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The preparation of novel photoactive compounds that liberate base upon irradiation is important for applications in microelectronics, polymer curing, and other light-triggered processes. In effect, light is used to create catalytic species within polymeric or other materials, and subsequent reactions catalyzed by the light-generated catalysts drive the overall chemical transformations. In this report, the search for novel photoprecursors of amines that are based on the chemistry of the desyl groups is reported. Several new chromophore designs in which the substitution pattern of the parent desyl chromophore was varied systematically were explored. A number of alternative synthetic routes have been explored using both symmetrical and unsymmetrical benzoins. Best results were obtained using the substituted benzoin chromophores with primary and secondary amines to form photosensitive α-keto carbamates. These substituted benzoin carbamates are easily obtained by reaction of the appropriate benzoin precursor with isocyanates or by reaction of activated derivatives with the free amine. The focus of this report is the preparation of the photoactive precursors of amines themselves, a second report will outline their photoactivity and quantum efficiency for practical applications in thin films or other formulations.

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Summary:

The preparation of novel photoactive compounds that liberate base upon irradiation is important for applications in microelectronics, polymer curing, and other light-triggered processes. In effect, light is used to create catalytic species within polymeric or other materials, and subsequent reactions catalyzed by the light-generated catalysts drive the overall chemical transformations. In this report, the search for novel photoprecursors of amines that are based on the chemistry of the desyl groups is reported. Several new chromophore designs in which the substitution pattern of the parent desyl chromophore was varied systematically were explored. A number of alternative synthetic routes have been explored using both symmetrical and unsymmetrical benzoins. Best results were obtained using the substituted benzoin chromophores with primary and secondary amines to form photosensitive α-keto carbamates. These substituted benzoin carbamates are easily obtained by reaction of the appropriate benzoin precursor with isocyanates or by reaction of activated derivatives with the free amine. The focus of this report is the preparation of the photoactive precursors of amines themselves, a second report will outline their photoactivity and quantum efficiency for practical applications in thin films or other formulations.

Introduction.

The chemistry of photogenerated catalysts has taken additional importance as numerous materials used in a variety of high technology applications, sensors, or even bioactive systems have been designed to take advantage of their availability. For these applications, phototriggering of activity is desirable either for patterning, sensing, or a simple non-intrusive mode of initiation. It is in the area of microelectronics that photogenerated catalysts have had the most visible impact. The concept of chemical amplification, which we have pioneered more than fifteen years ago, was reduced to practice in the mid-80's for the mass production of memory and other microlectronic devices. It is this technology,[1] based on the in situ photogeneration of a catalyst, that both represents today's state of the art and a leading candidate for to-morrow's approaches to advanced semiconductor devices.

Photolabile protecting groups have received considerable attention in synthetic organic chemistry because of the mild, neutral conditions which can be used to effect deprotection. Indeed, a variety of photolabile protecting groups have been developed for most common functional groups[2]. For instance, several photolabile groups based on the well known *o*-nitrobenzyl photorearragenment have been used to mask such diverse functional groups as alcohols, amines, carboxylic acids and carbonyl compounds. These photolabile protecting groups can also be used advantageously in imaging processes, resist chemistry, or other advanced technologies. For example, in light-flash physiology, caged nucleoside triphosphates[3], photolabile calcium chelators[3] and photoactive precursors of neurotransmitters[4] all rely on efficient photodeprotection strategies for their success.

Recently, we have developed a new photorelease strategy by masking amines and diamines as photoactive carbamates[5-7]. Under the action of light, these neutral carbamates decompose to liberate the free amine. However, it was found that commonly used photolabile amino protecting groups, such as the 3,5-dimethoxy-α,α-dimethylbenzyloxycarbonyl and *o*-nitrobenzyloxycarbonyl moieties, undergo somewhat complex photochemical processes that may be further hindered by deleterious side reactions upon prolonged photolysis.

We have recently reported our preliminary work on a new type of photolabile amino protecting group based on substituted desyl chromophores[8]. We now describe the full details of the design concepts and synthetic principles used in creating new chromophores for photolabile protecting groups. It is anticipated that these novel photoactive materials based on these design concepts could be of great

importance in polymer curing and imaging processes. In this early report, the emphasis is placed on the broader concept of chromophore design for the creation of new photolabile amino protecting groups. We focus on the desyl chromophore and its substituted analogs because they offer significant advantages over current photolabile protecting groups. The literature describing the photochemistry of the desyl chromophore suggests that in comparison with o-nitrobenzyl photochemistry, the 3',5'-dimethoxybenzoin chromophore will exhibit: (1) increased stability of photo byproducts; (2) improved photoefficiency and (3) enhanced rate of photorelease.

It is well known that the parent desyl chromophore undergoes photocleavage via classical photochemical pathways such as α-cleavage (Norrish Type I). In contrast, meta methoxy substitution causes photocyclization to become the major photocleavage pathway[9,10]. The photolysis of 3',5'-dimethoxybenzoin acetate affords 5,7-dimethoxy-2-phenylbenzo[b]furan and acetic acid as the major products (Scheme 1). In comparison, *o*-nitrobenzyl photochemistry is complicated by the formation of photochemically active *o*-nitroso carbonyl byproducts. Second, upon using 3',5'-dimethoxybenzoin esters as photolabile carboxyl protecting groups[10,11], they liberated the free acid quantitatively, with a quantum yield of 0.64 at 365 nm[10]. In contrast, the photoefficiency for photocleavage of simple *o*-nitrobenzyl esters is typically 0.10. The unique mode of photoreactivity offered by substituted benzoins has been applied to the caged release of phosphate esters[12-14] and inorganic phosphate[15] (Scheme 1). In these applications, 3',5'-dimethoxybenzoin phosphate was found to cyclize with a photoefficiency of 78%, which is more than double that of related unsubstituted benzoin phosphates[16]. Third, the photorelease of phosphate from desyl phosphates proceeds at least 1000 times faster and up to 1.24 times as efficiently as *o*-nitrobenzyl derived phosphate esters[13,16].

Results and Discussion.

1) General Design Considerations

A substituted benzoin chromophore may be envisioned as a light sensitive protecting group for a variety of common functional groups. In this report, we focus on their role in masking amines as α-keto carbamates because these materials may offer significant advantages over current photolabile amino protecting groups. Interest in these α-keto carbamates was two fold. First, the facile synthesis of these materials gave an early indication as to the ease of introduction of the desyl based photolabile group. In

general, α-keto carbamates are synthetically accessible; substituted benzoin carbamates may be synthesized via the appropriate benzoin by reaction with isocyanates or by activation as a mixed carbonate followed by reaction with the free amine. Second, these photosensitive α-keto carbamates may be used for rapid evaluation of novel desyl based chromophores. In the accompanying paper, the diverse array of photoactive α-keto carbamates prepared herein provides the basis for investigating chromophore structure -photosensitivity relationships in photoliberation of amino groups.

2) Design and Synthesis

i) Preparation of Unsubstituted α-Keto Carbamates

Simple unsubstituted α-keto carbamates may be prepared reacting an α-hydroxy ketone with an isocyanate. For example, benzoin cyclohexyl carbamate (**1**) was prepared by the reaction of benzoin with cyclohexyl isocyanate under a variety of conditions (Scheme 2). Previously, we had found methyllithium to be an excellent catalyst for the addition of a diverse array of alcohols to isocyanates[5,6]. Accordingly, the methyllithium catalyzed addition was investigated first. Under these conditions, reaction to give benzoin cyclohexyl carbamate (**1**) proceeded smoothly with a yield of about 50% for the addition itself. However, the anionic conditions resulted in the intramolecular cyclization of the α-keto carbamate (**1**) to 3-cyclohexyl-4-hydroxy-4,5-diphenyl-4-oxazolidin-2-one (**2**) which reacted further to give 3-cyclohexyl-4,5-diphenyl-4-oxazolin-2-one (**3**) as the major product. Cyclization of α-keto carbamates to oxazolidin-2-ones followed by elimination of water is known to proceed in the presence of base[17]. In order to minimize the cyclization-elimination reaction, we developed mild, neutral conditions for the preparation of desyl carbamates. We found that heating a solution of the benzoin and isocyanate in toluene proceeded smoothly in most cases to give the required desyl carbamate. Under these conditions, the yield of benzoin cyclohexyl carbamate (**1**) was 77%. The direct addition of a benzoin to an isocyanate was commonly accompanied by some minor oxidation of the benzoin to the corresponding benzil (vide infra). The efficiency of the direct addition was largely unaffected by amine type catalysts, such as DMAP and DBU. In contrast, stannous 2-ethyl hexanoate, which is a well known catalyst for urethane formation[18], failed to take the reaction to completion.

ii) Preparation of Aryl Substituted α-Keto Carbamates

a) Photolabile Amino Protecting Groups Based on Symmetrical Benzoins

Since symmetrical benzoins are more accessible than their unsymmetrical counterparts, the first generation of new photosensitive protecting groups were based on symmetrical benzoins. Based on the pronounced activating effect of meta methoxy substitution on the photocyclization of benzoin esters, we chose to investigate the novel 3,3',5,5'-tetramethoxybenzoin chromophore as a photolabile group. Despite a literature report that this benzoin (**4**) was unavailable by benzoin condensation[19], we succeeded in preparing this material in 31% yield by reaction of 3,5-dimethoxybenzaldehyde in DMF in the presence of potassium cyanide and tetrabutylammonium iodide[20] (Scheme 3). Subsequent reaction with cyclohexyl isocyanate in refluxing toluene gave the cyclohexylamine photoprecursor (**5**) in 77% yield (Scheme 2). The direct addition of benzoin (**4**) to cyclohexyl isocyanate was accompanied by a trace of 1,2-bis-(3,5-dimethoxyphenyl)ethanedione.

The cyclohexyl carbamate of 3,3'-dimethoxybenzoin (**6**) also attracted our attention because it would allow comparison of the effect of 2 versus 4 meta activating groups in the chromophore. 3,3'-Dimethoxybenzoin[21] reacted with cyclohexyl isocyanate to give the requisite carbamate (**6**) in 49% yield (Scheme 2). The addition of this particular benzoin to cyclohexyl isocyanate was plagued by cyclization of the carbamate to various isomers of 3-cyclohexyl-4-hydroxy-4,5-di-(3-methoxyphenyl)-4-oxazolidin-2-one (**7**). The crude gum isolated from the reaction itself was indeed the desired cyclohexyl carbamate (**6**), as indicated by ^{1}H NMR spectroscopy. However, during subsequent chromatographic operations cyclization tended to occur and subsequent crystallization only succeeded in depositing various isomers of 3-cyclohexyl-4-hydroxy-4,5-di-(3-methoxyphenyl)-4-oxazolidin-2-one (**7**). A trace amount of 1,2-bis-(3-methoxyphenyl)ethanedione was also isolated from the direct addition of this benzoin to cyclohexyl isocyanate.

Sheehan *et. al.*[10] reported that the photolability of piperoin derived esters is close to that of esters derived from the less readily available unsymmetrical benzoins. With this in mind, commercially available piperoin was derivatized with cyclohexyl isocyanate to give cyclohexyl carbamate (**8**) (Scheme 2).

All the carbamates prepared so far are synthesized by the direct addition of an isocyanate with the requisite benzoin. While this strategy allows for the facile synthesis of masked primary amines, it is somewhat restricted by the availability of the requisite isocyanates. If the substituted desyl chromophores are to find widespread use as light sensitive amino protecting groups then a general strategy which allows for the masking of free amines is required. This is illustrated by the masking of

piperidine as piperoinyl carbamate (**9**) (Scheme 4). Piperoin was converted to piperidinyl carbamate (**9**) in 43% yield via its p-nitrophenyl mixed carbonate followed by treatment with piperidine. A trace amount of 1,2-bis-(1,3-benzodioxol-5-yl)ethanedione was isolated from the preparation of piperidinyl carbamate (**9**). The protection of a secondary amine as an α-keto carbamate is particularly attractive as it does not suffer from any competing cyclization reactions observed during masking of primary amines via direct addition to an isocyanate. This competing cyclization reaction may severely limit the utility of photosensitive α-keto carbamates of primary amines

To further clarify the nature of the meta activating effect on the photochemistry of benzoin carbamates, carbamate (**10**) containing a 4,4'-dimethoxy substituted benzoin chromophore was synthesized. In contrast to the 3',5'-dimethoxybenzoin chromophore, the α-(4-methoxyphenyl)-4-methoxyphenacyl chromophore as in (**10**) is known to photocleave by a variety of mechanisms of which cyclization is a minor pathway[9]. Carbamate (**10**) was prepared in 46% yield by reaction of anisoin with cyclohexyl isocyanate in refluxing toluene (Scheme 2).

b) Photolabile Amino Protecting Groups Based on Unsymmetrical Benzoins

Before being able to prepare a variety of carbamates derived from unsymmetrical benzoins, an efficient synthesis of unsymmetrical benzoins was required. Because 3',5'-dimethoxybenzoin (**11**) is known to be an efficient chromophore for photocyclization, several synthetic strategies towards this particular unsymmetrical benzoin were investigated. The diverse chemistry offered by masked cyanohydrins is particularly well suited to the synthesis of unsymmetrical benzoins. This chemistry offers two complementary approaches to the problem of preparing unsymmetrical benzoins such as (**11**). First, one can use a TMS masked cyanohydrin as an electrophilic α-hydroxy carbonyl synthon in a reaction with a Grignard reagent[22]. Second, TMS masked cyanohydrins offer the prospect of Umpolung; deprotonation of a TMS masked cyanohydrin gives a nucleophilic benzoyl anion synthetic equivalent which reacts with electrophiles[23].

Using the first approach, 3',5'-dimethoxybenzoin (**11**) was isolated in an overall yield of 10% from 3,5-dimethoxybenzaldehyde (Scheme 5). Conversion of the aldehyde to α-(3,5-dimethoxyphenyl)-α-(trimethylsiloxy)acetonitrile was achieved by the zinc iodide catalyzed reaction with trimethylsilylcyanide[24]. Subsequent reaction with phenylmagnesium bromide, followed by acid mediated hydrolysis of the intermediate imine, gave the desired 3',5'-dimethoxybenzoin (**11**). In contrast, the

original conditions of Sheehan and Wilson[10], where 3,5-dimethoxybenzaldehyde cyanohydrin is simply reacted with a large excess of phenylmagnesium bromide, failed to provide any of the desired benzoin. This failure illustrates the need for protection of the hydroxyl group during the Grignard reaction.

Second, the Umpolung approach, in which α-(phenyl)-α-(trimethylsiloxy)acetonitrile was used as a benzoyl anion equivalent, was also used to prepare 3',5'-dimethoxybenzoin (**11**). Lithiation of α-(phenyl)-α-(trimethylsiloxy)acetonitrile, followed by reaction with 3,5-dimethoxybenzaldehyde gave the corresponding TMS masked benzoin. Subsequent hydrolysis using tetrabutylammonium fluoride gave 3',5'-dimethoxybenzoin (**11**) in 24% yield (Scheme 5).

With the 3',5'-dimethoxybenzoin chromophore available, carbamates containing this moiety were prepared. First, 3',5'-dimethoxybenzoin cyclohexyl carbamate (**12**) was prepared in 59% yield from 3',5'-dimethoxybenzoin (**11**) and cyclohexyl isocyanate (Scheme 2). This material is the masked amine equivalent of the highly photosensitive 3',5'-dimethoxybenzoin acetate reported by Sheehan *et. al.*.[10] Again, the direct addition of the benzoin to cyclohexyl isocyanate formed a trace of the corresponding benzil. In this case, 1-(3,5-dimethoxyphenyl)-2-(phenyl)ethanedione was isolated in a trace amount. A piperidine photoprecursor (**13**) containing the 3',5'-dimethoxybenzoin chromophore was prepared in 38% yield (Scheme 4). This photogenerator was prepared in a similar fashion to the piperoin piperidinyl carbamate (**9**).

For future evaluation of the meta activating effect of methoxy groups on the photocyclization we proposed to prepare the cyclohexyl carbamate of the isomeric 3,5-dimethoxybenzoin. Interestingly, on attempting to isolate the isomeric 3,5-dimethoxybenzoin from the analogous reaction of α-(3,5-dimethoxyphenyl)-α-(trimethylsiloxy)acetonitrile anion with benzaldehyde, only 3',5'-dimethoxybenzoin (**11**) was isolated in 50% yield. Corrie and Trentham[16] have recently reported the synthesis of 3,5-dimethoxybenzoin (**14**) in 65% yield by this same strategy. In their case, the TMS moiety was removed under acidic conditions, rather than by fluoride mediated hydrolysis. Thus, it seems that fluoride anion may be sufficiently basic as to effect isomerization of some unsymmetrical benzoins, as well as retro addition (vide infra).

A carbamate (**15**), derived from an unsymmetrical benzoin (**16**) containing the 1,3-methylenedioxy substituent, was also prepared in the usual way (Scheme 2). In similar fashion to 3,3'-dimethoxybenzoin cyclohexyl carbamate (**6**), the addition of the benzoin to cyclohexyl isocyanate proved troublesome

because the crude carbamate readily undergoes intramolecular cyclization on purification. Some of the desired carbamate was separable by chromatography, but the majority of the fractions from the column consisted of a mixture of the desired carbamate (**15**) (cyclohexyl CH, m, δ 3.50), 5-(1,3-benzodioxol-5-yl)-4-phenyl-4-oxazolin-2-one (**17**) (cyclohexyl CH, m, δ 3.29) and 5-(1,3-benzodioxol-5-yl)-4-phenyl-4-hydroxy-oxazolidin-2-one (**18**) (cyclohexyl CH, m, δ 2.87). The required benzoin (**16**) was prepared in 35% yield over two steps involving conversion of piperonal to α-(1,3-benzodioxol-5-yl)-α-(trimethylsiloxy)acetonitrile (**19**) followed by reaction with phenylmagnesium bromide (Scheme 5).

For some applications with inherently light sensitive substrates e.g., tryptophan, pyrimidines, efficient red shifted photolabile protecting groups would be of significant value. Accordingly, we investigated extending the UV absorption these benzoinyl based carbamates. The general approach used was to modify the benzoyl chromophore while retaining the photocyclization efficiency offered by the 3',5'-dimethoxyphenyl moiety. In an attempt to extend the n-π* transition of these novel benzoin carbamates to longer wavelength, a variety of bathochromic substituted analogs of 3',5'-dimethoxybenzoin cyclohexyl carbamate were prepared.

One strategy used was to modify the 3',5'-dimethoxybenzoin chromophore by incorporating a 4-methoxy substituent into the 1-phenyl ring. Through this modification, the new chromophore may be considered as the α-(3,5-dimethoxyphenyl)-4-methoxyphenacyl moiety and as such may be expected to be similar to the known photolabile 4-methoxyphenacyl group and its α substituted analogs. The 4-methoxyphenacyl and the α-methylphenacyl group have been widely used as both carboxyl[25] and amino[26] photolabile protecting groups. Thus, the new chromophore should possess the combined photosensitivity of the 3',5'-dimethoxybenzoin chromophore with the known photolability of α-substituted 4-methoxyphenacyl protecting groups. The required benzoin (**20**), was prepared from α-(4-methoxyphenyl)-α-(trimethylsiloxy)acetonitrile by lithiation and subsequent reaction of the carbanion with 3,5-dimethoxybenzaldehyde. Fluoride ion mediated hydrolysis gave the desired benzoin (**20**) in 47% yield (Scheme 5). With this benzoin in hand, conversion to the masked cyclohexylamine (**21**) was accomplished in 66% yield by reaction with cyclohexyl isocyanate in refluxing toluene (Scheme 2).

Using a similar strategy to the described above, a 4-methylthio substituent was incorporated into the 1-phenyl moiety. In the case of α-keto sulfonates, such a structural modification greatly increases the absorption maxima above 300 nm[27]. Because of such improved absorption characteristics, these

materials function as efficient red shifted photoacid generators. By analogy, cyclohexyl carbamate (**22**) containing the 4-methylthio modification chromophore may be expected to be an efficient source of cyclohexylamine beyond 300 nm. Furthermore, we anticipate carbamate (**22**) will also gain additional photosensitivity through the substituted phenacyl nature of the chromophore, similar to carbamate (**21**). Carbamate (**22**) was prepared from benzoin (**23**) in 92% yield by reaction with cyclohexyl isocyanate in refluxing toluene (Scheme 2). The required benzoin (**23**) was prepared from the masked TMS cyanohydrin of 4-methylthiobenzaldehyde by lithiation and reaction with 3,5-dimethoxybenzaldehyde. Subsequent fluoride assisted desilylation gave benzoin (**23**) in 58% yield (Scheme 5).

Following modification of the 3',5'-dimethoxybenzoin chromophore to photoactive substituted phenacyl groups it seemed appropriate to evaluate carbamates containing simple substituted phenacyl groups for comparison. Hence, two other cyclohexyl carbamates containing basic phenacyl chromophores were prepared (Scheme 2). Firstly, cyclohexyl carbamate (**24**) incorporating the parent α-methyl-4-methoxyphenacyl photolabile moiety was prepared in 59% yield from 1-phenyl-2-hydroxypropanone[28]. In this reaction, a trace of the corresponding 4-oxazolin-2-one (**25**) was also isolated. A similar addition reaction with 4-methoxybenzoin proceeded smoothly to give the corresponding cyclohexyl carbamate (**26**) in 52% yield. This carbamate contains the α-(phenyl)-4-methoxyphenacyl photolabile group. 4-Methoxybenzoin was prepared by the benzoin reversion synthesis from benzoin and 4-methoxybenzaldehyde[29].

Introduction of a 4-nitro substituent on the 1-phenyl moiety by reaction of α-(4-nitrophenyl)-α-(trimethylsiloxy)acetonitrile with 3,5-dimethoxybenzaldehyde was also investigated. In this case, attempted formation of the carbanion of with LDA at -78_C resulted in a complex mixture. Hunig *et. al.*[23] reported a similar difficulty on attempted alkylation of α-(4-nitrophenyl)-α-(trimethylsiloxy)acetonitrile.

In another approach, the 1-phenyl substituent was replaced by a 1-(2-naphthalenyl) substituent as in carbamate (**27**). The required benzoin (**28**) was prepared by reaction of the carbanion of α-(2-naphthalenyl)-α-(trimethylsiloxy)acetonitrile with 3,5-dimethoxybenzaldehyde in the usual way (Scheme 5). Addition of substituted benzoin (**28**) to cyclohexyl isocyanate proceeded in 70% yield to give the requisite carbamate (**27**) (Scheme 2). Once again, a trace amount of the corresponding benzil, 1-(3,5-dimethoxyphenyl)-2-(2-naphthalenyl)ethanedione was formed during the direct addition.

iii) Preparation of 2,2'-Di-Substituted α-Keto Carbamates

Previous experience in improving the photoefficiency of the *o*-nitrobenzyl photorearrangement[6] suggested that we apply similar design principles to improve the photosensitivity of substituted benzoin chromophores. One of the most successful structural modifications made during studies of the *o*-nitrobenzyl photorearrangement was α-substitution at the benzylic carbon atom[30]. The increased photoefficiency offered by this structural change is believed to stem from increased stabilization of the intermediate benzylic radical species. Since a benzylic radical may be an intermediate in the photocyclization of the desyl masking group, application of this strategy towards improved photosensitivity appeared promising. Accordingly, a variety of 2,2'-disubstituted α-hydroxy ketones were prepared as potentially improved chromophores for amine photogeneration via benzoin photocyclization. The first carbamate (**29**), containing a 2,2-disubstituted α-hydroxy keto chromophore was prepared in 94% by reaction of α-hydroxy ketone (**30**) with cyclohexyl isocyanate in the presence of a catalytic amount of stannous 2-ethyl hexanoate (Scheme 2). This tin(I) salt was reported to be a useful catalyst for the preparation of tertiary carbamates[18] and proved to be the catalyst of choice for reaction of our α-keto substituted tertiary alcohols with isocyanates. The requisite α-hydroxy ketone (**30**) was prepared in 46% yield by reaction of benzil and 3,5-dimethoxyphenylmagnesium chloride (Scheme 6). The preparation of the necessary Grignard reagent required somewhat forcing conditions: near complete reaction was achieved by heating a solution of 1-chloro-3,5-dimethoxybenzene and magnesium turnings in THF at reflux overnight.

In carbamate (**29**) an α-phenyl group has been incorporated into the 3',5'-dimethoxybenzoin chromophore. This substitution pattern may suffer from steric interference in the benzoin photocyclization. Accordingly, it seemed appropriate to prepare the α-methyl derivative in which the potentially favorable 2,2'-disubstitution pattern is retained but steric congestion is reduced. The required α-hydroxy ketone (**31**) was prepared by lithiation of α-(phenyl)-α-(trimethylsiloxy)acetonitrile and reaction with 3,5-dimethoxyacetophenone (Scheme 7). In this case, the TMS masked benzoin (**32**) was cleanly isolated in 99% yield and ultimately deprotected by acidolysis. The resulting α-hydroxy ketone (**31**) was converted to the cyclohexyl carbamate (**33**) in 66% yield, via the tin(I) catalyzed carbamoylation reaction described above (Scheme 2).

The 3,5-dimethoxy substitution pattern has been shown to play a particularly important role in the photocyclization of substituted benzoins when substitution is on the benzylic aromatic ring[8-10,12-16]. In the case of the *o*-nitrobenzyl photorearrangment, substitution by an additional *o*-nitro group is reported to cause a near five fold increase in photoefficiency, relative to the mono *o*-nitrobenzyl chromophore[6,30]. It may be possible to combine these two observations to further improve the photosensitivity of the benzoin photocyclization by incorporating both features into a single chromophore. Cyclohexyl carbamate (**34**) derived from α-hydroxy ketone (**35**) incorporating two 3,5-dimethoxyphenyl substituents adjacent to the hydroxyl derived carbon was quantitatively prepared from α-hydroxy ketone (**35**), by the stannous 2-ethyl hexanoate catalyzed addition to cyclohexyl isocyanate (Scheme 2). The TMS masked hydroxy ketone (**36**) was prepared in good yield from α-(phenyl)-α-(trimethylsiloxy)acetonitrile, by reaction with 3,3',5,5'-tetramethoxybenzophenone (**37**). Fluoride ion mediated hydrolysis of the TMS masked intermediate (**36**) resulted in 85% recovery of the substituted ketone (**37**) whilst acidolysis provided the desired α-hydroxy ketone (**35**) in 77% yield (Scheme 8). The efficient recovery of starting benzophenone from the fluoride mediated hydrolysis implies that fluoride is sufficiently basic as to cause the TMS masked benzoin to undergo a retro aldol type reaction. This is in contrast to the reaction of TMS masked cyanohydrins and aldehydes in which fluoride mediated hydrolysis of the crude TMS masked benzoin products proceeds smoothly while acidolysis suffers from significant side reactions. 3,3',5,5'-Tetramethoxybenzophenone (**37**) was prepared in 66% yield by reaction of 3,5-dimethoxybenzonitrile and 3,5-dimethoxyphenylmagnesium chloride (Scheme 8). On acidic work-up, the ketimine intermediate was isolated as the corresponding hydrochloride salt and hydrolyzed to the free ketone (**37**) using 30% sulfuric acid in refluxing toluene[31].

To further gauge the importance of double 3,5-dimethoxy substitution adjacent to the hydroxyl derived carbon as in (**34**), a carbamate in which the substitution pattern is reversed should provide the required contrast in photoactivity. For this purpose cyclohexyl carbamate (**38**) was prepared. This particular carbamate (**38**) was conveniently prepared in 81% yield via the usual tin(I) catalyzed reaction (Scheme 2). The required α-hydroxy ketone (**39**) was prepared by lithiation of α-(3,5-dimethoxyphenyl)-α-(trimethylsiloxy)acetonitrile followed by reaction with benzophenone (Scheme 9). The TMS masked benzoin (**40**) was isolated in reasonable purity and deprotected by acidolysis to give (**39**) in 81% yield.

Since a significant amount of this α-hydroxy ketone (**39**) was readily available, the opportunity was taken to evaluate several other methods of masking amines as tertiary carbamates. Initially, the conditions used to prepare other benzoin carbamates were investigated. However, heating a solution of the α-hydroxy ketone (**39**) with cyclohexyl isocyanate failed to give any of the desired carbamate (**38**). The cuprous chloride catalyzed addition of tertiary alcohols to isocyanates was also investigated[32]. In the case of α-hydroxy ketone (**39**), smooth addition to cyclohexyl isocyanate took place initially but as the reaction progressed a complex multicomponent mixture resulted. The reaction of tertiary alcohols with carbamoyl chlorides is reported to give the corresponding tertiary carbamates directly[33]. However, in the case of α-hydroxy ketone (**39**), DMAP catalyzed reaction with N,N'-diethylcarbamoyl chloride also failed. The synthesis of tertiary carbamates can also be approached by activation of the tertiary alcohol as a mixed carbonate followed by reaction with an amine. In the case of α-hydroxy ketone (**39**), attempted activation by derivatization to the p-nitrophenyl mixed carbonate afforded only recovered starting material.

Conclusions.

In order to allow the preparation of novel photogenerators of amines, the synthesis of a variety of substituted benzoin chromophores has been investigated. These chromophores hold significant potential as new photolabile protecting groups for a variety of functional groups. For instance, the masking of amino groups with these chromophores gave photoactive α-keto carbamates. The required benzoin chromophores were prepared by a variety of synthetic routes, depending on the structure of the benzoin chromophore desired. The benzoin condensation was used to prepare symmetrical benzoins. The synthetic versatility of TMS masked cyanohydrins was particularly useful in preparing unsymmetrical benzoins,. Firstly, upon reaction with a Grignard reagent, TMS masked cyanohydrins function as an α-hydroxy carbonyl equivalent to form α-hydroxy ketones. Alternatively, lithiation of a TMS masked cyanohydrin generates a benzoyl anion equivalent which reacts with aldehydes and ketones to generate benzoins and 2,2-disubstituted α-hydroxy ketones respectively. These chromophores were used to mask primary and secondary amines. Masking of primary amines was achieved by direct addition of the substituted benzoin to an isocyanate. The reaction of benzoins generally proceeded smoothly in refluxing toluene but on occasion was complicated by intramolecular cyclization of the α-keto carbamate

functionality to give substituted oxazolidin-2-one heterocycles. In contrast, carbamoylation of 2,2-disubstituted α-hydroxy ketones required tin (1) catalysis for efficient reaction. Protection of secondary amines was readily achieved by activation of the benzoin as a mixed p-nitrophenyl carbonate followed by reaction with the free amine. The novel protected amines with photochemically removable groups should find uses as photoactive compounds for chemically amplified resist materials in microlithography[1,38].

Experimental Procedures

General Procedures

Melting points and boiling points are uncorrected; melting points were recorded on a Gallenkamp melting point instrument. Unless stated otherwise, infrared spectra were obtained as KBr Disks using a Nicolet FTIR/44 spectrometer. Ultraviolet-visible spectra were measured in acetonitrile solution using a Hewlett-Packard 8450 Diode Array Spectrophotometer. NMR spectra were recorded in $CDCl_3$ on a Bruker AF250 spectrometer using tetramethylsilane as internal standard. Microanalyses were performed by Desert Analytics, Tucson, AZ.

Preparation of Symmetrical Benzoins

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-(3,5-dimethoxyphenyl)ethanone (4).

To a solution of 3,5-dimethoxybenzaldehyde (6.64g, 40.0mmol) in DMF (25ml) at room temperature under nitrogen was added tetra-n-butylammonium iodide (1.256g, 3.4mmol) followed by potassium cyanide (0.521g, 8.0mmol) and the resulting solution stirred at room temperature for 18h. The reaction mixture was poured into water (150ml) and the product extracted into dichloromethane (3 x 50ml). The combined organic extracts were washed with brine (2 x 25ml) and dried ($MgSO_4$). Removal of the solvent in vacuo gave a yellow oil (11.16g) which solidified on cooling. Recrystallization (CH_2Cl_2/EtOH) allowed isolation of the crude benzoin as an off-white solid (4.47g). Recrystallization from EtOH gave the requisite benzoin (**4**) as a white solid (4.18g, 31%).

m.p. 102-103_C (lit.[16] m.p. 102-103_C) Microanalysis: Calculated for $C_{18}H_{20}O_6$ (332.34) C 65.05, H 6.07; Found C 65.11, H 6.00%. IR ν 3460, 1683, 1595, 1459, 1428, 1351, 1301, 1207, 1158, 1065 cm^{-1}. ^1H NMR δ 3.74 and 3.79 (each 6H, each s, 3,3',5,5'-OCH_3), 4.48 (1H, d (J=6.2Hz), OH (D_2O

exch.)), 5.70 (1H, d (J=6.2Hz), 2-CH), 6.36 (1H, t (J_m=2.2Hz), Ar(2) 4-H), 6.47 (2H d (J_m=2.2Hz), Ar(2) 2,6-H), 6.61 (1H, t (J_m=2.3Hz), Ar(1) 4-H), 7.06 ppm (2H, d (J_m=2.3Hz), Ar(1) 2,6-H). ^{13}C NMR δ 55.25 and 55.42 (each q), 76.18 (d), 100.39 (d), 106.21 (d), 105.60 (d), 106.76 (d), 135.06 (s), 140.99 (s), 160.64 (s), 161.15 (s), 198.34 ppm (s).

Preparation of Unsymmetrical Benzoins

i) Preparation of Mono Substituted Benzoins

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-(phenyl)ethanone (11).

a) via Grignard Route.

To a solution of phenylmagnesium bromide (3M in Et_2O, 20.0ml, 60.0mmol), in anhydrous tetrahydrofuran (40ml) under nitrogen was added a solution of α-(3,5-dimethoxyphenyl)-α-(trimethylsiloxy)acetonitrile[16] (13.27g, 50.0mmol) in anhydrous tetrahydrofuran (40ml). The resulting solution was stirred at room temperature for 2h, then quenched with cold saturated ammonium chloride. The tetrahydrofuran was removed in vacuo and the residue extracted with ether (3 x 100ml). The combined ether extract was washed with water (2 x 50ml) and brine (1 x 50ml), dried ($MgSO_4$) and concentrated under reduced pressure. The residue (14.59g) was taken up in a mixture of methanol (100ml) and 10% hydrochloric acid (35ml) and the resulting solution heated at reflux for 6h. After cooling, the solvent was removed in vacuo and the residue taken up in ether (150ml). The solution was washed with water (3 x 50ml) and brine (1 x 50ml). After drying ($MgSO_4$), removal of the solvent under reduced pressure gave a red oil (9.25g). Attempts to crystallize the desired bemzoin from this crude oil failed. However, using flash chromatography (20% EtOAc/80% Hexane), the desired benzoin (2.16g) was isolated as a yellow solid. Recrystallization from methanol furnished the desired benzoin **(11)** as a light yellow crystalline solid (1.49g, 11%). This material had spectroscopic data consistent with 3',5'-dimethoxybenzoin **(11)** (vide infra).

b) via Umpolung Route.

To a solution of dry, distilled diisopropylamine (9.25ml, 66.0mmol) in anhydrous 1,2-dimethoxyethane (50ml) at -78_C under nitrogen was added a solution of n-butyllithium in hexanes (1.6M, 37.5ml, 60.0mmol). The solution was stirred at -78_C for 1h, then treated dropwise with a

solution of α-(phenyl)-α-(trimethylsiloxy)acetonitrile[24] (12.32g, 60.0mmol) in dry 1,2-dimethoxyethane (50ml). After 1h at -78_C, a solution of 3,5-dimethoxybenzaldehyde (10.97g, 66.0mmol) in dry 1,2-dimethoxyethane (150ml) was added and the reaction allowed to slowly warm up to 0_C over 4h. Once at 0_C, saturated ammonium chloride (75ml) was added and the mixture stirred for 5 min. Ether (150ml) was added and the layers separated. The organic layer was washed with saturated ammonium chloride (1 x 50ml), dried ($MgSO_4$) and concentrated in vacuo to give a orange oil (23.20g). The oil was taken up in tetrahydrofuran (75ml) and a solution of tetrabutylammonium fluoride in tetrahydrofuran (1M, 66ml, 66.0mmol) added. The resulting solution was stirred at room temperature under nitrogen for 4h, concentrated in vacuo and the residue partitioned between ether (200ml) and water (50ml). The layers were separated and the organic layer washed with water (2 x 50ml) and brine (1 x 50ml). After drying ($MgSO_4$), removal of the solvent in vacuo gave a yellow oil (18.27g) which on trituration with methanol gave a solid which was recrystallized from methanol to afford the substituted benzoin (**11**) as a white crystalline solid (3.97g, 24%).

m.p. 109-110_C (lit.[10] m.p. 110-111.5_C). Microanalysis: Calculated for $C_{16}H_{16}O_4$ (272.27): C 70.58, H 5.92; Found C 70.58, H 5.95%. IR ν 3450, 1682,1608, 1597, 1462, 1450, 1431, 1206, 1159, 1065 cm^{-1}. ^1H NMR δ 3.73 (6H, s, Ar(2) 3,5-OCH_3), 4.54 (1H, d (J=6.2Hz), OH (D2O exch.)), 5.87 (1H, d (J=6.2Hz), 2-CH), 6.37 (1H, t (J_m=2.2Hz), Ar(2) 4-H), 6.49 (1H, d (J_m=2.2Hz), Ar(2) 2,6-H), 7.41 (2H, m approximates to t (J_o=7.6Hz), Ar(1) 3,5-H), 7.54 (1H, m approximates to t (J_o=7.6Hz), Ar(1) 4-H), 7.94 ppm (2H, m approximates to d (J_o=7.6Hz), Ar(1) 2,6-H). ^{13}C NMR δ 55.26 (q), 76.06 (d), 100.35 (d), 105.69 (d), 128.59 (d), 129.01 (d), 133.36 (s), 133.87 (d), 140.92 (s), 161.15 (s), 198.61 (s) ppm.

*Attempted preparation of 1-(3,5-dimethoxyphenyl)-2-hydroxy-2-(phenyl)ethanone (**14**): Isolation of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-(phenyl)ethanone (**11**).*

α-(3,5-Dimethoxyphenyl)-α-(trimethylsiloxy)acetonitrile[16] (13.27g, 50.0mmol) was lithiated and the carbanion treated with freshly distilled benzaldehyde (5.81g, 55.0mmol) in a similar manner to that described above. The usual work-up followed by fluoride mediated hydrolysis gave the crude product as a red oil (15.87g). Trituration with a little methanol gave a solid which was recrystallized from methanol to give a white crystalline solid (6.79g, 50%). Spectroscopic analysis (^1H NMR/^{13}C NMR) revealed this

material to be the isomeric benzoin (**11**) previously prepared from reaction of α-(phenyl)-α-(trimethylsiloxy) acetonitrile and 3,5-dimethoxybenzaldehyde (vide supra).

α-(1,3-Benzodioxol-5-yl)-α-(trimethylsilyloxy)acetonitrile (19).

To a mixture of piperonal (15.01g, 0.10mol) and anhydrous zinc iodide (0.059g, 0.185mmol) under nitrogen at room temperature was added trimethylsilyl cyanide (10.91g, 0.11mol) in one portion The resulting solution was then stirred at 95_C overnight. Vacuum distillation of the red oil afforded the TMS masked cyanohydrin (**19**) as a pale yellow oil (21.60g, 87%).

b.p. 90-95_C at 0.5mmHg. IR ν 2242, 1506, 1490, 1447, 1235, 1103, 1085, 1041, 938, 875 cm^{-1}. ^1H NMR δ 0.24 (9H,s, $OSi(CH_3)_3$), 5.41 (1H, s, CH), 6.01 (2H, s, OCH_2O), 6.82 (1H, d (J_o=8.0Hz), 7-H), 6.93 (1H,dd (J_o=8.0Hz, J_m=1.8Hz), 6-H), 6.98 ppm (1H, d (J_m=1.8Hz), 4-H). ^{13}C NMR δ -0.47 (q), 63.22 (d), 101.29 (t), 106.76 (d), 108.13 (d), 118.95 (s), 120.02 (d), 130.00 (s), 148.02 (s), 148.28 (s) ppm.

2-(1,3-Benzodioxol-5-yl)-2-hydroxy-1-(phenyl)ethanone (16).

To an ice cooled solution of phenylmagnesium bromide (3M in Et_2O, 13.2ml, 39.4mmol), in anhydrous tetrahydrofuran (40ml) under nitrogen was added a solution of α-(1,3-benzodioxol-5-yl)-α-(trimethylsilyloxy)acetonitrile (8.94g, 35.9mmol) in anhydrous tetrahydrofuran (40ml). The resulting solution was stirred at 0_C for 2h, then quenched by pouring into a mixture of ice(350g)/concentrated sulfuric acid (20ml) and stirring for 1h. The tetrahydrofuran was removed in vacuo and the residue extracted with ether (3 x 100ml). The combined ether extract was washed with 10% hydrochloric acid (2 x 50ml) and brine (1 x 50ml), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was taken up in a mixture of methanol (100ml) and 10% hydrochloric acid (35ml) and the resulting solution stirred at room temperature for 60h. During this time a significant amount of solid was precipitated, the reaction mixture was cooled to 0_C and the solid collected by filtration. The white solid (4.53g) was identified as the desired benzoin albeit in a crude form. Recrystallization from methanol furnished the desired benzoin (**16**) as a white crystalline solid (3.63g, 40%).

m.p. 127-129_C (lit.[34] m.p. 120_C). Microanalysis: Calculated for $C_{15}H_{12}O_4$ (256.25); C 70.30, H 4.72; Found C 70.46, H 4.79%. IR ν 3458, 1681, 1502, 1488, 1443, 1247, 1099, 1039, 975, 695 cm^{-1}. ^1H NMR δ 4.39 (1H, br. s, OH), 5.87 (1H, s, 2-CH), 5.92 (2H, m, OCH_2O), 6.73-6.78 (2H, m, Ar(2)

6,7-H), 6.85 (1H, dd (J_o=8.0Hz, J_m=1.6Hz), Ar(2) 4-H), 7.44 (2H, m approximates to t, Ar(1) 3,5-H), 7.56 (1H, m approximates to t, Ar(1) 4-H), 7.92 ppm (2H, m approximates to d, Ar(1) 2,6-H). ^{13}C NMR δ 75.71 (d), 101.15 (t), 107.70 (d), 108.69 (d), 121.75 (d), 128.58 (d), 129.03 (d), 132.76 (s), 133.32 (s), 133.81 (d), 147.76 (s), 148.13 (s), 198.66 (s) ppm.

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-(4-methoxyphenyl)ethanone (20).

α-(4-Methoxyphenyl)-α-(trimethylsiloxy)acetonitrile[35] (11.77g, 50.0mmol) was lithiated and the carbanion treated with 3,5-dimethoxybenzaldehyde (9.14g, 55.0mmol) in an analogous manner to that described above. The usual work up followed by fluoride mediated hydrolysis gave the crude product as a yellow orange oil (18.33g). Trituration with a little methanol gave a solid which was recrystallized from methanol to give the substituted benzoin (**20**) as a white crystalline solid (8.03g, 53%).

m.p. 100-101_C. Microanalysis: Calculated for $C_{17}H_{18}O_5$(302.31); C 67.54, H 6.00; Found C 67.74, H 5.93%. IR ν 3366, 1678, 1675, 1601, 1264, 1244, 1207, 1177, 1164, 1087 cm^{-1}. ^1H NMR δ 3.74 (6H, s, Ar(2) 3,5-OCH_3), 3.83 (3H, s, Ar(1) 4-OCH_3), 4.62 (1H, d (J=5.8 Hz), OH (D2O exch.)), 5.79 (1H, d (J=5.8 Hz), 2-CH), 6.36 (1H, t (J_m = 2.2Hz), Ar(2) 4-H), 6.48 (2H, d (J_m=2.2Hz), Ar(2) 2,6-H), 6.87 and 7.93 ppm (each 2H, ABq (J_o=8.9Hz), Ar(1) 3,5-H and 2,6-H respectively). ^{13}C NMR δ 55.23 (s), 55.37 (s), 75.64 (d), 100.20 (d), 105.64 (d), 113.84 (d), 126.14 (s), 131.43 (d), 141.56 (s), 161.11 (s), 164.00 (s), 196.81 (s) ppm.

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-(4-methylthiophenyl)ethanone (23):

α-(4-Methylthiophenyl)-α-(trimethylsiloxy)acetonitrile[36] (12.57g, 50.0mmol) was lithiated and the carbanion treated with 3,5-dimethoxybenzaldehyde (9.14g, 55.0mmol) in an analogous manner to that described above. The usual work-up followed by fluoride mediated hydrolysis gave the crude product as a yellow oil (19.32g). Trituration with a little methanol gave a solid which was recrystallized from methanol to give the substituted benzoin (**23**) as a white crystalline solid (9.79g, 62%).

m.p. 112-113_C. Microanalysis: Calculated for $C_{17}H_{18}O_4S$ (318.47); C 64.13, H 5.70, S 10.07; Found C 64.28, H 5.76, S 9.74%. IR ν 3370, 1678, 1670, 1608, 1596, 1591, 1206, 1162, 1156, 1088 cm^{-1}. ^1H NMR δ 2.47 (3H, s, SCH_3), 3.74 (6H, s, Ar(2) 3,5-OCH_3), 4.58 (1H, d (J=6.1Hz), OH (D_2O exch.)), 5.80 (1H, d (J=6.1Hz), 2-CH), 6.36 (1H, t (J_m=2.1Hz), Ar(2) 4-H), 6.47 (2H, d (J_m=2.1Hz),

Ar(2) 2,6-H), 7.21 and 7.84 ppm (each 2H, ABq (J_o=7.8Hz), Ar(1) 3,5-H and 2,6-H respectively). ^{13}C NMR δ 14.42 (q), 55.25 (q), 75.85 (d), 100.25 (d), 105.69 (d), 124.70 (d), 129.34 (d), 141.22 (s), 147.36 (s), 161.15 (s), 197.37 (s) ppm. One carbon resonance missing.

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-(2-naphthalenyl)ethanone (28).

α-(2-Naphthalenyl)-α-(trimethylsiloxy)acetonitrile[37] (11.42g, 44.7mmol) was lithiated and the carbanion treated with 3,5-dimethoxybenzaldehyde (8.17g, 49.2mmol) in the usual manner. The usual work-up followed by fluoride mediated hydrolysis gave the crude product as an orange oil (14.71g). Attempts to crystallize this oil failed and the crude benzoin was isolated by flash chromatography using 25% EtOAc/75% hexane.

Microanalysis: Calculated for $C_{20}H_{18}O_4$ (322.34); C 74.52, H 5.63; Found C 74.32, H 5.42%. IR ν 3454, 1677, 1608, 1596, 1466, 1430, 1283, 1205, 1158, 1065 cm^{-1}. ^1H NMR δ 3.74 (6H, s, 3,5-OCH_3), 4.62 (1H, br. d (J=5.2Hz), OH), 6.02 (1H, br. d (J=5.2Hz), 2-CH), 6.35 (1H, t (J_m=2.2Hz), Ar(2) 4-H), 6.55 (2H, d (J_m=2.2Hz), Ar(2) 2,6-H), 7.50-7.65 (2H, m, Ar(1) 6,7-H), 7.81-8.03 (4H, m, Ar(1) 3,4,5,8-H), 8.49 ppm (1H, br. s, Ar(1) 1-H). ^{13}C NMR δ 55.25 (q), 76.13 (d), 100.32 (d), 105.74 (d), 124.13 (d), 126.88 (d), 127.68 (d), 128.50 (d), 128.93 (d), 129.65 (d), 130.68 (s), 131.20 (s), 132.12 (s), 135.75 (s), 141.12 (s), 161.17 (s), 198.55 (s) ppm.

ii) Preparation of 2,2-Disubstituted Benzoins

2-(3,5-Dimethoxyphenyl)-2-hydroxy-(1,2-diphenyl)ethanone (30)

To a suspension of clean, dry magnesium turnings (3.62g, 0.149mol) in dry tetrahydrofuran (20ml) at room temperature was added a few drops of a solution of 1-chloro-3,5-dimethoxybenzene (23.38g, 0.135mol) in dry tetrahydrofuran (100ml). No visible reaction took place even on adding a few drops of 1,2-dibromoethane. The suspension was then brought to reflux whereupon the addition of a few drops of 1,2-dibromoethane caused a vigorous reaction. The remainder of the aryl chloride solution was added dropwise over 30 min and the solution heated at reflux overnight. After cooling, the magnesium residues were filtered off under nitrogen and rinsed with tetrahydrofuran (2 x 10ml). Based on the weight of these residues (0.65g), the Grignard solution was assumed to contain 0.122 mol of 3,5-dimethoxyphenylmagnesium chloride. This Grignard reagent was added dropwise to a solution of benzil

(25.65g, 0.122mol) in dry tetrahydrofuran (200ml). The solution was brought to reflux and stirred there at for 16h. After cooling, the reaction was quenched with saturated ammonium chloride (100ml) and the tetrahydrofuran removed in vacuo. The residue was extracted with ether (3 x 100ml), the combined ether extracts were washed with water (2 x 75ml) and brine (1 x 75ml) and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave a dark brown viscous oil (45.71g) which failed to crystallize. The crude product was purified in a batch mode by flash chromatography using 10% EtOAc/90% hexane as eluant. In this way, a total of 5.92g of benzil was recovered from the early fractions of each column. The latter fractions from each column were combined to give the crude product as a colorless oil (18.94g) which crystallized on trituration with ethanol. Recrystallization from ethanol gave the desired benzoin (**30**) as a white crystalline solid (15.14g, 46% based on recovered starting benzil).

m.p. 111.5-113_C. Microanalysis: Calculated for C_{22} $H_{20}O_4$ (348.38); C 75.84, H 5.79; Found C 75.95, H 5.71%. IR ν 3429, 1674, 1611, 1597, 1426, 1235, 1205, 1158, 1068, 703 cm^{-1}. ^1H NMR δ 3.71 (6H, s, Ar(2) 3,5-OCH_3), 4.96 (1H, s, OH (D_2O exch.)), 6.42 (1H, t (J_m=2.2Hz) Ar(2) 4-H), 6.59 (2H, d (J_m=2.2Hz) Ar(2) 2,6-H), 7.29-7.51 (8H, m, Ph(2) 2,6-H and Ph(1) 3,4,5-H), 7.72 ppm (2H,d (Jo = 6.7Hz), Ph(2) 2,6-H). ^{13}C NMR δ 55.23 (q), 84.91 (s), 100.02 (d), 106.51 (d), 128.04 (d), 128.11 (d), 128.19 (d), 128.26 (d), 130.67 (d), 132.86 (d), 135.18 (s), 141.68 (s), 143.79 (s), 160.55 (s), 200.48 (s) ppm.

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-(phenyl)propanone (31).

To a solution of diisopropylamine (4.45ml, 3.21g, 31.75mmol) in dry 1,2-dimethoxyethane (50ml) at -78_C under nitrogen was added a solution of n-butyl lithium (1.6M in hexanes, 18.94ml, 30.30mmol) and the solution stirred at -78_C for 1h. A solution of α-(phenyl)-α-(trimethylsiloxy)acetonitrile[24] (5.93g, 28.86mmol) in dry 1,2-dimethoxyethane (50ml) was added and the solution stirred at -78_C for 1h, then a solution 3,5-dimethoxyacetophenone (5.20g, 28.86mmol) was added. The resulting mixture was allowed to warm up to 0_C over 4h. Saturated ammonium chloride (50ml) was added and the mixture stirred for 5 min. Ether (150ml) was added, the layers separated and the organic layer washed with saturated ammonium chloride (1 x 50ml). After drying ($MgSO_4$), removal of the solvent under reduced pressure gave the TMS masked benzoin (**32**) as an orange oil (10.82g).

IR(Liquid Film) ν 1685, 1607, 1597, 1425, 1253, 1207, 1157, 1066, 1012, 843 cm^{-1}. ^1H NMR δ 0.00 (9H, s, $OSi(CH_3)_3$), 1.74 (3H, s, CH_3), 3.72 (6H, s, Ar(2) 3,5-OCH_3), 6.30 (1H, t (J_m=2.2Hz), Ar(2) 4-H), 6.62 (2H, d (J_m=2.2Hz), Ar(2) 2,6-H), 7.23 (2H, t (J_o=7.8Hz), Ar(1) 3,5-H), 7.34 (1H, t (J_o=7.8Hz), Ar(1) 4-H), 7.90 ppm (2H, d (J_o=7.8Hz), Ar(1) 2,6-H). ^{13}C NMR δ 1.60 (q), 29.83 (q), 55.14 (q), 83.35 (s), 98.41 (d), 102.48 (d), 127.57 (d), 130.70 (d), 132.19 (d), 134.63 (s), 147.55 (s), 160.82 (s), 200.42 (s) ppm.

The TMS ether (**32**) was dissolved in a mixture of 1,4-dioxane (60ml), methanol (40ml) and 10% hydrochloric acid (50ml) and the resulting solution stirred at room temperature for 2h. After concentration under reduced pressure, the residue was partitioned between ether (200ml) and water (50ml) and the organic layer washed with water (2 x 35ml) and brine (1 x 35ml) and dried ($MgSO_4$). Removal of the solvent in vacuo gave the crude benzoin as an orange oil (9.64g) which failed to crystallize. The oil was purified by flash chromatography using 15% EtOAc/85% hexane to afford the desired benzoin (**31**) as a colorless oil (8.20g, 99%).

Microanalysis: Calculated for $C_{17}H_{18}O_4$ (286.31): C 71.31, H 6.34; Found C 71.17, H 6.26%. IR(Liquid Film) ν 3462, 1679, 1607,1597,1458, 1427, 1206, 1157, 1063, 1047 cm^{-1}. ^1H NMR δ 2.12 (3H, s, CH_3), 3.76 (6H, s, Ar(2) 3,5-OCH_3), 4.70 (1H, s, OH (slow D_2O exch.)), 6.41 (1H, t (J_m=2.2Hz), Ar(2) 4-H), 6.61 (2H, d (J_m=2.2Hz), Ar(2), 2,6-H), 7.31 (2H, m approximates to t, Ar(1) 3,5-H), 7.46 (1H, m approximates to t, Ar(1) 4-H), 7.75 ppm (2H, m approximates to d, Ar(1) 2,6-H). ^{13}C NMR δ 26.17 (q), 55.25 (q), 78.99 (s), 99.69 (d), 104.05 (d), 128.18 (d), 130.02 (d), 132.91 (d), 133.41 (s), 144.78 (s), 161.10 (s), 201.48 (s) ppm.

1,1'-Di-(3,5-dimethoxyphenyl)methanone (37)

To a suspension of clean, dry magnesium turnings (3.09g, 0.127mol) in dry tetrahydrofuran (20ml) at room temperature was added a few drops of a solution of 1-chloro-3,5-dimethoxybenzene (19.85g, 0.115mol) in dry tetrahydrofuran (100 ml). No visible reaction took place even on adding a few drops of 1,2-dibromoethane. The suspension was then brought to reflux whereupon the addition of a few drops of 1,2-dibromoethane caused a vigorous reaction. The remainder of the aryl chloride solution was added dropwise over 30 min. and the solution heated at reflux overnight. After cooling, the magnesium residues were filtered off under nitrogen and rinsed with tetrahydrofuran (2 x 10ml). Based on the weight

of these residues (0.55g), the Grignard solution was assumed to contain 0.104mol of 3,5-dimethoxyphenylmagnesium chloride. To a solution of 3,5-dimethoxybenzaldehyde (16.97g, 0.104mol) in dry tetrahydrofuran (200ml) at room temperature under nitrogen was added dropwise a solution of 3,5-dimethoxyphenylmagnesium chloride in tetrahydrofuran (0.104mol, 65ml). Once the addition was complete, the solution was heated at reflux for 14h. After cooling, the tetrahydrofuran was removed in vacuo and the residue partitioned between saturated ammonium chloride (150ml) and ether (200ml). The layers were separated and the aqueous phase extracted with ether (2 x 100ml). The combined ether extracts was treated with concentrated hydrochloric acid (5ml) which caused precipitation of a large amount of a fawn solid. The solid was collected by filtration, washed with water (2 x 50ml) and ether (2 x 50ml) and dried in vacuo overnight. The solid which amounted to 27.50g was identified as the ketimine hydrochloride salt. Hydrolysis was achieved by heating a suspension of the salt in a mixture of toluene (100ml) and 30% sulfuric acid (200ml) at reflux for 6h. After cooling, ether (300ml) was added and the mixture stirred overnight to dissolve the precipitated ketone. The layers were separated and the aqueous phase extracted with ether (2 x 75ml). The combined ether extracts were washed with water (2 x 75ml) and brine (1 x 75ml), dried ($MgSO_4$) and concentrated in vacuo to give the crude product as a light brown solid (23.38g). Recrystallization from ethanol furnished the desired benzophenone (**37**) as a pale yellow solid (20.72g, 66%).

m.p. 106-108_C. Microanalysis: Calculated for $C_{17}H_{18}O_5$ (302.31); C 67.54, H 6.00: Found C 67.52, H 5.96%. IR ν 1661, 1600, 1459, 1417, 1345, 1307, 1208, 1201, 1155, 753 cm^{-1}. ^1H NMR δ 3.83 (12H, s, 3,3',5,5'-OCH_3), 5.49(1H, s, CH), 6.67 (2H, t (J_m=2.3Hz), 4,4'-H), 6.94 ppm (4H, d (J_m=2.3Hz), 2.2',6,6'-H). ^{13}C NMR δ 55.45 (q), 104.72 (d), 107.70 (d), 139.23 (s), 160.39 (s), 195.80 (s) ppm.

2,2-Di-(3,5-dimethoxyphenyl)-2-hydroxy-1-(phenyl)ethanone (35).

α-(Phenyl)-α-(trimethylsiloxy) acetonitrile[24] (5.13g, 25.0mmol) was lithiated and the carbanion treated with 3,3',5,5'-tetramethoxybenzophenone (**37**) (7.94g, 26.3mmol) in an analogous manner to that described above. The usual work-up allowed isolation of the TMS masked benzoin (**36**) as an orange gum (13.15g). This material contained a trace amount of starting 3,3',5,5'-tetramethoxybenzophenone which was recovered after acidolysis and chromatography (vide infra).

For TMS Masked Benzoin (36):

IR ν 1685, 1596, 1457, 1426, 1312, 1251, 1206, 1157, 1068, 842 cm^{-1}. ^1H NMR δ 0.24 (9H, s, $OSi(CH_3)_3$), 3.72 (12H, s, 3,3',5,5'-OCH_3), 6.37 (2H, t (J_m=2.2Hz), Ar(2) 4,4'-H), 6.58 (4H, d (J_m=2.2Hz), Ar(2) 2,2',6,6'-H), 7.30 (2H, m approximates to t, Ar(1) 3,5-H), 7.42 (1H, m approximates to t, Ar(1) 4-H), 7.92 ppm (2H, m approximates to d, Ar(1) 2,6-H). ^{13}C NMR δ 1.28 (q), 55.22 (q), 88.29 (s), 99.47 (d), 106.85 (d), 127.48 (d), 130.21 (d), 131.92 (d), 136.86 (s), 144.87 (s), 160.20 (s), 201.60 (s) ppm.

Acidolysis of the crude TMS masked benzoin (**36**) gave an orange oil (11.95g) which on flash chromatography furnished the following; elution with 10% EtOAc/90% hexane allowed for the recovery of starting 3,3',5,5'-tetramethoxybenzophenone (**37**) as a white solid (1.07g). Further elution with 25% EtOAc/75% hexane gave a white foam (9.64g) which was recrystallized from MeOH then EtOAc/hexane to furnish the desired benzoin (**35**) as a fluffy white solid (7.12g, 77% based on recovered starting ketone).

For Benzoin (35):

M.p. 98-99C. Microanalysis: Calculated for $C_{24}H_{24}O_6$(408.43); C 70.57, H 5.92; Found C 70.76, H 5.89%. IR ν 3441, 1676, 1596, 1459, 1426, 1230, 1209, 1159, 1071, 1063 cm^{-1}. ^1H NMR δ 3.70 (12H, s, 3,3',5,5'-OCH_3), 4.97 (1H, s, OH (slow D_2O exch.)), 6.42 (2H, t (J_m= 2.2Hz), both Ar(2) 4,4'-H), 6.58 (4H, d (J_m=2.2Hz), Ar(2) 2,2',6,6'-H), 7.31 (2H, m approximates to t, Ar(1) 3,5-H), 7.47 (1H, m approximates to t, Ar(1) 4-H), 7.73 ppm (2H, m approximates to d, Ar(1) 2,6-H). ^{13}C NMR δ 55.21 (q), 84.88 (s), 100.08 (d), 106.52 (d), 128.06 (d), 130.62 (d), 132.86 (d), 135.47 (s), 143.72 (s), 160.52 (s), 200.26 (s) ppm.

3,5-Dimethoxyphenyl-2-hydroxy-(2,2-diphenyl)ethanone (39).

α-(3,5-Dimethoxyphenyl)-α-(trimethylsiloxy) acetonitrile[16] (6.63g, 25.0mmol) was lithiated and the carbanion treated with benzophenone (4,78g, 26.3mmol) in a similar manner to that described above.

The usual work-up allowed isolation of the TMS masked benzoin (**40**) as an orange oil (11.19g). This material contained a trace amount of starting benzophenone.

For TMS Masked Benzoin (40):

IR (Liquid Film) ν 1685, 1593, 1424, 1252, 1206, 1157, 1075, 1067, 890, 700 cm^{-1}. ^1H NMR δ -0.20 (9H, s, $OSi(CH_3)_3$), 3.75 (6H, s, 3,5-OCH_3), 6.55 (1H, t (J_m=2.2Hz), Ar(1) 4-H), 7.17 (2H, d (J_m=2.2Hz), Ar(1) 2,6-H), 7.25-7.50 ppm (10H, m, both Ar(2) 2,2-diPh). ^{13}C NMR δ 1.29 (q), 55.29 (q), 88.61 (s), 104.89 (d), 108.06 (d), 127.69 (d), 127.88 (d), 128.26 (d), 138.18 (s), 142.95 (s), 159.75 (s), 201.03 (s) ppm.

Acidolysis of the crude TMS masked benzoin (**40**) gave the crude benzoin as an orange oil (10.07g) which crystallized on standing. Subsequent recrystallization from methanol gave the desired substituted benzoin (**39**) as a white crystalline solid (7.02g, 81%).

For Benzoin (39):

M.p. 93-94_C. Microanalysis: Calculated for $C_{22}H_{20}O_4$ (348.38); C 75.84, H 5.79; Found C 75.83,H 5.83%. IR ν 3446, 1679, 1607, 1597, 1458, 1427, 1206, 1157, 1063, 1047 cm^{-1}. ^1H NMR δ 3.63 (6H, s, Ar(1) 3,5-OCH_3), 5.08 (1H, s, OH (D_2O exch.)), 6.56 (1H, t (J_m=2.3Hz), Ar(1) 4-H), 6.85 (2H, d (J_m=2.3Hz), Ar(1) 2,6-H), 7.29-7.48 ppm (10H, m, both Ar(2) 2,2-diPh). ^{13}C NMR δ 55.28 (q), 84.88 (s), 105.88 (d), 108.38 (d), 128.08 (d), 128.16 (d), 128.28 (d), 136.87 (s), 144.74 (s), 160.10 (s), 200.39 (s) ppm.

Preparation of Unsubstituted Carbamates

Cyclohexyl carbamate of 2-hydroxy-2-(phenyl)-1-(phenyl)ethanone (1).

1) Methyllithium Catalyzed Reaction

To a solution of 2-hydroxy-2-(phenyl)-1-(phenyl)ethanone (5.31g, 25.0mmol) in anhydrous tetrahydrofuran (80ml) at room temperature was added methyllithium (1.4M in Et_2O, 1.79ml, 2.50mmol). After stirring for 1h, a solution of cyclohexyl isocyanate (4.87ml, 4.77g, 26.25mmol) in dry tetrahydrofuran (20ml) was added and the resulting solution heated at reflux for 14h. After cooling, the tetrahydrofuran was removed in vacuo and the residue taken up in dichloromethane (200ml) and washed

with water (3 x 25ml) and brine (1 x 25ml). After drying ($MgSO_4$), removal of the solvent under reduced pressure gave a pale yellow solid (7.17g). Flash chromatography (10% EtOAc/90% Hexane) allowed isolation of the following three fractions. Firstly, a yellow gum (0.05g) was isolated and identified as 1,2-bis-(phenyl)ethanedione by ^1H, ^{13}C NMR and IR spectroscopy. Next, a white solid (2.82g) was isolated and recrystallized from Et_2O/Hexane. In this way, 3-cyclohexyl-4,5-diphenyl-4-oxazolin-2-one (**3**) was isolated as a white crystalline solid (2.04g). Lastly, a white foam (2.67g) was isolated. This material proved to be a mixture of 3-cyclohexyl-4-hydroxy-4,5-diphenyl-4-oxazolidin-2-one (**2**) and the desired carbamate (**1**). Trituration with EtOAc/Hexane allowed crystallization of the oxazolidin-2-one (**2**) as a cream solid (0.40g). This material was purified by recrystallization from EtOAc/Hexane to give the oxazolidin-2-one (**2**) as a white solid (0.069g). The mother liquor rich in the desired carbamate was concentrated and the residue crystallized from CH_2Cl_2/Hexane to afford the desired carbamate (**1**) as a white solid (1.78g, 21%).

a) Cyclohexyl carbamate of 2-hydroxy-2-(phenyl)-1-(phenyl)ethanone (1).

M.p. 87-88_C. Microanalysis: Calculated for $C_{21}H_{23}NO_3$ (337.40); C 74.75, H 6.87, N 4.15; Found C 74.90, H 6.96, N 4.22%. UV: $\varepsilon_{(246)}$13120, $\varepsilon_{(325)}$296. IR ν 3342, 2934, 1706, 1678, 1531, 1449, 1251, 1229, 1059, 697 cm^{-1}. ^1H NMR δ 1.05-2.15 (10H, m, cyclohexyl $(CH_2)_5$), 3.47 (1H, m, cyclohexyl CH), 4.68 and 5.00 (total 1H, each br. d, NH), 6.87 (1H, s, 1-CH), 7.14-7.55 (8H, m, Ar(1) 2,3,4,5,6-H and Ar(2) 3,4,5-H), 7.96 ppm (2H, m approximates to d (J_o= 8.1Hz) 2,6-H). ^{13}C NMR δ 24.63 (t), 25.33 (t), 33.10 (t), 50.06 (d), 77.15 (s), 128.48 (d), 128.53 (d), 128.71 (d), 128.93 (d), 129.04 (d), 133.24 (d), 133.97 (s), 134.73 (s), 154.60 (s), 194.98 (s) ppm.

b) 3-Cyclohexyl-4-hydroxy-4,5-diphenyl-4-oxazolidin-2-one (2)

M.p. 185-188_C. Microanalysis: Calculated for $C_{21}H_{23}NO_3$ (337.40); C 74.75, H 6.87, N 4.15; Found C 74.44, H 6.99, N 4.19%. UV: $\varepsilon_{(251)}$519, $\varepsilon_{(257)}$588, $\varepsilon_{(261)}$478, $\varepsilon_{(263)}$475, $\varepsilon_{(267)}$328, $\varepsilon_{(284)}$102. IR ν 3417, 3262, 2933, 1712, 1450, 1360, 1350, 1101, 703, 695 cm^{-1}. ^1H NMR δ 0.95-2.24 (10H, m, cyclohexyl $(CH_2)_5$), 2.23 (1H, s, OH), 2.82-2.94 (1H, m, cyclohexyl CH), 5.53 (1H, s, 1-CH), 7.12-7.17 (2H, m, 2 ArH), 7.36-7.58 ppm (8H, m, 8 ArH). ^{13}C NMR δ 24.90 (t), 25.78 (t), 25.99 (t), 29.86 (t), 30.69 (t), 53.85 (d), 85.98 (d), 92.17 (s), 125.98 (d), 126.60 (d), 128.65 (d) 128.72 (s), 128.79 (d), 128.94 (d), 129.19 (d), 131.99 (s), 155.85 (s) ppm.

c) 3-Cyclohexyl-4,5-diphenyl-4-oxazolin-2-one (3)

M.p. 161-163_C. Microanalysis: Calculated for $C_{21}H_{21}NO_2$ (319.39); C 78.97, H 6.63, N 4.39; Found C 79.11, H 6.59, N 4.26%. UV: $\varepsilon_{(292)}$14590. IR ν 2939, 1747, 1367, 1354, 1347, 991, 750, 704, 694, 668 cm^{-1}. ^1H NMR δ 1.05-2.27 (10H, m, cyclohexyl $(CH_2)_5$), 3.23-3.39 (1H, m, cyclohexyl CH), 7.11-7.21 (5H, m, 5 ArH), 7.35-7.43 (2H, m, 2 ArH), 7.48-7.58 ppm (3H, m 3, ArH). ^{13}C NMR δ 24.66 (t), 25.63 (t), 29.62 (t), 54.31 (d), 123.55 (s), 124.05 (d), 127.25 (d) 127.61 (s), 127.90 (s), 128.27 (d), 129.41 (d), 129.98 (d), 130.66 (d), 133.94 (s), 155.85 (s) ppm.

2) Uncatalyzed Reaction

To a solution of benzoin (9.02g, 42.5mmol) in toluene (100ml) at room temperature under nitrogen was added cyclohexyl isocyanate (5.97ml, 5.85g, 46.7mmol) and the resulting solution heated at reflux for 48h. After cooling, the reaction mixture was diluted with ether (100ml) and washed with water (2 x 75ml) and brine (1 x 50ml) and dried ($MgSO_4$). Removal of the solvent in vacuo gave the crude product as a yellow solid (12.10g). Flash chromatography (10% EtOAc/90% Hexane) followed by recrystallization from CH_2Cl_2/Hexane gave the desired carbamate (**1**) as a white solid (11.10g, 77%). This material had spectroscopic data identical to an authentic sample prepared above.

Preparation of Mono Aryl Substituted Carbamates

1) Derived From Symmetrical Benzoins

Cyclohexyl carbamate of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-(3,5-dimethoxyphenyl)-ethanone (5).

To a solution of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-(3,5-dimethoxyphenyl)ethanone (**4**) (1.50g, 4.51mmol) in toluene (80ml) at room temperature under nitrogen was added cyclohexyl isocyanate (0.63ml, 0.62g, 4.96mmol) and the resulting solution heated at reflux for 48h. After cooling, the reaction mixture was diluted with ether (100ml) and washed with water (2 x 50ml) and brine (1 x 50ml) and dried ($MgSO_4$). Removal of the solvent in vacuo gave the crude product as a yellow solid (3.57g). Flash chromatography (25% EtOAc/75% Hexane) gave the following fractions. Firstly, a yellow solid (0.10g) was isolated and recrystallized from ethyl acetate/hexane to give light yellow crystals (0.057g). This material was identified as 1,2-bis-(3,5-dimethoxyphenyl)ethanedione by spectroscopy and elemental analysis. Next the crude carbamate was isolated as a light yellow foam (1.67g). Subsequent

recrystallization (CH_2Cl_2/Hexane) allowed isolation of the desired substituted benzoin carbamate (**5**) as a fluffy white solid (1.58g, 77%).

M.p. 116-118_C. Microanalysis: Calculated for $C_{25}H_{31}NO_7$ (457.51) C 65.63, H 6.83, N 3.06; Found C 65.57, H 6.82 , N 2.95%. UV: $\varepsilon_{(202)}$20770, $\varepsilon_{(267)}$6421, $\varepsilon_{(320)}$2256. IR ν 3406, 3326, 2933, 1694, 1598, 1429, 1232, 1214, 1159, 1054 cm^{-1}. ^1H NMR δ 1.05-2.15 (10H, m, cyclohexyl $(CH_2)_5$), 3.48 (1H, m, cyclohexyl CH), 3.76and 3.78 (each 6H, each s, 3,3',5,5'-OCH_3), 4.62 and 4.92 (total 1H, each br. d, NH), 6.41 (1H, t (J_m=2.2Hz), Ar(2) 4-H), 6.57-6.61 (3H m, Ar(1) 4-H and Ar(2) 2,6-H), 6.68 (1H, s, 2-CH), 7.10 ppm (2H, d (J_m=2.0Hz), Ar(1) 2,6-H). ^{13}C NMR δ 24.61 (t), 25.32 (t), 33.06 (t), 50.04 (d), 55.31 (q), 55.42 (q), 77.26 (d), 101.11 (d), 105.86 (d), 106.38 (d), 106.45 (d), 135.94 (s), 136.40 (s), 154.46 (s), 160.60 (s), 161.04 (s), 194.34 (s) ppm.

Cyclohexyl carbamate of 2-hydroxy-2-(3-methoxyphenyl)-1-(3-methoxyphenyl)ethanone (6).

2-Hydroxy-2-(3-methoxyphenyl)-1-(3-methoxyphenyl)ethanone[21] (3.64g, 13.37mmol) was treated with cyclohexyl isocyanate (1.87ml, 1.84g, 14.70mmol) in refluxing toluene (75ml) in a similar manner to that described above. The usual work-up gave a yellow oil (6.32g) which on flash chromatography (20% EtOAc/80% Hexane) gave the following fractions. Firstly, a colorless oil (0.12g) was isolated and recrystallized from ethanol to give a white crystalline solid (0.034g). This material was identified as 1,2-bis-(3-dimethoxyphenyl)ethanedione by spectroscopy and elemental analysis. Next, the crude carbamate was isolated as a white foam (2.02g). Trituration with EtOAc/Hexane gave an isomer of 3-cyclohexyl-4-hydroxy-4,5-di-(3-methoxyphenyl)-4-oxazolidin-2-one (**7**) as a white crystalline solid (0.61g). Concentration of the mother liquor gave the desired carbamate (**6**) as a white gum (1.23g). The mixed fractions from the column were combined and concentrated to give a white foam (2.95g). This material was rechromatographed as above to afford additional 1,2-bis-(3-dimethoxyphenyl)ethanedione (0.05g), along with the crude carbamate as white gum (2.33g). In this case trituration with aqueous ethanol led to crystallization of another isomer of 3-cyclohexyl-4-hydroxy-4,5-di-(3-methoxyphenyl)-4-oxazolidin-2-one (**7**) as a white crystalline solid (0.27g). Concentration of the mother liquor afforded more of the desired carbamate (**6**) as a white gum (1.38g). The carbamate gum resisted all attempts at crystallization. Invariably attempted crystallization would lead to cyclization to form the crystalline 4-

oxazolidin-2-one form. Overall 2.61g of the desired carbamate **(6)** was isolated, this corresponds to a 49% yield.

a) Cyclohexyl carbamate of 2-hydroxy-2-(3-methoxyphenyl)-1-(3-methoxyphenyl)ethanone (6).

Microanalysis: Calculated for $C_{23}H_{27}NO_5$ (397.46) C 69.50, H 6.85, N 3.52; Found C 69.83, H 7.00 , N 3.31%. UV: $\varepsilon_{(218)}$26523, $\varepsilon_{(252)}$7597, $\varepsilon_{(282)}$2763, $\varepsilon_{(309)}$2260. IR ν 3360, 1727, 1673, 1610, 1593, 1591, 1525, 1226, 1204, 1160 cm^{-1}. ^1H NMR δ 1.05-2.05 (10H, m, cyclohexyl $(CH_2)_5$), 3.49 (1H, m, cyclohexyl CH), 3.77 and 3.80 (each 3H, each s, 3,3'-OCH_3), 4.63 and 4.95 (total 1H, each br. d, NH), 6.79 (1H, s, 2-CH), 6.87 (1H dd (J_o=8.0Hz, J_m=1.8Hz), Ar(1) 4-H), 6.99 (1H, br. t, Ar(2) 2-H), 7.02-7.08 (2H, m, Ar(2) 4,6-CH), 7.28 (2H, overlapping t (J_o=8.0Hz), Ar(1) and Ar(2) 5,5'-H), 7.48 (1H, br. t, Ar(1) H-2), 7.56 ppm (1H, dt (J_o=8.0Hz, J_m=1.8Hz), Ar(1) 6-H). ^{13}C NMR δ 24.62 (t), 25.32 (t), 33.10 (t), 50.05 (d), 55.18 (q), 55.29 (q), 77.16 (d), 112.77 (d), 113.67 (d), 120.03 (d), 120.86 (d), 121.34 (d), 129.45 (d), 129.97 (d), 135.32 (s), 135.93 (s), 154.54 (s), 159.60 (s), 159.86 (s), 194.63 (s) ppm.

b) Isomer A of 3-cyclohexyl-4-hydroxy-4,5-di-(3-methoxyphenyl)-4-oxazolidin-2-one (7)

M.p. 151-154_C. Microanalysis: Calculated for $C_{23}H_{27}NO_5$ (397.46); C 69.50, H 6.85, N 3.52; Found C 69.65, H 6.84, N 3.45%. UV: $\varepsilon_{(276)}$3612, $\varepsilon_{(283)}$3331. IR ν 3295, 1739, 1604, 1495, 1461, 1453, 1429, 1369, 1265, 1036 cm^{-1}. ^1H NMR δ 0.95-2.45 (10H, m, cyclohexyl $(CH_2)_5$), 2.94 (1H, m, cyclohexyl CH), 3.61 and 3.63 (each 3H, each s, 3,3'-OCH_3), 4.46 (1H, s, OH), 5.47 (1H, s, Ox 5-CH), 6.45 (1H, 1 ArH) 6.56-6.71 (4H,m, 4 ArH), 6.79 (1H, br. d (J=7.3Hz), 1 ArH), 6.94-7.08 ppm (2H, m, 2 ArH). ^{13}C NMR δ 25.00 (t), 25.82, (t), 26.01 (t), 29.91 (t), 30.95 (t), 53.72 (d), 55.02 (s), 55.07 (q), 87.44 (d), 95.21 (s), 110.75 (d), 112.43 (d), 113.99 (d) 114.47 (d), 117.92 (d), 119.59 (d), 128.54 (d), 128.67 (d), 136.67 (s), 138.49 (s), 156.76(s), 158.92 (s) ppm. One carbon resonance missing

c) Isomer B of 3-cyclohexyl-4-hydroxy-4,5-di-(3-methoxyphenyl)-4-oxazolidin-2-one (7)

M.p. 173-175_C Microanalysis: Calculated for $C_{23}H_{27}NO_5$ (397.46); C 69.50, H 6.85, N 3.52 Found C 69.49, H 6.95, N 3.54%. UV: $\varepsilon_{(275)}$4367, $\varepsilon_{(281)}$4094. IR ν 3316, 2929, 1708, 1608, 1357, 1287, 1271, 1259, 1047, 753 cm^{-1}. ^1H NMR δ 0.95-2.22 (10H, m, cyclohexyl $(CH_2)_5$), 2.42 (1H, s,

OH), 2.90 (1H, m, cyclohexyl CH), 3.77 and 3.85 (each 3H, each s, 3,3'-OCH_3), 5.49(1H, s, CH), 6.66-6.74 (2H, m, 2 ArH), 6.88-7.00 (2H, m, 2 ArH), 7.07-7.15 (2H, m, 2 ArH), 7.24-7.43 ppm (2H, m, 2 ArH). ^{13}C NMR δ 24.92 (t), 25.78 (t), 26.02 (t), 29.91 (t), 30.66 (t), 53.89 (d), 55.21 (q), 55.28 (q), 85.85 (d), 92.11 (s), 111.25 (d), 112.37 (d), 114.40 (d) 114.93 (d), 118.10 (d), 118.91 (d), 129.72 (d), 129.93 (d), 133.56 (s), 141.20 (s), 155.77 (s), 159.75 (s), 159.89 (s) ppm.

Cyclohexyl carbamate of 2-(1,3-benzodioxol-5-yl)-2-hydroxy-1-(1,3-benzodioxol-5-yl)ethanone (8).

2-(1,3-Benzodioxol-5-yl)-2-hydroxy-1-(1,3-benzodioxol-5-yl)ethanone (2.252g, 7.5mmol) was treated with cyclohexyl isocyanate (1.07ml, 1.05g, 8.25mmol) in refluxing toluene (50ml) in a similar manner to that described above. The usual work-up followed by flash chromatography (CH_2Cl_2) gave the crude carbamate as a white gummy solid (1.12g). Recrystallization from CH_2Cl_2/Hexane furnished the desired carbamate (**8**) as a white solid (0.852g, 27%).

M.p. 148-149_C Microanalysis: Calculated for $C_{23}H_{23}NO_7$ (425.47); C 64.92, H 5.45, N 3.29; Found C 64.60, H 5.39, N 3.44%. UV: $\varepsilon_{230)}$21959, $\varepsilon_{(278)}$8839, $\varepsilon_{(296)}$8858, $\varepsilon_{(312)}$9401. IR ν 3426, 2934, 1712, 1678, 1505, 1492, 1447, 1253, 1222, 1039 cm^{-1}. ^1H NMR δ 1.05-2.15 (10H, m, cyclohexyl $(CH_2)_5$), 3.49 (1H, m, cyclohexyl CH), 4.59 and 4.95 (total 1H, each br. d, NH), 5.90 (2H, d (J=2.8Hz), OCH_2O), 5.96 (2H, s, OCH_2O), 6.67 (1H, s, 2-CH), 6.78 (2H, m (J_o=8.2Hz), Ar(1) and Ar(2) 7,7'-H), 6.92 (2H, m, Ar(2) 4,6-H), 7.42 (1H, s, Ar(1) 4-H), 7.57 ppm (1H, d(J_o= 8.1Hz), Ar(1) 6-H). ^{13}C NMR δ 24.62 (t), 25.33 (t), 33.10 (t), 50.03 (d), 76.77 (s), 101.25 (t), 101.74 (t), 107.89 (d), 108.46 (d), 108.56 (d), 108.63 (d), 122.69 (d), 125.11 (d), 127.85 (s), 129.24 (s), 148.01 (s), 148.22 (s), 151.88 (s), 154.57 (s), 192.75 (s) ppm. One carbon resonance missing.

Piperidinyl carbamate of 2-(1,3-benzodioxol-5-yl)-2-hydroxy-1-(1,3-benzodioxol-5-yl)ethanone (9).

To a solution of 2-(1,3-benzodioxol-5-yl)-2-hydroxy-1-(1,3-benzodioxol-5-yl)ethanone (3.00g, 10.0mmol) and p-nitrophenylchloroformate (2.02g, 10.0mmol) in dichloromethane (25ml) at 0-5_C under nitrogen was added a solution of triethylamine (2.13g, 10.0mmol) in dichloromethane (10ml). The resulting solution was stirred at room temperature for 6h at which point TLC indicated complete consumption of the starting benzoin. A solution of piperidine (0.895g, 10.5mmol) in dichloromethane (25ml) was added and the mixture stirred at room temperature for 48h. At this point TLC indicated a

trace of mixed carbonate remained, to complete the reaction the mixture was heated at reflux for 4h. After cooling, the reaction mixture was washed with water (1 x 20ml), 0.5N NaOH (2 x 20ml), water (1 x 20ml), 2.5% HCl (1 x 20ml), and brine (1 x 20ml). After drying ($MgSO_4$), removal of the solvent under reduced pressure gave an orange-brown foam (3.85g). Flash chromatography (20% EtOAc 80% Hexane) gave the following fractions. Firstly, a white solid (0.17g) was isolated and recrystallized from ethyl acetate/hexane to give light yellow crystals (0.088g). This material was identified as 1,2-bis-(1,3-benzodioxol-5-yl)ethanedione by spectroscopy and elemental analysis. Next, an off white solid (2.41g) was isolated and recrystallized from EtOAc/Hexane to give the desired carbamate (**9**) as pale yellow platelets (1.70g, 43%)

M.p. 147-149_C. Microanalysis: Calculated for $C_{22}H_{21}NO_7$ (411.40); C 64.22, H 5.15, N 3.40; Found C 64.30, H 5.20, N 3.40%. UV: $\varepsilon_{(230)}$21536, $\varepsilon_{(278)}$8964, $\varepsilon_{(296)}$8848, $\varepsilon_{(312)}$9702. IR ν 1692(sh), 1678, 1678, 1504, 1490, 1468, 1444, 1251, 1237, 1037, 931 cm^{-1}. ^1H NMR δ 1.59 (6H, br. s, piperidinyl 3,4,5-CH_2), 3.44 (4H, m, piperidinyl 2,6-CH_2), 5.95 (2H, m, OCH_2O), 6.00 (2H, s, OCH_2O), 6.60 (1H, s, 2-CH), 6.78 (2H, overlapping d (J_o=8.2Hz), Ar(1) and Ar(2) 7,7'-H), 6.90-7.00 (2H, m, Ar(2) 4,6-H), 7.43 (1H, d (J_m=1.8Hz), Ar(1) 4-H), 7.59 ppm (1H, dd (J_o=8.2Hz, J_m=1.8Hz), Ar(1) 6-H). ^{13}C NMR δ 24.21 (t), 25.62 (t), 45.04 (t), 77.03 (s), 101.23 (t), 101.72 (t), 107.89 (d), 108.42 (d), 108.54 (d), 122.55 (d), 125.06 (d), 128.04 (s), 129.34 (s), 147.98 (s), 148.13 (s), 151.83 (s), 154.47 (s), 192.82 (s) ppm. Two carbon resonances missing.

Cyclohexyl carbamate of 2-hydroxy-2-(4-methoxyphenyl)-1-(4-methoxyphenyl)ethanone (10).

2-Hydroxy-2-(4-methoxyphenyl)-1-(4-methoxyphenyl)ethanone (4.05g, 15.0mmol) was treated with cyclohexyl isocyanate (2.11ml, 2.07g, 16.5mmol) in refluxing toluene (75ml) in a similar manner to that described above. The usual work-up followed trituration with CH_2Cl_2 gave the crude product as a white solid (3.45g). Recrystallization from CH_2Cl_2/Hexane furnished the desired carbamate (**10**) as large white crystals (2.75g, 46%).

M.p. 119-121_C. Microanalysis: Calculated for $C_{23}H_{27}NO_5$ (397.46) C 69.50, H 6.85, N 3.52; Found C 69.75, H 6.87, N 3.67%. UV: $\varepsilon_{(219)}$17355, $\varepsilon_{(274)}$16666, $\varepsilon_{(325)}$770. IR ν 3330, 1710, 1686, 1600, 1513, 1308, 1265, 1250, 1233, 1169 cm^{-1}. ^1H NMR δ 1.05-2.15 (10H, m, cyclohexyl $(CH_2)_5$), 3.50 (1H, m, cyclohexyl CH), 3.75 and 3.80 (each 3H, each s, 4,4'-OCH_3), 4.65 and 4.99 (total 1H, each

br. d, NH), 6.80 (1H, s, 2-CH), 6.85 (4H d (J_o=8.8Hz), 3,3',5,5'-H), 7.38 (2H, d (J_o=8.8Hz), Ar(2) 2,6-H), 7.94 ppm (2H, d (J_o=8.8Hz), Ar(1) 2,6-H). ^{13}C NMR δ 24.64 (t), 25.34 (t), 33.11 (t), 49.98 (d), 55.12 (q), 55.29 (q), 76.45 (d), 113.66 (d), 114.32 (d), 126.47 (s), 127.58 (s), 129.98 (d), 131.01 (d), 154.73 (s), 160.01 (s), 163.46 (s), 193.29 (s) ppm.

2) Derived from Unsymmetrical Benzoins

Cyclohexyl carbamate of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-(phenyl)ethanone (12).

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-(phenyl)ethanone (**11**) (1.487g, 5.46mmol) was treated with cyclohexyl isocyanate (0.77ml, 0.75g, 6.01mmol) in refluxing toluene (50ml) in a similar manner to that described above. The usual work-up followed by flash chromatography (CH_2Cl_2) gave the following fractions. Firstly, a colorless oil (0.04g) was isolated and recrystallized from ethyl acetate/hexane to give light yellow crystals (0.020g). This material was identified as 1-(3,5-dimethoxyphenyl)-2-(phenyl)ethanedione by spectroscopy and elemental analysis. Next, the crude carbamate was isolated as a white solid (1.54g). Subsequent recrystallization (CH_2Cl_2/Hexane) furnished the desired carbamate (**12**) as a white crystalline solid (1.279g, 59%).

M.p. 149-151_C. Microanalysis: Calculated for $C_{23}H_{27}NO_5$ (397.46) C 69.50, H 6.85, N 3.52: Found C 69.33, H 6.81 N 3.59%. UV: $\varepsilon_{(243)}$16633, $\varepsilon_{(280)}$2994. IR ν 3428, 3371, 2935, 1712, 1698, 1680, 1610, 1597, 1205, 1158 cm^{-1}. ^1H NMR δ 1.05-2.15 (10H, m, cyclohexyl $(CH_2)_5$), 3.46 (1H, m, cyclohexyl CH), 3.75 (3H, s, 3',5'-OCH_3), 4.62 and 4.95 (total 1H, each br. d, NH), 6.41 (1H, t (J_m=2.2Hz), Ar(2) 4-H), 6.61 (2H d (J_m=2.2Hz), Ar(2) 2,6-H), 6.75 (1H, s, 2-CH), 7.40 (2H, m approximates to t, Ar(1) 3,5-H), 7.52 (1H, m approximates to t, Ar(1) 4-H), 7.96 ppm (2H, m approximates to d, Ar(1) 2,6-H). ^{13}C NMR δ 24.62 (t), 25.33 (t), 33.11 (t), 50.06 (d), 55.30 (q), 77.16 (d), 101.07 (d), 106.43 (d), 128.46 (d), 128.69 (d), 133.26 (d), 134.72 (s), 135.91 (s), 154.51 (s), 161.03 (s), 194.77 (s) ppm.

Piperidinyl carbamate of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-(phenyl)ethanone (13).

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-(phenyl)ethanone (**11**) (1.363g, 5.01mmol) was converted to the corresponding piperidinyl carbamate (**13**) via the p-nitrophenyl mixed carbonate method previously

described for piperidinyl carbamate (**9**). The usual work-up followed by trituration with ether and recrystallization (Et_2O) furnished the desired carbamate (**13**) as a white solid (0.719g, 38%).

M.p. 124-125.5_C. Microanalysis: Calculated for $C_{22}H_{24}NO_5$ (382.42); C 68.91, H 6.57, N 3.65; Found C 68.63, H 6.45, N 3.53%. UV: $\varepsilon_{(243)}$14511, $\varepsilon_{(280)}$2854. IR ν 1697, 1680, 1612, 1595, 1433, 1266, 1234, 1164, 1156, 1063 cm^{-1}. ^1H NMR δ 1.59 (6H, br. s, piperidinyl 3,4,5-$(CH_2)_3$), 3.50 (4H, br. d, piperidinyl 2,6-CH_2), 3.75 (6H, s, Ar(2) 3,5-OCH_3), 6.41 (1H, t (J_m=2.2Hz), Ar(2) 4-H), 6.62 (2H, d (J_m=2.2Hz), Ar(2) 2,6-H), 6.73 (1H, s, 2-CH), 7.40 (2H, m approximates to t, Ar(1) 3,5-H), 7.51 (1H, m approximates to t, Ar(1) 4-H), 7.97 ppm (2H, m approximates to d, Ar(1) 2,6-H). ^{13}C NMR δ 24.21 (t), 25.63 (t), 45.04 (t), 55.28 (q), 77.70 (d), 100.59 (d), 106.42 (d), 128.43 (d), 128.70 (d), 133.15 (d), 134.83 (s), 136.19 (s), 154.40 (s), 160.93 (s), 194.81 (s) ppm.

*Cyclohexyl carbamate of 2-(1,3-benzodioxol-5-yl)-2-hydroxy-1-(phenyl)ethanone (**15**).*

2-(1,3-Benzodioxol-5-yl)-2-hydroxy-1-(phenyl)ethanone (**16**) (1.44g, 5.62mmol) was treated with cyclohexyl isocyanate (0.75ml, 0.74g, 5.90mmol) in refluxing toluene (60ml) in a similar manner to that described above. The usual work-up followed by flash chromatography (10% EtOAc/90%Hexane) allowed isolation of the crude carbamate as a white gummy solid (0.59g). Recrystallization from EtOAc/Hexane furnished the desired carbamate (**15**) as a white powder (0.412g, 19%).

M.p. 124-126_C. Microanalysis: Calculated for $C_{22}H_{23}NO_5$ (381.41); C 69.27, H 6.08, N 3.67; Found C 69.06, H 6.10, N 3.72%. UV: $\varepsilon_{(241)}$15148, $\varepsilon_{(288)}$4964. IR ν 3363, 1705, 1682, 1502, 1490, 1447, 1250, 1235, 1061, 1041 cm^{-1}. ^1H NMR δ 1.05-2.25 (10H, m, cyclohexyl $(CH_2)_5$), 3.50 (1H, m, cyclohexyl CH), 4.52 and 4.92 (total 1H, each br. d, NH), 5.94 (2H, m, OCH_2O), 6.73-6.79 and 6.91-6.97 (each 2H, each m, Ar(2) 4,6,7-H and 2-CH), 7.37 (2H, m approximates to t, Ar(1) 3,5-H), 7.48 (1H, m approximates to t, Ar(1) 4-H), 7.94 ppm (2H, m approximates to d, Ar(1) 2,6-H). ^{13}C NMR δ 24.63 (t), 25.33 (t), 33.11 (t), 50.05 (d), 76.77 (s), 101.27 (t), 108.59 (d), 108.72 (d), 122.84 (d), 127.49 (d), 128.48 (d), 128.67 (d), 133.25 (s), 134.66 (s), 148.04 (s), 148.27 (s), 154.57 (s), 194.77 (s) ppm.

The mixed fractions from the column (1.21g) consisted of the desired carbamate (**15**) (cyclohexyl CH, m, δ 3.50), the corresponding 4-oxazolin-2-one (**17**) (cyclohexyl CH, m, δ 3.29) and 4-hydroxy-oxazolidin-2-one (**18**) (cyclohexyl CH, m, δ 2.87).

Cyclohexyl carbamate of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-(4-methoxyphenyl)ethanone (21).

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-(4-methoxyphenyl)ethanone (**20**) (2.27g, 7.5mmol) was treated with cyclohexyl isocyanate (1.05ml, 1.03g, 8.25mmol) in refluxing toluene (60ml) in a similar manner to that described above. The usual work-up followed by trituration with cold toluene gave the crude carbamate as a white solid (2.14g). Recrystallization from CH_2Cl_2/Hexane furnished the desired carbamate (**21**) as a white solid (2.10g, 66%).

M.p. 105-107_C Microanalysis: Calculated for $C_{24}H_{29}NO_6$ (427.58); C 67.41, H 6.84, N 3.28; Found C 67.52, H, 6.94, N 3.31%. UV: $\varepsilon_{(280)}$18776. IR ν 3347, 2934, 1713, 1684, 1599, 1513, 1251, 1229, 1172, 1158 cm^{-1}. ^1H NMR δ 1.20-2.05 (10H, m, cyclohexyl $(CH_2)_5$), 3.46 (1H, m, cyclohexyl CH), 3.75 (6H, s, Ar(2) 3,5-OCH_3), 3.83 (3H, s, Ar(1), 4-OCH_3) 4.55 and 4.93 (total 1H, each br. d, NH), 6.40 (1H, t (J_m=2.2Hz), Ar(2) 4-H), 6.61 (2H, d (J_m=2.2Hz), Ar(2) 2,6-H), 6.73 (1H, s, 2-CH), 6.87 and 7.96 ppm (each 2H, ABq (J_o=7.0Hz), Ar(1) 3,5-H and 2,6-H respectively). ^{13}C NMR δ 24.62 (t), 25.32 (t), 33.10 (t), 50.02 (d), 55.29 (q), 55.32 (q), 76.83 (d), 100.94 (d), 106.37 (d), 113.69 (d), 127.52 (s), 131.04 (d), 136.43 (s), 154.54 (s), 160.97 (s), 163.57 (s); 193.02 (s) ppm.

Cyclohexyl carbamate of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-(4-methylthiophenyl)ethanone (22).

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-(4-methylthiophenyl)ethanone (**23**) (2.39g, 7.5mmol) was treated with cyclohexyl isocyanate (1.05ml, 1.03g, 8.25mmol) in refluxing toluene (50ml) in a similar manner to that described above. The usual work-up followed by trituration with cold toluene gave the crude carbamate as a white solid (3.15g). Recrystallization from CH_2Cl_2/Hexane furnished the desired carbamate (**22**) as a white solid (3.06g, 92%).

M.p. 152-154_C. Microanalysis: Calculated for $C_{24}H_{29}NO_5S$ (443.54) C 64.99, H 6.59, N 3.16, S 7.23; Found C 64.46, H 6.62, N 3.11, S 7.46%.UV: $\varepsilon_{(312)}$20991. IR ν 3365, 1727, 1673, 1610, 1593, 1591, 1525, 1226, 1204, 1160 cm^{-1}. ^1H NMR δ 1.05-2.05 (10H, m, cyclohexyl $(CH_2)_5$), 2.48 (3H, s, SCH_3), 3.46 (1H, m, cyclohexyl CH), 4.54 and 4.93 (total 1H, each br. d, NH), 6.40 (1H, t (J_m=2.2Hz), Ar(2) 4-H), 6.59 (2H, d (J_m=2.2Hz), Ar(2) 2,6-H), 6.71 (1H, s, 2-CH), 7.19 and 7.87 ppm (each 2H, ABq (J_o=8.6Hz), Ar(1) 3,5-H and 2,6-H respectively). ^{13}C NMR δ 14.52 (q), 24.62 (t), 25.33 (t),

33.10 (t), 50.04 (d), 55.29 (q), 76.45 (d), 100.98 (d), 106.40 (d), 124.76 (d), 129.07 (d), 130.76 (s), 136.15 (s), 146.37 (s), 154.50 (s), 161.02 (s), 193.56 (s) ppm.

Cyclohexyl carbamate of 2-hydroxy-1-(4-methoxyphenyl)propanone (24).

2-Hydroxy-1-(4-methoxyphenyl)propanone[28] (2.70g, 15.0mmol) was treated with cyclohexyl isocyanate (2.10ml, 2.07g, 16.5mmol) in refluxing toluene (50ml) in a similar manner to that described above. The usual work-up followed by flash chromatography (20% EtOAc/80% Hexane) allowed isolation of two major components. The minor less polar fraction was recrystallized from aqueous ethanol to afford 3-cyclohexyl-4-(4-methoxyphenyl)-5-methyl-4-oxazolin-2-one (**25**) as a white crystalline solid (0.144g). The major more polar fraction was recrystallized from EtOAc/Hexane to give the desired carbamate (**24**) as a white solid (3.32g, 73%).

For cyclohexyl carbamate of 2-hydroxy-1-(4-methoxyphenyl)propanone (24):

M.p. 117-118_C. Microanalysis: Calculated for $C_{17}H_{23}NO_4$ (305.36) C 66.86, H 7.59, N 4.59: Found C 66.28, H 7.62 N 4.57%. UV: $\varepsilon_{(217)}$11591, $\varepsilon_{(272)}$16797. IR ν 3325, 2937, 1711, 1686, 1603, 1537, 1263, 1237, 1144, 1089 cm^{-1}. ^1H NMR δ 1.05-2.15 (10H, m, cyclohexyl $(CH_2)_5$), 1.46 (3H, d (J=6.9Hz)), 3-CH_3), 3.47 (1H, m, cyclohexyl CH), 3.86 (3H, s, 4-OCH_3), 4.62 and 4.89 (total 1H, each br. d, NH), 5.92 (1H, q (J=6.9Hz), 2-CH), 6.93 and 7.95 ppm (each 2H, ABq (J_o=8.8Hz), Ar(1) 3,5-H and 2,6-H respectively). ^{13}C NMR δ 17.42 (q), 24.63 (t), 25.32 (t), 33.10 (t), 49.90 (d), 55.36 (q), 70.64 (d), 113.78 (d), 127.35 (s), 130.74 (d), 154.68 (s), 163.64 (s), 196.35 (s) ppm.

For 3-cyclohexyl-4-(4-methoxyphenyl)-5-methyl-4-oxazolin-2-one (25):

M.p. 114-115_C. Microanalysis: Calculated for $C_{17}H_{21}NO_3$ (287.35); C 71.05, H 7.37, N 4.88: Found C 70.95, H 7.35, N 4.97%. UV: $\varepsilon_{(280)}$21203. IR ν 2933, 1747, 1513, 1364, 1348, 1295, 1252, 1237, 1180, 758 cm^{-1}. ^1H NMR δ 1.10-2.27 (10H, m, cyclohexyl $(CH_2)_5$), 2.25 (3H, s, CH_3), 3.52-3.74 (1H, m, cyclohexyl CH), 3.83 (3H, s, 4-OCH_3), 6.92 and 7.39 ppm (each 2H, ABq (J_o=8.5Hz), 2,6-H and 3,5-H respectively). ^{13}C NMR δ 9.76 (q), 24.90 (t), 25.86 (t), 30.08 (t), 54.14 (d), 55.19 (q), 114.01 (d), 117.23 (s), 121.03 (s), 126.83 (d), 133.99 (s), 154.21 (s), 158.87 (s) ppm.

Cyclohexyl carbamate of 2-hydroxy-2-(phenyl)-1-(4-methoxyphenyl)ethanone (26).

2-Hydroxy-2-(phenyl)-1-(4-methoxyphenyl)ethanone[29] (1.75g, 7.22mmol) was treated with cyclohexyl isocyanate (1.01ml, 0.99g, 7.95mmol) in refluxing toluene (25ml) in a similar manner to that

described above. The usual work-up followed by flash chromatography (20% EtOAc/80%Hexane) and recrystallization (CH_2Cl_2/Hexane) furnished the desired carbamate (**26**) as a fine white powder (1.37g, 52%).

M.p. 87-90_C. Microanalysis: Calculated for $C_{22}H_{25}NO_5$ (367.43) C 71.91, H 6.86, N 3.81; Found C 71.71, H 6.90, N 3.88%. UV: $\varepsilon_{(280)}$16757. IR ν 3348, 1712, 1687, 1601, 1512, 1261, 1252, 1232, 1172, 1062 cm^{-1}. ^1H NMR δ 1.05-2.15 (10H, m, cyclohexyl $(CH_2)_5$), 3.50 (1H, m, cyclohexyl CH), 3.81 (3H, s, 4-OCH_3), 4.62 and 4.97 (total 1H, each br. d, NH), 6.85 (1H, s, 2-CH), 6.87 (2H d (J_o=8.8Hz), Ar(1) 3,5-H), 7.33 (3H, m, Ar(2) 3,4,5-H), 7.47 (2H, m, Ar(2) 2,6-H), 7.95 ppm (2H, d (J_o=8.8Hz), Ar(1) 2,6-H). ^{13}C NMR δ 24.63 (t), 25.34 (t), 33.13 (t), 50.03 (d), 55.31 (q), 76.83 (d), 113.71 (d), 127.59 (s), 128.47 (d), 128.87 (d), 131.07 (d), 134.51 (s), 154.62 (s), 163.55 (s), 193.23 (s) ppm.

Cyclohexyl carbamate of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-(2-naphthalenyl)ethanone (27).

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-(2-naphthalenyl)ethanone (**28**) (0.3385g, 1.205mmol) was treated with cyclohexyl isocyanate (0.17ml, 0.17g, 1326mmol) in refluxing toluene (25ml) in a similar manner to that described above. The usual work-up followed by flash chromatography (CH_2Cl_2) gave the following fractions. Firstly, a white solid (0.05g) was isolated and recrystallized from ethyl acetate/hexane to give white crystals (0.038g). This material was identified as 1-(3,5-dimethoxyphenyl)-2-(2-naphthalenyl)ethanedione by ^1H, ^{13}C NMR and IR spectroscopy. Next, the crude carbamate was isolated as a white gummy solid (0.40g) Subsequent recrystallization (EtOAc/Hexane) furnished the desired carbamate (**27**) as a fine white powder (0.379g, 70%).

M.p. 160-161_C. Microanalysis: Calculated for $C_{27}H_{28}O_5$ (446.50); C 72.63, H 6.32, N 3.14; Found C 72.59, H 6.63, N 3.15%. UV: $\varepsilon_{(204)}$59671, $\varepsilon_{(245)}$41242, $\varepsilon_{(251)}$47901, $\varepsilon_{(284)}$10503, $\varepsilon_{(292)}$9464, $\varepsilon_{(334)}$2022. IR ν 3426, 3380, 1725, 1711, 1692, 1675, 1610, 1598, 1253, 1158 cm^{-1}. ^1H NMR δ 1.05-2.15 (10H, m, cyclohexyl $(CH_2)_5$), 3.52 (1H, m, cyclohexyl CH), 3.74 (6H, s, 3,5-OCH_3), 4.55 and 4.97 (total 1H, each br. d, NH), 6.40 (1H, t (J_m=2.2Hz), Ar(2) 4-H), 6.66 (2H, d (J_m=2.2Hz), Ar(2) 2,6-H), 6.93 (1H,s, 2-CH), 7.46-7.65 (2H, m, Ar(1) 6,7-H), 7.80-8.05 (4H, m, Ar(1) 3,4,5,8-H), 8.49 ppm (1H, br. s, Ar(1) 1-H). ^{13}C NMR δ 24.62 (t), 25.33 (t), 33.12 (t), 50.08 (d), 55.29 (q), 77.16 (d),

101.02 (d), 106.46 (d), 124.19 (d), 126.65 (d), 127.60 (d), 128.37 (d), 128.53 (d), 129.59 (d), 130.57 (d), 132.08 (s), 132.24 (s), 135.54 (s), 136.06 (s), 154.59 (s), 161.04 (s), 194.77 (s) ppm.

Preparation of 2,2-Disubstituted Carbamates

Cyclohexyl carbamate of 2-(3,5-Dimethoxyphenyl)-2-hydroxy-(1,2-diphenyl)ethanone (29).

To a solution of 2-(3,5-dimethoxyphenyl)-2-hydroxy-(1,2-diphenyl)ethanone (**30**) (1.74g, 4.99mmol) in benzene (50 ml) at room temperature under nitrogen was added stannous 2-ethylhexanoate (0.1g) followed by cyclohexyl isocyanate (0.70ml, 0.69g, 5.49mmol). After stirring for 24h, the reaction mixture was pre-absorbed onto silica gel (20g) and purified by flash chromatography using 15% EtOAc/85% hexane as eluant. In this way the requisite carbamate was isolated as an off-white solid (2.42g). Recrystallization from EtOAc/hexane furnished the desired carbamate (**29**) as a fluffy white solid (2.23g, 94%).

M.p. 173-174.5_C. Microanalysis: Calculated for $C_{29}H_{31}NO_5$ (473.55); C 73.55, H 6.60, N 2.96; Found C 73.64, H 6.55, N 2.86%. UV: $\varepsilon_{(244)}$15324, $\varepsilon_{(278)}$2934. IR ν 3350, 2933, 1726, 1711, 1608, 1588, 1510, 1316, 1200, 1161 cm^{-1}. ^1H NMR δ 0.74-2.10 (10H, m, cyclohexyl $(CH_2)_5$), 3.19 (1H, m, cyclohexyl CH), 3.75 (6H, s, Ar(2) 3,5-OCH_3), 4.38 and 4.82 (total 1H, each br. d, NH), 6.38 (1H, t (J_m=2.2Hz), Ar(2) 4-H), 6.78 (2H, d (J_m=2.2Hz), Ar(2) 2,6-H), 7.26-7.46 (6H, m, Ar(1) and Ar'(2) 3,4,5-H), 7.58 (2H, m approximates to d, Ar(2) 2,6-H), 7.81 ppm (2H, m approximates to d, Ar(1) 2,6-H). ^{13}C NMR δ 24.48 (t), 25.23 (t), 32.66 (t), 49.62 (d), 55.25 (q), 87.70 (s), 99.25 (d), 105.31 (d), 127.53 (d), 127.56 (d), 127.69 (d), 127.77 (d), 128.98 (d), 131.32 (d), 136.86 (s), 140.17 (s), 142.39 (s), 153.03 (s), 160.43 (s), 195.30 (s) ppm.

Cyclohexyl carbamate of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-(phenyl)propanone (33).

A solution of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-(phenyl)propanone (**31**) (2.87g, 10.24mmol) in benzene (50ml) was treated with stannous 2-ethylhexanoate (0.1g) followed by cyclohexyl isocyanate (1.54ml, 1.51g, 12.03mmol) in a similar manner to that described above. Flash chromatography (15% EtOAc/85% Hexane) followed by recrystallization (PhH/hexane) furnished the desired carbamate (**33**) as white platelets (2.79g, 66%).

M.p. 114-116_C. Microanalysis: Calculated for $C_{24}H_{29}NO_5$ (411.48); C 70.05, H 7.10, N 3.40; Found C 70.13, H 7.05, N 3.39%. UV: $\varepsilon_{(228)}$12783, $\varepsilon_{(242)}$12532, $\varepsilon_{(278)}$3082. IR ν 3376, 3267, 2936,

1712, 1694, 1601, 1451, 1208, 1158, 1048 cm^{-1}. ^1H NMR δ 0.65-2.10 (10H, m, cyclohexyl-$(CH_2)_5$), 1.96 (3H, s, 3-CH_3), 3.22 (1H, m, cyclohexyl CH), 3.77 (6H, s, Ar(2) 3,5-OCH_3), 4.48 and 4.75 (total 1H, each br. d, NH), 6.38 (1H, t (J_m=2.2Hz), Ar(2) 4-H), 6.66 (2H, d (J_m=2.2Hz), Ar(2) 2,6-H), 7.27 (2H, m approximates to t, Ar(1) 3,5-H), 7.36 (1H, m approximates to t, Ar(1) 4-H), 7.76 ppm (2H, m approximates to d, Ar(1) 2,6-H). ^{13}C NMR δ 24.59 (t), 25.25 (t,) 27.14 (q), 32.80 (t), 49.56 (d), 55.30 (q), 86.16 (s), 99.03 (d), 102.62 (d), 127.73 (d), 128.96 (d), 131.61 (d), 135.46 (s), 143.06 (s), 153.10 (s), 160.99 (s), 196.97 (s) ppm.

Cyclohexyl carbamate of 2,2-di-(3,5-dimethoxyphenyl)-2-hydroxy-1-(phenyl)ethanone (34).

A solution of 2,2-di-(3,5-dimethoxyphenyl)-2-hydroxy-1-(phenyl)ethanone (**35**) (2.04g, 5.0mmol) in benzene (50ml) was treated with stannous 2-ethylhexanoate (0.1g) followed by cyclohexyl isocyanate (0.70 ml, 0.69g, 5.5mmol) in a similar manner to that described above. Flash chromatography (20% EtOAc/80% Hexane) followed by recrystallization (EtOAc/hexane) furnished the desired carbamate (**34**) as a white solid (2.67g, 100%).

M.p. 170-172_C. Microanalysis: Calculated for $C_{31}H_{35}NO_7$ (533.60); C 69.77, H 6.61, N 2.63; Found C 69.64, H 6.92, N 2.84%. UV: $\varepsilon_{(234)}$23321, $\varepsilon_{(278)}$5205. IR ν 3353, 1726, 1688, 1604, 1597, 1523, 1457, 1209, 1157, 1057 cm^{-1}. ^1H NMR δ 0.80-2.10 (10H, m, cyclohexyl $(CH_2)_5$), 3.16 (1H, m, cyclohexyl CH), 3.75 (12H, s, Ar(2), 3,3',5,5'-OCH_3), 4.39 and 4.83 (total 1H, each br. d, NH), 6.37 (2H, t (J_m=2.2Hz), Ar(2) 4,4-H), 6.78 (4H, d (J_m=2.2Hz), Ar(2) 2,2',6,6'-H), 7.27 (2H, m approximates to dt, Ar(1) 3,5-H), 7.38 (1H, m approximates to t, Ar(1) 4-H). 7.79 ppm (2H, m approximates to d, Ar(1) 2,6-H). ^{13}C NMR δ 24.44 (t), 25.22 (t), 32.65 (t), 49.61 (d), 55.22 (q), 87.16 (s), 99.26 (d),105.57 (d), 127.68 (d), 128.95 (d), 131.30 (d), 136.90 (s,), 142.36 (s), 152.96 (s), 160.24 (s), 195.19 (s) ppm.

Cyclohexyl carbamate of 2,2-(diphenyl)-2-hydroxy-1-(3,5-dimethoxyphenyl)ethanone (38).

A solution of 2,2-(diphenyl)-2-hydroxy-1-(3,5-dimethoxyphenyl)ethanone (**39**) (1.337g, 3.84mmol) in benzene (50ml) was treated with stannous 2-ethylhexanoate (0.1g) followed by cyclohexyl isocyanate (0.59ml, 0.577g, 4.61mmol) in a similar manner to that described above. Flash

chromatography (15% EtOAc/85% Hexane) followed by recrystallization (EtOAc/hexane) furnished the desired carbamate (**38**) as a white solid (1.48g, 81%).

M.p. 171-173_C. Microanalysis: Calculated for $C_{29}H_{31}NO_5$ (473.55): C 73.55, H 6.60, N 2.96; Found C 73.61, H 6.55, N 2.96%. UV: $\varepsilon_{(264)}$7373, $\varepsilon_{(318)}$2061. IR ν 3427, 2935, 1715, 1689, 1596, 1451, 1295, 1206, 1157, 1045 cm^{-1}. ^1H NMR δ 0.86-2.10 (10H, m, cyclohexyl-$(CH_2)_5$), 3.25 (1H, m, cyclohexyl CH), 3.72 (6H, s, Ar(1) 3,5-OCH_3), 4.40 and 4.89 (total 1H, each br. d, NH), 6.50 (1H, t (J_m=2.2Hz), Ar(1) 4-H), 7.02 (2H, d (J_m=2.2Hz), Ar(1) 2,6-H), 7.29 (6H, m, Ar(2) 3,3',4,4',5,5'-H), 7.54 ppm (4H, m approximates to d, Ar(2) 2,2',6,6'-H). ^{13}C NMR δ 24.46 (t), 25.26 (t), 32.73 (t), 49.69 (d), 55.28 (q), 88.24 (s), 104.07 (d), 106.96 (d), 127.31 (d), 127.64 (d), 127.94 (d), 138.23 (s), 140.30 (s), 153.24 (s), 159.92 (s), 194.58 (s) ppm.

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References

1. S.A. MacDonald, C.G. Willson and J.M.J. Fréchet, *Acc. Chem. Res.*, **1994**, *27*, 151.

2. R.W. Binkley and T.W. Flechtner in *Synthetic Organic Photochemistry*, W.M. Horspool, Ed, Plenum, New York.1984. Chapter 7, p 375; V.N.R. Pillai in *Organic Photochemistry* , A. Padwa, Ed. Marcel Dekkar, New York, 1987, Volume 9, Chapter 3, p 225; V.N.R. Pillai, *Synthesis*. **1980**,

3. J.H. Kaplan, B.Forbush III and J.F. Hoffman, *Biochemistry*, **1978**, *17*, 1929. G.C.R. Ellis-Davies and J.H. Kaplan, *J. Org. Chem.*, **1988**, *53*, 1966; S.R. Adams, J.P.Y. Kao, G. Grynkiewicz and R.Y. Tsien, *J. Am. Chem. Soc.*, **1988**, *110*, 3212.

4. M. Wilcox, R.W. Viola, K.W. Johnson, A.P. Billington, B.K. Carpenter, J.A. McCray, A.P. Guzikowski and G.P. Hess, *J. Org. Chem.*, **1990**, *55*, 1585.

5. J.F. Cameron and J.M.J. Fréchet, *J. Org. Chem.*, **1990**, *55*, 5919; J.F. Cameron and J.M.J. Fréchet, *J. Photochem. Photobiol. A*, **1991**, *59*, 105.

6. J.F. Cameron and J.M.J. Fréchet, *J. Am. Chem. Soc.*, **1991**, *113*, 4303; J.F. Cameron and J.M.J. Fréchet, *Polym. Mat. Sci. Eng.*, **1991**, *64*, 55.

7. J.E. Beecher, J.F. Cameron and J.M.J. Fréchet, *Polym. Mat. Sci. Eng.*, **1991**, *64*, 71; J.E. Beecher, J.F. Cameron and J.M.J. Fréchet, *J. Mater. Chem.*, **1992**, *2*, 811.

8. J.F. Cameron, C.G. Willson and J.M.J. Fréchet, *J. Chem. Soc., Chem. Commun.*, **1995**, in press; J.F. Cameron, C.G. Willson and J.M.J. Fréchet, Presented at the 209th National Meeting of the American Chemical Society, Anaheim, CA, April 1995, Paper ORGN 237.

9. J.C. Sheehan and R.M. Wilson, *J. Am. Chem. Soc.*, **1964**, *86*, 5277.

10. J.C. Sheehan, R.M. Wilson and A.W. Oxford, *J. Am. Chem. Soc.*, **1971**, *93*, 7222.

11. G.L. Eian and J.F. Trend U.S. Patent 4 369 244, 1983; G.L.Eian and J.E. Trend, U.S. Patent 4 980 096, 1990; R. A. Lee, U.S. Patent 4 469 774, 1984.

12. R. S. Givens and B. Matuszewski, *J. Am. Chem. Soc.*, **1984**, *106*, 6860; R. S. Givens, P.S. Athey, L. William Kueper III, B. Matuszewski and J.Y. Xue, *J. Am. Chem. Soc.*, **1992**, *114*, 8708; R. S. Givens, P.S. Athey, B. Matuszewski, L. William Kueper III, J.Y. Xue and T. Fister, *J. Am. Chem. Soc.*, **1992**, *114*, 8708.

13. R. S. Givens and L. William Kueper III, *Chem. Rev.*, **1993**, *93*, 55.

14. M.C. Pirrung and S.W. Shuey, *J. Org. Chem.*, **1994**, *59*, 3890.

15. J.E. Baldwin, A.W. McConnaughie, M.G. Maloney, A.J. Pratt and S. Bo Shim, *Tetrahedron*, **1990**, *46*, 6879.

16. J.E.T. Corrie and D.R. Trentham, *J. Chem. Soc., Perkin Trans. 1*, 1992, 2409.

17. R. Gompper, *Chem. Ber.*, **1956**, *89*, 1748; M.F. Saettone, *J. Org. Chem.*, **1966**, 31, 1959; J.C. Sheehan and FS. Guziec Jr., *J. Am. Chem. Soc.*, **1972**, *94*, 6562.

18. T. Francis and M.P. Thorne, *Can. J. Chem.*, **1976**, *54*, 24.

19. J.L. Hartwell and S.R.L. Kornberg, *J. Am. Chem. Soc.*, **1945**, *67*, 1606.

20. G.H. Hakimelahi, C.B. Boyce and H.S. Kasmei, *Helv. Chim. Acta*, **1977**, *60*, 342.

21. A. Schonberg and W. Malchow, *Chem. Ber.*, **1922**, *55*, 3746.

22. L.R. Krepski, S.M. Heilmann and J.K. Rasmussen, *Tetrahedron Lett.*, **1983**, *24*, 1983.

23. S. Hunig and G. Wehner, *Chem. Ber.*, **1979**, *112*, 2062; S. Hunig and G. Wehner, *Synthesis*, **1975**, 391.

24. D.A. Evans, L.K. Truesdale and G.L. Carrol, *J. Chem. Soc., Chem. Commun.*, **1973**, 55.

25. J.C. Sheehan and K. Umezawa, *J. Org. Chem.*, **1973**, *38*, 3771.

26. G. Church, J.M. Ferland and J. Gauthier, *Tetrahedron Lett.*, **1989**, *30*, 1901.

27. G. Berner, G. Rist, R. Kirchmayr and W. Rutsch, *Radcure Europe*, **1985**, 446.

28. I. Elphimoff-Felkin and M. Verrier, *Bull. Soc. Chim. Fr.*, **1967**, 1047.

29. J.S. Buck and W.S. Ide, *J. Am. Chem. Soc.*, **1930**, *52*, 220.

30. E. Reichmanis, B.C. Smith and R. Gooden, *J. Polym. Sci., Polym. Chem. Ed.*, **1985**, *23*, 1; E. Reichmanis, R. Gooden, C.W.Wilkins Jr., and H Schonhorn, *J. Polym. Sci., Polym. Chem. Ed.*, **1983**, *21*, 1075.

31. F.A. Vingiello and A. Borkovec, *J. Am. Chem. Soc.*, **1956**, *78*, 1240; F.A. Vingiello and A. Borkovec, *J. Am. Chem. Soc.*, **1955**, *77*, 4823.

32. M.E. Duggan and J.S. Imagire, *Synthesis*, **1989**, 131.

33. R.F. Atkinson, T.W. Balko, T.R. Westman, G.C. Sypniewski, M.A. Carmody, C.T. Pauler, C.L. Schade, D.E. Coulter, H.T. Pham and F. Barea, *J. Org. Chem.*, **1981**, *46*, 2804.

34. S. Yoshini and K. Yamamoto, *Yakugaku Zasshi*, **1972**, *92*, 359.

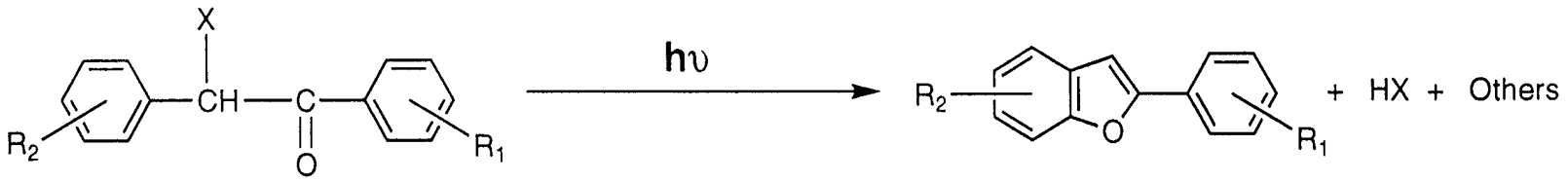
35. J.K. Rasmussen and S.M. Heilmann, *Synthesis*, **1978**, 219.

36. K. Mai and G. Patil, *Tettahedron Lett.*, **1984**, *25*, 4583.

37. M. Hayashi, T. Matsuda and N. Oguni, *J. Chem. Soc., Perkin Trans. 2*, **1992**, 3135.

38. J.M.J. Fréchet, et al. *Polym. Mat. Sci. Eng.*, **1995**, *72*, 4

Scheme 1

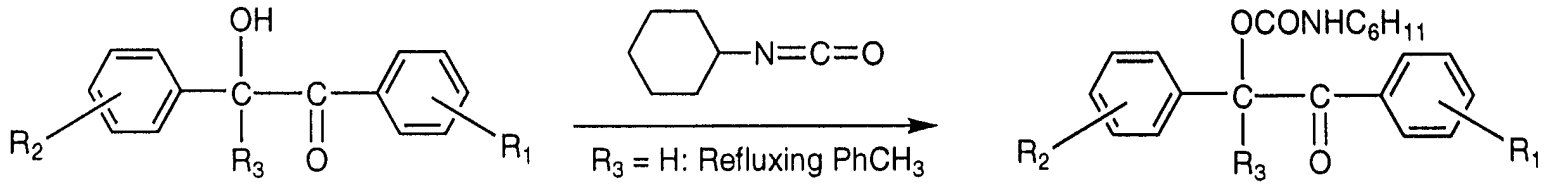


Where X = OAc, $OP(O)(OEt)_2$, $OP(O)O_2^{2-}$

R_1, R_2 = H

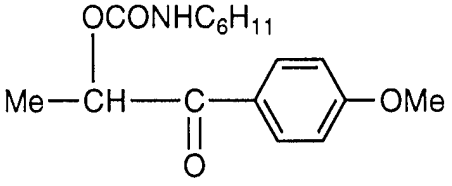
R_1 = H, R_2 = 3,5-$(OMe)_2$

Scheme 2



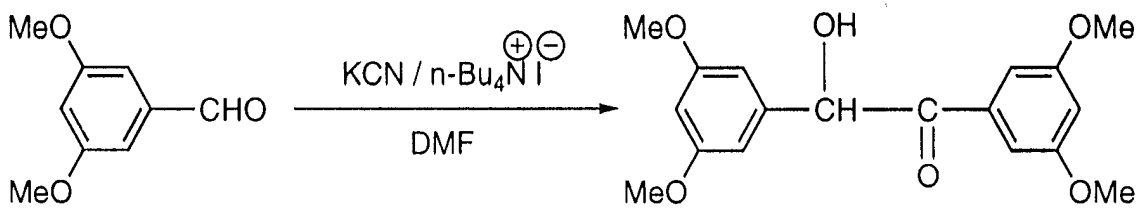
R_3 = aryl, alkyl: $Sn(O_2CC_7H_{15})$ in PhH

Where : $R_1 = R_2 = H$, $R_3 = H$ (**1**)
$R_1 = R_2 = 3,5\text{-OMe}$, $R_3 = H$ (**5**)
$R_1 = R_2 = 3\text{-OMe}$, $R_3 = H$ (**6**)
$R_1 = R_2 = 3,4\text{-}OCH_2O$, $R_3 = H$ (**8**)
$R_1 = R_2 = 4\text{-OMe}$, $R_3 = H$ (**10**)
$R_1 = H$, $R_2 = 3,5\text{-OMe}$, $R_3 = H$ (**12**)
$R_1 = H$, $R_2 = 3,4\text{-}OCH_2O$, $R_3 = H$ (**15**)
$R_1 = 4\text{-OMe}$, $R_2 = 3,5\text{-OMe}$, $R_3 = H$ (**21**)
$R_1 = 4\text{-SMe}$, $R_2 = 3,5\text{-OMe}$, $R_3 = H$ (**22**)
$R_1 = 4\text{-OMe}$, $R_2 = H$, $R_3 = H$ (**26**)
$R_1 = 3,4\text{-}C_4H_4$ (2-Naphth), $R_2 = 3,5\text{-OMe}$, $R_3 = H$ (**27**)
$R_1 = H$, $R_2 = 3,5\text{-OMe}$, $R_3 = Ph$ (**29**)
$R_1 = H$, $R_2 = 3,5\text{-OMe}$, $R_3 = Me$ (**33**)
$R_1 = H$, $R_2 = 3,5\text{-OMe}$, $R_3 = 3,5\text{-DiOMePh}$ (**34**)
$R_1 = 3,5\text{-OMe}$, $R_2 = H$, $R_3 = Ph$ (**38**)



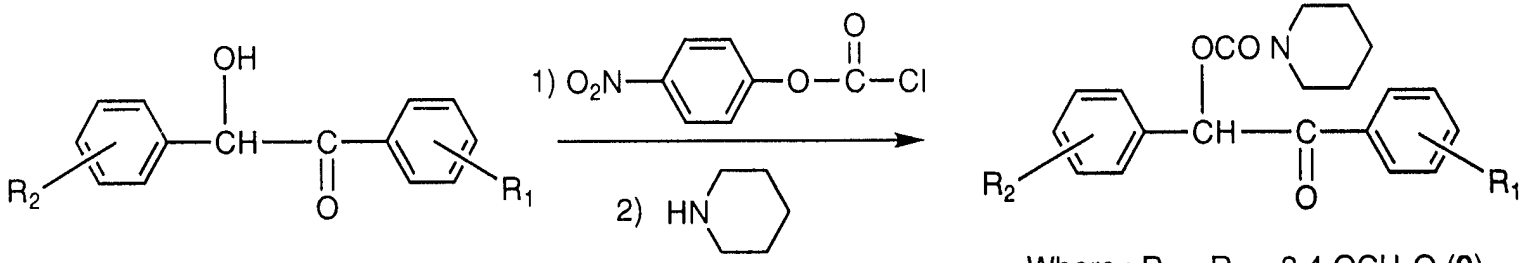
(**24**)

Scheme 3



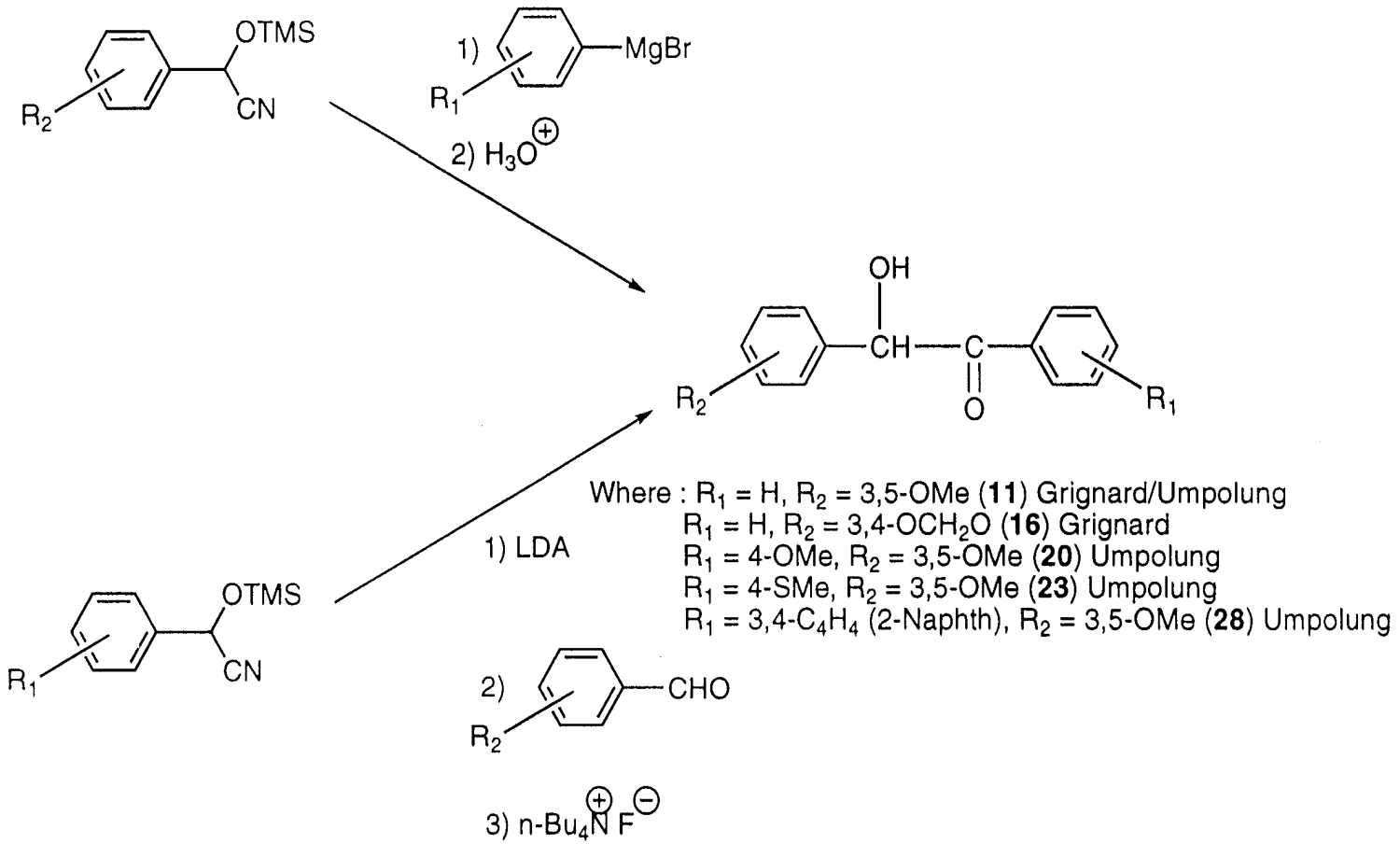
(**4**)

Scheme 4

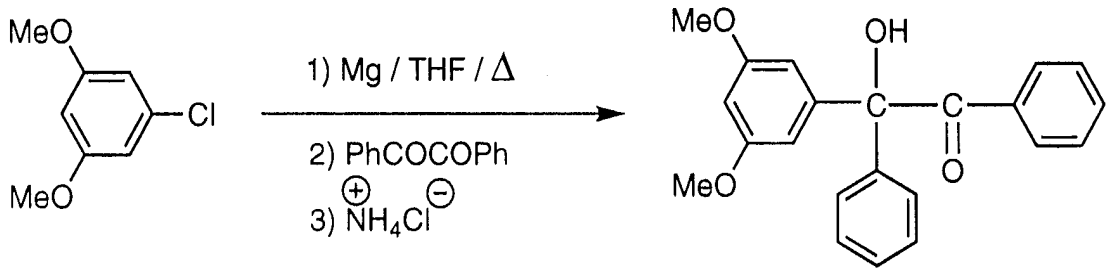


Where : $R_1 = R_2 = 3,4\text{-}OCH_2O$ (**9**)
$R_1 = H$, $R_2 = 3,5\text{-}OMe$ (**13**)

Scheme 5

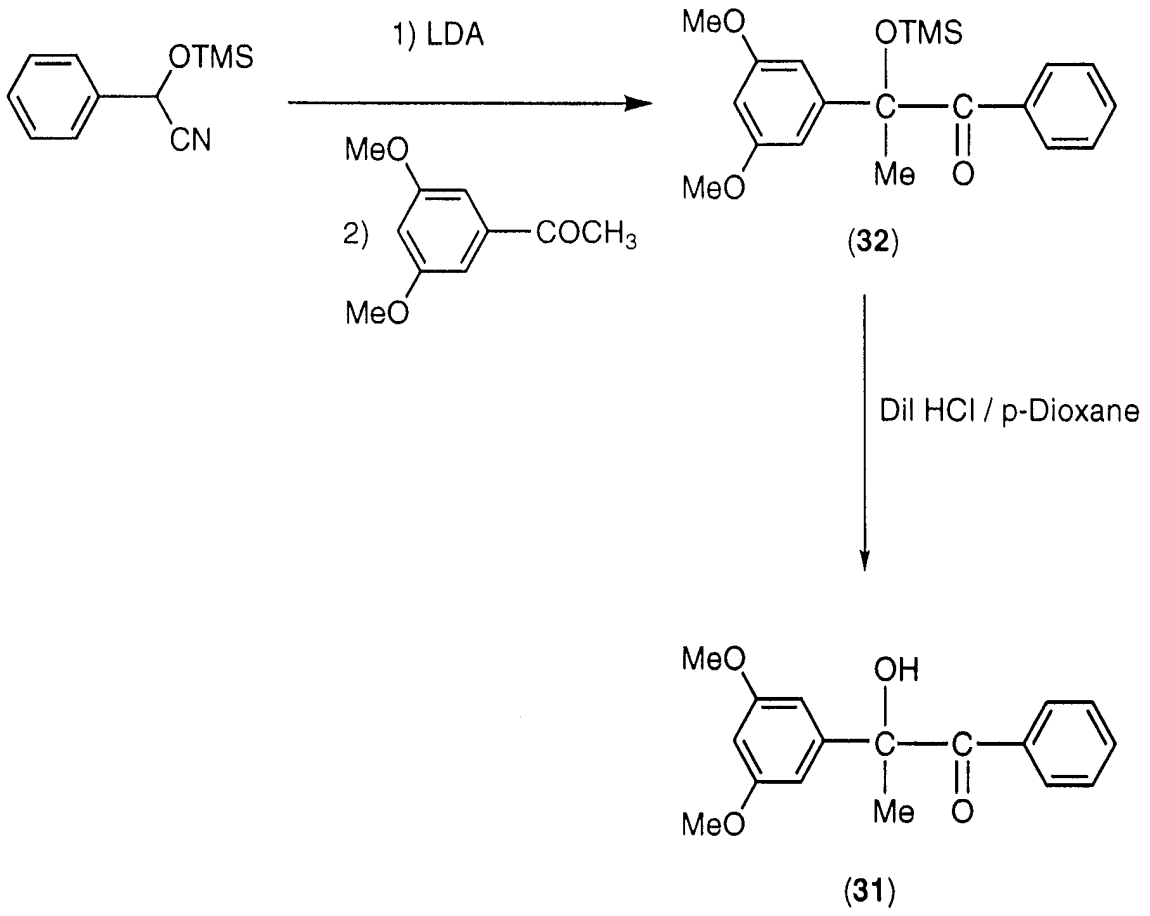

OTMS
CN
R2
1)
MgBr
R1
2) H3O⊕
OH
CH
C
O
R2
R1
Where : R1 = H, R2 = 3,5-OMe (11) Grignard/Umpolung
R1 = H, R2 = 3,4-OCH2O (16) Grignard
R1 = 4-OMe, R2 = 3,5-OMe (20) Umpolung
R1 = 4-SMe, R2 = 3,5-OMe (23) Umpolung
R1 = 3,4-C4H4 (2-Naphth), R2 = 3,5-OMe (28) Umpolung
1) LDA
OTMS
CN
R1
2)
CHO
R2
3) n-Bu4N⊕ F⊖

Scheme 6



(**30**)

Scheme 7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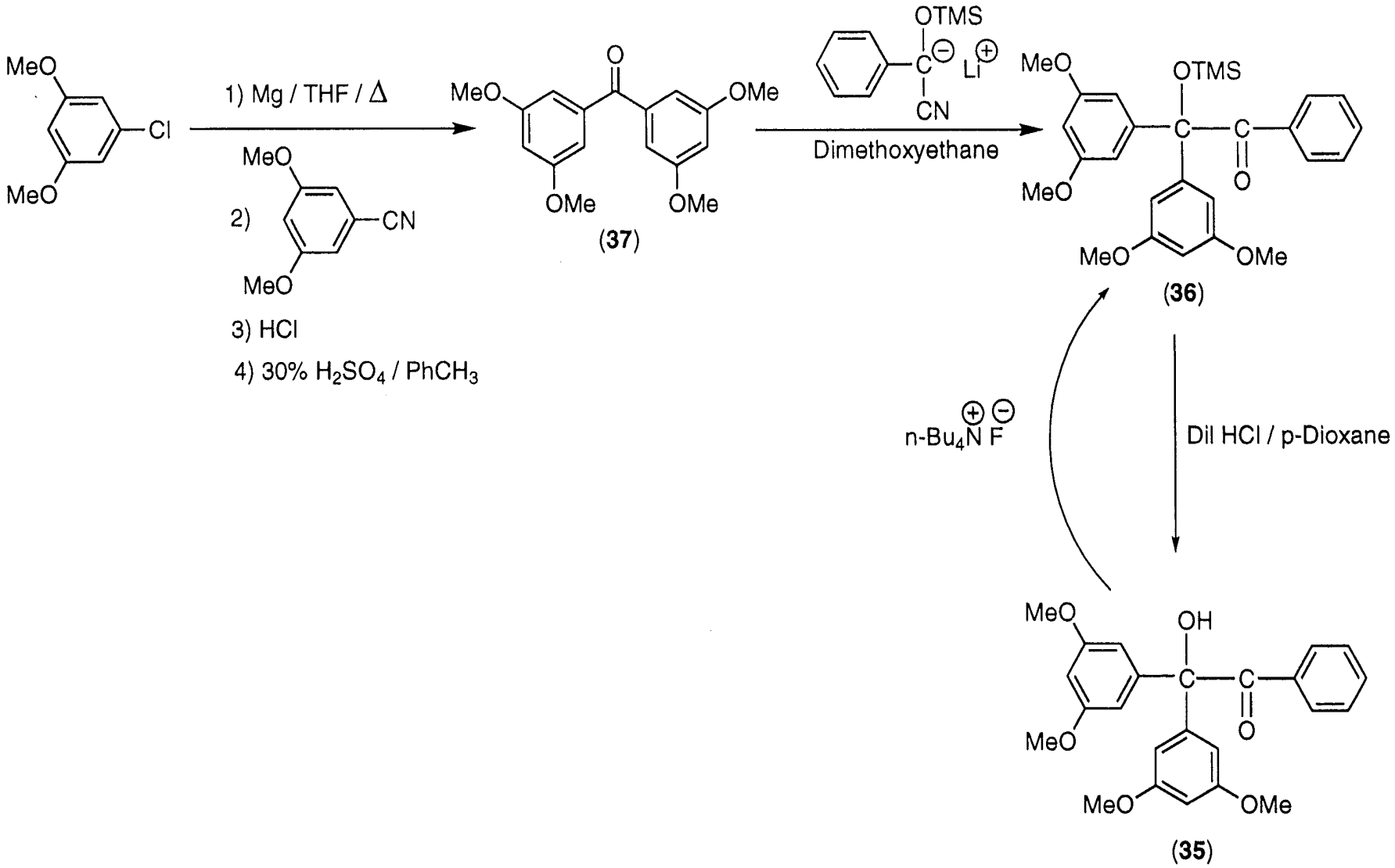
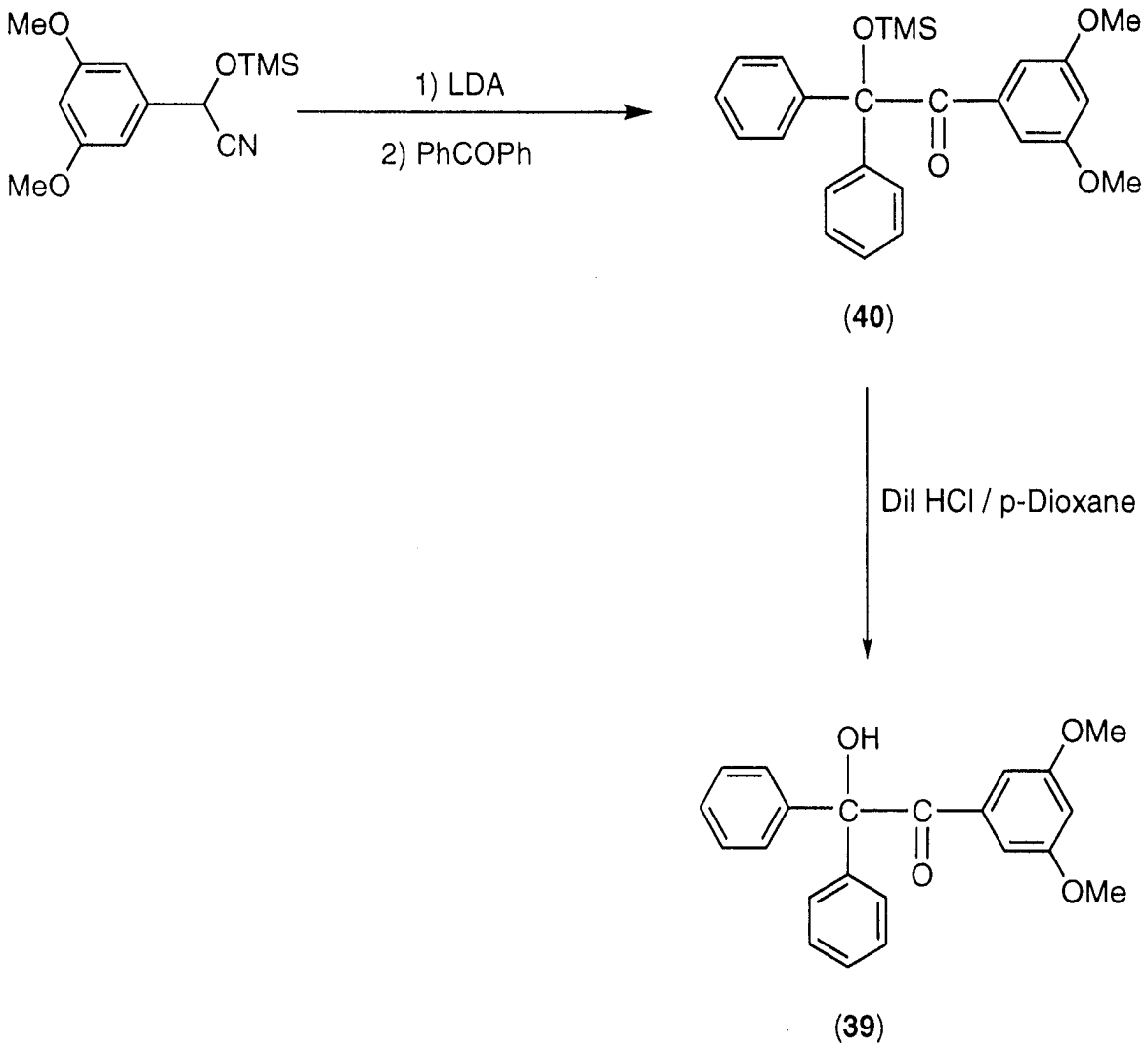
CN
1) LDA
MeO
2)
COCH3
MeO
MeO
OTMS
C
C
Me
O
MeO
(32)
Dil HCl / p-Dioxane
MeO
OH
C
C
Me
O
MeO
(31)

Scheme 8


MeO
Cl
MeO
1) Mg / THF / Δ
MeO
CN
MeO
2)
3) HCl
4) 30% H_2SO_4 / $PhCH_3$
MeO
OMe
O
OMe
OMe
(37)
OTMS
C
Li
CN
Dimethoxyethane
MeO
OTMS
C
C
O
MeO
MeO
OMe
(36)
n-Bu_4N F
Dil HCl / p-Dioxane
MeO
OH
C
C
O
MeO
MeO
OMe
(35)

Scheme 9


MeO
OTMS
CN
MeO
1) LDA
2) PhCOPh
OTMS
OMe
C
C
O
OMe
(40)
Dil HCl / p-Dioxane
OH
OMe
C
C
O
OMe
(39)