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Preparation of β- and γ-lactams *via* ring closures of unsaturated carbamoyl radicals derived from 1-carbamoyl-1-methylcyclohexa-2,5-dienes

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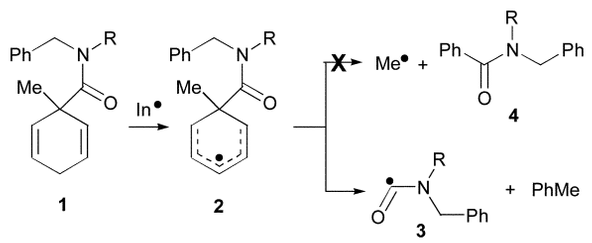
1-Carbamoyl-1-methylcyclohexa-2,5-dienes produced the corresponding delocalised 1-carbamoyl-1-methylcyclohexa-2,5-dienyl radicals on treatment with radical initiators. At temperatures above *ca.* 300 K dissociation to produce toluene and aminoacyl (carbamoyl) radicals took place. The alternative dissociation of the 1-carbamoyl-1-methylcyclohexa-2,5-dienyl radicals to release methyl radicals and an aromatic amide did not compete. Aminoacyl radicals with allyl, butenyl or similar side chains underwent cyclisations. Moderate yields of *N*-benzyl-azetidin-2-ones and *N*-benzyl-pyrrolidin-2-ones were isolated for a range of substituents. The main by-products were *N*-benzyl-*N*-alkenylformamides. Ring closure did not take place to a significant extent for precursors with alk-2-ynyl or 2-cyanoalkyl side chains. An improved yield of 1,3-dibenzylazetidin-2-one was obtained by use of lauroyl peroxide as initiator and by inclusion of methyl thioglycolate as polarity reversal catalyst.

Introduction

The β- and γ-lactam structural units occur in many biologically active molecules.[1] Synthetic routes to β-lactams include Ugi reactions,[2] Paterno–Büchi type [2+2] cycloadditions of ketenes and imines[3] and numerous base promoted condensations of imines and oxime ethers with a variety of enolate types.[4] In addition, reactions of the dianion derived from trisylhydrazone with aldehydes yield β-lactams,[5] as do rhodium catalysed intramolecular C–H insertion reactions of diazoamides.[6] Various other methods are also available.[7] Most of these synthetic routes employ powerful bases (or other stringent conditions) that necessitate tedious protection/deprotection strategies. Free-radical based synthetic methods usually involve neutral conditions and, because these reactive species seldom attack functional groups, this permits key steps to proceed without the need for protection. Recently, several free-radical mediated syntheses of β- and γ-lactams have been reported. For example, organotin hydride promoted cyclisations of unsaturated β-chloroamides yielded lactam rings and were employed in syntheses of PS-5 and thienamycin.[8] Modest yields of β-lactams were also obtained from 4-*exo*-cyclisations of carbamoylcobalt salophens.[9] To date, radical methods for lactams have suffered either from poor yields or have employed toxic organotin reagents.

1-Alkyl-cyclohexa-2,5-diene-1-carboxylic acids,[10] esters of 1-methylcyclohexa-2,5-diene-1-carboxylic acid,[11] and of 1-phenylcyclohexa-2,5-diene-1-carboxylic acid,[12] as well as silylated cyclohexadienes,[13] have been successfully used as precursors in ring-forming free-radical processes. The main drawback to their use was unwanted competition from an alternative dissociation of the intermediate 1-methyl-1-carboxalatocyclohexadienyl radicals that released methyl radicals and benzoate esters.

These findings suggested, however, that analogous amides **1** could function as precursors of aminoacyl radicals **3** (Scheme 1) and that suitably functionalised examples could ring close to afford lactams as the main products. Synthetic routes to a representative series of 1-carbamoyl-1-methylcyclohexa-2,5-dienes (CHD-amides, **1**) are described in this paper, together with an investigation of aminoacyl (carbamoyl) radical generation and subsequent cyclisation reactions. Part of the work described here was summarised in a preliminary communication.[14]



Scheme 1 Aminoacyl radical generation from *N*-benzyl-*N*-alkenyl-(1-methyl)cyclohexa-2,5-diene-1-carboxamides.

Results and discussion

The 1-methyl substituted compounds **1** were chosen because methyl is the least stabilised of the simple alkyl radicals. It follows that the unwanted β-scission of the intermediate cyclohexadienyl radicals **2**, to produce methyl radicals and aromatic amides **4**, should be markedly disfavoured. 1-Methylcyclohexa-2,5-diene-1-carbonyl chloride (**6**) is readily available from the corresponding acid prepared by Birch reduction/methylation of benzoic acid.[10,15] Preliminary experiments with amides derived from primary amines were less successful and therefore *N*-benzyl protected-amides **1** were utilised in most subsequent experiments. Secondary amines **5**, with unsaturation at the 2- or 3-positions of side chains R, were obtained either by borohydride reduction of alkenylimines or by treatment of benzylamine with an appropriate alkenyl, alkynyl or cyanoalkyl halide. The CHD-amides (**1**) were obtained in satisfactory yields on addition of **6** to DCM solutions of individual amines containing Et_3N and a catalytic amount of DMAP (Scheme 2).

Scheme 3 shows the anticipated course of the reaction. The unsaturated aminoacyl radical **8**, released from the initial cyclohexadienyl radical **7**, should either abstract a bisallylic hydrogen from more **1** to produce formamide **10**, or cyclise to give the corresponding azetidin-2-one, or pyrrolidine-2-one, **11**. The formation of pyrrolidinones was tested by examining the thermally induced decomposition of the but-3-enyl amide **1e** with dibenzoyl peroxide.

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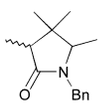
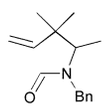
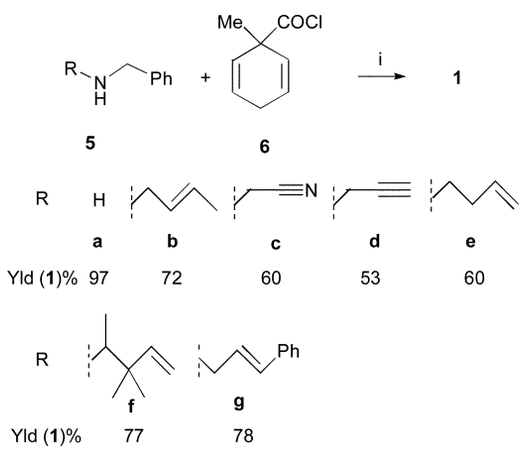
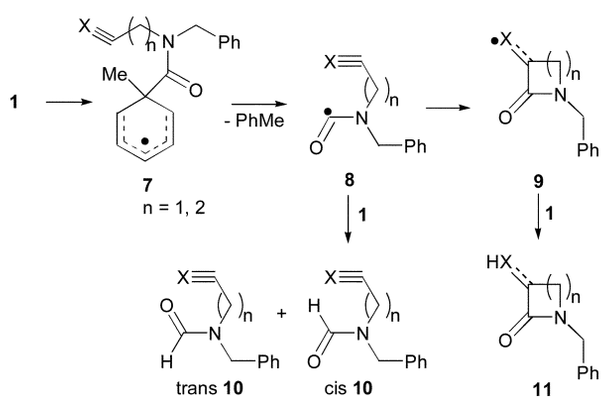
Table 1 Preparation of pyrrolidinones from induced decompositions of *N*-substituted-*N*-benzyl-(1-methyl)cyclohexa-2,5-diene-1-carboxamides[a]

CHD-amide	Conditions	Lactam **11** % (unreacted **1** %)	Formamide **10** %
1e	$(BzO)_2$, PhH, reflux, 24 h	 **11e** 53	 **10e** 37[f]
1e	DTBPOO,[d] PhH, reflux	**11e** 21[b] (57)[b]	**10e** 22[b]
1e	DTBP, UV, 60 °C, 4 h	**11e** 43[b] (44)[b]	**10e** 13[b]
1f	$(BzO)_2$, PhH, reflux, 24 h	 **11f** 17 de 60%[e]	 **10f** trace
1f	DTBP, UV, 60 °C, 7 h.	**11f** 21[c] de 69%	**10f** 8[b]

[a] Yields are for isolated products except those marked[b,c]. [b] Obtained by GC. [c] Obtained by NMR. [d] Di-*t*-butylperoxy oxalate. [e] 4 : 1 mixture of *trans*- and *cis*-diastereoisomers. [f] 1.1 : 1 mixture of rotamers.

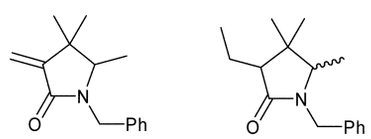


Scheme 2 *Reagents and conditions:* (i) Et_3N, cat. DMAP, DCM reflux.



Scheme 3 Induced decomposition of cyclohexa-2,5-diene-1-carboxamides.

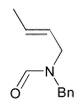
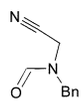
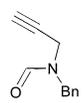
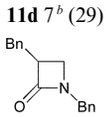
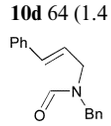
On refluxing **1e** and dibenzoyl peroxide in benzene for 24 h, the 3-methyl-*N*-benzylpyrrolidin-2-one **11e** was isolated in 53% yield along with a significant amount of the corresponding formamide **10e** as a mixture of *trans*- and *cis*-isomers (Table 1). Thermally induced decomposition of **1e** using di-*t*-butyl peroxyoxalate (DTBPOO) as initiator gave the same products but in reduced yields because much of the starting amide remained unreacted (Table 1). The reaction was also carried out using photolysis of di-*t*-butyl peroxide (DTBP) as the initiation mode. The yield of pyrrolidinone **11e** obtained was 43% on a conversion of 56%. Amide **1f** contained bis-methyl substitution of the butenyl chain and it was hoped that ring closure of the carbamoyl radical derived from this compound would be more efficient because of a Thorpe–Ingold effect. Thermally initiated decomposition of **1f** led to the isolation of the tetramethylpyrrolidinone **11f** as a mixture of diastereoisomers (60–70% de) in a disappointing 17% yield. The chromatograms of the product mixture were comparatively clean, except for debris from the dibenzoyl peroxide. The low yield was partly due to losses sustained during purification and separation from these by-products. A similar yield was obtained in the UV/DTBP initiated reaction (Table 1), the problem here being unreacted starting amide. Interestingly, the GC-MS chromatograms showed minor amounts of two additional products having molecular ions and fragmentation patterns consistent with structures **12** (4%) and **13** (6%).



The 3-methylenepyrrolidinone **12f** was probably formed by disproportionation of the intermediate **9f** with other radicals in the system. Likewise, the 3-ethyl-derivative **13** probably resulted from combination of **9f** with methyl radicals derived from β-scission of the initiator-derived *t*-butoxyl radicals. The presence of these radical–radical products suggested that chain propagation by H-atom abstraction from the starting amides was inefficient.

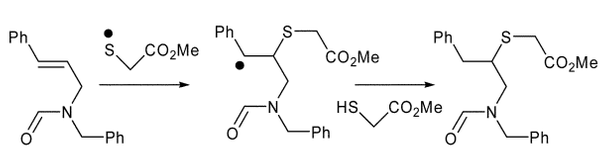
The use of cyclohexadienyl-amides **1** for the preparation of β-lactams was next investigated. The induced decomposition of **1b** was carried out thermally with dibenzoyl peroxide as initiator in refluxing benzene. The products were shown to be 1-benzyl-3-ethylazetidin-2-one (**11b**) accompanied by a significant amount of *N*-benzyl-*N*-but-2-enylformamide (**10b**) as a 1.3 : 1 mixture of *trans*- and *cis*-isomers. Considering that this ring closure is of the unfavourable 4-*exo*-variety, the yield of β-lactam (Table 2) was encouraging. Thermally initiated reactions of the cyanomethyl derivative **1c** gave solely the uncyclised formamide product of type **10**. In the photochemically initiated reactions with DTBP, amide conversions of only 60–70% could be achieved. The only products isolated from the thermally induced reaction of the propynylamide **1d** were the formamide isomers **10d**. However, the GC-MS chromatogram showed a small amount of a second product having the correct molecular mass for the product of 4-*exo*-*dig* cyclisation. The MS of this component showed the characteristic cross-ring fragmentation of a 4-membered ring and hence it was probably *N*-benzyl-3-methyleneazetidin-2-one (**11d**), although this was not confirmed by isolation and NMR spectral characterisation. In these reactions of **1c** and **1d** the cyclised species contain exocyclic double bonds, as well as 4-membered rings, so it was not at all surprising that ring closure of the aminoacyl radicals was too slow to compete effectively with hydrogen abstraction.

Table 2 Preparation of azetidinones from induced decompositions of *N*-substituted-*N*-benzyl-(1-methyl)cyclohexa-2,5-diene-1-carboxamides[a]

CHD-amide	Conditions	Lactam **11** % (unreacted **1** %)	Formamide **10** % (isomer ratio)
1b	$(BzO)_2$, PhH, reflux, 24 h		
		11b 34	**10b** 31 (1.3 : 1)
1b	DTBP, UV, rt, 2 h	**11b** 42[b]	**10b** 38[b]
1c	$(BzO)_2$, PhH, reflux, 24 h	**11c** 0	
			10c 57 (3.8 : 1)
1d	$(BzO)_2$, PhH, reflux, 24 h		
		11d 7[b] (29)[b]	**10d** 64 (1.4 : 1)
1g	$(BzO)_2$, PhH, reflux, 48 h		
		11g 12[b] (64)	**10g** 5
1g	DTBP/PhH, 70 °C, hν, 8 h	**11g** *ca.* 12[b]	**10g** *ca.* 5[b]
1g	DTBPOO[d], PhH, reflux, 24 h	**11g** 15[b] (16) **13g** 5[b]	**10g** 10[b]
1g	DTBPOO[d], PhH, RSH[e], reflux, 12 h	**11g** 24[c]	**14g** 65[b]
1g	DTBPOO[d], PhH, cat. RSH[e], reflux, 12 h	**11g** 38[c] **13g** 28[c]	**10g** 11[c]
1g	Lauroyl, PhH, RSH[e], reflux	**11g** 66[b] (10)	**14g** 24[b]

[a] Yields are for isolated products except those marked[b,c]. [b] Obtained by GC. [c] Obtained by NMR. [d] Di-*t*-butylperoxy oxalate. [e] RSH = Methyl thioglycolate.

The cinnamyl-substituted amide **1g** was chosen for more detailed study because the Ph substituent was expected to confer resonance stabilisation on the cyclised radical **9g** and hence to expedite the *4-exo*-cyclisation step. However, as an additional consequence of this resonance stabilisation of **9g** it was anticipated that the H-atom abstraction step would be disfavoured. The thermal and photochemical reactions initiated with dibenzoyl peroxide, DTBPOO and DTBP gave the corresponding azetidin-2-one **11g** but the yields were low (Table 2). We reasoned that addition of a good H-atom donor would enable the ring closed benzyl type radical **9g** to be trapped more easily. Accordingly, we carried out a reaction initiated with DTBPOO but including 1.2 mol eq. of methyl thioglycolate (RSH). The yield of 1,3-dibenzylazetidinone **11g** did significantly increase under these conditions (24%, Table 2), but a new product, {1-benzyl-2-[benzyl(formyl)amino]ethyl}sulfanyl acetate (**14g**) was a major by-product. It is probable that **14g** was formed by radical addition of the thioglycolate to the first formed formamide **10g** (Scheme 4).



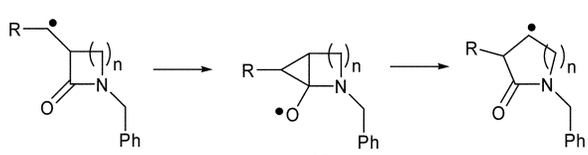
10g **14g**

Scheme 4 Formation of thiol adduct **14g**.

When a catalytic amount of RSH was employed, formation of **14g** was suppressed, and the β-lactam (**11g**) yield increased (Table 2), but radical–radical reactions again became important leading to formation of **13g**.

Use of lauroyl peroxide as initiator, in concert with 1 eq. of RSH, led to a greatly improved β-lactam yield (66%, Table 2). Some thiol adduct **14g** was still produced, but the termination product **13g** was undetectable under these conditions. It is likely that polarity reversal catalysis[16] played a part in enhancing the yield of **11g**. The azetidinylbenzyl radical **9g** will be resonance stabilised and nucleophilic. Hence a polar effect should favour H-abstraction from the electronegative RSH. The electrophilic thiyl radical ($RS^{\bullet}$) generated in this way will, in turn, H-abstract more readily from the cyclohexadienyl site of **1g**, thus regenerating RSH and continuing the chain. In the lauroyl peroxide initiated reactions, products derived from the initiator included undecane and docosane. These compounds significantly increased the viscosity of the reaction medium thus slowing radical–radical reactions which are normally diffusion controlled. This may account for the suppression of termination products **12g** and **13g** with this initiator.

Under certain experimental conditions, ring expansion of β-oxocycloalkyl radicals might take place *via* azabicyclo[*n*.1.0]-alkyloxyl radicals **15** (Scheme 5).[17] However, no five-membered ring containing pyrrolidinones were observed from reactions of **1b–d**. It is likely that higher reaction temperatures would be required for this alternative to become viable.



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Scheme 5 Potential ring enlargement of β-oxoazetidinylmethyl and related radicals.

Conclusions

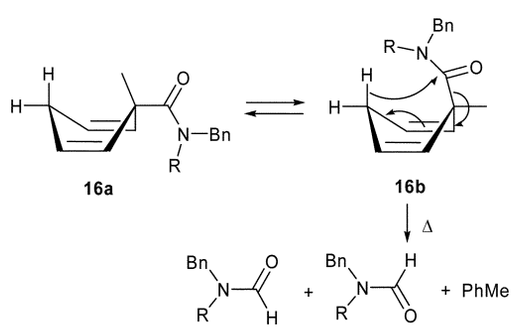
The results show that induced decompositions of cyclohexadienyl amides of type **1** readily afford aminoacyl (carbamoyl) radicals. No products from the undesired methyl radical release process *i.e.* aromatic amides **4** (Scheme 1) were detected for any of the precursors studied. Thus, the dissociations of the delocalised amide radicals **2** are clean and are more efficient than for the analogous 1-alkylcyclohexa-2,5-diene-1-carboxylic

acids or the analogous esters. In several cases, the cyclohexadienyl radicals **2**, and released aminoacyl radicals **3**, were observed by EPR spectroscopy. These observations supported the proposed mechanism and enabled kinetic data for dissociation of **2** to be obtained in certain cases.[18] It is probable that the comparatively efficient extrusion of aminoacyl radicals from **2** is because they are somewhat more thermodynamically stabilised (by the amide FG) than the alkyl or alkoxycarbonyl radicals released in the cases of the acids and esters respectively.

The only previous reports of cyclisations of aminoacyl radicals are those of Pattenden from his work with cobalt salophens.[9] We found that 5-*exo*-*trig*-ring closures took place efficiently, without complications from ring expansion *via* azabicyclo[*n*.2.0]alkyloxyl radicals. As expected, 4-*exo*-*trig*-cyclisations were more difficult and the isolated yield of the β-lactam **11b** was modest.

One reason for the modest yields was the comparatively slow donation of hydrogen by the cyclohexadienyl amides during chain propagation. Chain propagation was consequently not very efficient and comparatively large quantities of dibenzoyl peroxide initiator had to be added to maintain the reactions. Yields were reduced because of having to remove initiator debris from the products. Although cleaner systems were achieved with DTBPOO initiator, and in photochemical systems with DTBP, reactions were difficult to drive to completion under these conditions. Inclusion of methyl thioglycolate in the reaction medium led to increased β-lactam yields, probably because polarity reversal catalysis resulted from favourable polar effects on the H-atom abstractions.

Significant yields of formamides accompanied all the cyclisations. A possible cause of this appeared to be a non-radical electrocyclic elimination. The lowest energy conformation of **1** is probably **16a** with the Me group pseudo-axial. However, there will be a minor population of conformer **16b** with the amide group pseudo-axial. Direct electrocyclic elimination of formamide, as shown, can be envisaged from this structure (Scheme 6).



Scheme 6 Possible electrocyclic elimination of formamide from cyclohexadienyl amides.

When a solution of **1b** in benzene (no initiator) was heated at 60 °C and photolysed with UV light for 4 h, GC-MS analysis showed only unreacted amide. Similarly, a solution of **1f** in $CDCl_3$ was heated continuously at 82 °C in a sealed tube. However, monitoring by ^{1}H NMR showed no reaction after 23 h. Production of formamide by the electrocyclic process of Scheme 6 can therefore be ruled out and its formation must be attributed to H-abstraction (Scheme 3). Overall, the induced carbamoyl-cyclohexadiene decompositions represent comparatively 'clean' tin-free radical routes that are applicable for the preparation of a range of lactams from secondary amine starting materials.

Experimental

^{1}H NMR spectra were recorded at 300 MHz and ^{13}C NMR spectra at 75 MHz, in $CDCl_3$ solution with tetramethylsilane ($\delta_H = \delta_C = 0$) as reference. Coupling constants are expressed in Hz. Ether refers to diethyl ether. Light petroleum refers to the fraction boiling in the range 40–60 °C. EI mass spectra were obtained with 70 eV electron impact ionisation and CI spectra with isobutane as the target gas on a VG Autospec spectrometer. GC-MS analyses were run on a Finnigan Incos 50 quadrupole instrument, and/or on the VG Autospec, coupled to a Hewlett Packard HP 5890 chromatograph fitted with a 25 m HP 17 capillary column (50% phenyl methyl silicone). For the calculation of yields from GC data, the detector response was calibrated with known amounts of authentic materials (or close analogues). Chromatographic purifications were carried out using either Sorbsil C60 40/60A or BDH 40–63 μm silica gel eluting with the given solvent mixture. Ammonia was obtained from BOC and used directly from the cylinder; drying and distillation had no perceptible effect on the yields. *N*-Benzyl-*N*-but-2-enylidineamine,[9] *N*-benzyl-*N*-but-2-enylamine,[9] benzylaminoacetonitrile,[19] prop-2-ynylbenzylamine,[20] 1-methylcyclohexa-2,5-diene-1-carbonyl chloride (**6**),[10] 2,2-dimethylbut-3-enoic acid,[21] 3,3-dimethylpent-4-en-2-one,[22] *N*-benzyl-3-phenylprop-2-enylamine[23] and but-3-enylbenzylamine[24] were prepared according to literature procedures.

N-Benzyl-*N*-but-2-enyl-(1-methyl)cyclohexa-2,5-diene-1-carboxamide (1b). (General procedure for cyclohexadienyl amides)

1-Methylcyclohexa-2,5-diene-1-carbonyl chloride **6** (2.0 g, 13 mmol) was dissolved in dry dichloromethane (10 cm^3) and added dropwise to a mixture of *N*-benzyl-*N*-but-2-enylamine (1.6 g, 10 mmol), triethylamine (1.0 g, 10 mmol) and a catalytic amount of DMAP in dry dichloromethane (20 cm^3). The resultant mixture was refluxed for 5 h before washing with H_2O (2 × 100 cm^3) and drying ($MgSO_4$). The solvent was evaporated to give the product as a brown oil, which was purified by column chromatography, eluting with 2% ethyl acetate in light petroleum, in order to furnish **1b** (2.02 g, 72%) as a pale yellow oil; δ_H 1.38 (3 H, s, CH_3), 1.68 (3 H, br s, CH_3), 2.67 (2 H, m, allylic-H), 3.70–3.97 (2 H, m, CH_2), 4.48–4.72 (2 H, m, Ar–CH_2), 5.25–5.48 (2 H, m, 2 × CH), 5.70–5.81 (4 H, br s, 4 × CH), 7.08–7.34 (5 H, m, Ar H); δ_C 17.7 (CH_3), 25.8 (CH_2), 28.8 (CH_3), 45.0 (C), 47.7 (CH_2), 48.6 (CH_2), 122.9, 125.7, 126.9, 127.3, 127.4, 127.8, 128.4, 128.6, 129.4, 130.0, 130.6 (11 × CH), 138.0 (C), 173.5 (C=O); HRMS *m*/*z* found M$^+$ 281.1776, $C_{19}H_{23}NO$ requires 281.1780.

Thermally initiated reaction of *N*-benzyl-*N*-but-2-enyl-(1-methyl)-cyclohexa-2,5-diene-1-carboxamide (1b)

Amide **1b** (0.5 g, 1.8 mmol) was dissolved in benzene (10 cm^3) and heated to reflux before dibenzoyl peroxide (0.5 g) was added portion wise over a period of 24 h. After complete addition, the solvent was evaporated before dissolving the impure product in ether (50 cm^3), washing with NaOH (2 × 50 cm^3), HCl (2 × 50 cm^3) and water (2 × 50 cm^3) and drying ($MgSO_4$). The solvent was evaporated under reduced pressure to yield a brown oil (0.42 g), which was purified by column chromatography, eluting with 5% ethyl acetate in light petroleum. A sample of the purified product was analysed by GC-MS; peak no. 902, β-lactam **11b** *m*/*z* (relative intensity) 189 (M$^+$, 6), 160 (3), 133 (38), 119 (3), 105 (50), 91 (100), 77 (16), 65 (37), 55 (22), 41 (46), 39 (43), 27 (33); peak no. 908, *cis*- or *trans*-*N*-benzyl-*N*-but-2-enylformamide **10b** (31% combined *cis* + *trans*), 189 (M$^+$, 7), 160 (1), 148 (2), 134 (36), 115 (2), 106 (34), 98 (30), 91 (100), 79 (39), 77 (17), 70 (33), 65 (49), 55 (27), 39 (46), 28 (95); peak no. 914, *cis*- or *trans*-*N*-benzyl-*N*-but-2-enylformamide **10b** 189 (M$^+$, 20), 160 (6), 134 (21), 118 (13), 106 (28), 98 (28), 91 (100), 79 (25), 77 (19), 70 (18), 65 (44), 55 (26), 39 (56), 28 (77), 18 (100). The *N*-benzyl-3-ethylazetidin-2-one **11b** was finally isolated as a colourless oil (34%) by preparative TLC, eluting with 2% ethyl acetate in pentane; δ_H 0.98 (3 H, t, *J* 6.0, CH_3), 1.51–

1.90 (2 H, m, CH_2), 2.84 (1 H, m, CH), 3.12–3.20 (1 H, m, CH), 3.20–3.25 (1 H, m, CH), 4.38 (2 H, AB, Ar–CH_2), 7.19–7.41 (5 H, m, ArH); δ_C 11.2 (CH_3), 21.9 (CH_2), 44.5 (CH_2), 45.8 (Ar–CH_2), 51.3 (CH), 127.8, 128.1, 128.8 (5 × CH), 135.8 (C), 170.6 (C=O); HRMS *m/z* found M^+ 189.1149, $C_{12}H_{15}NO$ requires 189.1154. The mixture of *cis*- and *trans*-**10b** (31%, major : minor = 1.25 : 1) was also isolated as a colourless oil; δ_H (major isomer shifts first) 1.68, 1.72 (2 × 3 H, d, *J* 6.0, CH_3), 3.67, 3.80 (2 × 2 H, d, *J* 6.0 CH_2), 4.37, 4.52 (2 × 2 H, s, CH_2) 5.24–5.71 (2 × 2 H, br m, CH), 7.18–7.42 (2 × 5 H, m, Ar H), 8.21, 8.30 (2 × 1 H, s, HC=O); δ_C 17.7, 30.3 (CH_3), 43.3, 44.8 (CH_2), 48.6, 50.3 (CH_2), 124.6, 125.6, 127.4, 127.6, 128.0, 128.3, 128.5, 128.9, 129.5 (CH), 136.0, 136.4 (C), 162.5, 162.6 (C=O).

In a control experiment **1b** (0.1 g) in benzene (2 cm^3) was heated at 60 °C in a quartz tube and photolysed with UV light from a 400 W Hg lamp for 4 h. At the end of this period GC-MS analysis showed only unchanged **1b**.

Photochemically initiated reaction of 1b

Amide **1b** (0.2 g, 0.7 mmol) was dissolved in DTBP (250 μl) and added to a quartz tube (od 0.4 cm). The tube was capped and irradiated with light from a 400 W medium pressure Hg lamp for 2 h. Analysis of the reaction mixture by GC-MS indicated that all of the cyclohexadienyl amide had been consumed, leading to identical peaks in the GC-MS to those observed with the thermally initiated radical reaction. GC yield measurements, using a formamide standard, confirmed that the β-lactam **11b** was formed in 42% and the two formamide isomers **10b** in a combined yield of 38%.

N-Benzyl-1-methylcyclohexa-2,5-diene-1-carboxamide (1a)

The general method described for **1b** was employed with benzylamine (0.77 g, 7.2 mmol) and **6**. The crude product was purified by crystallisation with pentane/ethyl acetate yielding **1a** as a white crystalline solid (1.4 g, 97%); mp 79–80 °C; δ_H 1.4 (3H, s, CH_3), 2.7 (2H, s, bisallylic H), 4.42 (2H, m, PhN–CH_2), 5.7–6.0 (4H, br m, =CH), 6.0–6.2 (1H, br s, NH), 7.1–7.4 (5H, m, ArH); δ_C 25.4 (CH_3), 25.9 (CH_2), 43.6 (C), 45.0 (CH_2), 127.3 (CH), 128.6 (CH), 130 (CH), 138.5 (C), 174.6 (C=O); found: C, 78.81; H, 7.49; N, 6.09. Calc. for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16%; *m/z* (relative intensity), 227 (M^+, 5), 212 (5), 134 (5), 94 (5), 91 (100), 77 (50), 65 (38), 51 (18), 39 (24).

N-Benzyl-*N*-cyanomethyl-(1-methyl)cyclohexa-2,5-diene-1-carboxamide (1c)

Prepared from **6** and benzylaminoacetonitrile (2.28 g, 16 mmol) as for **1b**. The solvent was evaporated to give the product as a brown oil, which was purified by column chromatography, eluting with 5% ethyl acetate in hexane, in order to furnish the title compound **1c** (2.54 g, 60%) as a pale yellow oil; δ_H 1.26 (3 H, s, CH_3), 2.63 (2 H, s, allylic-H), 3.99 (2 H, s, CH_2), 4.64 (2 H, s, Ar–CH_2), 5.83 (4 H, m, 4 × CH), 7.18–7.39 (5 H, m, Ar H); δ_C 22.1 (CH_3), 33.4 (CH_2), 34.7 (CH_2), 46.1 (C), 54.6 (CH_2), 114.4 (CN), 127.3, 127.5, 127.8, 128.3, 128.6, 129.2, 129.7, 130.1, 130.4 (9 × CH), 137.2 (C), 170.2 (C=O); *m/z* (relative intensity), 266 (M^+, 1), 251 (1), 175 (2), 173 (2), 93 (74), 91 (100), 77 (53), 65 (37), 51 (32), 39 (36); HRMS, *m/z* found M^+ 266.1416, $C_{17}H_{18}N_2O$ requires 266.1419.

Thermally initiated reaction of *N*-benzyl-*N*-cyanomethyl-(1-methyl)cyclohexa-2,5-diene-1-carboxamide (1c)

Amide **1c** (0.5 g, 1.9 mmol) was dissolved in benzene (10 cm^3) and heated to reflux before dibenzoyl peroxide (0.5 g) was added portion wise over a period of 24 h. After complete addition, the solvent was evaporated before dissolving the impure product in ether (50 cm^3), washing with NaOH (50 cm^3), HCl (50 cm^3) and water (2 × 50 cm^3) and drying ($MgSO_4$). The solvent was evaporated under reduced pressure to yield a brown oil (0.38 g), which was analysed, by ^1H NMR and GC-MS; peak no. 104, toluene, peak no. 687, benzoic acid (from initiator); peak no. 768, biphenyl (from initiator); peak nos. 882 and 890 (essentially identical MS) *cis*- and *trans*-*N*-benzyl-*N*-cyanomethylformamide, **10c**; *m/z* (%) 174 (M^+, 16), 134 (71), 106 (83), 91 (100), 79 (97), 65 (76), 51 (61), 39 (81), 28 (92), 18 (13); peak no. 913, phenyl benzoate (from initiator); peak no. 1097, unreacted **1c**. The product was purified by column chromatography, eluting with 10% ethyl acetate in light petroleum, to give *N*-benzyl-*N*-cyanomethylformamide **10c** as a mixture of the two isomers (3.8 : 1) (0.19 g, 57%) major isomer (79 rel.%) δ_H 4.12 (2 H, s, CH_2), 4.55 (2 H, s, Ar–CH_2), 7.24–7.49 (5 H, m, Ar H), 8.31 (1 H, s, HC=O); δ_C 29.4 (CH_2), 51.1 (CH_2), 114.3 (CN), 127.9, 128.9, 129.3 (3 × CH), 133.5 (C), 162.0 (C=O); minor isomer (21 rel.%) δ_H 4.02 (2 H, s, CH_2), 4.68 (2 H, s, CH_2), 7.24–7.49 (5 H, m, ArH), 8.23 (1 H, s, HC=O), δ_C 35.0 (CH_2), 45.8 (CH_2), 114.3 (CN), 128.5, 128.7, 129.1 (3 × CH), 134.0 (C), 161.6 (C=O). HRMS *m/z* found M^+ 174.0786, $C_{10}H_{10}N_2O$ requires 174.0793.

Photochemically initiated reaction of 1c

Amide **1c** (0.2 g, 0.75 mmol) was dissolved in DTBP (250 μl) in a quartz tube and irradiated at ambient temperature with light from a 400 W high pressure Hg lamp for 2 h. Analysis of the reaction mixture by GC-MS confirmed the presence of both isomers of *N*-benzyl-*N*-cyanomethylformamide (**10c**) (together with unreacted **1c**) in an approximate ratio of 2 : 1. The only detectable impurities were those derived from the photolytic breakdown of DTBP.

N-Benzyl-*N*-prop-2-ynyl-(1-methyl)cyclohexa-2,5-diene-1-carboxamide (1d)

Prepared from **6** and prop-2-ynylbenzylamine (3.19 g, 22 mmol) by the method described for **1b**. The solvent was evaporated to give the product as a brown oil, which was purified by column chromatography, eluting with 10% ethyl acetate in hexane, in order to furnish **1d** (3.09 g, 53%) as a pale yellow oil; δ_H 1.41 (3 H, s, CH_3), 2.24 (1 H, s, CH), 2.73 (2 H, br s, allylic-H), 4.16 (2 H, s, CH_2), 4.80 (2 H, s, Ar–CH_2), 5.82 (4 H, m, 4 × CH), 7.18–7.42 (5 H, m, Ar H); δ_C 21.9 (CH_3), 32.1 (CH_2), 33.2 (CH_2), 45.2 (C), 55.1 (CH_2), 72.8 (C), 80.9 (CH), 126.8, 127.2, 127.8, 128.2, 128.7, 129.0, 129.5, 130.1, 130.6 (9 × CH), 139.2 (C), 172.2 (C=O); *m/z* (relative intensity), 174 (3), 172 (6), 134 (3), 105 (5), 93 (26), 91 (100), 77 (27), 65 (20), 51 (11), 39 (23), 28 (8), 18 (29); HRMS *m/z* found M^+ 265.1465, $C_{18}H_{19}NO$ requires 265.1467.

Thermally initiated reaction of *N*-benzyl-*N*-prop-2-ynyl-(1-methyl)cyclohexa-2,5-diene-1-carboxamide (1d)

Amide **1d** (0.5 g, 1.9 mmol) was dissolved in benzene (10 cm^3) and heated to reflux before dibenzoyl peroxide (0.5 g) was added portion wise over a period of 24 h. After complete addition, the solvent was evaporated before dissolving the impure product in ether (50 cm^3), washing with NaOH (50 cm^3), HCl (50 cm^3) and water (2 × 50 cm^3) and drying ($MgSO_4$). The solvent was evaporated under reduced pressure to yield a brown oil (0.47 g). GC-MS; peak no. 190, toluene; peak no. 692, benzoic acid (from initiator); peak no. 772, biphenyl (from initiator); peak no. 843, *N*-benzyl-*N*-prop-2-ynylformamide (**10d**) (62%, both isomers); *m/z* (relative intensity) 173 (M^+, 6), 144 (2), 134 (65), 128 (12), 115 (9), 106 (42), 91 (64), 79 (58), 65 (50), 51 (35), 39 (100), 28 (88); peak no. 867, probably *N*-benzyl-3-methyleneazetidin-2-one (**11d**) (7%); *m/z* (relative intensity) 173 (M^+, 11) 172 (18), 144 (7), 133 (22), 105 (45), 104 (33), 91 (100), 77 (26), 65 (42), 51 (48), 39 (89); peak no. 915, phenyl benzoate (from initiator); peak no. 1086, unreacted **1d** (31%). The crude product was purified by column chromatography, eluting with 10% ethyl acetate in light petroleum, to give **10d**

(64%, mixture of isomers, 1.4 : 1) as a colourless oil; major isomer, δ_H 2.26 (1 H, t, *J* 3.0, CH), 4.07 (2 H, d, *J* 3.0, CH_2), 4.55 (2 H, s, Ar–CH_2), 7.23–7.42 (5 H, m, Ar H), 8.30 (1 H, s, HC=O); δ_C 30.6 (CH_2), 50.3 (CH_2), 72.4 (C≡), 77.2 (C≡), 127.8, 128.6, 129.0 (3 × CH), 135.0 (C), 161.98 (C=O); minor isomer δ_H 2.40 (1 H, t, *J* 3.0, CH), 3.87 (2 H, d, *J* 3.0, CH_2), 4.66 (2 H, s, CH_2), 7.2–7.4 (5 H, m, ArH), 8.25 (1 H, s, HC=O); δ_C 36.2 (CH_2), 45.0 (CH_2), 73.8 (HC≡), 77.0 (C≡), 128.3, 128.8, 129.0 (3 × CH), 135.4 (C), 162.04 (C=O), HRMS *m*/*z* found M^+ 173.0838, $C_{11}H_{11}NO$ requires 173.0841.

Photochemically initiated reaction of 1d

Amide **1d** (0.5 g, 1.9 mmol) was dissolved in benzene (2 cm^3), which contained DTBP (1.10 g, 7.5 mmol). The resultant solution was placed in a quartz tube, heated to 60 °C using a quartz paraffin oil bath and the sample irradiated with light from a 400 W high pressure Hg lamp over a 3 h period. Analysis of the reaction mixture by GC-MS confirmed the formation of both formamide **10d** plus minor amounts of *N*-benzyl-3-methyleneazetidin-2-one (**11d**) and unreacted amide **1d**. The only detectable impurities were those derived from the photolytic breakdown of DTBP.

N-Benzyl-*N*-but-3-enyl-(1-methyl)cyclohexa-2,5-diene-1-carboxamide (1e)

Prepared from **6** (2.0 g, 14.5 mmol) and but-3-enylbenzylamine (2.24 g, 14.0 mmol) as described for **1b**. The solvent was evaporated to give a brown oil, which was purified by column chromatography, eluting with 10% ethyl acetate in hexane, in order to furnish **1e** (2.44 g, 60%) as a pale yellow oil; δ_H 1.37 (3 H, s, CH_3), 2.27 (2 H, m, CH_2), 2.69 (2 H, br s, allylic-H), 3.21–3.50 (2 H, m, CH_2), 4.67 (2 H, s, Ar–CH_2), 4.99 (2 H, d, *J* 7, CH_2), 5.59–5.84 (5 H, m, 5 × CH), 7.10–7.46 (5 H, m, Ar H); δ_C 25.7 (CH_2), 28.8 (CH_3), 31.3 (CH_2), 32.8 (CH_2), 44.9 (C), 51.0 (CH_2), 116.3 (CH_2), 126.8, 127.2, 128.3, 128.6, 130.3 (9 × CH), 135.4 (CH), 137.7 (C), 173.6 (C=O); *m*/*z* (relative intensity), 281 (M^+ 1), 240 (1), 190 (2), 188 (19), 174 (1), 160 (1), 148 (3), 93 (21), 91 (100), 77 (19), 65 (20), 51 (4), 39 (11), 28 (4), 18 (3); HRMS *m*/*z* found M^+ 281.1784, $C_{19}H_{23}NO$ requires 281.1780.

Thermally initiated reaction of *N*-benzyl-*N*-but-3-enyl-(1-methyl)cyclohexa-2,5-diene-1-carboxamide (1e)

Amide **1e** (0.5 g, 1.8 mmol) was dissolved in benzene (10 cm^3) and heated to reflux before dibenzoyl peroxide (0.5 g) was added portion wise over a period of 24 h. After complete addition, the solvent was evaporated before dissolving the mixture in ether (50 cm^3), washing with NaOH (50 cm^3), HCl (50 cm^3) and water (2 × 50 cm^3) and drying ($MgSO_4$). The solvent was evaporated under reduced pressure to yield a brown oil (0.56 g). GC-MS; toluene, plus benzoic acid and biphenyl (from initiator); peak no. 895, *N*-benzyl-*N*-but-3-enylformamide (isomers unresolved) (**10e**), *m*/*z* (relative intensity) 189 (M^+, 2), 148 (16), 134 (2), 130 (2), 119 (2), 106 (2), 98 (2), 91 (100), 77 (4), 65 (20), 51 (6), 39 (21), 28 (13), 18 (10); peak no. 915, 1-benzyl-3-methylpyrrolidin-2-one (**11e**), 189 (M^+, 69), 174 (10), 160 (12), 146 (5), 132 (13), 118 (10), 106 (23), 98 (25), 91 (100), 77 (10), 65 (32), 55 (19), 51 (12), 39 (35), 28 (23), 18 (9); peak no. 1118, unreacted **1e**. The product was purified by column chromatography, eluting with 10% ethyl acetate in light petroleum, and by preparative TLC to give the γ-lactam, **11e** (53%) as a colourless oil; δ_H 1.24 (3 H, d, *J* 7, CH_3), 1.63 (1 H, dq, *J* 7, 9 CH), 2.18–2.28 (1 H, m, CH), 2.55 (1 H, sextet, *J* 7, CH), 3.19 (2 H, m, CH_2), 4.47 (2 H, AB, Ar–CH_2), 7.21–7.37 (5 H, m, Ar H); δ_C 16.4 (CH_3), 27.1 (CH_2), 36.8 (CH), 44.6 (CH_2), 46.8 (CH_2), 127.3, 127.9, 128.5 (5 × CH), 136.7 (C), 177.4 (C=O); HRMS *m*/*z* found M^+ 189.1158, $C_{12}H_{15}NO$ requires 189.1154. The pair of formamides **10e** was isolated as a colourless oil (37%, 1.1 : 1); major isomer δ_H 2.18–2.35 (2 H, m, CH_2), 3.14–3.27 (2H, m, CH_2), 4.46 (2 H, s, Ar–CH_2), 4.9–5.19 (2 H, m, =CH_2), 5.59–5.85 (1 H, m, =CH), 7.18–7.41 (5 H, m, Ar H), 8.25 (1 H, s, HC=O); δ_C 32.6 (CH_2), 45.4 (CH_2), 51.5 (Ar–CH_2), 118.1 (=CH_2), 127.9, 128.2, 128.7 (5 × CH), 134.0 (CH), 136.4 (C), 162.8 (HC=O); minor isomer δ_H 2.18–2.35 (2 H, m, CH_2), 3.14–3.27 (2H, m, CH_2), 4.58 (2 H, s, Ar–CH_2), 4.9–5.19 (2 H, m, =CH_2), 5.59–5.85 (1 H, m, =CH), 7.18–7.41 (5 H, m, ArH), 8.30 (1 H, s, HC=O); δ_C 32.6 (CH_2), 45.4 (CH_2), 51.5 (Ar–CH_2), 122.8 (=CH_2), 127.2, 127.5, 128.3 (5 × CH), 134.0 (CH), 135.8 (C), 162.9 (HC=O) HRMS *m*/*z* found M^+ 189.1149, $C_{12}H_{15}NO$ requires 189.1154. The experiment was repeated using DTBPOO (1.9 mmol) as the thermally activated radical initiator. GC analysis indicated **10e** (21%), **11e** (22%) and unreacted **1e** (57%).

Photochemically initiated reaction of 1e

Amide **1e** (0.5 g, 1.8 mmol) was dissolved in benzene (2 cm^3), which contained DTBP (1.3 g, 9 mmol). The resultant solution was placed in a quartz tube, heated to 60 °C using a quartz paraffin oil bath and the sample was irradiated with light from a 400 W medium pressure Hg lamp over a 4 h period. Analysis of the reaction mixture by GC-MS confirmed the presence of both 1-benzyl-3-methylpyrrolidin-2-one (**11e**) and the *N*-benzyl-*N*-but-3-enylformamide (**10e**) in an approximate ratio of 2 : 1. The only detectable impurities were those derived from the photolytic breakdown of DTBP, with no evidence for the competitive release of methyl radicals to form *N*-benzyl-*N*-but-3-enylbenzamide.

N-Benzyl-3,3-dimethylpent-4-enylamine

Sodium borohydride (0.2 g, 5.3 mmol) was added portion wise over a period of 10 min to a stirred and cooled (0 °C) solution of the imine (2.56 g, 12.7 mmol) in dry methanol (40 cm^3) under an atmosphere of nitrogen. The solution was allowed to warm to ambient temperature and then stirred for 20 h, during which time the yellow colour of the solution faded. The solution was cooled (0 °C) before concentrated HCl was added dropwise until the mixture attained pH 1. The resulting suspension was evaporated under reduced pressure to leave a white solid. The residue was dissolved in water (50 cm^3) and the resulting aqueous solution was washed with ether (2 × 100 cm^3). The remaining aqueous solution was brought to pH 10 by careful addition of potassium hydroxide pellets, and the liberated amine was extracted into ether (3 × 100 cm^3). The combined organic phases were dried ($MgSO_4$) and then evaporated to dryness to leave a pale yellow oil. The product was purified by distillation to yield the title amine (1.63 g, 63%) as a colourless liquid; δ_H 0.9–1.0 (9H, 3 × CH_3), 2.3 (1H, q, CH, ^3J = 6.3), 3.7 (2H, AB system, Ar–CH_2, ^2J = 13.5), 5.0 (2H, m, =CH_2), 5.7 (1H, m, =CH), 7.2–7.3 (5H, m, ArH). δ_C 14.5 (CH_3), 21.9 (CH_3), 24.4 (CH_3), 40.9 (C), 52.2 (CH_2), 59.8 (CH), 112.0 (=CH_2), 126.7, 128.1, 128.2 (5 × ArCH), 140.9 (C), 146.8 (=CH); HRMS *m*/*z* found $(M + 1)^+$ 204.1745, $C_{14}H_{22}N$ requires 204.1752.

N-Benzyl-1-methyl-*N*-(1,2,2-trimethylbut-3-enyl)cyclohexa-2,5-diene-1-carboxamide (1f)

Prepared from *N*-benzyl-3,3-dimethylpent-4-enylamine (1.63 g, 8.0 mol), and **6** as described for **1b**. The amide was obtained as a pale yellow oil (1.91 g, 74%). δ_H 1.00 (3H, s, CH_3), 1.10 (3H, s, CH_3), 1.13 (3H, d, CH_3), 1.30 (3H, s, CH_3), 2.43–2.87 (2H, br m, allylic-CH_2), 4.14 and 4.73 (2H, AB, Ph–CH_2), 4.46 (1H, q, *J* 6.8, CH), 4.99–5.05 and 5.80–6.05 (7H, m, =CH), 7.05–7.37 (5H, m, ArH); δ_C 15.1 (CH_3), 23.5 (CH_3), 25.8 (CH_3), 28.0 (CH_3), 29.7 (CH_2), 41.5 (C), 45.7 (C), 47.1 (CH_2), 59.3 (CH), 112.7 (=CH_2), 122.3 (=CH), 122.4 (=CH), 126.1, 126.4, 129.1 (5 × CH), 130.8 (=CH), 132.4 (=CH), 139.7 (C), 145.3 (=CH), 174.4 (C=O); HRMS *m*/*z* found M^+ + 1 324.2339, $C_{22}H_{30}NO$ requires 324.2327.

Thermally initiated reaction of *N*-benzyl-1-methyl-*N*-(1,2,2-trimethylbut-3-enyl)cyclohexa-2,5-diene-1-carboxamide (1f)

Amide **1f** (0.15 g, 0.46 mmol) was dissolved in benzene (5 cm^3) and heated to reflux before dibenzoyl peroxide (0.12 g, 0.50 mmol) was added portion wise over a period of 24 h. After complete addition, the solvent was evaporated, the impure product was dissolved in ether (30 cm^3), washed with NaOH (30 cm^3), HCl (30 cm^3) and water (2 × 50 cm^3) and dried ($MgSO_4$). The solvent was evaporated to yield a brown oil 0.028 g (26%), which was analysed by GC-MS; peak nos. 583 and 590 (identical MS), *cis*- and *trans*-1-benzyl-3,4,4,5-tetramethyl-2-pyrrolidinone, (**11f**), 231 (M^+, 59), 216 (42), 161 (6), 140 (9), 134 (17), 106 (10), 91 (100), 83 (11), 70 (10), 65 (9), 55 (14); peak no. 717, unreacted **1f**; by-products from dibenzoyl peroxide were also observed. The product was purified by column chromatography, eluting with 10% ethyl acetate in hexane, to give γ-lactam **11f** as a mixture of two diastereoisomers (4 : 1) (0.018 g, 17%). Major isomer (60% de) δ_H 0.80 (3H, s, CH_3), 0.98 (3H, s, CH_3), 1.02 (3H, d, CH_3, ^3J 6.8), 1.07 (3H, d, CH, ^3J 7.7), 2.29 (1H, q, CH, ^3J 7.2), 2.98 (1H, q, CH, ^3J 6.8), 3.87 (1H, d, Ar–CH_2, ^2J 14.9), 5.02 (1H, d, Ph–CH_2, ^2J 14.9), 7.22–7.31 (5H, m, ArH); major isomer δ_C 9.1 (CH_3), 13.1 (CH_3), 22.8 (2 × CH_3), 38.9 (C), 44.3 (CH), 45.4 (CH_2), 60.8 (CH), 127.4, 128.3, 128.5 (5 × ArH), 136.9 (C), 176.1 (C=O). Minor isomer δ_H 0.74 (3H, s, CH_3), 0.95 (3H, s, CH_3), 1.03 (3H, d, CH_3, ^3J 6.8), 1.11 (3H, d, CH, ^3J = 7.2), 2.17 (1H, q, CH, ^3J = 7.2), 3.14 (1H, q, CH, ^3J = 6.8), 4.00 (1H, d, Ph–CH, ^2J = 14.9), 4.94 (1H, d, Ph–CH, ^2J = 14.9), 7.22–7.31 (5H, m, ArH); minor isomer δ_C 12.6 (CH_3), 16.3 (CH_3), 22.5 (2 × CH_3), 39.0 (C), 43.9 (CH), 48.2 (CH_2), 60.9 (CH), 127.2, 128.1, 128.2 (5 × ArH), 137.3 (C), 169.1 (C=O).

Photochemically initiated reaction of 1f

Amide **1f** (0.03 g) was dissolved in DTBP (200 μl) and placed in a quartz tube. The tube was capped and irradiated at ambient temperature with light from a 400 W medium pressure Hg lamp for 7 h. Analysis of the reaction mixture by GC-MS confirmed the presence of *cis*- and *trans*-1-benzyl-3,4,4,5-tetramethyl-2-pyrrolidinone isomers (**11f**) (ratio 1 : 5.4, de 69%) together with unreacted **1f** and by-products derived from the photolytic breakdown of DTBP. Benzyl-(1,2,2-trimethyl-3-butenyl)formamide (**10f**) was formed in only a trace, but 1-benzyl-4,4,5-trimethyl-3-methylenepyrrolidin-2-one (**12f**) *m*/*z* (%) 229 (M^+, 54), 228 (54), 214 (13), 196 (31), 131 (37), 119 (54), 105 (35), 91 (100), 77 (22) and 1-benzyl-3-ethyl-4,4,5-trimethylpyrrolidin-2-one (**13f**) *m*/*z* (%) 245 (M^+, 19), 231 (16), 178 (15), 162 (29), 134 (26), 105 (30), 91 (100), 57 (15) were observed as minor components.

***N*-Benzyl-1-methyl-*N*-3-phenyl-2-propenylcyclohexa-2,5-diene-1-carboxamide (1g)**

Prepared from *N*-benzyl-3-phenyl-2-propenylamine (1.5 g, 6.7 mmol), and **6** according to the general procedure. Amide **1g** was obtained as a colourless oil (1.5 g, 65%); IR (nujol) cm^{-1}: 1712 (C=O, stretch), 1586 (C=C), 1270 (C=C), δ_H 1.40 (3H, s, CH_3), 2.43–2.86 (2H, m, bisallylic-CH_2), 4.00–4.17 (2H, m, N–CH_2), 4.60–4.72 (2H, m, Ar–CH_2), 5.66–6.32 (6H, m, =CH), 7.18–7.34 (10H, m, ArH); δ_C 25.8 (CH_2), 28.8 (CH_3), 45.1 (C), 48.1, 48.4 (N–CH_2), 48.8, 52.8 (CH_2), 123.1 (2 =CH), 126.3, 127.0, 127.2, 128.4, 128.5 (10 × ArH), 127.6 (=CH), 130.4 (2 × =CH), 132.7 (=CH), 136.6 (C), 137.8 (C), 173.7 (C=O); HRMS *m*/*z* found M^++1 344.2022, $C_{30}H_{26}NO$ requires 344.2014.

Thermally initiated reaction of 1g

Amide **1g** (0.15 g) was dissolved in benzene (5 cm^3) and heated to reflux before dibenzoyl peroxide (0.12 g, 0.50 mmol) was added portion wise over a period of 24 h. After complete addition, the solvent was evaporated and the products were examined by GC-MS. Peak 569 *N*-benzylbenzamide, peak 618 1,3-dibenzylazetidin-2-one, (**11g**) *m*/*z* (%) 251 (M^+, 8), 160 (11), 118 (100), 117 (57), 115 (23), 91 (54), 65 (13), peak 648 *N*-benzyl-*N*-(3-phenylallyl)formamide (**10g**) *m*/*z* (%) 251 (M^+, 24), 160 (54), 115 (100), 91 (67), 65 (13).

Dibenzoyl peroxide mediated thermolysis of 1g

Dibenzoyl peroxide (0.3 g, 1.2 mmol) was dissolved in benzene (2 cm^3) and added dropwise over a period of 24 h, by using a syringe pump, to a refluxing benzene solution (7 cm^3) containing amide **1g** (0.3 g, 0.9 mmol). After complete addition, the mixture was left to reflux for 24 h. The solvent was evaporated before dissolving the impure product in ether (50 cm^3), washing with NaOH (2 × 50 cm^3), HCl (2 × 50 cm^3) and water (2 × 50 cm^3) and drying ($MgSO_4$). The solvent was evaporated under reduced pressure to yield a brown oil (0.25 g); GC-MS peak no. 330, biphenyl (from initiator); peak no 438 phenyl benzoate; (from initiator); peak no 569, *N*-benzylbenzamide, peak no. 618, 1,3-dibenzylazetidin-2-one **11g** (12%), *m*/*z* (relative intensity) 251 (M^+, 7) 160 (9), 118 (100), 117 (82), 105 (5), 91 (55), 77 (7), 65 (15), peak no.648 *N*-benzyl-(3-phenyl-2-propenyl)formamide **10g** (5%), *m*/*z* (relative intensity) 251 (M^+, 20), 160 (55), 134 (8), 115 (100), 105 (10), 91 (65), 77 (9), 65 (12); peak no. 772, unreacted amide **1g** (64%).

DTBP mediated photolysis 1g

Amide **1g** (0.2 g, 0.6 mmol) was dissolved in benzene (2 cm^3), which contained DTBP (0.5 g, 3.42 mmol). The resultant solution was placed in a quartz tube, heated to 70 °C using a quartz paraffin oil bath, and the sample was irradiated with light from a 400 W medium pressure Hg lamp over an 8 h period. Analysis of the reaction mixture by GC-MS indicated that photolytic radical fragmentation of amide **1g** led to identical peaks in the GC-MS to those observed with the thermally initiated radical reaction (except for initiator-derived products). GC measurements using *N*,*N*-dimethylbenzamide as a standard, demonstrated that the β-lactam **11g** and formamide **10g** were formed in a similar percentage to that obtained from thermal decomposition.

DTBPOO mediated thermolysis of 1g

Amide **1g** (0.2 g, 0.6 mmol) was dissolved in benzene (10 cm^3) and heated to reflux before DTBPOO (0.25 g, 1 mmol) was added, by syringe pump, over a period of 8 h. After complete addition, the solvent was evaporated before dissolving the mixture in ether (30 cm^3); a residue separated from the organic layer which was filtered off. The solvent was evaporated under reduced pressure to yield a yellow oil (0.25 g). GC-MS, peak 14.8 min, biphenyl (from initiator); peak 23.9 min, 1,3-dibenzylazetidin-2-one (**11g**), (15.4%); peak 24.7 min, *N*-benzyl-(3-phenyl-2-propenyl)formamide (**10g**), (10.1%), (unresolved isomers); peak 25.5 min, 1-benzyl-3-(1-phenylethyl)-2-azetidinone (**13g**) (4.5%), *m*/*z* (relative intensity), 265 (M^+, 5), 237 (8), 207 (15), 174 (58), 105 (63), 91 (100), 77 (43), 65 (10), 28 (100), 18(32), peak 29.1 min, unreacted amide **1g** (15.7%). The product was purified by column chromatography, eluting with 20% ethyl acetate in hexane to give the β-lactam, **11g**; δ_H 2.87–2.90 and 3.17 (2H, m, ^3J = 2.4, J_{gem} = 5.3, CH_2), 2.91–3.13 (2H, ddd, ^2J = 14.5, ^3J = 4.8 and 8.2, AB system, Ar–CH_2), 3.51 (1H, m CH), 4.17–4.47 (2H, dd, J = 15.4, AB system, Ar–NCH_2), 7.18–7.40 (10H, m, ArH), δ_C 34.2 (Ar–CH_2), 43.9 (CH), 45.7 (Ar–CH_2), 50.7 (CH_2), 126.6, 127.6, 127.9, 128.6, 128.7, 129.1 (10 × CH), 135.5 (C), 138.0 (C), 169.7 (C=O); IR (ν_{max} cm^{-1}) 1740; HRMS (FAB) *m*/*z* found M^+ + 1 252.1390, $C_{17}H_{18}NO$: requires 252.1388. The mixture of *cis*- and *trans*-*N*-benzyl-(3-phenyl-2-propenyl)formamides (**10g**) (major : minor = 1.4 : 1); δ_H (major isomer shifts first), 3.89, 4.01 (2 × 2 H, d, J = 6.8 CH_2), 4.41, 4.57 (2 × 2 H, s, CH_2), 5.98–6.50 (2 × 2 H, br m, CH), 7.12–7.45 (2 × 10 H, m, Ar H), 8.30, 8.36 (2 × 1 H, s, HC=O).

Thermolysis of 1g with DTBPOO and thiol

DTBPOO (0.1 g, 0.43 mmol) was dissolved in benzene (1.5 cm^3) and added portion wise, over 12 h, to a refluxing benzene solution containing amide **1g** (0.1 g, 0.3 mmol) and methyl thioglycolate (0.032 g, 0.3 mmol). After complete addition the solution was refluxed for 24 h, the solvent evaporated at reduced pressure leaving a crude product which was dissolved in DCM (20 cm^3) and treated with a warm 6 M solution of KOH (50 cm^3). The aqueous phase was extracted with DCM (3 × 25 cm^3) and the combined organic layer evaporated at reduced pressure to leave a yellow product. GC-MS, peak 23.9 min 1,3-dibenzylazetidin-2-one (**11g**) (24%), peak 28.6 min *cis* and *trans*-methyl({1-benzyl-2-[benzyl(formyl)amino]ethyl}sulfanyl) acetate (**14g**) (65%), *m*/*z* (relative intensity) 357 (M^+, 2) 284 (22), 252 (40), 222 (25), 177 (10), 160 (8), 149 (28), 116 (20), 91 (100), 77 (5), 65 (12), peak 29.1 min, unreacted amide. When only a catalytic amount of thiol was used the yield of β-lactam increased to 38%, sulfanylformamide **14g** was not detected, only 11% of formamide **10g** together with 28% of azetidin-2-one **13g** was formed under these conditions.

Thermolysis of 1g with lauroyl peroxide and thiol

Amide **1g** (0.1 g, 0.3 mmol) was dissolved in benzene (7 cm^3) and heated to reflux before lauroyl peroxide (total 0.18 g, 0.45 mmol) in benzene (3 cm^3) was added in portions (0.35 cm^3 of soln.) over a period of 8 h. Following the first addition, the solution was refluxed for 5 min and then methyl thioglycolate (0.032 g, 0.3 mmol) was added. After complete addition, the solvent was evaporated to yield a yellow crude product. GC-MS, peak 3.6 min, methyl thioglycolate, peak 10.3 min, undecane (from initiator), peak 16.1 min, disulfide (dimer of thiol), peak 17.1 min, lauric acid (from initiator) peak. 23.5 min, docosane (from initiator), peak 23.9 min, 1,3-dibenzyl azetidin-2-one (**11g**) (66%); peak 25.7 min, undecyl laurate (from initiator), peak 28.6 min *cis*- and *trans*-methyl({1-benzyl-2-[benzyl(formyl) amino]ethyl}sulfanyl) acetate (**14g**) (24%), peak 29.1 min unreacted amide **1g** (10%).

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References and notes

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