k_d+k_{H_2O}[H_2O]}) \tag{47}$$

is the rate constant for water-catalyzed dehydration process, k_{MeOH} and k'_{H2O} are the rate constants for nucleophilic attack of MeOH and H_2O towards the *o*-QM, respectively. In eq. 47, the second bracketed quantity on the right hand side is the quantum yield for formation of *o*-QM ($(\Phi_p)_{QM}$), while the first bracketed quantity is the fraction of photogenerated *o*-QM that leads to methyl ether product, which is set equal to α. Thus eq. 47 may be rewritten as eq. 48. According to the

$$\phi_p=\alpha(\phi_p)_{QM} \tag{48}$$

results of a previous section, the nucleophilicity of MeOH to *o*-QM's was found to be about 10 times that of H_2O. Thus, $\alpha \approx 0.8$ in 50% MeOH-H_2O solution. Therefore, the quantum yields ($(\Phi_p)_{QM}$) for formation of *o*-QM's **1** and **113** in the above solvent system are calculated as 0.29 and 0.58, respectively.

2.3 Fluorescence and Lifetime Measurements

Photoexcited *o*-hydroxybenzyl alcohols may give *o*-QM's *via* either a step-wise or a concerted pathway. In the concerted pathway, *o*-hydroxybenzyl alcohols dehydrate directly from S_1 to give the corresponding *o*-QM's. In the step-wise

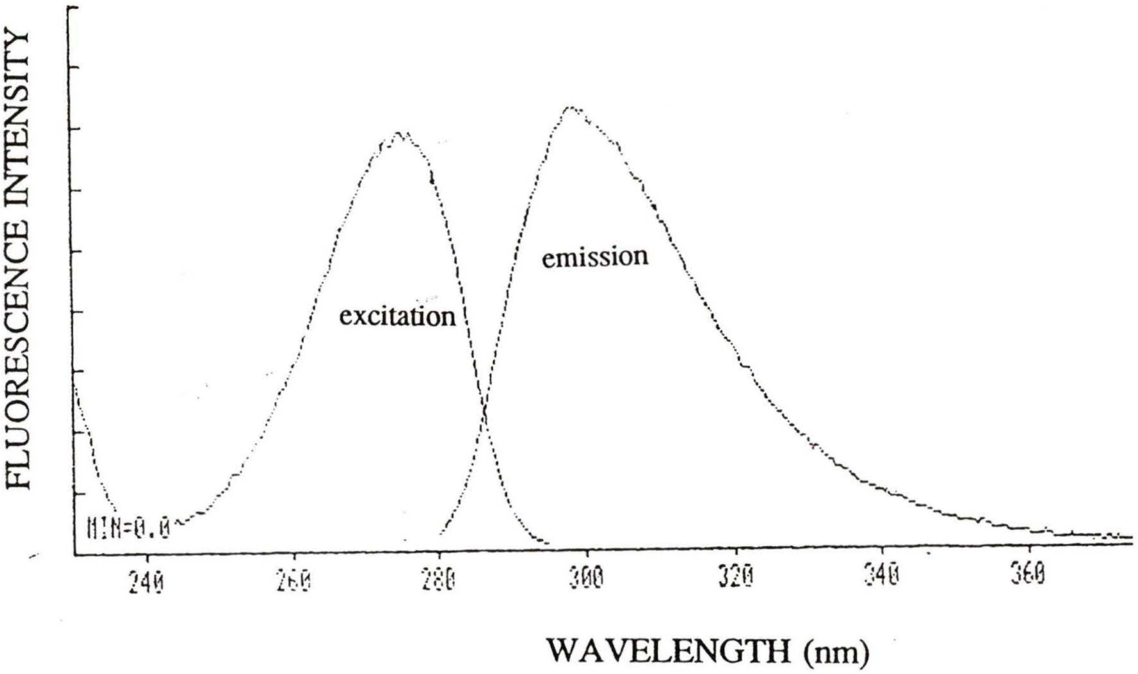


Figure 2.4 Fluorescence excitation and emission spectra of **43** in pH 1.0 solution (λ_{ex} = 265 nm, λ_{em} = 300 nm)

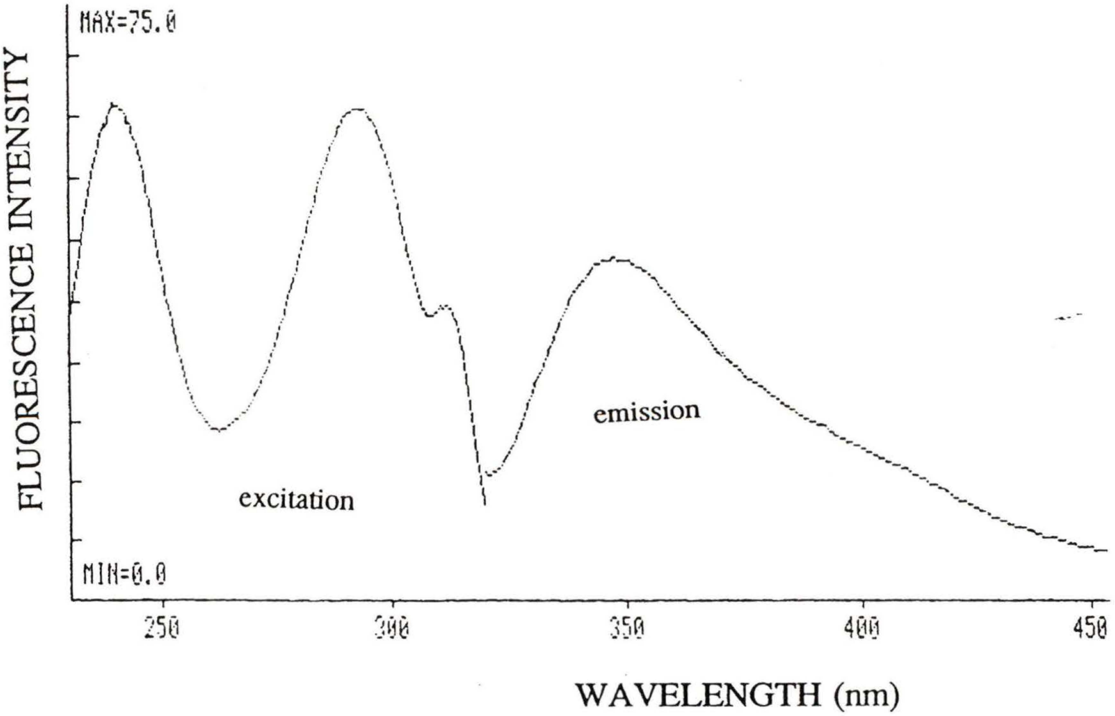


Figure 2.5 Fluorescence excitation and emission spectra **43** in pH 14.0 solution (λ_{ex} = 265 nm, λ_{em} = 350 nm)

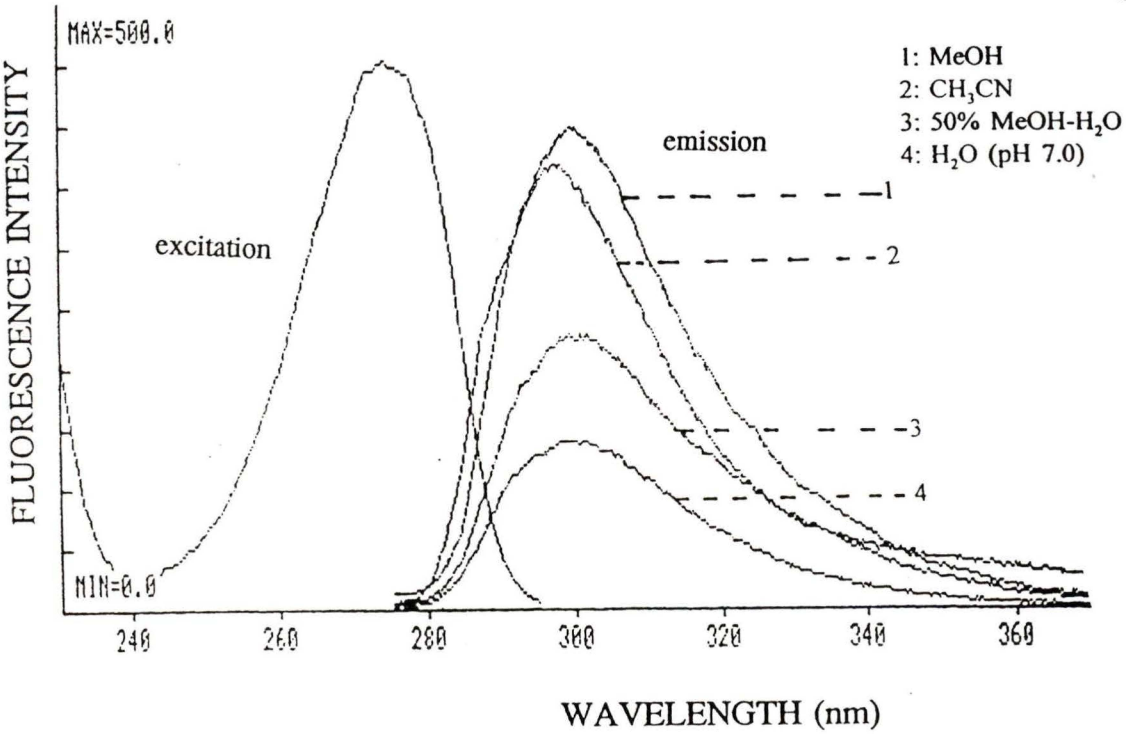


Figure 2.6 Fluorescence spectra of **43** in different solvents (OD = 0.038 ± 0.002 at λ_{ex} = 265 nm, λ_{em} = 300 nm)

pathway, the initially obtained S_1 state deprotonates adiabatically, to give the corresponding phenolates in S_1, which subsequently dehydroxylates to afford the *o*-QM's. The known enhanced acidity of phenols in S_1 is consistent with either pathway. Fluorescence measurements may provide additional information with regards to actual pathway leading to *o*-QM's.

Steady state fluorescence spectra of **43** were recorded in several solvents (λ_{ex} = 265 nm) at ambient temperature. The fluorescence emission and excitation spectra of **43** in wholly aqueous pH 1.0 is shown in **Figure 2.4** (λ_{max} = 300 nm). It is well known that the $pK_a(S_1)$ of phenols is ≤ 3.[139] Thus the singlet excited state of phenol **43** should be fully protonated at pH 1.0. Therefore, the observed emission band at 300 nm is assignable to the phenol form of **43**. When the fluorescence spectrum was taken in basic solution (pH 14), where **43** exist completely in its phenolate form, the emission band at 300 nm no longer observed. Instead, a very weak new band at 350 nm was observed which required much higher instrument sensitivity (**Figure 2.5**). This band is assigned as the fluorescence emission of the phenolate form of **43**. Fluorescence spectra of **43** in dry CH_3CN, pure MeOH, 50% MeOH-H_2O (pH 7.0 for H_2O portion) and H_2O (buffer solution pH 7.00) are shown in **Figure 2.6**. Only the phenol form emission band (300 nm) were observed in those solvents. Absolute fluorescence quantum yields (Φ_f) were measured in above solvents using 2-aminopyridine ($\Phi_f = 0.60 \pm 0.05$ in 0.05 **M** H_2SO_4)[137] and anisole ($\Phi_f = 0.29$ in cyclohexane)[138] as external

Table 2.5 Fluorescence quantum yields (Φ_f) and lifetimes (τ) of **43** in selected solvents

Solvent	τ	Φ_f
CH_3CN	5.2 ± 0.2 ns	0.21 ± 0.02^a 0.19 ± 0.02^b
MeOH		0.22 ± 0.02^a 0.20 ± 0.02^b
50% MeOH-H_2O (H_2O at pH 7)		0.14 ± 0.02^a 0.14 ± 0.02^b
H_2O (pH 7)	1.6 ± 0.2 ns	0.079 ± 0.003^a 0.075 ± 0.003^b

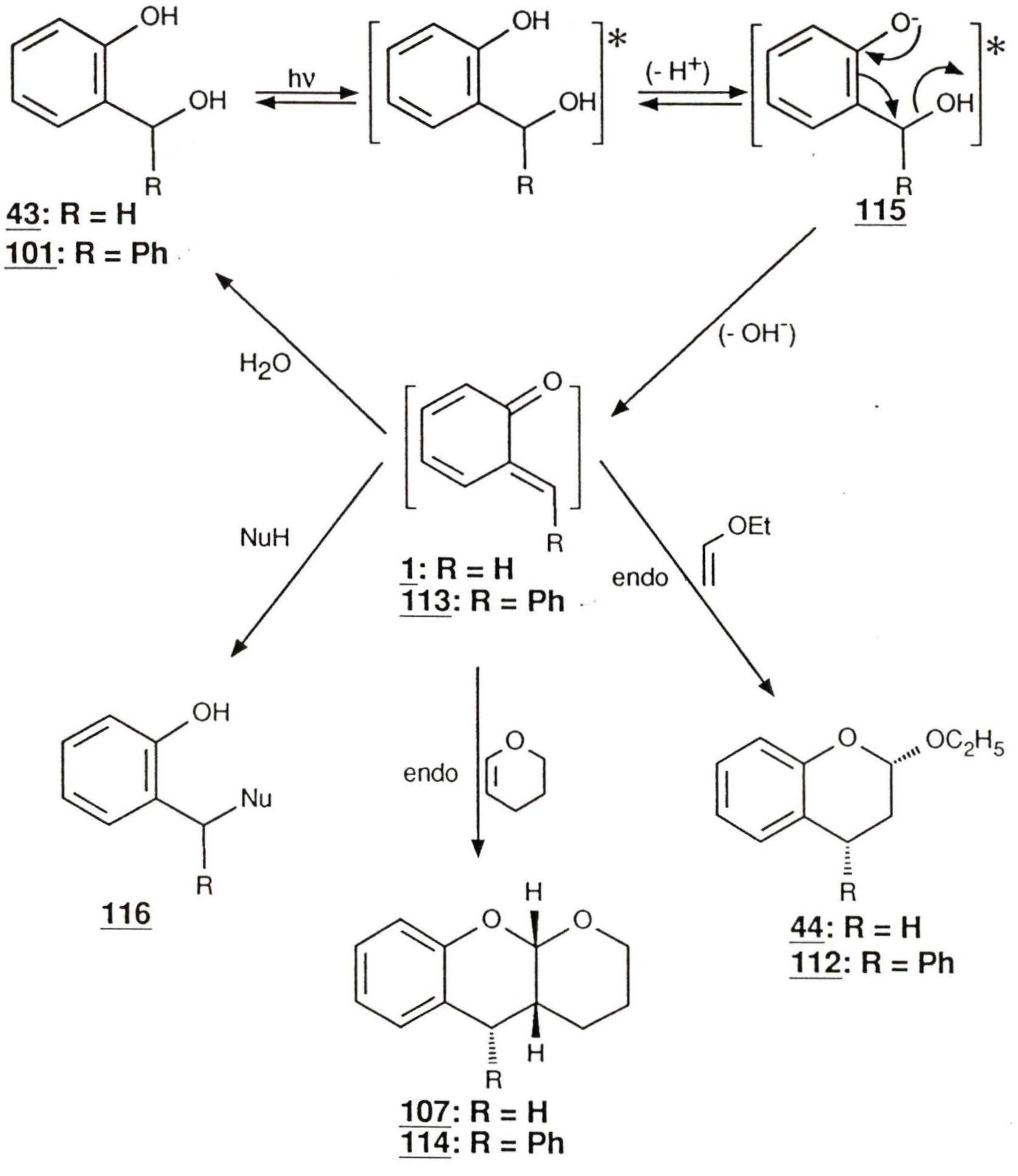
[a] using 2-aminopyridine as external standard.
[b] using anisole as external standard.

standards (**Table 2.5**). Φ_f of **43** in pure dry CH_3CN, where it is non-reactive, was found to be 0.21 with a lifetime $\tau = 5.2$ ns. The fluorescence quantum yield is about three fold lower in H_2O at pH 7 ($\Phi_f = 0.079$, $\tau = 1.6$ ns). This can be attributed to either the adiabatic deprotonation, which leads to the excited phenolate,[139] or the dehydration from S_1, which affords *o*-QM (**1**). Both processes are promoted by H_2O. Interestingly, fluorescence quantum yield of **43** in MeOH was found to be $\Phi_f = 0.22$, which is about the same as that in pure CH_3CN, although photosolvolysis of **43** was observed in pure MeOH. Φ_f in 50% MeOH-H_2O is about two times as that in pure H_2O (**Table 2.5**). As mentioned in a previous section, the maximum in photomethanolysis efficiency of **43** was observed in 50% MeOH-H_2O. Thus, if the phenol form in S_1 is directly responsible for the formation of *o*-QM (**1**), its fluorescence emission should be very weak in 50% MeOH- H_2O.

Phenols are known to undergo efficient adiabatic ionization of the phenolic hydroxyl groups to give the corresponding phenolates in excited state in aqueous solution.[115,139] Therefore, it is reasonable to assume that *o*-hydroxybenzyl alcohols undergo similar adiabatic deprotonation to lead the corresponding excited phenolate, upon irradiation in aqueous solution. It has been shown that the fluorescence emission of the phenolates of photochemically stable phenols are comparable with that of the phenol form.[115,139] Thus, the weak emission of the phenolate of **43** in aqueous media, together with the results of fluorescence quantum yields of the phenol form in aqueous MeOH, suggest that the phenolate ion in the S_1 state is the reactive species responsible for the formation of *o*-QM (**1**). That is, almost all of the phenolate form generated appears to be removed efficiently.

2.4 Mechanism

The results of this study have shown that *o*-hydroxybenzyl alcohols undergo efficient photosolvolysis in aqueous solution. This reaction is believed to proceed *via* *o*-QM intermediates, which are trapped by alcohol nucleophiles, and by electron-rich dienophiles to give the expected [4 + 2] cycloaddition products. The proposed mechanism for photosolvolysis and photoinduced [4 + 2] cycloaddition of *o*-hydroxybenzyl alcohols in aqueous solution is shown in **Scheme 2.4**. In neutral aqueous solution, *o*-hydroxybenzyl alcohols exist as the phenol forms in the ground state. Phenols in S_1 are much more acidic than in the ground state and undergo an efficient adiabatic deprotonation to give the corresponding phenolates, which remain on the excited singlet state.[115,139] For the phenols studied in this work, phenolate **115** would be expected to be formed efficiently. Excited phenolates are powerful electron-donors, even better than the corresponding hydroxy and methoxy groups. The methoxy group has been shown to efficiently facilitate the photodehydroxylation on irradiation of methoxybenzyl alcohols.[103] It is not surprising then that the excited state phenolates can also assist the dehydroxylation. Fluorescence studies also indicate that the excited phenolate is


OH
OH
R
43: R = H
101: R = Ph
hν
OH
OH
R
*
(- H+)
O-
OH
R
*
115
(- OH-)
H2O
O
R
1: R = H
113: R = Ph
NuH
endo
OEt
endo
O
OH
Nu
R
116
H
O
O
H
R
107: R = H
114: R = Ph
O
OC2H5
R
44: R = H
112: R = Ph

Scheme 2.4

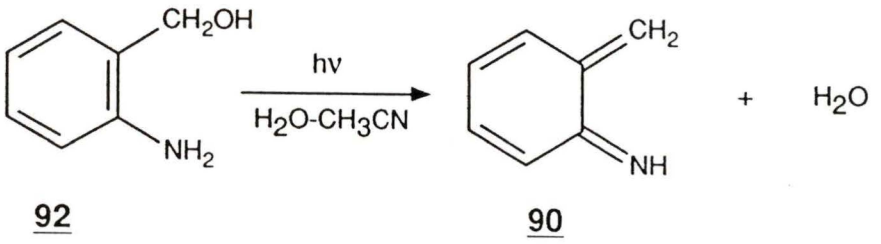
the reacting species since its observed emission is very weak under reaction conditions. Therefore, it is phenolate **115** that activates the heterolysis of the benzylic C-OH bond. The result of the cleavage of the benzylic C-OH bond is the formation of the corresponding *o*-QM. Although both *transoid-o*-QM and *cisoid-o*-QM could be formed from some substrates, for steric reasons, the *transoid*-isomer is believed to be formed predominately. The resulting *transoid-o*-QM can then either react with nucleophiles to give the Michael addition product **116**, or add H_2O to regenerate the starting material. It can also react with electron-rich dienophiles to give a [4 + 2] cycloaddition product in a totally regiospecific manner. The cycloaddition may proceed *via* either an *endo* or an *exo* manner. The *exo*-addition between the *transoid-o*-QM and the dienophile affords the thermodynamically more stable *trans*-chroman derivative, while the *endo* addition affords the kinetically favorable *cis*-chroman derivative. The major products observed are the *cis*-chroman derivatives, indicating that the reaction is dominated by an *endo*-addition manner.

The photosolvolysis and the photoinduced [4 + 2] Diels-Alder type reaction of *o*-hydroxybenzyl alcohols are very clean and efficient as well. Thus, this work provides an additional general route for generation of *o*-QM's, and a regiospecific and diastereoselective route for assembling polycyclic structures under very mild conditions.

3. Photogeneration and Trapping of *o*-Quinone Methide Imine from 2-Aminobenzyl Alcohol in Acidic Solution

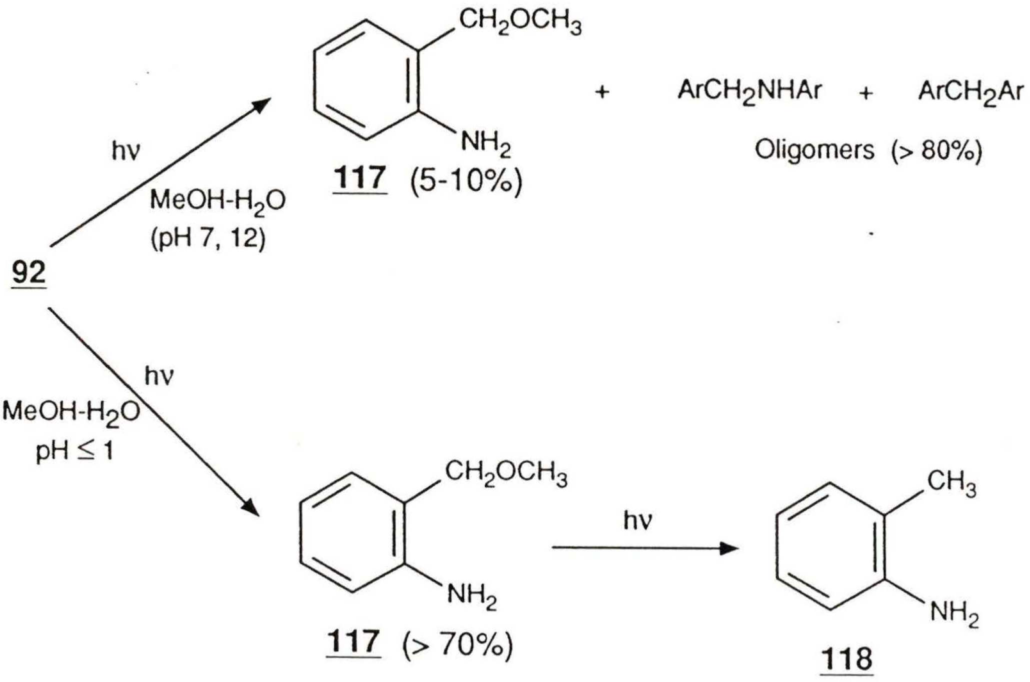
3.1 Product Studies

It has been shown in the previous chapter that photolysis of *o*-hydroxybenzyl alcohols in aqueous solution results in the formation of *o*-QM's. The compound under study in this chapter is 2-aminobenzyl alcohol (**92**), a close relative of the *o*-hydroxybenzyl alcohols. If a similar photochemical mechanism operates for **92**, then *o*-QMI (**90**) would be the expected intermediate (eq. 49). Thus, the photosolvolysis of **92** in aqueous MeOH solution at different acidities is studied and compelling evidence for the formation of **90**, *via* initial adiabatic deprotonation of its photoexcited conjugate acid **116** followed by a dehydroxylation step, is presented in this chapter.



(49)

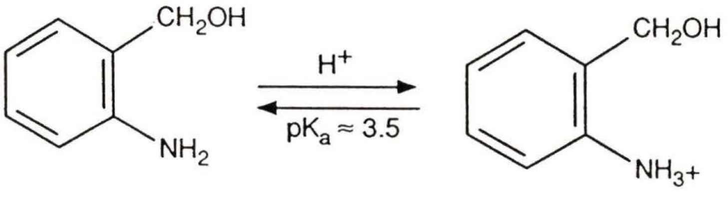
Photolysis of an argon purged 50% MeOH-H_2O solution (*v*/*v*) (pH 7 and pH 12 for the aqueous portion) of **92** (4.1×10^{-3} **M**) for 30 min resulted in substantial loss of starting material (> 90%), as indicated by the ^{1}H NMR integration of the benzylic methylene signal of the starting material at δ 4.6 relative to the aromatic protons. The expected 2-aminobenzyl methyl ether (**117**), assigned by the methoxy singlet at δ 3.3 (OCH_3) and the benzylic methylene ($ArCH_2O$) singlet at δ 4.4, was observed only as a minor product (< 10% percent of the product mixture by ^1H NMR integration). The ^1H NMR spectrum also showed several methylene peaks between δ 4.0-4.7, which are assigned as benzylic methylene groups attached to amino moiety ($ArCH_2NHAr$), implicating formation of dimers, trimers and probably



Scheme 3.1

higher oligomers. In addition, a broad peak observed between δ 3.7-4.0 (not exchangeable with D_2O) suggests the formation of oligomers of the structural type $ArCH_2Ar$ (**Scheme 3.1**). These two types of photochemical products ($ArCH_2NHAr$ and $ArCH_2Ar$) arise, respectively, *via* nucleophilic attack of the methylene position of the proposed *o*-QMI (**90**) intermediate by amine nitrogen, and by the *ortho*- and *para*-positions of the benzene ring activated by the amine. Mass spectral analysis of these samples gave molecular ions consistent with the formation of dimers and trimers. Photolysis of an argon purged 50% CH_3CN-H_2O solution of **92** at pH 7 and pH 12 also resulted in loss of starting material and the formation of oligomers, except that **117** was absent.

Photolysis of **92** in acidic 50% MeOH-H_2O solution (pH 1 or less for the aqueous portion) as above gave clean conversion to **117**, no self-condensation products were observed (**Scheme 3.1**). Ether **117** was isolated by preparative TLC and characterized by ^1H NMR and mass spectroscopy. Control experiments in the dark at pH 1 and higher acidities for similar periods of time gave no detectable reaction. This observation is expected since the amine would be fully protonated, and the resulting ammonium ion **119** is highly electron-withdrawing ($\sigma \approx +1$), hence deactivating with respect to thermal solvolysis. Photolysis at higher pH gave increasing amounts of self-condensation products at the expense of **117**. A pK_a of 3.5 for **119** was determined by UV-Vis titration and is in the region expected for typical aryl amines (eq. 50). The ammonium ion, unlike the free amine, is no



92 119

(50)

longer a nucleophile. It would not react with the photogenerated *o*-QMI intermediate to give the self-condensation products. Thus, protonation of ground state **92** results in the photosolvolysis being clean and free from oligomers.

High conversions to ether **117** could be achieved on photolysis of **92** in acidic MeOH-H_2O solution (pH $\leq$ 1 for aqueous portion). This is shown by a plot of conversion *vs* photolysis time (**Figure 3.1**) carried out in 50% MeOH-H_2O (*v*/*v*) at pH 1.0. At high conversion (> 30%), the reduced product, *o*-toluidine (**118**), was formed as a minor product. The identity of **118** was determined by ^{1}H NMR (benzylic methyl singlet at δ 2.1) and GC (by comparing its retention time with that of an authentic sample, which is commercially available). *o*-Toluidine (**118**) is a secondary photochemical product, formed *via* photolysis of **117**, as shown by independent photolysis of an authentic sample of **117**. The mechanism of this reaction is assumed to be *via* initial $ArCH_2$-O bond homolysis followed by hydrogen abstraction from the solvent or from the methoxy radical.

Attempts were made to measure Φ_p for formation of **117** using GC as the

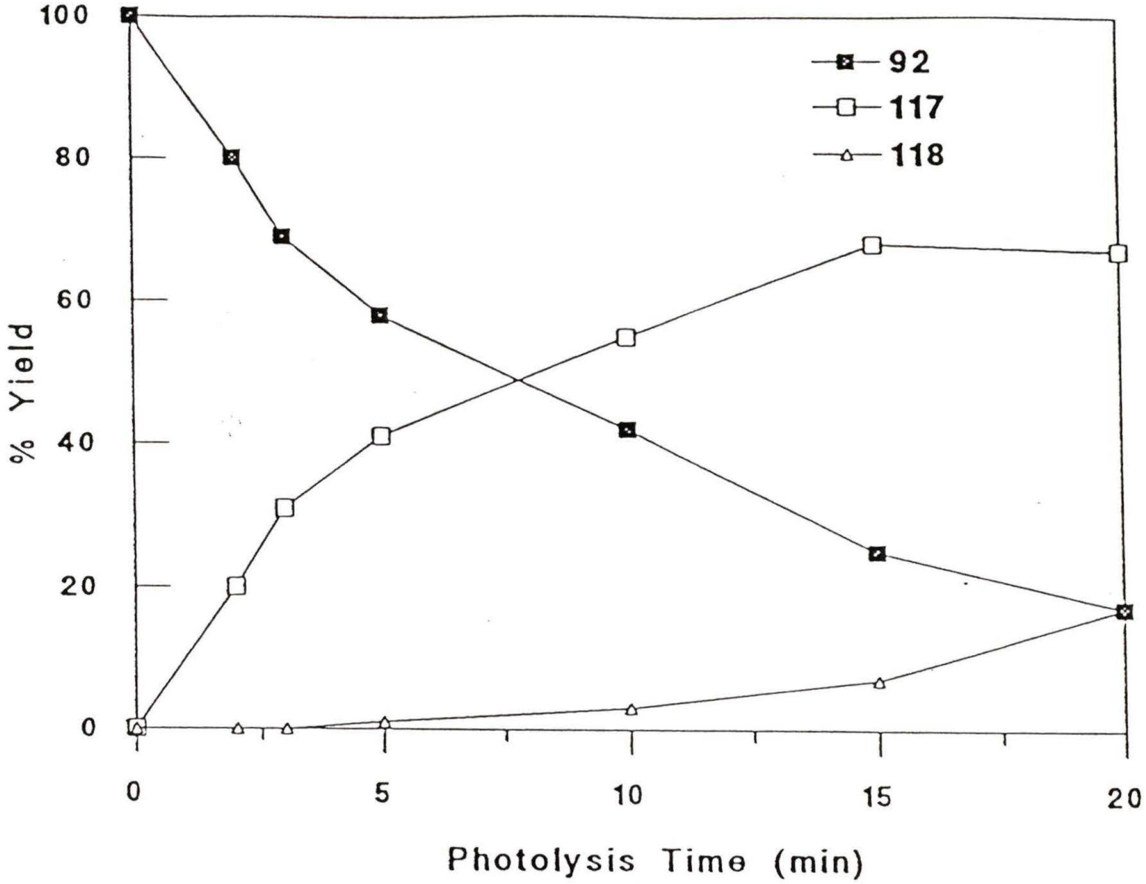


Figure 3.1 Plot of conversion of **92** to **117** in 50% MeOH-H_2O (*v*/*v*) as a function of photolysis time at pH 1.0

analytical technique. However, the starting material **92** always appeared as a broad poorly resolved band, limiting the accuracy of the method. As an alternative, ^1H NMR integration of the product mixture of small scale preparatory photolyses (254 nm, 4 lamps, Rayonet reactor) was used to estimate Φ_p. The photosolvolysis of **43** in 50% MeOH-H_2O ($\Phi_p = 0.23 \pm 0.03$) was used as the secondary actinometric reference for **92** in the same solvent system except that the H_2O portion was at pH 1.0. Chemical and quantum yields for formation of **117** on photolysis at different acidities beginning at pH 7.0 are given in **Table 3.1**. Clean reaction and high

Table 3.1 Chemical and quantum yields of **117** on photolysis of **92** in 50% MeOH-H_2O as a function of acidity

acidity[a]	yield (%)[b]	Φ_p[c]
pH 7.0	≈ 8%[d]	--
pH 3.0	≈ 8%[d]	--
pH 2.0	20%[d]	--
pH 1.0	67%	0.31 ± 0.05
5%[e] (H_o = +0.08)[f]	62%	0.29 ± 0.05
10%[e] (H_o = -0.36)[f]	67%	0.41 ± 0.05
20%[e] (H_o = -1.08)[f]	69%	0.32 ± 0.05
30%[f] (H_o = -1.72)[f]	66%	0.30 ± 0.05

[a] acidity of H_2O portion of solvent.
[b] calculated by ^1H NMR integration; estimated error ± 10% of quoted value.
[c] Φ_p's measured using the photolysis of **43** in 50% MeOH-H_2O as reference.
[d] estimated since oligomers are the major products at this pH.
[e] *w/w* H_2SO_4.
[f] approximate H_o acidity function value of the H_2SO_4 portion.

yields for **117** were observed only below pH 2. However, overall conversions, as measured by loss of starting material **92** by ^1H NMR integration, were independent of the acidity.

Photolyses of 50% ROH-H_2O solutions of **92** for several alcohols at pH 1.0 all gave clean photosolvolyses to afford the corresponding ethers, as shown in **Table 3.2**. The yields of ethers decreased with increasing branching of the alkyl

Table 3.2 Yields of ethers o-$NH_2C_6H_4CH_2OR$ on photolysis of **92** in 50% ROH-H_2O at pH 1.0

ROH	Yield of o-$NH_2C_6H_4CH_2OR$ (%)[a]
MeOH	67
EtOH	41
2-PrOH	18
t-BuOH	≤ 3

[a] calculated by ^1H NMR integration; estimated error ± 15% of quoted value.

group of the alcohols. This observation is similar to that for the photosolvolysis of **43** in aqueous alcohols. The relative yields again reflect the relative nucleophilicities of the alcohols employed.

3.2 Fluorescence and Lifetime Measurements

That the clean photosolvolysis of **92** was only observed in acidic solution suggests that acid-base dissociation of **119** in the S_1 state is important in the overall reaction mechanism. Aryl ammonium ions are stronger acids in S_1 than in the ground state.[139-141] For example, the ground and singlet excited state pK_a for 2-naphthylammonium ion is 4.1 and -0.8, respectively.[141] This has been rationalized as being the result of the enhanced electron donation of the lone pair electrons on nitrogen to benzene ring in S_1, making the benzene ring electron-rich and the nitrogen less basic.

Fluorescence emission and excitation spectra of **92** in wholly aqueous solution at pH 7.00 are shown in **Figure 3.2** (λ_{em} = 345 nm; τ = 1.4 ± 0.1 ns; Φ_f = 0.048 ± 0.005). On increasing the acidity of the solution to 1.25 **M** H_2SO_4 (H_o ≈ -0.56), the emission intensity at 345 nm decreased by a fact of > 20, but no new emission band were observed (**Figure 3.3**). However, the excitation spectrum now resembles the absorption band of the ammonium ion **117**. This is expected since at this acidity, the ground state is fully protonated. At intermediate acidities, it was possible to see two excitation bands assignable to **92** and **117**. However, only one

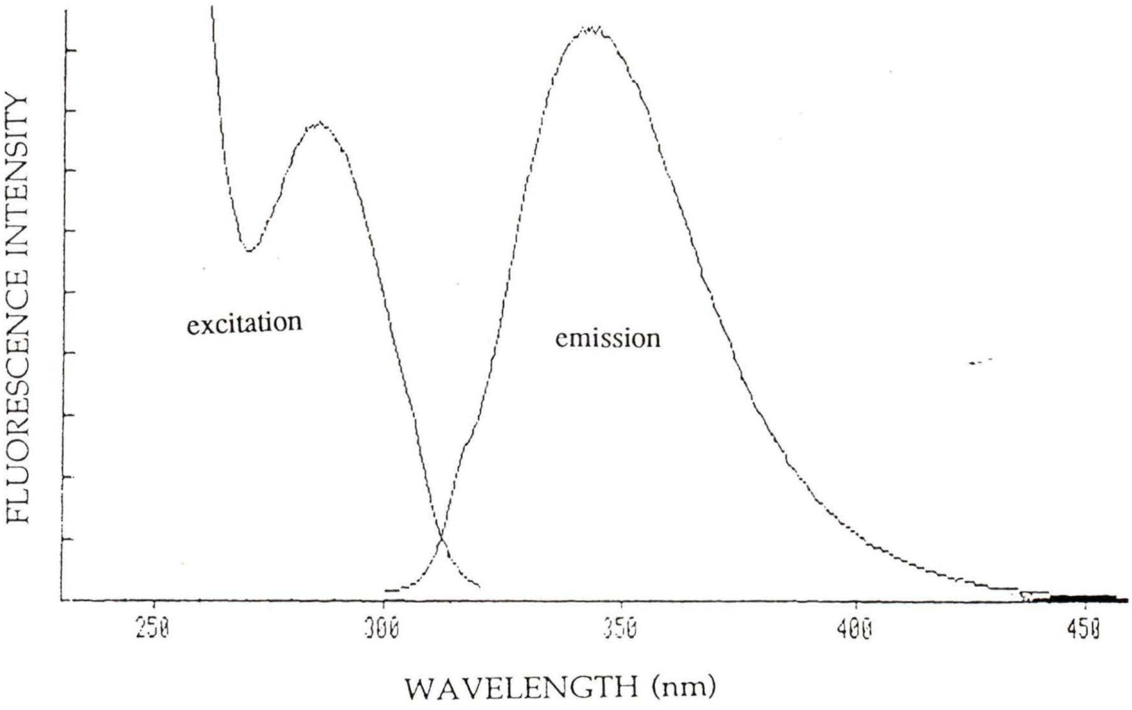


Figure 3.2 Fluorescence excitation and emission spectra of **92** in pH 7.00 buffer solution (OD = 0.041 ± 0.002 at λ_{ex} = 265 nm, λ_{em} = 345 nm)

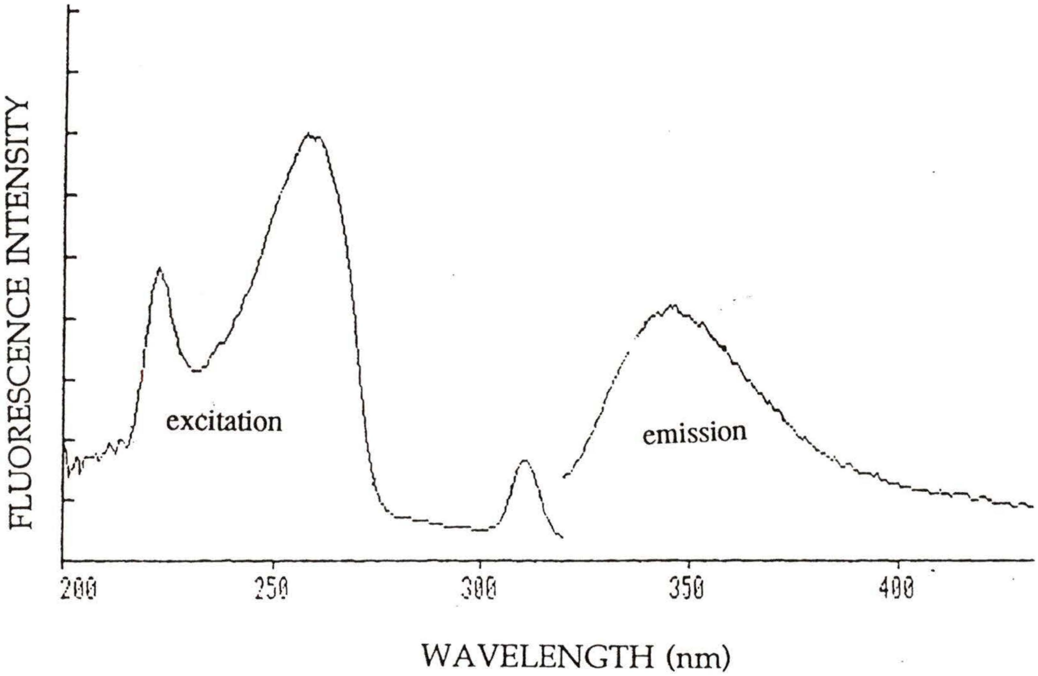


Figure 3.3 Fluorescence excitation and emission spectra of **92** in 1.25 **M** H_2SO_4 (λ_{ex} = 265 nm, λ_{em} = 345 nm)

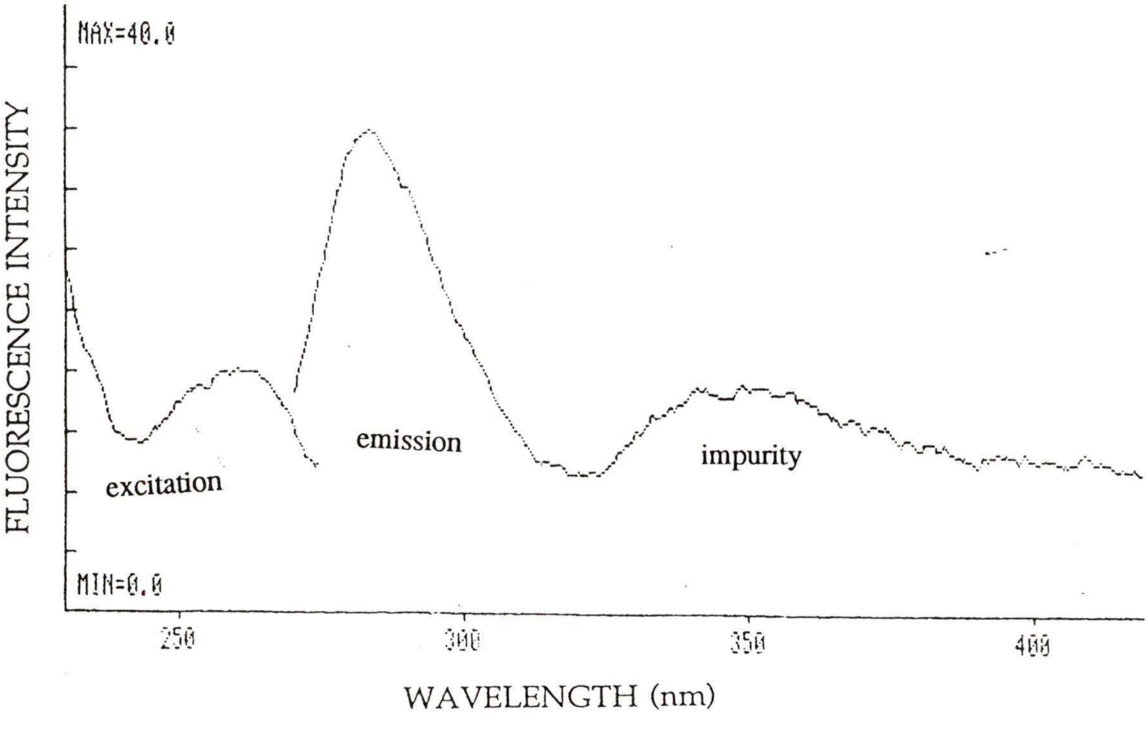
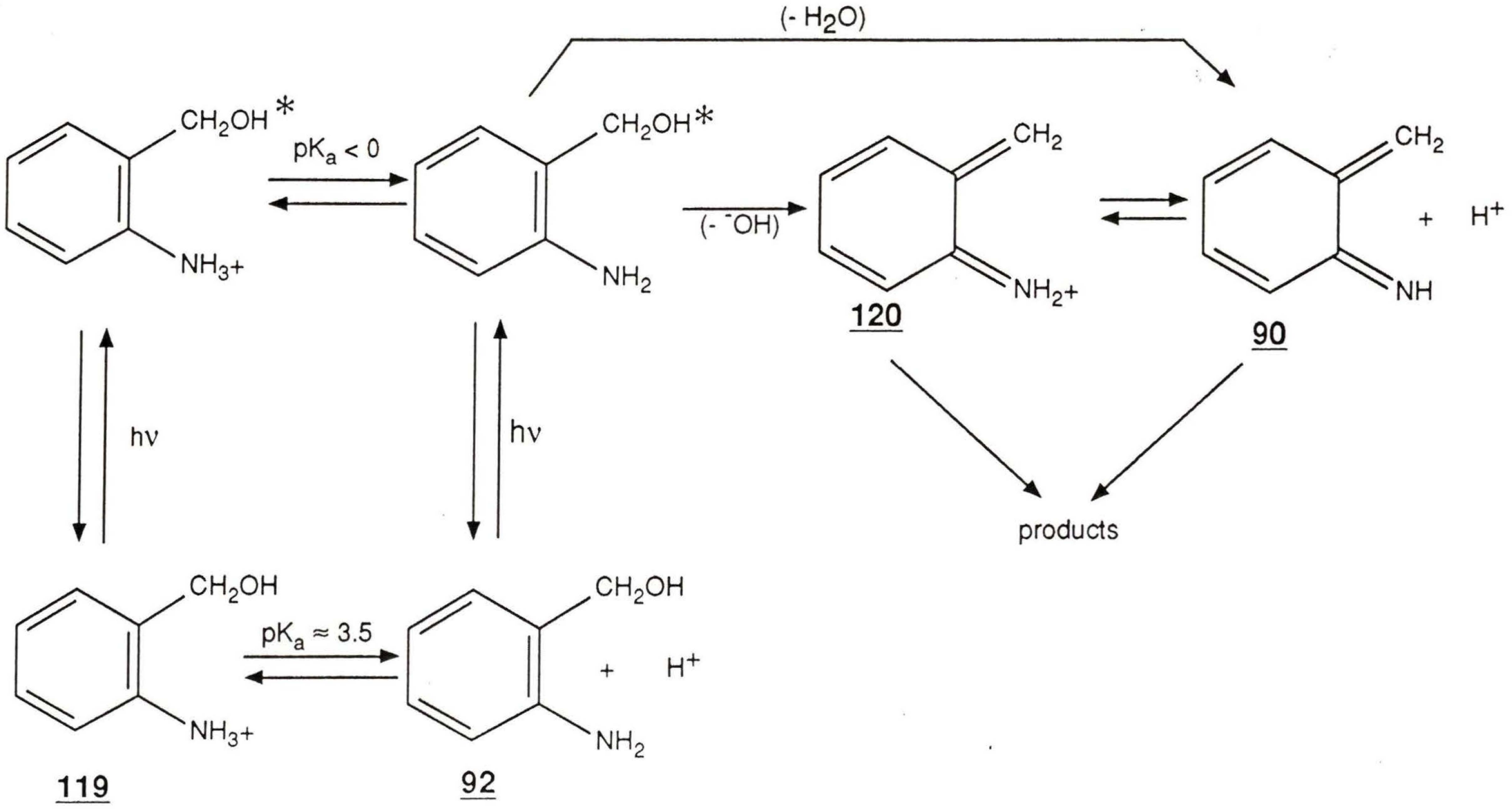


Figure 3.4 Fluorescence excitation and emission spectra of **92** in 5.0 **M** H_2SO_4 (λ_{ex} = 265 nm, λ_{em} = 285 nm)

emission band assignable to **92** was observed. In 3.5 **M** ($H_o \approx -1.62$) and 5.0 **M** ($H_o \approx -2.28$) H_2SO_4, a weak blue shifted band maximumed at 285 nm assignable to **117** was observed **(Figure 3.4)**. The even weaker band at 350 nm arises from impurities in the 5.0 **M** H_2SO_4. This has been confirmed by taking the fluorescence spectra of the "pure" acid solution under identical conditions. Thus, the excited state pK_a value of **117** can be estimated to be in the -0.6 to -1.62 range. The Φ_f of **92** in pure dry CH_3CN ($\Phi_f = 0.16 \pm 0.05$, $\tau = 2.8 \pm 0.2$ ns), where it is not reactive, is about three fold higher than that in pure H_2O. The fluorescence emission of **92** was also quenched by MeOH ($\Phi_f = 0.050 \pm 0.05$), indicating that the S_1 state of the free amine is the species responsible for the photosolvolysis.

3.3 Mechanism

Whereas *o*-aminobenzyl alcohol (**92**) in its free amine or protonated form (**119**) is stable to thermal photolysis, we have found that photolysis of **119** results in a very cleanly reacting photosolvolytic system. The proposed mechanism for photosolvolysis of **92** (**119**) is shown in **Scheme 3.2** which is consistent with the experimental data available and results for related systems. Direct excitation of **92** (pH > 3.5) does result in reaction, giving rise to either **120** or **90**. This was expected since it has already shown by the previous chapter that **43** is reactive towards photosolvolysis. It is unlikely that loss of hydroxide ion would be assisted by protons at these pH's.[100,103] The complexity of the product mixture observed at these pH's is the direct consequence of the availability of **92**, which is


(- H2O)
CH2OH *
pKa < 0
NH3+
CH2OH*
NH2
(- ⁻OH)
CH2
NH2+
120
CH2
+ H+
NH
90
hν
hν
products
CH2OH
pKa ≈ 3.5
NH3+
119
CH2OH
+ H+
NH2
92

Scheme 3.2

nucleophilic at nitrogen (as well at the *ortho* and *para*-positions of the benzene ring). It is evidenced that attack of **120** or **90** by **92** competes effectively with attack by MeOH solvent. Although MeOH is in great excess, the much greater nucleophilicity of the amino group compensates for this.

Photolysis in more acidic medium ($pH \leq 1$) excites **119** exclusively. Because aryl ammonium ions are much acidic in S_1, adiabatic deprotonation follows, giving rise to excited **92**. Subsequent dehydroxylation gives rise to either **120** or **90**. The much weaker fluorescence emission observed for excited **92** obtained *via* this adiabatic route is consistent with an additional pathway to **120** or **90**, *viz.*, acid catalyzed loss of hydroxide ion. Precedent for the interaction of free amines with protons has been reported by Shizuka *et al.*[140,141], who reported proton quenching of singlet excited naphthylamines as their free bases, although no net chemistry was observed for these substrates. The clean photolysis in acid is explained by the lack of free base **92** acting as a competing nucleophile at these acidities. Attempts to trap of **120** or **90** *via* [4 + 2] cycloaddition reactions were all met with failure. This is probably due to the fact that in acid solutions, *o*-QMI exists in the protonated form **120**, which is electron-deficient, and hence does not react with electron-deficient dienophiles. The protonated *o*-QMI **120** may be trappable with electron-rich dienophiles, which, unfortunately, are unstable in acid solutions.

4. Conclusions

The photochemistry of several *o*-hydroxybenzyl alcohols has been studied in aqueous alcohol solution. In general, photolysis of these compounds results in very clean and efficient photosolvolysis. Evidence has been presented to support that the photosolvolysis proceeds *via* an *o*-QM intermediate, as shown by trapping with nucleophiles, as well as by several electron-rich dienophiles. The latter reaction gave rise to formal [4 + 2] cycloaddition products in a regiospecific and diastereoselective manner in good yields. The mechanism is believed to involve adiabatic deprotonation of the phenol form upon excitation to S_1, to generate the corresponding phenolate, which subsequently reacts by dehydroxylation, to give the *o*-QM. It is believed that the *transoid-o*-QM (where relevant) is the reacting species, which reacts with electron-rich dienophiles in an *endo* manner, to give the corresponding chroman derivative. This work provides a clean and efficient route for *o*-QM generation and a regiospecific method for assembling polycyclic structures under very mild conditions.

The photosolvolytic behavior of *o*-aminobenzyl alcohol has also been studied over a range of pH and in moderately concentrated aqueous H_2SO_4 solution. Although reactive in all pH's studied, clean solvolytic reaction was observed only when pH ≤ 1. The reaction in acidic medium is believed to proceed *via* adiabatic deprotonation of the protonated substrate ($ArNH_3^+$) in S_1 to give the excited free base. Subsequent dehydroxylation gives *o*-QMI as the reactive intermediate.

Nucleophilic attack by added ROH gives the photosolvolytic product.

Finally, this thesis has shown that interesting and expected photochemistry can result from studying simple aromatic compounds in aqueous solution. It is evident that much more can be learned in this area by exploring related substrates.

5. Experimental

5.1 General

Gas chromatography (GC) was carried out on a Varian 3700 gas chromatograph with a Hewlett-Packard 3390A integrator using a DB-5 capillary column. Analytical thin layer chromatography (TLC) was performed on precoated silica gel plates (Macherey-Nagel, Sil/UV-Vis$_{254}$), using solvent systems as indicated in each experiment. Preparative TLC was performed on Analtech GF 1000 micrometer silica gel plates. Mass spectra were taken on either a Finnigan 3300 or a Kratos Concept H instrument. ^{1}H NMR spectra were recorded on either a Perkin-Elmer R32 (90 MHz), a Bruker WM 250 (250 MHz) or a Bruker AM 360 (360 MHz) instrument using $CDCl_3$ or acetone-d_6 as solvents. Tetramethylsilane (TMS) was used as an internal standard on the 90 MHz instrument. Chemical shifts are reported in ppm down field from TMS and splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet and b, broad. UV-Vis spectra were recorded on a Phillips PU 8740 UV/Vis, a Cary 1 UV-Vis or a Pye Unicam SP8-400 UV/Vis spectrophotometer. IR spectra were recorded on NaCl plates using a Perkin-Elmer 1320 infrared spectrophotometer. All preparative photolyses were carried out in a Rayonet RPR 100 photochemical reactor equipped with 16 × 254 nm lamps, using quartz tubes (100-200 mL) which were cooled with an internal cold finger (< 15°C). The solutions were continuously purged with a stream of argon *via* a long fine needle for 10 min before and during the irradiation, to effect stirring and deoxygenation.

5.2 Materials

o-Hydroxybenzyl alcohol (**43**), benzofuran-2(3*H*)-one (**5**) and *o*-aminobenzyl alcohol (**92**) were purchased from Aldrich and recrystallized before use (**43** from toluene; **5** and **92** from 95% ethanol in an acetone/dry ice bath). ^{1}H NMR and GC analysis showed that they were > 98% pure. Ethyl vinyl ether (EVE), 3,4-dihydro-2*H*-pyran and 2,3-dihydrofuran were all Aldrich reagents. Aqueous solutions of the appropriate pH were either commercially available phosphate buffers or diluted from standardized stock of known NaOH or H_2SO_4 concentration. The pH of the solutions used were checked by a pH meter prior to photolysis. Acetonitrile was HPLC grade and cyclohexane was spectrophotometric grade for fluorescence measurements. The solvents CH_3CN, MeOH, 95% EtOH, 2-propanol, *t*-butyl alcohol and diethyl ether for photolysis and work-up were all Aldrich or other commercially available reagents and used as received after purity checks. CH_2Cl_2 and THF were distilled before use. Spectrophotometric grade acetone was used as the solvent for GC and GC/MS analysis. Reagents such as $MgSO_4$, $NaBH_4$, and $NaHCO_3$ were used without further purification.

Work-up for photochemical reactions carried out in a wholly organic solvent was accomplished by simple evaporation of the solvent. Photochemical reactions carried out in aqueous solutions were worked up by adding a saturated aqueous solution of NaCl and extracting with 5 × 75 mL portions of CH_2Cl_2. The organic extracts were then combined and dried over $MgSO_4$. Filtration of the $MgSO_4$ and evaporation of CH_2Cl_2 under reduced pressure provided the crude photochemical products which were then separated by preparative TLC as required and characterized by ^1H NMR, mass spectrum, IR, GC and GC/MS.

α-Methyl-*o*-hydroxybenzyl Alcohol [2-(2'-hydroxyethyl)phenol] (100). This substance was prepared *via* a standard procedure for reduction of ketones.[142] To a stirred solution of 2'-hydroxyacetophenone (Aldrich, 5.0 g, 36.8 mmole) in methanol (150 mL) was carefully added a suspension of $NaBH_4$ (1.0 g, 26.3 mmole) in 20 mL methanol in an ice bath. The reaction mixture was then heated to 30-40 °C for one hour. TLC analysis (silica gel, CH_2Cl_2) showed that the reaction had been completed. The reaction mixture was then poured into 100 mL ice H_2O and quenched by addition of saturated NH_4Cl solution. The combined extracts (by 5 × 80 mL CH_2Cl_2) were dried over $MgSO_4$. Removal of the organic solvent under reduced pressure gave a pale yellow liquid (4.4 g, 86%). Distillation of the crude product under reduced pressure afforded pure **100** as a colorless liquid (2.0 g, 39%): mass spectrum (CI) m/z 121 ($(M-18)^+ + 1$, base peak), 139 ($M^+ + 1$); ^1H NMR (90 MHz, $CDCl_3$) δ 1.45 (d, J = 7 Hz, 3H), 3.1 (b, 1H, D_2O exchangeable), 5.0 (q, J = 7 Hz, 1H), 6.7-7.3 (m, 4H), 8.0 (s, 1H, D_2O exchangeable).

α-Phenyl-*o*-hydroxybenzyl alcohol (101). To a stirred solution of salicyladehyde (Aldrich, 2.0 g, 17.9 mmole) in 50 mL of dry THF was added 30 mL of 1.8 **M** phenyllithium solution (54 mmole), under nitrogen in a dry ice-acetone bath. After beibg refluxed for 4 hours, the reaction mixture was cooled to room temperature and 50 ml of wet THF was added carefully followed by a further 10 min. reflux to decompose the excess phenyllithium. The reaction mixture was then transferred to a 500 mL erlenmeyer flask and 100 mL of ice H_2O was added and then acidified with saturated NH_4Cl. The solution was extracted with diethyl ether (3 × 70 mL). Removal of the ether afforded an oil (3.2 g, 90%), which solidified overnight. Recrystallization from toluene afforded pure **101** (2.7 g, 76%): Mass spectrum m/z (CI) 183 (base peak, $(M-18)^+ + 1$); ^1H NMR (90 MHz, acetone-d_6) δ 4.3 (b, 1H, D_2O exchangeable), 6.1 (s, 1H), 6.7-7.3 (m, 9H), 8.6 (s, 1H, D_2O exchangeable). m.p. 53-54 °C (literature: 54-55 °C[103]).

***o*-Hydroxystyrene (67).** This compound was prepared by decarboxylation of 2-hydroxycinnamic acid according to the procedure of Fries and Fickewirth.[124,143] The acid was allowed to decarboxylate in a 230 °C oil bath under reduced pressure (~ 5-6 mm Hg). Compound **67** was distilled out during the reaction. The reaction was carefully controlled so that the temperature of the distillate did not exceed 60 °C. From 2.0 g (12.2 mmole) of the acid, there was obtained of 0.6 g (41%) of a white crystalline solid **67**: mass spectrum (CI) m/z 121 ($M^+ + 1$); ^1H NMR (90 MHz, $CDCl_3$) δ 5.0 (s, 1H, D_2O exchangeable), 5.35 (dd, J = 12 Hz, J' = 2 Hz, 1H), 5.7 (m, J = 18 Hz, J' = 2 Hz, 1H), 6.7-7.4 (m, 5H).

2,6-Dimethoxybenzyl Alcohol (89c). To a stirred suspension of lithium aluminum hydride (0.50 g, 13.1 mmole) in dry THF (50 mL), a solution of 2,6-dimethoxybenzoic acid (2.0 g, 11.0 mmole) in 75 mL dry THF was added at such a rate that the stirred solution refluxes gently. The reaction mixture was then refluxed gently with stirring for one hour and then was cooled to room temperature. About 30 mL of wet THF was added dropwise to the cooled reaction mixture, maintaining stirring to decompose excess hydride. The reaction mixture was then refluxed for a further 10 min to complete the decomposition and was allowed to cool once more. The reaction mixture was then transferred to a 500 mL erlenmeyer flask and 50 mL of ice H_2O was added carefully. After acidified by saturated NH_4Cl, the THF layer was separated, and the water layer was extracted by diethyl ether (3 × 75 mL). The THF layer and the ether extracts were then combined and washed with saturated $NaHCO_3$ solution (3 × 50 mL)and then dried over $MgSO_4$. Removal of the solvent gave crude **89c**, which was then recrystallized from toluene to afford white crystals (1.6 g, 79%): mass spectrum (CI) m/z 169 (M^+ + 1); ^1H NMR (90 MHz, $CDCl_3$) δ 2.4 (b, 1H, D_2O exchangeable), 3.8 (s, 6H), 4.7 (s, 2H), 6.5 (d, J = 8 Hz, 2H), 7.2 (q, J = 8 Hz, 2H). m.p. 86-87 °C (literature: 84-85 °C, uncrrected[144]).

***o*-(Methoxymethyl)phenol (4).** To a stirred solution of *o*-hydroxybenzyl alcohol (**43**) (2.0 g., 16.1 mmole) in 150 mL MeOH, 150 mL of 20% H_2SO_4 was added. The reaction mixture was left at room temperature for overnight. The solution was then extracted with CH_2Cl_2 (5 × 75 mL), washed with saturated $NaHCO_3$, dried over $MgSO_4$ and evaporated under reduced pressure. ^1H NMR analysis showed that about 75% of the substrate had converted to the methyl ether product. The product mixture was then separated by column chromatography, using CH_2Cl_2 as eluent (silica gel), to afford a pure colorless liquid of **4** (1.2 g, 55%): mass spectrum (CI) m/z 107 ($(M-32)^+ + 1$, base peak), 125 ($M^+ + 1$); ^1H NMR (90 MHz, acetone-d_6) δ 3.3 (s, 3H), 4.5 (s, 2H), 6.7-6.9 (m, 2H), 7.0-7.3 (m, 2H), 8.0 (s, 1H, D_2O exchangeable); IR (cm^{-1}) 3350 (broad), 1070.

5.3 Product Studies

Photolysis of *o*-hydroxybenzyl alcohol (43) in aqueous MeOH. A solution of **43** (50 mg, 100 mL 50% MeOH-H_2O *(v/v)*) was irradiated at 254 nm for 15 min. After photolysis, 50 mL of saturated NaCl was added, and the solution was extracted with 5 × 75 mL CH_2Cl_2. The combined extracts were dried over $MgSO_4$ and evaporated under reduced pressure to gave a pale yellow crude product mixture. GC analysis showed two products: *o*-(methoxymethyl)phenol (**4**) (45%) and *o*-cresol (17%, secondary product).

In an analytical experiment, a solution of 50 mg **43** in 100 mL 50% MeOH-H_2O in an 100 mL quartz tube was irradiated. At intervals, 1 mL of the irradiated solution was taken out and 1 mL of saturated NaCl was added. The mixture was then extracted with CH_2Cl_2 (5 × 2 mL) and the organic layer was separated and dried over Mg_2SO_4. The CH_2Cl_2 was carefully removed under reduced pressure.

The residue was then diluted with acetone and subjected to GC analysis. The conversion and the yields were calculated and the photoproducts identified by comparing their retention times with those of authentic samples.

For preparative scale photolysis, a solution of 100 mg **43** in 50% MeOH-H_2O (200 mL) was irradiated for 20 min. After work up, the major product was isolated by preparative TLC (silica gel, CH_2Cl_2) and confirmed to be **4** by ^1H NMR and MS.

Photolysis of 43 in aqueous EtOH. A solution of **43** (50 mg, 100 mL 50% EtOH-H_2O) was irradiated at 254 nm for 15 min. 1H NMR analysis of the reaction mixture showed that the corresponding ether **104** and the secondary product **48** were formed in 35% and 10% yields, respectively. Preparative scale photolysis (100 mg **43** in 200 mL 50% EtOH-H_2O at 254 nm for 30 min.) followed by preparative TLC (silica gel, CH_2Cl_2) afforded pure **104**: mass spectrum (CI) m/z 107 ($(M-46)^+ +1$, base peak), 153 ($M^+ + 1$); ^1H NMR (90 MHz, acetone-d_6) δ 1.2 (t, J = 7 Hz, 3H), 3.6 (q, J = 7 Hz, 2H), 4.6 (s, 2H), 6.7-6.9 (m, 2H), 7.0-7.3 (m, 2H), 8.1 (b, 1H, D_2O exchangeable); IR (cm^{-1}) 3350 (broad), 1070.

Photolysis of 43 in aqueous 2-propanol. A solution of **43** (50 mg, 100 mL 50% 2-propanol-H_2O) was irradiated at 254 nm for 15 min. ^1H NMR analysis showed that ether **105** and **48** were produced in 25% and < 5% yields, respectively. Preparative scale photolysis (200 mg **43** in 200 mL of 50% 2-PrOH-H_2O at 254 nm for 30 min.) followed by preparative TLC (silica gel, CH_2Cl_2) separation afforded pure **105**: mass spectrum (CI) m/z 107 ((M-60)$^+$ +1, base peak), 167 (M$^+$ +1); ^{1}H NMR (90 MHz, acetone-d_6) δ 1.2 (d, J = 6 Hz, 6H), 3.7 (septet, J = 6 Hz, 1H), 4.6 (s, 2H), 6.7-6.9 (m, 2H), 7.0-7.3 (m, 2H), 8.1 (s, 1H, D_2O exchangeable).

Photolysis of 43 in aqueous *t*-BuOH. A solution of 50 mg **43** in 100 mL of 50% *t*-BuOH-H_2O (*v*/*v*) was irradiated at 254 nm for 15 min. ^{1}H NMR analysis of the product mixture showed that ether **106** was formed in ≈ 9% yield. Preparative scale photolysis (200 mg **43** in 200 mL of 50% *t*-BuOH-H_2O at 254 nm for 30 min.) followed by preparative TLC (silica gel, CH_2Cl_2) separation afforded pure **106**: mass spectrum (CI) m/z 107 ((M - 74)$^+$ + 1, base peak), 181 (M$^+$ + 1); ^{1}H NMR δ 1.3 (s, 9H), 4.6 (s, 2H), 6.7-6.9 (m, 2H), 7.0-7.3 (m, 2H), 8.2 (s, 1H, D_2O exchangeable).

Dark reaction of 43 in aqueous MeOH. A solution of 50 mg **43** in 100 mL 50% MeOH-H_2O was purged with argon in the absence of UV light for one hour at room temperature. The reaction mixture was then worked up as usual. No reaction was observed by GC and ^{1}H NMR analysis.

Photolysis of α-methyl-*o*-hydroxybenzyl alcohol (100) in aqueous MeOH. A solution of 50 mg **100** in 100 mL of 50% MeOH-H_2O was photolyzed at 254 nm for 15 min. After photolysis, the reaction mixture was worked up by CH_2Cl_2 extraction as described above. ^{1}H NMR analysis showed that about *o*-(1'-methoxyethyl)phenol (**69**) (27%) and a small amount of *o*-ethylphenol (< 4%) were formed. A UV-Vis sectrume of the product mixture indicated that a trace amount of *o*-hydroxystyrene (λ_{max} = 255 nm) was also formed during the photolysis. ^{1}H NMR parameters for **69**: δ 1.4 (t, J = 7 Hz, 3H), 3.3 (s, 3H), 4.4 (q, J = 7 Hz, 1H), 6.7-6.9 (m, 2H), 7.0-7.3 (m, 2H), 7.8 (b, 1H, D_2O exchangeable).

Photolysis of α-phenyl-*o*-hydroxybenzyl alcohol (101) in aqueous MeOH. A solution of 80 mg **101** in 100 mL of 50% MeOH-H_2O was photolyzed at 254 nm for 15 min. ^{1}H NMR analysis showed that the yields of ether **102** and *o*-benzylphenol **103** were formed in 63% and 14% yields, respectively. Preparative TLC separation afforded pure **102**: mass spectrum (CI) m/z 183 ($(M-32)^+$ + 1, base peak); ^{1}H NMR δ 3.4 (s, 3H), 5.4 (s, 1H), 6.7-7.4 (m, 9H), 7.9 (b, 1H, D_2O exchangeable).

Photolysis of benzo-2(*3H*)-one (5) in aqueous ROH. A solution of 50 mg **5** in 100 mL of 50% MeOH-H_2O was irradiated at 254 nm for 8.5 min. 1H NMR analysis showed three products were formed: **4** (50%), **43** (4%) and **48** (9%).

Photolysis of 50 mg **5** in 100 mL of 50% EtOH-H_2O gave **104** (46%), **43** (15%) and **48** (≈ 4%).

Photolysis of 50 mg **5** in 100 mL of 50% 2-propanol-H_2O gave **105** (30%), **43** (31%) and a small amount of **48** (≈ 1%).

Photolysis of 50 mg **5** in 100 mL of 50% *t*-BuOH-H_2O gave **106** (12%) and **43** (56%). Secondary product **48** was not observed by ^{1}H NMR.

A solution of 50 mg **5** in 100 mL of 50% MeOH-H_2O left in the absence of light at room temperature for one hour gave no observable reaction. Unreacted starting material could be quantitatively recovered.

Photolysis of 4 in aqueous MeOH. A solution of 30 mg **4** in 100 mL of 50% MeOH-H_2O was irradiated at 254 nm for 15 min. ^{1}H NMR analysis showed that *o*-cresol (**48**) was formed as the only product in 30% yield. ^{1}H NMR data: δ 2.1 (s, 3H), 4.6 (b, 1H, D_2O exchangeable), 6.6-7.2 (m, 4H).

Photodecarbonylation efficiency of 5 in different solvents. To study the solvent dependence for the efficiency of photodecarbonylation of **5**, photolyses were carried out in the following solvents: MeOH, 95% EtOH, 2-PrOH, *t*-BuOH, CH_3CN-MeOH, H_2O, and aqueous alcohols. Irradiation of 5 mg of **5** in 20 mL of any of the above solvents resulted in the corresponding ether and/or alcohol products. The conversion of **5** (2.5 min photolysis at 254 nm in all of the above solvents was 30% ± 3%.

To obtain the relative reactivity of different nucleophiles towards *o*-QM (**1**), solutions of **5** (50 mg) in a series of nucleophile-H_2O-CH_3CN systems were irradiated at 254 nm for 8 min with 8 lamps. The results were summarized in **Table 4.1**. The relative reactivities were calculated by eq. 40 and listed in **Table 2.2**.

Photolysis of 43 in the presence of EVE. To a solution of 50 mg **43** in 100 mL of 50% CH_3CN-H_2O, 1.0 mL of EVE was added. The mixture was irradiated at 254 nm for one hour. GC and ^{1}H NMR analyses showed that 2-ethoxy-3,4-dihydro-2*H*-1-benzopyran (2-ethoxychroman, **44**) as the only product in 75% yield. Preparative scale photolysis (100 mg **43** with 1.0 mL EVE in 100 mL of 50% CH_3CN-H_2O), followed by preparative TLC separation afforded pure **44**: mass spectrum (CI) m/z 179 (M^+ + 1); ^1H NMR (250 MHz, $CDCl_3$), δ 1.95-2.10 (m, 3H), 2.60-2.67 (m, 1H), 2.93-3.02 (m, 1H), 3.59-2.72 (m, 1H), 3.85-3.98 (m, 1H), 5.26 (t, 1H, J = 2.92 Hz, OCHO), 6.83-6.91 (m, 2H), 7.05-7.15 (m, 2H). The ^1H NMR data are consistent with the reported ones.[11] Photolysis of **5** under identical conditions also gave **44** in > 80% yield.

Table 5.1 Products and yields on photolysis of **5** in different solvent systems

Solvent	recovery of **5** (%)[a]	Product yield (%)[a]	
		o-$HOC_6H_4CH_2OR$	**43**
$MeOH/H_2O/CH_3CN$ (10/20/70)[b]	77	17	6
$EtOH/H_2O/CH_3CN$ (31/18/51)[b]	76	20	4
2-$PrOH/H_2O/CH_3CN$ (38/9/53)[b]	78	17	5
t-$BuOH/H_2O/CH_3CN$ (47/9/44)[b]	80	7	13
$EVE/MeOH/CH_3CN$ (1.5/20/79)[b]	75	15	10[c]

[a] calculated by ^1H NMR integration; estimated error ± 10% of quoted value.
[b] *v*/*v*.
[c] yield of **44**.

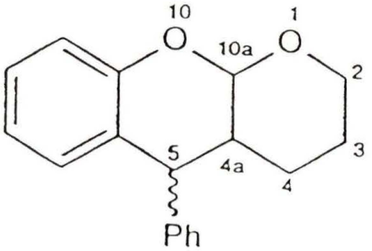
A solution of 50 mg **43**, in the presence of 1.0 mL of EVE, in 100 of 50% CH_3CN-H_2O left in the dark for one hour at room temperature gave no observable [4 + 2] addition products. However, polymers of EVE was formed under this condition.

Photolysis of **43** (50 mg), in the presence of 2,3-dihydrofuran (1.0 mL), in 100 mL 50% CH_3CN-H_2O at 254 nm for one hour gave the expected 2,3,3a,9a-tetrahydro-*cis*-2*H*-furo[2,3-b][1]benzopyran (**108**) in >50% yield; exact mass calculated for $C_{11}H_{12}O_2$ (M^+): 176.0837, found 176.0840; ^1H NMR (250 MHz, $CDCl_3$), δ 1.58-1.74 (m, 1H), 1.96-2.09 (m, 1H), 2.66-2.79 (m, 2H), 3.01-3.10 (dd, 1H, J = 16.40 Hz, J' = 6.24 Hz), 3.95-4.04 (m, 2H), 5.24 (d, 1H, J = 4.8 Hz, OCHO, *cis*-fused), 6.95-6.91 (m, 2H), 7.04-7.15 (m, 2H).

Photolysis of **43** (50 mg) in the presence of 3,4-dihydro-2*H*-pyran at 254 nm for one hour also gave the expected 3,4,4a,10a-tetrahydro-*cis*-2*H*,5*H*-pyrano[2,3-b][1]benzopyran (**107**) in > 50% yield; mass spectrum (CI) m/z 191 (M^+ + 1); ^1H NMR (250 MHz, $CDCl_3$), δ 1.58-1.73 (m, 4H), 2.12-2.18 (m, 1H), 2.65 (dd, J = 16.5 Hz, J' = 4.90 Hz), 2.93 (dd, J = 16.5 Hz, J' = 5.95 Hz), 3.67-3.75 (m, 1H), 3.96-4.05 (m, 1H), 5.32 (d, J = 2.60 Hz, OCHO, *cis*-fused), 6.80-6.87 (m, 2H), 6.99-7.13 (m, 2H). The MS and ^1H NMR data are consistent with the reported values.[11]

Photolysis of 101 in the presence of EVE. To a solution of 80 mg **101** in 100 mL of 50% CH_3CN-H_2O, 1.0 mL of EVE was added. The mixture was irradiated at 254 nm for one hour. The reaction mixture was worked up by CH_2Cl_2 extraction as usual. ^{1}H NMR analysis showed that the expected *cis*-2-ethoxy-4-phenyl-3,4-dihydro-2*H*-benzopyran (*cis*-**112**) and *trans*-2-ethoxy-4-phenyl-3,4-dihydro-2*H*-benzopyran (*trans*-**112**) are formed in 100% total yield. The two isomers were isolated as a mixture by preparative TLC (silica gel, diethyl ether-hexane, 2:1) and were characterized by GC/MS and ^{1}H NMR without further separation: MS/GC (CI) m/z 255 ($M^+ + 1$), ^{1}H NMR (360 MHz, $CDCl_3$), *cis*-**112** (93%), δ 1.25 (t, 3H), 2.18 (ddd, 1H, J = 13.34 Hz, J' = 11.2 Hz, J'' = 8.48 Hz), 2.38 (ddd, 1H, J = 13.34 Hz, J' = 6.50 Hz, J'' = 2.45 Hz), 3.61-3.70 (m, 1H), 4.02-4.10 (m, 1H), 4.18 (dd, 1H, J = 11.2 Hz, J' =6.5 Hz), 5.25 (dd, 1H, J = 8.48 Hz, J' = 2.45 Hz, OCHO), 6.68-7.34 (m, 9H); *trans*-**112** (7%), δ 1.20 (t, 3H), 2.11 (ddd, 1H, J = 13.00 Hz, J' = 11.30 Hz, J'' = 2.80 Hz), 2.22 (ddd, J = 13.00 Hz, J' = 6.30 Hz, J'' = 2.80 Hz), 3.64 (m, 1H), 3.90 (m, 1H), 4.28 (dd, J = 11.30 Hz, J' = 6.30 Hz), 5.25 (dd, J = J' = 2.80 Hz, OCHO), 6.68-7.34 (m, 9H). The ^{1}H NMR data are consistent with the reported values (*vide supra*).[27]

Photolysis of **101,** in the presence of 3,4-dihydro-2*H*-pyran, in aqueous CH_3CN at 254 nm for one hour also gave the expected *cis*-5-phenyl-3,4,4a,10a-tetrahydro-*cis*-2*H*,5*H*-pyrano[2,3-b][1]benzopyran (*cis*-**114**) and *trans*-**114** in 100% total yield. The two diastereomers were again obtained as a mixture by preparative TLC (silica gel, diethyl ether-hexane, 2:1) and characterized by GC/MS and ^{1}H NMR without further separation. Exact mass calculated for $C_{18}H_{18}O_2$: 266.1307, found: 266.1300; ^{1}H NMR (360 MHz, $CDCl_3$): Since *cis*-**114** and *trans*-**114** are structurally similar, most signals are overlap each other. The signals were assigned by comparison of that of **107**: δ 1.42-1.86 (m, 4H, H_3 and H_4), 2.10-2.18 (m, 1H, H_{4a}), 3.67-3.82 (m, 1H, H_2), 4.01-4.09 (m, 1H, H_2'), 4.48-4.66 (m, 1H, H_5), 5.24 (d, J = 2.7 Hz, H_{10a} for *cis*-**114**), 5.58 (d, J = 1.8 Hz, H_{10a} for *trans*-**114**), 6.8-7.4 (m, 9H, aromatic H's). The relative yield of *cis*-**114** based on the H_{10a} integration is 70%.



Photolysis of 89c in the presence of EVE. To a solution of 50 mg of 2,6-dimethoxybenzyl alcohol (**89c**) in 100 mL of 50% CH_3CN-H_2O, 2.0 mL of EVE was added. The mixture was photolyzed at 254 nm for one hour and was then worked up by CH_2Cl_2 extraction (5 × 75 mL). ^{1}H NMR analysis showed that 3-(2',6'-dimethoxyphenyl)propyl aldehyde (**111**) was formed in 30% yield. The identity of **111** was assigned by chemical shifts of ^{1}H NMR: δ 2.6 (dt, 2H), 2.9 (t, 2H), 3.8 (s, 6H), 6.4-6.7 (m, 2H), 7.0-7.3 (m, 2H), 9.7 (t, 1H, J = 2 Hz, aldehyde proton).

Photolysis of 92 in acidic aqueous alcohol solutions. In a typical procedure, 50-100 mg of **92** was dissolved in 50 mL ROH (R = Me, Et, 2-Pr, *t*-Bu) and added 50 mL of H_2O of the appropriate acidity. The solution was irradiated at 254 nm for 10-25 min. Acid solutions were neutralized to ≈ pH 7 before extracting with CH_2Cl_2 (5 × 75 mL). The identity of the secondary product of photolysis (*o*-toluidine (**118**)) was identified by comparison with an authentic sample, by GC. Ether photoproducts obtained on photolysis of **92** in 50% ROH-H_2O were isolated by preparative TLC (silica, CH_2Cl_2) and readily characterized by ^1H NMR. Spectroscopic data are listed below for each product.

2-aminobenzyl methyl ether (**117**): mass spectrum (CI) m/z 138 (M^+ + 1); ^1H NMR (90 MHz, acetone-d_6) δ 3.2 (s, 3H), 4.4 (s, 2H), 4.3-4.8 (b, 2H, D_2O exchangeable), 6.4-6.7 (m, 2H), 6.9-7.1 (m, 2H); IR (cm^{-1}) 3350, 3400, 1075.

2-aminobenzyl ethyl ether: mass spectrum (CI) m/z 152 (M^+ + 1); ^1H NMR (90 MHz, acetone-d_6) δ 1.1 (t, J = 7 Hz, 3H), 3.4 (q, J = 7 Hz, 2H), 4.4 (s, 2H), 4.3-4.8 (b, exchangeable with D_2O, 2H), 6.4-6.7 (m, 2H), 6.9-7.2 (m, 2H); IR (cm^{-1}) 3450, 2265, 1080.

2-aminobenzyl 2'-propyl ether: mass spectrum (CI) m/z 166 (M^+ + 1); ^1H NMR (90 MHz, acetone-d_6) δ 1.2 (d, J = 6 Hz, 6H), 3.7 (septet, J = 6 Hz, 1H), 4.3-4.9 (b, 2H, exchangeable with D_2O), 4.4 (s, 2H), 6.4-6.7 (m, 2H), 6.9-7.2 (m, 2H).

2-aminobenzyl *t*-butyl ether: mass spectrum (CI) m/z 180 (M^+ + 1); ^1H NMR (90 MHz, acetone-d_6) δ 1.3 (s, 9H), 4.4 (s, 2H), 4.3-4.9 (b, 2H, exchangeable with

D_2O), 6.5-6.7 (m, 2H), 6.9-7.2 (m, 2H).

A solution of **92** in 1:1 MeOH-10% H_2SO_4 (*v*/*v*) left in the dark for one hour gave no observable reaction. After work up, the starting material could be recovered unreacted.

5.4 Product Quantum Yield Measurements

Product quantum yields were obtained on an optical bench using 280 nm excitation with slits of 7.0 nm/7.0 nm from the output of an Oriel 200 W Hg lamp filtered through an Applied Physics monochromator and a 254-400 bandpass filter. Samples were prepared by mixing 1.50 mL of a 1.00×10^{-2} **M** stock solution and 1.50 mL of a standard pH 7.00 buffer solution in suprasil quartz cuvettes. UV-Vis analysis showed that the absorbance were > 3.0 at 280 nm for all the samples studied. The sample were then purged with argon for 10 min prior to the photolysis. Purging was continued during the photolysis to effect stirring the solutions. No cold finger was utilized since the intensity of the light source was not sufficient to heat up the samples appreciable. Photolysis times varied between 12-59 min depending on the conversion expected for the photoproducts. The conversion of the substrates were kept less than 20% to reduce secondary photolysis.

After photolysis, the solution was added 3 mL of saturated NaCl and extracted with five portions of CH_2Cl_2 (5×3 mL), which was performed utilizing a pasteur pipette to effect mixing the layers. The organic extracts were then collected and dried over $MgSO_4$. Filtration and evaporation under reduced pressure provided the photoproduct mixtures required for analysis. The product mixtures were the diluted by acetone and quantified by GC. No internal standard was used Recovery experiment showed that both products and substrates could be recovered in > 90% yields (by weight) by simple extraction and the substrate-product ratio remained unchanged after the extraction (by ^1H NMR integration). GC responses of substrates and products were were essentially identical at low conversion (≤ 20%). This was done by co-injecting a series of substrate-product mixture in different ratio.

The light intensity in einsteins/min was measured by potassium ferrioxalate chemical actinometry.[135,136] To 3.0 mL of the stock solution of 0.0060 **M** potassium ferrioxalate ($K_3Fe(C_2O_4)_3$) in 0.050 **M** H_2SO_4 was transferred into each of the two suprasil cuvettes. One of these cuvettes was irradiated at 280 nm for 5 min with argon purging to mimic the conditions used for product studies. The other was put under the dark without irradiation and serves as a blank.

Irradiation of the actinometer solution leads to reduction of the Fe^{3+} to Fe^{2+} (eq. 51).[135] The quantity of Fe^{2+} produced was measured by reacting it with 1,10-phenanthroline to produce a complex, which has an absorption at $\lambda_{max} = 510$ nm.

$$2Fe^{3+} + C_2O_4^{2-} \rightarrow 2Fe^{2+} + 2CO_2 \qquad (51)$$

The quantity of Fe^{2+} can be determined from the strength of this absorption.

To prepare the Fe^{2+}-1,10-phenanthroline complex, the photolyzed solution was worked up as follows. 1.0 mL of the photolyzed solution was taken from the cuvette into a 10 mL volumetric flask. 2.0 mL of a 0.1% (*w/w*) stock solution of 1,10-phenanthroline in water and 0.5 mL of a buffer solution (prepared from dissolve 41.0 g $NaOAc\cdot 3H_2O$ and 5 mL H_2SO_4 in H_2O to make 1 L solution) was added to this flask. The volume was adjusted into 10.00 mL with distilled water and the solution were mixed thoroughly by vigorously shaking and left in the dark for half of an hour. The above procedure was performed under a red light source and repeated for the blank. A portion of the complex samples were then transferred to UV cuvettes and the absorption at 510 nm was measured. The difference in absorption of the photolyzed and the blank potassium ferrioxalates was determined and substituted in the eq. 52 for light intensity .

$$I = \frac{\Delta A \ V_2 \ V_3}{\epsilon \ \phi_\lambda \ t \ V_1} \times 10^{-3} \qquad (52)$$

Where:

I is the light intensity in einsteins/min absorbed by the 3 mL cuvette solution.

ΔA is the difference in absorption between the irradiated sample and the blank sample.

V_1 is the volume of irradiated actinometer withdrawn (1.00 mL).

V_2 is the volume of the actinometer irradiated (3.0 mL).

V_3 is the volume of the volumetric flask (10.00 mL).

ε is the extinction coefficient for the Fe^{2+}-1,10-phenanthroline at 510 nm (1.11×10^4 L mol^{-1} cm^{-1}).

Φ_λ is the known quantum yield for Fe^{2+} formation at the wavelength used for the photolysis ($\Phi_\lambda = 1.25$ at 280 nm).

t is the time of photolysis (5 min).

The measured light intensity, along with the moles of photoproduct obtained, were then substituted into eq. 46 to calculate the product quantum yields (Φ_p).

Quantum yields (Φ_p) for formation of 4 in aqueous MeOH. A sample of **43** (1.00×10^{-5} mole) in 50% MeOH-H_2O was prepared by mixing 1.5 mL of the stock solution of **43** (1.00×10^{-2} **M** in MeOH) and 1.5 mL of pH 7.00 buffer in a suprasil quartz cuvette. This solution was photolyzed under argon on the optical bench for 30 min. The worked up reaction mixture was subjected to GC. The light intensity absorbed by **43** was obtained by the method described above. An average value of $\Phi_p = 0.23 \pm 0.03$ was obtained from five trials.

The Φ_p's for the formation of other ether products **104**, **105** and **106** from **43** was estimated from small scale preparatory photolyses (254 nm, Rayonet reactor) by ^{1}H NMR integration. The photolysis of **43** in 50% MeOH-H_2O (Φ_p = 0.23) was used as the secondary reference. The results are listed in **Table 2.4**.

The Φ_p's for the formation of 2-aminobenzyl methyl ether (**107**) in different acidities from **92** was also estimated from small scale preparatory photolysis (254 nm, Rayonet reactor) by ^{1}H NMR integration, using photomethanolysis of **43** in 50% MeOH-H_2O as the secondary reference. Using this method, $\Phi_p = 0.29 \pm 0.05$ for the formation of **107** at pH 1.

Quantum Yields (Φ_p) for formation of 44 in aqueous CH_3CN. The Φ_p's for the formation of **44** from **43** (5.00×10^{-3} **M** in 50% CH_3CN-H_2O) were measured in the presence of different concentration of EVE, *i.e.*, 3.4×10^{-3}, 3.4×10^{-2}, 6.8×10^{-2}, 0.10, 0.14, 0.17, 0.34 and 0.68 **M**. The solutions were irradiated at 280 nm on an optical bench for 59 min. The results were shown by **Figure 2.3** and **Table 2.4**.

Quantum yields for formation of 102 in aqueous MeOH. A solution of **101** (5.00×10^{-3} **M**) in 50% MeOH-H_2O was irradiated at 280 nm on an optical bench for 12 min. The average Φ_p for formation of **102** for **101** was 0.46 ± 0.03.

Quantum yields for formation of 112 in aqueous CH_3CN. A solution of **101** (5.00×10^{-3} **M**), in the presence of 0.14 **M** of EVE, in 50% CH_3CN-H_2O was irradiated at 280 nm for 25 min. The Φ_p for the formation of *cis*-**112** and *trans*-**112** are found to be 0.25 ± 0.03 and 0.0020 ± 0.0005, respectively.

5.5 Steady State Fluorescence and Lifetime Measurements

Steady state fluorescence spectra (uncorrected) were taken on a Perkin-Elmer MPF 66 instrument at ambient temperature. Solutions ($\approx 10^{-5}$ **M**) in four sided suprasil cuvettes were purged with a stream of argon prior to the measurement.

Fluorescence quantum yields (Φ_f) were measured by using 2-aminopyridine ($\Phi_f = 0.60 \pm 0.05$ in 0.05 **M** H_2SO_4)[137] and anisole ($\Phi_f = 0.29$ in cyclohexane)[138] as secondary standards. These particular standards were chosen since the region of their emission overlaps that of the substrates, *i.e.*, compounds **43** and **92**.

Dilute solutions of substrates and standards (OD = 0.038 ± 0.002 at excitation wavelength) were prepared in proper solvents to prevent self-quenching which can occur at high concentrations. Samples of each were placed in four-sided quartz cuvettes and a UV-Vis spectrum recorded for each on a Varian Cary 1 UV-Vis instrument to obtain a crossing point or area in the two spectra. The absorption of the sample and the standard must be the same to insure that each absorbs the same number of photons. Dilutions of standards and **43** were performed to obtain the crossing point at 265 nm. While dilutions of standards and **92** were performed at 285 nm to obtain the crossing point.

The matched solutions of standards and substrates were then purged with argon and fluorescence spectra were recorded with the excitation wavelengths at the matching points. The areas for each emission spectrum were then measured and substituted in eq. 53 to determine Φ_f^s for the substrates.

$$\Phi_f^s = \Phi_f^r \frac{A^s}{A^r} \left(\frac{n^s}{n^r}\right)^2 \qquad (53)$$

Where:

A^s is the area under the sample fluorescence emission curve.

A^r is the area under the reference standard emission curve.

Φ_f^s is the fluorescence quantum yield for the sample.

Φ_f^r is the fluorescence quantum yield for the standards.

n^s is the refractive index of the solvent used with the sample.

n^r is the refractive index of the solvent used with the reference standards.

Fluorescence lifetimes were measured at room temperature using single photon counting on a Photon Technology International instrument (PTI LS-100 spectrofluorimeter equipped with single photon electronics), using a standard hydrogen spark lamp as excitation source and deconvolution software provided by PTI for analysis of observed decays. All decays were good single exponential. These measurements were done by Mr. Deepak Shukla.

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1 Cheng Yang and Peter Wan, "Photosolvolysis of 2-aminobenzyl alcohol in aqueous solution", *J. Photochem. Photobiol., A*, in press.

2 Cheng Yang and Peter Wan, "*o*-Quinone methides from photolysis of *o*-hydroxybenzyl alcohols: trapping by nucleophiles as electron-rich dienophiles", *XVI International Conference on Photochemistry*, Vancouver, 1993.

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