Photogeneration of amines from α-keto carbamates: design and preparation of photoactive compounds

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The design and synthesis of substituted desyl (2-oxo-1,2-diphenylethyl) groups has been investigated to create new photolabile protecting groups. The photoreactivity of these chromophores stems from the diverse photochemistry of the desyl group. Several chromophore designs have been explored in which the substitution pattern of the parent desyl chromophore was varied systematically. The required benzoin chromophores are prepared by a variety of synthetic routes, depending on the structure of the benzoin chromophore desired. Symmetrical benzoins are readily available *via* the benzoin condensation. Unsymmetrical benzoins including 2,2-disubstituted α-hydroxy ketones are generally prepared *via* trimethylsilyl (TMS) masked cyanohydrins. On reaction with a Grignard reagent, the TMS masked cyanohydrin functions as an α-hydroxycarbonyl 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 substituted benzoins. These desyl chromophores have significant potential as new photolabile protecting moieties for a variety of functional groups and are used to mask primary and secondary amines as photosensitive α-keto carbamates. The substituted benzoin carbamates are readily prepared from the appropriate benzoin by reaction with isocyanates or by activation as a mixed carbonate followed by reaction with the free amine. These α-keto carbamates are interesting for two main reasons. First, the facile synthesis of these materials indicates the ease of introduction of the desyl based photolabile group. Second, these α-keto carbamates may be used for rapid evaluation of novel photoactive desyl based chromophores.

Introduction

The application of photolabile protecting groups in synthetic organic chemistry has received considerable attention due to the mild, neutral conditions which can be used to effect deprotection. Indeed, photolabile protecting groups have been developed for most common functional groups.[1] For instance, several photolabile groups based on the well known *o*-nitrobenzyl photorearrangement have been used to mask such diverse functional groups as alcohols, amines, carboxylic acids and carbonyl compounds. Traditionally used in classical synthetic organic applications, photolabile groups are now frequently used in advanced technologies. For example, in light-flash physiology, caged nucleoside triphosphates,[2] photolabile calcium chelators[3] and photoactive precursors of neurotransmitters[4] all rely on efficient photodeprotection strategies for their success.

Recently, we developed a new strategy for the photorelease of reactive organic bases by masking amines and diamines as photoactive carbamates.[5–7] Under the action of light, these neutral carbamates decompose to liberate free amines. However, we found that some commonly used photolabile amino protecting groups, *e.g.* the 3,5-dimethoxy-α,α-dimethylbenzyloxycarbonyl and *o*-nitrobenzyloxycarbonyl moieties, undergo somewhat complex photochemistry and suffer from deleterious side reactions upon prolonged photolysis.

We recently published a preliminary report on the utility of new photolabile amino protecting groups based on substituted desyl (2-oxo-1,2-diphenylethyl) chromophores.[8] We now describe the full details of the design concepts and synthetic principles used in creating new improved chromophores for photolabile protecting groups. Emphasis is placed on chromophore design with a view to creating new, practical photolabile amino protecting groups. The desyl chromophore and its substituted analogues 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 by-products; (2) improved photoefficiency and (3) enhanced rate of photorelease.

First, the parent desyl chromophore is well known to undergo photocleavage *via* classical photochemical pathways such as α-cleavage (Norrish Type I). In contrast, *m*-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 by-products. Second, 3′,5′-dimethoxybenzoin esters have been developed as photolabile carboxy protecting groups[10–12] and shown to liberate 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[13–15] and inorganic phosphate[16] (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

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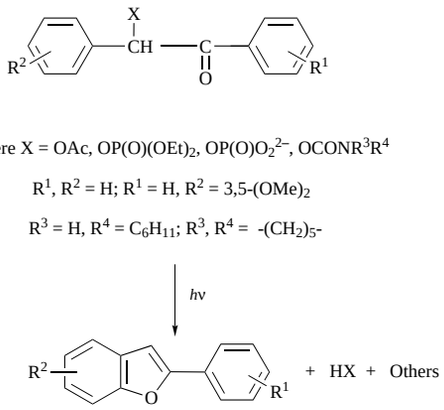
¶ IUPAC name: 1-(3,5-dimethoxyphenyl)-2-oxo-2-phenylethyl acetate.



Scheme 1

unsubstituted benzoin phosphates.[17] 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.[14,17]

Results and discussion

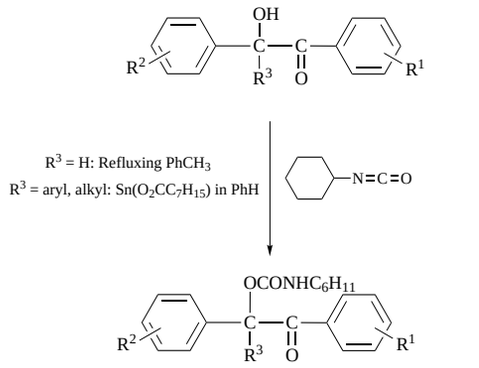
General design considerations

The substituted benzoin chromophore may be envisioned as a light sensitive protecting group for a variety of common functional groups. For instance, we initially reported on the utility of 3′,5′-dimethoxybenzoinyl‖ carbamates as photoprecursors of both primary and secondary amines[8] (Scheme 1). More recently, we have further developed these materials as novel amine base progenitors for use in polymer imaging and coating chemistry.[18] Independent of our investigation, Pirrung and coworkers have also developed the photolabile 3′,5′-dimethoxybenzoinyloxycarbonyl group specifically for the protection of secondary amines.[19] The same group have also extended the scope of the 3′,5′-dimethoxybenzoinyl chromophore to allow for protection of both alcohols[20,21] and thiols.[20]

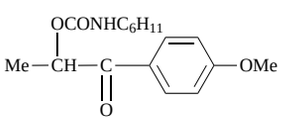
In this paper, emphasis is placed on developing desyl based α-keto carbamates as masked amines because these materials may offer significant advantages over current photolabile amino protecting groups. There were two main reasons for interest in these α-keto carbamates. First, the synthesis of these materials illustrates the relative ease with which desyl based photolabile protecting groups may be introduced. 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. The diverse array of photoactive α-keto carbamates prepared herein provided a materials base for our investigation of chromophore structure–photosensitivity relationships during photoliberation of amino groups.[22] The utility of α-keto carbamates derived from alkoxy substituted desyl chromophores has recently been described.[8,18,22]

Design and synthesis

Preparation of unsubstituted α-keto carbamates. Simple, unsubstituted α-keto carbamates may be prepared by reacting an α-hydroxy ketone with an isocyanate. For example, benzoin *N*-cyclohexylcarbamate **1** was prepared by the reaction of benzoin with cyclohexyl isocyanate under a variety of conditions



Where : **1** $R^1 = R^2 = H$, $R^3 = H$
2 $R^1 = R^2 = 3,5\text{-OMe}$, $R^3 = H$
3 $R^1 = R^2 = 3\text{-OMe}$, $R^3 = H$
4 $R^1 = R^2 = 3,4\text{-}OCH_2O$, $R^3 = H$
5 $R^1 = R^2 = 4\text{-OMe}$, $R^3 = H$
6 $R^1 = H$, $R^2 = 3,5\text{-OMe}$, $R^3 = H$
7 $R^1 = H$, $R^2 = 3,4\text{-}OCH_2O$, $R^3 = H$
8 $R^1 = 4\text{-OMe}$, $R^2 = 3,5\text{-OMe}$, $R^3 = H$
9 $R^1 = 4\text{-SMe}$, $R^2 = 3,5\text{-OMe}$, $R^3 = H$
10 $R^1 = 4\text{-OMe}$, $R^2 = H$, $R^3 = H$
11 $R^1 = 3,4\text{-}C_4H_4$ (2-Naphth), $R^2 = 3,5\text{-OMe}$, $R^3 = H$
12 $R^1 = H$, $R^2 = 3,5\text{-OMe}$, $R^3 = Ph$
13 $R^1 = H$, $R^2 = 3,5\text{-OMe}$, $R^3 = Me$
14 $R^1 = H$, $R^2 = 3,5\text{-OMe}$, $R^3 = 3,5\text{-diOMePh}$
15 $R^1 = 3,5\text{-OMe}$, $R^2 = H$, $R^3 = Ph$



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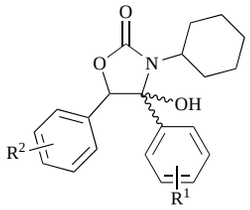
Scheme 2

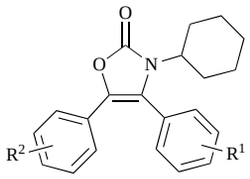
(Scheme 2). Previously, we had found methyllithium to be an excellent catalyst for the addition of a diverse array of alcohols to isocyanates.[5,6] Accordingly, the methyllithium catalysed addition was investigated first. Under these conditions, the addition of benzoin to cyclohexyl isocyanate afforded benzoin *N*-cyclohexylcarbamate **1** in only 21% yield. Under the anionic reaction conditions, the major reaction pathway involved a combination of cyclization and dehydration. Intramolecular cyclization of benzoin *N*-cyclohexylcarbamate **1** to give 3-cyclohexyl-4-hydroxy-4,5-diphenyloxazolidin-2-one **17** was followed by subsequent dehydration to give 3-cyclohexyl-4,5-diphenyl-2,3-dihydrooxazol-2-one **20** 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.[23] In order to minimize the cyclization–elimination reaction, we developed mild, neutral conditions for the preparation of desyl carbamates. We found that simply heating a solution of the benzoin and isocyanate in toluene gave the required desyl carbamate. Under these conditions, the yield of benzoin *N*-cyclohexylcarbamate **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 *e.g.* 1,2-diphenylethanedione (*vide infra*). The efficiency of the direct addition was largely unaffected by amine catalysts, such as 4-dimethylaminopyridine (DMAP) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). Stannous 2-ethylhexanoate, which is a well known catalyst for urethane formation,[24] failed to take the reaction to completion.

Preparation of aryl substituted α-keto carbamates. *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 was based on symmetrical benzoins.

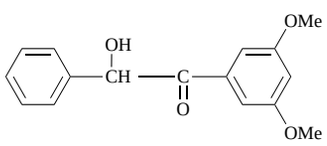
‖ IUPAC name: 1-(3,5-dimethoxyphenyl)-2-oxo-2-phenylethyl.





Where : **17** $R^1 = R^2 = H$
18 $R^1 = R^2 = 3\text{-OMe}$
19 $R^1 = H$, $R^2 = 3,4\text{-OCH}_2O$

Where : **20** $R^1 = R^2 = H$
21 $R^1 = H$, $R^2 = 3,4\text{-OCH}_2O$



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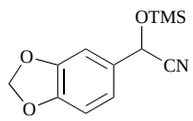

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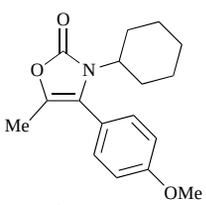

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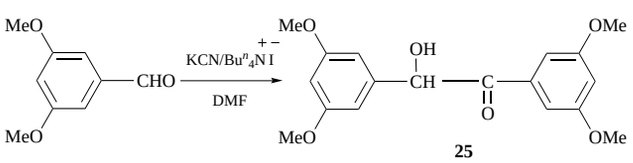
Because of the pronounced activating effect of *meta* methoxy substitution on the photocyclization of benzoin esters,[10,15] we chose to investigate the 3,3′,5,5′-tetramethoxybenzoin chromophore as a photolabile amino protecting group. Despite a literature report that this benzoin **25** was unavailable by benzoin condensation,[25] we succeeded in preparing this material in 31% yield by reaction of 3,5-dimethoxybenzaldehyde in DMF in the presence of potassium cyanide and tetra-*n*-butylammonium iodide[26] (Scheme 3). Subsequent reaction with cyclohexyl isocyanate in refluxing toluene gave the cyclohexylamine photoprecursor **2** in 77% yield (Scheme 2). This material is the masked amine equivalent of the highly photosensitive 3,3′,5,5′-tetramethoxybenzoinyl acetate and phosphate esters reported by Corrie and Trentham.[17] Interestingly, the direct addition of benzoin **25** to cyclohexyl isocyanate was accompanied by a trace of 1,2-bis(3,5-dimethoxyphenyl)ethanedione.



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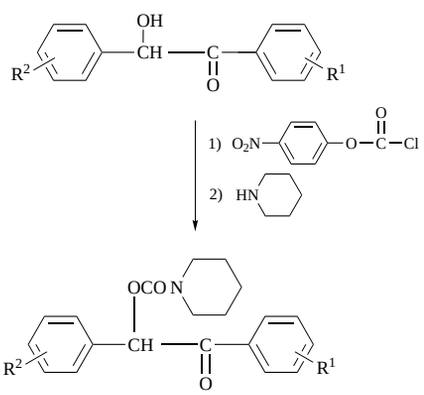
Scheme 3

The cyclohexylcarbamate of 3,3′-dimethoxybenzoin **3** was attractive because it would allow comparison of the effect of two *versus* four *meta* activating groups in the chromophore. 3,3′-Dimethoxybenzoin[27] reacted with cyclohexyl isocyanate to give the requisite carbamate **3** in 49% yield (Scheme 2). The addition of this particular benzoin to cyclohexyl isocyanate was plagued by cyclization of the carbamate to 3-cyclohexyl-4-hydroxy-4,5-bis(3-methoxyphenyl)oxazolidin-2-one **18**. In this case, the 4-hydroxyoxazolidin-2-one **18** was isolated in two crystal crops each of which proved to be a different stereoisomer as indicated by ^{1}H and ^{13}C NMR spectroscopy. The crude gum isolated from the reaction itself was indeed the desired cyclohexylcarbamate **3**, as indicated by ^{1}H NMR spectroscopy. However, cyclization tended to occur during subsequent chromatographic operations and crystallization only succeeded in separating stereoisomers of 3-cyclohexyl-4-hydroxy-4,5-bis(3-methoxyphenyl)oxazolidin-2-one **18**. 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 photosensitivity of piperoin [1,2-bis(1,3-benzodioxol-5-yl)-2-hydroxyethanone] 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 cyclohexylcarbamate **4** (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 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 **26** (Scheme 4). Piperoin was converted to piperidinocarbamate **26** *via* its *p*-nitrophenyl mixed carbonate followed by treatment with piperidine. A trace of 1,2-bis(1,3-benzodioxol-5-yl)ethanedione was isolated from the preparation of piperidinocarbamate **26**. The protection of a secondary amine as an α-keto carbamate is particularly attractive as it does not suffer from any competing cyclization reactions of the sort 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 derived from primary amines.



Where : **26** $R^1 = R^2 = 3,4\text{-OCH}_2O$
27 $R^1 = H$, $R^2 = 3,5\text{-OMe}$

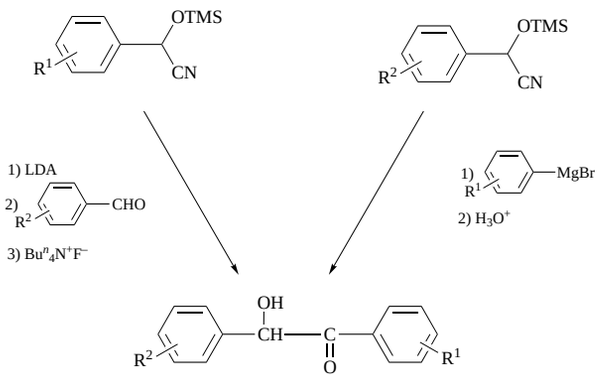
Scheme 4

To further clarify the nature of the *meta* activating effect on the photochemistry of benzoin carbamates, carbamate **5**, 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 **5** is known to photocleave by a variety of mechanisms of which cyclization is a minor pathway.[9] Carbamate **5** was prepared by reaction of anisoin [2-hydroxy-1,2-bis(4-methoxyphenyl)ethanone] with cyclohexyl isocyanate in refluxing toluene (Scheme 2).

Photolabile amino protecting groups based on unsymmetrical benzoins.—An efficient synthesis of unsymmetrical benzoins was required to enable the synthesis of a variety of carbamates derived from unsymmetrical benzoins. Because 3′,5′-dimethoxybenzoin **28** 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 **28**.

First, one can use a trimethylsilyl (TMS) masked cyanohydrin as an electrophilic α-hydroxycarbonyl synthon in reaction with a Grignard reagent.[28] 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.[29]

Using the first approach, 3′,5′-dimethoxybenzoin **28** was prepared from 3,5-dimethoxybenzaldehyde (Scheme 5). Conversion of the aldehyde to α-(3,5-dimethoxyphenyl)-α-(trimethylsiloxy)acetonitrile was achieved by zinc iodide catalysed reaction with trimethylsilyl cyanide.[30] Subsequent reaction with phenylmagnesium bromide, followed by acid mediated hydrolysis of the intermediate imine, gave the desired 3′,5′-dimethoxybenzoin **28**. In contrast, the original procedure of Sheehan *et al.*,[10] in which 3,5-dimethoxybenzaldehyde cyanohydrin is 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 hydroxy group during the Grignard reaction.



Where : **28** R^1 = H, R^2 = 3,5-OMe; Grignard/umpolung
29 R^1 = H, R^2 = 3,4-OCH_2O; Grignard
30 R^1 = 4-OMe, R^2 = 3,5-OMe; umpolung
31 R^1 = 4-SMe, R^2 = 3,5-OMe; umpolung
32 R^1 = 3,4-C_4H_4 (2-Naphth), R^2 = 3,5-OMe; umpolung

Scheme 5

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 **28**. Lithiation of α-phenyl-α-(trimethylsiloxy)acetonitrile, followed by reaction with 3,5-dimethoxybenzaldehyde gave the corresponding TMS masked benzoin. Subsequent hydrolysis using tetra-*n*-butylammonium fluoride gave 3′,5′-dimethoxybenzoin **28** (Scheme 5).

With 3′,5′-dimethoxybenzoin readily available,** carbamates containing the 3′,5′-dimethoxybenzoin chromophore were readily prepared. First, 3′,5′-dimethoxybenzoin *N*-cyclohexylcarbamate **6** was prepared from 3′,5′-dimethoxybenzoin **28** 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-phenylethanedione was isolated in a trace amount. A piperidine photoprecursor **27** containing the 3′,5′-dimethoxybenzoin chromophore was also prepared (Scheme 4). This photosensitive carbamate was prepared in a similar fashion to piperoin piperidinocarbamate **26**.

For future evaluation of the *meta* activating effect of methoxy groups on the photocyclization, we proposed to prepare the cyclohexylcarbamate 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 **28** was isolated in 50% yield. Corrie and Trentham[17] have recently reported the synthesis of 3,5-dimethoxybenzoin **22** 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 **7**, derived from an unsymmetrical benzoin **29**, containing the 1,3-methylenedioxy substituent, was also prepared in the usual way (Scheme 2). The addition of the benzoin to cyclohexyl isocyanate proved troublesome because the crude carbamate readily undergoes intramolecular cyclization during purification similar to that observed for 3,3′-dimethoxybenzoin *N*-cyclohexylcarbamate **3**. Some of the desired carbamate was separable by chromatography, but the majority of the column fractions consisted of a mixture of the desired carbamate **7** (cyclohexyl CH, m, δ_H 3.50), 5-(1,3-benzodioxol-5-yl)-3-cyclohexyl-4-hydroxy-4-phenyloxazolidin-2-one **19** (cyclohexyl CH, m, δ_H 2.87) and 5-(1,3-benzodioxol-5-yl)-3-cyclohexyl-4-phenyl-2,3-dihydrooxazol-2-one **21** (cyclohexyl CH, m, δ_H 3.29). The required benzoin **29** was prepared in two steps involving conversion of piperonal to α-(1,3-benzodioxol-5-yl)-α-(trimethylsiloxy)acetonitrile **23** followed by reaction with phenylmagnesium bromide (Scheme 5).

For some applications with inherently light sensitive substrates *e.g.* tryptophan and pyrimidines, efficient red shifted photolabile protecting groups would be of significant value. Accordingly, we investigated extending the UV absorption of these benzoinyl based carbamates. The general approach 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 analogues of 3′,5′-dimethoxybenzoin *N*-cyclohexylcarbamate 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 analogues. The 4-methoxyphenacyl and the α-methylphenacyl group have been widely used as both carboxy[32] and amino[33] photolabile protecting groups. Thus, the new chromophore should possess the combined photosensitivity of the 3′,5′-dimethoxybenzoin chromophore and the known photolability of α-substituted 4-methoxyphenacyl protecting groups. The required benzoin **30** was prepared from α-(4-methoxyphenyl)-α-(trimethylsiloxy)acetonitrile[22] by lithiation and subsequent reaction of the carbanion with 3,5-dimethoxybenzaldehyde. Fluoride ion mediated hydrolysis gave the desired benzoin **30** (Scheme 5). With this benzoin in hand, conversion to the masked cyclohexylamine **8** was accomplished by reaction with cyclohexyl isocyanate in refluxing toluene (Scheme 2).[22]

Using a strategy similar to that 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.[34] Because of such improved absorption characteristics, these materials function as efficient red shifted photoacid generators. By analogy, cyclohexylcarbamate **9** containing the 4-methylthio modified chromophore may be expected to be an efficient

** During preparation of this manuscript, a report on the use of classical dithiane umpolung synthons for the synthesis of unsymmetrical alkoxy substituted benzoins appeared.[31] In contrast to the initial report by Lee,[12] this latter work found the Corey–Seebach dithiane addition to be an effective route for the synthesis of unsymmerical benzoins including 3′,5′-dimethoxybenzoin.

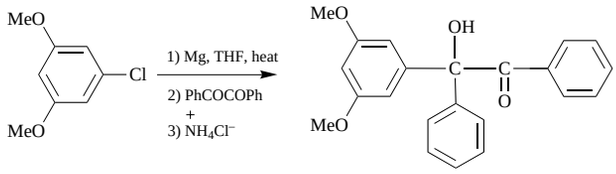
source of cyclohexylamine beyond 300 nm. The substituted benzoinyl chromophore in carbamate **9** may also be viewed as a thiomethyl substituted analogue of the light sensitive phenacyl chromophore. The additional photolability of the phenacyl chromophore in **9** may be expected to increase further the photosensitivity of the protecting group. In this regard, carbamate **9** is similar to carbamate **8**. Carbamate **9** was prepared from benzoin **31** by reaction with cyclohexyl isocyanate in refluxing toluene (Scheme 2). The required benzoin **31** was prepared from the masked TMS cyanohydrin of 4-methylthiobenzaldehyde by lithiation and reaction with 3,5-dimethoxybenzaldehyde. Subsequent fluoride assisted desilylation gave benzoin **31** (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 **16** incorporating the parent α-methyl-4-methoxyphenacyl photolabile moiety was prepared from 2-hydroxy-1-(4-methoxyphenyl)propanone.[35] In this reaction, a trace of the corresponding 2,3-dihydrooxazol-2-one **24** was also isolated. A similar addition reaction with 4-methoxybenzoin proceeded smoothly to give the corresponding cyclohexylcarbamate **10**. This carbamate contains the α-phenyl-4-methoxyphenacyl photolabile group. 4-Methoxybenzoin was prepared by the benzoin reversion synthesis from benzoin and 4-methoxybenzaldehyde.[36]

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 with LDA at −78 °C resulted in a complex mixture. Hunig and Wehner[29] 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-naphthyl) substituent as in carbamate **11**. The required benzoin **32** was prepared by reaction of the carbanion of α-(2-naphthyl)-α-(trimethylsiloxy)acetonitrile with 3,5-dimethoxybenzaldehyde in the usual way (Scheme 5). Addition of substituted benzoin **32** to cyclohexyl isocyanate gave the requisite carbamate **11** (Scheme 2). A trace amount of the corresponding benzil, 1-(3,5-dimethoxyphenyl)-2-(2-naphthyl)-ethanedione, was formed during the addition. Table 1 and Table 2 summarize the analytical data on α-hydroxy ketones and α-keto carbamates, respectively.

Preparation of 2,2-disubstituted 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.[37] 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 **12**, containing a 2,2-disubstituted α-hydroxy keto chromophore was prepared by reaction of α-hydroxy ketone **33** with cyclohexyl isocyanate in the presence of a catalytic amount of stannous 2-ethylhexanoate (Scheme 2). This tin(II) salt was reported to be a useful catalyst for the preparation of tertiary carbamates[24] and proved to be the catalyst of choice for reaction of our α-keto substituted tertiary alcohols with isocyanates. The requisite α-hydroxy ketone **33** was prepared by reaction of benzil and 3,5-

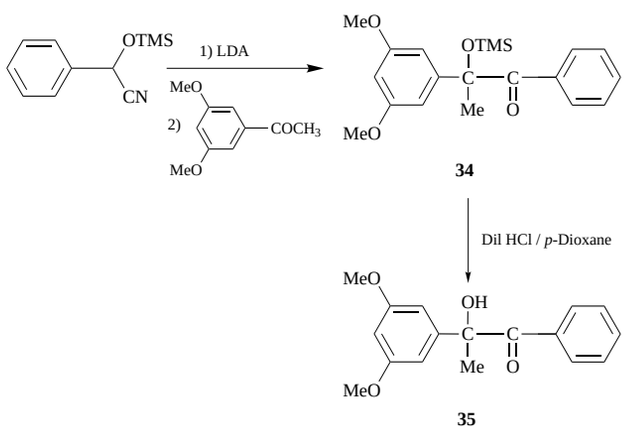


33

Scheme 6

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.

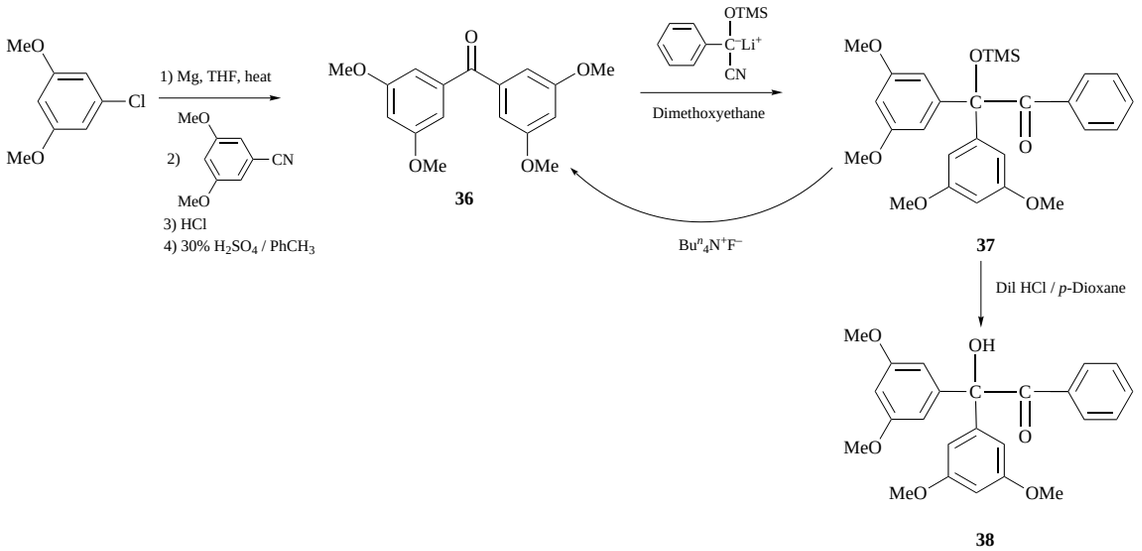
In carbamate **12**, an α-phenyl group has been incorporated into the 3′,5′-dimethoxybenzoin chromophore. This substitution pattern may suffer from steric interference in the benzoin photocyclization. Accordingly, it seemed appropriate to prepare the α-methyl derivative in which the potentially favourable 2,2-disubstitution pattern is retained but steric congestion is reduced. The required α-hydroxy ketone **35** was prepared by lithiation of α-phenyl-α-(trimethylsiloxy)acetonitrile followed by reaction with 3,5-dimethoxyacetophenone (Scheme 7). In



Scheme 7

this case, the TMS masked benzoin **34** was isolated and ultimately deprotected by acidolysis. The resulting α-hydroxy ketone **35** was converted to the cyclohexylcarbamate **13**, *via* the tin(II) catalysed 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.[8–21] In the case of the *o*-nitrobenzyl photorearrangement, substitution by an additional *o*-nitro group is reported to cause a near fivefold increase in photoefficiency, relative to the mono *o*-nitrobenzyl chromophore.[6,37] 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. Cyclohexylcarbamate **14**, incorporating two 3,5-dimethoxyphenyl substituents adjacent to the hydroxy substituted carbon, was prepared from α-hydroxy ketone **38**, by the stannous 2-ethylhexanoate catalysed addition to cyclohexyl isocyanate (Scheme 2).[22] The chromophore based on 2,2-bis(3,5-dimethoxyphenyl)-2-hydroxy-1-phenylethanone **38** warrants a special mention as it does not contain a chiral centre. By using this group, facile protection of optically active substrates may be envisioned without undesired formation of diastereoisomers. This feature may render α-hydroxy ketone **38** particularly useful as a photoremovable group in protection schemes involving optically active substrates *e.g.* peptides, phosphotriesters. The TMS masked hydroxy ketone **37** was prepared from α-phenyl-α-

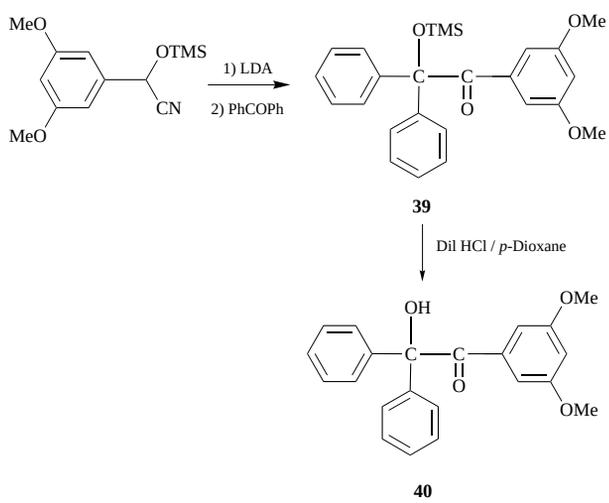


Scheme 8

(trimethylsiloxy)acetonitrile, by reaction with 3,3′,5,5′-tetramethoxybenzophenone **36**.[22] Interestingly, fluoride ion mediated hydrolysis of the TMS masked intermediate **37** resulted in recovery of the substituted ketone **36** while acidolysis provided the desired α-hydroxy ketone **38** (Scheme 8). The efficient recovery of starting benzophenone from the fluoride mediated hydrolysis implies that fluoride is sufficiently basic so as to cause reversion of the TMS masked benzoin back to the starting benzophenone **36**. 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 **36** was prepared by reaction of 3,5-dimethoxybenzonitrile with 3,5-dimethoxyphenylmagnesium chloride (Scheme 8). On acidic work-up, the ketimine intermediate was isolated as the corresponding hydrochloride salt and hydrolysed to the free ketone **36** using 30% sulfuric acid in refluxing toluene.[22]

To further gauge the importance of double 3,5-dimethoxy substitution adjacent to the hydroxy substituted carbon as in **14**, a carbamate in which the substitution pattern is reversed should provide the required contrast in photoreactivity. For this purpose cyclohexylcarbamate **15** was prepared. This particular carbamate **15** was conveniently prepared *via* the usual tin(II) catalysed reaction (Scheme 2). The required α-hydroxy ketone **40** was prepared by lithiation of α-(3,5-dimethoxyphenyl)-α-(trimethylsiloxy)acetonitrile followed by reaction with benzophenone (Scheme 9). The TMS masked benzoin **39** was isolated and deprotected by acidolysis to give **40** in 81% yield.

Since a significant amount of α-hydroxy ketone **40** was readily available, several other methods of masking amines as tertiary carbamates were investigated. Initially, the conditions used to prepare other benzoin carbamates were investigated. However, heating a solution of the α-hydroxy ketone **40** with cyclohexyl isocyanate failed to give any of the desired carbamate **15**. The cuprous chloride catalysed addition of tertiary alcohols to isocyanates was also investigated.[38] In the case of α-hydroxy ketone **40**, 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.[39] However, in the case of α-hydroxy ketone **40**, DMAP catalysed reaction with *N*,*N*′-diethylcarbamoyl chloride failed. The synthesis of tertiary carbamates can also be realized by activation of the tertiary alcohol as a mixed carbonate followed by reaction with an amine. In the case of α-hydroxy ketone **40**, attempted activation by derivatization to the *p*-nitrophenyl mixed carbonate afforded only recovered starting material. Table 1 and Table 2 summarize the analytical data on 2,2-disubstituted α-hydroxy ketones and α-keto carbamates, respectively.



Scheme 9

Conclusions

The synthesis of a variety of substituted benzoin chromophores was investigated. These chromophores hold significant potential as new photolabile protecting groups for a variety of functional groups. For instance, 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. In their reaction with a Grignard reagent, TMS masked cyanohydrins function as α-hydroxy carbonyl equivalents 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 the direct addition of the substituted benzoin to an

Table 1 Analytical data on α-hydroxy ketones

Comp.	Yield (%) mp (°C)	δ_H (ppm)[d]	δ_C (ppm)	ν/cm^{-1}	Elemental analysis (%) Calc.	Found
29	40 127–129[a]	4.39 [1 H, br s, OH (D_2O exch.)], 5.87 (1 H, s, 2-CH), 5.91 and 5.93 (each 1 H, ABq, J_{gem} 1.2, OCH_2O), 6.73–6.78 [2 H, m, Ar(2) 4,7-H], 6.85 [1 H, dd, J_o 8.0, J_m 1.6, Ar(2) 6-H], 7.44 [2 H, m approximates to t, Ar(1) 3,5-H], 7.56 [1 H, m approximates to t, Ar(1) 4-H], 7.92 [2 H, m approximates to d, Ar(1) 2,6-H]	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)	3458, 1681, 1502, 1488, 1443, 1247, 1099, 1039, 975, 695	$C_{15}H_{12}O_4$ (256.25) C, 70.3 H, 4.7	 C, 70.5 H, 4.8
31	62 112–113	2.47 (3 H, s, SCH_3), 3.74 [6 H, s, Ar(2) 3,5-OCH_3], 4.58 [1 H, d, J 6.1, OH (D_2O exch.)], 5.80 (1 H, d, J 6.1, 2-CH), 6.36 [1 H, t, J_m 2.1, Ar(2) 4-H], 6.47 [2 H, d, J_m 2.1, Ar(2) 2,6-H], 7.21 and 7.84 [each 2 H, ABq, J_o 7.8, Ar(1) 3,5-H and 2,6-H respectively]	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)[c]	3370, 1678, 1670, 1608, 1596, 1591, 1206, 1162, 1156, 1088	$C_{17}H_{18}O_4S$ (318.47) C, 64.1 H, 5.7 S, 10.0	 C, 64.3 H, 5.8 S, 9.7
32	*b*	3.74 (6 H, s, 3,5-OCH_3), 4.62 [1 H, br d, J 5.2, OH (D_2O exch.)], 6.02 (1 H, br d, J 5.2, 2-CH), 6.35 [1 H, t, J_m 2.2, Ar(2) 4-H], 6.55 [2 H, d, J_m 2.2, Ar(2) 2,6-H], 7.50–7.65 [2 H, m, Ar(1) 6,7-H], 7.81–8.03 [4 H, m, Ar(1) 3,4,5,8-H], 8.49 [1 H, br s, Ar(1) 1-H]	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)	3454, 1677, 1608, 1596, 1466, 1430, 1283, 1205, 1158, 1065	$C_{20}H_{18}O_4$ (322.34) C, 74.5 H, 5.6	 C, 74.3 H, 5.4
33	46 111.5–113	3.71 [6 H, s, Ar(2) 3,5-OCH_3], 4.96 [1 H, s, OH (D_2O exch.)], 6.42 [1 H, t, J_m 2.2, Ar(2) 4-H], 6.59 [2 H, d, J_m 2.2, Ar(2) 2,6-H], 7.29–7.51 [8 H, m, Ph(2) 2,6-H and Ph(1) 3,4,5-H], 7.72 [2 H, m approximates to d, J_o 6.7, Ph(1) 2,6-H]	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)	3429, 1674, 1611, 1597, 1426, 1235, 1205, 1158, 1068, 703	$C_{22}H_{20}O_4$ (348.38) C, 75.8 H, 5.8	 C, 75.95 H, 5.7
35	99 Oil	2.12 (3 H, s, CH_3), 3.76 [6 H, s, Ar(2) 3,5-OCH_3], 4.70 [1 H, s, OH (slow D_2O exch.)], 6.41 [1 H, t, J_m 2.2, Ar(2) 4-H], 6.61 [2 H, d, J_m 2.2, Ar(2) 2,6-H], 7.31 [2 H, m approximates to t, Ar(1) 3,5-H], 7.46 [1 H, m approximates to t, Ar(1) 4-H], 7.75 [2 H, m approximates to d, Ar(1) 2,6-H]	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)	3462, 1679, 1607, 1597, 1458, 1427, 1206, 1157, 1063, 1047	$C_{17}H_{18}O_4$ (286.31) C, 71.3 H, 6.3	 C, 71.2 H, 6.3
40	81 93–94	3.63 [6 H, s, Ar(1) 3,5-OCH_3], 5.08 [1 H, s, OH (D_2O exch.)], 6.56 [1 H, t, J_m 2.3, Ar(1) 4-H], 6.85 [2 H, d, J_m 2.3, Ar(1) 2,6-H], 7.29–7.48 [10 H, m, both Ar(2) 2,2-diPh]	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)	3446, 1679, 1607, 1597, 1458, 1427, 1206, 1157, 1063, 1047	$C_{22}H_{20}O_4$ (348.38) C, 75.8 H, 5.8	 C, 75.8 H, 5.8

[a] Lit.,[40] 120 °C, 112 °C. [b] Yield and mp not determined. [c] The carbon resonance unaccounted for is (are) assumed to be coincident with other carbon resonances. Although the ^{13}C NMR data alone are not definitive, the diverse array of analytical data including ^1H NMR, infrared and elemental results, strongly support the proposed identity of this compound especially when considered together with the ^{13}C NMR data. [d] In the assignments in Tables 1 and 2, Ar(1) refers to the phenyl group with the R^1 substituent and Ar(2) refers to the phenyl group with the R^2 substituent.

isocyanate. Derivatization of these photosensitive benzoins generally proceeded smoothly in refluxing toluene but in some cases 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(II) 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.

Experimental

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 FT-IR/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. *J* Values are quoted in Hz. Microanalyses were performed by Desert Analytics, Tucson, AZ. Piperoin was obtained from ICN Biomedicals. Table 1 and Table 2 summarize the analytical data on α-hydroxy ketones and α-keto carbamates, respectively. Ether refers to diethyl ether.

Benzoin synthesis

1,2-Bis(3,5-dimethoxyphenyl)-2-hydroxyethanone 25. To a solution of 3,5-dimethoxybenzaldehyde (6.64 g, 40 mmol) in DMF (25 cm^3) at room temperature under nitrogen was added tetra-*n*-butylammonium iodide (1.26 g, 3.4 mmol) followed by potassium cyanide (0.52 g, 8 mmol) and the resulting solution stirred at room temperature for 18 h. The reaction mixture was poured into water (150 cm^3) and the product extracted into dichloromethane (3 × 50 cm^3). The combined organic extracts were washed with brine (2 × 25 cm^3) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave a yellow oil (11.16 g) which solidified on cooling. Recrystallization (CH_2Cl_2–EtOH) allowed isolation of the crude benzoin as an off-white solid

Table 2 Analytical data on α-keto carbamates

Comp.	Yield (%) mp (°C)	δ_H (ppm)[q]	δ_C (ppm)	ν/cm^{-1}	λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})	Elemental analysis (%) Calc.	Found
1[a]	21/77 87–88	1.05–2.15 [10 H, m, cyclohexyl $(CH_2)_5$], 3.47 (1 H, m, cyclohexyl CH), 4.68 and 5.00 (total 1 H, each br d, NH), 6.87 (1 H, s, 2-CH), 7.14–7.55 [8 H, m, Ar(1) 3,4,5-H and Ar(2) 2,3,4,5,6-H], 7.96 [2 H, m approximates to d, J_o 8.1 Ar(1) 2,6-H]	24.63 (t), 25.33 (t), 33.10 (t), 50.06 (d), 77.15 (d), 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)	3342, 2934, 1706, 1678, 1531, 1449, 1251, 1229, 1059, 697	246 (13 120), 325 (296)	$C_{21}H_{23}NO_3$ (337.40) C, 74.75 H, 6.9 N, 4.15	 C, 74.9 H, 7.0 N, 4.2
2[b]	77 116–118	1.05–2.15 [10 H, m, cyclohexyl $(CH_2)_5$], 3.48 (1 H, m, cyclohexyl CH), 3.76 and 3.78 (each 6 H, each s, 3,3′, 5,5′-OCH_3), 4.62 and 4.92 (total 1 H, each br d, NH), 6.41 [1 H, t, J_m 2.2, Ar(2) 4-H], 6.57–6.61 [3 H, m, Ar(1) 4-H and Ar(2) 2,6-H], 6.68 (1 H, s, 2-CH), 7.10 [2 H, d, J_m 2.0, Ar(1) 2,6-H]	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)	3406, 3326, 2933, 1694, 1598, 1429, 1232, 1214, 1159, 1054	202 (20 770), 267 (6421), 320 (2256)	$C_{25}H_{31}NO_7$ (457.51) C, 65.6 H, 6.8 N, 3.1	 C, 65.6 H, 6.8 N, 2.95
3[c]	49 Gum	1.05–2.05 [10 H, m, cyclohexyl $(CH_2)_5$], 3.49 (1 H, m, cyclohexyl CH), 3.77 and 3.80 (each 3 H, each s, 3,3′-OCH_3), 4.63 and 4.95 (total 1 H, each br d, NH), 6.79 (1 H, s, 2-CH), 6.87 [1 H, dd, J_o 8.0, J_m 1.8, Ar(1) 4-H], 6.99 [1 H, br t, Ar(2) 2-H], 7.02–7.08 [2 H, m, Ar(2) 4,6-CH], 7.28 [2 H, overlapping t, J_o 8.0, Ar(1) and Ar(2) 5,5′-H], 7.48 [1 H, br t, Ar(1) H-2], 7.56 [1 H, dt, J_o 8.0, J_m 1.8, Ar(1) 6-H]	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)	3360, 1727, 1673, 1610, 1593, 1591, 1525, 1226, 1204, 1160	218 (26 523), 252 (7597), 282 (2763), 309 (2260)	$C_{23}H_{27}NO_5$ (397.46) C, 69.5 H, 6.85 N, 3.5	 C, 69.8 H, 7.0 N, 3.3
4[d]	27 148–149	1.05–2.15 [10 H, m, cyclohexyl $(CH_2)_5$], 3.49 (1 H, m, cyclohexyl CH), 4.59 and 4.95 (total 1 H, each br d, NH), 5.88 and 5.90 (each 1 H, ABq, J_{gem} 1.2, OCH_2O), 5.96 (2 H, s, OCH_2O), 6.67 (1 H, s, 2-CH), 6.78 [2 H, m, J_o 8.2, Ar(1) and Ar(2), 7,7′-H], 6.92 [2 H, m, Ar(2) 4,6-H], 7.42 [1 H, s, Ar(1) 4-H], 7.57 [1 H, d, J_o 8.1, Ar(1) 6-H]	24.62 (t), 25.33 (t), 33.10 (t), 50.03 (d), 76.77 (d), 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)[r]	3426, 2934, 1712, 1678, 1505, 1492, 1447, 1253, 1222, 1039	230 (21 959), 278 (8839), 296 (8858), 312 (9401)	$C_{23}H_{23}NO_7$ (425.47) C, 64.9 H, 5.45 N, 3.3	 C, 64.6 H, 5.4 N, 3.4
5[e]	46 119–121	1.05–2.15 [10 H, m, cyclohexyl $(CH_2)_5$], 3.50 (1 H, m, cyclohexyl CH), 3.75 and 3.80 (each 3 H, each s, 4,4′-OCH_3), 4.65 and 4.99 (total 1 H, each br d, NH), 6.80 (1 H, s, 2-CH), 6.85 [4 H, d, J_o 8.8, 3,3′,5,5′-H], 7.38 [2 H, d, J_o 8.8, Ar(2) 2,6-H], 7.94 [2 H, d, J_o 8.8, Ar(1) 2,6-H]	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)	3330, 1710, 1686, 1600, 1513, 1308, 1265, 1250, 1233, 1169	219 (17 355), 274 (16 666), 325 (770)	$C_{23}H_{27}NO_5$ (397.46) C, 69.75 H, 6.9 N, 3.5	 C, 69.5 H, 6.85 N, 3.5
6[f]	59 149–151	1.05–2.15 [10 H, m, cyclohexyl $(CH_2)_5$], 3.46 (1 H, m, cyclohexyl CH), 3.75 (3 H, s, 3′,5′-OCH_3), 4.62 and 4.95 (total 1 H, each br d, NH), 6.41 [1 H, t, J_m 2.2, Ar(2) 4-H], 6.61 [2 H, d, J_m 2.2, Ar(2) 2,6-H], 6.75 (1 H, s, 2-CH), 7.40 [2 H, m approximates to t, Ar(1) 3,5-H], 7.52 [1 H, m approximates to t, Ar(1) 4-H], 7.96 [2 H, m approximates to d, Ar(1) 2,6-H]	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)	3428, 3371, 2935, 1712, 1698, 1680, 1610, 1597, 1205, 1158	243 (16 633), 280 (2994)	$C_{23}H_{27}NO_5$ (397.46) C, 69.75 H, 6.9 N, 3.5	 C, 69.5 H, 6.8 N, 3.6

Table 2 (*Continued*)

Comp.	Yield (%) mp (°C)	δ_H (ppm)[q]	δ_C (ppm)	ν/cm^{-1}	λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})	Elemental analysis (%) Calc.	Found
7[g]	19 124–126	1.05–2.25 [10 H, m, cyclohexyl $(CH_2)_5$], 3.50 (1 H, m, cyclohexyl CH), 4.52 and 4.92 (total 1 H, each br d, NH), 5.93 and 5.95 (each 1 H, ABq, J_{gem} 1.2, OCH_2O), 6.73–6.79 and 6.91–6.97 [each 2 H, each m, Ar(2) 4,6,7-H and 2-CH], 7.37 [2 H, m approximates to t, Ar(1) 3,5-H], 7.48 [1 H, m approximates to t, Ar(1) 4-H], 7.94 [2 H, m approximates to d, Ar(1) 2,6-H]	24.63 (t), 25.33 (t), 33.11 (t), 50.05 (d), 76.77 (d), 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)	3363, 1705, 1682, 1502, 1490, 1447, 1250, 1235, 1061, 1041	241 (15 418), 288 (4964)	$C_{22}H_{23}NO_5$ (381.41) C, 69.3 H, 6.1 N, 3.7	 C, 69.1 H, 6.1 N, 3.7
9[h]	92 152–154	1.05–2.05 [10 H, m, cyclohexyl $(CH_2)_5$], 2.48 (3 H, s, SCH_3), 3.46 (1 H, m, cyclohexyl CH), 4.54 and 4.93 (total 1 H, each br d, NH), 6.40 [1 H, t, J_m 2.2, Ar(2) 4-H], 6.59 [2 H, d, J_m 2.2, Ar(2) 2,6-H], 6.71 (1 H, s, 2-CH), 7.19 and 7.87 [each 2 H, ABq, J_o 8.6, Ar(1) 3,5-H and 2,6-H respectively]	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)	3365, 1727, 1673, 1610, 1593, 1591, 1525, 1226, 1204, 1160	312 (20 991)	$C_{24}H_{29}NO_5S$ (443.54) C, 65.0 H, 6.6 N, 3.2 S, 7.2	 C, 64.7 H, 6.6 N, 3.1 S, 7.5
10[i]	52 87–90	1.05–2.15 [10 H, m, cyclohexyl $(CH_2)_5$], 3.50 (1 H, m, cyclohexyl CH), 3.81 (3 H, s, 4-OCH_3), 4.62 and 4.97 (total 1 H, each br d, NH), 6.85 (1 H, s, 2-CH), 6.87 [2 H, d, J_o 8.8, Ar(1) 3,5-H], 7.33 [3 H, m, Ar(2) 3,4,5-H], 7.47 [2 H, m, Ar(2) 2,6-H], 7.95 [2 H, d, J_o 8.8, Ar(1) 2,6-H]	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)[r]	3348, 1712, 1687, 1601, 1512, 1261, 1252, 1232, 1172, 1062	280 (16 757)	$C_{22}H_{25}NO_4$ (367.43) C, 71.9 H, 6.9 N, 3.8	 C, 71.7 H, 6.9 N, 3.9
11[j]	70 160–161	1.05–2.15 [10 H, m, cyclohexyl $(CH_2)_5$], 3.52 (1 H, m, cyclohexyl CH), 3.74 (6 H, s, 3,5-OCH_3), 4.55 and 4.97 (total 1 H, each br d, NH), 6.40 [1 H, t, J_m 2.2, Ar(2) 4-H], 6.66 [2 H, d, J_m 2.2, Ar(2) 2,6-H], 6.93 (1 H, s, 2-CH), 7.46–7.65 [2 H, m, Ar(1) 6,7-H], 7.80–8.05 [4 H, m, Ar(1) 3,4,5,8-H], 8.49 [1 H, br s, Ar(1) 1-H]	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)	3426, 3380, 1725, 1711, 1692, 1675, 1610, 1598, 1253, 1158	204 (59 671), 245 (41 242), 251 (47 901), 284 (10 503), 292 (9464), 334 (2022)	$C_{27}H_{28}NO_5$ (446.50) C, 72.6 H, 6.3 N, 3.1	 C, 72.6 H, 6.6 N, 3.15
12[k]	94 173–174.5	0.74–2.10 [10 H, m, cyclohexyl $(CH_2)_5$], 3.19 (1 H, m, cyclohexyl CH), 3.75 [6 H, s, Ar(2) 3,5-OCH_3], 4.38 and 4.82 (total 1 H, each br d, NH), 6.38 [1 H, t, J_m 2.2, Ar(2) 4-H], 6.78 [2 H, d, J_m 2.2, Ar(2) 2,6-H], 7.26–7.46 [6 H, m, Ar(1) and Ar′(2) 3,4,5-H], 7.58 [2 H, m approximates to d, Ar′(2) 2,6-H], 7.81 [2 H, m, approximates to d, Ar(1) 2,6-H]	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)	3350, 2933, 1726, 1711, 1608, 1588, 1510, 1316, 1200, 1161	244 (15 234), 278 (2934)	$C_{29}H_{31}NO_5$ (473.55) C, 73.55 H, 6.6 N, 3.0	 C, 73.6 H, 6.55 N, 2.9
13[l]	66 114–116	0.65–2.10 [10 H, m, cyclohexyl $(CH_2)_5$], 1.96 (3 H, s, 3-CH_3), 3.22 (1 H, m, cyclohexyl CH), 3.77 [6 H, s, Ar(2) 3,5-OCH_3], 4.48 and 4.75 (total 1 H, each br d, NH), 6.38 [1 H, t, J_m 2.2, Ar(2) 4-H], 6.66 [2 H, d, J_m 2.2, Ar(2) 2,6-H], 7.27 [2 H, m approximates to t, Ar(1) 3,5-H], 7.36 [1 H, m approximates to t, Ar(1) 4-H], 7.76 [2 H, m approximates to d, Ar(1) 2,6-H]	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)	3376, 3267, 2936, 1712, 1694, 1601, 1451, 1208, 1158, 1048	228 (12 783), 242 (12 532), 278 (3082)	$C_{24}H_{29}NO_5$ (411.48) C, 70.05 H, 7.1 N, 3.4	 C, 70.1 H, 7.05 N, 3.4

Table 2 (*Continued*)

Comp.	Yield (%) mp (°C)	δ_H (ppm)[q]	δ_C (ppm)	ν/cm^{-1}	λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})	Elemental analysis (%) Calc.	Found
15[m]	81 171–173	0.86–2.10 [10 H, m, cyclohexyl $(CH_2)_5$], 3.25 (1 H, m, cyclohexyl CH), 3.72 [6 H, s, Ar(1) 3,5-OCH_3], 4.40 and 4.89 (total 1 H, each br d, NH), 6.50 [1 H, t, J_m 2.2, Ar(1) 4-H], 7.02 [2 H, d, J_m 2.2, Ar(1) 2,6-H], 7.29 [6 H, m, Ar(2) 3,3′,4,4′,5,5′-H], 7.54 [4 H, m approximates to d, Ar(2) 2,2′-6,6′-H]	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)	3427, 2935, 1715, 1689, 1596, 1451, 1295, 1206, 1157, 1045	264 (7373), 318 (2061)	$C_{29}H_{31}NO_5$ (473.55) C, 73.55 H, 6.6 N, 3.0	 C, 73.6 H, 6.55 N, 3.0
16[n]	73 117–118	1.05–2.15 [10 H, m, cyclohexyl $(CH_2)_5$], 1.46 (3 H, d, J 6.9, 3-CH_3), 3.47 (1 H, m, cyclohexyl CH), 3.86 (3 H, s, 4-OCH_3), 4.62 and 4.89 (total 1 H, each br d, NH), 5.92 (1 H, q, J 6.9, 2-CH), 6.93 and 7.95 [each 2 H, ABq, J_o 8.8, Ar(1) 3,5-H and 2,6-H respectively]	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)	3325, 2937, 1711, 1686, 1603, 1537, 1263, 1237, 1144, 1089	217 (11 591), 272 (16 797)	$C_{17}H_{23}NO_4$ (305.36) C, 66.9 H, 7.6 N, 4.6	 C, 66.8 H, 7.6 N, 4.6
26[o]	43 147–149	1.59 [6 H, br s, piperidino 3,4,5 (CH_2)], 3.44 [4 H, m, piperidino 2,6 (CH_2)], 5.93 and 5.95 (each 1 H, ABq, J_{gem} 1.2, OCH_2O), 6.00 (2 H, s, OCH_2O), 6.60 (1 H, s, 2-CH), 6.78 [2 H, overlapping d, J_o 8.2, Ar(1) and Ar(2) 7,7′-H], 6.90–7.00 [2 H, m, Ar(2) 4,6-H], 7.43 [1 H, d, J_m 1.8, Ar(1) 4-H], 7.59 [1 H, dd, J_o 8.2, J_m 1.8, Ar(1) 6-H]	24.21 (t), 25.62 (t), 45.04 (t), 77.03 (d), 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)[r]	1692 (sh), 1678, 1504, 1490, 1468, 1444, 1251, 1237, 1037, 931	230 (21 536), 278 (8964), 296 (8848), 312 (9702)	$C_{22}H_{21}NO_7$ (411.40) C, 64.2 H, 5.15 N, 3.4	 C, 64.3 H, 5.2 N, 3.4
27[p]	38 124–124.5	1.59 [6 H, br s, piperidino 3,4,5 $(CH_2)_3$], 3.50 [4 H, br d, piperidino 2,6 (CH_2)], 3.75 [6 H, s, Ar(2) 3,5-OCH_3], 6.41 [1 H, t, J_m 2.2, Ar(2) 4-H], 6.62 [2 H, d, J_m 2.2, Ar(2) 2,6-H], 6.73 (1 H, s, 2-CH), 7.40 [2 H, m approximates to t, Ar(1) 3,5-H], 7.51 [1 H, m approximates to t, Ar(1) 4-H], 7.97 [2 H, m approximates to d, Ar(1) 2,6-H]	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)	1697, 1680 1612, 1595 1433, 1266 1234, 1164 1156, 1063	243 (14 511), 280 (2854)	$C_{22}H_{24}NO_5$ (382.42) C, 68.9 H, 6.6 N, 3.65	 C, 68.7 H, 6.45 N, 3.5

[a] Purified by flash chromatography (10% EtOAc–90% hexane) followed by recrystallization from CH_2Cl_2–hexane. [b] Purified by flash chromatography (25% EtOAc–75% hexane) followed by recrystallization from CH_2Cl_2–hexane. [c] Purified by successive flash chromatography (20% EtOAc–80% hexane). [d] Purified by flash chromatography (CH_2Cl_2) followed by recrystallization from CH_2Cl_2–hexane. [e] Purified by trituration with CH_2Cl_2 followed by recrystallization from CH_2Cl_2–hexane. [f] Purified by flash chromatography (CH_2Cl_2) followed by recrystallization from CH_2Cl_2–hexane. [g] Purified by flash chromatography (10% EtOAc–90% hexane) followed by recrystallization from EtOAc–hexane. [h] Purified by trituration with cold toluene followed by recrystallization from CH_2Cl_2–hexane. [i] Purified by flash chromatography (20% EtOAc–80% hexane) followed by recrystallization from CH_2Cl_2–hexane. [j] Purified by flash chromatography (CH_2Cl_2) followed by recrystallization from EtOAc–hexane. [k] Purified by flash chromatography (15% EtOAc–85% hexane) followed by recrystallization from EtOAc–hexane. [l] Purified by flash chromatography (15% EtOAc–85% hexane) followed by recrystallization from PhH–hexane. [m] Purified by flash chromatography (15% EtOAc–85% hexane) followed by recrystallization from EtOAc–hexane. [n] Purified by flash chromatography (20% EtOAc–80% hexane) followed by recrystallization from EtOAc–hexane. [o] Purified by flash chromatography (20% EtOAc–80% hexane) followed by recrystallization from EtOAc–hexane. [p] Purified by trituration with ether followed by recrystallization from Et_2O. [q] ^{1}H NMR of these cyclohexyl carbamates routinely showed two broad resonances for the carbamate NH proton and no apparent duplication of any other resonances. This effect is likely due to the presence of *anti* and *syn* rotamers as a result of rotational isomerism about the amide like bond.[41] Typically, the minor carbamate *syn* rotamer is often difficult to detect at room temperature since the resonances typically blend into the baseline (a hidden partner).[41] The fact that only the NH resonance was clearly duplicated suggest that all the other resonances in the hidden partner are sufficiently broadened and blend in to the baseline. [r] See Table 1, footnote *c*.

(4.47 g). Further recrystallization from EtOH gave benzoin **25** as a white solid (4.18 g, 31%); mp 102–103 °C (lit.,[17] 102–103 °C).

Representative synthesis of benzoins using α-aryl-α-(trimethylsiloxy)acetonitrile as an electrophilic α-hydroxycarbonyl synthon: preparation of 2-(1,3-benzodioxol-5-yl)-2-hydroxy-1-phenylethanone 29

(a) α-(1,3-Benzodioxol-5-yl)-α-(trimethylsiloxy)acetonitrile 23. To a mixture of piperonal (15.01 g, 0.1 mol) and anhydrous zinc iodide (59 mg, 0.2 mmol) under nitrogen at room temperature was added trimethylsilyl cyanide (10.91 g, 0.11 mol) in one portion. The resulting solution was then stirred at 95 °C overnight. Vacuum distillation of the red oil afforded the TMS masked cyanohydrin **23** as a pale yellow oil (21.60 g, 87%); bp 90–95 °C (0.5 mmHg); ν_{max}/cm^{-1} 2242, 1506, 1490, 1447, 1235, 1103, 1085, 1041, 938, 875; δ_H 0.24 [9 H, s, $OSi(CH_3)_3$], 5.41 (1 H, s, CH), 6.01 (2 H, s, OCH_2O), 6.82 (1 H, d, J_o 8.0, 7-H), 6.93 (1 H, dd, J_o 8.0, J_m 1.8, 6-H), 6.98 (1 H, d, J_m 1.8, 4-H); δ_C −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).

(b) 2-(1,3-Benzodioxol-5-yl)-2-hydroxy-1-phenylethanone 29. To an ice cooled solution of phenylmagnesium bromide (3 mol

dm^{-3} in Et_2O; 13.2 cm^3, 39.4 mmol) in anhydrous tetrahydrofuran (40 cm^3) under nitrogen was added a solution of α-(1,3-benzodioxol-5-yl)-α-(trimethylsiloxy)acetonitrile **23** (8.94 g, 35.9 mmol) in anhydrous tetrahydrofuran (40 cm^3). The resulting solution was stirred at 0 °C for 2 h, then quenched by pouring into a mixture of ice (350 g) and concentrated sulfuric acid (20 cm^3) and stirring for 1 h. The tetrahydrofuran was removed *in vacuo* and the residue extracted with ether (3 × 100 cm^3). The combined ether extracts were washed with 10% hydrochloric acid (2 × 50 cm^3) and brine (1 × 50 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was taken up in a mixture of methanol (100 cm^3) and 10% hydrochloric acid (35 cm^3) and the resulting solution stirred at room temperature for 60 h. During this time, a significant amount of solid precipitated. The reaction mixture was cooled to 0 °C and the solid collected by filtration. The white solid (4.53 g) was identified as the desired benzoin albeit in a crude form. Recrystallization from methanol furnished benzoin **29** as a white crystalline solid (3.63 g, 40%). See Table 1 for analytical data.

Representative synthesis of benzoins using α-aryl-α-(trimethylsiloxy)acetonitrile as a benzoyl anion synthon: preparation of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-(4-methylthiophenyl)-ethanone 31

To a solution of dry, distilled diisopropylamine (7.7 cm^3, 55 mmol) in anhydrous 1,2-dimethoxyethane (50 cm^3) at −78 °C under nitrogen was added a solution of *n*-butyllithium in hexanes (1.6 mol dm^{-3}; 31.3 cm^3, 50 mmol). The solution was stirred at −78 °C for 1 h, then treated dropwise with a solution of α-(4-methylthiophenyl)-α-(trimethylsiloxy)acetonitrile[42] (12.57 g, 50 mmol) in dry 1,2-dimethoxyethane (50 cm^3). After 1 h at −78 °C, a solution of 3,5-dimethoxybenzaldehyde (9.14 g, 55 mmol) in dry 1,2-dimethoxyethane (50 cm^3) was added and the reaction allowed to slowly warm up to 0 °C over 4 h. Once at 0 °C, saturated aqueous ammonium chloride (75 cm^3) was added and the mixture stirred for 5 min. Ether (150 cm^3) was added and the layers separated. The organic layer was washed with saturated aqueous ammonium chloride (1 × 50 cm^3), dried ($MgSO_4$) and concentrated *in vacuo* to give an orange oil (21.30 g). The oil was taken up in tetrahydrofuran (75 cm^3) and a solution of tetra-*n*-butylammonium fluoride in tetrahydrofuran (1 mol dm^{-3}; 55 cm^3, 55 mmol) added. The resulting solution was stirred at room temperature under nitrogen for 4 h, concentrated *in vacuo* and the residue partitioned between ether (200 cm^3) and water (50 cm^3). The layers were separated and the organic layer washed with water (2 × 50 cm^3) and brine (1 × 50 cm^3). After drying ($MgSO_4$), removal of the solvent *in vacuo* gave a yellow oil (18.73 g) which on trituration with a little methanol gave a solid which was recrystallized from methanol to give benzoin **31** as a white crystalline solid (9.79 g, 62%). See Table 1 for analytical data.

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-(2-naphthyl)ethanone 32

The title compound **32** was prepared from α-(2-naphthyl)-α-(trimethylsiloxy)acetonitrile[43] (11.42 g, 44.7 mmol) in the same manner as described for **31**. See Table 1 for analytical data.

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1,2-diphenylethanone 33

To a suspension of clean, dry magnesium turnings (3.62 g, 0.149 mol) in dry tetrahydrofuran (20 cm^3) at room temperature was added a few drops of a solution of 1-chloro-3,5-dimethoxybenzene (23.38 g, 0.135 mol) in dry tetrahydrofuran (100 cm^3). 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 × 10 cm^3). Based on the weight of these residues (0.65 g), 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 (25.65 g, 0.122 mol) in dry tetrahydrofuran (200 cm^3). The solution was brought to reflux and stirred at reflux for 16 h. After cooling, the reaction was quenched with saturated aqueous ammonium chloride (100 cm^3) and the tetrahydrofuran removed *in vacuo*. The residue was extracted with ether (3 × 100 cm^3) and the combined ether extracts were washed with water (2 × 75 cm^3) and brine (1 × 75 cm^3) and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave a dark brown viscous oil (45.71 g) which failed to crystallize. The crude product was purified in a batch mode by flash chromatography using 10% EtOAc–90% hexane as eluent. In this way, a total of 5.92 g of benzil was recovered from the early fractions of each column. The later fractions from each column were combined to give the crude product as a colourless oil (18.94 g) which crystallized on trituration with ethanol. Recrystallization from ethanol gave benzoin **33** as a white crystalline solid (15.14 g, 46% based on recovered starting benzil). See Table 1 for analytical data.

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-phenylpropanone 35

2-(3,5-Dimethoxyphenyl)-2-trimethylsiloxy-1-phenylpropanone **34** was prepared from α-phenyl-α-(trimethylsiloxy)-acetonitrile[30] (5.93 g, 28.9 mmol) and 3,5-dimethoxyacetophenone (5.2 g, 28.9 mmol) in the same manner as described for **31**. The TMS masked benzoin **34** was isolated as an orange oil (10.82 g); ν_{max}(liquid film)/cm^{-1} 1685, 1607, 1597, 1425, 1253, 1207, 1157, 1066, 1012, 843; δ_H 0.00 [9 H, s, $OSi(CH_3)_3$], 1.74 (3 H, s, CH_3), 3.72 [6 H, s, Ar(2) 3,5-OCH_3], 6.30 [1 H, t, J_m 2.2, Ar(2) 4-H], 6.62 [2 H, d, J_m 2.2, Ar(2) 2,6-H], 7.23 [2 H, t, J_o 7.8, Ar(1) 3,5-H], 7.34 [1 H, t, J_o 7.8, Ar(1) 4-H], 7.90 [2 H, d, J_o 7.8, Ar(1) 2,6-H]; δ_C 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).

The TMS ether **34** was dissolved in a mixture of 1,4-dioxane (60 cm^3), methanol (40 cm^3) and 10% hydrochloric acid (50 cm^3) and the resulting solution stirred at room temperature for 2 h. After concentration under reduced pressure, the residue was partitioned between ether (200 cm^3) and water (50 cm^3) and the organic layer washed with water (2 × 35 cm^3) and brine (1 × 35 cm^3) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave the crude benzoin as an orange oil (9.64 g) which failed to crystallize. The oil was purified by flash chromatography using 15% EtOAc–85% hexane to afford the desired benzoin **35** as a colourless oil (8.2 g, 99%). See Table 1 for analytical data.

1-(3,5-Dimethoxyphenyl)-2-hydroxy-2,2-diphenylethanone 40

1-(3,5-Dimethoxyphenyl)-2-trimethylsiloxy-2,2-diphenylethanone **39** was prepared from α-(3,5-dimethoxyphenyl)-α-(trimethylsiloxy)acetonitrile[17] (6.63 g, 25 mmol) and benzophenone (4.78 g, 26.3 mmol) in a manner similar to that described for **34**. The TMS masked benzoin **39** was isolated as an orange oil (11.19 g); ν_{max}(liquid film)/cm^{-1} 1685, 1593, 1424, 1252, 1206, 1157, 1075, 1067, 890, 700; δ_H −0.20 [9 H, s, $OSi(CH_3)_3$], 3.75 (6 H, s, 3,5-OCH_3), 6.55 [1 H, t, J_m 2.2, Ar(1) 4-H], 7.17 [2 H, d, J_m 2.2, Ar(1) 2,6-H], 7.25–7.50 [10 H, m, both Ar(2) 2,2-diPh]; δ_C 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). This material was contaminated by a trace amount of the starting benzophenone.

Acidolysis of the crude TMS masked benzoin **39** was performed as described for **35** and gave the crude benzoin as an orange oil (10.07 g) which crystallized on standing. Subsequent recrystallization from methanol gave benzoin **40** as a white crystalline solid (7.02 g, 81%). See Table 1 for analytical data.

Carbamate synthesis

Preparation of the cyclohexylcarbamate of 2-hydroxy-1,2-diphenylethanone 1†† *via* methyllithium catalysed reaction. To a solution of 2-hydroxy-1,2-diphenylethanone (5.31 g, 25 mmol) in anhydrous tetrahydrofuran (80 cm^3) at room temperature was added methyllithium (1.4 mol dm^{-3} in Et_2O; 1.8 cm^3, 2.5 mmol). After stirring for 1 h, a solution of cyclohexyl isocyanate (4.9 cm^3, 4.77 g, 26.3 mmol) in dry tetrahydrofuran (20 cm^3) was added and the resulting solution heated at reflux for 14 h. After cooling, the tetrahydrofuran was removed *in vacuo* and the residue taken up in dichloromethane (200 cm^3) and washed with water (3 × 25 cm^3) and brine (1 × 25 cm^3). After drying ($MgSO_4$), removal of the solvent under reduced pressure gave a pale yellow solid (7.17 g). Flash chromatography (10% EtOAc–90% hexane) allowed isolation of the following three fractions. First, a yellow gum (50 mg) was isolated and identified as 1,2-diphenylethanedione[44] by spectroscopy and elemental analysis. Next, a white solid (2.82 g) was isolated and recrystallized from Et_2O–hexane. In this way, 3-cyclohexyl-4,5-diphenyl-2,3-dihydrooxazol-2-one **20** was isolated as a white crystalline solid (2.04 g); mp 161–163 °C [Found: C, 79.1; H, 6.6; N, 4.3. Calc. for $C_{21}H_{21}NO_2$ (319.39): C, 79.0; H, 6.6; N, 4.4%]; λ_{max}/nm 292 (ε/dm^3 mol^{-1} cm^{-1} 14 590); ν_{max}/cm^{-1} 2939, 1747, 1367, 1354, 1347, 991, 750, 704, 694, 668; δ_H 1.05–2.27 [10 H, m, cyclohexyl $(CH_2)_5$], 3.23–3.39 (1 H, m, cyclohexyl CH), 7.11–7.21 (5 H, m, 5 ArH), 7.35–7.43 (2 H, m, 2 ArH), 7.48–7.58 (3 H, m, 3 ArH); δ_C 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).

Last, a white foam (2.67 g) was isolated. This material proved to be a mixture of 3-cyclohexyl-4-hydroxy-4,5-diphenyloxazolidin-2-one **17** and the desired carbamate **1**. Trituration with EtOAc–hexane allowed crystallization of the oxazolidin-2-one **17** as a cream coloured solid (0.4 g). This material was purified by recrystallization from EtOAc–hexane to give the oxazolidin-2-one **17** as a white solid (69 mg); mp 185–188 °C [Found: C, 74.4; H, 7.0; N, 4.2. Calc. for $C_{21}H_{23}NO_3$ (337.40): C, 74.7; H, 6.9; N, 4.15%]; λ_{max}/nm 251 (ε/dm^3 mol^{-1} cm^{-1} 519), 257 (588), 261 (478), 263 (475), 267 (328), 284 (102); ν_{max}/cm^{-1} 3417, 3262, 2933, 1712, 1450, 1360, 1350, 1101, 703, 695; δ_H 0.95–2.24 [10 H, m, cyclohexyl $(CH_2)_5$], 2.23 [1 H, s, OH (D_2O exch.)], 2.82–2.94 (1 H, m, cyclohexyl CH), 5.53 (1 H, s, 5-CH), 7.12–7.17 (2 H, m, 2 ArH), 7.36–7.58 (8 H, m, 8 ArH); δ_C 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).

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 (1.78 g, 21%). See Table 2 for analytical data.

Representative procedure for the non-catalysed synthesis of cyclohexylcarbamates: preparation of the cyclohexylcarbamate of 2-hydroxy-1,2-diphenylethanone 1

To a solution of benzoin (9.02 g, 42.5 mmol) in toluene (100 cm^3) at room temperature under nitrogen was added cyclohexyl isocyanate (6 cm^3, 5.85 g, 46.7 mmol) and the resulting solution heated at reflux for 48 h. After cooling, the reaction mixture was diluted with ether (100 cm^3) and washed with water (2 × 75 cm^3) and brine (1 × 50 cm^3) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave the crude product as a yellow solid (12.10 g). Flash chromatography (10% EtOAc–90% hexane) followed by recrystallization from CH_2Cl_2–hexane gave the desired carbamate **1** as a white solid (11.10 g, 77%). This material had spectroscopic data identical to an authentic sample prepared above (see Table 2).

†† IUPAC name: 2-oxo-1,2-diphenylethyl *N*-cyclohexylcarbamate. The other carbamates can be named similarly.

Cyclohexylcarbamate of 1,2-bis(3,5-dimethoxyphenyl)-2-hydroxyethanone 2

A solution of 1,2-bis(3,5-dimethoxyphenyl)-2-hydroxyethanone **25** (1.5 g, 4.5 mmol) was treated with cyclohexyl isocyanate (0.6 cm^3, 0.62 g, 5 mmol) in refluxing toluene (80 cm^3) in a manner similar to that described for **1**. Work-up and purification gave carbamate **2** as a fluffy white solid (1.58 g, 77%). See Table 2 for analytical data. Flash chromatography also gave a yellow solid (0.1 g) which was recrystallized from ethyl acetate–hexane to give light yellow crystals (57 mg). This material was identified as 1,2-bis(3,5-dimethoxyphenyl)ethanedione[17] by spectroscopic and elemental analysis.

Cyclohexylcarbamate of 2-hydroxy-1,2-bis(3-methoxyphenyl)-ethanone 3

2-Hydroxy-1,2-bis(3-methoxyphenyl)ethanone[27] (3.64 g, 13.4 mmol) was treated with cyclohexyl isocyanate (1.9 cm^3, 1.84 g, 14.7 mmol) in refluxing toluene (75 cm^3) in a similar manner to that described for **1**. The usual work-up gave a yellow oil (6.32 g) which on flash chromatography (20% EtOAc–80% hexane) gave the following fractions. First, a colourless oil (0.12 g) was isolated and recrystallized from ethanol to give a light yellow crystalline solid (34 mg). This material was identified as 1,2-bis(3-methoxyphenyl)ethanedione[45] by spectroscopic and elemental analysis. Next, a mixture enriched in the desired carbamate was isolated as a white foam (2.02 g). Trituration with EtOAc–hexane gave a stereoisomer of 3-cyclohexyl-4-hydroxy-4,5-bis(3-methoxyphenyl)oxazolidin-2-one **18** as a white crystalline solid (0.61 g); mp 151–154 °C [Found: C, 69.65; H, 6.8; N, 3.45. Calc. for $C_{23}H_{27}NO_5$ (397.46): C, 69.5; H, 6.85; N, 3.5%]; λ_{max}/nm 276 (ε/dm^3 mol^{-1} cm^{-1} 3612), 283 (3331); ν_{max}/cm^{-1} 3295, 1739, 1604, 1495, 1461, 1453, 1429, 1369, 1265, 1036; δ_H 0.95–2.45 [10 H, m, cyclohexyl $(CH_2)_5$], 2.94 (1 H, m, cyclohexyl CH), 3.61 and 3.63 (each 3 H, each s, 3,3′-OCH_3), 4.46 [1 H, s, OH (D_2O exch.)], 5.47 (1 H, s, Ox 5-CH), 6.45 (1 H, m, 1 ArH), 6.56–6.71 (4 H, m, 4 ArH), 6.79 (1 H, br d, *J* 7.3, 1 ArH), 6.94–7.08 (2 H, m, 2 ArH); δ_C 25.00 (t), 25.82 (t), 26.01 (t), 29.91 (t), 30.95 (t), 53.72 (d), 55.02 (q), 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).‡‡

Concentration of the mother liquor gave the desired carbamate **3** as a white gum (1.23 g). Besides the homogeneous materials described above, flash chromatography also generated a number of mixed fractions which were combined and concentrated to give a white foam (2.95 g). This material was rechromatographed as above to afford additional 1,2-bis(3-methoxyphenyl)ethanedione (50 mg),[45] along with a mixture greatly enriched in the desired carbamate as a white gum (2.33 g). In the case of the latter mixture, trituration with aqueous ethanol led to crystallization of another stereoisomer of 3-cyclohexyl-4-hydroxy-4,5-bis(3-methoxyphenyl)oxazolidin-2-one **18** as a white crystalline solid (0.27 g); mp 173–175 °C [Found: C, 69.5; H, 6.95; N, 3.5. Calc. for $C_{23}H_{27}NO_5$ (397.46): C, 69.5; H, 6.85; N, 3.5%]; λ_{max}/nm 275 (ε/dm^3 mol^{-1} cm^{-1} 4367), 281 (4094); ν_{max}/cm^{-1} 3316, 2929, 1708, 1608, 1357, 1287, 1271, 1259, 1047, 753; δ_H 0.95–2.22 [10 H, m, cyclohexyl $(CH_2)_5$], 2.42 [1 H, s, OH (D_2O exch.)], 2.90 (1 H, m, cyclohexyl CH), 3.77 and 3.85 (each 3 H, each s, 3,3′-OCH_3), 5.49 (1 H, s, CH), 6.66–6.74 (2 H, m, 2 ArH), 6.88–7.00 (2 H, m, 2 ArH), 7.07–7.15 (2 H, m, 2 ArH), 7.24–7.43 (2 H, m, 2 ArH); δ_C 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).

Concentration of the mother liquor afforded more of carbamate **3** as a white gum (1.38 g). The gum resisted all attempts

‡‡ See Table 1, footnote *c*.

at crystallization. As outlined above, attempted crystallization would lead to cyclization to form stereoisomers of oxazolidin-2-one **18**. Overall 2.61 g of carbamate **3** was isolated, this corresponds to a 49% yield. See Table 2 for analytical data.

Cyclohexylcarbamate of 1,2-bis(1,3-benzodioxol-5-yl)-2-hydroxyethanone 4

1,2-Bis(1,3-benzodioxol-5-yl)-2-hydroxyethanone (2.25 g, 7.5 mmol) was treated with cyclohexyl isocyanate (1.1 cm^3, 1.05 g, 8.3 mmol) in refluxing toluene (50 cm^3) in a manner similar to that described for **1**. Work-up and purification gave carbamate **4** as a white solid (0.85 g, 27%). See Table 2 for analytical data.

Representative procedure for the synthesis of piperidinocarbamates: preparation of the piperidinocarbamate of 1,2-bis(1,3-benzodioxol-5-yl)-2-hydroxyethanone 26

To a solution of 1,2-bis(1,3-benzodioxol-5-yl)-2-hydroxyethanone (3 g, 10 mmol) and *p*-nitrophenyl chloroformate (2.02 g, 10 mmol) in dichloromethane (25 cm^3) at 0–5 °C under nitrogen was added a solution of triethylamine (2.13 g, 21 mmol) in dichloromethane (10 cm^3). The resulting solution was stirred at room temperature for 6 h at which point TLC indicated complete consumption of the starting benzoin. A solution of piperidine (0.9 g, 10.5 mmol) in dichloromethane (25 cm^3) was added and the mixture stirred at room temperature for 48 h. At this point, TLC indicated that a trace of mixed carbonate remained. To complete the reaction, the mixture was heated at reflux for 4 h. After cooling, the reaction mixture was washed with water (1 × 20 cm^3), NaOH (0.5 M; 2 × 20 cm^3), water (1 × 20 cm^3), 2.5% hydrochloric acid (1 × 20 cm^3) and brine (1 × 20 cm^3). After drying ($MgSO_4$), removal of the solvent under reduced pressure gave an orange–brown foam (3.85 g). After purification, carbamate **26** was isolated as pale yellow platelets (1.7 g, 43%). See Table 2 for analytical data. Flash chromatography also gave a yellow solid (0.17 g) which was recrystallized from ethyl acetate–hexane to give light yellow crystals (88 mg). This material was identified as 1,2-bis(1,3-benzodioxol-5-yl)ethanedione[46] by spectroscopy and elemental analysis.

Cyclohexylcarbamate of 2-hydroxy-1,2-bis(4-methoxyphenyl)-ethanone 5

2-Hydroxy-1,2-bis(4-methoxyphenyl)ethanone (4.05 g, 15 mmol) was treated with cyclohexyl isocyanate (2.1 cm^3, 2.07 g, 16.5 mmol) in refluxing toluene (75 cm^3) in a similar manner to that described for **1**. Work-up followed by purification gave carbamate **5** as large white crystals (2.75 g, 46%). See Table 2 for analytical data.

Cyclohexylcarbamate of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-phenylethanone 6

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-phenylethanone[17] **28** (1.49 g, 5.5 mmol) was treated with cyclohexyl isocyanate (0.8 cm^3, 0.75 g, 6 mmol) in refluxing toluene (50 cm^3) in a manner similar to that described for **1**. Work-up followed by purification gave carbamate **6** as a white crystalline solid (1.28 g, 59%). See Table 2 for analytical data. Flash chromatography also afforded a colourless oil (40 mg) which was recrystallized from ethyl acetate–hexane to give 1-(3,5-dimethoxyphenyl)-2-phenylethanedione as light yellow crystals (20 mg) [Found: C, 71.2; H, 5.2. Calc. for $C_{16}H_{14}O_4$ (270.27): C, 71.1; H, 5.2%]; δ_H 3.83 (6 H, s, 3,5-OCH_3), 6.74 [1 H, t, J_m 2.2, Ar(2) 4-H], 7.10 [2 H, d, J_m 2.2, Ar(2) 2,6-H], 7.51 [2 H, m approximates to t, Ar(1) 3,5-H], 7.65 [1 H, m approximates to t, Ar(1) 4-H], 7.96 [2 H, m approximates to d, Ar(1) 2,6-H]; δ_C 55.56 (q), 107.27 (d), 107.44 (d), 128.89 (d), 129.78 (d), 132.84 (s), 134.59 (s), 134.77 (d), 161.02 (s), 194.31 (s), 194.35 (s).

Piperidinocarbamate of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-phenylethanone 27

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-phenylethanone[17] **28** (1.36 g, 5 mmol) was converted to the corresponding piperidinocarbamate **27** *via* the *p*-nitrophenyl mixed carbonate method described for **26**. Work-up followed by purification gave carbamate **27** as a white solid (0.72 g, 38%). See Table 2 for analytical data.

Cyclohexylcarbamate of 2-(1,3-benzodioxol-5-yl)-2-hydroxy-1-phenylethanone 7

2-(1,3-Benzodioxol-5-yl)-2-hydroxy-1-phenylethanone **29** (1.44 g, 5.6 mmol) was treated with cyclohexyl isocyanate (0.8 cm^3, 0.74 g, 5.9 mmol) in refluxing toluene (60 cm^3) in a similar manner to that described for **1**. Work-up and purification gave carbamate **7** as a white powder (0.41 g, 19%). See Table 2 for analytical data. The mixed fractions from the column (1.21 g) consisted of the desired carbamate **7** (cyclohexyl CH, m, δ_H 3.50), the corresponding 4-hydroxyoxazolidin-2-one **19** (cyclohexyl CH, m, δ_H 2.87) and 2,3-dihydrooxazol-2-one **21** (cyclohexyl CH, m, δ_H 3.29).

Cyclohexylcarbamate of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-(4-methylthiophenyl)ethanone 9

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-(4-methylthiophenyl)-ethanone **31** (2.39 g, 7.5 mmol) was treated with cyclohexyl isocyanate (1.1 cm^3, 1.03 g, 8.3 mmol) in refluxing toluene (50 cm^3) in a manner similar to that described for **1**. Work-up and purification gave carbamate **9** as a white solid (3.06 g, 92%). See Table 2 for analytical data.

Cyclohexylcarbamate of 2-hydroxy-1-(4-methoxyphenyl)-propanone 16

2-Hydroxy-1-(4-methoxyphenyl)propanone[35] (2.7 g, 15 mmol) was treated with cyclohexyl isocyanate (2.1 cm^3, 2.07 g, 16.5 mmol) in refluxing toluene (50 cm^3) in a manner similar to that described for **1**. Work-up and purification gave carbamate **16** as a white solid (3.32 g, 73%). See Table 2 for analytical data. Flash chromatography also allowed isolation of a minor, less polar, fraction which was recrystallized from aqueous ethanol to afford 3-cyclohexyl-4-(4-methoxyphenyl)-5-methyl-2,3-dihydrooxazol-2-one **24** as a white crystalline solid (0.14 g); mp 114–115 °C [Found: C, 70.95; H, 7.35; N, 5.0. Calc. for $C_{17}H_{21}NO_3$ (287.35): C, 71.05; H, 7.4; N, 4.9%]; λ_{max}/nm 280 (ε/dm^3 mol^{-1} cm^{-1} 21 203); ν_{max}/cm^{-1} 2933, 1747, 1513, 1364, 1348, 1295, 1252, 1237, 1180, 758; δ_H 1.10–2.27 [10 H, m, cyclohexyl $(CH_2)_5$], 2.25 (3 H, s, CH_3), 3.52–3.74 (1 H, m, cyclohexyl CH), 3.83 (3 H, s, 4-OCH_3), 6.92 and 7.39 [each 2 H, ABq, J_o 8.5, 2,6-H and 3,5-H respectively]; δ_C 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).

Cyclohexylcarbamate of 2-hydroxy-1-(4-methoxyphenyl)-2-phenylethanone 10

2-Hydroxy-1-(4-methoxyphenyl)-2-phenylethanone[36] (1.75 g, 7.2 mmol) was treated with cyclohexyl isocyanate (1 cm^3, 0.99 g, 8 mmol) in refluxing toluene (25 cm^3) in a similar manner to that described for **1**. Work-up and purification gave carbamate **10** as a fine white powder (1.37 g, 52%). See Table 2 for analytical data.

Cyclohexylcarbamate of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-(2-naphthyl)ethanone 11

2-(3,5-Dimethoxyphenyl)-2-hydroxy-1-(2-naphthyl)ethanone **32** (0.34 g, 1.2 mmol) was treated with cyclohexyl isocyanate (0.2 cm^3, 0.17 g, 1.4 mmol) in refluxing toluene (25 cm^3) in a manner similar to that described for **1**. Work-up and purification gave carbamate **11** as a fine white powder (0.38 g, 70%). See Table 2 for analytical data. Flash chromatography also gave a yellow solid (50 mg) which was recrystallized from ethyl acetate–hexane to give 1-(3,5-dimethoxyphenyl)-2-(2-naphthyl)-ethanedione as a pale yellow crystalline solid (38 mg) [Found: C, 74.7; H, 5.05. Calc. for $C_{20}H_{16}O_4$ (320.33): C, 75.0; H, 5.0%];

δ_H 3.83 (6 H, s, 3,5-OCH_3), 6.75 [1 H, t, J_m 2.2, Ar(2) 4-H], 7.15 [2 H, d, J_m 2.2, Ar(2) 2,6-H], 7.55–7.67 [2 H, m, Ar(1) 6,7-H], 7.88–7.98 [3 H, m, Ar(1) 4,5,8-H], 8.09 [1 H, dd, J_o 8.6, J_m 1.7, Ar(1) 3-H], 8.39 [1 H, d, J_m 1.7, Ar(1) 1-H]; δ_C 55.58 (q), 107.36 (d), 107.47 (d), 123.55 (d), 127.08 (d), 127.85 (d), 129.06 (d), 129.44 (d), 129.82 (d), 130.19 (s), 132.22 (s), 133.41 (d), 134.74 (s), 136.28 (s), 161.05 (s), 194.33 (s), 194.38 (s).

Representative procedure for the catalysed preparation of cyclohexylcarbamates: preparation of the cyclohexylcarbamate of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1,2-diphenylethanone 12

To a solution of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1,2-diphenylethanone **33** (1.74 g, 5 mmol) in benzene (50 cm^3) at room temperature under nitrogen was added stannous 2-ethylhexanoate (0.1 g) followed by cyclohexyl isocyanate (0.7 cm^3, 0.69 g, 5.5 mmol). After stirring for 24 h, the reaction mixture was purified to give carbamate **12** as a fluffy white solid (2.23 g, 94%). See Table 2 for analytical data.

Cyclohexylcarbamate of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-phenylpropanone 13

The cyclohexylcarbamate of 2-(3,5-dimethoxyphenyl)-2-hydroxy-1-phenylpropanone **13** was prepared in a manner similar to that described for **12**. After purification, carbamate **13** was isolated as white platelets (2.79 g, 66%). See Table 2 for analytical data.

Cyclohexylcarbamate of 1-(3,5-dimethoxyphenyl)-2-hydroxy-2,2-diphenylethanone 15

The cyclohexylcarbamate of 1-(3,5-dimethoxyphenyl)-2-hydroxy-2,2-diphenylethanone **15** was prepared in a similar manner to that described for **12**. After purification, carbamate **15** was isolated as a white solid (1.48 g, 81%). See Table 2 for analytical data.

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